



## Review article

# Efficacy and cost effectiveness of nucleic acid amplification testing (NAT) and serologic screening in preventing HBV, HCV and HIV transmission risk

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## Background

Previous cost effectiveness analyses of NAT systems only gave credit to detection of window period (WP) NAT yield donations [and occult HBV infections (OBIs) in settings without anti-HBc testing] while not considering the vast majority of concordant NAT and serology positive infections.<sup>1</sup> Moreover previous models ignored the fact that serology reactive, NAT nonreactive donations were less infectious than NAT yield donations. However, for proper comparison of the cost effectiveness of NAT and serology, both technologies should be placed on an equal footing. The efficacy (and cost effectiveness) of a certain screening scenario is determined by the amount of transmission risk that can be removed from baseline (i.e. in the absence of any screening). In order to estimate

screening efficacy, an international survey was conducted in twenty blood establishments in six geographical regions, i.e. 1) South Africa, 2) South-East Asia (Singapore, Hong Kong, Malaysia), 3) Egypt, 4) Mediterranean (Italy, Spain), 5) Central-North Europe (Switzerland, Slovenia, Poland, Finland, Denmark, Ireland) and 6) South Pacific (Australia, New Zealand). Intensive communication and data validation in collaboration with the co-investigators helped create a reliable screening database of 11 787 610 donations and to exclude false positive screening results.<sup>3</sup> Parallel screening of donations by ID-NAT (Ultrio, Novartis Diagnostics) and serology (usually Abbott PRISM) and through supplemental testing protocols enabled classification of 8458 HBV, 5147 HCV and 7100 HIV infections into different stages of high and low infectivity.<sup>2</sup>

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## Aim

The prevalence and residual transmission risk of HBV, HCV and HIV-1 infections was compared in six geographical regions. The international database was used to model the efficacy of different screening scenarios, i.e. (i) serology alone, (ii) Ag/Ab combo assays, (iii) serology and MP-NAT (iv) serology and ID-NAT and (v) ID-NAT alone.

## Methods

Screening data from twenty blood centers were collected in 1-5 year periods during 2005 to 2011 to establish the rate of HBV, HCV and HIV-1 infections in first time (FT), lapsed ( $> 365$  day interdonation interval) and repeat ( $\leq 365$  day) donations. Residual risk and screening efficacy was calculated for RBC transfusions by infectivity based modeling as published by Weusten et al.<sup>4</sup> and Bruhn et al.<sup>2</sup>

## Results

The screening efficacy of serology as compared to ID-NAT alone in first time donors (with the highest prevalence of NAT and serology positive infections) was as follows: HBsAg 96.1%, anti-HCV 99.3%, anti-HIV 98.7% versus HBV-DNA 98.7%, HCV-RNA 99.97% and HIV-RNA 99.77%. In repeat donations (with a much lower prevalence of acute infections) the efficacy levels were: HBsAg 53.9%, anti-HCV 71.2%, anti-HIV 86.4% versus HBV-DNA 88.1%, HCV-RNA 97.94% and HIV-RNA 97.64%. Adding HBsAg, anti-HCV or anti-HIV to ID-NAT had a negligible effect on the efficacy with a maximum improvement of 0.01% in first time donors. However, adding anti-HBc may have some impact by reducing low viral load OBI transmission risk. Preliminary modeling showed that adding anti-HBc test-

ing to ID-NAT may enhance the efficacy in FT and repeat donations by 0.2 and 1.4% to 99.0 and 89.5% respectively. Not surprisingly, the efficacy of ID-NAT alone was higher than that of serology and MP-NAT together. For example in repeat donations, pooling (MP8) reduced efficacy by 5.1%, 1.5% and 4.4% for HBV, HCV and HIV-1 respectively. Despite large geographic differences in prevalence of infections, similar efficacy levels were found for the various screening scenarios in the regions. The modelling data for HIV and HCV are solid, but those of HBV are still preliminary and need further review because of the variability of the Ultrio assay in detecting different HBV strains and the higher sensitivity of the new Ultrio Plus and Elite versions for different HBV genotypes.

## Conclusion and discussion

This large international database of confirmed infections detected by simultaneous screening with ID-NAT and serology allows for more accurate modeling of the efficacy of different screening scenarios in eliminating viral transmission risk. It now becomes possible to more reliably compare the cost effectiveness of serology and ID-NAT and to examine the health-economic impact of pooled NAT screening and of adding anti-HBc testing with regard to risk reduction and loss of donors/donations.<sup>3,4</sup> Our modeling results suggest that a robust ID-NAT system (with inbuilt redundancy to overcome mismatches of primers and probes for genetic variants)<sup>5</sup> could eventually replace serologic screening in some situations. In the context of availability of pathogen reduction technology (PRT) for platelet concentrates and FFP it seems feasible to only rely on ID-NAT screening, particularly for donations from regular repeat donors (although regulatory authorities are unlikely to approve such new blood safety

scenarios based on NAT and PRT). [However, also in an ID-NAT only screening scenario it is recommended to first select seronegative donors by pre-screening with serology in order to reduce the burden of ID-NAT repeat and discriminatory test work and to eliminate any residual transmission risk from serology yields that are mainly found in first time donors]. If NAT, serology and PRT were to receive equal credit for preventing transfusion transmitted infections, it could very well be that the current paradigm of incremental cost effectiveness modeling (starting from already established and regulated blood safety systems) will change in favor of new technologies which make the older systems redundant.

## References

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