### Criteria Grid
**Best Practices and Interventions for the Prevention and Awareness of Hepatitis C**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Date of Review:</strong></td>
<td>June 14, 2015</td>
</tr>
<tr>
<td><strong>Reviewer(s):</strong></td>
<td>Christine Hu</td>
</tr>
</tbody>
</table>

#### Part A

**Category:**

- Basic Science
- Clinical Science
- Public Health/Epidemiology
- Social Science
- Programmatic Review

**Best Practice/Intervention:**

- **Focus:** Hepatitis C, Hepatitis C/HIV, Other: Blood transfusions, HBV
- **Level:** Group, Individual
- **Target Population:** population who received blood transfusion in sub-Saharan Africa
- **Setting:** Health care setting/Clinic, Home
- **Country of Origin:** USA
- **Language:** English, French

#### Part B

**Is the best practice/intervention a meta-analysis or primary research? Please go to Comments section.**

- **YES**
- **NO**
- **N/A**

**COMMENTS**

Systematically evaluate the probability of acquiring either HIV, HBV or HCV from a single unit of whole blood in sub-Saharan Africa based on Pan American Health Organization’s estimate model of transfusion-associated risks in Central and South America.

- A systematic review of literature as well as data from WHO African region were used to parameterize the risk model.

**The best practice/intervention shows evidence of “scale up” ability**

- **YES**
- **NO**
- **N/A**
<table>
<thead>
<tr>
<th>The best practice/intervention shows evidence of transferability</th>
<th>□</th>
<th>☑</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>The best practice/intervention shows evidence of adaptation</td>
<td>☑</td>
<td>□</td>
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</tr>
<tr>
<td>Do the methodology/results described allow the reviewer(s) to assess the generalizability of the results?</td>
<td>□</td>
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</tbody>
</table>

Many of the studies were small, hospital-based, cross-sectional surveys with data collected from urban centers; results cannot be generalized to the rest of each sub-Saharan Africa countries.

<table>
<thead>
<tr>
<th>Are the best practices/methodology/results described applicable in developed countries?</th>
<th>□</th>
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</thead>
<tbody>
<tr>
<td>Are the best practices/methodology/results described applicable in developing countries?</td>
<td>□</td>
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</tbody>
</table>

Results of this study only applicable to sub-Saharan Africa countries.

<table>
<thead>
<tr>
<th>The best practice/intervention has utilized a program evaluation process</th>
<th>☑</th>
<th>□</th>
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</thead>
<tbody>
<tr>
<td>Consultation and feedback with community has taken place</td>
<td>□</td>
<td>☑</td>
<td>□</td>
</tr>
<tr>
<td>The best practice/intervention is sensitive to gender issues</td>
<td>□</td>
<td>☑</td>
<td>□</td>
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<tr>
<td>The best practice/intervention is sensitive to multicultural and marginalized populations</td>
<td>□</td>
<td>☑</td>
<td>□</td>
</tr>
<tr>
<td>The best practice/intervention is easily accessed/available electronically</td>
<td>□</td>
<td>☑</td>
<td>□</td>
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<table>
<thead>
<tr>
<th>Is there evidence of a cost effective analysis? If so, what does the evidence say? Please go to Comments section</th>
<th>□</th>
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<tr>
<td>How is the best practice/intervention funded? Please go to Comments section</td>
<td>□</td>
<td>□</td>
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</table>

No funding stated
<table>
<thead>
<tr>
<th>Is the best practice/intervention dependent on external funds?</th>
<th>☐</th>
<th>☒</th>
<th>☐</th>
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<tr>
<td><strong>Other relevant criteria:</strong></td>
<td>☐</td>
<td>☐</td>
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<tr>
<td><strong>Limitations:</strong></td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>- Utilized simplified model to make estimate, limiting the accuracy of findings</td>
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<tr>
<td>- Study relied on accuracy of available data</td>
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<tr>
<td>- Many assumptions were made about the susceptibility of recipient population due to limited data</td>
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<tr>
<td><strong>Result:</strong></td>
<td>☐</td>
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<tr>
<td>- The risk model gives a general description of transfusion risks in sub-Saharan Africa, though does not apply to all countries within the region</td>
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<tr>
<td>- Confirmed that the risks of transfusion-transmitted infections (HIV, HBV, or HCV) are substantially higher than those reported in high-income countries.</td>
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The risk of transfusion-transmitted infections in sub-Saharan Africa

Sudha Jayaraman, Zaid Chalabi, Pablo Perel, Carla Guerriero, and Ian Roberts

BACKGROUND: Blood transfusions carry the risk of transmitting infections. This risk has been studied in detail in high-income countries but not in sub-Saharan Africa. This study estimates the risks of acquiring human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) from a single unit of blood in sub-Saharan Africa.

STUDY DESIGN AND METHODS: A mathematical model was constructed to quantify transfusion risks across 45 sub-Saharan African countries using three components: the risk of a contaminated unit entering the blood supply, the risk that the unit will be given to a susceptible patient, and the risk that receipt of the unit will lead to infection in the recipient. Variables included prevalence of infection in donors, extent of blood testing, test sensitivity, and susceptibility of recipients. Data from the World Health Organization (WHO) African Region and a systematic review of the literature were used to parameterize the model. Uncertainty in the risk estimates was quantified using probabilistic sensitivity analysis.

RESULTS: The median overall risks of becoming infected with HIV, HBV, and HCV from a blood transfusion in sub-Saharan Africa were 1, 4.3, and 2.5 infections per 1000 units, respectively. If annual transfusion requirements projected by the WHO were met, transfusions alone would be responsible for 28,595 HBV infections, 16,625 HCV infections, and 6650 HIV infections every year. Sensitivity analysis suggests that the true risks may be even higher.

CONCLUSIONS: This study is the first to systematically quantify the risks of transfusion-transmitted infections across sub-Saharan Africa. Although the results are limited by the quality and quantity of available data, these may be the most reliable estimates at this time.
infections (TTIs) in these settings remains largely unknown.5

In sub-Saharan Africa, the risk of TTIs is thought to be substantial because of the high prevalence of these infections,6 the frequent use of paid or replacement donors,1,7-10 and incomplete screening coverage.1,4 In addition, TTIs could have major long-term social and economic consequences in this setting where blood transfusion recipients are mostly young people. Trauma predominantly affects young men, obstetric complications affect young women, and malaria is particularly important in children. Secondary infections could also occur if young infected patients, after recovery, pass on infection to sexual partners.

Several individual country reports of transfusion risks have sought to address this burden in isolated settings within sub-Saharan Africa. However, these reports do not reflect the risks across the continent. Currently, despite moves to massively increase funding to address blood safety in sub-Saharan Africa, the overall situation has not been evaluated systematically. In Central and South America, the Pan American Health Organization (PAHO) has used mathematical modeling to generate estimates of transfusion-associated risks.11 Based on this model, we sought to estimate the probability of acquiring one of three TTIs: HIV, HBV, and HCV, from a single unit of whole blood, across sub-Saharan Africa as a whole, using published data.

MATERIALS AND METHODS

Risk model
The probability of developing an infection after receiving 1 unit of blood in sub-Saharan Africa is the product of three independent risks: the risk of contamination of the blood supply, the risk of a susceptible patient receiving a contaminated unit, and the risk of acquiring an infection after receipt of a contaminated unit (i.e., the risk of seroconversion).

Contamination of the blood supply depends on the prevalence and incidence of infection in donors and the extent of screening and test accuracy in each country. Where less than 100% of donated blood is tested, the proportion of unscreened donations determines the exposure of the blood supply to contaminated units from prevalent infections (i.e., one minus screening coverage). If all donations are screened, then the sensitivity of the screening test becomes the key determinant of the risk that a tainted unit would enter the blood supply (i.e., one minus screening sensitivity). However, screening can miss infected patients who seroconvert during the window period of the screening test. Nevertheless, window period infections may be less important in sub-Saharan Africa where screening coverage and test sensitivity are likely to be suboptimal and thus more important contributing factors to the TTI risk. Therefore, in our model we considered only the prevalence of infection, screening coverage, and test sensitivity, to estimate the risk of blood supply contamination.

Second, the probability that a contaminated unit of blood will be given to a susceptible recipient depends on the prevalence of infection and the levels of immunity in the recipient population. Hospitalized patients in sub-Saharan Africa, who form the majority of the recipient population, tend to have higher rates of current or previous exposure to HIV, HBV, and HCV, and thus susceptibility, which was not included in the PAHO model, is relevant in this setting.12,13 Vaccine-mediated immunity is important but possible only for HBV. However, since HBV vaccine coverage is low in most of sub-Saharan Africa, we did not include it as a variable in our model.

Third, the probability of developing HIV, HBV, or HCV after receipt of a contaminated unit of blood has been established through follow-up studies of transfusion recipients who had received antibody-positive blood products in the 1980s. Rates of seroconversion were 90% for each infection in this population.14-16

Thus, we calculated the overall probability of acquiring a TTI after receipt of 1 unit of whole blood in each sub-Saharan African country as a weighted mean of the risks in screened and unscreened donations:

\[
\text{Overall risk (TTI)} = \text{Risk}_{\text{screened}} \times \text{Screening coverage} + \text{Risk}_{\text{unscreened}} \times \left(1 - \text{Screening coverage}\right),
\]

where the risk from unscreened donations is

\[
\text{Risk}_{\text{unscreened}} = \text{prevalence of TTI in donors} \times \text{proportion of susceptible patients} \times \text{infectivity risk}
\]

and the risk from screened donations is

\[
\text{Risk}_{\text{screened}} = \text{Risk}_{\text{unscreened}} \times \left(1 - \text{test sensitivity}\right).
\]

Systematic review
To parameterize our model, we conducted a systematic review of studies from 45 sub-Saharan countries published from 1998 to 2008 (Appendix S1, available as supporting information in the online version of this paper). Data on the prevalence of HIV, HBV, and HCV in the general population; each type of donor population (new, repeat, paid, replacement, or family); and the screening coverage in each country were retrieved. The search was limited to full journal publications and abstracts published in English and considered only data reported in adults. We searched MEDLINE, EMBASE, CAB Abstracts, and Global Health databases, as well as the World Health Organization (WHO) Web site. Study characteristics and results were reviewed for information regarding prevalence and screening patterns across countries, method descriptions, and general comments. The search included...
the following keywords: “Africa,” “blood donor,” “donor,” “screen,” “screening,” “prevalence,” “HIV,” “hepatitis B,” and “hepatitis C.” The following MeSH headings were exploded: “Africa South of the Sahara,” “prevalence,” and “blood donors.” The reference lists of identified articles were checked for other relevant studies. Studies that did not report data on the prevalence of HIV, HBV, and HCV or screening coverage information were excluded. Data were analyzed using computer software (Microsoft Office Excel, 2003, Microsoft Corp., Seattle, WA).

For many countries, there were very few sources of data to populate our model. Of the 45 countries in this region, no peer-reviewed publications were found in the systematic review for 28 countries. Through this systematic review, just one or two articles were identified for 12 of the 45 sub-Saharan African countries. In addition, since most of these studies were small, hospital-based, cross-sectional surveys, there are concerns for the precision, internal validity, and generalizability of these data. Sampling strategies and populations studied were not identical across articles. Others did not report details of their sampling method or types of donors. Furthermore, publication and reporting bias may have affected the quality of data from these hospital-based studies. The base case scenario for our model was conducted using the WHO’s 2007 African Region Report on the Safety of Blood Supply from the 2004 Global Database for Blood Safety survey, which had an overall 89% response rate with response rates also varying by infection. These data were also from national transfusion services, often from urban centers, and thus may not be generalizable to the rest of each country. However, since these are the best available data at this time, no study was excluded based on quality for this model. Sensitivity analysis was used to address some of these challenges to data quality. Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed for the conduct and reporting of the systematic review.17

Parameterization of the model
The prevalence of infection among donors in each country was determined as the mean of the prevalence in new and repeat donors as reported by the WHO.7 Where this information was not available, solely new donor or general population rates from our systematic review were used. For up to 25% of countries, the 2007 WHO African Region Report on the Safety of Blood Supply noted a lower prevalence of infection among donors than values reported in the published literature. In these cases, the mean of all reported values was used as the base case. Countries that reported 0% prevalence of any infection were assumed to have, at a minimum, risks equivalent to those reported in high-income countries. Appendix S2 (available as supporting information in the online version of this paper) summarizes the actual prevalence and susceptibility estimates used in our model.

Since country level data on screening coverage were not available from the literature, the WHO reports on screening rates across the African Region were assumed for the base case. According to the WHO, in 2004, a total of 1.48% of donated units were reportedly not screened for HIV, 5.47% for HBV, and 19.24% for HCV.7 The WHO does not indicate a breakdown of screening coverage by country and nor were these data available in the literature although there are many reports of financial constraints prohibiting countries from screening for HCV.18,19

The test sensitivities used in our deterministic model were based on the WHO’s rigorous evaluation of all commercially available tests for HIV, HBV, and HCV. We used the lowest test sensitivities reported in these evaluations (HIV, 95.3%; HBV, 96.3%; HCV, 97.1%).20-22 A recent quality control study of current screening tests at six African blood banks reported overall assay sensitivities of 98% for HIV, 75% for HBV, and 88% for HCV for the 13 enzyme immunoassays and eight simple/rapid tests evaluated against a reference laboratory.33 To take such reports into account in our estimates, we used a broad range of test sensitivities in our uncertainty analysis.

Some reports suggest that the prevalence of active TTIs in hospitalized patients is much higher than in the general population,12,13 but this information is not readily available at the country level in sub-Saharan Africa. We therefore estimated the current rates of infection in recipients by using general population or donor prevalence information. Finally, the infectivity risk for each infection was presumed to be 90% based on published reports.14-16

Probabilistic sensitivity analysis
Since there was substantial uncertainty in the values of variables used in our model and because the real values can vary within countries, we performed multivariate probabilistic sensitivity analyses on model variables using 1000 Monte Carlo simulations for each infection and for each sub-Saharan African country. Prevalence of HIV, HBV, and HCV infections among the donor populations, test sensitivity, screening coverage, infectivity risk, and proportion of susceptible patients for each of the sub-Saharan Africa countries in the model were varied simultaneously using the uniform distribution. A uniform distribution assumes that the value of a variable is located at any point between the bounds of the distribution with equal probability. Without prior information on the uncertainty in the values of the variables, for example from previous meta-analysis, uniform distributions present the most conservative form of characterizing uncertainty in each variable.24,25

The bounds of the distribution for the prevalence of infection in donors and recipients were base case ± 50%.
The base case values are summarized in Appendix S2. Because there are no confidence intervals reported in the data sources for these estimates and it is unclear how accurate the reported data are, the 50% boundary was chosen to define a large error margin in the estimates of prevalence and susceptibility risks. Our model used screening coverage rates reported by the WHO African Region and incorporated bounds of 50% to 100%, again to have a large margin of error based on the substantial variability in screening rates between countries. The bounds for infectivity risk were set at 80% to 100%. We used the test sensitivities for HIV, HBV, and HCV from the WHO’s assay reports for our model. However, because it is likely for test sensitivity to vary between and within countries based on the availability of testing equipment and the type of tests used,23 but the degree of this variability is unknown, we chose 75% to 100% as the boundaries around the test sensitivity estimates.

RESULTS

We identified 107 potential studies in the systematic review, of which 63 met the inclusion criteria. Of these, four described transfusion services across sub-Saharan Africa generally10,26-28 and three were cross-sectional survey reports from the WHO.1,7,29 Fifty-five articles reported prevalence data for individual countries (Appendix S1). The 2007 WHO African Region Report on the Safety of Blood Supply was identified through the search and included self-reported data from 41 countries but not from Nigeria, Niger, Liberia, Principe, Sao Tome, and Equatorial Guinea. No articles were identified through the systematic review for 28 countries.

Based on our deterministic model, which did not incorporate uncertainty, the median overall risk of acquiring a TTI in sub-Saharan Africa was estimated to be highest for HBV at 4.3 infections per 1000 donations, followed by HCV at 2.5 in 1000 and HIV at 1 in 1000 (Table 1). The risks of acquiring a TTI from screened and unscreened blood and the current modeled incidence of TTI from these transfusions are also reported in Table 1. While these specific estimates may be gross approximations, according to this model, the most likely infection to be acquired from a single unit of blood in sub-Saharan Africa is HBV, regardless of screening.

Annual volume of donations was publicly available for 16 countries.30 Using these data, we were able to estimate the annual number of TTIs per country, the ratio of infections to donations, and number of infections per 100,000 donations (Table 2). The WHO estimates that approximately 6.65 million units are required per year for this region’s population of 650 million although currently only 2 million units are collected and transfused.7 If this requirement was met, based on our model estimates, approximately 28,595 cases of HBV, 16,625 cases of HCV,
and 6650 cases of HIV could occur from contaminated transfusions, in sub-Saharan Africa, every year (Table 1). When we used probabilistic sensitivity analysis to determine the impact of the uncertainty in model variables on the risk estimates, the TTI risk across sub-Saharan Africa was higher than the base case scenario results outlined above. In the Monte Carlo simulation, the HIV and HCV risks most commonly ranged from 2 to 10 infections per 1000 units whereas the HBV risk ranged from 11 to 50 per 1000 units (Figs. 1-3), suggesting that our deterministic model may be underestimating the risks. HBV continued to be the most important TTI when uncertainty was addressed. Simulation runs for a sample country are shown in Figs. 4 through 6. Each of the Figs. 1 through 6 shows the histogram of the relevant risk estimate obtained from the Monte Carlo simulations and represents the uncertainty in these risks.

**DISCUSSION**

This is the first cross-country comparative study of the risks of acquiring HIV, HBV, or HCV from a blood transfusion in sub-Saharan Africa. Other studies have attempted to quantify the risks of acquiring HIV, HBV, or HCV from a single unit of blood in sub-Saharan Africa and cannot be used to make exact statements about the risks in the region. Our work in sub-Saharan Africa is based on the risk assessment in sub-Saharan Africa, which was the only region that used a model to generate individual risk estimates for each country. We sought to increase the accuracy of our findings by using the PAHO model, which is the basis of our model. Our model conservatively estimates the risk of acquiring HIV, HBV, or HCV from a single unit of blood in sub-Saharan Africa and is derived from our model.

**TABLE 2. Estimates of TTIs and TTI to donation ratios in 16 countries based on our model and all publicly available data**

<table>
<thead>
<tr>
<th>Countries</th>
<th>Reported number of donations per year</th>
<th>Estimated transfusion transmitted HIV infections per year, n (range)</th>
<th>TTI-HIV to annual donation, ratio (range)</th>
<th>Estimated transfusion transmitted HBV infections per year, n (range)</th>
<th>TTI-HBV to annual donation, ratio (range)</th>
<th>Estimated transfusion transmitted HCV infections per year, n (range)</th>
<th>TTI-HCV to annual donation, ratio (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botswana</td>
<td>12,000</td>
<td>154 (39-397)</td>
<td>1:78 (35-311)</td>
<td>1:78 (35-311)</td>
<td>1:78 (35-311)</td>
<td>1:78 (35-311)</td>
<td>1:78 (35-311)</td>
</tr>
<tr>
<td>Cameroon</td>
<td>69 (25-228)</td>
<td>1,362 (110-989)</td>
<td>276 (101-910)</td>
<td>276 (101-910)</td>
<td>276 (101-910)</td>
<td>276 (101-910)</td>
<td>276 (101-910)</td>
</tr>
<tr>
<td>Congo</td>
<td>21,000</td>
<td>1,313 (58-2,575)</td>
<td>76 (19-171)</td>
<td>76 (19-171)</td>
<td>76 (19-171)</td>
<td>76 (19-171)</td>
<td>76 (19-171)</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>80,000 (16-146)</td>
<td>11,321 (58-934)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
</tr>
<tr>
<td>DRC</td>
<td>100,000</td>
<td>1,177 (234-1,109)</td>
<td>129 (47-427)</td>
<td>129 (47-427)</td>
<td>129 (47-427)</td>
<td>129 (47-427)</td>
<td>129 (47-427)</td>
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<tr>
<td>Ethiopia</td>
<td>40,000</td>
<td>1,540 (134-2,130)</td>
<td>184 (78-698)</td>
<td>184 (78-698)</td>
<td>184 (78-698)</td>
<td>184 (78-698)</td>
<td>184 (78-698)</td>
</tr>
<tr>
<td>Gabon</td>
<td>15,000</td>
<td>1,433 (137-1,319)</td>
<td>303 (76-682)</td>
<td>303 (76-682)</td>
<td>303 (76-682)</td>
<td>303 (76-682)</td>
<td>303 (76-682)</td>
</tr>
<tr>
<td>Ghana</td>
<td>60,000</td>
<td>1,386 (309-1,736)</td>
<td>112 (36-32)</td>
<td>112 (36-32)</td>
<td>112 (36-32)</td>
<td>112 (36-32)</td>
<td>112 (36-32)</td>
</tr>
<tr>
<td>Guinea</td>
<td>20,000</td>
<td>1,932 (420-3,176)</td>
<td>106 (29-238)</td>
<td>106 (29-238)</td>
<td>106 (29-238)</td>
<td>106 (29-238)</td>
<td>106 (29-238)</td>
</tr>
<tr>
<td>Kenya</td>
<td>50,000</td>
<td>1,413 (135-1,218)</td>
<td>241 (82-739)</td>
<td>241 (82-739)</td>
<td>241 (82-739)</td>
<td>241 (82-739)</td>
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<tr>
<td>Malawi</td>
<td>25,000</td>
<td>1,430 (43-385)</td>
<td>771 (260-3,236)</td>
<td>771 (260-3,236)</td>
<td>771 (260-3,236)</td>
<td>771 (260-3,236)</td>
<td>771 (260-3,236)</td>
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<tr>
<td>Mali</td>
<td>25,000</td>
<td>1,125 (54-943)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
<td>81 (20-182)</td>
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<tr>
<td>South Africa 850,000</td>
<td>60 (22-202)</td>
<td>1,147 (420-3,781)</td>
<td>123 (31-277)</td>
<td>123 (31-277)</td>
<td>123 (31-277)</td>
<td>123 (31-277)</td>
<td>123 (31-277)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>130,000</td>
<td>1,691 (275-2,479)</td>
<td>416 (131-340)</td>
<td>416 (131-340)</td>
<td>416 (131-340)</td>
<td>416 (131-340)</td>
<td>416 (131-340)</td>
</tr>
<tr>
<td>Uganda</td>
<td>140,000</td>
<td>1,864 (383-3,447)</td>
<td>116 (29-261)</td>
<td>116 (29-261)</td>
<td>116 (29-261)</td>
<td>116 (29-261)</td>
<td>116 (29-261)</td>
</tr>
</tbody>
</table>

*Estimates are rough approximations based on publicly available data and do not indicate exact risks in each country.
† Risk based on general population prevalence of HIV instead of donor prevalence.
‡ Data not available.

We determined the impact of the uncertainty in model variables on the risk estimates by using the Monte Carlo simulation. In the base case scenario, the HIV risk in sub-Saharan Africa is higher than the base case scenario results outlined above. In the Monte Carlo simulation, the HIV and HCV risks most commonly ranged from 2 to 10 infections per 1000 units whereas the HBV risk ranged from 11 to 50 per 1000 units (Figs. 1-3), suggesting that our deterministic model may be underestimating the risks. HBV continued to be the most important TTI when uncertainty was addressed. Simulation runs for a sample country are shown in Figs. 4 through 6. Each of the Figs. 1 through 6 shows the histogram of the relevant risk estimate obtained from the Monte Carlo simulations and represents the uncertainty in these risks.
risk estimates. Nevertheless, based on the available data and despite the importance of country-specific risk factors, our model generates the most valid global risk assessments currently available in sub-Saharan Africa.

Our study has many limitations. It used a simplified model to make its estimates, which limits the accuracy of the findings. In this model, imperfect screening coverage and test sensitivity were assumed to make greater contributions to TTI risk in the African setting than residual risk from incidental infections occurring in the window period. However, Candotti and colleagues\textsuperscript{33} demonstrated the importance of residual risk in this region when they reported the high risk of HIV or HCV transmission through transfusions in Ghana despite adequate testing for anti-HIV, p24 antigen, and anti-HCV. They estimated the residual risk of HIV, HCV, and HBV in Ghana to be 1 in 2578, 1 in 1450, and 1 in 326. Thus, the risk of infection from seronegative window period donations can be substantial. Future versions of our model may need to incorporate this factor to describe the transfusion risks more accurately in settings with a high incidence of infections. In addition, our model did not incorporate the probability of laboratory or clinical errors,\textsuperscript{34} prevalence of viral variants that are not detected by testing, increasing use of component separation,\textsuperscript{30} and the proportion of asymptomatic chronic carriers in the population. These factors may also need to be considered in future models of transfusion risks.

Our study relied on the accuracy of limited available data. In order to estimate the prevalence of infection in donors accurately and to account for the lower rates of infection in repeat donors, our model used an average of the infection prevalence in first-time and repeat donors in each country.\textsuperscript{10,35,36} However, this assumption may lead to overestimates of TTI risks in settings where repeat donors make up a high proportion of all donors. For example, in South Africa, where repeat donors supplied 83% of units in 2001 through 2002, only 0.02% of donations from these donors were HIV positive compared to 0.59% of donations from first-time donors.\textsuperscript{37} Thus, our model may be less reliable in countries within sub-Saharan Africa that have greater proportions of repeat versus first-time donors. Voluntary, paid, and replacement donors are also known to be higher risk than repeat donors; however, these populations were not included in our study. Furthermore, there is a substantial difference in prevalence of infection in donors compared to the general public, which may have affected the validity of our estimates (Appendix S2). Additionally, “test-seeking behavior” by the public, that is, use of blood donation centers as testing facilities to avoid the potential stigma of attending voluntary counseling and testing centers, could artificially inflate the prevalence estimates reported in

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**Fig. 1. Distribution of HIV risk from blood transfusions across sub-Saharan Africa (n = 39 countries), based on 1000 simulations per country.**

**Fig. 2. Distribution of HBV risk from blood transfusions across sub-Saharan Africa (n = 39 countries), based on 1000 simulations per country.**

**Fig. 3. Distribution of HCV risk from blood transfusions across sub-Saharan Africa (n = 36 countries), based on 1000 simulations per country.**
donors. However, this behavior is probably rare since the majority of transfusions in Africa are collected through small-volume hospitals and probably take place in emergency situations from paid or family donors.\textsuperscript{30} Country-level data on screening coverage and test accuracy were not available in the literature for this region. Our model applied the overall screening rates and ideal sensitivities for rapid tests, as reported by the WHO, across sub-Saharan Africa, to project the prevalence of TTIs. However, differences in provision of transfusion services mean that screening rates and tests may vary within and between countries.\textsuperscript{30} Screening coverage in a centralized setting such as exists in Uganda or Zimbabwe may be much higher than that in many hospital-based systems in sub-Saharan Africa.\textsuperscript{30} The practice of predonation testing as one method of improving the quality of transfusions has been used in some settings, although it is not clear if this practice is common or if it has a substantial impact on TTI risks.\textsuperscript{3} In addition, even in countries that may have perfect or near perfect screening, the coverage rates and tests usage in the capital areas are not likely to reflect intracountry differences such as the situations in the regional or district settings. Low-volume hospitals away from major cities may be more likely to have supply shortages and be more likely to use rapid tests with lower sensitivities.\textsuperscript{10} The use of less sensitive screening tests such as simple and rapid tests are reported to be common in sub-Saharan Africa due to the cost of testing, although no estimates of the magnitude of this problem exist in the literature. In our model, we used the test sensitivities described by the WHO but attempted to account for the variations in test sensitivity across the continent by using broad ranges in our uncertainty analysis. Furthermore, we made many assumptions about the susceptibility of the recipient population because little data exist on the prevalence of infection in transfusion recipients. One important assumption was that general population or new donor prevalence rates were reasonable proxies for infection rates in hospitalized patients. However, many reports suggest that prevalence of HIV, HBV, and HCV in hospitalized patients is higher than in the general population, and thus our model may have overestimated the risk of TTIs.\textsuperscript{12,13}

Finally, in our uncertainty analysis, we addressed “first-order” uncertainty, which is uncertainty in the values of the model variables. “Second-order” uncertainty or uncertainty in the lower and upper bounds of the uniform distribution could be relevant as well but was not incorporated in our analysis because there is not sufficient information to do so at this time. However, such analyses may be incorporated in future models using Bayesian approaches, particularly as new data are reported. Based on our current assumptions, the deterministic model...
could result in underestimates, although the magnitude of this underestimation will not be evident without conducting Bayesian analysis.

As a result of many of these limitations, although our model describes the overall picture of transfusion risks in sub-Saharan Africa, it will not apply to all countries in this region. For example, the risks of transfusions in the Republic of South Africa clearly do not represent the risks across the continent. The South African National Blood Service has substantially reduced the risks of transfusions through the use of highly sensitive nucleic acid testing.38,39 Our model, which does not take such detailed screening practices into account, would overestimate the risks in that country. Thus, our model may be less accurate in countries with rigorous blood safety practices, although such countries are likely to be the exception rather than the rule in sub-Saharan Africa.

Nevertheless, in countries were the data quality is reasonable, our model is likely to be fairly accurate and could have potential for use as a tool for periodic monitoring and evaluation of blood safety initiatives. The United States President’s Emergency Plan for AIDS Relief (PEPFAR), starting in 2004, has allocated $1.2 billion in funding to 12 African “focus” countries to improve transfusion practices through support for universal testing, educational opportunities for clinicians, and evaluations of transfusion practices.40 This initiative has the potential to vastly improve the opportunities for clinicians, and evaluations of transfusion practices.40 This initiative has the potential to vastly improve the understanding of transfusion risks in the African setting. Our model, if populated with high-quality data from PEPFAR countries, could be used to assess the burden of TTIs in sub-Saharan Africa more accurately.

Many key areas exist for future research. Barriers to screening and the impact of direct and indirect costs to individual countries need to be closely evaluated. The costs and cost-effectiveness of preventing and treating TTIs need to be compared. In addition, the factors that affect TTI risk, such as epidemic stage, may be different for each infection and may vary between countries, and the increase or decrease in incidence rates of each infection may contribute to the residual risk. Country-level case studies could shed more light on the variations in risks and costs of TTIs.

Blood transfusions are an essential part of clinical care. Our study confirms that the risks of TTIs in sub-Saharan Africa are substantially higher than those reported in high-income countries. Although our estimates are based on country-level data and limited published reports from individual institutions in sub-Saharan Africa, our results reiterate the need for increased support from the global community to address transfusion-associated risks in this region.

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CONFLICT OF INTEREST

Authors have no conflicts of interest.

REFERENCES


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Results of systematic review.
Appendix S2. Prevalence and susceptibility estimates used in model, based on WHO data and systematic review.

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