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Cost-Effectiveness of Blood Donor Screening for *Babesia microti* in Endemic Regions of the United States

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Abstract

Background—*Babesia microti* is the leading reported cause of red blood cell (RBC) transfusion-transmitted infection in the United States (US). Donor screening assays are in development.

Study Design and Methods—A decision analytic model estimated the cost-effectiveness of screening strategies for preventing transfusion-transmitted babesiosis (TTB) in a hypothetical cohort of transfusion recipients in *Babesia*-endemic areas of the US. Strategies included: (1) No screening, (2) Uniform Donor Health History Questionnaire (UDHQ), “*status quo*”, (3) Recipient risk-targeting using donor antibody (Ab) and polymerase chain reaction (PCR) screening, (4) Universal endemic donor Ab screening, (5) Universal endemic donor Ab and PCR screening. Outcome measures were TTB cases averted, costs, quality-adjusted life years (QALYs) and incremental cost-effectiveness ratios (\$/QALY). We assumed a societal willingness to pay of \$1 million/QALY based on screening for other transfusion-transmitted infections.

Results—Compared to no screening, the UDHQ avoids 0.02 TTB cases per 100,000 RBC transfusions at an incremental cost effectiveness ratio (ICER) of \$160,000/QALY whereas recipient risk-targeted strategy using Ab/PCR avoids 1.62 TTB cases per 100,000 RBC transfusions at an ICER of \$713,000/QALY compared to the UDHQ. Universal endemic Ab screening avoids 3.39 cases at an ICER of \$760,000/QALY compared to the recipient-risk targeted strategy. Universal endemic Ab/PCR screening avoids 3.60 cases and has an ICER of \$8.8 million/QALY compared to universal endemic Ab screening. Results are sensitive to blood donor *Babesia* prevalence, TTB transmission probability, screening test costs, risk and severity of TTB complications, and impact of babesiosis diagnosis on donor quality of life.

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Conclusion—Antibody screening for *Babesia* in endemic regions is appropriate from an economic perspective based on the societal willingness to pay for preventing infectious threats to blood safety.

Keywords

Babesia microti; cost-effectiveness; transfusion; blood supply screening

INTRODUCTION

The intra-erythrocytic protozoan *Babesia microti* is currently the leading red blood cell (RBC) transfusion-transmitted pathogen reported to the United States (US) Food and Drug Administration (FDA).¹ Babesiosis most commonly occurs after an *Ixodes scapularis* tick bite and results in clinical manifestations that range from asymptomatic infection or influenza-like illness to organ failure and death.² Complications may include acute respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy, renal failure, or hemolytic anemia. In hospitalized or immunocompromised patients, mortality rates of 6–28% have been reported.^{3–7}

In the US, the disease has a regional focus in seven Northeast and Upper Midwest states (Connecticut, Massachusetts, Minnesota, New Jersey, New York, Rhode Island and Wisconsin) accounting for 97% of 1,124 babesiosis cases reported to the Centers for Disease Control and Prevention (CDC) in 2011.⁸ Over the past decade the geographic range of *Babesia microti* has expanded and more tick and transfusion-transmitted cases have been documented.^{4,9} In endemic states, donor seroprevalence¹⁰ can be as high as 2%, with incidence ranging from 1/604–1/100,000 cases per red blood cell (RBC) units transfused.^{11,12}

The current method of blood donor screening for asymptomatic *Babesia microti* infection relies on self-reported history through the Uniform Donor Health History Questionnaire (UDHQ) followed by indefinite deferral of donors acknowledging a history of infection.¹³ In 2010, a FDA Blood Products Advisory meeting concluded that alternative strategies to mitigate the risk of TTB were needed.¹⁴ One strategy is blood product screening with antibody and/or polymerase chain reaction (PCR) assays in regions with high *Babesia* prevalence. Another potential strategy is to test a fraction of donors and maintain a separate inventory of *Babesia*-negative RBC components for transfusion to high-risk recipients only. High-risk conditions include asplenia, organ transplantation, malignancy, human immunodeficiency virus (HIV), immunosuppressive medications, chronic heart, lung and liver disease, advanced age and premature infants.² In 2010, the Rhode Island Blood Center initiated the first laboratory-based blood donor screening program for *Babesia microti* targeting thalassemia, sickle cell disease and neonatal patients under an FDA investigational new drug (IND) protocol.¹⁵ The American Red Cross, in collaboration with industry, is evaluating high throughput immunofluorescence antibody (IFA) and PCR *Babesia microti* blood screening assays under an FDA IND and other assays are in development.^{16,17}

Since the HIV epidemic, public expectations are zero tolerance for infectious threats to blood safety.¹⁸ As diagnostic technology has improved and new infections, such as West

Nile virus have emerged, blood supply screening assays have been successfully implemented despite extremely high cost-effectiveness ratios.¹⁹ Experience suggests a societal willingness to adopt for blood safety interventions at, or above, 1 million dollars per quality-adjusted life-year (\$/QALY), a 10 to 20 fold higher threshold than for other medical and pharmaceutical interventions.^{20,21} The unique geographic, seasonal and microbiological characteristics of *Babesia*, combined with the difficulty of accurately identifying at-risk donors and recipients, have posed exceptional challenges for transfusion medicine in balancing the costs and benefits of potential screening interventions.²² We evaluated the cost-effectiveness of the status quo UDHQ and three laboratory based blood donor screening strategies as compared to no screening for *Babesia microti* in endemic US regions.

MATERIALS AND METHODS

Model Overview

We developed a decision analytic model (Figure 1) to simulate the health and economic consequences of blood supply screening for *Babesia microti* in a hypothetical cohort of transfusion recipients in endemic regions with a mean age of 60.²³ Transfusion recipients receive one unit of RBCs per donor. Recipients are assigned probabilities of receiving correctly or incorrectly identified *Babesia* infected or uninfected units of blood based on test sensitivity, specificity and on blood donor *Babesia* prevalence. When an infected RBC unit is transfused, transmission may or may not occur. If *Babesia microti* is transmitted, recipients may remain asymptomatic or develop symptomatic babesiosis. Recipients with babesiosis can recover and return to baseline health, experience long-term disability, or die from babesiosis or unrelated causes. Recipients who receive an uninfected unit can survive or die from unrelated causes. Model inputs and sensitivity analysis ranges are reported in Table 1. The model was programmed in TreeAge Pro 2012 (TreeAge Software Inc., Williamstown, Massachusetts).

The model projects the number of transfusion-transmitted babesiosis (TTB) cases averted, lifetime QALYs gained, and costs associated with transfusions and TTB. Costs and QALYs were projected for each strategy and used to calculate incremental cost-effectiveness ratios (ICERs) that were compared to an ICER threshold of \$1 million/QALY, representing a societal willingness to pay for blood safety.²⁰ The analysis was conducted from the societal perspective over a lifetime time horizon, with all costs in 2011 US dollars,²⁴ and future health costs and consequences were discounted at 3% annually.²⁵

Screening Strategies

For the purposes of the analysis, Connecticut, Massachusetts, Minnesota, New Jersey, New York, Rhode Island and Wisconsin were considered endemic states and we assumed that screening would only occur in counties with babesiosis incidence rates greater than 1.0 per 100,000 persons based on CDC or local health department surveillance data. For example, in New York State screening would occur in Dutchess county (incidence of 17.5 per 100,000), but not in Oswego county (incidence of 0 per 100,000).²⁶ We compared 5 screening strategies for *Babesia microti* in endemic regions: (1) No screening; (2) UDHQ, the *status quo*, a 48-item general medical history questionnaire that includes one question asking

donors if they have a history of babesiosis. (3) Recipient-risk targeted screening whereby only transfusion recipients in endemic regions identified as high-risk receive RBC units screened with both antibody (Ab) and polymerase chain reaction (PCR) assays in parallel (simultaneous testing). (4) Universal Ab screening where all donated RBC units in an endemic region are screened with an antibody assay. (5) Universal Ab/PCR screening where all donated RBC units in an endemic region are screened simultaneously with both Ab and PCR assays allowing for the additional detection of donors in the window period prior to serologic response. In all laboratory screening strategies, RBC units that screen positive are discarded and the corresponding donor is notified and referred for medical evaluation.

Data

We used the proportion of hematology/oncology (15%), organ transplant (1%), neonates (2%) and intensive care unit (11%) transfusion recipients (total of 29%) from the 2009 National Blood Collection and Utilization Survey (NBCUS) to estimate the transfusion population at high-risk for babesiosis complications.²⁷ This estimate was similar to previously published reports (25%–27%) of immunocompromised transfusion recipients used in cost-effectiveness analyses of West Nile virus blood supply screening^{19,28} In the base case, we assumed no shortage of blood products and that laboratory screened RBC units would always be available for high-risk transfusion recipients in the recipient risk-targeted strategy. Sensitivity and specificity estimates for the UDHQ were based on New York²⁹ and Rhode Island Blood Center¹⁵ data, and accuracy of Ab and PCR testing for babesiosis was based on published literature for diagnostic tests used in clinical practice.^{30–33} The base case prevalence of 0.9% was a weighted average of published serologic surveys of blood donors in endemic states.^{10,15,34,35} We assumed 4% of all donors with *Babesia* would have a window period infection (PCR positive; antibody negative).³⁶ The base case, transmission probability (0.4%) was derived from the Rhode Island Blood Center's incidence and prevalence data and represents the likelihood of developing symptomatic babesiosis after transfusion of a potentially infectious unit.¹⁵ In the base case we assumed that all positive units (Ab positive only, PCR positive only, or both Ab and PCR positive) were equally infectious. In sensitivity analysis, we examined the impact of increasing the transmission probability of *Babesia*-infected RBC unit from a window period donor (Ab negative and PCR positive). In the base case, high-risk transfusion recipients were assumed to have a 2-fold greater risk of developing symptomatic babesiosis and a 1.8-fold greater probability of developing complications compared to other recipients.³ The probability of death after blood transfusion was based on results from a survival study of a large cohort of US transfusion recipients.³⁷ Survival estimates for the non-high risk group were based on data from the 41–65 aged cohort and survival of the high risk group was modeled using the aged >65 cohort. We assumed a stable annual risk of death beyond year 3 and merged US life table annual mortality probabilities when these values exceeded the cohort-based estimates (at age 84 for non-high risk recipients and age 90 for high-risk recipients).³⁸ 99.9% of the cohort was deceased by age 100.

The baseline quality of life of transfusion recipients was derived from previously published cost-effectiveness analyses of blood supply screening.^{19,39} There are no data on quality of life for patients with babesiosis. Health state utility weights were extrapolated from quality

of life studies for influenza hospitalization,⁴⁰ ARDS,^{41–43} and intensive care unit patients.⁴⁴ Long-term disability associated with complicated babesiosis was based on quality of life data from survivors of ARDS, the most frequent complication of severe babesiosis.^{5,7} In the base case, we did not assign a quality of life change to blood donors who screen positive assuming that they would remain asymptomatic, resolve the infection and not require further treatment per Infectious Diseases Society of America (IDSA) recommendations.⁴⁵ In sensitivity analysis, we considered a temporary utility decrement for positive donors because the notification and medical follow-up process may result in emotional distress and life disruption.⁴⁶

All TTB-related costs were assumed to occur during the first year following transfusion. The per unit costs of Ab screening and Ab/PCR screening were estimated to be \$15 and \$30, respectively, since no FDA approved test currently exists. The Ab/PCR cost was increased by 10% in the recipient-risk targeted strategy to account for additional costs to maintain a separate inventory of blood products and potentially higher per unit costs. Babesiosis hospitalization costs were obtained from 2009 Healthcare Cost and Utilization Project data⁴⁷ and sub-acute rehabilitation stay costs for complicated babesiosis were extrapolated from Medicare data for sepsis.⁴⁸ Medication costs for azithromycin and atovaquone were based on average wholesale drug prices⁴⁹ and durations were per IDSA guidelines.⁴⁵ The cost to blood centers to investigate reported TTB cases included confirmatory testing of all potentially implicated RBC units and labor costs (Kessler DA. Personal communication). The costs of excluding donors who self-reported a history of babesiosis included blood center screening and pre-donation medical evaluation. Societal costs for discarding *Babesia*-positive RBC units included blood center costs, such as increased recruitment and unit destruction,⁵⁰ as well as donor medical work-up and time.^{51–54} Additional costs for false positives represented the opportunity costs for blood centers to collect, screen and process donated RBCs that were inappropriately discarded.

Additional details regarding the model inputs and data sources are available in the supplementary appendix.

Sensitivity Analyses

Parameters were varied individually in one-way sensitivity analysis to evaluate the sensitivity of results to plausible variations in model estimates. Overall model uncertainty was evaluated in probabilistic sensitivity analysis by simultaneously conducting 1,000 random draws from probability distributions for each variable and recalculating the cost-effectiveness of each strategy. All variables were assumed to have triangular probability distributions, with the base case estimate as the mode and with uncertainty ranges in Table 1 representing the lower and upper limits. To evaluate the stability of results to this assumption, probability distributions for key variables were changed from triangular to uniform to represent greater uncertainty.

RESULTS

Base case cost-effectiveness results are displayed in Table 2. The predicted TTB incidence was similar with no screening or the status quo UDHQ, (approximately 3.6 cases per

100,000 RBC transfusions). The projected number of TTB cases avoided per 100,000 RBC transfusions compared to no screening would be 1.6 for recipient risk-targeted strategy, 3.4 for universal endemic Ab screening and 3.6 for universal endemic Ab/PCR screening. The net costs per RBC transfusion for the recipient risk-targeted, universal endemic Ab and universal endemic Ab/PCR strategies would be \$11.72, \$20.42 and \$35.57, respectively; increases of 5%, 9% and 16% above the mean price (\$223) US hospitals paid per RBC unit in 2009.²⁷ The anticipated health benefit per 100,000 RBCs transfused would be 1.52 QALYs for recipient risk-targeting, an additional 1.14 QALYs for universal endemic Ab and a further 0.17 QALYs for universal endemic Ab/PCR screening. Compared to no screening, the status quo UDHQ strategy had an ICER of \$160,000/QALY. The ICER for recipient risk-targeted screening compared to the *status quo* was \$713,000/QALY and the ICER for universal endemic Ab screening compared to risk-targeted screening was \$760,000/QALY. Universal endemic Ab/PCR screening, the most effective and expensive strategy, had an ICER of \$8.8 million/QALY compared to universal endemic Ab screening. If the only policy option considered was screening all units in an endemic region with both Ab and PCR (versus do nothing), the cost-effectiveness ratio of this strategy would be \$1.2 million/QALY.

In one-way sensitivity analyses, variables that exerted the greatest influence on results were blood donor babesiosis prevalence, the transmission probability, screening test costs, the risk and severity of babesiosis complications and impact of babesiosis diagnosis on donor quality of life (Supplementary Table 1). Where babesiosis prevalence exceeds 0.6% (compared to 0.9% in the base case), universal endemic Ab screening is the preferred strategy at an ICER threshold of \$1 million/QALY (Figure 2). When the transmission probability was varied, universal endemic Ab screening is the preferred strategy at an ICER threshold of \$1 million/QALY when incidence exceeded 1/39,000 RBC units transfused, compared to 1/28,000 RBC units transfused in the base case (Supplementary Figure 1). The recipient-risk targeted strategy was preferred if the transmission probability for a RBC unit from a window period donor was greater than 4 times the transmission probability for a non-window period donor and universal endemic Ab/PCR was optimal if this value was 20 times greater.

Universal endemic Ab screening was no longer preferred when Ab screening cost \$18 or more per RBC unit or when Ab/PCR cost less than \$22. If pooled testing of multiple blood units could reduce the cost of combination Ab/PCR by 3-fold to \$10 per unit and sensitivity maintained at greater than 80%, universal endemic Ab/PCR would be preferred at a willingness to pay of \$1 million/QALY. If a recipient risk-targeted strategy employing Ab screening only (and not parallel Ab/PCR) was a viable policy option, the ICERs would be \$426,000/QALY and \$1.1 million/QALY for risk-targeted and universal Ab screening, respectively.

Risk-targeted screening was preferable to universal endemic Ab screening when high-risk recipients had a 8-fold greater relative risk of symptomatic transmission (compared to 2-fold in base case) or a 2.4 times greater relative risk of developing complicated babesiosis (compared to 1.8 in base case). Laboratory testing was no longer preferred when donor quality of life was temporarily decreased by 0.02 (on a scale from 0 to 1) following the diagnosis of asymptomatic babesiosis.

In probabilistic sensitivity analysis (Figure 3) at a cost-effectiveness threshold of \$1 million/QALY, laboratory screening was preferred to the status quo in 84% of simulations: universal Ab (62%), recipient risk-targeted (16%) and universal Ab/PCR (6%). If willingness to pay was \$5 million/QALY (reflecting the current practice for nucleic acid testing of donated blood for HIV, hepatitis B and hepatitis C viruses^{55,56}), universal Ab/PCR was preferred in 37% of simulations. At a cost-effectiveness threshold frequently used outside of blood screening (\$100,000/QALY) laboratory screening strategies were preferred in approximately 2 % of simulations. Results were stable after probability distributions for key variables were replaced with uniform distributions (Supplementary Figure 2).

DISCUSSION

Medical community and public expectations for TTB prevention have intensified as a result of reported increased incidence.^{57,58} We used a decision analytic model to evaluate the effectiveness and cost-effectiveness of laboratory-based blood supply screening for *Babesia microti*. We found that universal Ab screening in endemic regions could avoid approximately 3 cases of TTB per 100,000 RBC transfusions with a cost-effectiveness ratio of less than \$1 million/QALY, which compares favorably to currently adopted practices for preventing other transfusion-transmitted infections (Table 3).^{59,60}

Our analysis is the first to consider the cost-effectiveness of the current donor health history questionnaire for preventing transfusion-transmitted babesiosis. Using data from the Rhode Island and New York Blood Centers we estimated the UDHQ has a sensitivity of 0.5% and a positive predictive value of 24% when compared to antibody testing.^{15,29} Laboratory screening strategies with better test characteristics prevented more cases of TTB and had cost-effectiveness ratios below \$1 million/QALY. Although combining Ab and PCR screening of all donated blood would be the most effective strategy, the additional health benefit compared to Ab screening is likely to be small, and we found this strategy had an unfavorable cost-effectiveness ratio of >\$8 million/QALY. Importantly, this finding was sensitive to assumptions regarding the infectivity of *Babesia*-infected RBC units that came from a window period donor and estimates of assay cost. In the base case, we assumed the transmission probability was the same for all test positive units. However, when we assumed a window period donation was approximately 20 times more likely to transmit *Babesia*, the preferred strategy changed, and testing of all RBC units in an endemic region with Ab and PCR was the favored option.

In an effort to mitigate costs, policy makers have considered selectively applying Ab/PCR screening to immunocompromised transfusion recipients at risk for severe babesiosis.⁶¹ In clinical practice, determining an appropriate high-risk population is challenging because of diverse and common risk factors for severe babesiosis such as advanced age and heart disease. Our analysis captured additional costs associated with a selective transfusion strategy, such as maintaining a separate inventory of blood products, by assigning a 10% additional per unit cost for each unit tested under this strategy. We found that universal endemic Ab screening would be preferred to risk-targeted Ab/PCR screening because it offers greater overall health benefit (more TTB cases prevented and QALYs gained) with a

comparable cost-effectiveness ratio (approximately \$700,000–800,000 per QALY). This result is explained by the significant costs associated with *Babesia* Ab/PCR screening of approximately 30% of the blood supply for transfusion recipients with easily identifiable high-risk conditions and the likelihood of severe TTB cases occurring in transfusion recipients with other common comorbidities who would be difficult to target through risk-based algorithms. Furthermore, prior work has documented the logistical and ethical problems associated with selective transfusion protocols designed to prevent transfusion-related complications.^{62,63} Our model suggests that, in addition to these issues, a risk-targeted transfusion policy for TTB prevention in endemic regions is unlikely to offer greater value compared to a universal antibody screening strategy.

If universal screening were to be adopted in endemic regions, the exclusion of many potential donors raises additional concerns related to cost, blood availability and donor follow-up. In our model, the costs of donor medical evaluation and discarded blood amounted to approximately \$625 per donation testing positive. PCR based screening offers the potential to reduce these costs due to improved specificity. We did not consider PCR based screening on its own as important determinants of the performance of PCR assays in the donor population are unknown. These include optimal sample volume, primer selection, and the particular methodology employed (i.e real time PCR vs nested PCR). In our analysis, we did not assume a shortage of blood products from increased donor exclusion because, on average, the US blood supply operates on approximately a 10% margin above demand.²⁷ Excluding donors who were Group O or phenotype matched for chronically transfused populations could be of greater concern. Future analyses examining the blood center budget impact of *Babesia* screening and simulation modeling of donor re-entry protocols based on antibody clearance are important areas for further investigation. Lastly, to address additional unintended consequences of laboratory screening, we considered potential adverse quality of life effects on asymptomatic *Babesia* positive blood donors. Our results were sensitive to small changes in donor quality of life, which underscores the importance of effective donor notification programs that address potential anxiety, confusion and life disruption.⁴⁶

Our analysis supports universal screening of donated blood in regions with *Babesia* seroprevalence greater than 0.6%. *Babesia* prevalence among blood donors in non-endemic regions has not been well quantified, but 13% of 162 TTB cases reported to the CDC occurred outside of endemic regions through donor travel or imported blood products.⁹ Recent data indicates 0.2% seroprevalence in areas of New Hampshire and Maine⁶⁴ and 0.02% in Oklahoma and Arizona.⁶⁵ Our results do not apply to areas in the Western United States where *Babesia duncani* and other *Babesia* species are found since they would not be identified with current screening assays for *Babesia microti*. However, other *Babesia* species have been implicated in only a small fraction (2%) of TTB cases reported to the CDC.⁹

Our analysis has important limitations pertaining to the quality of data used to inform model inputs and other assumptions. The point estimates for assay sensitivity and specificity are based on diagnostic tests used in clinical settings (not blood donor screening) and test costs are based on other blood donor screening tests. We used the best available evidence describing babesiosis clinical outcomes, incorporating published studies of both tick and

transfusion-associated disease. However, robust clinical outcome data are limited, with the existing evidence base consisting of small studies lacking long-term follow-up on the frequency and severity of babesiosis morbidity. Clinical outcomes are better characterized for tick-associated babesiosis than transfusion-associated disease because of the small number of reported cases as well likely under-recognition and under-reporting. Evidence suggesting significantly worse outcomes for transfusion recipients with babesiosis than the estimates in this study would only improve the cost-effectiveness of screening. In order to account for the uncertainty around our estimates, we incorporated a broad range of plausible values in sensitivity analyses related to these and other important model inputs.

Models by their nature are simplified representations of complex real-world processes. We did not incorporate the dynamic interplay of ecological, host-parasite and human behavioral factors that may impact on tick and transfusion-associated *Babesia* transmission. Our model assumes prevalence is uniformly distributed throughout an endemic region when, in reality, it is focal without clearly defined geographic borders. Further research is needed to more precisely characterize *Babesia microti*'s geographic range and the appropriate boundaries for donor screening. We also did not consider a seasonally-targeted TTB mitigation strategy. Tick-associated babesiosis has a seasonal peak between June through September, whereas, transfusion-associated disease may occur year-round. The addition of PCR to antibody testing only during months of high tick activity could hypothetically enhance the cost-effectiveness of combination donor testing. However, seasonal variations in *Babesia* blood donor epidemiology and the duration of the window period are not well-characterized.

In conclusion, we found the cost-effectiveness of *Babesia microti* antibody screening of donated blood compares favorably to adopted blood safety interventions. Selective recipient risk-targeted screening offers less value than universal antibody screening using a cost-effectiveness threshold for blood safety of \$1 million/QALY. Based on this societal willingness to pay for preventing infectious threats to blood safety, donor antibody screening for *Babesia microti* is appropriate in endemic areas of the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Model Schematic

Decision tree structure for blood supply screening for *Babesia microti*. Closed circles represent chance events and open circles represent Markov processes where transfusion recipients transition between alive and dead health states to project lifetime outcomes. The model was run separately for high-risk and non-high risk transfusion recipients and results are a weighted average for all transfusion recipients.

Figure 2.

Cost-effectiveness of each screening strategy as a function of *Babesia microti* prevalence in blood donors. At prevalence greater than 0.6%, universal antibody screening is the most cost-effective strategy given a willingness to pay for blood safety of \$1 million per quality-adjusted life-year.

Figure 3.

Cost-effectiveness acceptability curve showing the probability that a screening strategy is optimal (provides the greatest health benefit) at a specified willingness to pay value.

Table 1

Model parameters

Inputs	Base case	Sensitivity Range	Reference(s)
Probability values			
Screening test characteristics *			
Questionnaire			
Sensitivity	0.5%	(0.1–5)	15,29
Specificity	99.9%	(90–100)	15,29
Ab			
Sensitivity	94.0%	(80–100)	30,31
Specificity	97.7%	(80–100)	30,31
Ab/PCR in parallel			
Sensitivity	99.9%	(90–100)	32,33
Specificity	97.7%	(80–100)	32,33
Babesiosis prevalence *			
Seropositive	0.9%	(0.1–2.0)	10,15,34,35
Window period (Ab negative/PCR positive)	0.04%	(0.01–0.09)	36
Proportion of transfusion recipients at high risk for severe babesiosis *	29%	(25–75)	19,27,28
Transmission probability *	0.4%	(0.1–2.2)	15
Probability of complicated babesiosis †			
High risk	57%	(20–80)	7
Non-high risk	32%	(10–50)	3
Babesiosis case fatality rate			
High risk	21%	(6–28)	5–7
Non-high risk	6%	(1–10)	3,4
All-cause mortality post-RBC transfusion ‡			
Year 1			
High risk	38%	(27–49)	37
Non-high risk	27%	(19–35)	37
Year 2			
High risk	19%	(13–25)	37
Non-high risk	11%	(5–15)	37
Year 3			
High risk	15%	(10–20)	37
Non-high risk	8%	(4–12)	37
Utility values			
Baseline transfusion recipient	0.90	(0.60–0.90)	19,39
Uncomplicated babesiosis §	0.87	(0.80–0.89)	40
Complicated babesiosis /	0.67	(0.40–0.80)	41,44
Costs, 2011 US \$			

Inputs	Base case	Sensitivity Range	Reference(s)
Blood donation screening tests			
Universal Ab	\$15	(8–23)	See text
Universal Ab/PCR	\$30	(15–45)	See text
Targeted Ab/PCR	\$33	(30–39)	See text
Babesiosis hospitalization [¶] (per day)	\$1,940	(970–2,920)	47
Outpatient costs			
Sub-acute rehabilitation care following complicated babesiosis ^{**}	\$9,420	(4,710–14,130)	48
Medication costs (per week) ^{††}			
Atovaquone	\$650	(325–975)	49
Azithromycin	\$22	(11–33)	49
Physician office visit			
Initial	\$152	(76–228)	52
Follow-up	\$61	(31–92)	52
Laboratory workup of positive donor ^{‡‡}	\$157	(79–326)	53,54
Blood center costs			
Specimen collection ^{§§} (per positive unit)	\$143	(72–215)	50
Screening and processing ^{§§} (per positive unit)	\$67	(34–101)	50
Donor recruitment ^{//} (per positive unit)	\$18	(9–27)	50
Unit destruction ^{//} (per positive unit)	\$12	(6–18)	50
Investigation of transfusion transmitted babesiosis case ^{¶¶}	\$1,000	(500–1,500)	See text
Donor time			
Office visit	\$49	(25–73)	51
Blood donation	\$37	(18–55)	50

Abbreviations: Ab=antibody; PCR =polymerase chain reaction; RBC=red blood cell; IDSA = Infectious Diseases Society of America

* See supplementary materials for additional information regarding model input calculations and sources.

[†] High risk conditions were presumed to confer a 1.8 increase in risk of complications based on the relative risk increase of babesiosis complications associated with asplenia.³

[‡] High risk and non-high risk transfusion recipient survival was modeled using outcomes for the 65-year old cohort and the 45–65 year old cohort from the referenced study.³⁷

[§] Utility value applied for 2 weeks in non-high risk recipient and 4 weeks in high risk recipient after which time the recipient returns to baseline health state.

[/] Assumes permanent disability.

[¶] Length of hospital stay is 5.3 days⁴⁷ and 12.7 days⁵ for uncomplicated and complicated babesiosis, respectively.

^{**} Mean 2009 Medicare payment to sub-acute nursing facility for diagnosis of severe sepsis.

^{††} Average wholesale price adjusted by average Medicaid discount and pharmacy dispensing fee. Azithromycin and atovaquone were assumed to be prescribed for outpatient therapy whereas hospitalized patients could receive clindamycin and quinine depending on severity as per IDSA guidelines.

^{††} Laboratory workup includes repeat *Babesia microti* serology, blood smear, nucleic acid testing, *Borrelia burgdorferi* serology, complete blood count, liver function tests and basic chemistry panel.

^{§§} Costs applied only for false positives representing opportunity cost of inappropriate deferral.

^{//} Costs applied for both true and false positives.

^{¶¶} Includes costs of testing all potentially implicated RBC units and labor costs.

Table 2
Cost-effectiveness results of blood supply screening for *Babesia microti* in endemic regions

Screening strategy	TTB cases averted (per 100,000 RBCs transfused)	Cost* (per RBC unit)	Incremental Cost* (per 100,000 RBCs transfused)	QALYs (per transfusion recipient)	Incremental QALYs (per 100,000 RBCs transfused)	ICER† (\$/QALY)
No screening						
UDHQ (<i>status quo</i>)	0.02	\$0.83		5.9143787		
Recipient risk targeted (Ab/PCR)	1.62	\$11.72	\$1,086,000	5.9143942	1.52	713,000
Universal Ab‡	3.39	\$20.42	\$871,000	5.9144056	1.14	760,000
Universal Ab/PCR‡	3.60	\$35.57	\$1,515,000	5.9144073	0.17	8,778,000

Abbreviations: RBC = red blood cell; TTB=transfusion-transmitted babesiosis; ICER = incremental cost-effectiveness ratio; QALY =quality-adjusted life year; UDHQ=Uniform Donor Health Questionnaire; Ab=antibody; PCR =polymenase chain reaction

* 2011 US dollars

† In strict incremental analysis the ICERs represent the difference in costs and effects between a strategy and the next most effective alternative. The cost effectiveness results for each strategy compared to no screening were 1) Recipient risk-targeted (Ab/PCR) \$708,000/QALY; 2) Universal Ab \$730,000; 3) Universal Ab/PCR \$1,220,000/QALY.

‡The term “universal” refers to a strategy of screening all donated blood units within an endemic region and not national screening.

Table 3

League table of blood safety interventions for transfusion-transmitted infection prevention

Source	Intervention	Comparator	Year of FDA licensure	ICER* (\$/QALY)
Eisenstade et al, 1988 ⁵⁹	HIV Ab	No screen	1985	Cost saving
Bush et al, 1995 ⁶⁰	HCV Ab	No screen	1990	Cost saving
Custer et al, 2005 ¹⁹	West Nile Virus NAT [†]	No screen	2006	701,000
Current study	Babesiosis Ab	No screen	Investigational	733,000
Agapova et al, 2010 ³⁹	Chagas Disease Ab [‡]	No screen	2006	863,000
Jackson et al, 2003 ⁵⁵ Marshall et al, 2004 ⁵⁶	HBV/HCV/HIV minipool NAT [§]	HBsAg, anti-HBc HCV Ab HIV Ab	1999–2005	5.4 million

ICER= incremental cost-effectiveness ratio; HIV=human immunodeficiency virus; Ab=antibody; HCV=hepatitis C virus; NAT=nucleic acid testing; ID=individual donation; HBV=hepatitis B virus; HBsAg=hepatitis B surface antigen; hepatitis B core antibody

* All costs updated to 2011 US dollars.

[†] Strategy of minipool testing of RBC units and individual unit testing in a geographic region experiencing West Nile virus outbreak.

[‡] Strategy of universal one-time donor testing.

[§] ICER represents the averaged incremental cost-effectiveness ratio from the two referenced studies.