INFORMATION BRIEF

Review of the Cost Effectiveness of Nucleic Acid Test for Transfusion Transmitted Infections in other Countries

By the Health Technology Assessment Study Group – Health Policy Development and Planning Bureau

KEY MESSAGE

- There is a need to strengthen current testing algorithms using serologic screening before introducing a complementary/confirmatory test.
- Evidence from other settings show that nucleic acid test (NAT) is not a cost-effective screening test for transfusion transmitted infections (TTIs).
- Significant price reduction in the cost of NAT (e.g., cost of reagents) is needed to make it cost effective in most contexts. A local economic evaluation using Philippine data may help determine a cost-effective price for NAT.

CONTEXT

Transfusion Transmitted Infection[1]

- TTIs are conditions spread through blood transfusion. The risk factors for contracting TTIs include the presence of high viral titer in the blood and asymptomatic blood donor.
- The risks of TTI leading to chronic illnesses and serious complications may be decreased if blood donations are screened prior to blood transfusion.

Nucleic Acid Testing[1]

- Tests have been developed to screen blood for infection, most of which are designed to detect antibodies, antigens, or the nucleic acid of the infectious agent.
- NAT detects the presence of viral nucleic acid, DNA and RNA, in the blood samples even at low viral titer
- NAT assays can either be in mini pools (i.e., testing simultaneous samples) or through individual donations (ID) (i.e., single sample is run through the assay).
- Countries with high incidence rate of infections would benefit from NAT by decreasing the risk of transfusing blood collected in the window period of infection.

Policies

- The National Council for Blood Services, through the Department Circular 2013-0132, recommends strategies to test all blood donations for TTI prior to cross-matching and transfusion.[2]
- TTI screening tests are mandatory for the following diseases: human immunodeficiency virus 1 and 2 (HIV-1 and HIV-2, respectively) hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis *(Treponema pallidum),* and, for endemic locations, malaria (*Plasmodium sp.*). Specific tests for these diseases are tabulated in Table 1.[1]
- According to the Department of Health, all blood donations found to be reactive in any of these tests are sent for confirmatory testing (Figure 1).[2]

Table 1. Serologic tests for transfusion transmitted infection

Disease	Serologic test
HIV	Combination of HIV Ag/Ab test or HIV Ab test
Hepatitis B	HBsAg test
Hepatitis C	Combination of Hepatitis C Ag/Ab or Hepatitis C Ab test
Syphilis	Specific treponemal Abs screening test
Malaria	Malaria Ag and Ab screening test

Ab=antibody; Ag=antigen; HBs=Hepatitis B surface; HIV=human immunodeficiency virus.

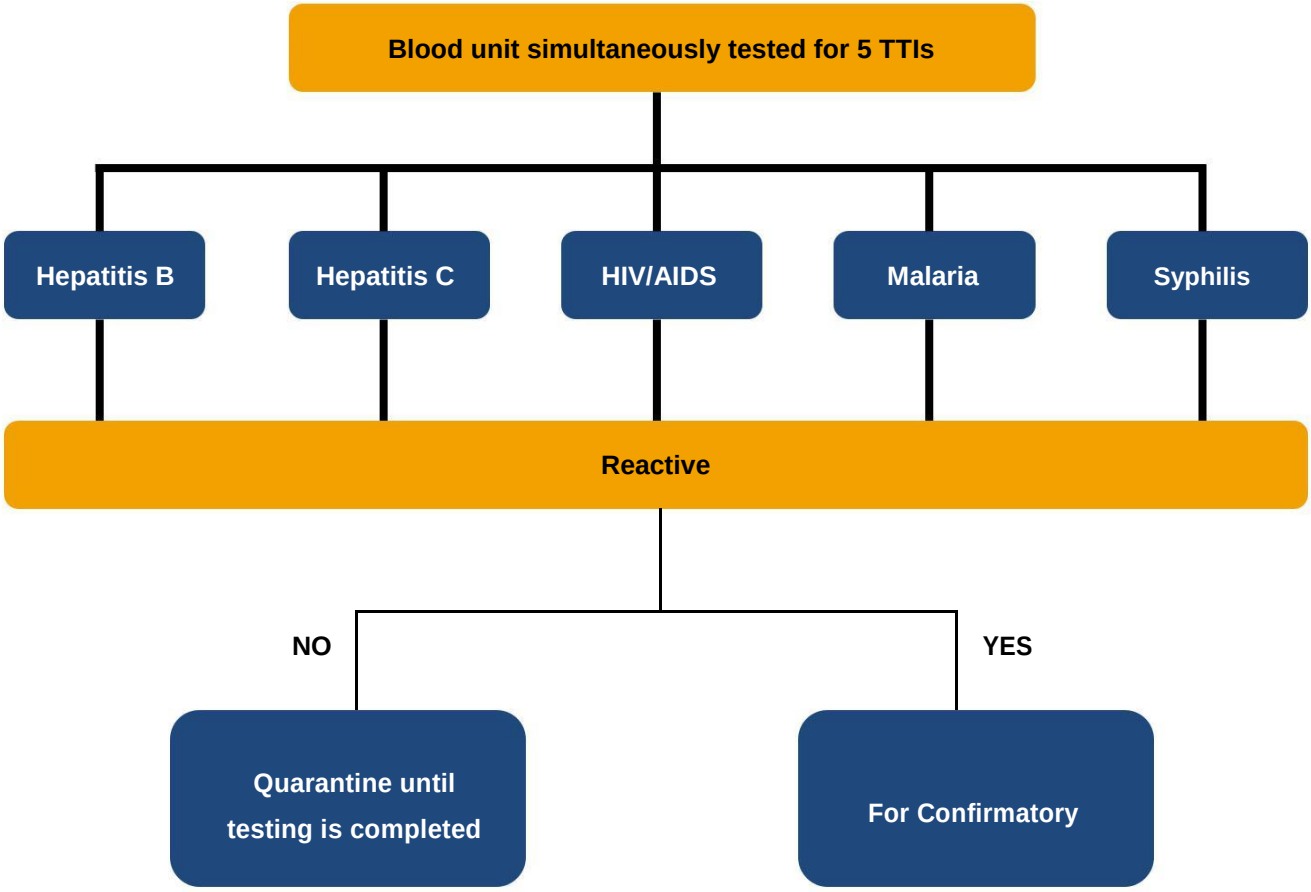

Figure 1. Blood units testing algorithm for screening and diagnosing transfusion transmitted infections
AIDS=acquired immunodeficiency syndrome; HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus; TTI=transfusion transmitted infection.

COST EFFECTIVENESS OF NAT IN OTHER COUNTRIES

Methods

A systematic literature search on PubMed, Cochrane Library, Center for Reviews and Dissemination, Cost-effectiveness Analysis Registry of Tufts Medical Center, and HERDIN database was conducted. Only 8 economic evaluations were included in the final report. The review protocol and the summary of the included studies are presented in Appendix A and Appendix B, respectively.

Relevant Studies
A summary is provided in Table 2.

- Zimbabwe
  - The authors concluded that implementing this additional screening cannot be cost effective in their local context, as it is considered very expensive for the meager benefit it provides for HIV, HBV, and HCV. Lowering the cost of NAT significantly by improving testing and donor recruitment efficiency and negotiating the price of reagents may improve its cost effectiveness.[3]

- Sweden
  - Because the baseline risks are already low in Sweden (less than 0.5 per million transfusions for HBV and HCV and less than 0.2 per million for HIV), and ID-NAT costs US$ 29.5 per blood donation, adding NAT on top of serologic screening cannot be considered cost-effective in their context. The benefit of NAT comes at a very high cost, falling above the usual threshold in Sweden.[4]

- US
  - A study concluded that NAT is not cost effective compared to usual antigen test for the detection of TTIs in whole-blood donations. However, they also argued that NAT can still improve the safety of overall blood supply in the US.[5]
  - A similar study compared various permutations of screening including mini pool NAT, ID-NAT, serologic screening, p24/hepatitis B surface antigen (HBsAg) test, and anti-hepatitis B core antibody test. This study concluded that current serologic screening protocols have already reduced HIV, HCV, and HBV transmission among blood donors therefore incremental benefits of NAT are minimal.[6]

- France
  - Enzyme immunoblot assay plus NAT compared to other screening and management options is not a cost-effective intervention to be integrated into the French health policy. Other factors, such as social benefits, ethical aspects, and public risk, should be considered.[7]

- European Union
  - In a study comparing current HBsAg assays, new HBsAg assays with enhanced-sensitivity, and single-sample HBV NAT, results show that the single-sample HBV NAT test yields only modest health benefit but at very high costs and is therefore deemed not cost effective. The study recommends expanding the protocol that supports the implementation of HBsAg assays rather than the HBV NAT.[8]

- Cross country
  - A study by Custer et al. used a web-based application to conduct a cost-utility analysis of NAT for HIV, HBV, and HCV in 6 different countries, namely Brazil, Ghana, Netherlands, South Africa, Thailand, and United States of America. Results show that across the 6 countries, both the multiplex and individual NAT screening strategy are not cost effective compared to common serological test for HIV, HBV, and HCV. HIV antibody test, HCV antibody test, and HBsAg test remain the most cost effective options in all 6 countries.[9]
  - Individual donor NAT was not cost effective in Ghana, Thailand, and the Netherlands. MP24-NAT was not cost effective in Thailand and Netherland, while it is deemed cost effective in Ghana.[10]

Table 2. Summary of cost effectiveness analyses of NAT in other countries

Study	Country	Disease Targeted	Intervention	Comparator	Result
Mafirakureva et al., 2016	Zimbambwe	HIV, HCV, and HBV	HBsAg, HCV-Ab, and HIV Combo Ag/Ab + ID-NAT	HBsAg, HCV-Ab, and HIV Combo Ag/Ab	Not cost effective
Davidson et al., 2011	Sweden	HIV, HCV, and HBV	HBsAg, HCV-Ab, and HIV Combo Ag/Ab + ID-NAT	HBsAg, HCV-Ab, and HIV Combo Ag/Ab	Not cost effective
Jackson, et al., 2003	US	HIV, HCV, and HBV	HBsAg, HCV-Ab, and HIV Combo Ag/Ab + ID-NAT	HBsAg, HCV-Ab, and HIV Combo Ag/Ab	Not cost effective
Marshall et al., 2004	US	HIV, HCV, and HBV	HBsAg, HCV-Ab, and HIV Combo Ag/Ab + ID-NAT	HBsAg, HCV-Ab, and HIV Combo Ag/Ab	Not cost effective
Loubierer, Rotily, & Moatti, 2003	France	HCV	EIA + NAT	No screening + No management; Wait and treat cirrhosis; EIA + EIA	Not cost effective
Pereira, 2003	European Union	HBV	Single-sample HBV NAT	Current HbsAg assay ; new HbsAg	Not cost effective
Custer et al., 2017	Brazil, Ghana, Netherlands, South Africa, Thailand, and United States of America	HIV, HCV, and HBV	Mini pool mutiplex NAT (pool size 16) ; Individual donor NAT	HBsAg, HCV-Ab, and HIV Combo Ag/Ab ; HIV combo Ag/Ab + HCV combo HBsAg	Not cost effective
Van Hulst et al., 2009	Ghana, Thailand, and Netherlands	HIV, HCV, and HBV	Mini pool mutiplex NAT (pool size 6) ; Mini pool mutiplex NAT (pool size 24) ; ID-NAT	HIV combo + HCV combo + HBsAg	Not cost effective

Ab=antibody; Ag=antigen; combo=combination; EIA=enzyme immunoblot assay; HBV=hepatitis B virus; HBsAg=hepatitis B virus surface antigen; HCV=hepatitis C virus; HIV=human immunodeficiency virus; ID=individual donor; NAT=nucleic acid test.

***Disclaimer**: This information brief merely collated evidence of cost effectiveness of NAT in other countries. Results are neither directly transferable nor generalizable to Philippine context as the variables used in each analysis are unique to each study setting. The intent is to provide a list of sources of the best evidence on the topic that the HPDPB-Research Division could identify using all reasonable efforts within the time allowed. A cost-effectiveness analysis using local data on costs and epidemiological information is needed to provide health economic evidence on NAT relevant to Philippine setting. The producers of this brief are not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.*

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Appendix A. Information brief review protocol

Research Question
Is nucleic acid test (NAT) a cost-effective intervention among patients with transfusion transmitted infection (TTI) in other countries?

Objective
To provide information on the cost effectiveness of NAT among TTI patients in other countries

Search Strategy and Selection Criteria
Electronic databases such as PubMed/Medline, Cochrane Database of Systematic Reviews, Cochrane Central Registry of Controlled Trials, Center for Reviews and Dissemination, Cost-effectiveness Analysis Registry of Tufts Medical Center, and Health Research Development Information Network were searched for research articles on the cost effectiveness of NAT among TTI patients in other countries. The search strategy is constructed by combining search terms with appropriate Boolean operators as described in detail in Table 3. Studies that satisfy the selection criteria will be subjected to full-text review. Studies are appraised by reviewers prior to inclusion in the final report. The number of hits per database searched and the keywords used is tabulated in Table 4.

Table 3. Selection Criteria

Criteria	Description
Population	Patients with transfusion transmitted infection
Intervention	Nucleic acid test
Study Design	Cost-effectiveness analysis, cost-utility analysis, systematic review of cost-effectiveness analysis

Table 4. Database search results

Database	Keywords and Search terms	Hits
PubMed	(((((((Nucleic acid test[Mesh] OR Nucleic acid test OR Nucleic Acid Amplification Test[Mesh] OR Nucleic Acid Amplification Test)) AND (transfusion transmitted infections[Mesh] OR transfusion transmitted infections))) AND (Cost-effectiveness Analysis OR "cost effectiveness analysis" OR CEA OR cost effectiveness)))) Filters: English	31
Cochrane Libraries	Nucleic acid test OR Nucleic acid amplification test in All Text AND transfusion transmitted infections in All Text AND cost-effectiveness Analysis OR cost effectiveness analysis OR cost effective OR cost effectiveness in All Text - (Word variations have been searched)	3
TUFTS	Nucleic acid test	9
CRD	Nucleic acid test	2
HERDIN	Nucleic acid test and transfusion transmitted infection	1

CRD=Center for Reviews and Dissemination; HERDIN= Health Research Development Information Network;
TUFTS= Cost-effectiveness Analysis Registry of Tufts Medical Center;

Appendix B. Detailed summary of included studies

Author	Year	Country	Disease Condition	Intervention	Comparator	Perspective	Outcomes	Currency	Sponsor
Custer et al.	2017	Brazil, Ghana, Netherlands, South Africa, Thailand, USA	HIV, HCV, HBV	HIV Ab + HCV Ab + HBsAg	HIV Combo + HCV Combo + HBsAg ; Mini pool Multiplex NAT (pool size 16); Individual Donation NAT	-	Number of infections remaining, costs and QALY gained	USD	ISBT Transfusion-Transmissible Infectious Diseases Working Party
Pereira	2003	EU	HBV	HBV NAT	HBsAg assays (current and new)	payers	Life expectancy (i.e. LYs and QALYs), lifetime costs of treating HBV complications	Euro	Ministry of Health of the Gov't of Spain
Loubiere et al.	2003	France	HCV	NAT	No HCV screening or treatment	health systems	1. # of true positive HCV-infected detected; 2. # of cases of HCV infection averted; 3. # of potential life years saved.	USD	-
van Hulst et al.	2009	Ghana, Thailand, and Netherlands	HIV, HCV, HBV	HBsAg, HCV-Ab, and HIV-Ab;	1. HBsAg, HCV-Ab + Ag, and HIV- Ab + Ag/p24, 2. MP24-NAT + HIV-Ab, HCV-Ab, and HBsAg, 3. MP6-NAT + HIV-Ab, HCV-Ab, and HBsAg, and 4. ID-NAT (on HBV, HCV, and HIV) + HIV-Ab, HCV-Ab, and HBsAg.	health care	DALYs averted	USD	Landsteiner Foundation for Blood Transfusion Research and the Ghanaian-Dutch Collaboration for Health Research and Development program
Mafirakureva et al.	2016	Zimbabwe	HIV, HCV, HBV	NAT + SS	SS	health care	infections averted, QALYs	USD	EU Seventh Framework Program
Davidson et al.	2010	Sweden	HIV, HCV, HBV	NAT + SS	SS	societal	infections avoided, QALY	SEK/USD	-
Marshall et al.	2004	US	HIV, HCV, HBV	MP NAT + SS, p24, ID NAT + SS, p24	SS	healthcare system	years of life gained and QALY	USD	Chiron Corporation
Jackson et al.	2003	US	HIV, HCV, HBV	Minipool NAT, ID NAT	HIV p24 Ag, anti-HBc Ab	societal	infections avoided, QALY	USD	NHLBI Retrovirus Epidemiology Study

Ab=antibody; Ag=antigen; combo=combination; EIA=enzyme immunoblot assay; DALY=Disability-adjusted life years; HBc=Hepatitis B core antibodies HBV=hepatitis B virus; HBsAg=hepatitis B virus surface antigen; HCV=hepatitis C virus; HIV=human immunodeficiency virus; ID=individual donor; LY=life years; NAT=nucleic acid test; QALY=Quality-adjusted life years; SEK=Swedish krona; SS=serologic screening; USD=United States dollars