

The Transfusion-Transmissible Infections Monitoring System (TTIMS): Donation Database Coordinating Center

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Transfusion
Transmissible
Infections
Monitoring
System

Speaker Notes for Slide #1

Hello my name is Dr. Whitney Steele and I am the Co-PI of the TTIMS Donation Database Coordinating Center. Today I will be presenting on the objectives of the TTIMS DDCC and data on the prevalence and incidence of three transfusion transmissible infections in the blood donor population.

Monitoring of TTIs in the US Blood Supply

- There are many independent blood centers and blood systems in the US
- Therefore, no one blood collector can provide a complete picture of TTI prevalence and incidence rates, and projected risks nationally
- Overall donor infection rates are low, so large datasets are needed to monitor possible trends
- Until recently there was no mechanism for routine, central collection of US blood donor, donation and TTI data
- Such data are essential for monitoring blood safety, and the results of policy changes and evolving collection practices

Speaker Notes for Slide #3

There are many independent blood centers and blood systems in the United States. Because of this no one blood collector is capable of providing a complete picture of transfusion transmitted infection or TTI rates and projected risks nationally. As overall donor infection rates are low, large datasets are needed to monitor possible trends. Until recently there was no mechanism for monitoring risks on a routine basis as there was no centralized on-going collection of data on US blood donors and donations including testing information. These data are essential for monitoring blood safety, the results of policy changes and evolving collection practices.

Objectives of TTIMS: DDCC

- Monitor HBV, HCV and HIV in US blood donors by developing and maintaining a complete database including data from participating blood centers representing nearly 60% of the US blood supply
 - Develop consensus definitions for concordant positives and NAT yields
 - Daily data exports, QC, data sharing, identification of key units for LRCC
- Perform relevant data analyses; report results
 - Prevalence
 - By sex, donation status, age, self-reported race/ethnicity, DHHS reporting region
 - Incidence and Residual Risk

Speaker Notes for Slide #5

The objectives of the DDCC fall into 2 main categories – collect and maintain high quality data and analyze the data to provide reliable nation estimates.

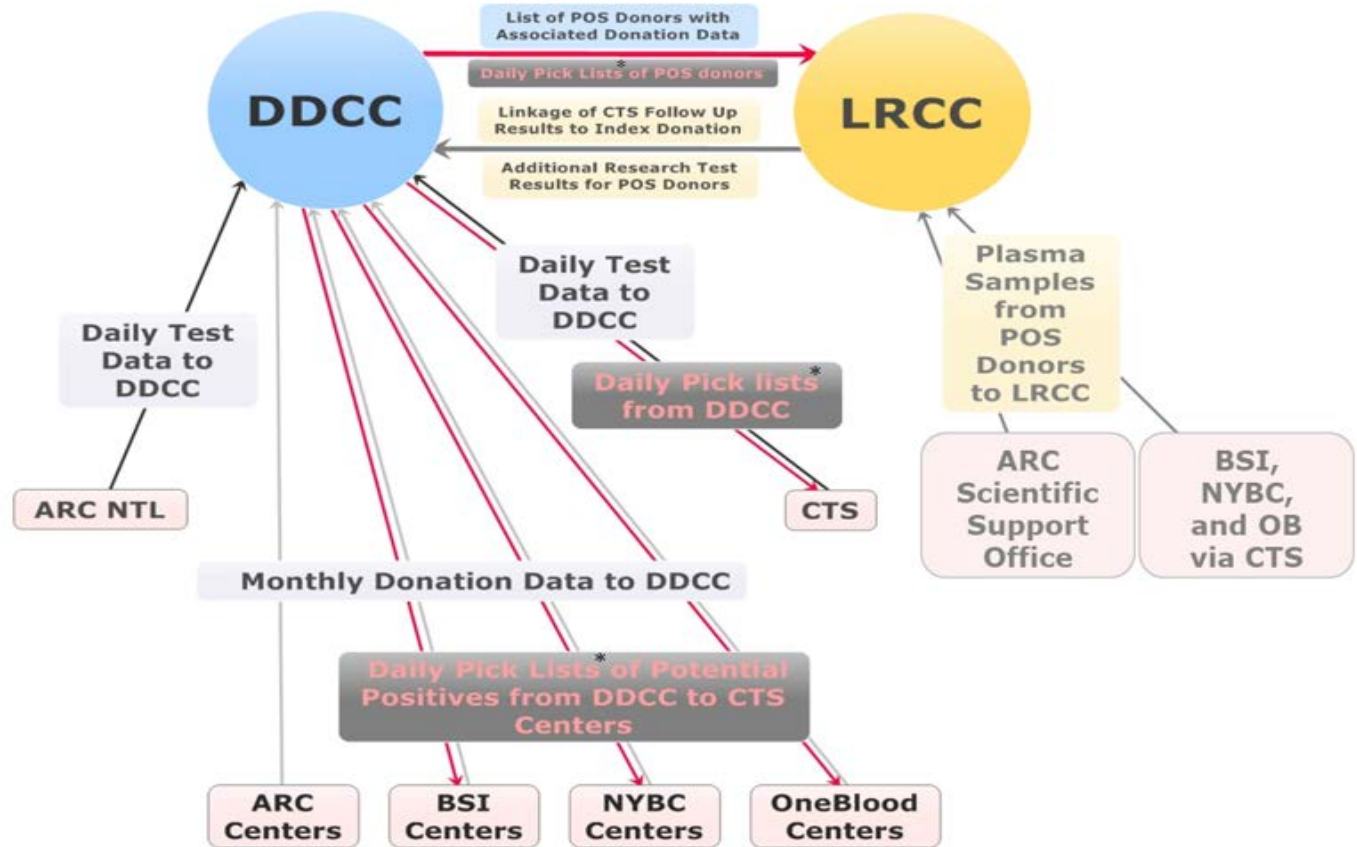
More specifically the DDCC monitors HBV, HCV and HIV in US blood donor by developing and maintaining a database that includes information on nearly 60% of the blood supply.

To do this it was essential to develop consensus positive definitions that could be used across all participating blood systems.

In addition the DDCC was charged with developing daily data exports, quality control processes and facilitating the work of the LRCC.

The DDCC also performs relevant data analyses and reports results to stakeholders. This includes calculation of prevalence by categories of interest and calculating incidence by various methods as well as residual risk.

TTIMS Data File and Sample Transfers



* Potential positive units for retention are reported in Pick Lists

Methods

- Prevalence and incidence rates calculated for the first 24 months of TTIMS data collection
- Incident donor = repeat donor with a positive donation and a preceding negative donation within the 2-year interval of interest
- Incidence rate is the number of incident donors ÷ total person-time accumulated within the interval (by repeat donors with at least 2 donations in the interval)

positives among repeat donors

Total time at risk (person-years)



½ of the person years of incident donors + All person years of negative repeat donors

- Residual Risk = Incidence Rate * Window Period

Speaker Notes for Slide #8

Prevalence and incidence rates were calculated for the first 2 years of TTIMS data

Prevalence is presented here for donations

For TTIMS to be considered incident, a donor must have a negative tested donation followed by a positive donation within the two-year interval

Incidence density is calculated using the traditional formula shown here of the number of incident donors divided by the total person time at risk.

The residual risk was calculated using the window period method, which is the incidence rate multiplied by the window period.

DDCC: Consensus Positive Definitions

Marker	Confirmed NAT-Yield	Concordant NAT/Serology
HIV	RNA (dHIV positive) + RNA confirmed (independent sample) and/or Ab seroconversion	Ab repeat reactive + RNA (dHIV)
		HIV controllers (NAT neg)*
HCV	RNA (dHCV positive) + RNA confirmed (independent sample) and/or Ab seroconversion	Ab RR + RNA (dHCV)
HBV	DNA (dHBV positive) + DNA confirmed (independent sample) and/or Ag/Ab seroconversion	Ag RR+ DNA (dHBV) Ag RR + Ab RR + DNA (dHBV) Ab RR + DNA (dHBV)

*Confirmed by subsequent testing of an independent sample as HIV-1 Ab positive & HIV NAT reactive in at least one replicate of 10x testing

Speaker Notes for Slide #10

One of the important first aspects of TTIMS was to build consensus positive definitions for each agent.

For each marker donors are considered consensus positive if they are either confirmed NAT-yield or have concordant serology and nucleic acid reactivity.

Confirmed NAT yields are serology negative and discriminatory NAT reactive on an independent sample

Concordant NAT/Serology positives are repeat reactive on serology and discriminatory NAT reactive.

In addition, HIV consensus positives also include HIV controllers. True HIV Controllers suppress their HIV infection in such a way that very little RNA is present. To confirm them their Antibody reactivity is retested and 10x NAT panel testing is used to ensure that RNA is present in at least one replicate.

DDCC: 4 Centers of Donations for 24 Months

TTIMS – Sep 2015 - Aug 2017

Year	ARC	BSI	NYBC	OB	All Centers
Total by Center	9,683,685	1,889,756	748,546	1,608,307	13,930,294
Percent by Center	69.5%	13.6%	5.4%	11.5%	100.0%

Speaker Notes for Slide #12

The data presented here are from the first 24 months of TTIMS. The TTIMS database contains testing and demographic information on nearly 14 million donations from 4 major US blood systems. The American Red Cross, Blood Systems, New York Blood Center and OneBlood. All 4 together represent more than 60% of the blood supply.

Overall Consensus Positive Rates

HIV, HBV and HCV prevalence per 100k donations with 95% CI

Sept 2015 - Aug 2017

Consensus Positive Rate (NAT Yield + Concordant Positive)*

	Positives	Rate/100k	95% CI
HIV	365	2.6	(2.4 - 2.9)
HBV	912	6.5	(6.1 - 7.0)
HCV	2,762	19.8	(19.1 - 20.6)

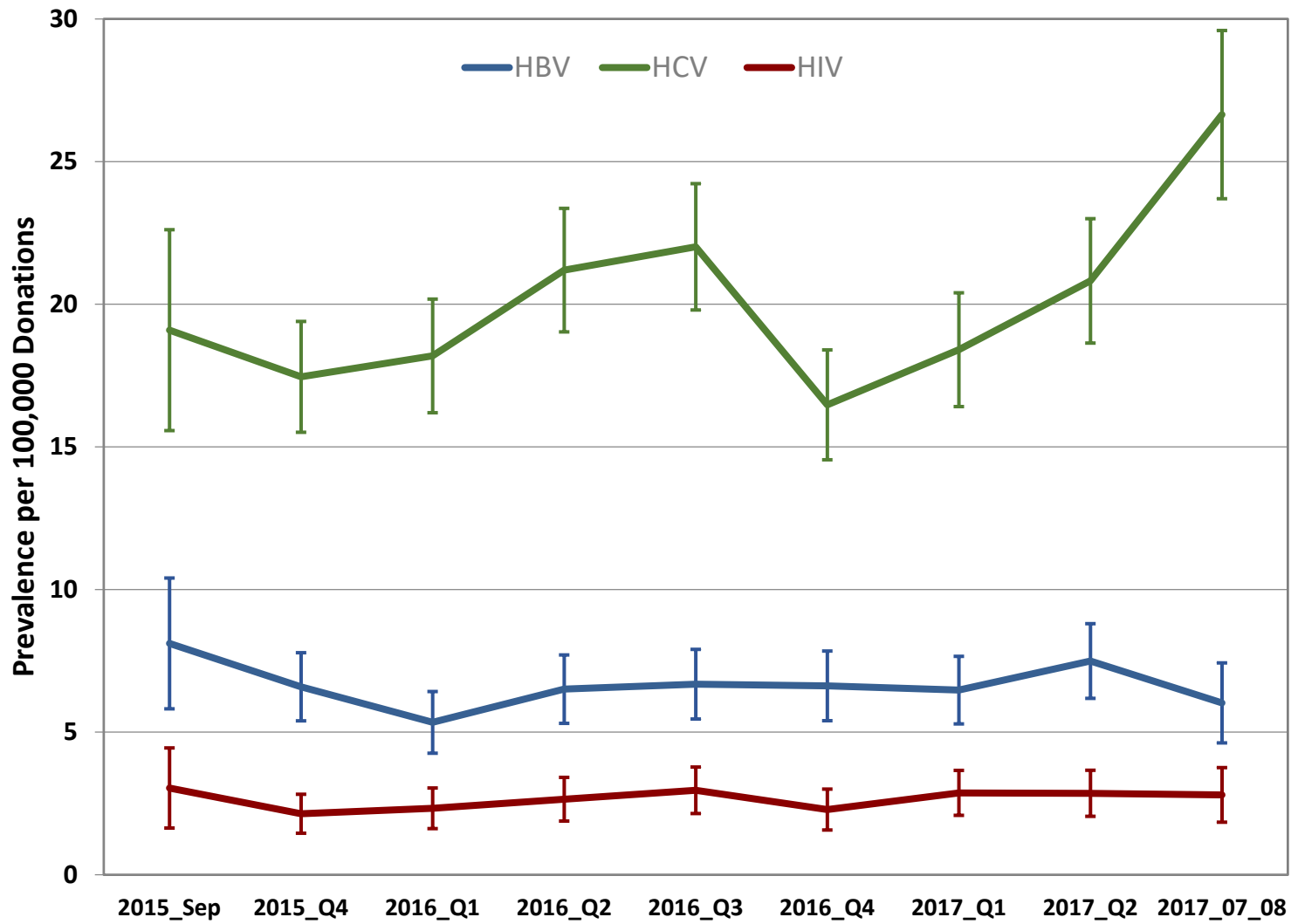
*HIV Consensus Positives include HIV Controllers

Speaker Notes for Slide #14

The overall prevalence rates for each agent are shown here and are presented per 100k donations. The number of consensus positives includes both NAT yield positive and serology plus NAT reactive samples. There were 365 HIV positives which includes the few identified HIV controllers for a rate of 2.6 per 100k, 912 HBV positives for a rate of 6.5 per 100k and 2,762 HCV consensus positives for a prevalence rate of approximately 20 per 100K donation.

**Overall
Consensus
Positive Rates
per 100k
donations with
95% CI**

HIV
2.6 (2.4 - 2.9)
HBV
6.5 (6.1 - 7.0)
HCV
19.8 (19.1-20.6)



Consensus Positive Rates by Sex

HIV, HBV and HCV prevalence per 100k donations with 95% CI

Sept 2015 – Aug 2017

Number of Positives and Prevalence Rates				
		Positives	Rate/100k	95% CI
HIV	Male	296	4.0	(3.5 – 4.4)
	Female	69	1.1	(0.8-1.3)
HBV	Male	651	8.8	(8.1-9.4)
	Female	261	4.0	(3.5-4.5)
HCV	Male	1808	24.3	(23.2-25.4)
	Female	954	14.7	(13.8-15.6)

53.4% Male donations / 46.6% Female donations

Speaker Notes for Slide #17

Overall 53% of the donations in the database are from males and 47% are from females.

The prevalence of all markers is higher in males than females.

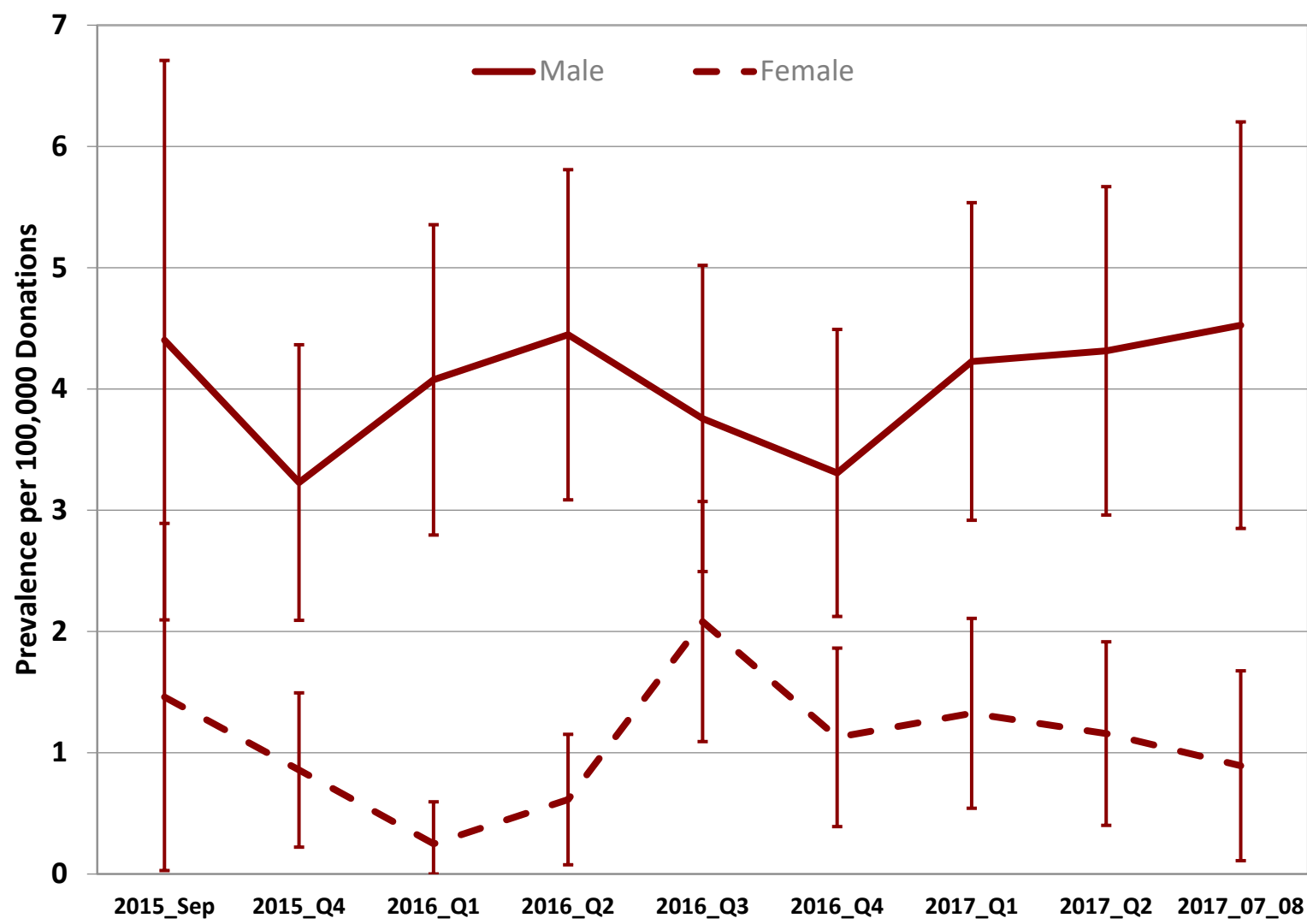
The Prevalence of HIV in males is 4 per 100k donations compared to 1 in females.

The prevalence rate of HBV of nearly 9 per 100k in males is more than twice that of females

The prevalence rate of HCV in males of 24 is greater than that of 15 in the female donations.

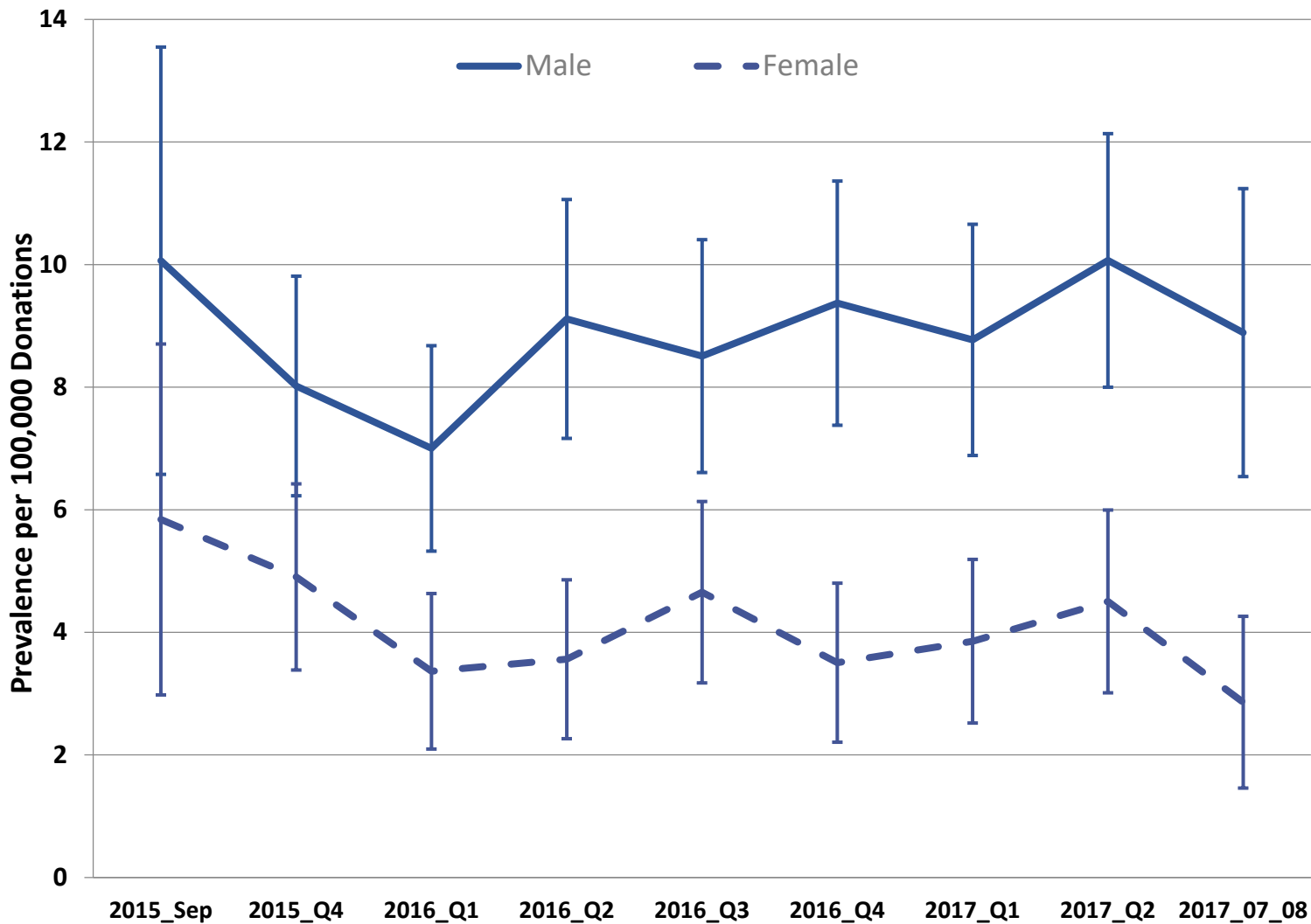
HIV Consensus Positive Rates per 100k Donations with 95% CI by Sex

Male
4.0 (3.5 – 4.4)
Female
1.1 (0.8 - 1.3)



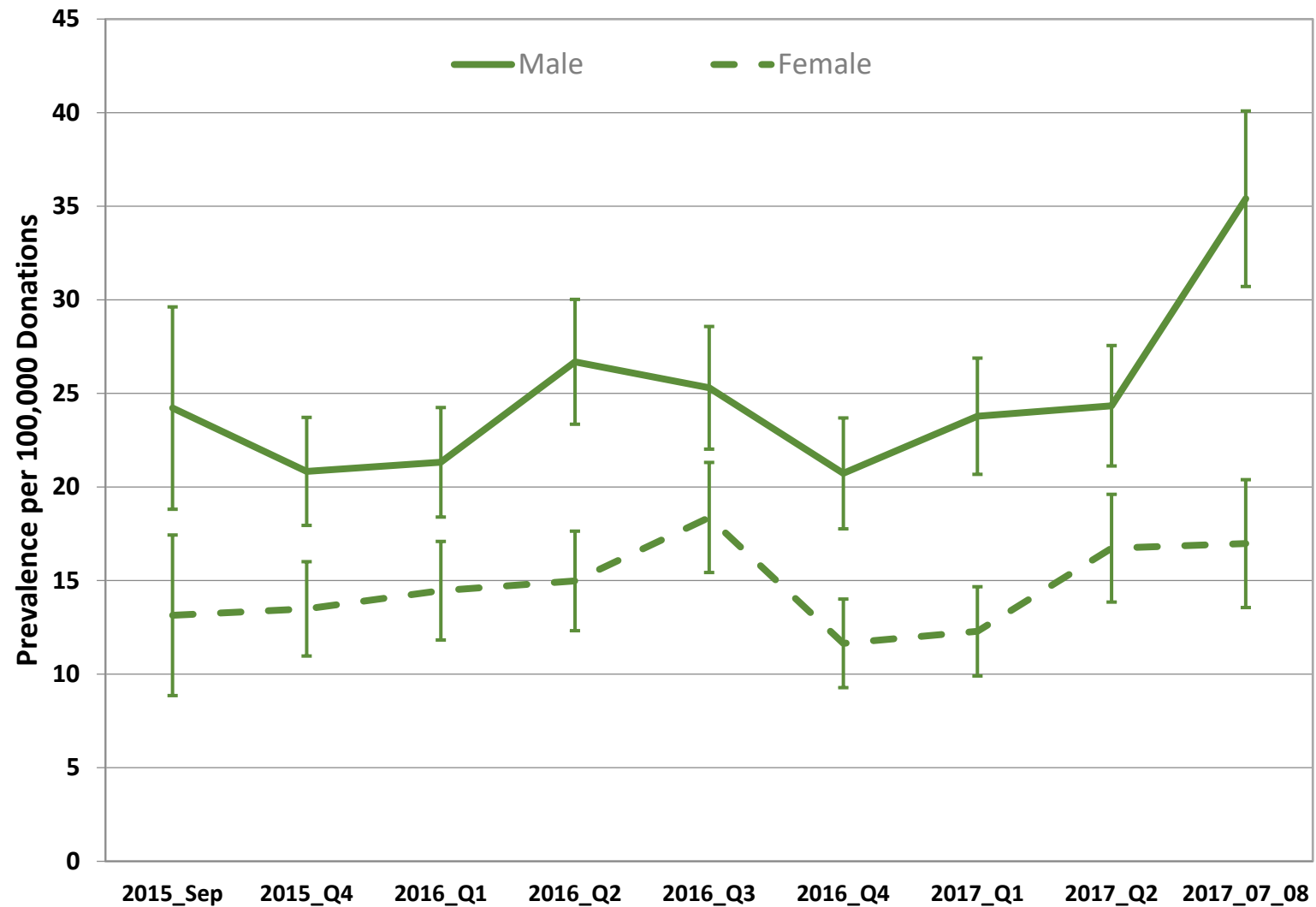
HBV
Consensus
Positive Rates
per 100k
Donations with
95% CI by
Sex

Male
8.8 (8.1 – 9.4)
Female
4.0 (3.5 - 4.5)



HCV
Consensus
Positive Rates
per 100k
Donations with
95% CI by
Sex

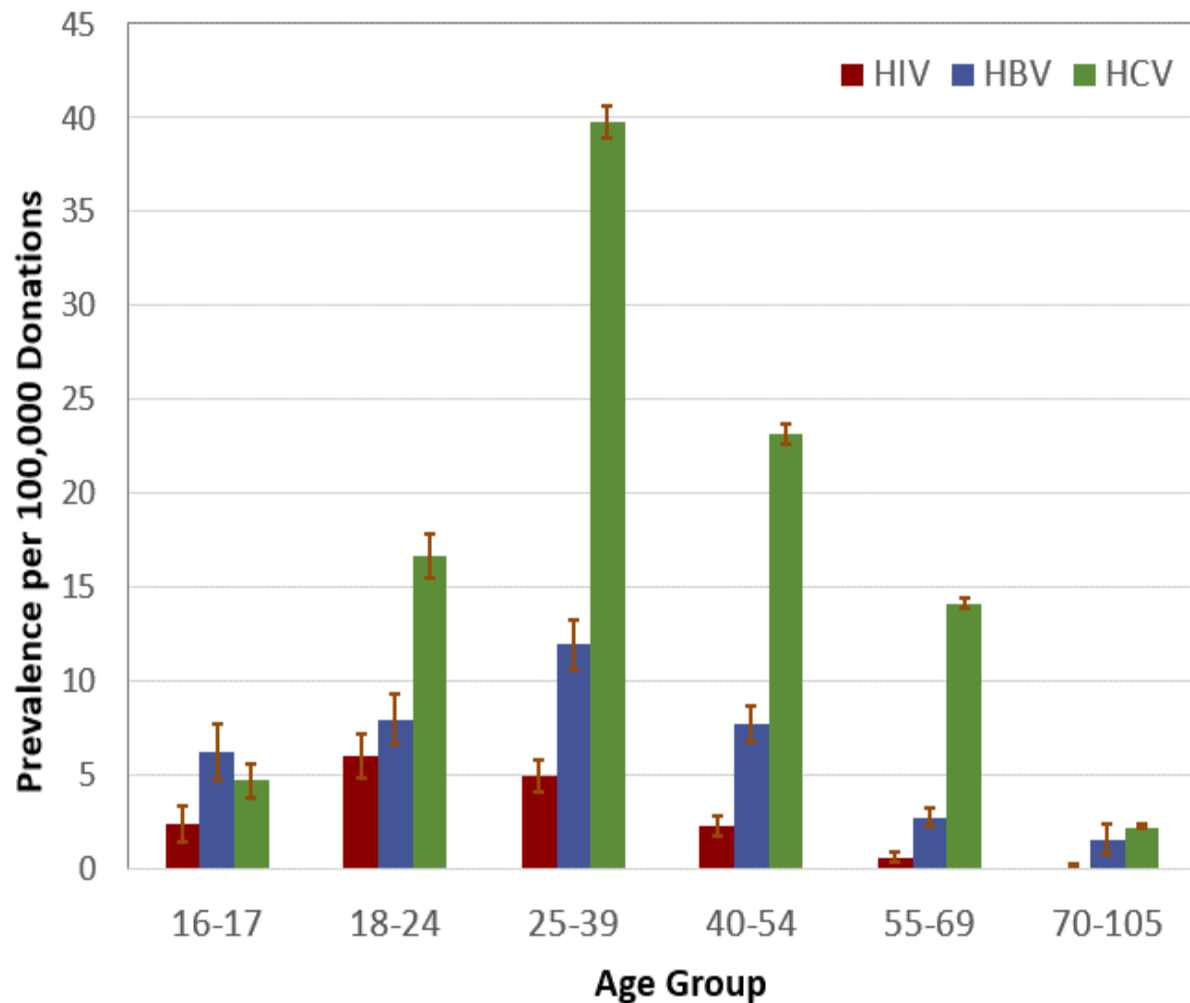
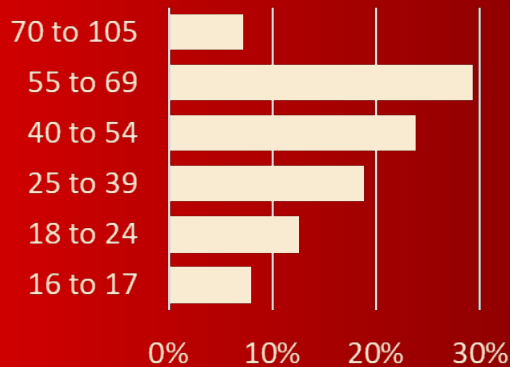
Male
24.3 (23.2 – 25.4)
Female
14.7 (13.8 – 15.6)



Consensus Positive Rates by Age in Years

HIV, HBV, and HCV prevalence per 100k donations with 95% CI
Sept 2015 – Aug 2017

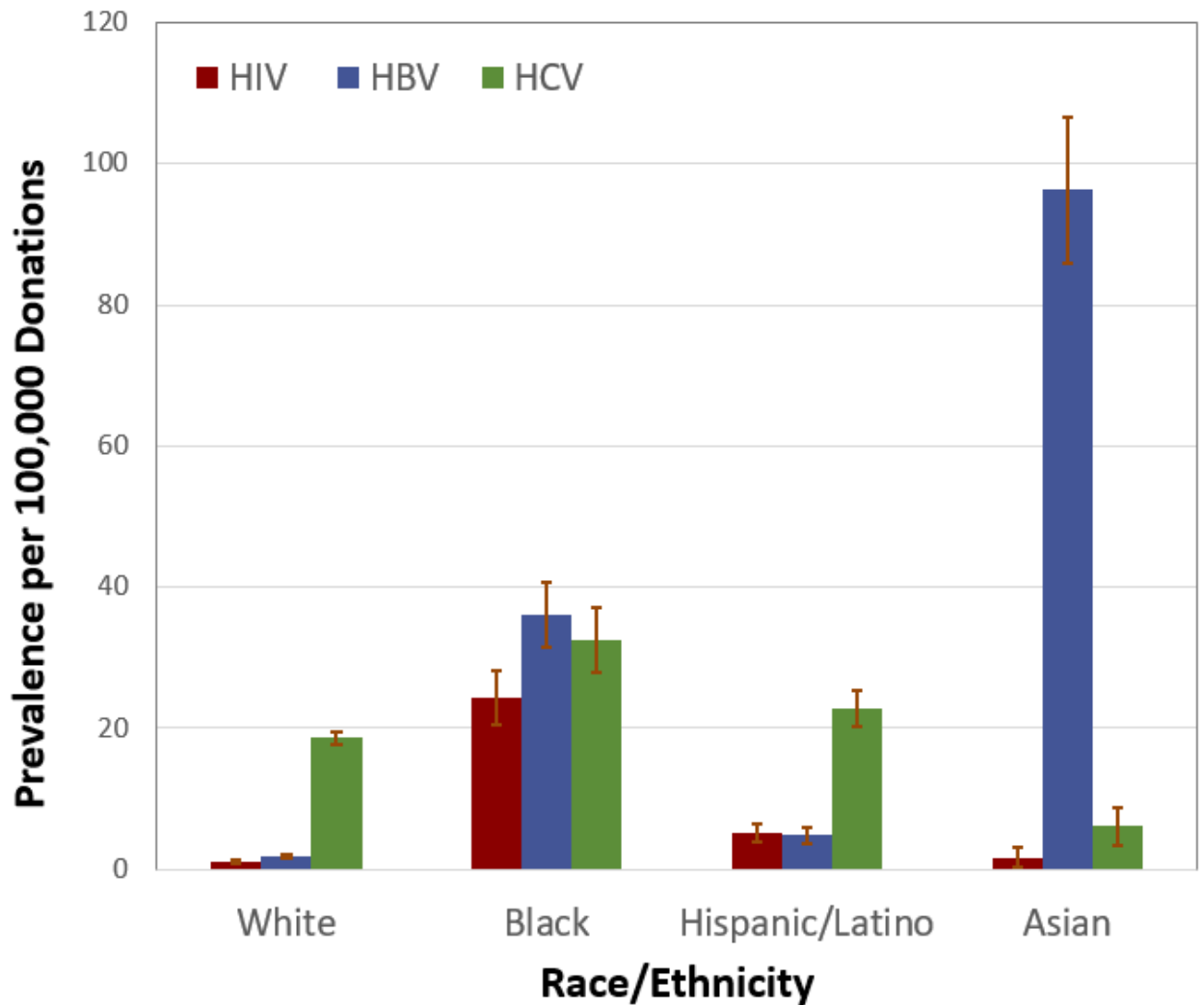
% Donations by Age in Years



Consensus Positive Rates By Race/Ethnicity

HIV, HBV and HCV
Prevalence per 100k
donations with 95% CI
Sept 2015 - Aug 2017

White	80.2%
Hispanic/Latino	9.3%
Black	4.4%
Asian	2.5%



Consensus Positive Rates by Donor Status

HIV, HBV and HCV prevalence per 100k donations with 95% CI

Sept 2015 – Aug 2017

Number of Positives and Prevalence Rates				
		Positives	Rate/100k	95% CI
HIV	First-time	197	8.8	(7.6 -10.0)
	Repeat	168	1.4	(1.2 -1.7)
HBV	First-time	803	35.8	(33.3 - 38.2)
	Repeat	109	0.9	(0.8 - 1.1)
HCV	First-time	2285	101.8	(97.6 – 106.0)
	Repeat	477	4.1	(3.7 - 4.5)

13.9 million total donations

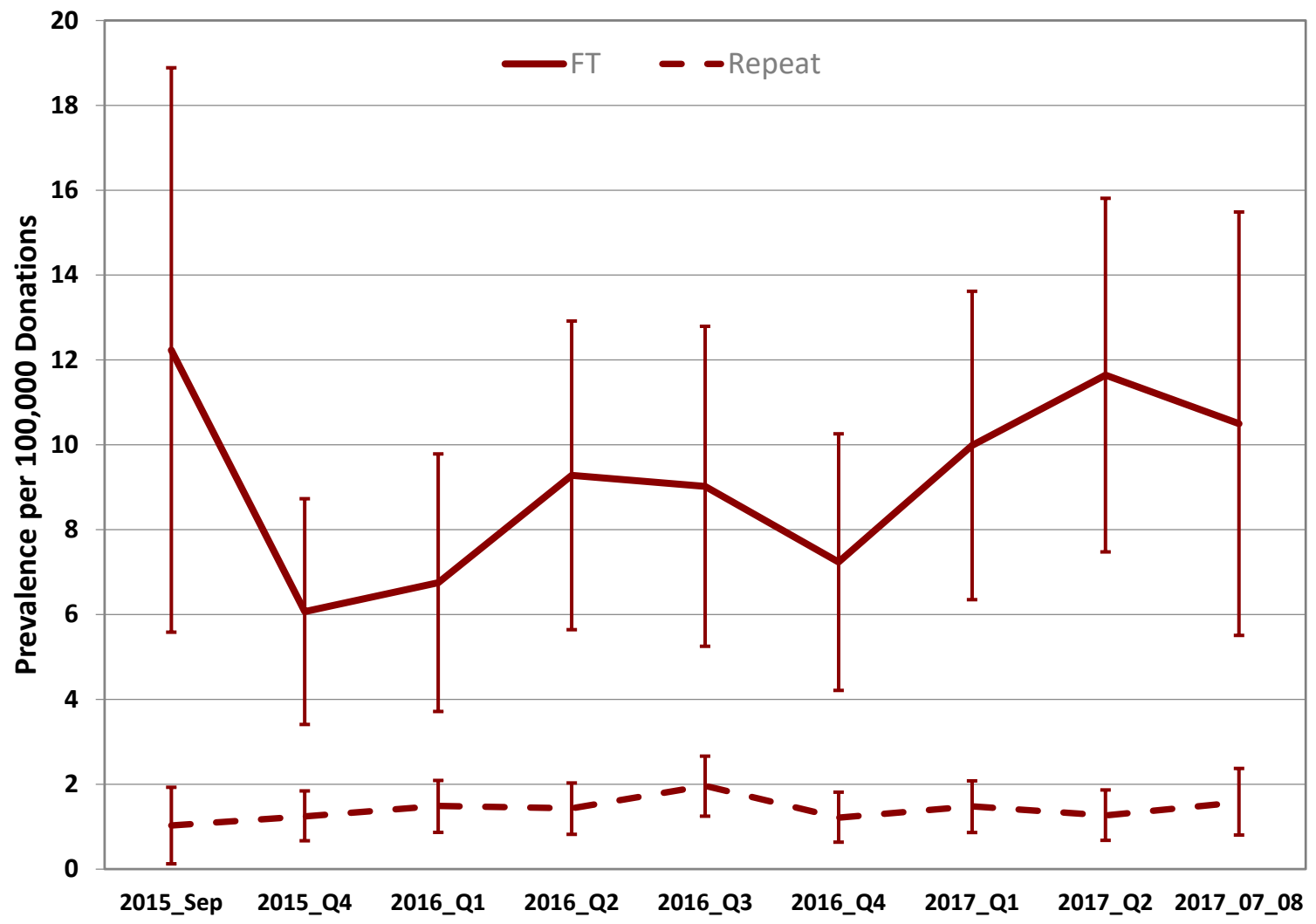
16.1% First-time donations / 83.9% Repeat donations

Speaker Notes for Slide #24

- The majority of donations are from repeat donors – 84% with 16% from first time donors.
- The Prevalence of HIV in First-time donations is 6 times that in Repeat donations
- The Prevalence of HBV in First-time donations is approximately 40 times that in Repeat donations
- The prevalence of HCV in first-time donations is 25 times higher than that in repeat

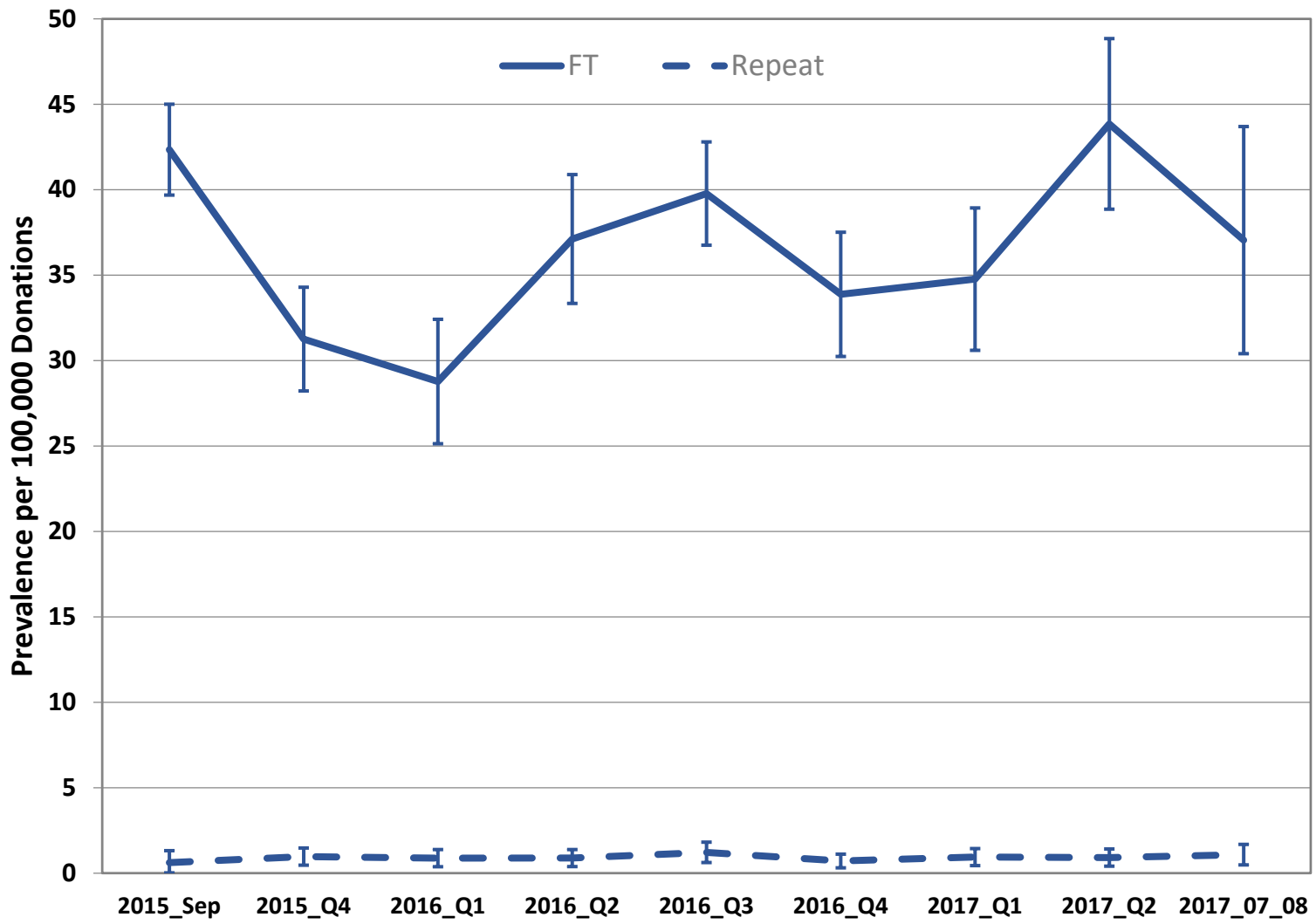
HIV
Consensus
Positive Rates
per 100k
donations
with 95% CI
by
Donor Status

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



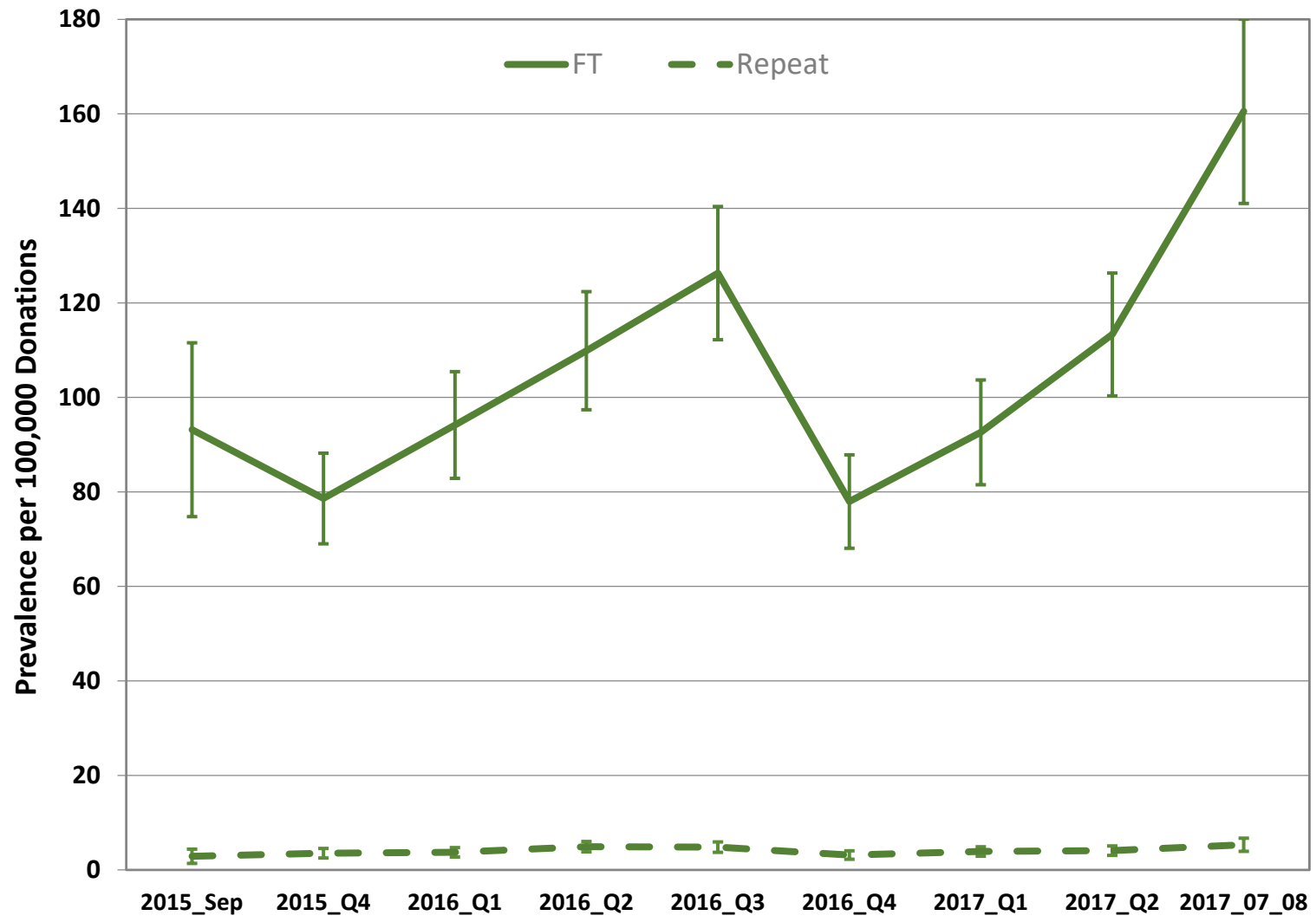
HBV
Consensus
Positive Rates
per 100k
donations
with 95% CI
by
Donor Status

First-Time
35.8 (33.3 – 38.2)
Repeat
0.9 (0.8 - 1.1)



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

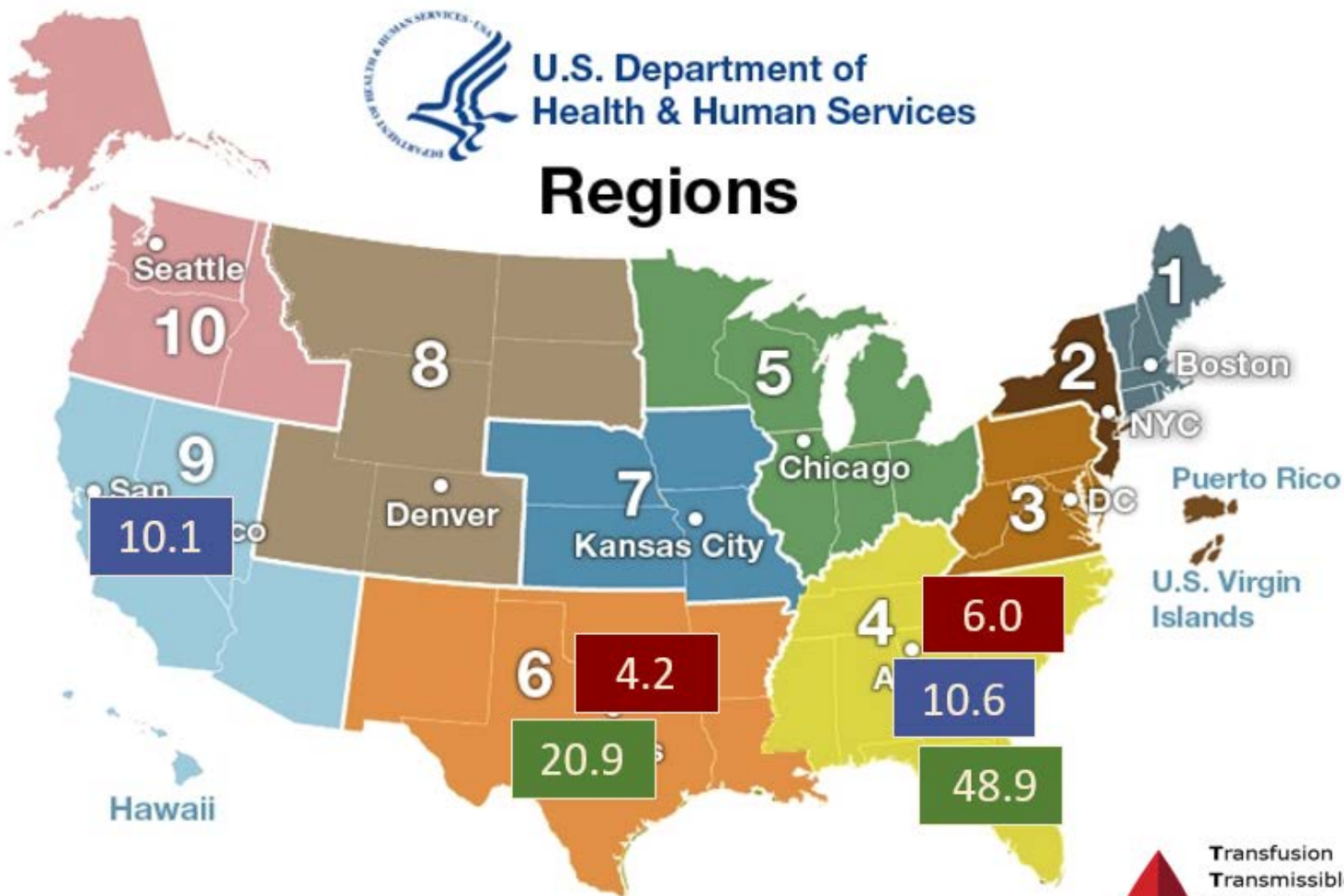
First-time
101.8 (97.6-106.0)
Repeat
4.1 (3.7-4.5)





U.S. Department of Health & Human Services

Regions



Highest
 Consensus
 Positive Rates
 per 100k
 donations
 by
DHHS Region*

* Cities shown
 indicate DHHS
 Regional Offices

HIV

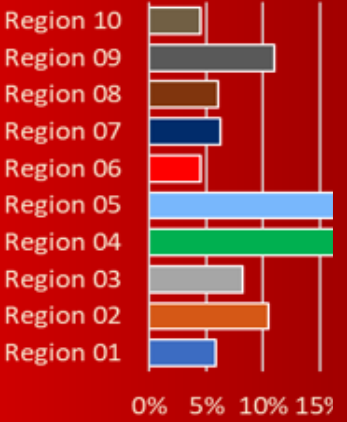
HBV

HCV

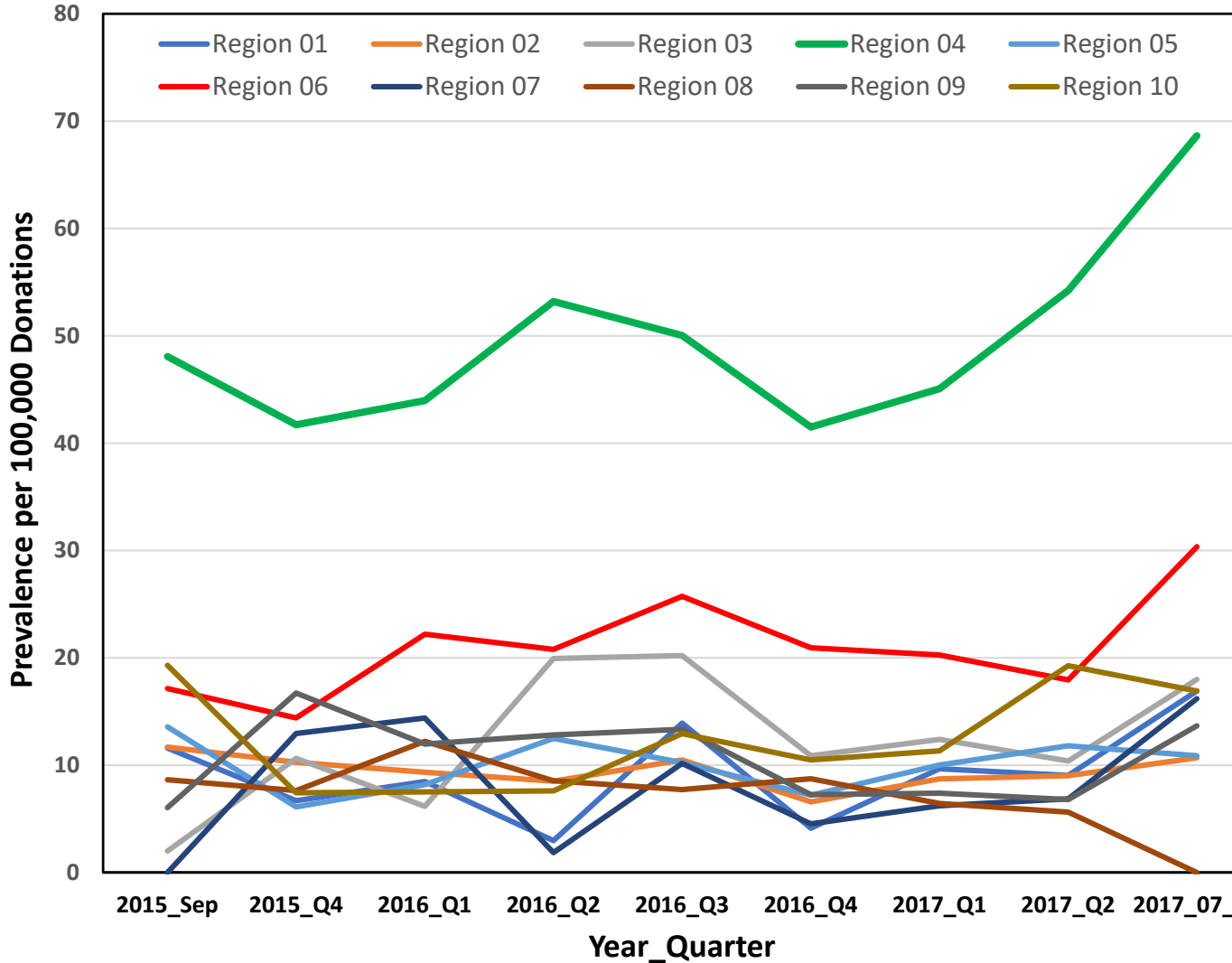


HCV Overall Consensus Positive Rates by DHHS Region

% Donations by Region



Quarterly Donations by Region, Sept 2015 – Aug 2017

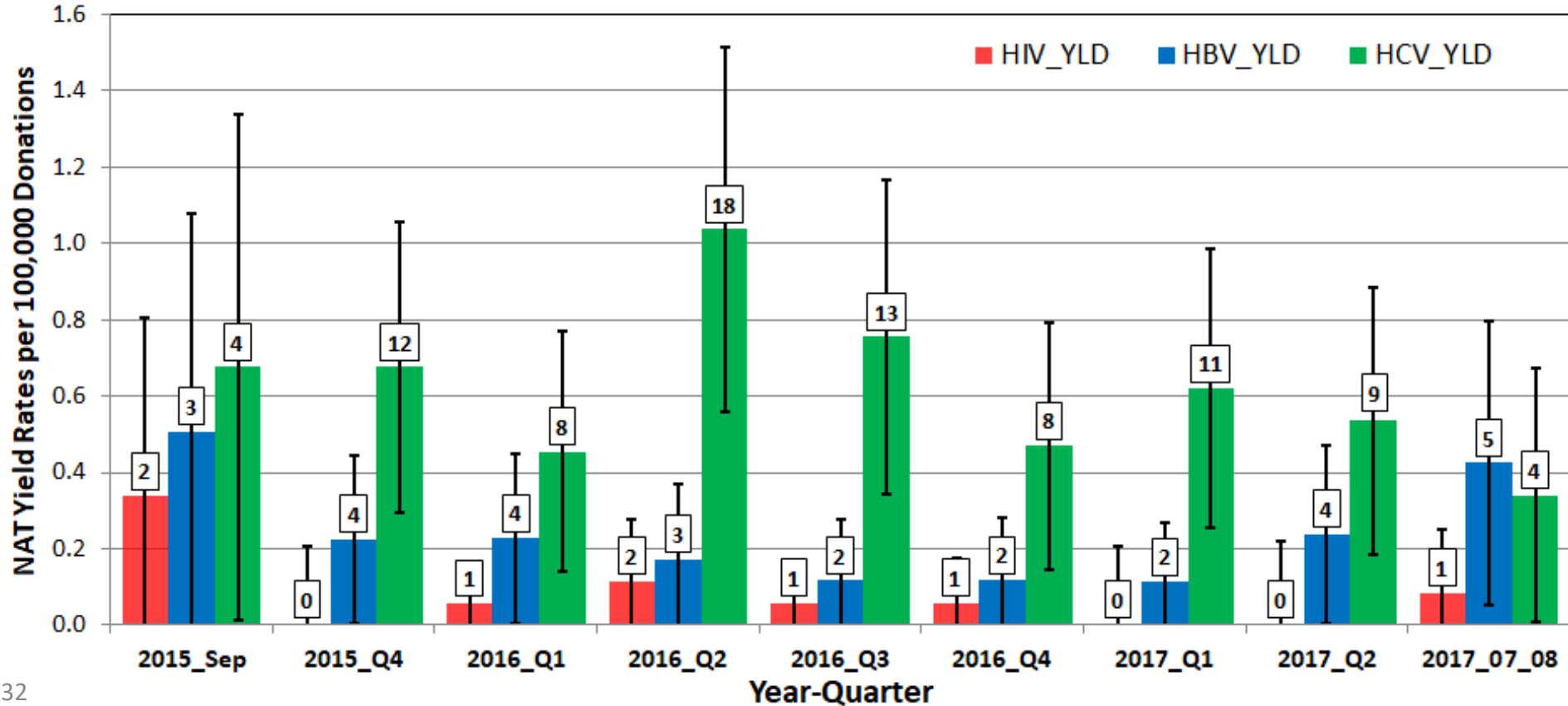


Incidence and Residual Risk

- TTIMS plans to monitor incidence in multiple ways
 - Incidence density using seroconverting repeat donors
 - relies on having complete data for a certain period (24 months for TTIMS)
 - NAT Yield as a proxy
 - Recency testing as part of the LRCC activities
- Residual Risk (window period x incidence)

NAT Yield Rates by Quarter

HIV, HBV and HCV yield prevalence per 100k donations with 95% CI



Incidence Rates for HIV, HBV and HCV

Sept 2015 – Aug 2017

	Number of Incident Cases	Incidence /100,000 PY (95% CI)	Window Period	Residual Risk
HIV	59	2.1 (1.6 – 2.7)	9.1 days	1 : 1,896,914
HBV	24	0.9 (0.5 – 1.2)	18.5 days	1 : 2,291,522
HCV	52	1.9 (1.4 – 2.4)	7.4 days	1 : 2,646,234

Speaker Notes for Slide #33

These are the incidence rates for HIV, HBV and HCV. Incidence density rates are only calculated using repeat donors that have 2 or more tested donations in the period of study. Only a fraction of repeat positive donors met these conditions - 34% of HIV repeat positives were considered incident, 22% of HBV repeat positives were incident and only 10% of HCV repeat positives. HIV incidence was 2.1 per 100,000 person years, HBV was 1 per 100,000 person year and HCV was 1.9 per 100,000 person years.

For residual risk the window periods used are shown on the slide reflecting the periods associated with the testing in use at all centers. The residual risk for HIV was 1 in 1.9 million, for HBV 1 in 2.3 million and for HCV 1 in 2.6 million.

This is due to a large number of the consensus positive repeat donors not meeting the requirement of having a prior donation during the 24 month TTIMS study period as outlined previously i.e. 2 tested donations between September 2015 and August 2017.

HIV – 59 Inc/168 Rpt Pos = 34.5%

HBV – 24 Inc/109 Rpt Pos = 22.0%

HCV – 52 Inc/477 Rpt Pos = 10.9%

Summary – Fulfilling the Objectives of TTIMS: Monitoring

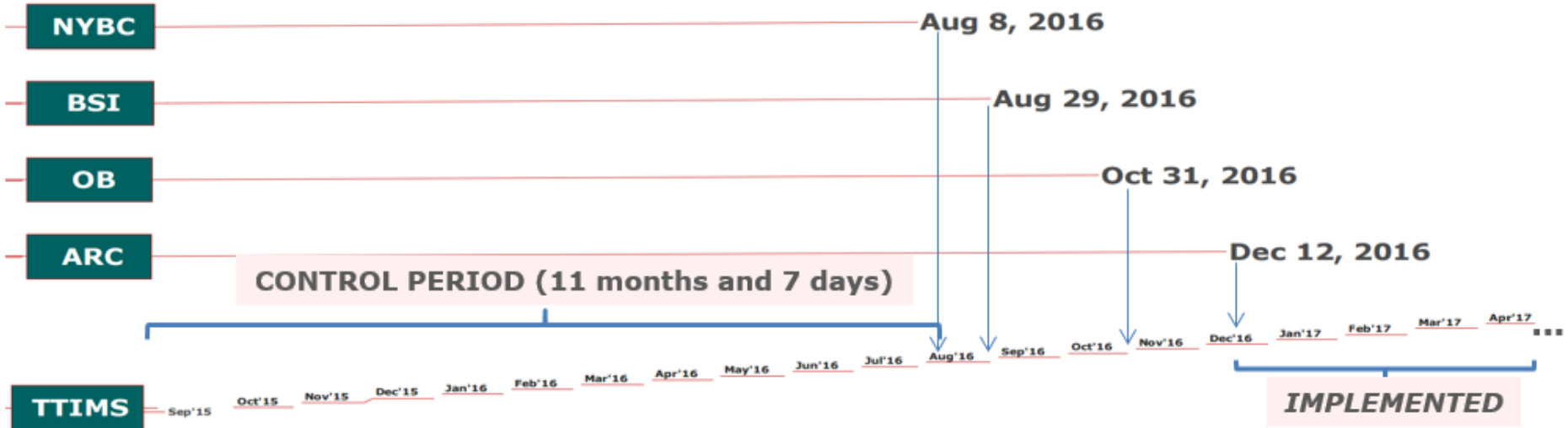
- The DDCC portion of TTIMS has established the capacity to monitor infection prevalence in ~60% of US blood donations using data from 4 major blood systems
 - Developed Consensus Positive definitions used across all systems
 - Established processes for secure data transfer, quality control and identification of positive units
 - Developed analysis programs to generate routine quarterly and annual monitoring reports
 - Analyzed and reported on 24 months of tracking including ~14 million donations

Summary – Fulfilling the Objectives of TTIMS: Analysis of Prevalence and Incidence

- Prevalence rates are very low among donations from US blood donors ranging from 2.6 per 100k (HIV) to 19.8 per 100k (HCV); highest in donations from:
 - First-time donations (4-35x higher than repeat donations)
 - Males (2-4x times higher than females)
 - HCV- and HIV-positive donors from the SE and SC (especially for HCV where rates in the SE are 49 per 100k)
 - HBV-positive Asian donors and for HBV in the SE and West (10 per 100k each)
 - Younger donors, especially for HIV and HBV (18-39 year-olds)
 - Only significant trend to date is increase in HCV prevalence in donations collected in the SE/SC US (particularly from FT, male donors); risk factor analyses will investigate risks for HCV-yield donors
- Incidence rates are low compared to historic rates with corresponding residual risks of between 1 in 1.9 million (HIV) to 1 in 2.6 million (HCV)

Summary – Fulfilling the Objectives of TTIMS: Policy Changes

- While data from the TTIMS DDCC can be used to look at changes in infection rates in response to changes in policy, it is important to keep in mind that:
 - A relatively large change in infection rates would be needed for statistical significance
 - Changes in rates are also influenced by collection practices (e.g. impact of the current focus on “right type” of donors), shifts in donor demographics and the epidemiology of the disease in the general population
- For example, once sufficient data are available, TTIMS could evaluate TTI prevalence and incidence before and after participating blood systems implemented the MSM 77 → MSM 1 change



Thank You!



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