ARV and PrEP Use In US Blood Donors

IPFA/PEI 27th International Workshop on Surveillance and Screening of Blood-borne Pathogens

Brian Custer, MPH, PhD
bcuster@vitalant.org
5 May 2021

Disclosures

Research grants and speaker's bureau funding from Grifols Diagnostic Solutions – not related to the content of this presentation

Employed by Vitalant

Outline

- Review the issue of HIV detection in the era of Antiretrovirals (ARV) and Pre-Exposure Prophylaxis (PrEP) or Post-Exposure Prophylaxis (PEP)
- Describe findings from US studies of donors who are taking ARV or PrEP/PEP
- Explain current and planned research to assess whether there is a risk to the blood supply

hivma

hiv medicine association

UNDETECTABLE = UNTRANSMITTABLE

In 2017, HIVMA endorsed the *U=U Consensus Statement*, saying definitively that when a person living with HIV has an undetectable viral load, they will not transmit HIV.

The science is clear.

HPTN 052

PARTNER

Opposites Attract

PARTNER 2

Combined data from 2008-2016 show that **there were ZERO linked HIV transmissions** after more than **a hundred thousand condom-less sex acts** within both heterosexual and male-male serodiscordant couples where the partner living with HIV had a **durably undetectable viral load**.

But the need remains great.

- Only 11% of young adults 18-30 believe that ART is "very effective" in preventing HIV.
- Only 50% of people living with HIV are engaged in care and virally suppressed.

*"The body of scientific evidence to-date has established that there is **effectively no risk of sexual transmission of HIV** when the partner living with HIV has a durably undetectable viral load, **validating the U=U message of HIV treatment as prevention."***

Anthony S. Fauci, MD
July 2018

www.HIVMA.org Oct. 2018 #UequalsU

Ending the HIV Epidemic: A Plan for America

HHS is proposing a once-in-a-generation opportunity to eliminate new HIV infections in our nation. The multi-year program will infuse 48 counties, Washington, D.C., San Juan, Puerto Rico, as well as 7 states that have a substantial rural HIV burden with the additional expertise, technology, and resources needed to end the HIV epidemic in the United States. Our four strategies – diagnose, treat, protect, and respond – will be implemented across the entire U.S. within 10 years.

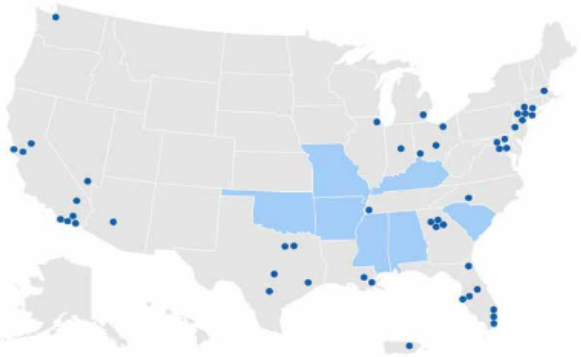
GOAL:

HHS will work with each community to establish local teams on the ground to tailor and implement strategies to:

75% reduction in new HIV infections in 5 years and at least **90%** reduction in 10 years.

- **Diagnose** all people with HIV as early as possible.
- **Treat** people with HIV rapidly and effectively to reach sustained viral suppression.
- **Prevent** new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).
- **Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.

The Initiative will target our resources to the 48 highest burden counties, Washington, D.C., San Juan, Puerto Rico, and 7 states with a substantial rural HIV burden.



Geographical Selection:
Data on burden of HIV in the US shows areas where HIV transmission occurs more frequently. More than 50% of new HIV diagnoses* occurred in only 48 counties, Washington, D.C., and San Juan, Puerto Rico. In addition, 7 states have a substantial rural burden – with over 75 cases and 10% or more of their diagnoses in rural areas.

*2016-2017 data

Ending the HIV Epidemic

www.HIV.gov

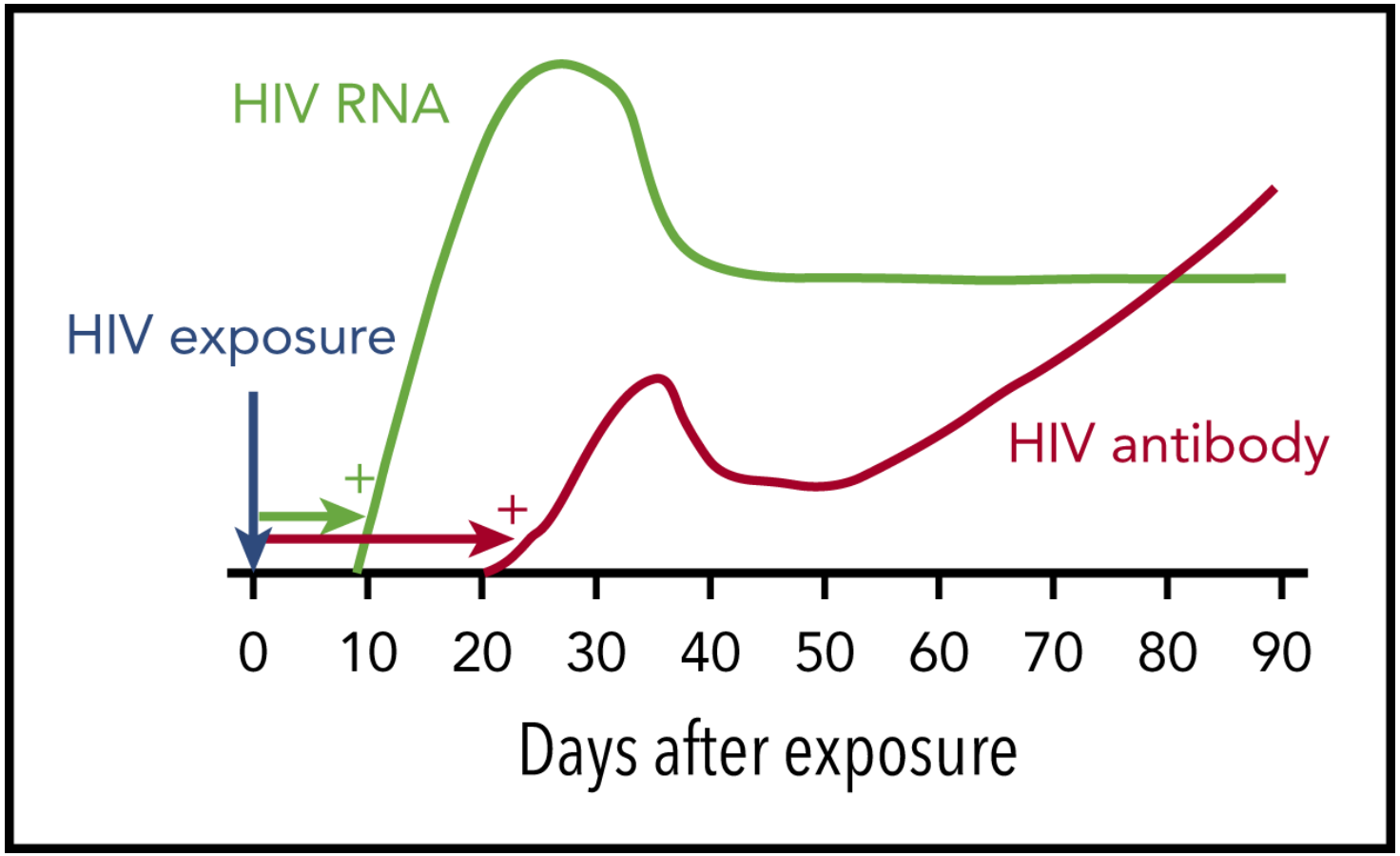
TRANSFUSION MEDICINE

Comment on Grebe et al, page 1359, and Custer et al, page 1351

ART and science of keeping HIV out of the blood supply

Richard Kaufman | Brigham and Women's Hospital

blood® 10 SEPTEMBER 2020 | VOLUME 136, NUMBER 11 **1223**



In developed countries, blood centers protect the safety of the blood supply by deferring high-risk donors and screening all donations for HIV and other pathogens using exquisitely sensitive and specific assays. This multilayered approach has been highly successful. In the United States and many other countries, the per-unit risk of HIV transfusion-transmission is <1 per million.[3] However, medical policies and practices continue to evolve, and so do the risks of transfusion-transmitted infection. In this issue of *Blood*, Custer and colleagues report 2 important studies about current risks of transfusion-transmitted HIV. One of these studies is reassuring[1]; the other is not.[2]

ashpublications.org/blood/pages/blood_podcast

Impact of early ART on HIV test performance

Incomplete HIV Type 1 Antibody Evolution and Seroreversion in Acutely Infected Individuals Treated with Early Antiretroviral Therapy

Sigall Kassutto,[1,2] Mary N. Johnston,[2] and Eric S. Rosenberg[2]

Clinical Infectious Diseases 2005; 40:868–73

- 3/150 patients did not develop fully evolved Ab pattern (2%)
- Ab testing performed using HIV-1/2 ELISA (Abbott) and HIV-1 Western blot (BioRad)
- VL measured using Roche Amplicor and Chiron branched DNA

Seroreversion in Subjects Receiving Antiretroviral Therapy during Acute/Early HIV Infection

C. Bradley Hare,[1] Brandee L. Pappalardo,[4,a] Michael P. Busch,[4] Annika C. Karlsson,[2,a] Bruce H. Phelps,[5] Steven S. Alexander,[6] Christopher Bentsen,[7] Clarissa A. Ramstead,[1] Douglas F. Nixon,[2] Jay A. Levy,[3] and Frederick M. Hecht[1]

Clinical Infectious Diseases 2006; 42:700–8

- 6/87 subjects developed seroreversion (7%)
- Ab testing performed using 2nd-gen EIAs (BioMérieux, Bio-Rad), 3rd-gen EIA (Bio-Rad), strip immunoblot assay (Chiron), and Western blot assays (Ortho, Bio-Rad)

Generation	Capture reagent	Detects
1st	Whole viral lysate	IgG antibody
2nd	Recombinant proteins or synthetic peptides	IgG antibody
3rd	Recombinant proteins or synthetic peptides	IgM and IgG
4th	Recombinant proteins or synthetic peptides; anti-p24 antibody	IgM, IgG and p24
5th	Recombinant proteins or synthetic peptides; anti-p24 antibody	Distinguishes between p24 and antibodies

Positive or Not, That Is the Question: HIV Testing for Individuals on Pre-exposure Prophylaxis

Jason Zucker, MD, MS*†
Caroline Carnevale, FNP, MPH, AAHIVS‡
Alex J. Rai, PhD§
Peter Gordon, MD*
Magdalena E. Sobieszczyk, MD, MPH*

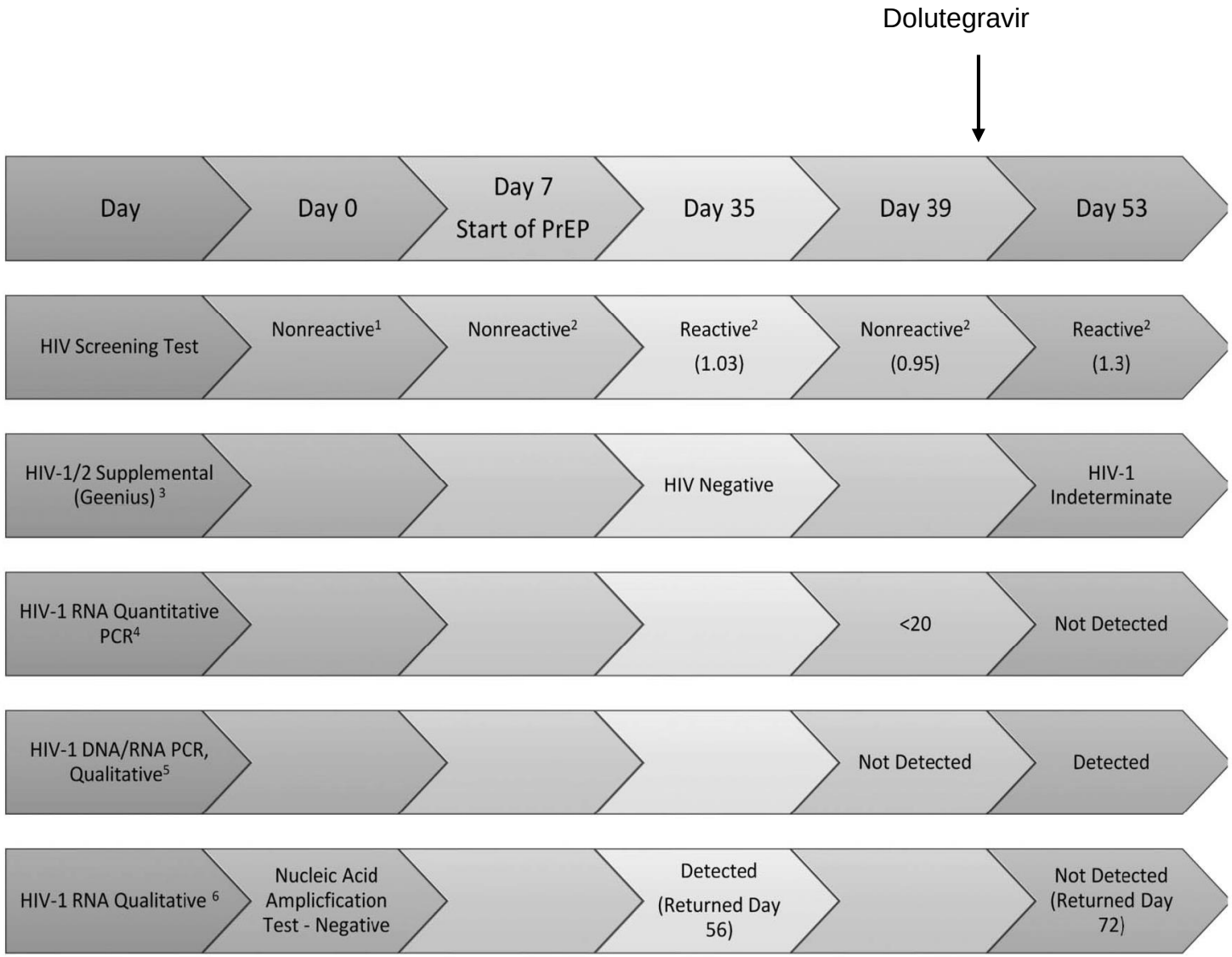


FIGURE 1. Timeline of HIV diagnostics for patient initiating PrEP. [1]OraQuick Rapid HIV-1/2 Antibody Test, Orasure Technologies, Inc., Bethlehem, PA. [2]Abbott Architect HIV Ag/Ab Combo, Abbott Laboratories, Abbott Park, IL. [3]Geenius, Bio-Rad, Marne la Coquette, France. [4]COBAS AmpliPrep/TaqMan HIV-1 Test kit, version 2.0, Indianapolis, IN. [5]COBAS AmpliPrep/TaqMan HIV-1 Qual Test, Indianapolis, IN. [6]APTIMA HIV-1 RNA qualitative assay, Hologic, Inc., San Diego, CA.

ARV Use in HIV+ Donors

Question: What is the proportion of ARV use among HIV-positive blood donors in the USA?

Motivations

- Assess ARV use in HIV+ blood donors to begin to understand possible blood safety concerns
- Distinguish between true elite and false elite controllers (in HIV seropositive-only donors)

Design/Approach

- Test 300 HIV-positive and 300 infection-negative plasma samples, using Liquid Chromatography-Mass Spectrometry (LC-MS/MS), for 13 drug metabolites of ARVs

Transfusion Transmissible Infections Monitoring System

List of analytes tested for using LC-MS/MS and their biologic half-lives

Drug	Minimum plasma half-life (in hours)*
Lamivudine, Epivir (3TC)	5-7
Cobicistat (Cobi)	3-4
Etravirine (ETV)	30-40
Rilpivirine (RPV)	45
Darunavir (DRV)	15
Raltegravir (RAL)	7-12
Abacavir (ABC)	1.5
Emtricitabine (FTC)	8.2-10
Tenofovir (TDF and TAF)	17
Efavirenz (EFV)	40-55
Ritonavir (RTV)	3-5
Elvitegravir (EVG)	9-15
Dolutegravir (DTG)	12-15

*Plasma and intracellular elimination half-lives of antiretroviral components of once-daily single-tablet antiretroviral regimens. ARV therapies include combinations of drugs that enhance and improve the half-lives of these drugs. **Limit of Quantitation (LOQ) 10-50 ng/mL**

Transfusion Transmissible Infections Monitoring System

ARV Use in HIV+ Donors

HIV Infection Classification	HIV-positive donors at TTIMS blood centers during period*	Samples tested for ARVs	ARVs detected n (% & 95%CI based on tested samples)
HIV Negative		300	0
HIV Positive	463	299	46 (15.4%; 11.5 – 20.0%)

* 9/1/2015 – 12/31/2017

Transfusion Transmissible Infections Monitoring System

ARV Use in HIV+ Donors

Identifying true and false elite controllers

- Criteria for true elite controllers
  - Seropositive
  - Viral load <75 copies/mL
  - Not taking antiretroviral drugs

HIV + samples tested for ARVs

Viral Load	ARV –	ARV +
Low/Not Detectable	1	22
Above 75 copies/mL	244	3
Not Available/Not Tested	8	21

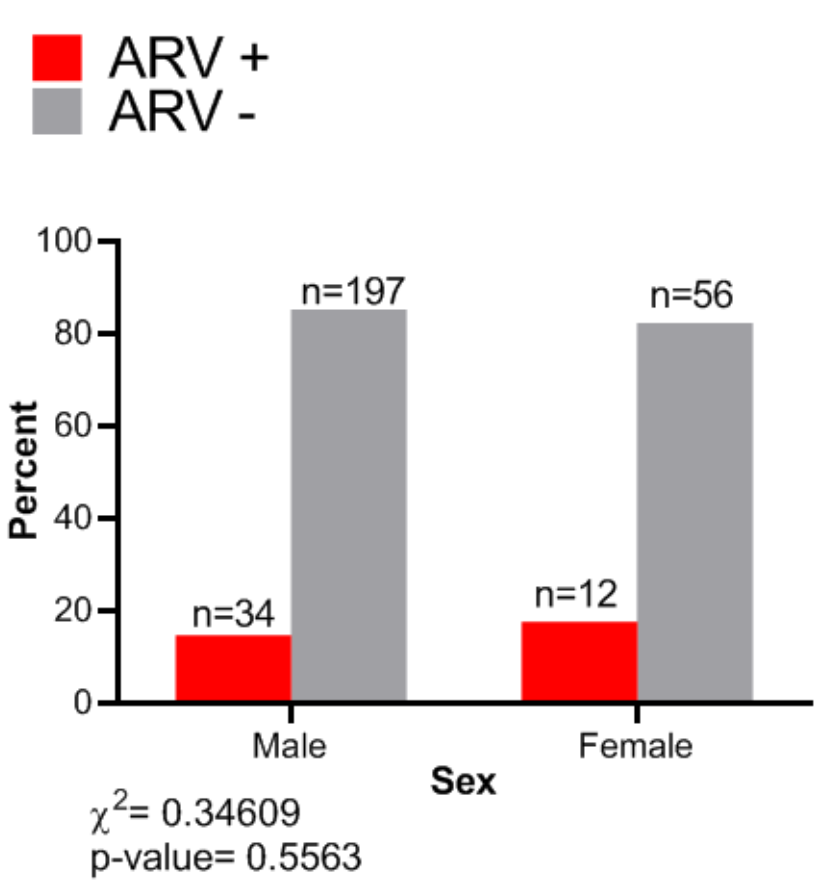
True elite controller

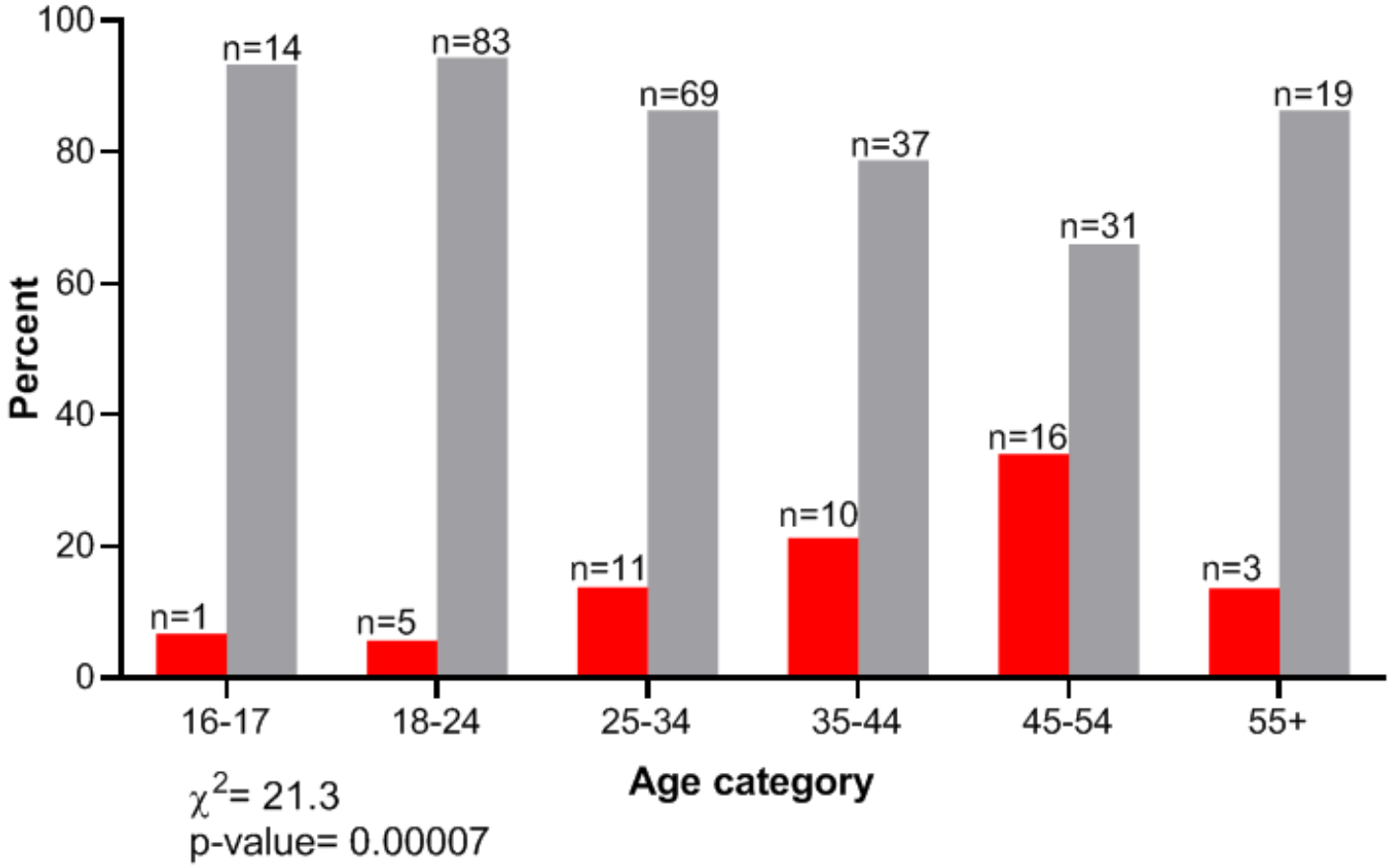
False elite controllers

Transfusion Transmissible Infections Monitoring System

ARV Use in HIV+ Donors

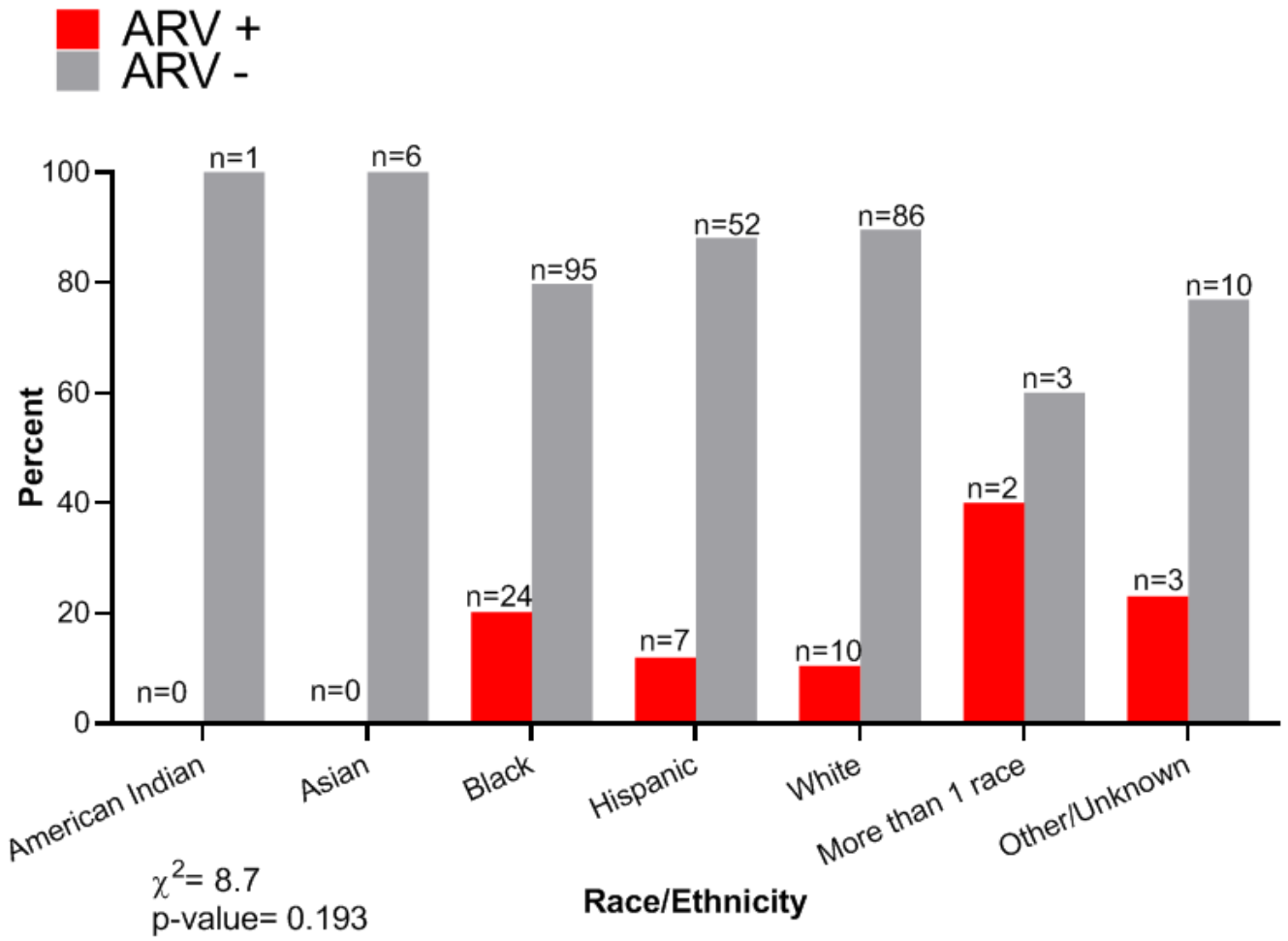
Demographics of ARV Use

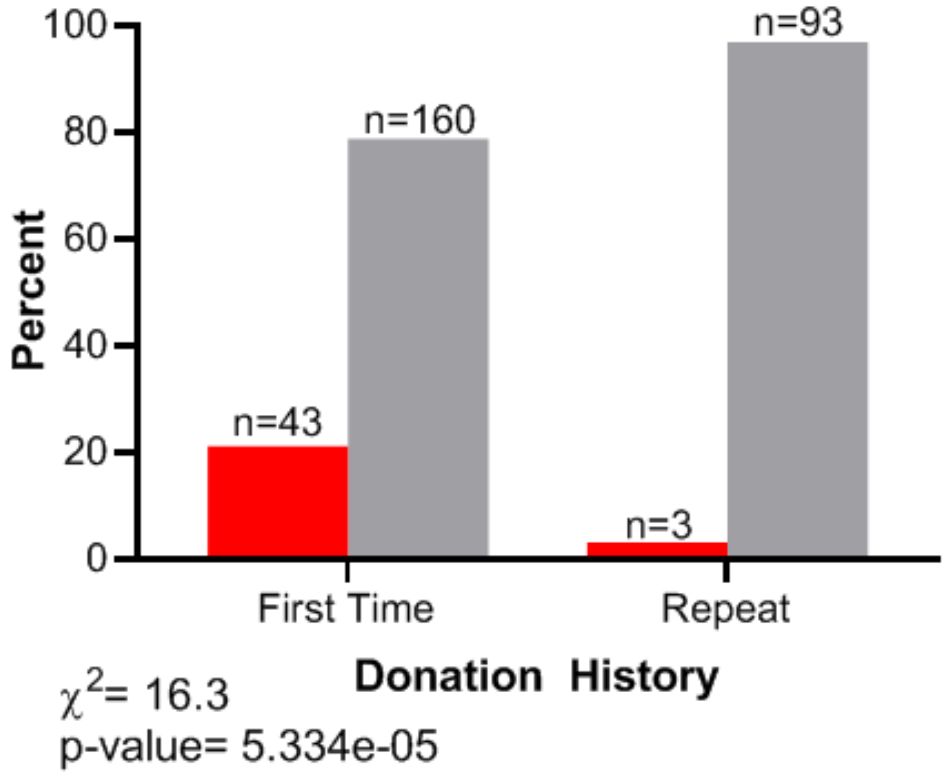




ARV Use in HIV+ Donors

Demographics of ARV Use





PrEP Use in Infection Negative Donors

Background

- Truvada® consists of dual therapy of emtricitabine and tenofovir disoproxil fumarate (TDF)
  - PrEP first approved for use in the US in 2012
- Use has steadily increased among populations targeted for public health interventions (MSM, higher risk heterosexuals, PWID)
- Estimates of prevalence of PrEP use is limited and only among higher-risk behavior populations
- Descovy® consists of dual therapy of emtricitabine and tenofovir alafenamide (TAF)
  - Approved for PrEP in 2019

Motivations for conducting PrEP studies in donors:

- Concern over possible breakthrough HIV infection
- Could be additional indicator for risk of TTIs
- Identify sub-groups with possible PrEP use in donor population

Transfusion Transmissible Infections Monitoring System

PrEP Use in Infection Negative Donors

Question: What is the proportion of PrEP use among infection-negative blood donors in the US?

Design/Approach (Pilot Study)

- De-identified infection-negative samples from a selected population:
  - 18–45-year-old, first-time, male donors with successful donations
  - Donation negative for all markers routinely screened for (HIV-1/2, HBV, HCV, HTLV-I/II, WNV, ZIKV, *Treponema pallidum*, and *Trypanosoma cruzi*)
  - Donations from 6 urban metropolitan centers with elevated HIV prevalence and notable PrEP availability

Transfusion Transmissible Infections Monitoring System

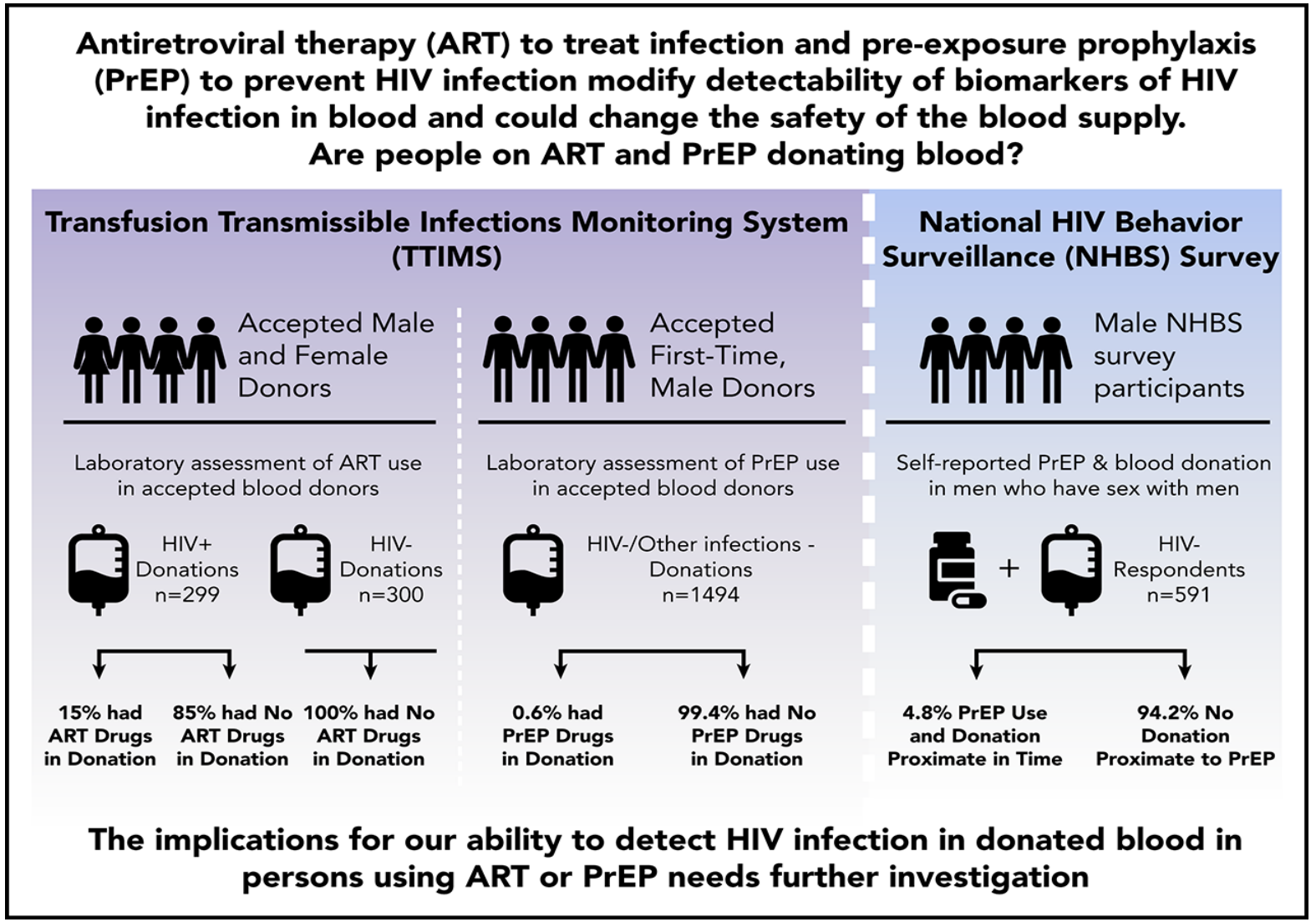
PrEP Use in Infection Negative Donors

Geographic Location	Samples	PrEP Drugs Detected n (% & 95%CI)
Boston, MA	176	0 (0)
Los Angeles, CA	344	2 (0.6)
Miami, FL	243	1 (0.4)
New York City, NY	350	2 (0.6)
San Francisco, CA	211	2 (1.0)
Washington, DC	170	2 (1.2)
Total	1494	9 (0.6%; 0.03 – 1.1%)

Transfusion Transmissible Infections Monitoring System

HIV antiretroviral therapy and prevention use in US blood donors: a new blood safety concern

Brian Custer,[1,2] Claire Quiner,[1,3] Richard Haaland,[4] Amy Martin,[4] Mars Stone,[1,2] Rita Reik,[5] Whitney R. Steele,[6] Debra Kessler,[7] Phillip C. Williamson,[8] Steven A. Anderson,[9] Alan E. Williams,[9] Henry F. Raymond,[10] Willi McFarland,[11] William T. Robinson,[12,13] Sara Glick,[14] Kwa Sey,[15] C. David Melton,[16] Simone A. Glynn,[17] Susan L. Stramer,[18] and Michael P. Busch,[1,2] for the Transfusion-Transmissible Infections Monitoring System

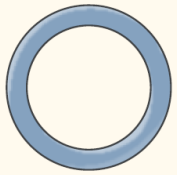
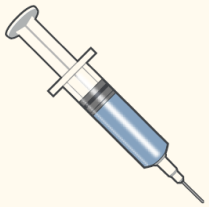
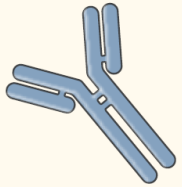


Transfusion Transmissible Infections Monitoring System

PrEP – Dosing Options and Formulations in Development

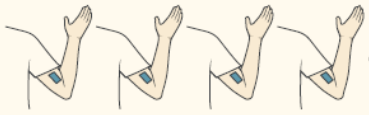
1. Daily dosing
2. On demand, event-based, or 2-1-1
3. Long-acting, in development:

NIAID is funding research on 4 types of long-acting HIV prevention.

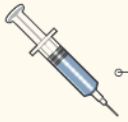
INTRAVAGINAL RING (IVR)	IMPLANT	INJECTABLE	ANTIBODY
			
Polymer ring inserted into the vagina releases antiretroviral drug over time.	Device implanted in the body releases antiretroviral drug over time.	Long-acting antiretroviral drug is injected into the body.	Antibody is infused or injected into the body.

How many products are under investigation?

dapivirine IVR (MTN 034/REACH clinical trials)
tenofovir IVR (CONRAD)
Truvada IVR (Oak Crest Institute of Science)



cabotegravir (SLAP-HIV project)
dolutegravir (University of North Carolina)
tenofovir alafenamide(Oak Crest Institute of Science)
tenofovir alafenamide & emtricitabine (Houston Methodist Research Institute)



cabotegravir (HPTN 077, 083 & 084 clinical trials)

CAP256V2LS (NIAID VRC & CAPRISA)
N6LS (VRC 609 clinical trial)
PGT121.414.LS (NIAID)
Sanofi trispecific antibody (NIAID VRC & Sanofi)
VRC01
(AMP Studies, HVTN 116 & IMPAACT P1112 clinical trials)
VRC01LS (HVTN 116 & IMPAACT P1112 clinical trials)
VRC07-523LS
(VRC 610, HVTN 127/HPTN 087 & IMPAACT P1112 clinical trials)

https://www.hiv.gov/hiv-basics/hiv-prevention/potential-future-options/long-acting-prep

Impact on US Blood Donor Eligibility

1. Updated the AABB Donor History Questionnaire and related materials
   - Questions and language about medication taken to:
     - prevent HIV infection (PrEP/PEP)
     - treat HIV infection (ARV)

2. Deferral of individuals taking PrEP or PEP (HIV *uninfected*)
   - Until 3 months after the last dose, and after routine lab tests have been completed by prescriber

3. Deferral of individuals taking ARV (HIV-infected)
   - Indefinite

Association Bulletin #20-04
May 5, 2020

Changes to the AABB DHQ

PrEP or pre-exposure prophylaxis involves taking a specific combination of medicines as a prevention method for people who are HIV negative and at high risk of HIV infection.

PEP or post-exposure prophylaxis is a short-term treatment started as soon as possible after a high-risk exposure to HIV.

ART or anti-retroviral therapy is the daily use of a combination of HIV medicines (called an HIV regimen) to treat HIV.

CONTENT	Yes	No
4. Have you taken any medications on the Medication Deferral List in the time frames indicated? (Review the Medication Deferral List.)	❑	❑

HIV Prevention (PrEP and PEP)	Truvada, Descovy, Tivicay, Isentress	Tenofovir, Emtricitabine Dolutegravir, Raltegravir	3 months
HIV Treatment or Anti-retroviral Therapy (ART)			Ever

REVISIONS FOR v2.0	Yes	No
37. In the **past 3 months**, have you taken any medication to prevent an HIV infection?	❑	❑
45. Have you **EVER** taken any medication to treat an HIV infection?	❑	❑

New DHQ data from Vitalant

Implemented on 8/15/2020, data from 8/16/2020 to 3/31/2021:

Have you EVER taken any medication to treat an HIV infection?

Sex of donor	Female	Male	Total
Total Interviews	369,785	353,023	722,808
NO	369,765	353,010	722,775
UNSURE	8	1	9
YES	12	12	24
YES per 100,000 DHQ responses (95% CI)	3.2 (1.4 – 5.1)	3.4 (1.5 – 5.3)	3.3

In the past 3 months, have you taken any medication to prevent an HIV infection?

Sex of donor	Female	Male	Total
Total Interviews	369,786	353,023	722,809
NO	369,771	352,979	722,750
UNSURE	6	4	10
YES	9	40	49
YES per 100,000 DHQ responses (95% CI)	2.4 (0.8 – 4.0)*	11.3 (7.8 – 14.8)*	6.8

* significantly different ($p<0.0001$)

Specific Risk Questions on DHQ

5I. In the past 3 months, have you had a blood transfusion?	☐ Yes	☐ No
5J. In the past 3 months, have you had a transplant such as organ, tissue, or bone marrow?	☐ Yes	☐ No
5L. In the past 3 months, have you had a graft such as bone or skin?	☐ Yes	☐ No
5M. In the past 3 months, have you come into contact with someone else's blood?	☐ Yes	☐ No
5N. In the past 3 months, have you had an accidental needle stick?	☐ Yes	☐ No
5O. In the past 3 months, have you had sexual contact with anyone who has ever had HIV/AIDS or has ever had a positive test for the HIV/AIDS virus?	☐ Yes	☐ No
5R. In the past 3 months, have you had sexual contact with a prostitute or anyone else who has ever taken money or drugs or other payment for sex?	☐ Yes	☐ No
5S. In the past 3 months, have you had sexual contact with anyone who has ever used needles to take drugs or steroids, or anything not prescribed by their doctor?	☐ Yes	☐ No
MALE DONORS: 7N. In the past 3 months, have you had sexual contact with another male?	☐ Yes	☐ No
FEMALE DONORS: 5Y. In the past 3 months, have you had sexual contact with a male who had sexual contact with another male in the past 3 months?	☐ Yes	☐ No
6M. In the past 3 months, have you had a tattoo?	☐ Yes	☐ No
6N. In the past 3 months, have you had ear or body piercing?	☐ Yes	☐ No
6O. In the past 3 months, have you had or been treated for syphilis or gonorrhea?	☐ Yes	☐ No
7Q. In the past 3 months, have you used needles to take drugs, steroids, or anything not prescribed by your doctor?	☐ Yes	☐ No
7M. In the past 3 months, have you received money, drugs, or other payment for sex?	☐ Yes	☐ No

New DHQ data from Vitalant – Disclosed specific risks

(Implemented on 8/15/2020, data from 8/16/2020 to 3/31/2021)

ARV use

- Among the 24 who answered yes to the ARV question, only 5 donors answered yes to the question ‘Have you ever had a positive test for the HIV/AIDS virus?’

- 18 other donors answered yes to testing HIV-positive but not to taking ARVs.

New DHQ data from Vitalant – Disclosed specific risks

(Implemented on 8/15/2020, data from 8/16/2020 to 3/31/2021)

PrEP/PEP use: 12 of 49 disclosed specific risk questions

Females

- Majority are PEP-exposures

Males

- PrEP use and PEP-exposures
- 7 of the 40 male donors reported MSM behavior within 3-months of donating.
  - **This means that of those male donors reporting PrEP/PEP, 33 (82.5%) didn't report MSM behavior in the 3-months of donation**

Blood safety implications and advancing testing for screening donors with HIV infections taking ART and PrEP therapies

REDS-IV-P
Optimizing Transfusion Across the Lifespan

1. Characterization of the altered dynamics of viremia and seroconversion and performance of blood donor screening assays in HIV-infected individuals who took ART early after being infected, and in people who became infected with HIV while on PrEP.
2. Assess whether testing of whole blood (WB) using simple WB processing methods by donor screening NAT and viral load (VL) assays/platforms enables detection of HIV infections not detectable by current blood screening plasma-based testing algorithms.
3. Demonstration that novel, sensitive multiplexed HIV antigen assays could detect low level humoral immune responses not detectable by current commercially available donor screening and diagnostic serological assays, which will lead to enhancement of those assays.

Planned testing
Abbott Alinity s HIV Ag/Ab Combo
Ortho Vitros HIV Combo
Roche Elecsys HIV Duo
Grifols Procleix Ultrio Elite dHIV
Roche cobas MPX

Summary

- Do not know if or how residual risk of HIV in the blood supply has changed with increased availability of ARV and PrEP/PEP
- REDS-IV-P is studying the issue of HIV detection in the ARV and PrEP/PEP era
  - Testing being conducted in 2021
- New PrEP dosing options and therapeutic approaches will further complicate blood safety matters – each will have to be assessed for our ability to detect HIV in blood donations
- Initial data suggest that taking PrEP does not necessarily mean donors have recent high-risk behaviors
- TTIMS plans to expand ARV testing of HIV-positive donations
- TTIMS plans to conduct a PrEP study to assess use in a broader range of donors
  - Motivations research – surveys and qualitative interviews to understand factors contributing to donation in persons taking ART and PrEP

Acknowledgements

Vitalant/VRI

- Roberta Bruhn
- Michael Busch
- Eduard Grebe
- Dan Hindes
- Zhanna Kaidarova
- Mars Stone
- Nelly Gefter
- Eric Delwart
- Eda Altan
- Sonia Bakkour
- Eric Peters
- Hany Kamel
- Jackie Vannoy
- Claire Quiner
- Marj Bravo

CTS

- Phillip Williamson
- Sherri Cyrus
- Val Winkelman
- Tracy Fickett

FDA

- Steve Anderson
- Alan E. Williams
- Angela Moy
- Hong Yang
- Rich Forshee
- Peter Marks

NHLBI

- Simone A. Glynn

NYBC

- Debra Kessler
- Carlos Delvalle
- Lisa Milan-Benson

OneBlood

- Rita Reik
- Tisha Foster
- Melissa Lopez
- Cathy Shea
- Adam Rosenzweig
- Shalet Verghese
- Vilson Ortiz
- Harold Olieberg

ARC

- Susan Stramer
- Whitney Steele
- Ed Notari
- Roger Dodd
- Diane Nelson
- James Haynes
- David Krysztof
- Rebecca Townsend
- Rahima Fayed
- Meng Xu
- Barbara Deisting
- Stephanie Acocella

Quality Analytics

- Jaye Brodsky
- Marjory Manske
- Maureen Barr

OASH/HHS

- James Berger

CDC

- Rich Haaland
- Amy Martin

Transfusion Transmissible Infections Monitoring System

Thank You

bcuster@vitalant.org

ARV Use Conclusions

- ARV use in HIV-positive donors was associated with first-time donor status and increasing age, but not sex or race/ethnicity
- The relatively high S/CO values from PRISM suggest recent initiation of ARV therapy in first-time donors
- Seropositive donors with measurable HIV RNA may be on therapy that is not working for them or may be inconsistently taking medication
- For these HIV-positive/ARV-positive donors we do not know the motivations but the previous DHQ was not effective in achieving disclosure
  - Brings attention back to the issue of test seeking and use of blood centers for infection monitoring
- These findings may have direct blood safety implications

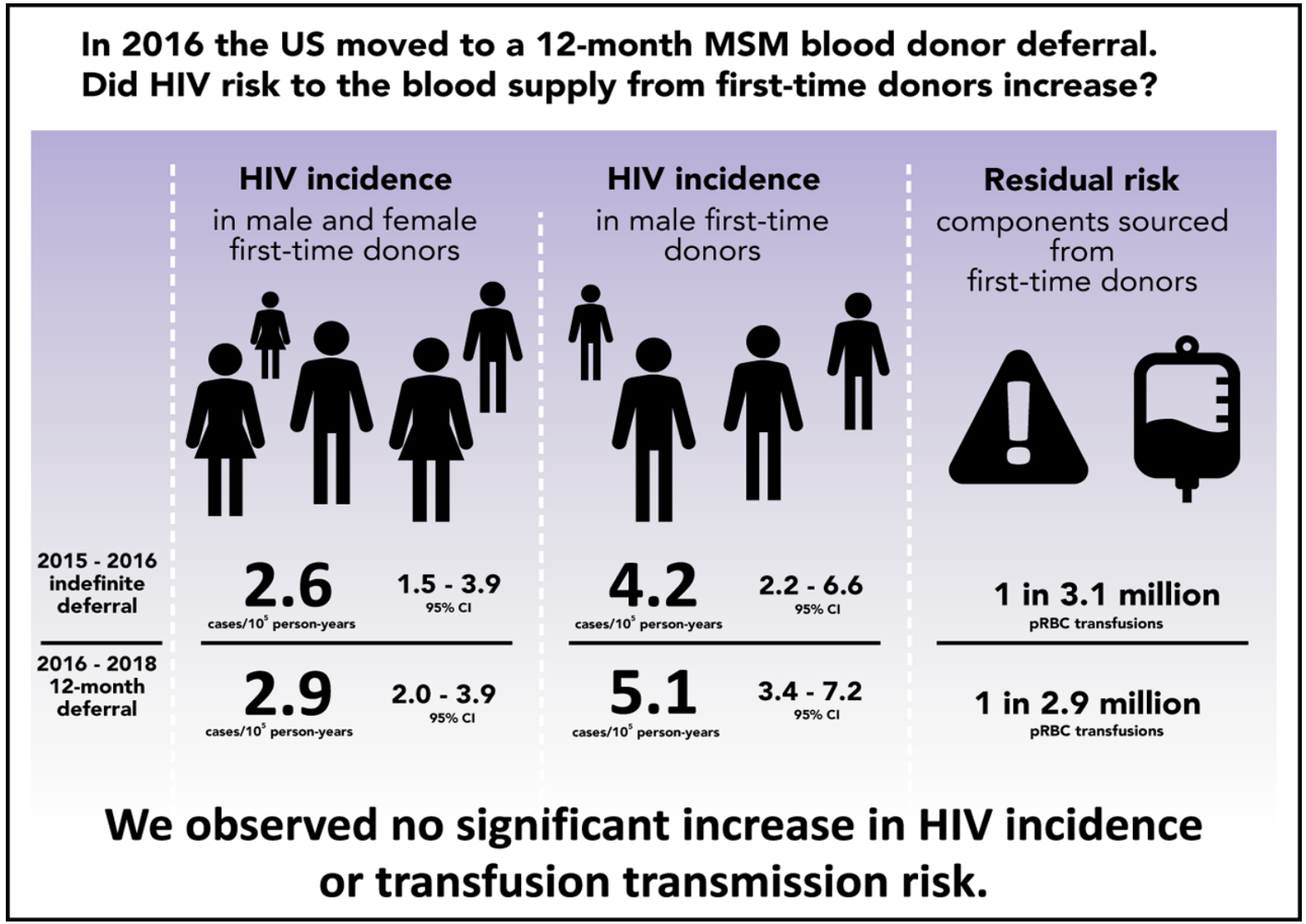
PrEP Use Conclusions

- For donors with measurable PrEP drugs, the pilot study was focused on a selected group of the donor population – results are not generalizable to the overall donor population
  - Evidence of HIV-negative/PrEP-positive donors raises concerns about possible increased risk of HIV-breakthrough infections
  - Results contribute to the decision to adopt PrEP/PEP questions on the DHQ
  - We do not know the motivations of the donors we have identified:
    - Is this also a form of test-seeking or monitoring?
    - Do these donors have risk behaviors?
- REDS-IV-P project to fully investigate the blood screening implications and our ability to identify HIV infection in era of widespread ART and increasing PrEP use

HIV incidence in US first-time blood donors and transfusion risk with a 12-month deferral for men who have sex with men

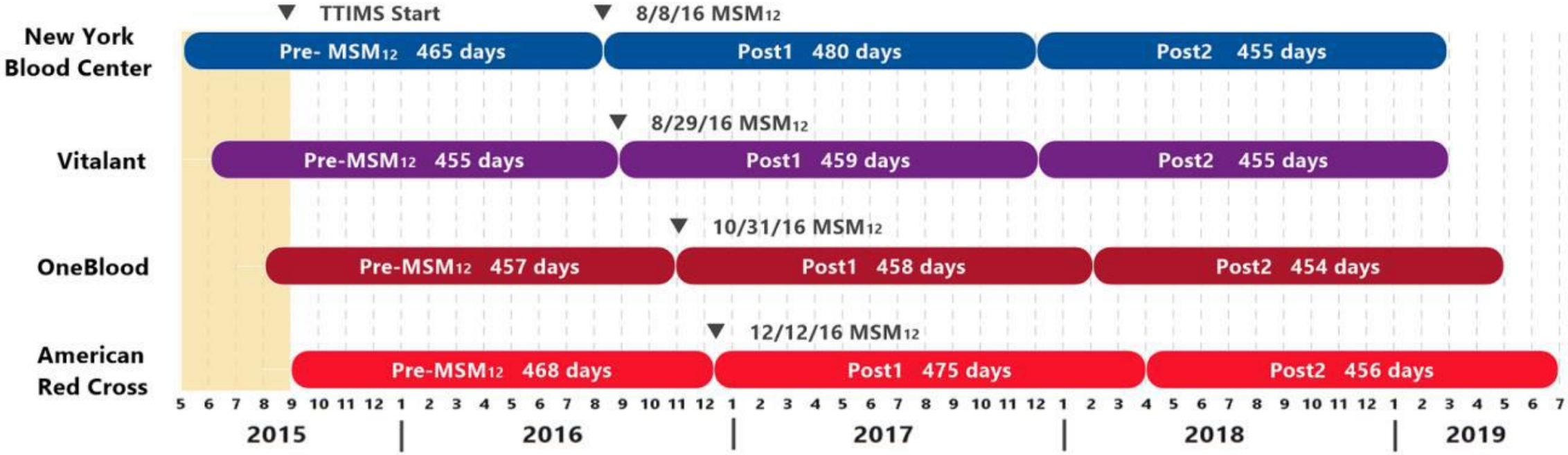
Eduard Grebe,[1,2] Michael P. Busch,[1,2] Edward P. Notari,[3] Roberta Bruhn,[1,2] Claire Quiner,[1,4] Daniel Hindes,[1] Mars Stone,[1,2] Sonia Bakkour,[1,2] Hong Yang,[5] Phillip Williamson,[6] Debra Kessler,[7] Rita Reik,[8] Susan L. Stramer,[3] Simone A. Glynn,[9] Steven A. Anderson,[5] Alan E. Williams,[5] and Brian Custer,[1,2] for the Transfusion-Transmissible Infections Monitoring System

TTIMS: HIV incidence first-time donors



Transfusion Transmissible Infections Monitoring System

TTIMS: HIV Incidence in Repeat and First Time Donors



HIV		Pre-MSM	Post1-MSM	Post2-MSM
Repeat donors	Repeat incident cases	27	24	18
	Incidence rate* (95% CI)	2.19 (1.45-3.19)	1.88 (1.21-2.80)	1.57 (0.93-2.49)
	Residual risk† per donation	1:1,831,502	1:2,133,505	1:2,554,770
First-time donors	Incidence rate‡ (95% CI)	8.54 (5.66-12.44)	7.33 (4.72-10.92)	6.12 (3.63-9.71)
	Residual risk† per donation	1:469,565	1:546,993	1:654,998
All donors, weighted	Incidence rate§ (95% CI)	4.09 (2.70-5.95)	3.54 (2.28-5.28)	2.96 (1.75-4.70)
	Residual risk‖ per donation	1:1,151,127	1:1,337,943	1:1,606,972

Steele et al. Transfusion *In Press*

HIV Diagnosis

Elliott T et al. *Journal of the International AIDS Society* 2019, **22**:e25419
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25419/full | https://doi.org/10.1002/jia2.25419

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

REVIEW

Challenges of HIV diagnosis and management in the context of pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), test and start and acute HIV infection: a scoping review

Tamara Elliott[1,2], Eduard J Sanders[3,4], Meg Doherty[5], Thumbi Ndung'u[6,7,8,9], Myron Cohen[10], Pragna Patel[11], Gus Cairns[12,13], Sarah E Rutstein[10], Jintanat Ananworanich[14,15], Colin Brown[16,17] and Sarah Fidler[1,18,§]

Discussion: Missed acute HIV infection prevents people living with HIV (PLHIV) from accessing early treatment, increases likelihood of onward transmission, and allows for inappropriate initiation or continuation of PrEP, which may result in HIV drug resistance. While immediate ART is recommended for all PLHIV, studies have shown that starting ART in the setting of acute HIV infection may result in a delayed or complete absence of development of HIV-specific antibodies, posing a diagnostic challenge that is particularly pertinent to resource-limited, high HIV burden settings where HIV-antibody POCTs are standard of care. Similarly, ART used as PrEP or PEP may supress HIV RNA viral load, complicating current HIV testing algorithms in resource-wealthy settings where viral detection is included. As rollout of PrEP continues, HIV testing algorithms may need to be modified.

Conclusions: With increasing use of PrEP and ART in acute infection we anticipate diagnostic challenges using currently available HIV testing strategies. Research and surveillance are needed to determine the most appropriate assays and optimal testing algorithms that are accurate, affordable and sustainable.