MSM and blood donation: shifting to individualized risk assessment

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Deferring donors at higher risk for transfusion transmissible infections is an important part of ensuring blood safety. The deferral for gay, bisexual, and other men who have sex with men (gbMSM) was implemented in the 1980s in many countries, since they were identified as a high-risk group for AIDS/HIV. With the introduction of increasingly sensitive HIV antibody testing, augmented by nucleic acid testing, the window period for HIV infection—when a donor may be infectious but have negative test results—has shrunk dramatically. In Canada, this has led to progressively shorter deferral periods for gbMSM, decreasing from a permanent deferral for sex with another male since 1977 to a 5-year, 12-month, and eventually 3-month deferral period. These time-based deferrals maintained safety; however, they are seen as stigmatizing by many and still result in the deferral of sexually active gbMSM. More recently, several countries have moved to a donor screening approach based on assessing sexual risk behaviors in all donors. This article outlines research supporting changes in policy, current eligibility screening policies in several countries, and preliminary results postimplementation of new eligibility policies in Canada in September 2022.

LEARNING OBJECTIVES

- Explain the evolution of deferral policies for high-risk sexual behaviors over time
- Compare time-based deferrals for gay, bisexual, and other men who have sex with men with sexual risk–based policies for all donors
- Identify methods of evaluating the safety of policy changes postimplementation

CLINICAL CASE

Walter, a married gay man, and his husband, Bill, who have been in a mutually exclusive sexual relationship for many years, hear an urgent appeal for blood donors on the radio and decide to overcome their fear of needles and make an appointment to donate blood. While waiting to be seen by the screener at the Toronto fixed site, they see their neighbor, Casanova, who is always boasting about his success finding new lady partners on Tinder.

Who do you think will be eligible to donate?

Introduction

Blood safety depends on donor selection, testing, and for some components, pathogen reduction. In many countries, including the US, Canada, the UK, and Australia, blood establishments performing collection, testing, and distribution are highly regulated, and a standardized donor health questionnaire (DHQ) and criteria manual are used. The DHQ questions divide donors into standard and higher risk groups, with the higher risk group undergoing additional testing or, more often, deferring from donation for a period of time or indefinitely. If testing is unavailable for an infectious agent in a nonpathogen-reduced component, donor selection is vital to reduce risk. Once testing is developed, the importance of donor selection decreases.

Introduction of criteria for gay, bisexual, and other men who have sex with men

Donor criteria for gay, bisexual, and other men who have sex with men (gbMSM) were introduced in the 1980s, when it was recognized that AIDS could be transmitted by blood.[1,2] Initially, donors were provided written materials instructing them to self-defer if they fell into risk categories, including male homosexuals with multiple partners. These policies are thought to have resulted in an approximately 90% reduction in the risk of AIDS/HIV transfusion

Table 1. Postimplementation monitoring over shorter time-based deferral periods, Canadian Blood Services

• HIV rates remained low (0.2–0.4 per 100,000 donations)
• No HIV NAT-only positive cases
• HIV-positive donors were noncompliant or denied risk factors
• No positive lookback or traceback cases for HIV
• Noncompliance rate remained low (<1%) as assessed by anonymous donor surveys
• Residual risk of HIV calculated as 1 in 12.9 million units transfused

transmission in high-risk areas, such as San Francisco.[2,3] Once antibody testing began, interviews with HIV-positive donors indicated that many did not necessarily identify as gay or have multiple partners. In 1985, the deferral for a man who has had sex with another man even once since 1977 was mandated by the Food and Drug Administration (FDA); 1977 was thought to be the time AIDS appeared in North America.[4] Many other countries introduced similar criteria. Many other criteria were also put in place to reduce the risk of HIV and/or hepatitis B and C transmission, including deferrals for having an HIV-positive sexual partner, for paying or receiving money or drugs for sex, or for using injection drugs.[4]

The epidemiology of HIV differs in different geographic areas. This discussion is focused on deferral policies in countries where gbMSM have a higher prevalence and incidence of HIV compared with the general population.

Evolution of criteria over time: shorter time-based deferrals for gbMSM

The relative importance of donor screening questions for HIV risk decreased with the introduction of increasingly sensitive tests for HIV 1/2 antibodies, antigen testing (p24), and eventually nucleic acid testing (NAT). Improved automation, process control, and quality systems have virtually eliminated errors in testing and blood center quarantine procedures. The window period, when donors may be infectious but have negative test results, is estimated at 9 days for NAT tests performed in minipools in North America. Additionally, individuals are more aware of risk factors for HIV transmission, and rapid, confidential testing is easily available.

However, criteria for gbMSM were slow to change, in part because of a highly precautionary system born out of the tragedy of transmission of HIV and hepatitis C (known as non-A, non-B hepatitis at the time) to thousands of blood- and plasma-derived clotting factor recipients in the 1980s and early 1990s.[5]

In 2000, Australia implemented a 12-month deferral policy for gbMSM, with no increase in HIV positivity rates.[6] Risk modeling done in several countries suggested that moving from a permanent to a 5-year or 12-month deferral would lead to a negligible increase in HIV risk of under 1 in 5 million transfusions.[7] The US REDS-III Blood Donation Rules Opinion Study (BloodDROPS), in surveys of the gbMSM community and noncompliant gbMSM who donated blood, demonstrated that the HIV prevalence in gbMSM donors was 0.25%, considerably lower than the estimated rate in the general US gbMSM population.[8]

Based on the above, in addition to advocacy group pressure, many countries moved from a permanent deferral for gbMSM to progressively shorter time-based deferrals.[9] In Canada, the permanent deferral was replaced by a 5-year, 12-month, and 3-month deferral in 2013, 2016, and 2019, respectively.[10] In the US, the FDA issued revised recommendations for reducing the risk of HIV transmission in 2015, including a 12-month deferral for gbMSM, and again in 2020, including a 3-month deferral.[11]

Postimplementation monitoring studies (Table 1) showed that changing to shorter deferral periods maintained safety.[12]

Change to sexual risk behavior policies

Although shorter time-based deferrals allow some men who had remote experiences with male-to-male sex to donate, they still result in the deferral of most sexually active gbMSM. Additionally, asking male donors about sex with another male can be seen as stigmatizing and the deferrals seen as discriminatory, generating "ban the ban" campaigns and cancelled blood drives on university campuses, and legal challenges in several countries.[1,13] Under these criteria, our possible donors, Walter and Bill, would be deferred, while Casanova may likely be eligible.

Italy and Spain

Several countries, including Spain and Italy, implemented policies based on sexual behaviors considered to be at higher risk, regardless of whether the partner is same sex or opposite sex; these are sometimes referred to as gender-neutral or risk-based behavior policies. For example, in Spain, donors were deferred for 12 months after sex with more than 1 concurrent partner, or sex with an occasional partner. In Italy, donors were deferred for 4 months after sexual contact with a new or occasional partner whose risk behavior is unknown, and indefinitely deferred for usual/recurrent sex with more than 1 partner whose risk behaviors are unknown or multiple new partners. Published HIV rates, including NAT-only positives, were higher compared with countries using time-based deferrals; it is unclear if this was related to the criteria, methods of questionnaire administration (use of medical doctors), and/or poor donor understanding and compliance. Both differences in blood center functioning and higher donor HIV rates impeded adoption on these approaches in other countries.[14-16]

The UK FAIR approach

UK policies evolved from a permanent deferral for male-to-male sex to a 12- and then 3-month deferral. The UK FAIR (For the Assessment of Individual Risk) steering group, comprising the UK blood services, Public Health England, Nottingham University researchers, and stakeholders including 2SLGBTQI+ (two-spirit, lesbian, gay, bisexual, transgender, queer, intersex, and other people who identify as part of sexual and gender diverse communities) groups, reviewed the literature on individual risk sexual

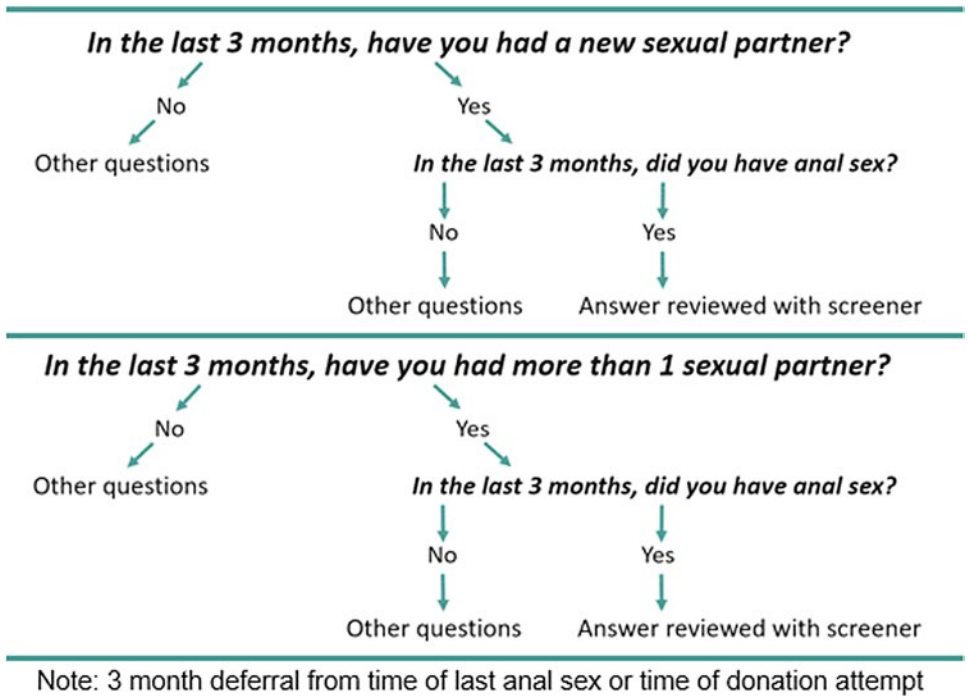

Figure 1. Current sexual risk behavior questions, Canadian Blood Services. Identical criteria are included in the FDA Guidance for Industry and the AABB DHQ_, version 4.[26,27]

behaviors and markers of risk. Focus groups and surveys of stakeholders were undertaken to assess the feasibility and acceptability of potential questions. FAIR recommended deferring donors with a new partner or multiple sexual partners in the last 3 months only if they had anal sex, since anal sex carries the highest rate of HIV transmission and deferral of all donors with a new partner or multiple partners would have too great an impact on the adequacy of the blood supply.[17] Donors who participated in chemsex (use of drugs such as amyl nitrite to enhance sexual experience) in the past 3 months are also deferred since this was identified as a marker of HIV risk. These recommendations were implemented by the blood services in the UK in 2021.

Canadian research programs and policy changes

In 2017, the Canadian federal government funded research programs, administered by Canadian Blood Services and Héma-Québec, the two Canadian blood suppliers, to develop the evidence for a sexual risk behavior approach for whole blood, plateletpheresis, and source plasma donation. Research themes, developed at a kickoff meeting, included safety, operational feasibility, acceptability to donors and gbMSM community members, and the impact of pathogen reduction. Nineteen projects at 11 different research sites were funded, resulting in over 20 publications to date.[18] Many studies, such as risk modeling of possible changes, risks for HIV infection identified in a prospective cohort of gbMSM, operational feasibility of various policies, and acceptability of various approaches to donors and high-interest stakeholder groups, proved critical to supporting a successful regulatory submission to move to an approach very similar to FAIR.[19-23]

Criteria implemented at Canadian Blood Services for all donors and all donation types (whole blood, plasma and plateletpheresis, source plasma) in September 2022 are shown in Figure 1. Implementation was preceded by an extensive staff training program. Héma-Québec implemented identical criteria, first for source plasma and then for all other donation types, slightly later in 2022. Results in the first 6 months postimplementation have shown no increase in HIV rates, no HIV NAT-only positive donors, few complaints from donors, and lower than expected donor deferral rates. Walter and Bill may now be eligible, while Casanova may find himself deferred, depending on specific sexual behaviors. Table 2 shows actual compared with predicted deferral rates.[19,24] A similar discordance between expected and observed rates was seen at Héma-Québec, the blood supplier for the province of Québec. Reasons for this discordance are unclear but may relate to how thoughtful people are about answering survey questions compared with the actual donor questionnaire. As expected, younger donors are more likely to be deferred by the new criteria. These observations would be strengthened by a longer observation period. Additionally, an anonymous donor survey will be performed in late 2023 to access compliance and provide some data on the

Table 2. Observed vs expected answers to new donor questions, % of all donation attempts

In the last 3 months:			Deferrals
Sex with a new partner	2.1% **(5.2%)**	+ anal sex →	0.06% **(0.4%)**
Sex with >1 partner	0.94% **(2.7%)**	+ anal sex →	0.03% **(0.4%)**
One or both	2.3% **(6.3%)**	+ anal sex →	0.085% **(0.6%)**

number of currently eligible male donors who previously would have been deferred. It is possible that noncompliance has been reduced as some gbMSM may not have answered questions truthfully that they considered discriminatory.

US ADVANCE Study and upcoming policy changes in the US and other countries

The US ADVANCE (Assessing Donor Variability and New Concepts in Eligibility) Study, funded by the FDA, enrolled close to 1600 sexually active gbMSM, from 18 to 39 years old in 8 participating communities. Study participants completed a questionnaire and were tested for HIV antiretroviral drugs (medications that can be used as pre-exposure prophylaxis for HIV, known as PrEP). The goal of the study was to evaluate whether sexual behavior risk questions could identify participants who recently became infected with HIV.[25] The FDA used study data, as well as implementation data and risk modeling studies performed internationally, to issue recommendations for evaluating donor eligibility using individual risk-based questions to reduce the risk of HIV transmission by blood and blood products (in draft guidance in January 2023, final guidance in May 2023). The questions and criteria proposed are similar to what has been implemented in the UK and Canada, shown in Figure 1.[26] The Association for the Advancement of Blood & Biotherapies has incorporated these changes into the DHQ version 4.0 and prepared resources to assist in training and implementation.[27]

Many other countries, such as Israel, France, the Netherlands, and Germany, have implemented or will soon implement criteria based on sexual risk behaviors and remove time-based deferrals for gbMSM.

Future considerations

Some future considerations are outlined in Table 3. PrEP therapy with antiretroviral medications is highly effective at preventing sexual transmission of HIV. However, if donors get infected by HIV on or shortly after discontinuing PrEP, viral kinetics and the host immune response may be altered, possibly prolonging testing window periods. Many blood centers have added PrEP-related criteria, deferring some otherwise eligible donors.[28]

Treatment of HIV with antiretroviral medications is highly effective at reducing sexual transmission risk, leading to public health messaging that undetectable equals untransmissible (U=U). However, this is not necessarily the case for transfusion of a large volume intravenously. Communicating this message is challenging.

Pathogen reduction technologies are used in manufacturing plasma protein derivatives and more recently have been introduced for platelets and plasma for transfusion. These technologies result in several log reduction of many pathogens, such as HIV, hepatitis B virus, and hepatitis C virus. Theoretically, criteria could be less stringent when pathogen reduction technology is used. A good place to start may be PrEP/post-exposure prophylaxis criteria.

Trans or *transgender* is an umbrella term that refers to people whose current gender identity differs from their biological sex assigned at birth. Trans people may identify as trans males (assigned female at birth, gender identity male), as trans females (assigned male at birth, gender identity female), or as nonbinary. Blood centers have grappled with several complex issues in attempting to respectfully screen trans donors while ensuring donor and recipient safety.[29] Screening is simplified by the use of a sexual risk behavior approach, since all donors are asked the same questions, regardless of their sex or gender, and the questions focus on behavior, regardless of the sex or gender of the donor's sexual partner(s) (gender-neutral questions). However, most blood centers do not have a nonbinary option, partly due to software limitations.[30]

Table 3. Future considerations

Issue	Comments
PrEP	PrEP use is increasing ↓ Will otherwise eligible gbMSM donors be deferred for PrEP use?
Pathogen reduction	Methods in use for source plasma, platelets, and transfusible plasma are highly effective against HIV ↓ Can eligibility criteria be modified if pathogen reduction is being performed? HIV-infected donors on PrEP or who have recently taken PrEP and have negative test results have very low viremia, so are deferrals for PrEP needed for pathogen-reduced components?
Trans donors	A binary donor registration system does not adequately cover the gender identity spectrum ↓ Can we modify our computer systems to be more inclusive of all potential donors?

Conclusions

After many decades of using male-to-male sex as a surrogate marker for high-risk sexual behavior, blood services are moving to criteria based on sexual risk behaviors in all donors. Initial implementation in the UK and Canada have shown promising results but would be strengthened by further observation. These changes are an important step toward a more inclusive approach to blood donor selection.

Conflict-of-interest disclosure

Mindy Goldman is on the biomedical advisory board of ITL. She has given a presentation at a Roche corporate event about donor diversity.

Off-label drug use

Mindy Goldman: There is nothing to disclose.

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References

1. Goldman M, W-Y Shih A, O'Brien SF, Devine D. Donor deferral policies for men who have sex with men: past, present and future. *Vox Sang.* 2018;113(2):95-103.
2. Goldman M. HIV risk factors. In: Screening Blood Donors With the Donor History Questionnaire. Eder A, Goldman M, eds. Bethesda, Maryland: AABB Press; 2019.

3. Busch MP, Young MJ, Samson SM, et al. Risk of human immunodeficiency virus transmission by blood transfusions prior to the implementation of HIV antibody screening in the San Francisco Bay Area. *Transfusion*. 1991;31(1):4-11.
4. Pindyk J, Waldman A, Zang E, et al. Measures to decrease the risk of acquired immunodeficiency syndrome transmission by blood transfusion. Evidence of volunteer blood donor cooperation. *Transfusion*. 1985;25(1):3-9.
5. Goldman M, Lapierre D, Lemay L, Devine D, Sher G. Donor criteria for men who have sex with men: a Canadian perspective. *Transfusion*. 2014;54(7): 1887-1892.
6. Seed CR, Kiely P, Law M, Keller AJ. No evidence of a significantly increased risk of transfusion-transmitted human immunodeficiency virus infection in Australia subsequent to implementing a 12-month deferral for men who have had sex with men. *Transfusion*. 2010;50(12):2722-2730.
7. Germain M. The risk of allowing blood donation from men having sex with men after a temporary deferral: predictions versus reality. *Transfusion*. 2016;56(6 pt 2):1603-1607.
8. Custer B, Sheon N, Siedle-Khan B, et al; NHLBI Recipient Epidemiology and Donor Evaluation Study-III (REDS-III). Blood donor deferral for men who have sex with men: the Blood Donation Rules Opinion Study (Blood DROPS). *Transfusion*. 2015;55(12):2826-2834.
9. Benjamin RJ, Bianco C, Goldman M, et al. Deferral of males who had sex with other males. *Vox Sang*. 2011;101(4):339-367.
10. Goldman M, Caffrey N, O'Brien SF. Screening for high-risk sexual behavior in Canada. *Transfusion*. 2022;62(12):2419-2422.
11. US Food and Drug Administration. Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products. Guidance for Industry. https://resource.nlm.nih.gov/9918227270706676. Updated August 2020. Accessed 9 May 2023.
12. Caffrey N, Goldman M, Osmond L, Yi Q-L, Fan W, O'Brien SF. HIV incidence and compliance with deferral criteria over three progressively shorter time deferrals for men who have sex with men in Canada. *Transfusion*. 2022;62(1):125-134.
13. Grace D, Gaspar M, Lessard D, et al. Gay and bisexual men's views on reforming blood donation policy in Canada: a qualitative study. *BMC Public Health*. 2019;19(1):772.
14. Suligoi B, Pupella S, Regine V, Raimondo M, Velati C, Grazzini G. Changing blood donor screening criteria from permanent deferral for men who have sex with men to individual sexual risk assessment: no evidence of a significant impact on the human immunodeficiency virus epidemic in Italy. *Blood Transfus*. 2013;11(3):441-448.
15. Raimondo M, Facco G, Regine V, Pupella S, Grazzini G, Suligoi B. HIV-positive blood donors unaware of their sexual at-risk behaviours before donation in Italy. *Vox Sang*. 2016;110(2):134-142.
16. Bes M, Piron M, Casamitjana N, et al. Epidemiological trends of HIV-1 infection in blood donors from Catalonia, Spain (2005-2014). *Transfusion*. 2017;57(9):2164-2173.
17. FAIR. Can donor selection policy move from a population-based donor selection policy to one based on a more individualized risk assessment? Conclusions from the For the Assessment of Individualised Risk (FLAIR) group; 2022. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/21001/fair_sabto_20201211.pdf. Accessed 9 May 2023.
18. Caffrey N, O'Brien SF, Walsh GM, Haw J, Goldman M. Evolving the gay, bisexual and other men who have sex with men time-based deferral to sexual risk screening for all donors: The contribution of Canadian research programmes. *Vox Sang*. 2023;118(8):605-615.
19. O'Brien SF, Goldman M, Robillard P, Osmond L, Myhal G, Roy E. Donor screening question alternatives to men who have sex with men time deferral: potential impact on donor deferral and discomfort. *Transfusion*. 2021;61(1):94-101.
20. Caffrey N, Goldman M, Lewin A, Grégoire Y, Yi Q-L, O'Brien S-F. Removing the men who have sex with men blood donation deferral: informing risk models using Canadian public health surveillance data. *Transfus Clin Biol*. 2022;29(3):198-204.
21. Lambert G, Cox J, Fourmigue A, et al; Engage Study Team. HIV incidence and related risks among gay, bisexual, and other men who have sex with men in Montreal, Toronto, and Vancouver: informing blood donor selection criteria in Canada. *Transfusion*. 2022;62(12):2555-2567.
22. Grace D, Gaspar M, Klassen B, et al. Stepping stones or second class donors?: a qualitative analysis of gay, bisexual, and queer men's perspectives on plasma donation policy in Canada. *BMC Public Health*. 2021;21(1):444.
23. Haw J, Woo H, Kohut T, Fisher W. Sexual risk behavior questions: understanding and mitigating donor discomfort. *Transfusion*. 2022;62(2): 355-364.
24. Caffrey N, Goldman M, Lewin A, Osmond L, O'Brien SF. Behaviour based screening questions and potential donation loss using the "For the Assessment of Individualised Risk" screening criteria: a Canadian perspective. *Transfus Med*. 2022;32(5):422-427.
25. ADVANCE Study – Assessing Donor Variability and New Concepts in Eligibility. https://advancestudy.org/. Accessed 9 May 2023.
26. US Food and Drug Administration. Recommendations for Evaluating Donor Eligibility Using Individual Risk-Based Questions to Reduce the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products. Guidance for Industry, May 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-evaluating-donor-eligibility-using-individual-risk-based-questions-reduce-risk-human. Accessed 6 July 2023.
27. Association for the Advancement of Blood & Biotherapies. IDA and DHQ_v4.0 and Accompanying Materials – Toolkit for Implementation. https://www.aabb.org/news-resources/resources/donor-history-questionnaires/blood-donor-history-questionnaires. Accessed 6 July 2023.
28. Association for the Advancement of Blood & Biotherapies. AABB Association Bulletin #22-03. Updated Recommendations on Donor Deferral for Use of Antiretroviral Medications for HIV Prevention and Treatment Including Long-Acting Injectable PrEP and the Impact on Blood Safety. https://www.aabb.org/news-resources/news/article/2022/09/08/association-bulletin-22-03-outlines-updated-deferral-recommendations-for-medications-to-prevent-treat-hiv-infection. Updated 8 September 2022. Accessed 9 May 2023.
29. Goldman M, Butler-Foster T, Lapierre D, O'Brien SF, Devor A. Trans people and blood donation. *Transfusion*. 2020;60(5):1084-1092.
30. Pandey S, Gorlin JB, Townsend M, et al. International Forum on Gender Identification and Blood Collection: summary. *Vox Sang*. 2022;117(3): 447-456.

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