TTIMS: Transfusion-Transmissible Infections Monitoring System

Program Overview

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Transfusion
Transmissible
Infections
Monitoring
System

TTIMS: Transfusion-Transmissible Infections Monitoring System

A representative and sustainable system initiated in September 2015, to collect HIV, HCV and HBV incidence and prevalence, risk factors, advanced laboratory measures, and associated demographic variables among US blood donors reflecting approximately 60% of the US blood supply.

- *BPAC December 2015 HIV Recency Discussion*
- *BPAC December 2016 Update*
- *BPAC December 2017 Data Presentation*

Ref: Custer B et al. Transfusion-transmissible infection monitoring system: a tool to monitor changes in blood safety.

Transfusion 2016:56;1499-1502

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TTIMS Structure and Governance

- FDA, NIH/NHLBI, and HHS/OASH funding
  - Donor Database Coordinating Center (DDCC) – Contracted through 2020
  - Laboratory and Risk Factor Coordinating Center (LRCC) – IDIQ Contract through 2021
- Steering Committee
- Executive Committee
- Analysis Workgroups

DDCC - Donation Database Coordinating Center

American Red Cross

Data collection sites:

- American Red Cross
- Vitalant (formerly Blood Systems, Inc.)
- New York Blood Center
- OneBlood

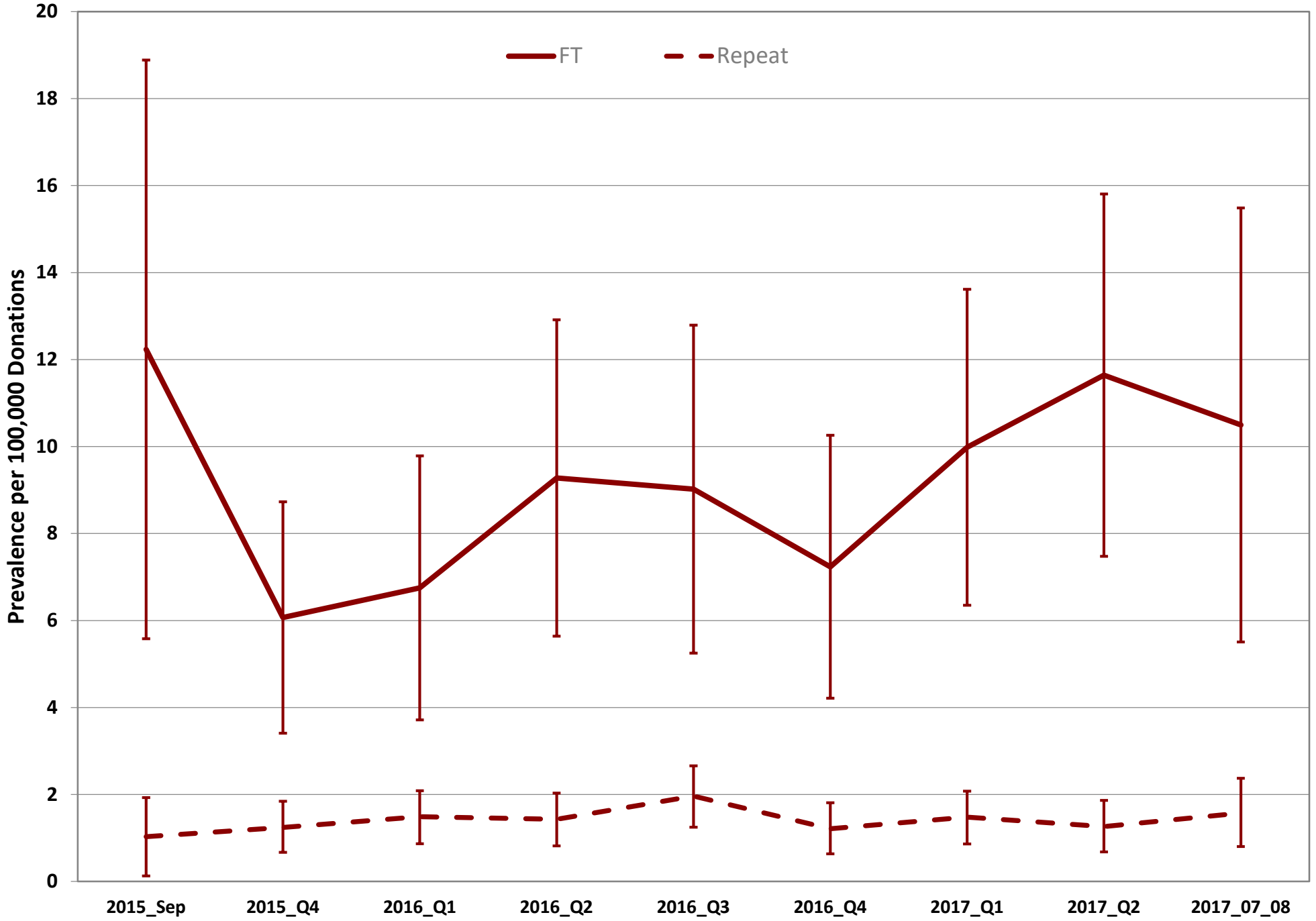
- Creative Testing Solutions (laboratory results)

DDCC Work Scope

- Maintains central database - 60% of US blood supply monitored for HBV, HCV, and HIV markers
  - Consensus test result definitions
  - Validated data exchange
  - Quarterly data analysis
    - Prevalence (donors)
    - Prevalence (donations)
    - Incidence Estimates (NAT yield; repeat donor seroconversion)
    - Residual Risk Estimates (incidence rate x window period (wp)

HIV Consensus Positive Rates per 100k donations with 95% CI by **Donor Status**

First-time
8.8 (7.6-10.0)
Repeat
1.4 (1.2-1.7)



LRCC – Laboratory and Risk Factor Coordinating Center

- Vitalant Research Institute

  Data and samples contributed by:

  Vitalant
  American Red Cross Blood Services
  New York Blood Center
  OneBlood

  Creative Testing Solutions (laboratory results)

LRCC Work Scope

- Risk Factor (RF) Interviews - HIV, HCV (yield), HBV (yield)
- Integrate TTIMS RF data with marker data
- Biospecimen repository
  - HIV, HCV, HBV samples within TTIMS
  - Historical HIV+ samples from TTIMS sites
- Laboratory studies

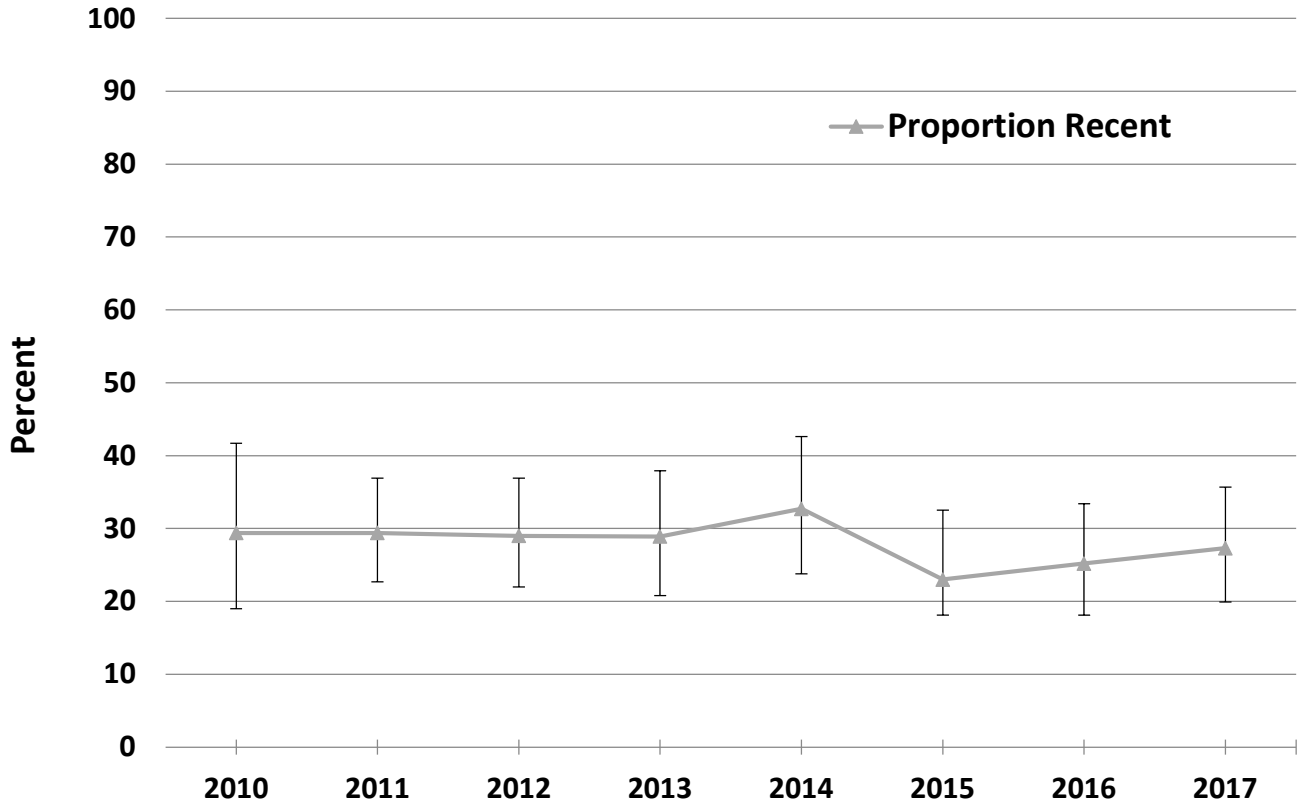
Current TTIMS LRCC Laboratory Research

- Evaluation of donor HIV antibodies using LAg avidity assays capable of characterizing “recent” HIV infection*
  - LAg Avidity testing of stored donor samples to assess performance in blood donation setting
  - Use of recency analysis and modeling to estimate infection incidence in first time (FT) donors increases the power to assess changes in overall donor HIV incidence over time (e.g. pre/post- policy change)

**Persons with recently acquired HIV-1 infections typically exhibit HIV-1 specific IgG populations with higher proportions of lower antigen-binding strength (avidity); those with long-term infections typically have higher IgG avidity. Mean duration of recent infection (MDRI) ~ 130 days. LAg testing may also be available soon for HCV infection.*

TTIMS - LAg Testing Results by Year

Donation Year	Total Tested	Recent n (%)
2010	68	20 (29.4)
2011	170	50 (29.4)
2012	155	45 (29.0)
2013	118	34 (28.9)
2014	104	34 (32.7)
2015*	112	24 (21.4)
2016	136	34 (25.0)
2017	149	41 (27.5)



* Includes period before and during TTIMS

No evidence of significant differences by year – including year following change to 1-year deferral for MSM

LRCC Laboratory Research

- HIV/HCV/HBV genetic sequence analysis of viral isolates (and drug resistance for HIV)

  Genotypes and drug resistance mutations reflect the patterns observed in public health surveillance initiatives in the US general population

TTIMS Accomplishments – EOY 2018

- TTIMS donations database – 23,982,383 (09/15 –12/18)
- Risk interviews
  - All HIV+ 144
  - HCV+ (NAT Yield) 28
  - HBV+ (NAT Yield) 13
  - All Controls 296
- HIV Recency testing – 1,012 (397 w/in TTIMS)

TTIMS Analysis Strategies - 2019

- Major analyses targeted for 2019 to gain two years of data and adequate power to assess prevalence and incidence time trends surrounding the $MSM_{12mo.}$ deferral change:

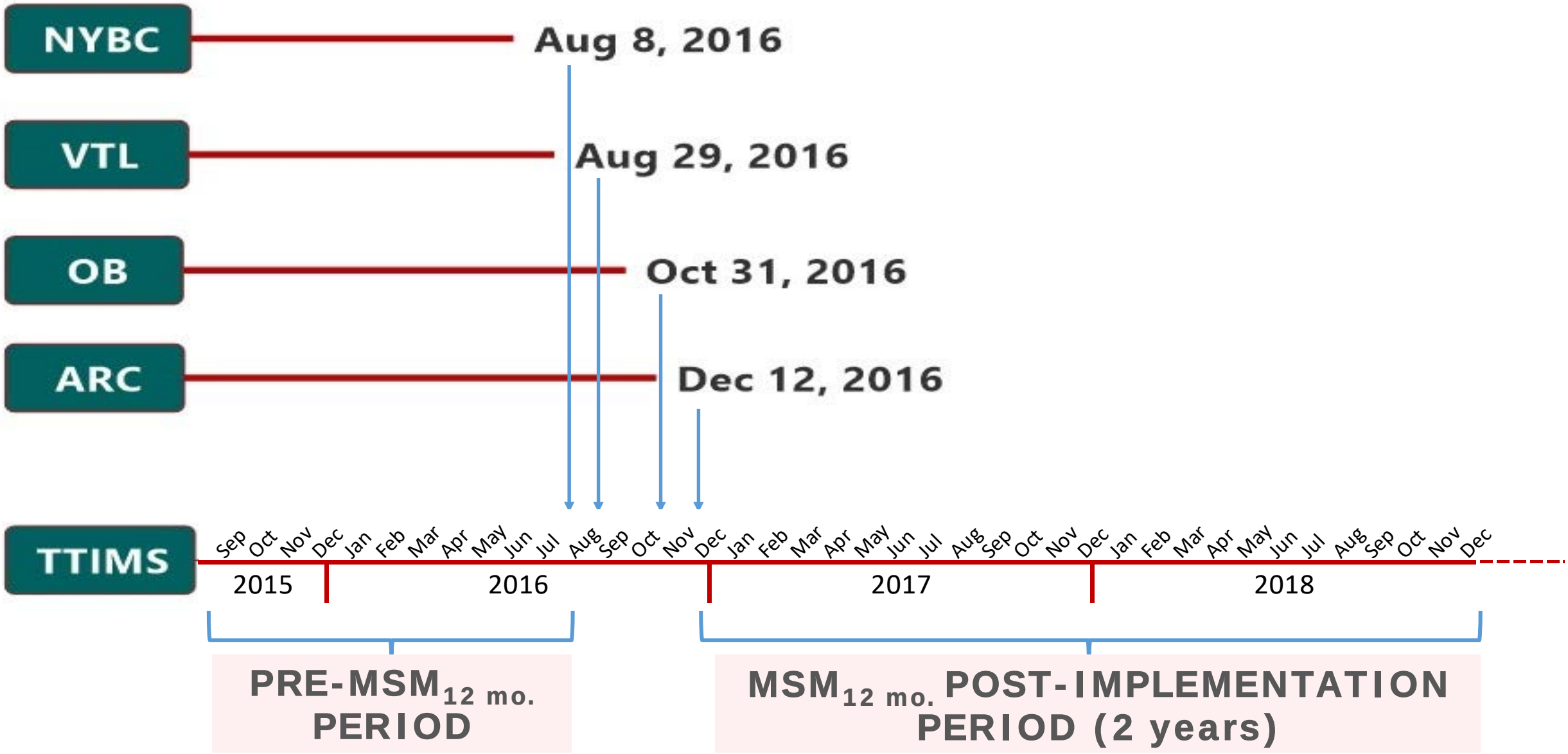
- PRE – $MSM_{12mo.}$

  TTIMS defined TTIMS data available September, 2015 – $MSM_{12\ mo.}$ policy implementation as the blood establishment-specific "pre" period.

- POST – $MSM_{12mo.}$

  TTIMS defined December 31, 2018 as establishing a minimum two year period for donor/donation data collected after blood establishment implementation of $MSM_{12\ mo.}$ policy at TTIMS sites.

Staggered Implementation of $MSM_{12\ mo.}$ at TTIMS Sites



Proposed Analytic Strategies for 2019 Related to $MSM_{12\ mo.}$ Policy Change

- Donation Prevalence by strata (FT/Rpt, Age, Sex, USPH Region)

- Classical Incidence Calculations – Repeat Donors
  - Method 1: Equal "$MSM_{12\ mo.}$ pre-implementation periods" + assumptions
  - Method 2: Modeling to minimize bias related to use of true different policy implementation dates + assumptions

- Estimates of FT HIV+ donors with specified MDRI by LAg Avidity testing
  - Modeling to estimate HIV incidence in First-Time donors

- Donor/Control Risk Interviews (cf: 2004-2009 REDS-II data)

TTIMS New PrEP and ARV Initiatives

Pre-Exposure Prophylaxis (PrEP) for high risk exposures and Anti-Retroviral Therapies (ARV) for HIV infection are highly effective medications. However dosing compliance failures may result in incomplete protection and the theoretical possibility of transmissible HIV infection in blood that may not be detected by current blood establishment screening.

- PrEP use among current donors (collaboration with CDC HIV/AIDS)
  - HPLC study of n=1500 anonymous, but geographically targeted FT male donor samples tested anonymously
- ARV use among HIV+ donors (collaboration with CDC HIV/AIDS)
  - HPLC study of all TTIMS and archived HIV+ blood samples

TTIMS - Overview Summary

- Since its initiation in September, 2015 TTIMS has established a comprehensive and sophisticated monitoring capability for the safety of the US blood supply.

- Major analyses are planned for 2019 to assess prevalence, incidence, and risk factors for HIV, HCV, and HBV infection among both FT and repeat donors and assess time trends that may be associated with policy changes such as $MSM_{12\ mo.}$

- TTIMS has been responsive to contemporary needs for data related to PrEP and ARV use among individuals who attempt to donate blood.

- Data for the specific TTIMS studies described will be presented by the responsible investigators in the coming year

Special thanks to CBER/FDA, NHLBI/NIH, and OASH/HHS for continued TTIMS funding *

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TTIMS Team and Acknowledgements

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- **TTIMS Executive Committee Member**

Staggered Implementation of $MSM_{1\ Year}$ at TTIMS Sites – 508 Addendum for Slide 14

- The TTIMS program began data collection in September, 2015. FDA issued guidance recommending a change in the MSM deferral to 12 months in December, 2015. TTIMS sites implemented the new deferral between August and December, 2016 – resulting in variable periods of TTIMS observational data prior to the policy change. As of December 2018, a full two years of post-policy change data are available for comparative analysis.