Gay and bisexual men should be allowed to donate blood. An agent-based analysis of HIV incidence and blood collections when revoking the MSM deferral policy.

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Abstract

Background

Since 2008, there has been a chronic shortfall of transfusable blood products, which delays critical treatments for patients and inflates the financial burden of transfusion procedures. Alleviating this blood shortfall is a national health priority. This statistical simulation determines the efficacy of allowing men who have sex with men (MSM) to donate blood as a strategy for reducing the blood shortfall by studying the effects of the MSM deferral policy on HIV incidence and blood product collections.

Methods and Materials

An agent-based model was developed to simulate blood collection and transfusion behavior in the United States. The model can either exclude MSM from donation or allow MSM to donate, and calculates the HIV incidence in both cases. The magnitude of the difference in RBC collections, platelet collections, and HIV incidence between models that enforce and lack an MSM exclusion policy is determined by regression analysis.

Results

With a 95% confidence interval, models where MSM were not excluded from blood donation saw an increased HIV incidence of 0.032 ± 0.018 $\frac{\text{infections}}{100{,}000 \times \text{year}}$ ($0.269 \pm 0.151\%$), which entails 45 to 160 additional HIV infections in the United States per year, while the volume of red blood cell and platelet collections increased by 1.7 ± 0.10 million units per year($10.1 \pm 0.55\%$) and 460 ± 25 thousand units per year($10.0 \pm 0.49\%$), respectively. The models excluding MSM from donation predict a real-world HIV infection rate via the transfusion route of approximately 55 infections in the United States per year, which falls into the bounds of observed values.

Conclusion

The additional volume of blood products collected from revoking the MSM deferral policy can treat nearly 150,000 trauma ward patients or the severe anemia of 250,000 cancer sufferers. Overall, the quantity of new available treatments dwarfs the increase in the HIV incidence rate; suggesting that the MSM deferral policy likely harms more patients than it safeguards.

Key Words: Blood Management, MSM, HIV, Deferrals, Blood Donation, Controversy

Introduction

Blood banks have the herculean task of collecting and distributing millions of liters of blood donations every year, and ensuring that every blood donation is safe.[1,2] This undertaking is complicated by a growing demand for blood transfusions and a falling rate of blood donation.[2] The AABB, formerly the American Association of Blood Banks, estimates that the volume of blood products collected for transfusion in the United States has decreased by 21.4% from 2008 to 2013, the last year that data is publicly available.[2–4] A recent meta analysis concludes that this trend has continued at least through 2015.[5] With the lack of progress in attracting donations, the only reasonable recourse to remedy acute blood shortages is to exercise increasingly strict stewardship over existing blood stockpiles.[6] At times of scarcity, many patients can have operations and treatments delayed, while hospitals inventories can be limited to less than a day's supply of blood.[7,8]

With the prospect of a chronic shortfall of blood donations, unorthodox options should be considered to alleviate the risk to public health. A simple solution is to allow a larger portion of the population to donate blood products. To ensure that blood stockpiles are not contaminated by infectious diseases, the United States Food and Drug Administration sets standards on who can and cannot donate blood. The FDA's blood donation criteria excludes 62% of the U.S. population from donating blood.[9]

The policy this study focuses on is the 1983 mandate, made in response to the AIDS pandemic, to exclude all men who have had sex with men (MSM) after 1977 from blood donation.[10] At the time, there were no accurate tests to indicate the presence of the HIV virus in a blood sample Hence, the FDA banned several at-risk groups, including MSM, from donating blood to safeguard transfusion recipients. Almost 15,000 individuals contracted AIDS from blood transfusions before accurate testing became available in 1985.[11] In 2016, this policy was relaxed to exclude only men who have had sex with men in the past year. But this still excludes a large majority of MSM from donating blood products, including men who are in low-risk, monogamous relationships.[10] The median MSM reports four sexual partners per year, essentially rendering the post-2016 policy a blanket ban on all MSM.[12]

Allowing gay and bisexual men to donate would immediately enable an additional 2-5% of the population to donate blood; bolstering existing blood stocks.[13,14] MSM represent 67% of HIV diagnoses per year, and the FDA has argued that allowing MM to donate blood could potentially induce a public health risk by exposing blood recipients to an increased risk of HIV infection.[15] On the other hand, every blood donation is tested with modern HIV testing regimes that have an immensely high specificity, and, in principle, can determine the presence of the HIV virus with high accuracy.[16] This would allow blood banks to remove any contaminated blood from the general supply. However, HIV infections have an approximately 50-day "window period" occurring immediately after infection where the probability that the virus will be detected even with modern HIV tests is small.[17] Even after the window period, the

probability of a false negative never quite reaches zero and asymptotically approaches a value between 1 in 10,000 and 1 in 100,000.[22] Revoking the MSM ban would immediately result in an increase to the population of eligible donors, but would put more recipients of blood transfusions at risk of HIV infection.

The present study was designed to quantify the increased risk of HIV infection in transfusion recipient and increase in the volume of blood collected if MSM were allowed to donate regardless of recent sexual contact. The key question is how many more people can we treat compared to how many people contract HIV.

Materials and methods

An agent-based model (ABM) was developed to evaluate the potential risks of allowing MSM to donate blood. The agents were designed to reflect the donation and transfuion rates illustrated in the 2013 AABB Blood Survey. Each model contains 200,000 agents and each agent starts with several parameters determining the conditions under which it donates or is forbidden from donating blood, such as its HIV status.

To accurately reflect the U.S. population, 2 - 5% of agents are MSM, and the proportion of agents who contract HIV and donate blood are designed to mimic the data provided by the Centers for Disease Control (CDC) and the 2013 AABB Blood Survey, respectively.[2,13,14] Agents that recognize that they are HIV-positive will exclude themselves from donation without exception, but a portion of HIV-infected agents are unaware of their HIV infection, and willingly donate. Following CDC estimates, approximately 15% of HIV-infected persons are unaware of their HIV status, and an equal proportion of HIV sufferers in the model are not aware of their infection.

When an HIV-positive agent donates blood, the donation is accepted into the blood supply if an HIV test on their blood results in a false negative. The probability of a false negative in the window period is shown in Fig. 2.

A monte-carlo method using a pseudo-random Mersenne Twister determines the results of the test, either true positive or false negative, and thus whether the blood is accepted into or rejected from the blood supply.

To account for the uncertainty in estimating the proportion of the population defined as MSM, the proportion of MSM agents in each model are sampled from a uniform distribution ranging from 0.02 to 0.05. This allows the study to control for this quantity across our regressions without having to make a precise estimation as to the true proportion of the population that is MSM. Likewise, while the volume of plasma and platelets transfused is well estimated in the 2013 AABB Blood Survey Report, the number of recipients of these blood products is not. To control for this confounding variable, the average volume of plasma and platelets transfused per recipient is allowed to vary between 1 and 4 $\frac{\text{Units}}{\text{Recipient}}$ inclusive in the ABM.

Each model is run over the course of a year, with a time step of one day. At each time step, monte-carlo methods are used to govern which agents contract HIV, donate blood, and receive blood. At every time step, each agent can

execute a whole blood donation, plateletpheresis, or a double red donation and also request a transfusion of red blood cells, platelets, and/or plasma. The model was completed 2,104 times. 67% of model runs were a control, with all MSM excluded from donation, while 33% of model runs allowed MSM to donate if they lacked a positive HIV test result in the past. The number of HIV transmissions from transfusions, volume of blood products collected, and the number of donors with HIV are then extracted from each model run to use as dependent variables in regression models.

A multitude of potentially significant independent variables are extracted at the conclusion of each model execution: the average volume of platelets transfused per recipient and average volume of plasma transfused per recipient, the proportion of agents that are MSM, and a dummy variable representing whether that model excluded MSM from donation. An ordinary least squares multiple linear regression with heteroscedasticity-consistent standard errors is used to determine the correlation of increased HIV incidence and the above-mentioned independent variables, with a p-value > 0.05 being considered insignificant and removed from the model to avoid overfitting. The coefficients of these regressions determines the prediction of the net increase in HIV infections and volume of blood product collections if the MSM exclusion policy were revoked.

The proportion of HIV infected donations that occurred during the window period and the quantity of HIV transmissions via transfusions per infected donation are also calculated. The python code for the ABM and a link to a detailed description of the model is provided in the Appendix.

Results

Table 1 illustrates that models excluding MSM have a 65% lower HIV infection rate from transfusions than models that allow MSM to donate.

The multiple linear regression for HIV incidence via transfusion indicates that allowing MSM to donate blood is significantly correlated with a higher HIV incidence even after controlling for the number of agents who receive platelet transfusions, receive plasma transfusions, and are MSM (see Table 2).

The number of agents that are MSM and the number that receive plasma transfusions were not significantly correlated with HIV incidence. It's important to note that the coefficient of determination is incredibly small, R^2=0.010, which is likely due to the huge quantity of random variate in each agent based model. Since the fit is so poor, the coefficient for the exclusion variable has a large confidence interval. However, the entirety of the 95% confidence interval is greater than 0, still indicating a positive correlation between allowing MSM to donate and HIV incidence. The statistics for the regression model specify a 95% confidence interval of 0.014 to 0.050 $\frac{\text{infections}}{100{,}000 \times \text{year}}$ for the exclusion coefficient.

Models that excluded MSM collected approximately 10% fewer blood products on average than models that allow MSM to donate (see Table 3).

The number of agents that receive platelet and plasma transfusions is independent of blood product collections, and they are excluded from the multiple linear regressions for the volume of RBC and platelets collected. The quantity of blood products collected is positively correlated with allowing MSM to donate as shown in Table 4. Doing so is expected to increase the volume of RBC and platelet collections by 553 $\frac{\text{units}}{100{,}000}$ and 144 $\frac{\text{units}}{100{,}000}$, respectively. The 95% confidence interval specifies a range of 553 $\pm$ 29 and 144 $\pm$ 8 $\frac{\text{units}}{100{,}000}$ for RBC and platelet collections, respectively.

The number of days infected with HIV for donors whose blood test resulted in a false negative and whose blood was incorporated into the blood supply is shown in Fig. 3.

Of HIV-contaminated donations that make it into the blood supply, 76.3% occur during the 50-day window period. The MSM exclusion policy has little effect on the distribution.

A single contaminated donation has the potential to infect up to three recipients through the three blood products collected from a single donation: red blood cells, platelets, and plasma, all of which can each be transfused into a different recipient. Averaged across all models, there are 1.115 $\frac{\text{HIV Infections}}{\text{Infected Donation}}$. The number of transmissions per infected donation is dependent upon the donor's blood type as depicted in Table 5.

Since AB- is such a rare blood type, only a single agent donated HIV-infected AB- blood in all 2,104 model runs, and no agent received any of the blood products from that donation. With more model executions, the AB- value in Table 5 will be nonzero, but likely less than the value associated with AB+.

Discussion

Scaled to the population of the United States, allowing MSM to donate blood would increase the volume of red blood cells and platelets collected by 1.7 million and 0.45 million $\frac{\text{units}}{\text{year}}$, respectively. That volume of red blood cells would provide treatment for 280,000 cancer patients with severe anemia or 150,000 trauma ward victims and the additional platelets would provide 250,000 transfusions to acute myeloid leukemia sufferers.[3, 22–24] It is difficult to weigh the costs and benefits of revoking the MSM exclusion policy since so little data is available on the human and material costs of blood shortages, but this study indicates that the increase in the quantity of available treatments clearly dwarfs the expected quantity of HIV infections by three orders of magnitude. The MSM deferral policy likely harms more patients than it safeguards.

In addition, RBC and platelet transfusions cost patients approximately $350 and $530 per unit transfused, respectively.[25] This imposes a large financial burden on transfusion recipients, either directly through out-of-pocket payments or indirectly for higher insurance premiums. Increasing the supply of transfusable blood would reduce the

price of transfusions and ease this financial risk to families.

As shown in Table 1, the average number of infections per 100,000 in the models that exclude MSM is 0.0171 infections per 100,000. This implies that, when scaled to the population of the United States, 55 people are infected with HIV by transfusions in the U.S. every year. This is larger than the CDC estimate of 11 $\frac{\text{Infections}}{year}$. However, the CDC estimate has a significant variance stemming from its back-of-the-envelope calculation of assuming 1 in 1.5 million blood units is infected, and the estimate is admittedly conservative. Nevertheless, it is a reasonable lower bound. From 2011 to 2016, an average of 88 adults per year were diagnosed with HIV from a source other than injection drug use and sexual contact, which serves as an upper bound on the actual number of HIV-infected transfusions per year.[21] This study's prediction of 55 infections per year via the transfusion route lies nearly halfway between the lower bound of 11 and the upper bound of 88 and can be considered a reasonable estimate.

The mean estimate indicates that revoking the MSM exclusion policy would increase the number of infections per 100,000 to 0.0487 $\frac{\text{Infections}}{100{,}000}$. This entails that the U.S. would experience 156 $\frac{\text{Infections}}{year}$ if MSM could donate. This increase of 101 infections would constitute 0.2607% of the 38,739 HIV diagnoses made in the United States in 2017.[15] The 95% confidence interval suggests 45 to 160 additional HIV infections in the United States per year.

A cursory inspection of Fig[?] indicates that a majority (71%) of HIV-infected donations occur within 30 days of infection, and suggests that another possible policy might be to exclude men who have had sex with men in the past month instead of a full year. Given the conservative attitude of government agencies, it may be easier to adopt this policy in lieu of allowing all MSM to donate. Doing so would pose even less risk than a full revocation of the MSM deferral policy, which this analysis suggests is already tiny relative to the overall HIV incidence rate, but would also result in fewer blood product collections that a full revocation.

Author summary

Robert Gottesman has a B.A. in Physics from Reed College, and specializes in public policy analysis.

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I would like to thank my friend and former coworker Eric Shierman, who helped me to interpret the results of this study and whose constant encouragement and wisdom is a great privilege.

I'd like to extend an honorable mention to the man who I met in a coffee shop in Portland, Oregon, who couldn't donate blood despite being perfectly healthy, and turned me onto this subject in the first place.

Appendix

A walk through of this model is presented here:

https://github.com/Robdei/Blood-Donation-Simulation/blob/master/SimulationDescription.pdf

See my GitHub to view the python code for this model:

https://github.com/Robdei/Blood-Donation-Simulation/blob/master/BloodDonationSimulation.py

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Tables

Table 1. Average and standard deviation of HIV infections from transfusions per 100,000 in models by MSM exclusion policy.

Model exclusion policy	Average of infections (per 100,000)	SD of infections (per 100,000)
Exclude MSM	0.0171	0.1282
Include MSM	0.0488	0.2252

Table 2. Coefficients, standard error, and p-value of the multiple linear regression of HIV incidence via transfusion onto the independent variables.

	Dependent variable: HIV Incidence from Transfusions		
Variable	Model 1	Model 2	Model 3
Exclusion‡	0.0316†	0.0316†	0.0317†
	(0.009)	(0.009)	(0.009)
$\frac{\text{Platelets}}{\text{Recipient}}$	-0.0077†	-0.0077†	-0.0077†
	(0.003)	(0.003)	(0.003)
$\frac{\text{Plasma}}{\text{Recipient}}$		-0.0027	-0.0027
		(0.003)	(0.003)
MSM Proportion			-8.8e-07
			(0.00)
Intercept	0.0359†	0.0429†	0.0491†
	(0.009)	(0.013)	(0.020)
Adj. R^2	0.010	0.009	0.009

$^{*}p < 0.05$, $^{\dagger}p < 0.01$, ‡Reference is to exclude MSM
(Standard errors in parentheses)

Table 3. Average volume (in units per 100,000) of red blood cells and platelets collected in models that exclude and include MSM

Model exclusion policy	RBC volume collected ($\frac{\text{units}}{100,000}$)	Platelet volume collected ($\frac{\text{units}}{100,000}$)
Exclude MSM	5,472	1,434
Include MSM	6,031	1,580

Table 4. Coefficients, standard error, and p-value of the multiple linear regression of RBC collected and platelets collected onto the exclusion dummy and proportion of agents that are MSM.

	Dependent variable	
Variable	RBC collected ($\frac{Units}{100{,}000}$)	Platelets collected ($\frac{Units}{100{,}000}$)
Exclusion†	553.1	144.1
	(15.02)	(3.977)
MSM Proportion	0.1146	0.0299
	(0.014)	(0.004)
Intercept	4673	1225
	(114.6)	(30.12)
Adj. R^2	0.341	0.336

*All variables have $p < 0.01$, †Reference is to exclude MSM
(Standard errors in parentheses)

Table 5. Average quantity of HIV transmissions per contaminated donation by blood type.

Blood type of infected donation	HIV infections per false negative
O-	1.86
A-	1.75
A+	1.64
O+	1.48
B-	1.00
B+	0.400
AB+	0.286
AB-	0.000

Figures

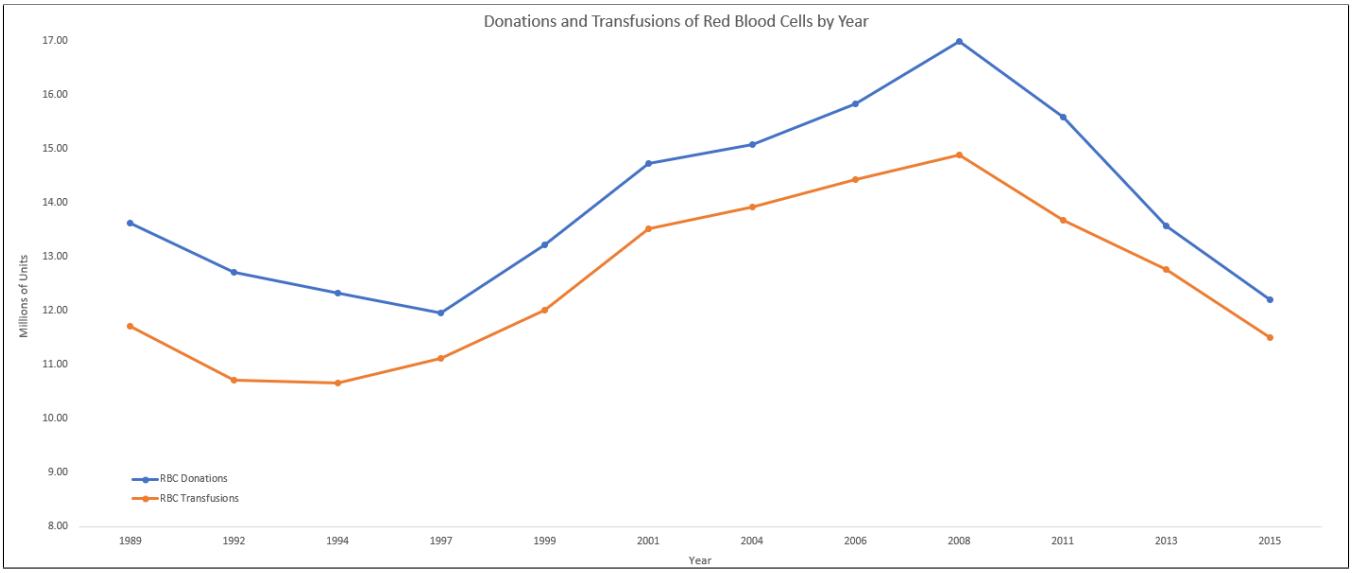

Fig 1. Volume of red blood cells (RBC) and whole blood (WB) donated and transfused in the United States from 1989 to 2015.[2,5] The volume of blood products collected has been declining since 2008.

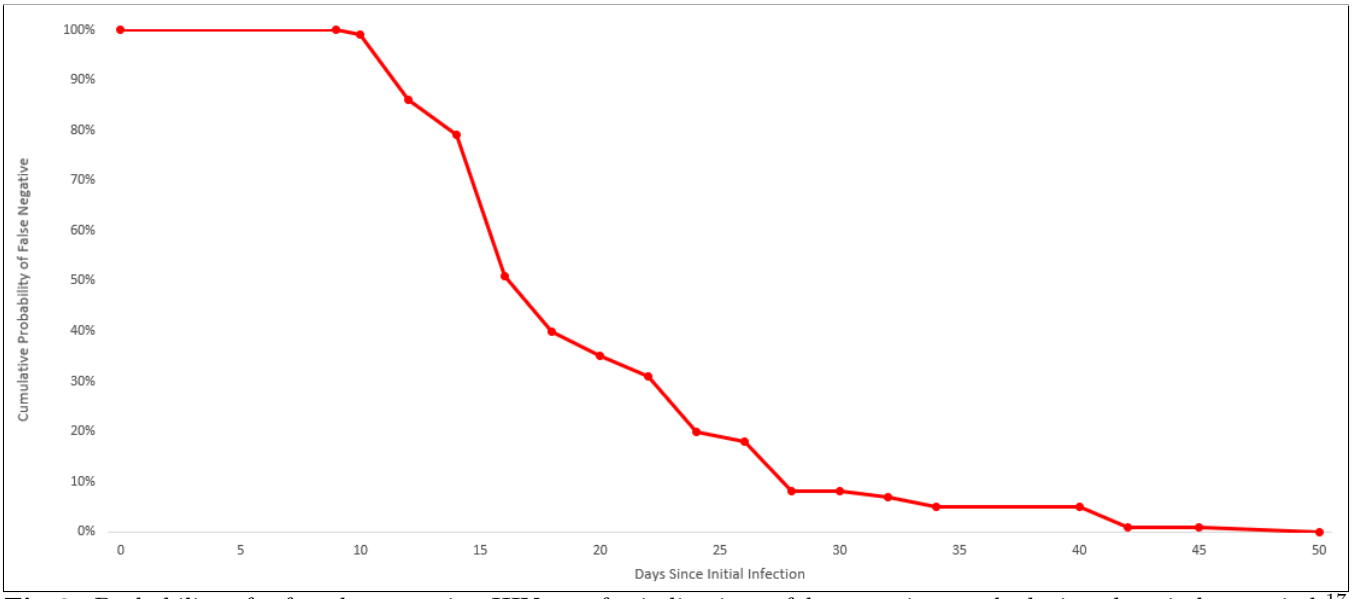

Fig 2. Probability of a fourth-generation HIV test for indicating a false negative result during the window period.[17]

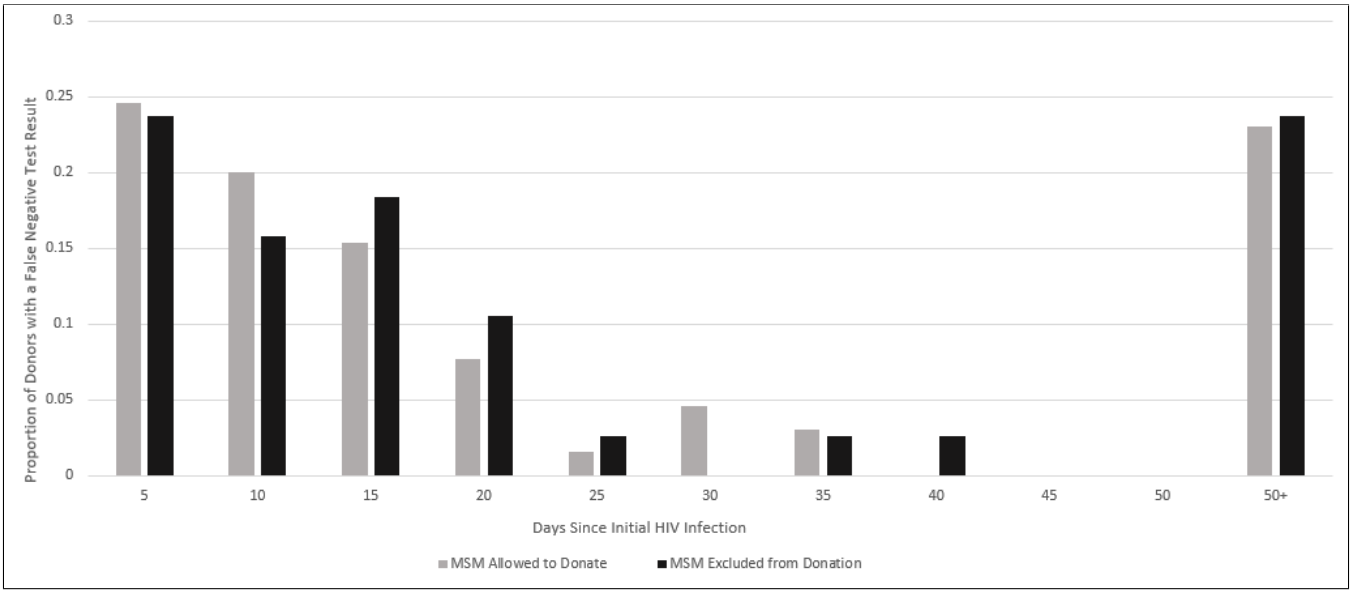

Fig 3. Histogram of the proportion of blood donations that result in a false negative test result as a function of days since initial infection.

Figure Captions

Fig 1. Volume of red blood cells (RBC) and whole blood (WB) donated and transfused in the United States from 1989 to 2015.[2,5] The AABB estimates that the number of blood donations has been declining since 2008. The volume of RBC collections in 2015 is less than any time since 1999, and the net difference between donations and transfusions is smaller in 2015 than at any other time since at least 1989.

Fig 2. Probability of a fourth-generation HIV test for indicating a false negative result during the window period.[17] HIV tests have an incredibly high accuracy if used more than 50 days after exposure, but there is a relatively high chance of a false reading if used before that time. The above chart is used to determine the probability that an HIV-infected agent's blood donation will be collected.

Fig 3. Histogram of the proportion of blood donations that result in a false negative test result as a function of days since initial infection. The occasions where HIV-contaminated blood made it into the general blood supply was compiled across every model and the number of days since HIV exposure were calculated. 76.3% of HIV-infected donations that make it into the blood supply occurred during the 50-day window period.