50th Meeting

HHS Advisory Committee on Blood & Tissue Safety & Availability

April 15-16, 2019

Hubert H. Humphrey Building | Washington, DC

Welcome

Jacquelyn Fredrick, PhD (Chair)
Retired CEO
Versiti, Inc.

Emily A. Blumberg, MD, FACP (Vice-Chair)
Director, Transplant Infectious Diseases
Hospital of the University of Pennsylvania

Advisory Committee for Blood and Tissue Safety and Availability (ACBTSA)

Established in September of 1997 by Executive Order to provide the Secretary of HHS with advice, information, and recommendations on policies and programs related to blood and tissue safety and availability.

OBJECTIVES AND SCOPE OF ACTIVITIES: The Secretary is responsible for issuing and enforcing regulations concerning the collection, preparation, and distribution of blood, blood products, tissues and organs; for issuing and enforcing regulations related to the transmission of communicable diseases; and for carrying out research in health fields including diseases involving these products.

The ACBTSA will advise, assist, consult with, and make policy recommendations to the Secretary, through the Assistant Secretary for Health, regarding these broad responsibilities related to the safety of blood, blood products, tissues and organs as further delineated under Description of Duties. For solid organs and blood stem cells, the Committee's work will be limited to policy issues related to donor derived infectious disease complications of transplantation.

Learn more: https://www.hhs.gov/ohaidp/initiatives/blood-tissue-safety/index.html

FDA/BPAC UPDATE

Carlos H. Villa, MD, PhD
Medical Officer
CRS/DBCD/OBRR/CBER/FDA

120th Meeting of the Blood Products Advisory Committee

U.S. Food and Drug Administration
Center for Biologics Evaluation and Research
Silver Spring, MD
March 20-21, 2019

Carlos H. Villa, MD PhD
Medical Officer
Division of Blood Components and Devices
Office of Blood Research and Review

Topics for Discussion

- **Topic I:** Evaluation of strategies to reduce the risk of Zika Virus (ZIKV) transmission by blood and blood components
- **Topic II:** Review of intramural research programs
- **Topic III:** Blood donation policies regarding men who have sex with men (MSM)

Topic I: Evaluation of strategies to reduce the risk of Zika Virus (ZIKV) transmission by blood and blood components

- Introduction to the topic
- Update on the current status of the ZIKV epidemic
- AABB ZIKV Biovigilance Network
- Current Considerations for Reducing the Risk of Transfusion Transmitted ZIKV
- Open Public Hearing / Committee Discussion

Summary of Topic I

- Current FDA guidance (July 2018) recommends universal ZIKV testing for blood donations by nucleic acid testing (minipool or individual donation)
- Large declines in ZIKV disease cases and confirmed ZIKV positive blood donors from 2016 to 2018
- FDA is re-evaluating July 2018 recommendations

Committee Discussion of Topic I

- Committee supported continuing the current strategy of universal testing by minipool or individual donation testing
- Committee felt that additional information and continued surveillance are needed before implementing further policy change

Question 1

- At this time, do the available data support continuing universal testing for ZIKV using MP or ID NAT as recommended in the July 2018 Final Guidance (no policy change at this time)?
  - 11 yes, 4 no

Question 2

- Do the available data support a regional testing option strategy for ZIKV using MP or ID NAT in at-risk U.S. states and territories?
  - 6 yes, 9 no

Question 3

- Do the available data support the elimination of all testing for ZIKV without re-introduction of donor screening for risk factors (e.g. travel) in areas with no risk of ZIKV infection, pending another outbreak in the United States?
  - 14 no, 1 yes

Topic III: Blood Donation Policies Regarding Men Who Have Sex with Men (MSM)

IIIA: Update on Donor Deferral Policies and Donor HIV Risk Questionnaire Study

IIIB: Pathogen Reduction of Platelet Donations as an Alternative Procedure to MSM Donor Deferral

Topic IIIA: Update on Donor Deferral Policies and Donor HIV Risk Questionnaire Study

- Blood Donation Policies Regarding MSM
- International Perspectives on Blood Donor Eligibility in MSM Donors
- Epidemiology of HIV in the United States
- Overview of the Transfusion-Transmitted Infections Monitoring System (TTIMS)
- Donor HIV Risk Questionnaire Study
- Open Public Hearing / Committee Discussion

Summary of Topic IIIA

- FDA MSM deferral policy for blood donation was revised in 2015 FDA guidance to a 12 month deferral
- International policies on MSM donation vary from individual risk-based criteria deferral, to variable time-based deferrals, and to alternative strategies
- Numbers of new HIV infections continue to decline overall, although decline has slowed and certain populations are disproportionately and increasingly affected (e.g. young Black and Latino MSM)

Summary of Topic IIIA (continued)

- Effective antiretroviral therapy has improved lifespan and preexposure prophylaxis is an effective prevention tool
- Since its inception in 2015, TTIMS has established a comprehensive and sophisticated monitoring capability for the U.S. blood supply
- A pilot study assessing the discriminant function of behavioral history questions for predicting recent HIV infection in MSM aims to provide FDA with evidence by which to consider changes in MSM deferral policy

Committee Discussion of Topic IIIA

- The committee was asked to comment on what has been learned from implementing other MSM policies internationally and how this information can inform current U.S. MSM deferral policy
- The committee was also asked to comment on the questions proposed for study in the HIV Risk Questionnaire

Committee Discussion of Topic IIIA (continued)

- Differences in HIV epidemiology and donor screening practices between countries were discussed by the committee
- The committee provided recommendations regarding the proposed questions in the HIV Risk Questionnaire study
- The committee agreed that FDA should pursue data to consider alternative deferral strategies while ensuring the current level of safety and supported improved assessment of risk for all individuals

Topic IIIB: Pathogen Reduction of Platelet Donations as an Alternative Procedure to MSM Donor Deferral

- Introduction the topic
- Proposal for Pathogen Reduction of Platelet Donations from MSM
- Open Public Hearing / Committee Discussion

Summary of Topic IIIB

- FDA may issue an exception or alternative to regulatory requirements ("variance") regarding blood, blood components, or blood products (21 CFR 640.120)
- FDA has received a request for an alternative procedure to MSM deferral in which otherwise eligible MSM donors will donate apheresis platelets that will be pathogen reduced using an FDA-approved device
  - Donations will be tested for all relevant transfusion transmitted infections, including HIV

Committee Discussion

- The majority of the committee expressed the opinion that pathogen reduction as an alternative to MSM deferral would result in safe products intended for transfusion, while noting that care would need to be taken to implement this approach
- The committee emphasized the need to engage stakeholders
- The committee reemphasized the need to study and develop individual risk assessment

Purpose of the Meeting

Emily A. Blumberg, MD, FACP (Vice-Chair)
Director, Transplant Infectious Diseases
Hospital of the University of Pennsylvania

Overview of Federal Agency Roles and Responsibilities Regarding Transplant Safety

MARILYN E. LEVI, MD
Physician of Division of Transplantation
Health Resources Services Administration

Organ and Blood Stem Cell Transplantation in the United States: The role of HRSA

Marilyn E. Levi M.D., Medical Officer
Division of Transplantation (DoT)
Healthcare Systems Bureau (HSB)
Health Resources and Services Administration (HRSA)
Department of Health and Human Services (HHS)

Health Resources and Services Administration (HRSA)

- The primary federal entity responsible for oversight of the solid organ and blood stem cell transplant systems in the U.S. and for initiatives to increase the level of organ and tissue donation in this country

- HRSA oversight is exercised according to:
  - statutory requirements
  - federal regulations
  - federal contracts

Solid Organ Transplantation Statutory Authorities through HRSA

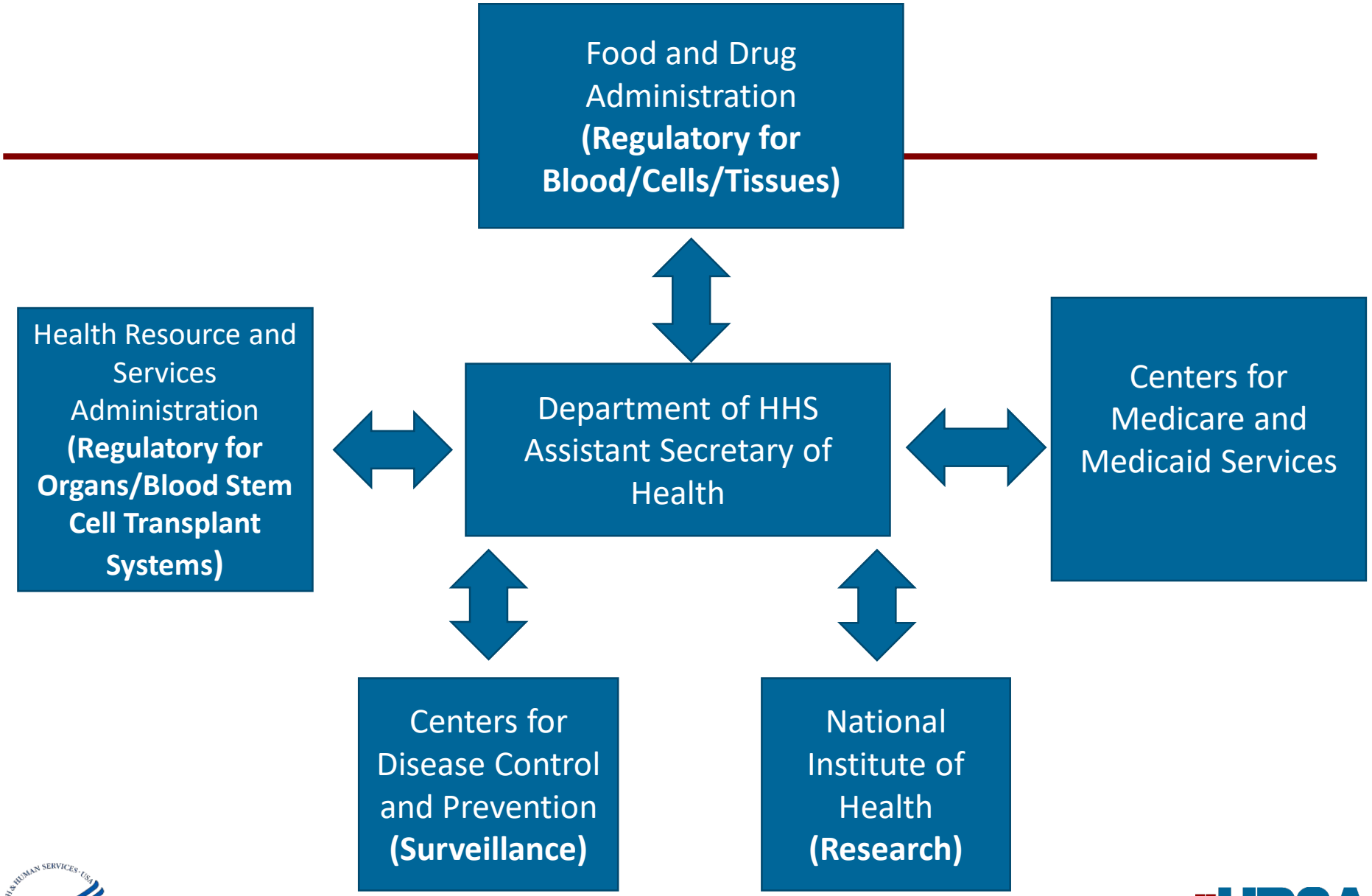
- NOTA (P.L. 98-105, October 19, 1984), as amended, enables:
  - OPTN
  - SRTR
  - Grant authority – including public and professional education
  - Congressional report on the Scientific and Clinical Status of Organ Transplantation

- *The Organ Donation and Recovery Improvement Act* (P.L 108-216, April 5, 2004) enables:
  - Public education
  - Living donor assistance – grant mechanism for travel, subsistence and expenses
  - Congressional Report on Organ Donation and the Recovery, Preservation, and Transportation of Organs

Solid Organ Transplantation Statutory Authorities

- *The Charlie W. Norwood Living Organ Donation Act* (Norwood) (P.L. 110-144, Dec. 21, 2007):
  - Enables and clarifies that organ paired donation is not valuable consideration
  - Congressional report on the Long-Term Health Effects of Living Organ Donation

- *HIV Organ Policy Equity Act* (HOPE) (P.L. 113-51, Nov 21, 2013) enables:
  - Development and publication of research criteria relating to transplantation of HIV positive organs into HIV positive individuals by Nov 21, 2015
  - Limited to living and deceased kidney and liver transplantation


Food and Drug Administration **(Regulatory for Blood/Cells/Tissues)**
Health Resource and Services Administration **(Regulatory for Organs/Blood Stem Cell Transplant Systems)**
Department of HHS Assistant Secretary of Health
Centers for Medicare and Medicaid Services
Centers for Disease Control and Prevention **(Surveillance)**
National Institute of Health **(Research)**

Division of Transplantation Oversight

Organ Transplantation

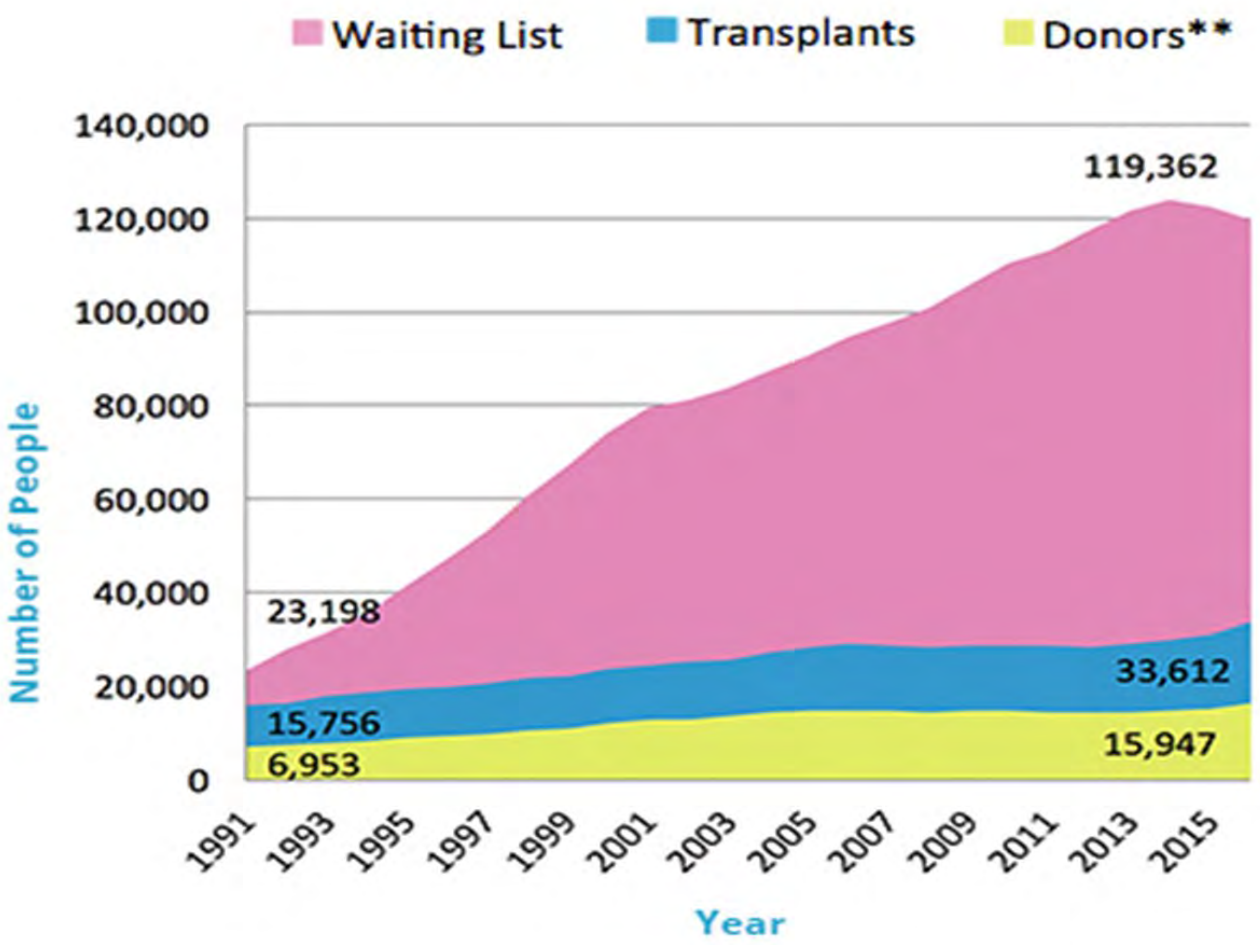
- Organ Procurement and Transplantation Network (OPTN)
- Scientific Registry of Transplant Recipients (SRTR)
- Studies and demonstration projects to increase organ donation and recovery rates
- Organ Donation Public Awareness Program
- National Living Donor Assistance Center (NLDAC)
- Advisory Committee on Organ Transplantation (ACOT)

Division of Transplantation Oversight

Blood Stem Cell Transplantation

- CW Bill Young Transplantation Program
  - Single Point of Access - Coordinating Center
  - Office of Patient Advocacy
  - Stem Cell Therapeutics Outcomes Database (SCTOD)
- National Cord Blood Inventory (NCBI)
- Advisory Council on Blood Stem Cell Transplantation (ACBSCT)

Solid Organ Transplant Data



2017-2018 U.S. Organ Transplant Data

	2017	2018
Total Transplants	34, 770	35, 694
Deceased Donation	10, 281	10, 721
Living Donation	6, 186	6, 834

As of March 3, 2019
113, 727 transplant candidates on the waiting list

2017 - 2018 U.S. Solid Organ Transplant Data

	Deceased Donor	Living donor
Kidney	14,037	5,811
Liver	7,715	367
Lung	2,449	0
Heart	3,244	0
Kidney/Pancreas	7,713	367
Pancreas	213	0

HRSA Contract Oversight

- OPTN – operated under contract with HHS/HRSA by the United Network for Organ Sharing (UNOS)

- http://optn.transplant.hrsa.gov

- This website provides data and educational information about organ donation, transplantation, and the matching process

Scientific Registry of Transplant Recipients

- Supports the ongoing performance evaluation of solid organ transplantation in the United States

- Provides analytical support to the OPTN:
  - in the formulation and evaluation of OPTN policies
  - simulation of allocation models using analytic tools to support organ allocation policy development
  - statutory outcomes reporting (patient and graft survival)

- Current contractor is Minneapolis Medical Research Foundation - Chronic Disease Research Group

Critical Balance Organ Availability Versus Patient Safety

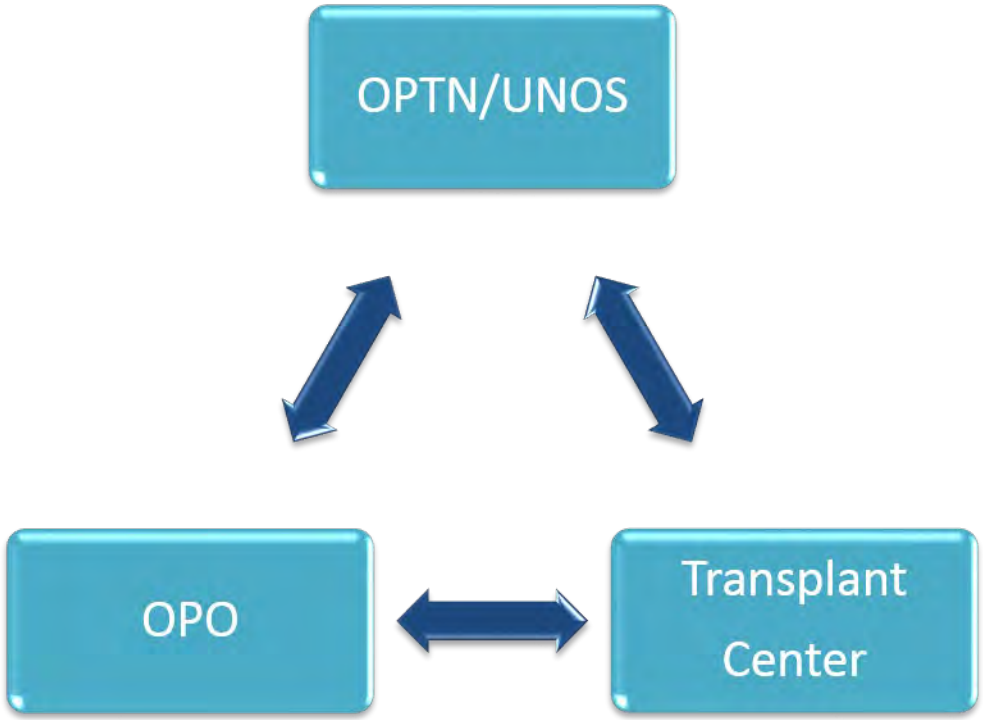
Biovigilance in the United States

HRSA Healthcare Systems

HRSA Biovigilance Monitoring and Safety

- OPTN: *ad hoc* Donor Transmission Advisory Committee
- UNOS Patient Safety Portal
- Public Health Service (PHS) Biovigilance Working Group
- PHS Guidelines
- National Marrow Donor Program (NMDP)
- DPSM Advisory Committee of the NMDP

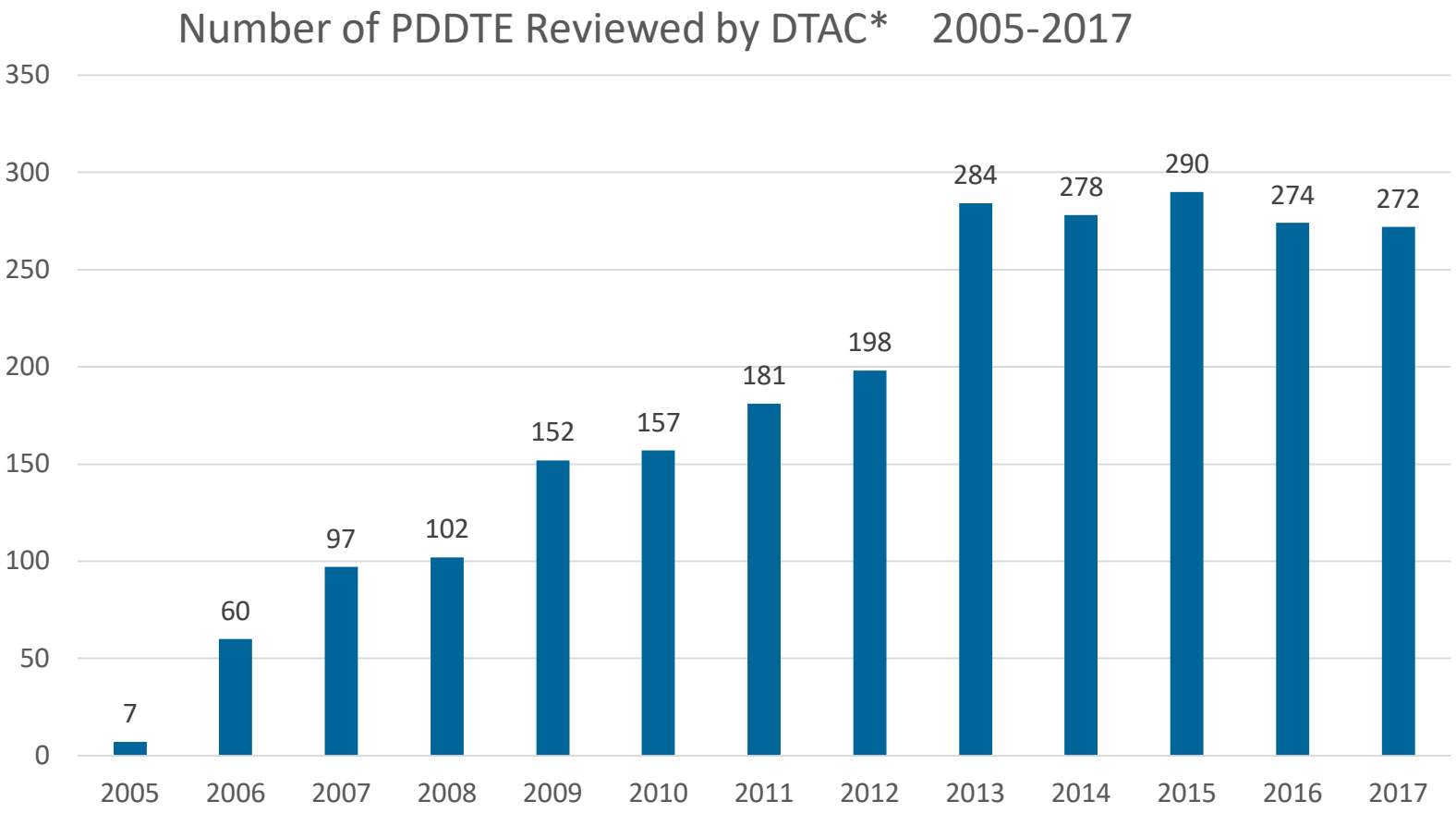
Chain of Events if a Potential Donor Derived Transmission Event is Suspected



Ad Hoc Disease Transmission Advisory Committee

- Part of OPTN patient safety program
- Examine unexpected potential donor-derived transmission events mainly consisting of infection or malignancy
  - Categorize as to whether or not they are donor derived
  - Reviews aggregate data on all reported cases to assess the risk of donor disease transmission
  - Inform policy change and improve existing processes
  - Educate transplant community

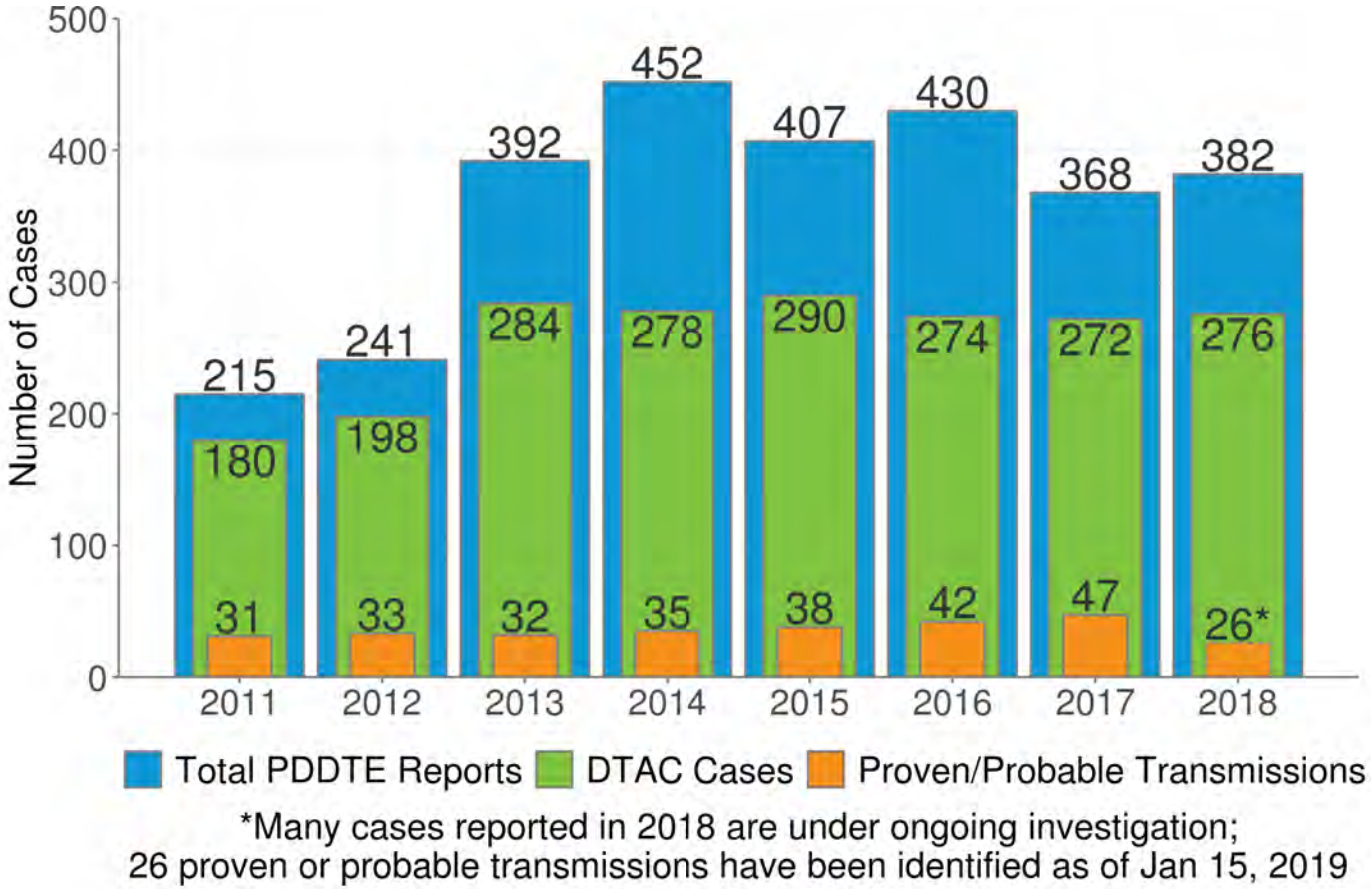
Potential Donor Derived Transmission Events



For an extended description of this chart, please see the description on **page 230.**

Updated Potential Donor Derived Transmission Events

- Number of cases reviewed and those with proven/probable transmission are relatively stable
- Community continues to use the reporting system appropriately



For an extended description of this chart, please see the description on **page 231.**

Donor-Derived Diseases
DTAC Data

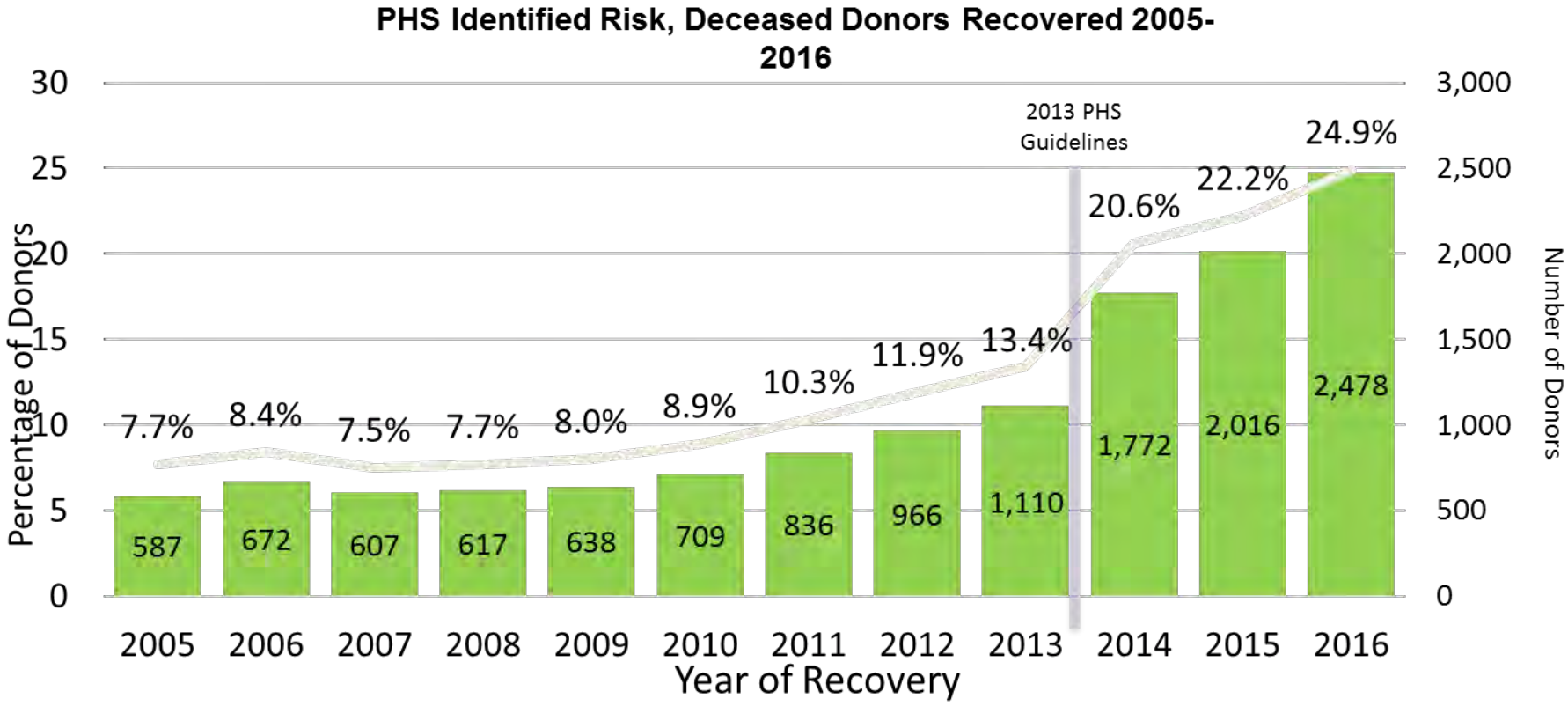
	2011	2018
Reports made to OPTN	236	438
Reports with DTAC review	181	276
Donors transmitting Proven/Probable	17%	10.5% (as of Feb 5, 2019, tentative)

Public Health Service Increased Risk Donors (2013)

Exposures within past 12 months:

- Intravenous drug use
- Imprisonment for 72 hours
- Sexually transmitted infection
- Sexual activity:
  - MSM
  - Exchange of sexual activity for drugs or money
  - HIV, hepatitis B or hepatitis C infected partner
  - Sexual partner with history of IVDA
- Hemodiluted blood sample
- Hemodialysis (for HCV risk only)
- Children <18 months of age born to mother infected with or at increased risk for HIV, HBV or HCV
- Children breastfed from mother with known HIV infection or at increased risk

More Donors at "Increased Risk"



For an extended description of this chart, please see the description on **page 232**.

10 Year Review of Probable/ Proven DDTE The Fear and the Reality

- FEAR:
  - 2005-2015: 219 donors transmitted unexpected diseases to 254 recipients with 71 fatalities
  - Numbers of transmission seem large

- REALITY:
  - 219 / 63,382 (0.34%) deceased donors involved
  - 254 / 174,388 (0.14%) recipients had DDD
  - 71 (0.04%) died

DTAC Develops OPTN/UNOS Guidance

Patient safety

- PHS increased risk donor organs (6/2017)
- Identifying risk factors for West Nile Virus in living donors (6/2013)
- HTLV-1 screening and reporting (2/2014)
- Recognizing central nervous system infections (2/2014)
- PHS guideline for reducing HIV, HBV, and HCV (12/2013)
- Recognizing seasonal and geographically endemic infections in living donors (11/2014)

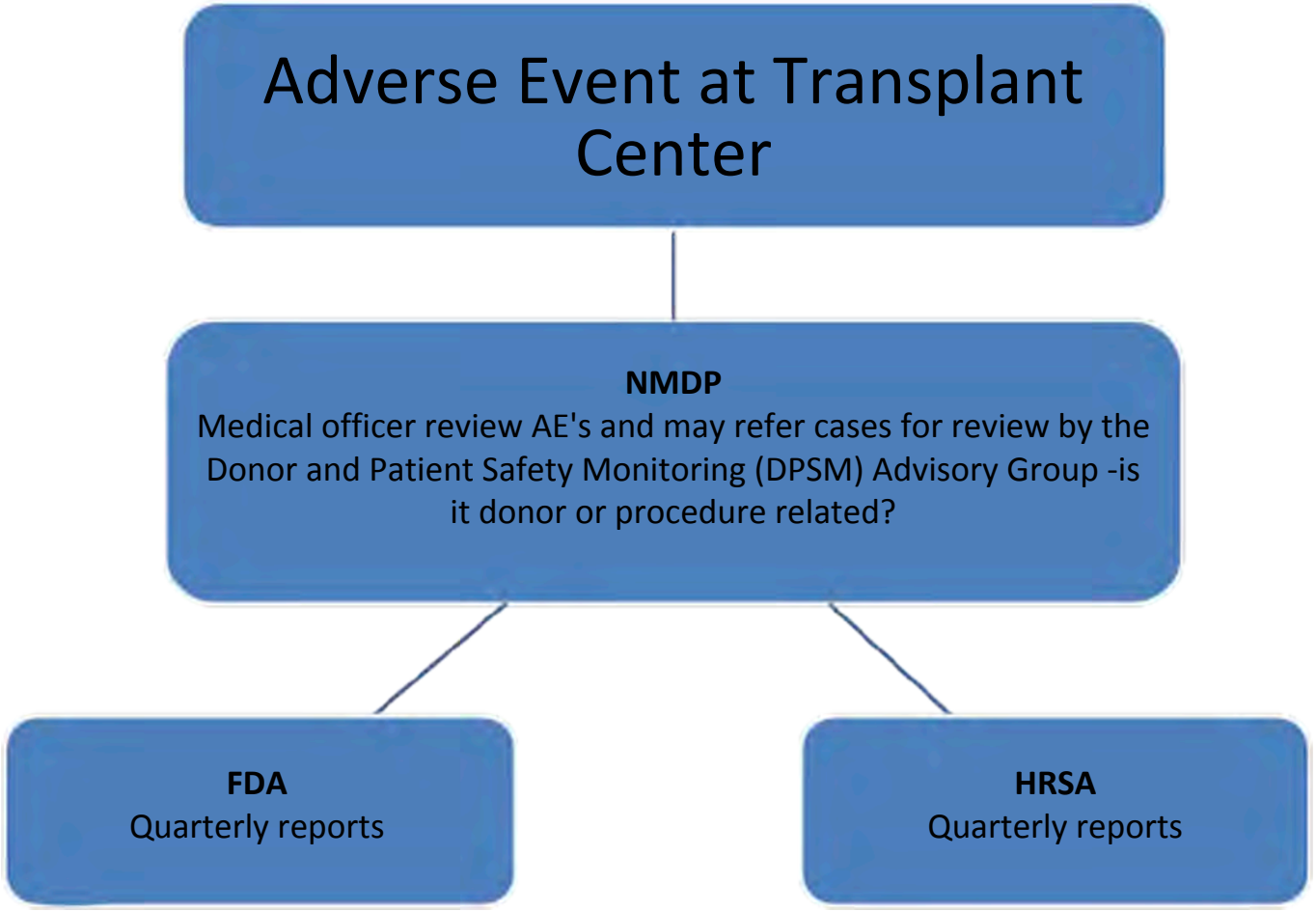
Centers for Diseases Control (CDC) OPTN Final Rule, §121.4:

- Coordinate possible disease transmission (rabies, HIV, TB, WNV, cancers) with investigations
- CDC and HRSA DoT staff serve as ex-officio members of the DTAC
- HRSA, CDC and FDA:
  - coordinate issues relating to donor screening
  - serve as ex-officio members of the Advisory Committee on Blood Safety and Availability (ACBTSA)
- OPTN Final Rule §121.4: Board of Directors are responsible for developing policies consistent with CDC recommendations

Improving Patient Safety Electronic Reporting in UNet^{SM}

- Improving Patient Safety electronic reporting system (implemented 2006):
  - **Goal**: Use more organs for transplantation and reduce the morbidity and mortality of transplant candidates and living donors.
- Many other pathways exist for data or issues to be reported to the OPTN

Stem Cell and Cord Blood Transplantation:
How are adverse events handled?



Contact Information

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organdonor.gov
optn.transplant.hrsa.gov
srtr.transplant.hrsa.gov
bloodcell.transplant.hrsa.gov

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Leadership Remarks

ADM Brett Giroir, MD

Assistant Secretary for Health,
U.S. Department of Health and Human Services (HHS)

Leadership Remarks

Robert R. Redfield, MD
Director
Centers for Disease Control and Prevention (CD)

OVERVIEW OF OPTN-ROLES/RESPONSIBILITIES

DAVID KLASSEN, MD
Chief Medical Officer
UNOS

Overview of the Organ Procurement and Transplantation Network (OPTN)

David Klassen, M.D.
OPTN Medical Director
Chief Medical Officer, UNOS

Acknowledgment

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Transplantation in the 1970's and early 1980's

- No coordinating national system
- Ad hoc or collaborative regional organ sharing
- Inconsistent pattern/model/service areas for organ recover
- Concerns around equity and commercialization

National Organ Transplant Act of 1984

- Organ Procurement & Transplantation Network (OPTN)
  - Private nonprofit entity by contract with HHS
  - Establish membership criteria and medical criteria for allocating organs
  - National policy and system; nationwide coordination
  - Original scope recommended by 1986 task force
  - Original enforcement authority not clearly defined
- Created the modern OPO system
- Created SRTR for data analysis

Key OPTN responsibilities

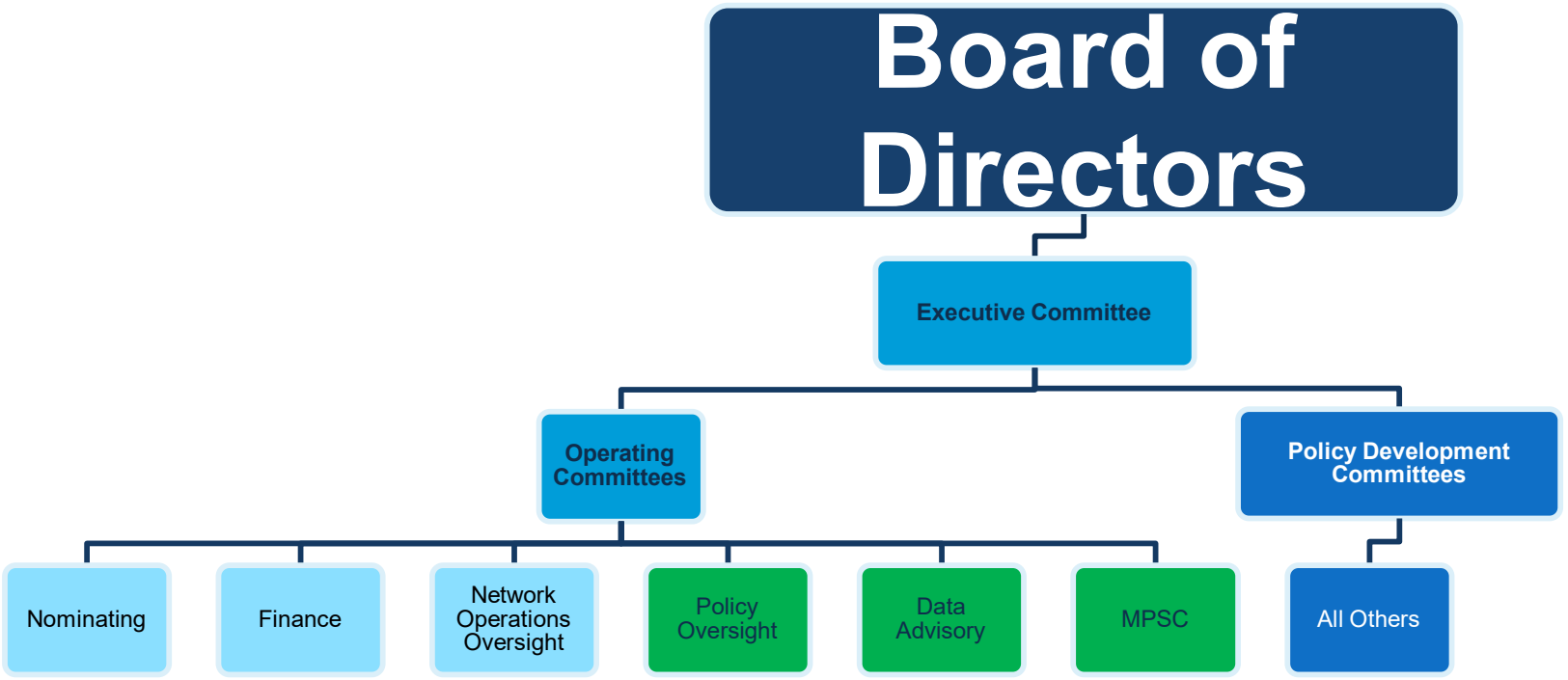
- Maintain national transplant list
- Facilitate organ distribution, transplantation
- Establish equitable policies and membership standards
- Monitor members for compliance, safety, quality
- Collect/validate/report transplant data
- Promote most/best use of available organs

OPTN is a Membership Organization

As of January 2019

Transplant Hospitals	253
Organ Procurement Orgs.	58
Histocompatibility Labs	149
Public Orgs.	6
Medical/Scientific Orgs.	13
Individual Members	8

OPTN Governance Structure



Policy Development Committees

18 total policy development committees

- Roughly 18 members on each committee
- Serve in advisory capacity to the Board

Each committee has its own focus

- Some are organ-specific (Liver and Intestine, Thoracic, Kidney, etc.)
- Some are focused on a particular constituency (Pediatric Transplantation, Living Donor, Patient Affairs, etc.)
- Others are task-based (Operations and Safety, Disease Transmission Advisory, etc.)

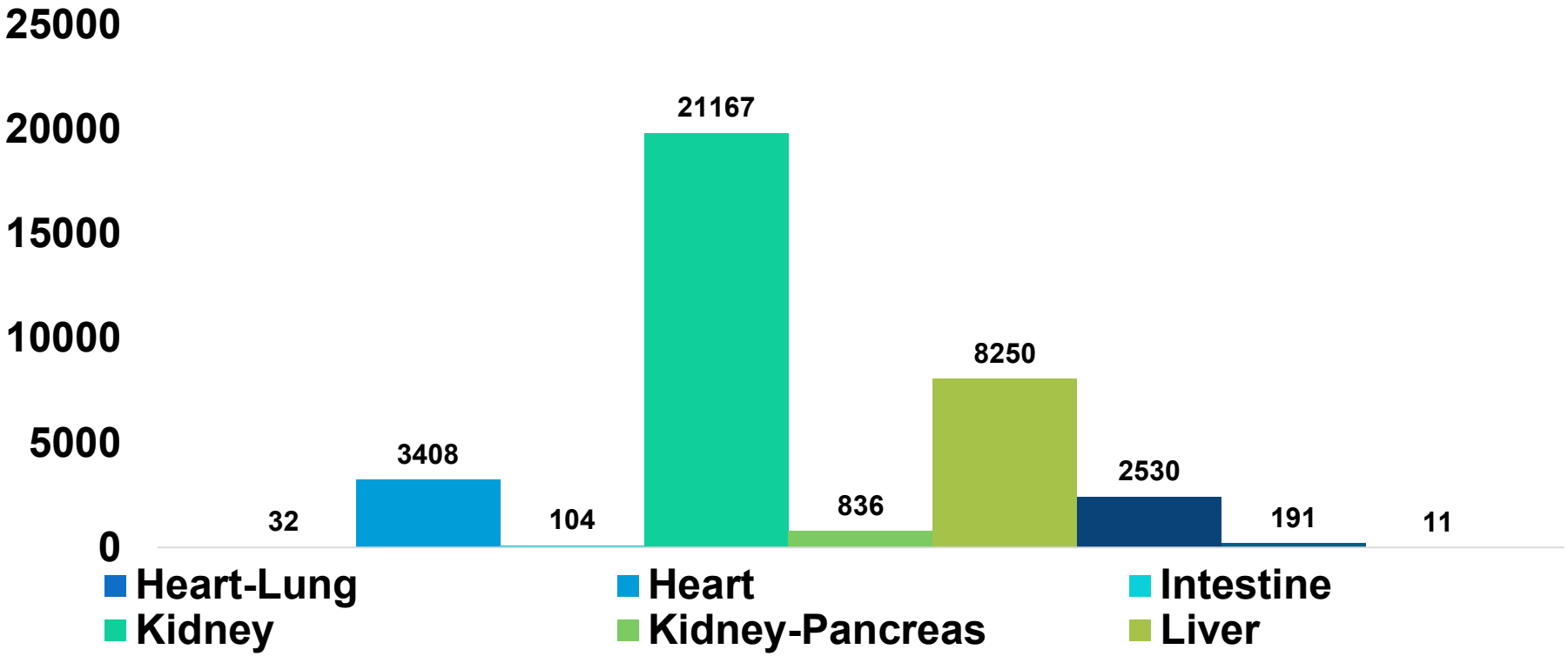
Provide initial review and analysis of proposed policies, guidance documents, education projects, and other projects

- Develop projects from idea phase through public comment
- Responsible for pre- and post-implementation evaluation as well

OPTN High Level Data

- 36,527 solid organ transplants performed in 2018
  - 23 percent increase in five years
- 10,721 deceased organ donors in 2018
  - 25 percent increase in five years
- More than 250,000 transplant recipients alive today
- About 114,000 transplant candidates currently listed nationwide
  - Below historic peak in 2014
  - 150 candidates added each day on average, 18 die waiting

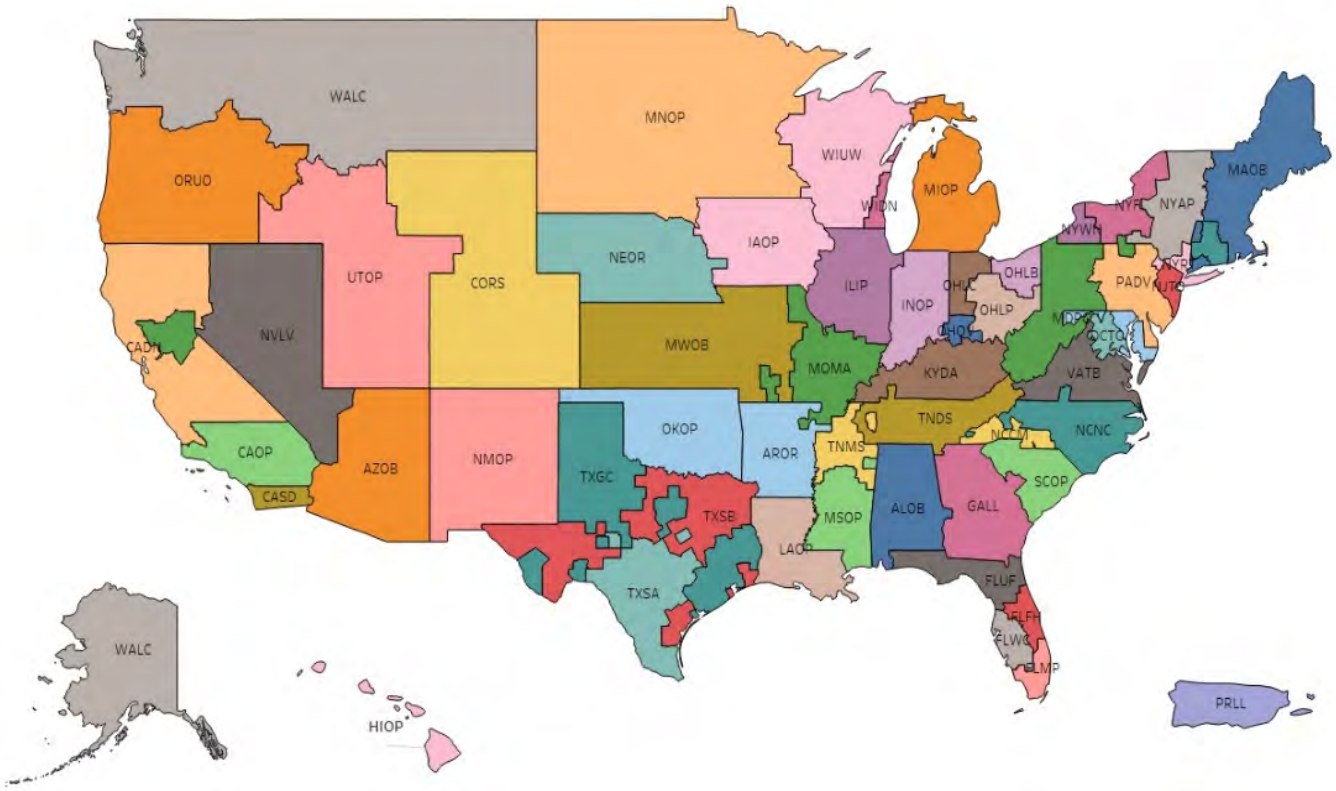
U.S. Transplants Performed by Organ, 2018



OPTN: Geographic Structure

- Organ Procurement Organizations (OPOs) or Donor Service Areas (DSAs): 58 defined geographic territories
- Regions: 11 larger areas also have administrative functions
- These geographical boundaries are not designed to optimize allocation, largely political and historical in nature and their use for allocation is currently being revised

OPTN DSA Map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WALC
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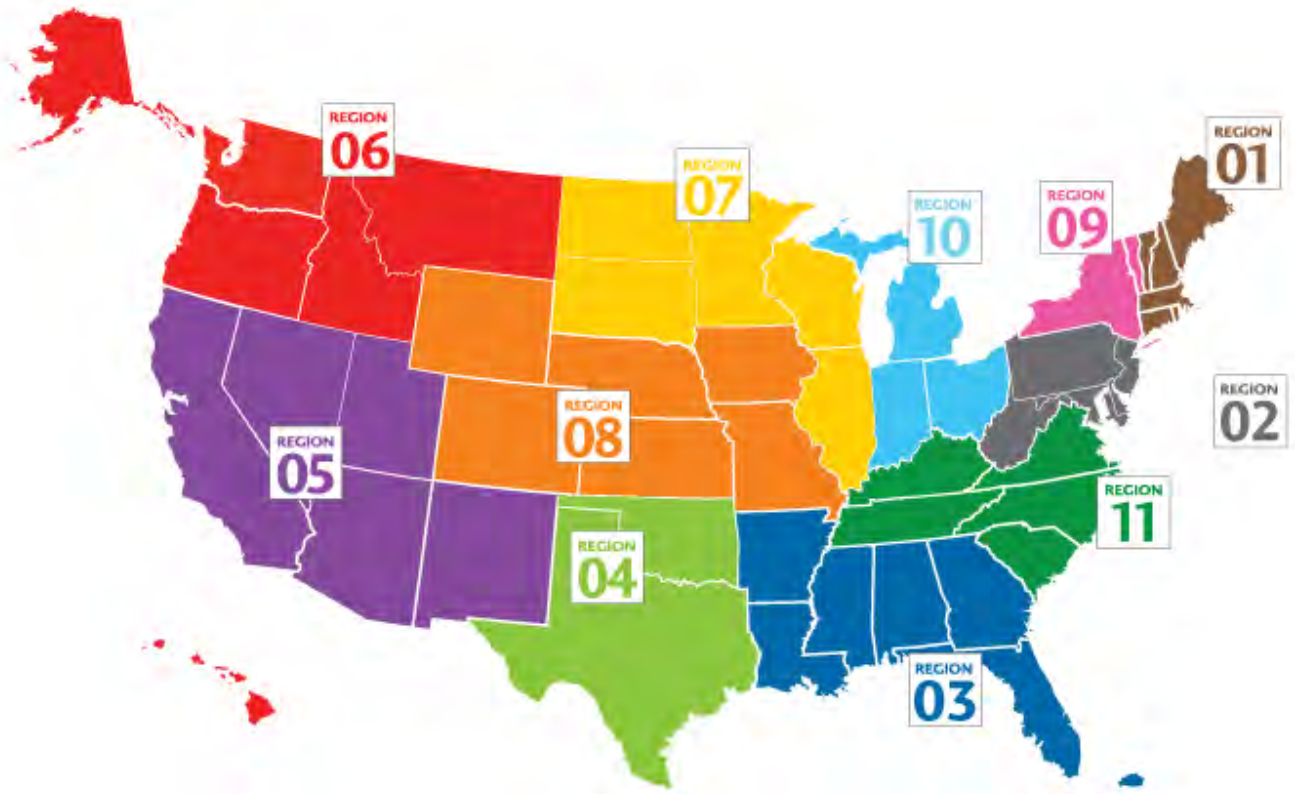
OPTN Regional Map



Regions

Region 1: Maine, New Hampshire, Massachusetts, Rhode Island, Connecticut
Region 2: Pennsylvania, New Jersey, Washington, DC, Maryland, West Virginia
Region 3: Arkansas, Louisiana, Mississippi, Alabama, Georgia, Florida
Region 4: Oklahoma, Texas
Region 5: California, Nevada, Utah, Arizona, New Mexico
Region 6: Washington, Oregon, Idaho, Montana, Alaska, Hawaii
Region 7: North Dakota, South Dakota, Minnesota, Wisconsin, Illinois
Region 8: Wyoming, Colorado, Nebraska, Kansas, Iowa, Missouri
Region 9: New York, Vermont
Region 10: Michigan, Indiana, Ohio
Region 11: Kentucky, Tennessee, Virgina, North Carolina, South Carolina

Who is UNOS?

- Incorporated in 1984 as a 501(c)3
- 370 Employees
- Headquartered in Richmond, VA
- Manage the OPTN system under cost-share contract with the federal government
- 24-hour call center for organ matching
- Provide research, technology and education to the transplant community

www.unos.org

UNOS Relationship to the Government

- UNOS is a private corporation
- Health Resources and Services Administration (HRSA) is part of HHS within the Federal Government
- HRSA contracts with UNOS to operate the OPTN

OPTN Core Functions

- Running the “match”
- Managing the data
- Quality oversight
- Policy Development

Allocation: organ specific systems

- **Kidney**: utility and equity, recipient health, organ quality
- **Liver**: sickest first, varied sharing by MELD score and zones
- **Heart**: sickest first, geography by 500 mile zones
- **Lung**: Lung allocation score, a balance of pre and post transplant survival, geography by 250 mile zones

OPTN Database

- 24 billion records
- 8 database environments, including a hot site with full fail-over capabilities
- 30,000 database elements
- 8 terabytes of data storage

OPTN Quality Oversight

- Patient Safety
- Disease transmission
- Clinical transplantation outcomes
- Policy compliance

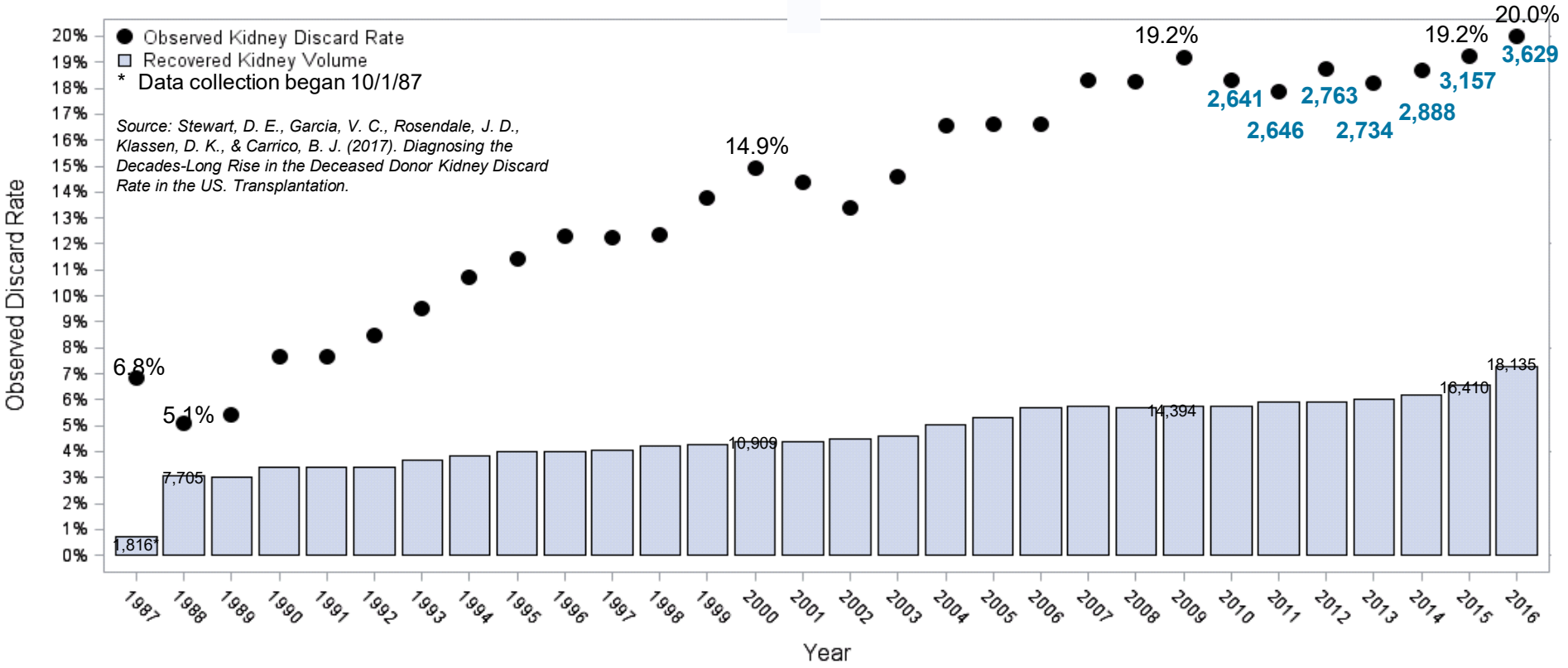
Policy Development

- Broad transplant community input
- Public comment
- Board of Directors approval

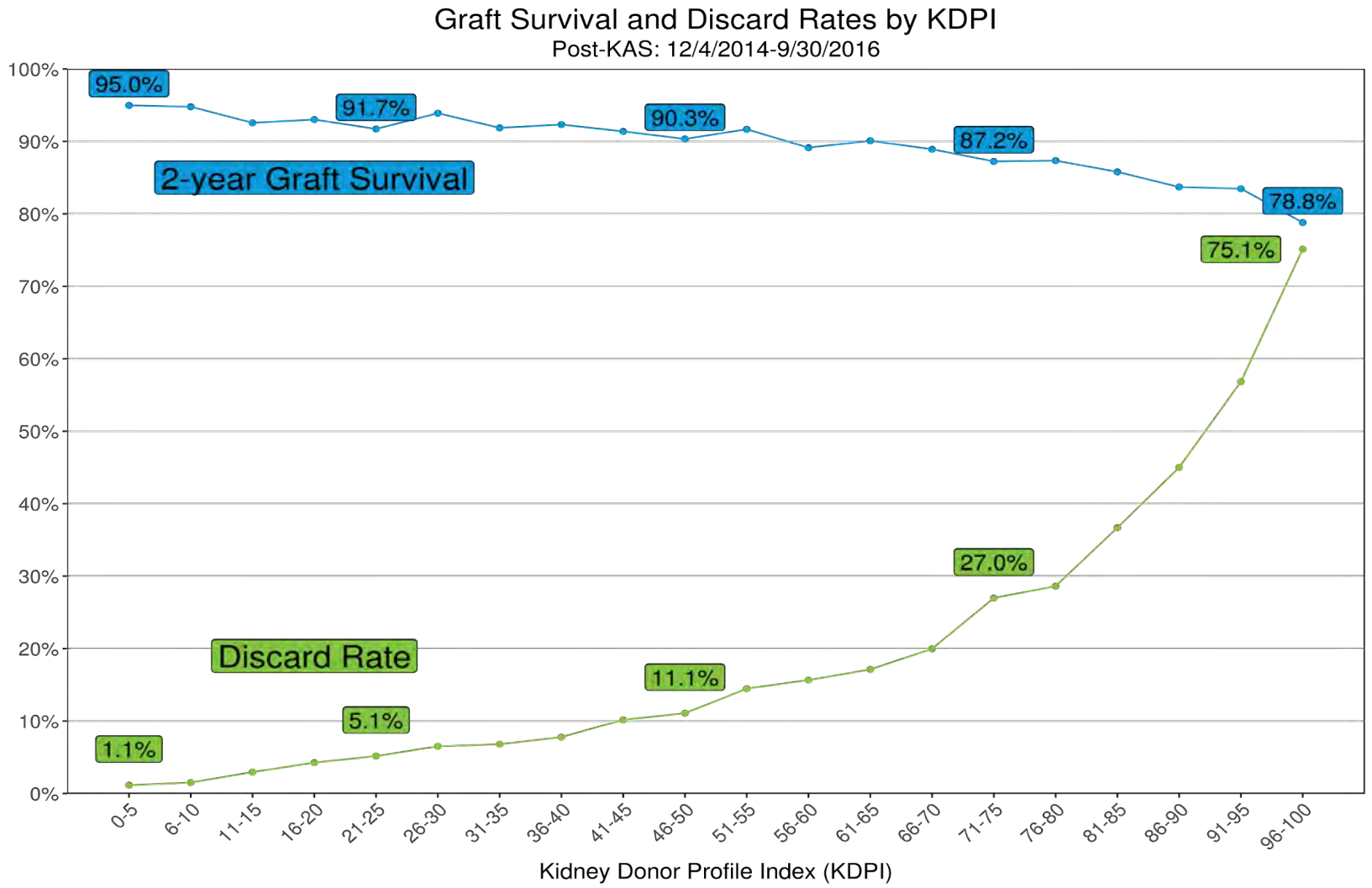
OPTN Policy Relating to Transmissible Disease Risk and Consent

- Required consent by recipients to general risks of potential malignancy or infectious disease Transmission
- Required consent by recipients for donors with risk identified pre-transplant
- Required consent for recipients of organs from donors with increased risk of disease transmission as specified in the *U.S. Public Health Services (PHS) Guideline*

Discard rate trends - kidney



For an extended description of this chart, please see the description on page 233.

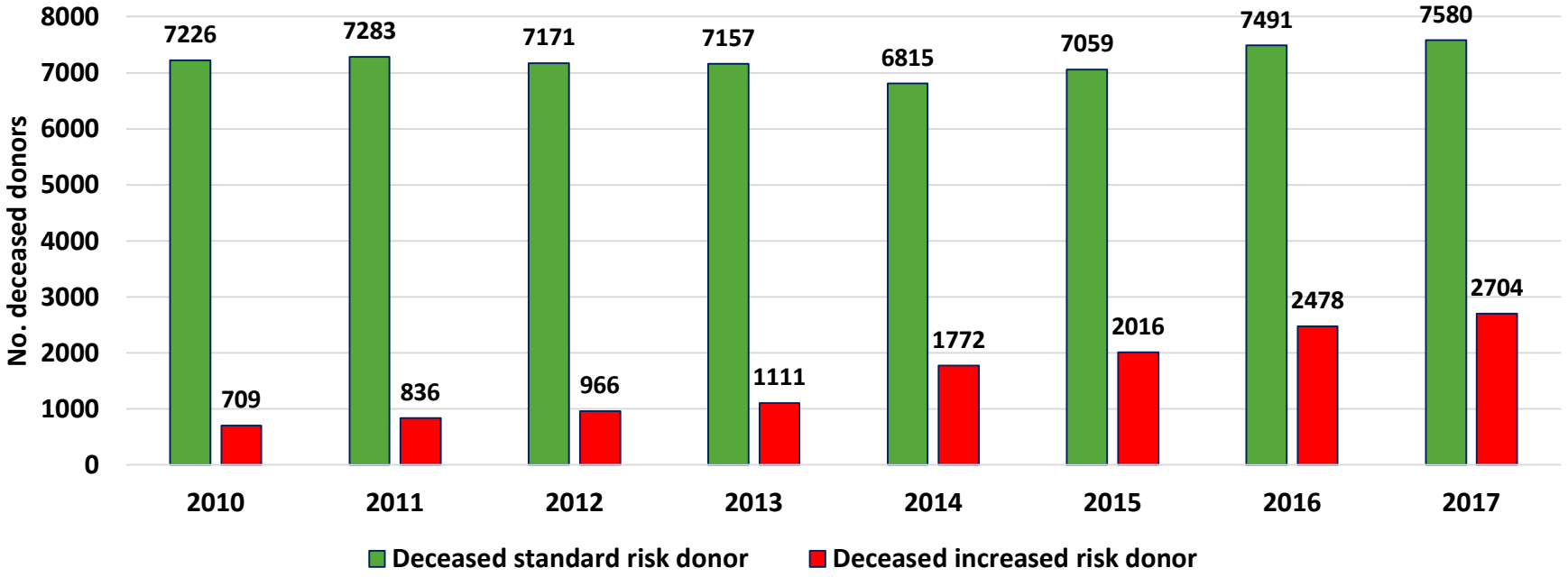


For an extended description of this chart, please see the description on **page 234**.

Kidney donor profile index - KDPI

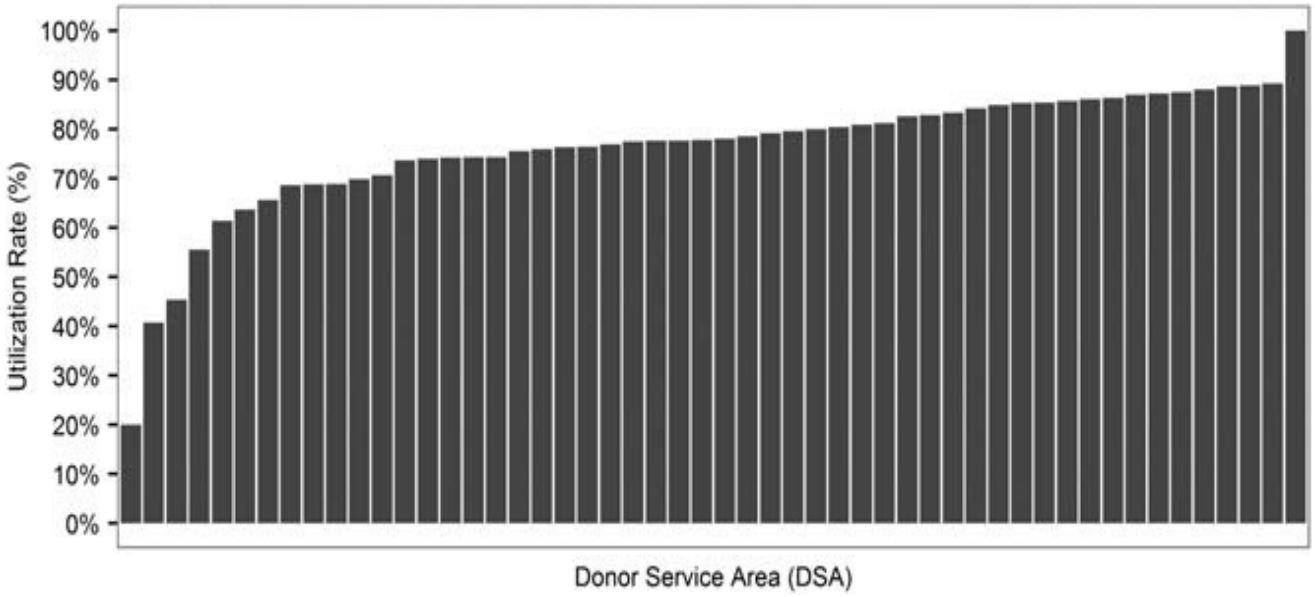
- Age
- Height
- Weight
- Ethnicity
- History of hypertension
- History of diabetes
- Cause of death
- Serum creatinine
- Hepatitis C status
- DCD status

Deceased Organ Donors in the United States by PHS Increased Risk Status

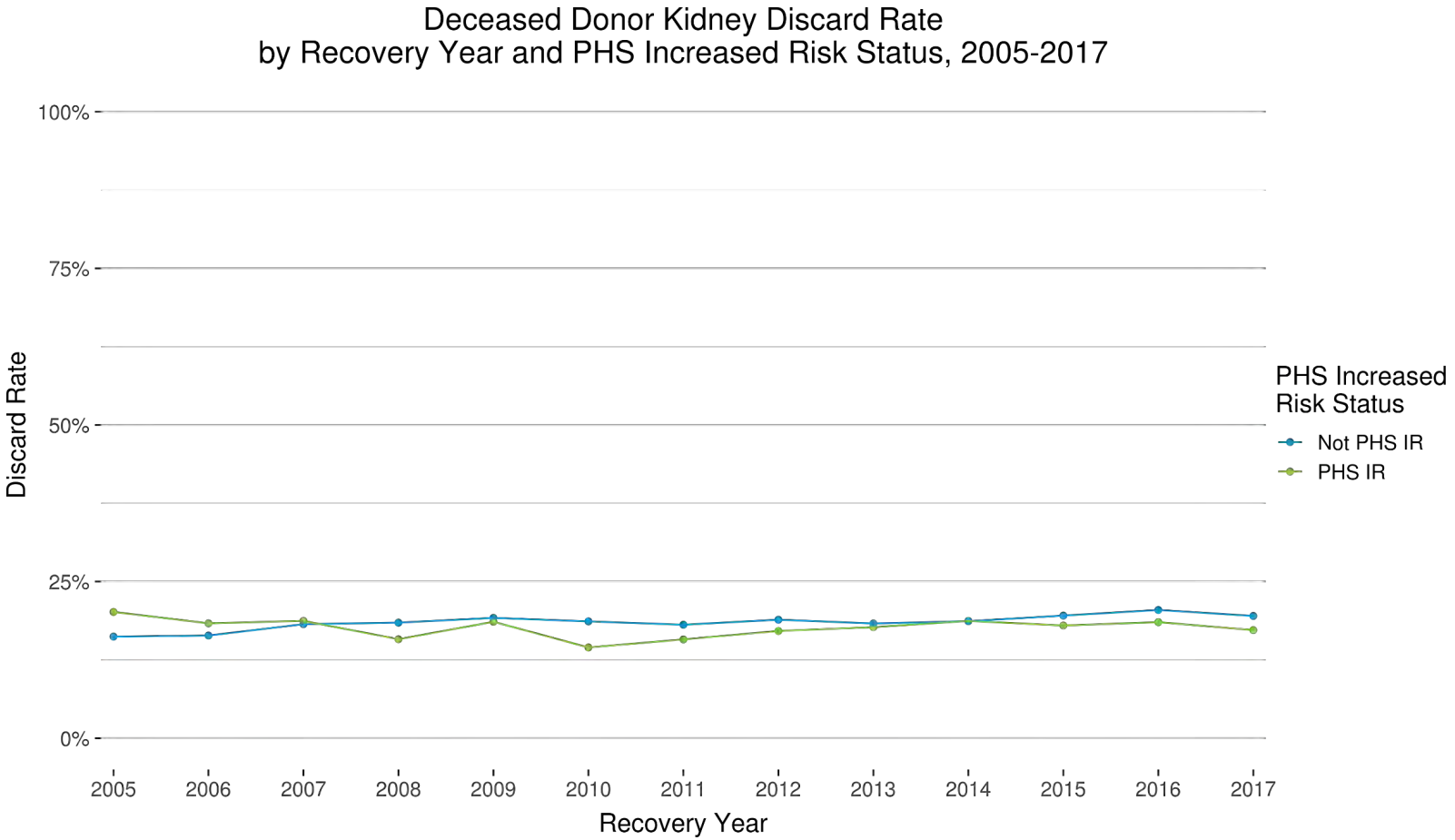


For an extended description of this chart, please see the description on **page 235.**

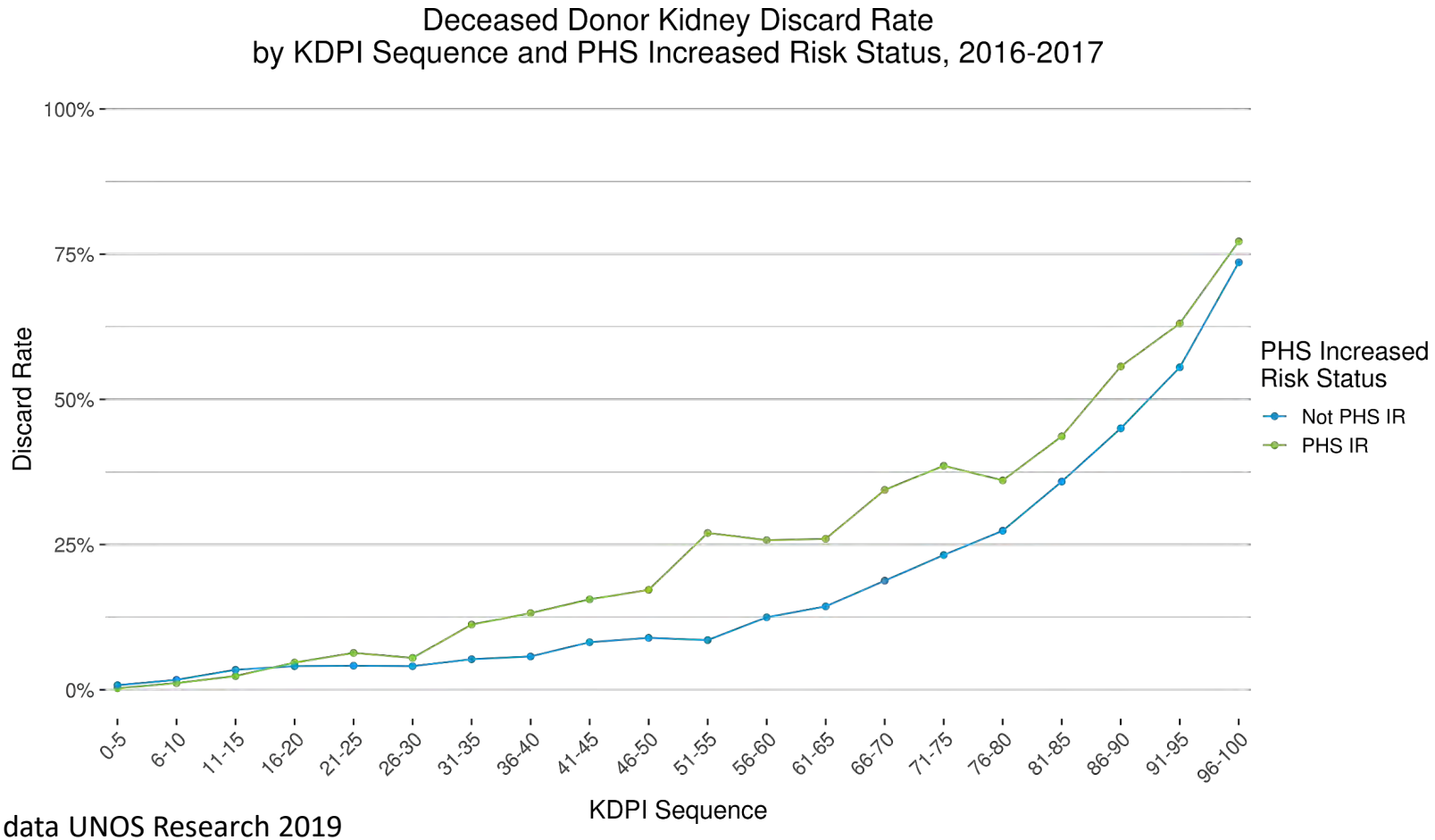
PHS IRD Kidney Utilization



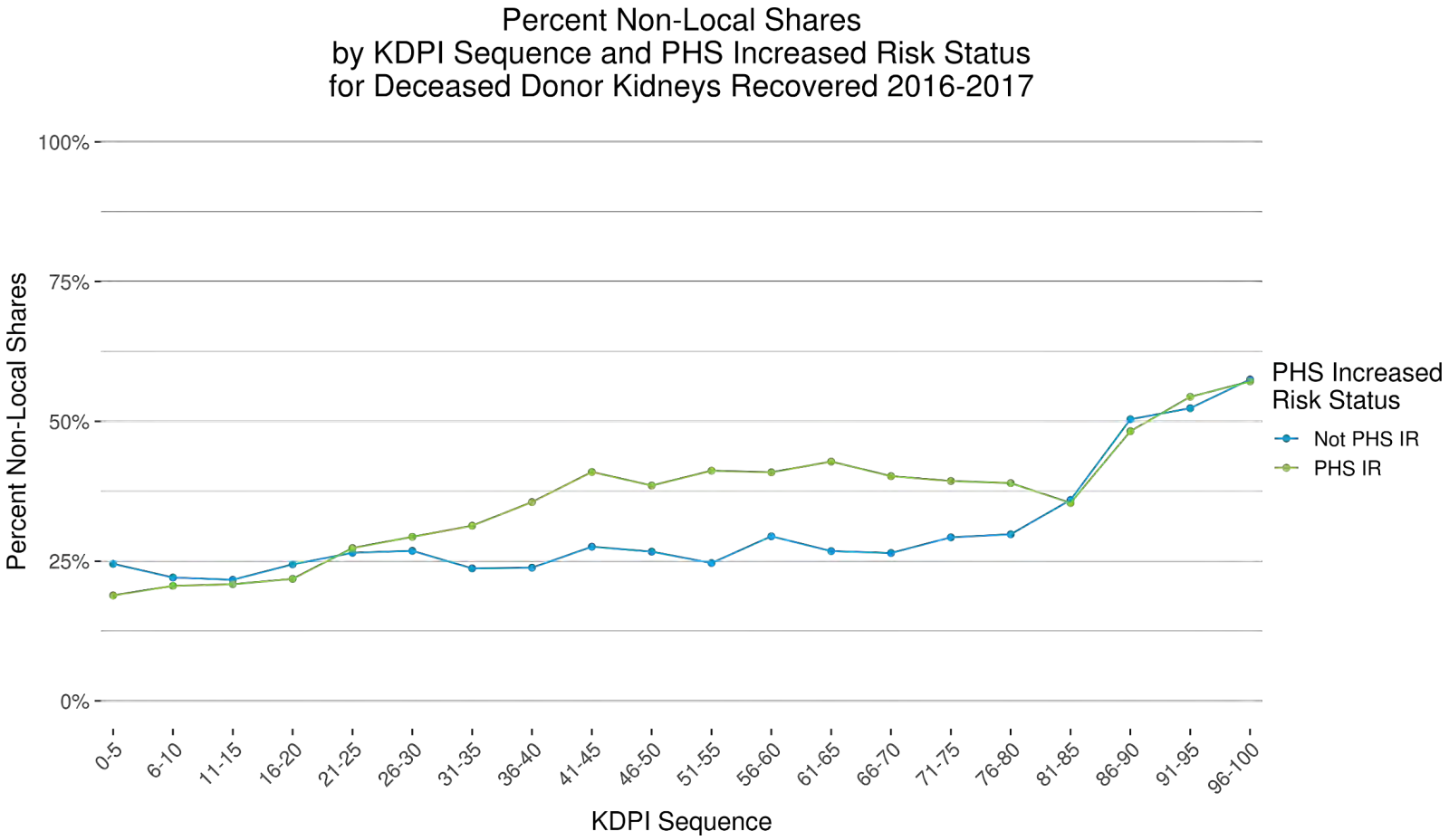
Volk et al., Transplantation 2017 101:1666 - 1669

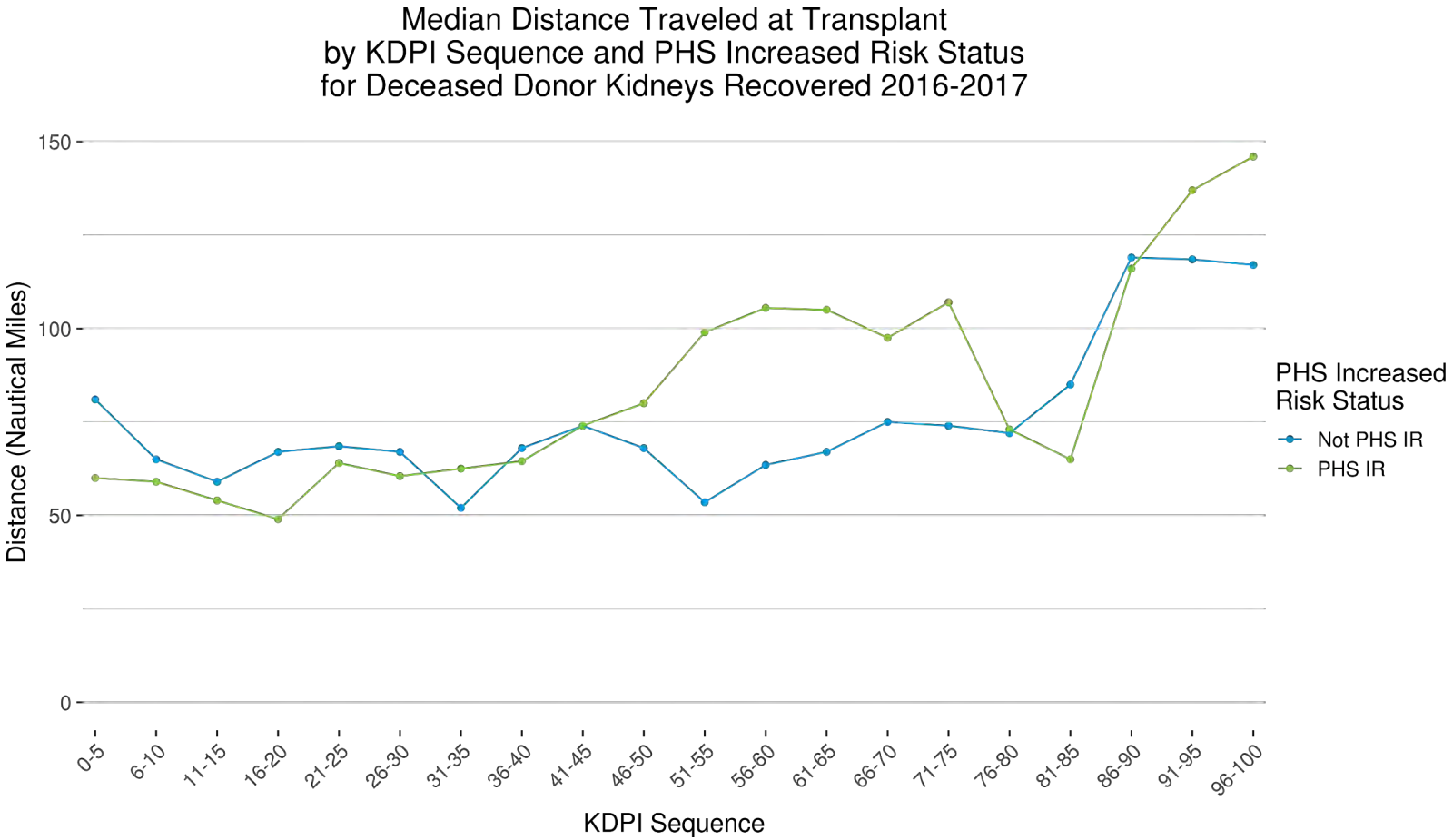


OPTN data UNOS Research 2019



OPTN data UNOS Research 2019

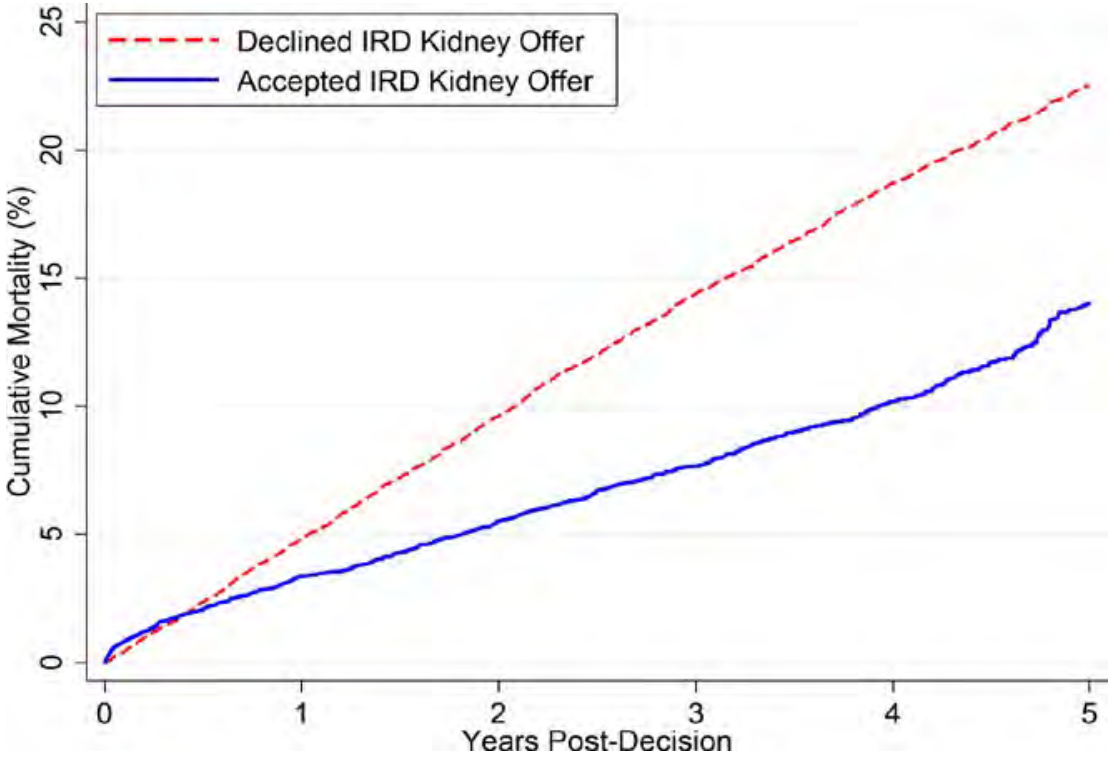

Percent Non-Local Shares
by KDPI Sequence and PHS Increased Risk Status
for Deceased Donor Kidneys Recovered 2016-2017
100%
75%
50%
25%
0%
Percent Non-Local Shares
0-5
6-10
11-15
16-20
21-25
26-30
31-35
36-40
41-45
46-50
51-55
56-60
61-65
66-70
71-75
76-80
81-85
86-90
91-95
96-100
KDPI Sequence
PHS Increased Risk Status
Not PHS IR
PHS IR


Median Distance Traveled at Transplant
by KDPI Sequence and PHS Increased Risk Status
for Deceased Donor Kidneys Recovered 2016-2017
Distance (Nautical Miles)
150
100
50
0
0-5
6-10
11-15
16-20
21-25
26-30
31-35
36-40
41-45
46-50
51-55
56-60
61-65
66-70
71-75
76-80
81-85
86-90
91-95
96-100
KDPI Sequence
PHS Increased Risk Status
Not PHS IR
PHS IR

Organ Acceptance Decisions
Risks vs. Benefits of IRD Organs

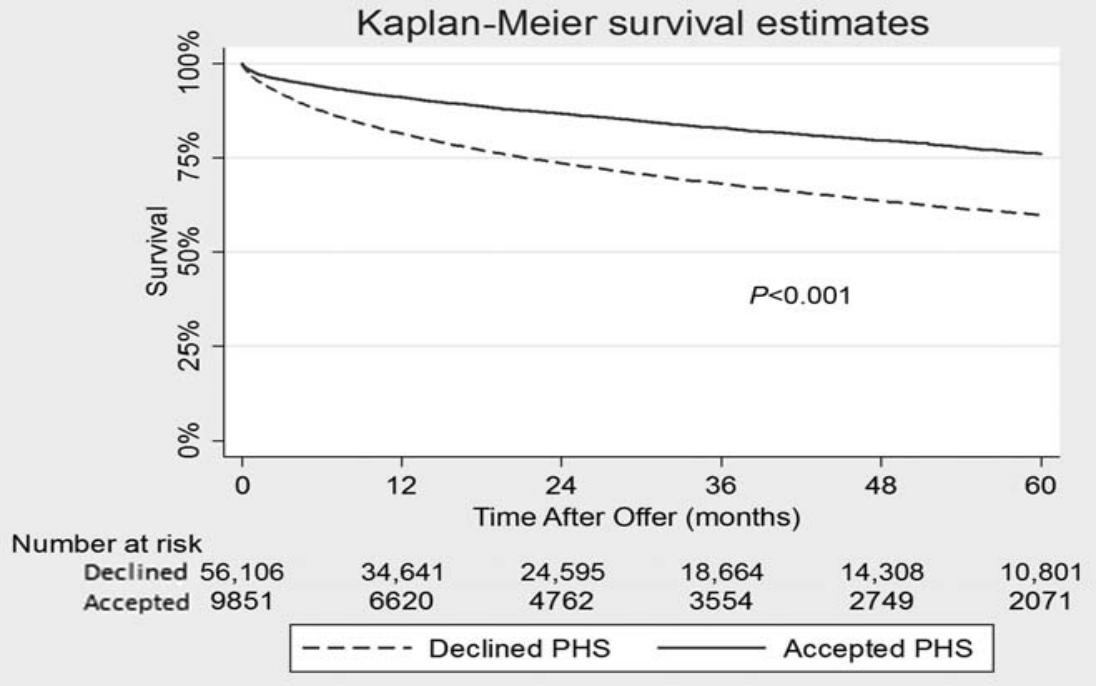
- Transplantation environment is unique
- Time Pressures: 30 minutes to decide
- Recipient concerns and consent
- Transplant center considerations

Survival Benefit of IRD Kidneys



Bowring et al., Am J Trans 2018 18:617-624

Survival Benefit of IRD Livers



Croome et al. Liver Transplantation 2018 24:497-504

For an extended description of these maps, please see the descriptions on **page 236.**

Questions?

BREAK

Historical background of PHS role in prevention of HIV, HBV, HCV transmission through organ transplantation: focus on 1994 to 2013

MATT KUEHNERT, MD
Medical Director
Musculoskeletal Transplant Foundation (MTF)

HISTORICAL BACKGROUND OF PHS ROLE IN PREVENTION OF HIV AND HEPATITIS TRANSMISSION THROUGH ORGAN TRANSPLANTATION

Matthew J. Kuehnert, MD

April 15th 2019

Disclaimer and potential conflicts:

- Employee of MTF Biologics (nonprofit tissue bank)
- Member, American Association of Tissue Banks
- Liaison member of AABB Transfusion Transmitted Diseases committee
- Former CDC employee and commissioned officer of USPHS (retired!)

Opinions and any policy positions conveyed are purely of my own, and do not necessarily reflect the opinions or positions of my employer or any committees or groups of which I am a part.

- IN THE BEGINNING…

- Soon after FDA approved HIV antibody testing and screening was required for blood donors, CDC made recommendations for screening of organ and tissue donors (1985)

- Transmission of HIV through organ transplantation **occurred despite antibody testing**, including in the setting of
  - Hemodilution (heart/kidney/liver, MMWR 1987)
  - Testing too long before recovery (living donor kidney, Quarto NEJM 1989)
  - Window period (Simonds NEJM 1992)
    - 41 organ/tissue recipients, 7 infected (heart, liver, kidneys [2], fresh-frozen bone [3])

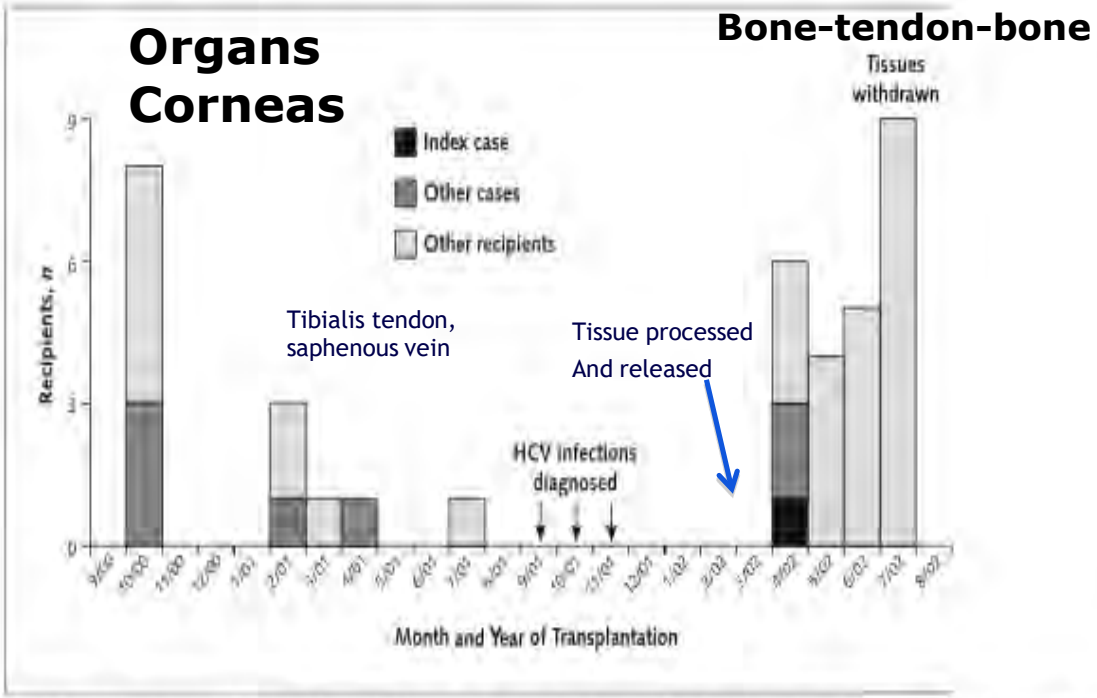
- PHS Workgroup on Organ and Tissue Transplantation formed (1991)

- “CDC Guideline” for Preventing Transmission of HIV through human tissue/organs published (1994)
- Recommended “to exclude potential organ and tissue donors who had risk factors for HIV, unless the transplant center determined that the risk of not performing the transplant outweighed the potential risk of HIV transmission…”
- Update to 1994 guidance (1996) encouraged transplant centers to consider organs from donors with negative antibody testing but HIV risk factors for transplantation, following an informed discussion of risks and benefits
- Also importantly, retained recommendation to test recipients before transplant and at 3, 6, and 12 months after transplant (but not implemented as a requirement)

- Unfortunately, transmissions continued, not only involving HIV but also with another recognized pathogen, hepatitis C virus (HCV)
- Multiple reports of transmission of HCV through organ transplantation, beginning in 1991
- HCV transmission continued despite antibody screening
    - Large cluster of HCV transmission from an infected donor to organ and tissue recipients in 2000-2002 (published 2003, 2005)

Interface between organs and tissues – the need for communication

Figure 1. Transplantation of grafts from a donor with hepatitis C virus (*HCV*) infection, by month of transplantation and case status (n = 38), United States, 2000–2002.



Dates of transplantation for 2 recipients were unknown. Hepatitis C virus infection was diagnosed in 3 recipients in September, October, and November 2001. These recipients had undergone transplantation in February 2001, October 2000, and April 2001, respectively.

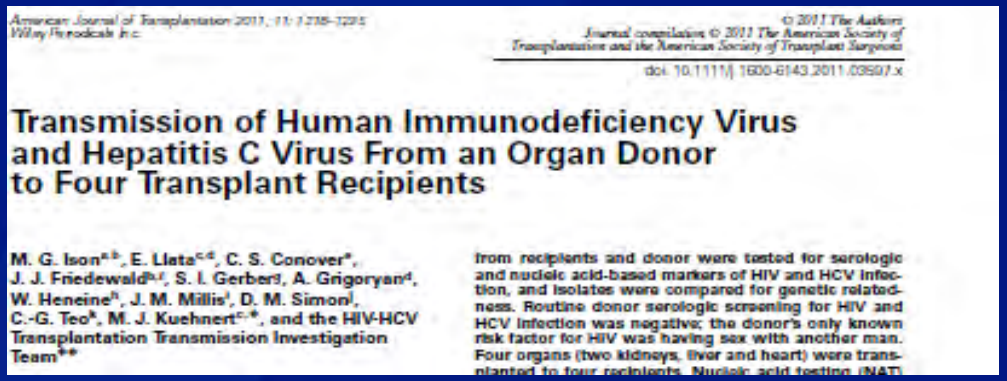
MMWR 52(13): 273-276, 2003. Tugwell BD, et al. ***Ann Intern Med*** 143:648-654, 2005

- Nucleic acid testing (NAT) developed to reduce “window period” of antibody

  (time during which patient is infected with transmissible virus, but test is falsely negative)

  - Implemented for blood donor screening in 1999
  - Implemented for tissue donor screening in 2005

  - By 2007, organ donors still were not being tested using NAT…



American Journal of Transplantation 2011; 11: 1238–1245
Wiley Periodicals Inc.

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Journal compilation © 2011 The American Society of Transplantation and the American Society of Transplant Surgeons

doi: 10.1111/j.1600-6143.2011.03597.x

Transmission of Human Immunodeficiency Virus and Hepatitis C Virus From an Organ Donor to Four Transplant Recipients

M. G. Ison[a,b], E. Llata[c,d], C. S. Conover[e], J. J. Friedewald[b,f], S. I. Gerber[g], A. Grigoryan[d], W. Heneine[h], J. M. Millis[i], D. M. Simon[j], C.-G. Teo[k], M. J. Kuehnert[c,*], and the HIV-HCV Transplantation Transmission Investigation Team[**]

from recipients and donor were tested for serologic and nucleic acid-based markers of HIV and HCV infection, and isolates were compared for genetic relatedness. Routine donor serologic screening for HIV and HCV infection was negative; the donor's only known risk factor for HIV was having sex with another man. Four organs (two kidneys, liver and heart) were transplanted to four recipients. Nucleic acid testing (NAT)

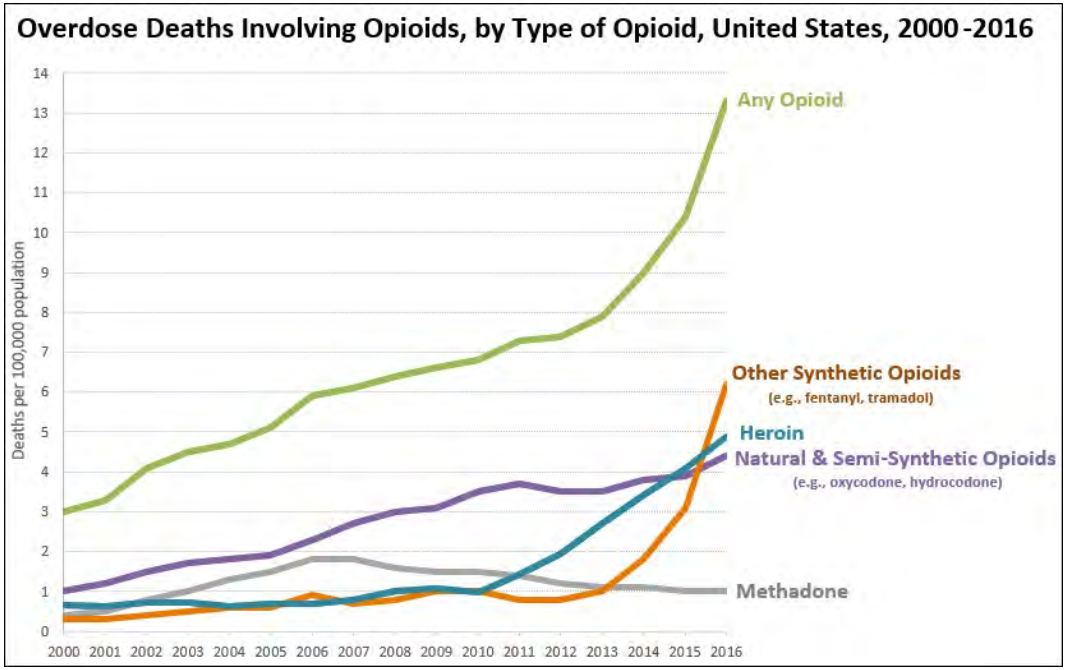
- In 2007, donor with increased risk (MSM, died after hit by car) transmitted both HIV and HCV to 4 organ transplant recipients

- Donor tested using antibody screening only
- Recognition of donor derived infection took months
- Two recipients died
- Two other recipients lost graft due to complications

- In 2009, HIV transmitted by kidney transplant to a living donor
- Donor was screened and tested 79 days before transplant
- One year after transplant, donor was diagnosed with HIV; had unprotected sex (MSM) between screening and organ recovery
- Recommendation that living donors be screened no more than 7 days before recovery (still with antibody required only)…

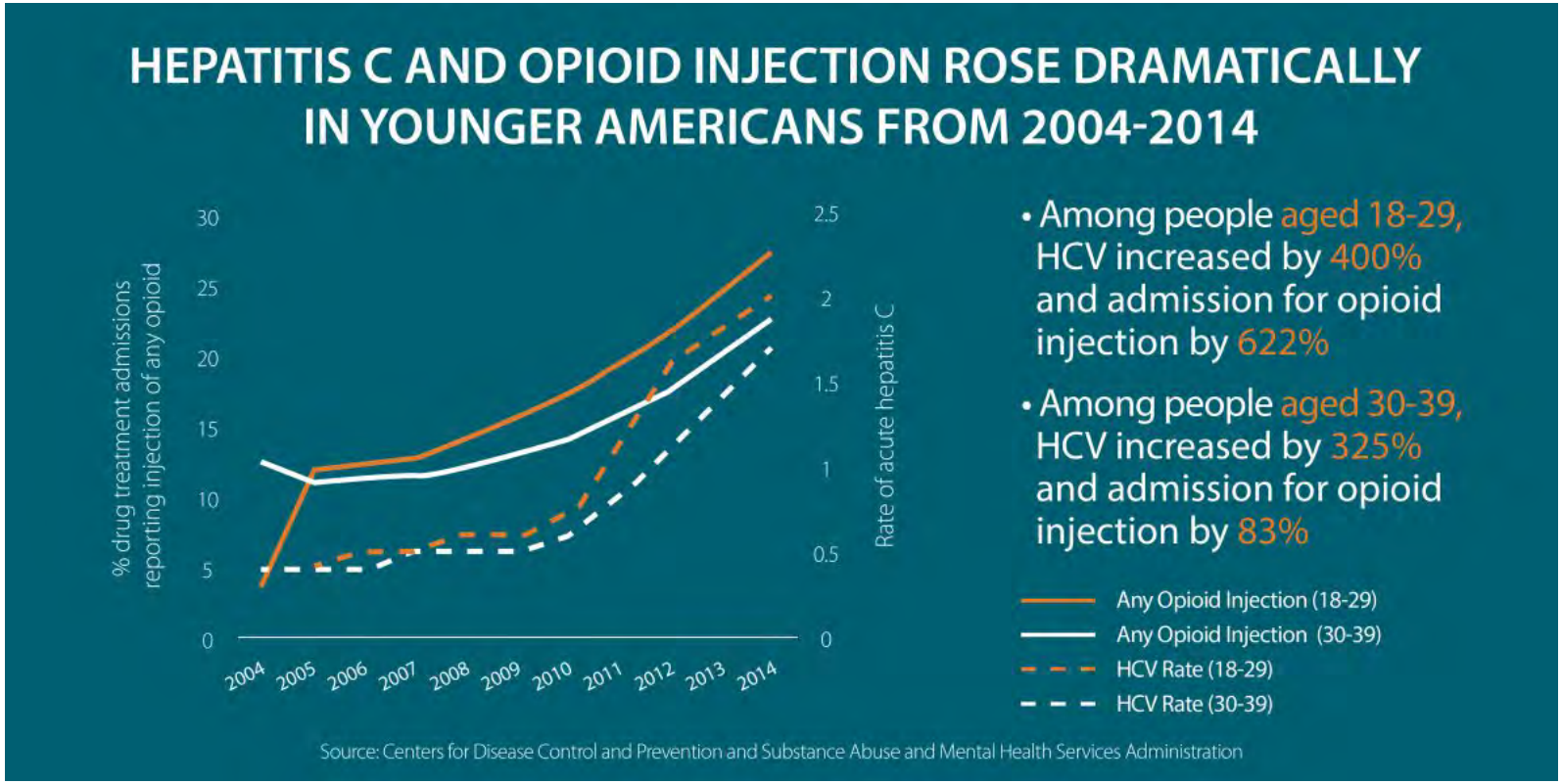
OPIOID EPIDEMIC IN THE U.S. IS STILL WORSENING

- Increases in deaths from use of synthetic opioids and heroin reaching exponential scale
- Patients become addicted from prescribed oral medications, then search for other drugs/routes



Source: CDC/NCHS

OPIOID USE AND NEW HCV INFECTIONS ARE INCREASING



HCV Prevalence in Potential Organ Donors

Risk Status	Prevalence (%) for Donors in Study
Normal Risk	3.45 (CI: 3.10-3.85)
High Risk	18.20 (CI: 15.74-20.91)
Missing Risk	12.88 (CI: 10.83-15.08)
All Potential Donors	5.58 (CI: 5.15-6.06)

Ellingson K et al, AJT, 2011

Comparison of Residual Risk despite lab screening – HIV, Hepatitis B virus (HBV), and Hepatitis C virus (HCV)

	DONORS (000)			
Marker	Organs* (HR) Serology	Organs* (NR) Serology	Tissues** Serology	Blood*** MP-NAT
HIV	1:11	1:50	1:55	1:1,467
HBV	---	--	1:34	1:282 /1:357
HCV	1:1	1:5	1:42	1:1,149

*Ellingson et al., Am.J. Transpl, 2011
**Zou et al., NEJM 351:2004
***Zou, et al., Transfusion 50:1495, 2010
HR = High Risk
NR = Normal Risk
MP-NAT = minipool nucleic acid testing

Slide courtesy of D. Michael Strong

PHS Guideline Development

- "Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs" published in 1994 by PHS was deemed out of date
- Agreement that PHS guidelines needed revision
  - Association for Organ Procurement Organizations (AOPO), followed by other transplant organizations, sent letters to CDC suggesting guideline revision in 2008
- Intent of revised PHS guideline
  - reducing risk of infectious transmission, while preserving availability of high quality organs
  - providing best available information for transplant teams and their patients to make informed decisions
- Objective process developed for PHS guideline revision and update with input from community experts

How Do We Preserve Availability, Yet Keep Organs Safe As Possible?

- Donor eligibility (procurement) issues
  - Risk of transmission
  - Risk of not transplanting an organ with low risk of transmitting an infectious disease
  - Impact of methods to mitigate risks
- Organ suitability (transplantation) issues
  - Outcomes of patients who do not receive an at-risk organ, remain on transplant list
  - Outcomes of patients who receive infected organs
  - Patient preference (informed consent)

Important Differences in Focus (1994 versus 2013 PHS Guideline)

- 1994: *PHS Guideline for Preventing Transmission of Human Immunodeficiency Virus through Transplantation of Human Tissue and Organs*
  - Organs and tissues; banked breast milk and semen
  - Transmission of HIV only
  - Developed via ad hoc expert input
- 2013: *PHS Guideline for Reducing HIV, HBV and HCV Infection Transmitted through Organ Transplantation*
  - Organs and blood vessel conduits used for transplantation
  - Transmission of HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV)
  - Developed via evidence-based process and expert input

Important Differences in Focus (1994 versus 2013 PHS Guideline)

- Expanded to include HBV and HCV
- Term “CDC High Risk donor” changed to “Increased Risk Donor (IRD)”
- Criteria resulting in IRD designation updated to 12 categories
  - time period during which risk behaviors result in IRD designation standardized to 12 months (previously 5 years or 12 months)
- Special recipient informed consent prior to IRD organ transplant (previously CDC high risk donors excluded unless deemed emergency
- Donor and recipient laboratory testing recommendations updated
  - includes HCV NAT for all donors and HIV NAT or HIV p24 antigen for IRD
  - post-transplant HIV, HBV, HCV recipient testing

Evidence-based Process for Revision

- HHS agencies and external experts from transplant community provided input
- On behalf of PHS, CDC led development of draft
- Recommendations based on systematic review of the best available evidence
- Evidence review conducted by:
  - Center for Evidence-based Practice at University of Pennsylvania
  - ECRI Institute/Evidence-based Practice Center

Technical Advisors for Guideline Development

- Expert Panel
  - Experts in consent Issues, hepatitis and HIV content, and laboratory medicine;
  - Individuals with background in organ recovery, transplantation, and infectious disease
- Review Committee
  - Representatives from organ recovery, transplantation, and public health professional organizations (e.g., Council of State and Territorial Epidemiologists, Association of Organ Procurement Organizations, American Society for Transplantation, American Society of Transplant Surgeons, United Network for Organ Sharing); laboratory test manufacturers; patient advocate; and ad hoc members
- PHS representatives from CDC, FDA, HHS/OPHS, HRSA, and NIH

Categories of PHS Guideline Recommendations

- Summary of Recommendations
  - Risk Factors for Recent HIV, HBV or HCV Infection
  - Risk Assessment (Screening) of Living and Deceased Donors
  - Testing of Living and Deceased Donors
  - Informed Consent Discussion with Transplant Candidates
  - Testing of Recipients Pre- and Post-transplant
  - Collection and/or Storage of Donor and Recipient Specimens
  - Tracking and Reporting of HIV, HBV and HCV
- Recommendations for Further Study

Process for Revision of PHS Guideline

- HHS offices and agencies, including CDC, HHS/OPHS, HRSA, FDA, and NIH, reviewed and approved the draft PHS Guideline
- Federal Register Notice
  - 90-day public comment period
- **Approximately 100 comments were received and reviewed**
- PHS Guideline Revision Work Group convened to review and discuss changes to recommendations
  - Agreed on changes to the guideline
- Expert Panel and Review Committee
  - Provided further input

Issues Raised During Guideline Development

- Revised risk factors identified for HIV, HBV or HCV infection may result in more donors defined as at increased risk, raising fears of reduced acceptance of organs
- New recommendations for nucleic acid testing (NAT) may result in more false positive tests, raising fears of decreased organ availability
- New recommendations for pre- and post-transplant testing of transplant recipients may increase costs

Categories of PHS Guideline Recommendations – initial draft

- **Donor Risk Assessment**
- **Donor Screening**
  - Includes Table of risk factors for recent infection of HIV, HBV, HCV
- **HBV-Infected Donors and Transplantation**
- **HCV-Infected Donors and Transplantation**
- **Recipient Informed Consent**
- **Recipient Testing**
- **Donor and Recipient Specimen Collection and Storage**
- **Tracking and Reporting of HIV, HBV and HCV**

Major Changes to PHS Guideline In Response to Public Comment and External Input

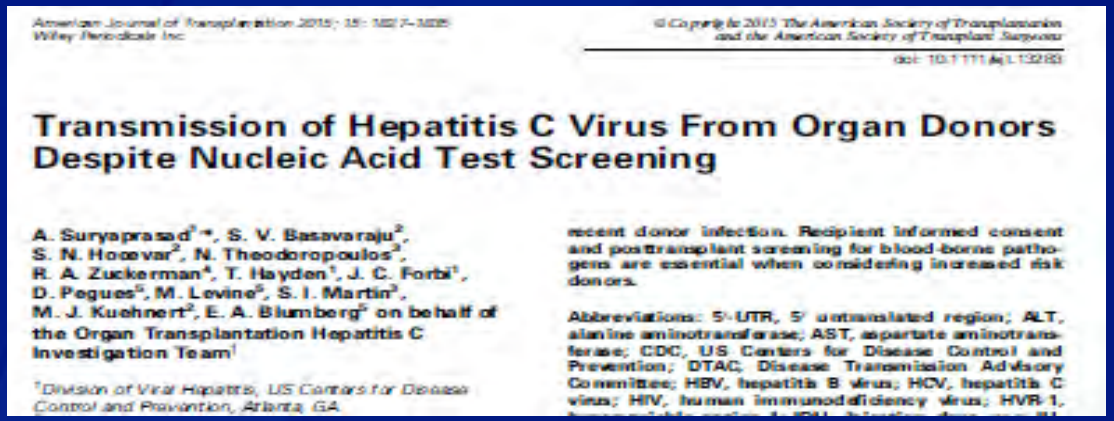
- Number of recommendations decreased from 54 to 32
- Sections on HBV- and HCV-infected Donors and Transplantation were deleted
- Donor testing for HIV changed from NAT for all donors to NAT or Ag/Ab for increased risk donors
- Donor testing for HBV changed from NAT for increased risk donors to no recommendation
- Living Donor testing changed from within 7 to within 28 days of organ recovery
- Recipient testing (based on increased donor risk) reduced and changed to broader timeframes after transplant

Major Changes to PHS Guideline In Response to Public Comment and External Input

- **Regarding storing blood specimens for future testing (for the possibility of donor-derived disease transmission investigation)**
  - Recommendations changed to limit to storing specimens from deceased donors only (no recommendations for living donors or recipients)
  - Recommendations on division of donor specimens into multiple aliquots for storing was deleted

Items to Consider In the Wake of the Finalized PHS Guideline

- **Risk-Benefit Analysis**
  - how many transmissions prevented because they would have received HIV/HBV/HCV infected organs?
  - how many recipients die because of turning down a donor with a false positive test (serology or NAT)?
- **Cost-Benefit Analysis?**
  - what is the cost of serology and NAT?
  - what is the cost of keeping a candidate on the wait list?
  - what is the cost of treating HIV, HBV, HCV?
- **Can safety be preserved while increasing availability?**
  - reduce the 12 month deferral period for risk behaviors?
  - reduce number of risk factors?
  - why not get rid of risk factors altogether, and “trust the NATs”?



American Journal of Transplantation 2015; 15: 1827–1835
Wiley Periodicals Inc.

doi: 10.1111/ajt.13283

Transmission of Hepatitis C Virus From Organ Donors Despite Nucleic Acid Test Screening

A. Suryaprasad[1,*], S. V. Basavaraju[2], S. N. Hoosvar[2], N. Theodoropoulos[3], R. A. Zuckerman[4], T. Hayden[1], J. C. Forbi[1], D. Pegues[5], M. Levine[5], S. I. Martin[3], M. J. Kuehnert[2], E. A. Blumberg[5] on behalf of the Organ Transplantation Hepatitis C Investigation Team[†]

[1]Division of Viral Hepatitis, US Centers for Disease Control and Prevention, Atlanta, GA

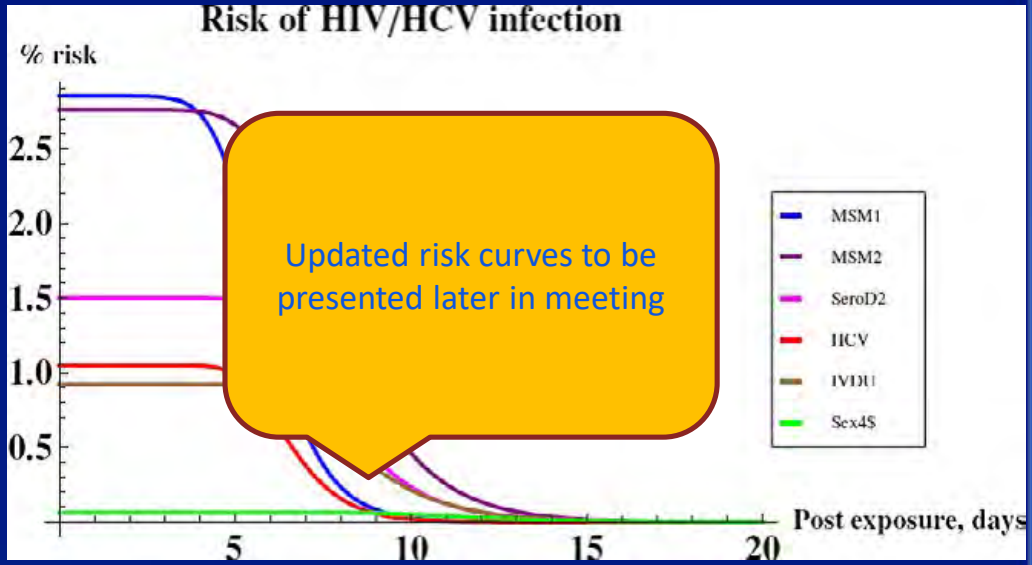
recent donor infection. Recipient informed consent and posttransplant screening for blood-borne pathogens are essential when considering increased risk donors.

Abbreviations: 5′-UTR, 5′ untranslated region; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CDC, US Centers for Disease Control and Prevention; DTAC, Disease Transmission Advisory Committee; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HVR-1,

- 3 clusters of HCV transmitted via organ transplantation despite NAT screening, 2011-2013 (one each year), affecting 8/12 recipients
- Donor risk factors: 1 heroin overdose (found down w/needles), 1 MVA (found w/needle marks), 1 history IVDU
- Detection was attributable to careful post-transplant testing which is not universal practice in recipients of organs from increased risk donors (Theodoropoulos, 2013)
- Outcomes poor when donor HCV infection is recent, reipcient treatment not given quickly (unrecognized infection or treatment not feasible)

Modeling Risk of undetected HIV and HCV infection if nucleic acid test (NAT) negative

- Antibody tests have window period (before immunologic response to infection)
- NAT closes the window period, but there is still an “eclipse period” of 5-7 days where virus is present, but undetectable
- Risk of undetected infection despite NAT can be modeled
- Recent publication applied model of increased risk organ donors
- Challenge to find “safe subset”



Risk of HIV or HCV infection being present despite negative NAT for different types of behavior, 0 to 20 days between testing and exposure.

Source: Annambhotla PD, et al. Transpl Infect Dis 2017.

Morbidity and Mortality Weekly Report

Characteristics of Deceased Solid Organ Donors and Screening Results for Hepatitis B, C, and Human Immunodeficiency Viruses — United States, 2010–2017

Winston E. Abara, MD[1]; Melissa G. Collier, MD[1]; Anne Moorman, MPH[1]; Danae Bixler, MD[1]; Jefferson Jones, MD[2]; Pallavi Annambhotla, PhD[2]; James Bowman, MD[3]; Marilyn E. Levi, MD[3]; John T. Brooks, MD[4]; Sridhar V. Basavaraju, MD[2]

TABLE 2. Characteristics of deceased increased risk donors (IRDs) (N = 12,592) — Organ Procurement and Transplantation Network, United States, 2010–2017

Characteristic	2010 No. (%)	2011 No. (%)	2012 No. (%)	2013 No. (%)	2014 No. (%)	2015 No. (%)	2016 No. (%)	2017 No. (%)	Total 2010–2017 No. (%)
IRDs (% among all deceased donors)	709 (8.9)	836 (10.3)	966 (11.9)	1,11[illegible] (13.4)	1,772 (20.6)	2,016 (22.2)	2,478 (24.9)	2,704 (26.3)	12,592 (17.9)
HCV RNA by NAT									
Positive	—	—	—	—	7 (8.6)†	252 (14.5)§	363 (14.7)¶	423 (15.7)**	1,045 (14.9)
Negative	—	—	—	—	74 (91.4)	1,488 (85.5)	2,114 (85.3)	2,280 (84.3)	5,956 (85.1)
Percentage of IRDs tested for HCV RNA by NAT	—	—	—	—	81 (4.6)	1,740 (86.3)	2,477 (>99.9)	2,703 (>99.9)	7,001 (78.1)

† Six of the seven HCV RNA–positive donors were anti-HCV positive; one was negative.
§ 243 of 252 (96.4%) HCV RNA–positive donors were anti-HCV positive; nine (3.6%)were negative.
¶ 344 of 363 (94.8%) HCV RNA–positive donors were anti-HCV positive; 19 (5.2%) were negative.
** 397 of 423 (93.9%) HCV RNA–positive donors were anti-HCV positive; 26 (6.1%) were negative.
†† The HIV Organ Policy Equity Act (HOPE Act) of 2013 allows transplantation, under research protocols, of organs from donors infected with HIV into recipients who are also infected with HIV. https://optn.transplant.hrsa.gov/governance/public-comment/changes-to-hope-act-open-variance/.
§§ Fiveof the six HIV RNA-positive donors were anti-HIV positive; one(16.7%) was negative.

Organ Safety: Progress and Challenges

What is missing?

- Knowledge of how many transmissions prevented
- Outcomes for management of known infected donor ("expectant transmissions")
  - HBV and HCV transmission
  - HIV transmission (HOPE Act)
- Need for better informed consent understanding/discussion
- Models to understand what donors are at risk
  - study of donors with true positive laboratory screening tests, correlated with known risk factors as evident in history questionnaire
  - Would require participation of most OPOs

Organ Safety: Progress and Challenges

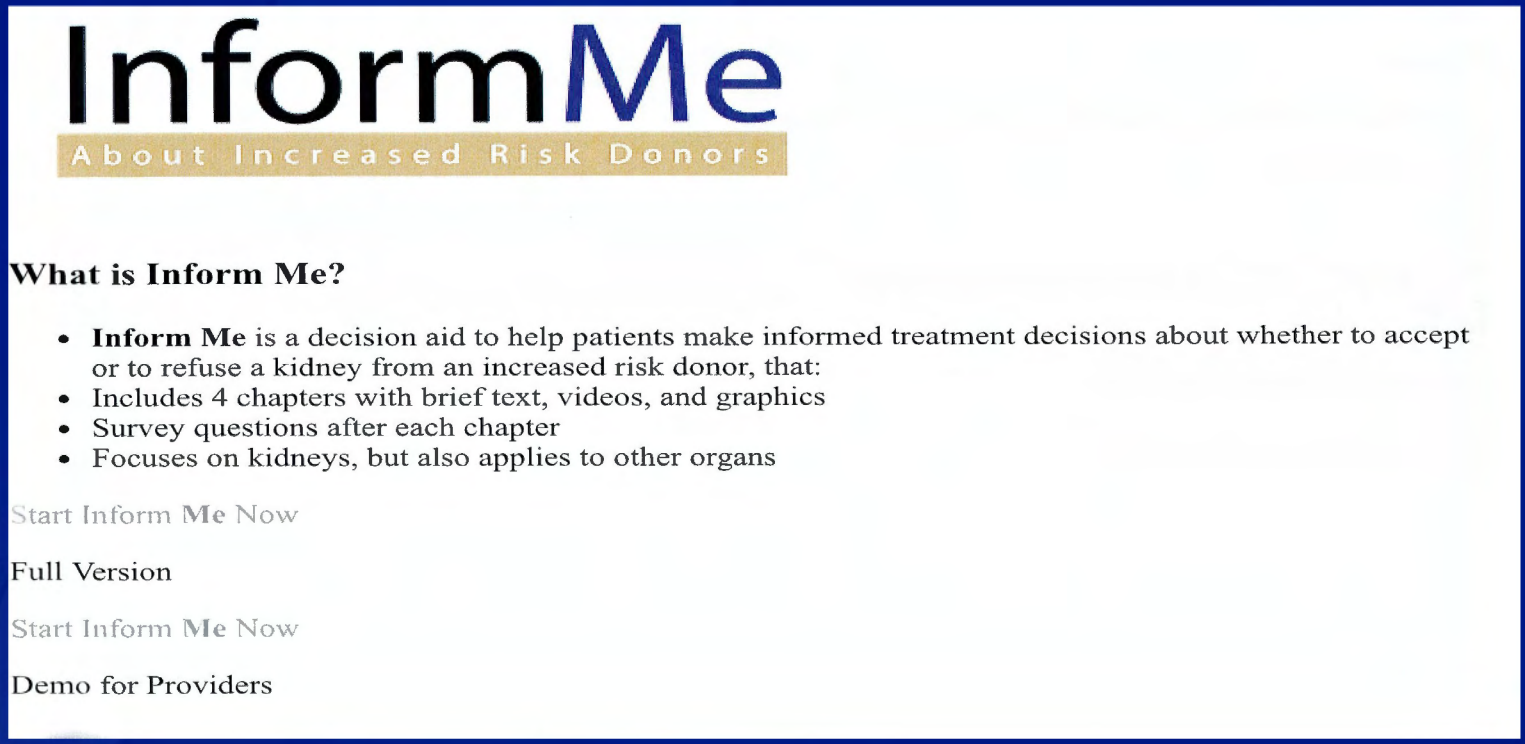
What are the dangers?

- Risks of eliminating risk factor assessment entirely, and rely on laboratory screening
  - Still have eclipse period
  - Lack of assessment for organ donors may lessen attention to evaluate same donors for tissue eligibility (risk of transmission to organ and tissue recipients)
  - There are other pathogens besides HIV/HBV/HCV
    - Human herpesvirus 8
    - Hepatitis E virus
    - Pegivirus 2 (not same as Pegivirus 1/Hep G virus)

Organ Safety: Progress and Challenges

What needs to be done?

- Testing of all recipients receiving transplant from increased risk donors
  - document lack of transmission
  - rapid diagnosis and treatment to improve outcome
- Recommendations for management of known infected donor ("expectant transmissions")
- **Models for risk quantification**
  - **June 2017 OPTN document https://optn.transplant.hrsa.gov/resources/guidance/understanding-hiv-hbv-hcv-risks-from-increased-risk-donors/**
  - **there are few projects moving forward in this area (e.g., risk-benefit score that can be based on individual data to illustrate risk to both surgeon and recipient)**



https://informme.cbits.northwestern.edu/system/

Improving Organ Transplant Availability by Evaluating Risk of Infection Transmission

Dec 19, 2016 | Atlanta, GA

The demand and the average time on the waiting lists for organ transplants are growing, while the supply of organs remains comparatively limited.

According to UNOS, the United Network for Organ Sharing, currently more than 121,480 people across the United States are waiting for an organ, while 30,970 people received transplants in 2015. In the same year, 6,648 people died on the transplant waitlist, while 6,702 were removed from the list after waiting so long that they became too sick to undergo transplant surgery.

A possible resolution to this problem is to increase the availability of organs. In the past, organs with a small risk of infection were often not chosen for transplant. After several transmissions of infectious diseases that occurred through transplants where these infections (or the risk) were not detected ahead of time, use of many more organs were discouraged because of problems with understanding the risk.

A collaborative project between ISyE and the Centers for Disease Control and Prevention (CDC) addresses this issue of risk estimation and perception, with the goal of assessing the risk of infection in an organ donor, and evaluating the options of receiving an increased-risk donor (IRD) organ versus staying on the waitlist for a patient. Ultimately, the goals are to reduce deaths due to organ transplants transmitting infections, boost the availability of organs without infection for transplant, and reduce the number of patients who die while on the waiting list.

The collaboration started with a Senior Design project, initially focusing on infectious encephalitis in liver transplants.

ORIGINAL ARTICLE

WILEY

Assessment of risk for transplant-transmissible infectious encephalitis among deceased organ donors

Hannah K. Smalley[1,2] | Nishi Anand[1] | Dylan Buczek[1] | Nicholas Buczek[1] | Timothy Lin[1] | Tanay Rajore[1] | Muriel Wacker[1] | Sridhar V. Basavaraju[3] | Brian M. Gurbaxani[1,4] | Teresa Hammett[5] | Pinar Keskinocak[1,2] | Joel Sokol[1] | Matthew J. Kuehnert[3]

[1]H. Milton Stewart School of Industrial and Systems Engineering, Georgia Institute of Technology, Atlanta, GA, USA

[2]Center for Health and Humanitarian Systems, Georgia Institute of Technology, Atlanta, GA, USA

[3]Office of Blood, Organ, and Other Tissue Safety, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases, Atlanta, GA, USA

Abstract

Background: There were 13 documented clusters of infectious encephalitis transmission via organ transplant from deceased donors to recipients during 2002-2013. Hence, organs from donors diagnosed with encephalitis are often declined because of concerns about the possibility of infection, given that there is no quick and simple test to detect causes of infectious encephalitis.

Methods: We constructed a database containing cases of infectious and non-infectious encephalitis. Using statistical imputation, cross-validation, and regression techniques,

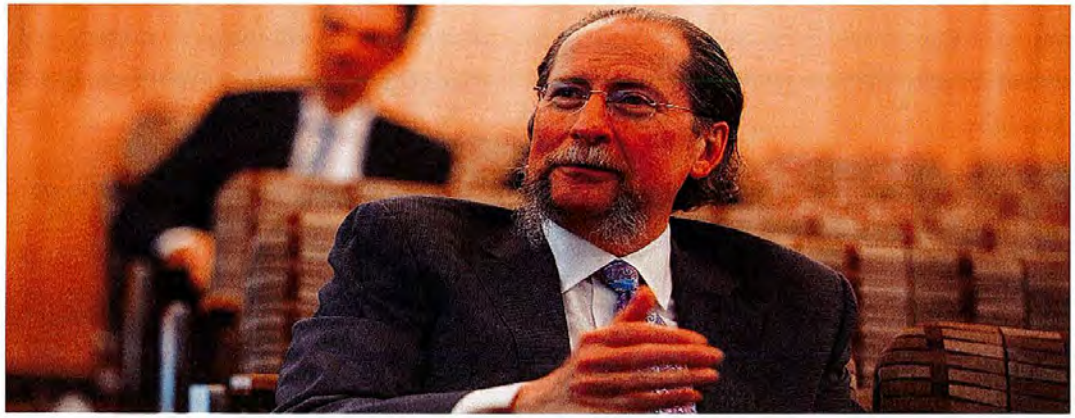
FIGURE 1 User interface of the infectious encephalitis risk calculator

The Bottom Line

- Risk of infectious disease transmission is small, but important for there to be trust in the system, including for organ recipients
- Risks are poorly understood clinically; no guideline or mandated testing will fix this gap
- Informed consent and assessment tools at the bedside level are key, unless you're an expert yourself
- Real life story illustration….

PATIENT CARE, IN THE MEDIA | JANUARY 28, 2019

The Wall Street Journal: Leading Transplant Surgeon Accepts a Hepatitis C–Positive Heart for Himself



Transplant surgeon Dr. Robert Montgomery, a long-time advocate for the use of organs from high-risk donors, has now received a hepatitis C–positive heart transplant.

PHOTO: NYU LANGONE STAFF

Robert Montgomery, MD, professor of surgery and director of NYU Langone Transplant Institute, has advocated for his patients to accept organs from high-risk donors for years. In September 2018, he had to make that decision for himself, as a heart transplant recipient.

"I actually hired the people that did my transplant, not knowing they would be saving my life at some point," says Dr. Montgomery. Five days after entering the hospital, he had an offer of a hepatitis C-positive heart. Nader Moazami, MD, professor of cardiothoracic surgery and surgical director of heart transplantation at NYU Langone, performed Dr. Montgomery's transplant.

The Transplant Institute now successfully transplants hepatitis C-positive organs to hepatitis C-negative recipients in their heart, lung, kidney, and liver programs. Patients are immediately treated for hepatitis C with medications, which are more than 95 percent effective. Dr. Montgomery tested positive for the disease five days after the surgery. He took oral medication every day for eight weeks, and the infection cleared. He returned to work part time two weeks after the surgery, and was back to full time two months later.

QUESTIONS?

Historical perspective on the establishment of DTAC

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Historical Perspective on the Establishment of DTAC

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Northwestern University Feinberg School of Medicine

Advisory Committee on Blood and Tissue Safety and Availability

Washington, DC – 15 April 2019

Disclosures

- Research Support°
  - AiCuris, Chimerix, Emergent BioScience, Genentech/Roche, Gilead, Janssen, Shire
- Paid Consultation
  - Celltrion, Genentech/Roche, Janssen, Shionogi, Viracor Eurofins, VirBio
- Unpaid Consultation
  - GlaxoSmithKline, Romark, Vertex
- Data & Safety Monitoring Board Participation
  - Janssen, Vitaeris

As of 3/12/19; ° Paid to Northwestern University.

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Donor-Derived Infections: *Definitions*

- Any infection of a recipient that results from an infection present in the donor and transmitted by the donated organ
- Types:
  - Expected:
    - Common everyday occurrence
    - HBV, HCV, EBV, CMV, Toxo
  - Unexpected
    - True incidence is unknown: Lower but not absent for living donors
    - Best estimate: ~0.15%
    - LCMV, Rabies, malaria
    - Bacterial, fungal pathogens

Ison MG, Nalesnik MA. ***Am J Transplant***. 2011;11: 1123-30.
Garzoni C, Ison MG. ***Transplantation***. 2011; 92: 1297-1300.

The Early Days: *Pre-DTAC*

illustration: Don Smith

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Donor-Derived Disease Transmissions: *Setting the Stage*

- 54 yo WM with HBV/HCV/HCC
- Day 5: Fever to 102.4, mild frontal HA since time of transplant
- IS: ATG, Tacrolimus, Azathioprine
- Abx: Pip-Tazo, HBIg, 3TC, Famciclovir, TMP-SMX
- SH: Suburbs, Iron worker
- PE: Non-focal except for a tender RUE peripheral IV catheter

Donor-Derived Disease Transmissions: *Setting the Stage*

- Continued with fever, LFTs increased
- Seizure (? Hypoxemic)
- Progressive “sepsis” with elevated LFTs and renal dysfunction
- Call from another Transplant ID doc

Donor-Derived Disease Transmissions: *Setting the Stage*

Fischer *et al*. ***N Eng J Med***. 2006;354:2235-2249.

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Donor-Derived Diseases: *Regulations*

- OPTN Policy 4.6 (Screening of Donors)
  - Donor testing must use use a FDA licensed, approved or cleared serologic test *if commercially available*
  - *In the event that such screening tests are not commercially available prior to transplant, then a FDA approved diagnostic test is permissible to assess the donor*
  - The Host OPO shall obtain a history to determine if the donor is "high risk"
  - Known conditions that may be transmitted by the donor organ must be communicated to the transplant centers
  - Exceptions
    - Organs from donors with a positive screening test or confirmed medical conditions that may be transmittable, with the exception of HIV, may be transplanted at the discretion of the transplanting program with the informed consent of the recipient

http://www.optn.org/policiesAndBylaws/policies.asp. Accessed 4/1/09

Background: *OPTN Policy 4.7*

- 'When a transplant program is informed that an organ recipient at that program is confirmed positive for or has died from a transmissible disease or medical condition for which there is substantial concern that it could be from donor origin, the transplant program must notify by phone and provide available documentation, as soon as possible and not to exceed one complete working day, to the procuring OPO.'
- OPO shall then:
  - Communicate the results to all recipient Transplant Centers & Tissue Banks
  - Manage the investigation
  - Notify the OPTN as soon as possible
  - Submit a final written report to the OPTN within 45 days

http://www.optn.org/policiesAndBylaws/policies.asp. Accessed 4/1/09

Disease Transmission Advisory Group

- Created in October 16, 2006
  - A working group of the Operations Committee
  - Initial Members
    - ID: Jay Fishman, Emily Blumberg, Michael Ison
    - Malignancy: Mike Nalesnik
    - Ops Members: Rick Hasz, Kevin Myer, Myron Kauffman
    - External Members: Matt Kuehnert (CDC), Elizabeth Ortiz-Rios (HRSA)
- First Report Reviewed by Group in October 31, 2006
  - First report was of probable transmission of leukemia
  - Truly the wild west: No plan on how to handle the case, no guidelines
  - Goal per Jay "our real job will be to define the role of DTAG at UNOS over time"
  - Generally started as discussion among the members
  - Quickly added Amit Tevar to help with malignancy cases

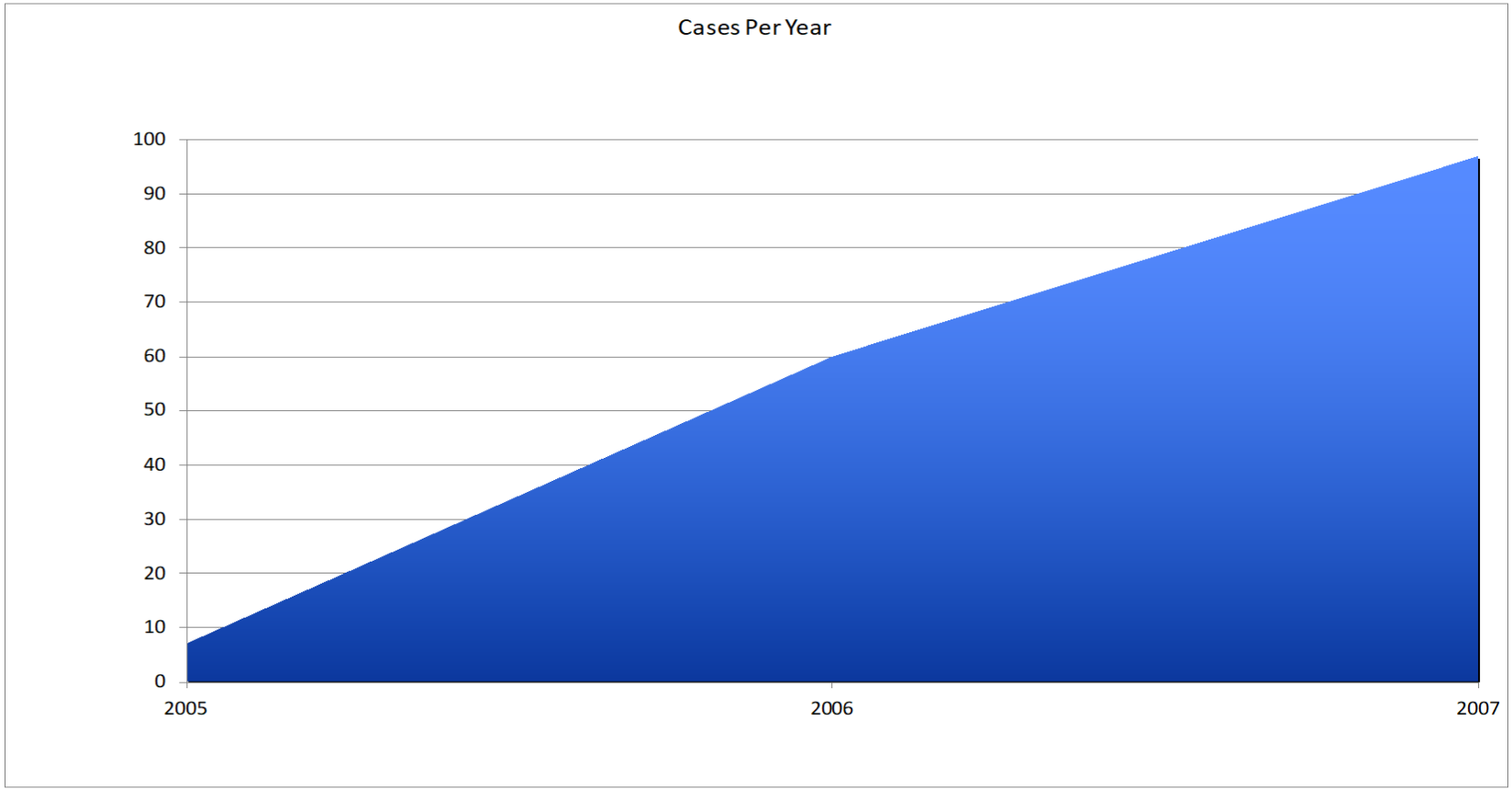
Disease Transmission Advisory Group

- First Leadership Transition: August 2007
  - Michael Ison became the second DTAG chair
- First case of a reportable disease emerged August 2007: Legionella
  - A lot of confusion about roles of various partners
  - Initially reported through health department and independent investigation initiated with CDC leadership
  - Quickly established need for DTAG involvement in case
    - Matt quickly invited DTAG chair to become involved in all calls related to the case
- Initial work all conducted manually
  - Email discussion
  - Paper/simple electronic management system

DTAG Membership by end of 2007

Name	Specialty	Affiliation
Michael Ison, MD MS (Chair)	Transplant ID	Northwestern
Michael Nalesnik, MD (Vice Chair)	Transplant Path	U. Pittsburgh
Emily Blumberg, MD	Transplant ID	U. Pennsylvania
Kevin Carney, RN/CCTC	Transplant Coordinator	U. Pennsylvania
James Cutler, CPTC	OPO	SW Transplant Alliance
Michael DiMaio, MD	CT Surgery	UT Southwestern
Rick Hasz, MFS	OPO	Gift of Life
Lewis Teperman, MD	Transplant Surgery	NYU
Amit Tevar, MD	Transplant Oncology	U. Cincinnati
Matt Kuehnert, MD	*Ex officio*	CDC
James Burdick, MD	*Ex officio*	HRSA/DoT
Chris McLaughlin	*Ex officio*	HRSA/DoT
Elizabeth Ortiz-Rios, MD	*Ex officio*	HRSA/DoT
Joyce Hager, MPH	Patient Safety Manager	UNOS
Vicki McEwen	Patient Safety Coordinator	UNOS
Gloria Taylor, MA RN	Standards & Process	UNOS

DTAG: *Quick Growth*



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Focus in Increased Risk Donors: *The Start*

Index Patient: 30 yo M with nephrotic syndrome

- HIV, HCV antibody negative in 2003 for listing for 2nd transplant
- Highly sensitized, consented for IRD kidney: November 2006

- 3 months Post-Transplant
  - Elevated LFTs, negative hepatitis serology
  - Liver biopsy: inflammation, stage II/III fibrosis -> HCV RNA (>10M IU/mL)
- 10 months Post-Transplant
  - Kidney biopsy: Banff 1A ACR, HIVAN (Proliferative GN)
  - HIV Ab+, HIV Viral Load 520c/mL and CD4 Count 16 cells/µL
  - Referred to ID for evaluation and management
- 11 months Post-Transplant
  - Presented to hospital after syncope in train station
  - Significant diarrhea
  - Alerted OPO, UNOS, CDC of transmission

Ison *et al*. ***Am J Transplant***. 2011; 11: 1218-1225.

Focus in Increased Risk Donors: *The Start*

- Donor
  - Negative serology for HIV & HCV
  - Appropriately labeled as "high risk" by PHS guidelines
  - Subsequent testing of post-transfusion serum was + for HIV and HCV by PCR

Table 1: Detection of HIV and HCV through laboratory testing in organ donor samples

Specimen	Hemodilution[1]	Anti-HIV antibody	HIV Viral Load	Anti-HCV IgG	HCV Viral Load
Pretransfusion (Routine screening results)	None	Negative	ND	Negative	ND
Pretransfusion Investigation results	–	Unavailable for testing	Unavailable for testing	Unavailable for testing	Unavailable for testing
Posttransfusion Investigation results	Yes	Negative	Positive[2]	Negative	Positive (898 IU/mL)

Table 2: Investigation results of HIV and HCV laboratory testing in four organ recipients

	Pretransplant			Posttransplant values at initial assessment—November 2007					
Organ	Date	Anti-HIV IgG	Anti-HCV IgG	Date	Anti-HIV IgG	HIV Viral Load (copies/mL)	Anti-HCV IgG	HCV RNA	HCV Viral Load (IU/mL)
Left kidney	2003[1]	NR	NR	10/07	Reactive	520	NR	Reactive	23 million
Right kidney	1/07	NR	NR	11/07	Reactive	35,000	NR	Reactive	4–5 million
Liver	12/06	NR	NR	11/07	Reactive	500,000	NR	Reactive	5 million
Heart	12/06	NR	NR	11/07	Reactive	1 million	NR	Reactive	4–5 million

Ison *et al*. ***Am J Transplant***. 2011; 11: 1218-1225.

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Response to HIV-HCV Transmission Event

- Community quickly responded with processes to improve consent and monitoring
- OPTN Developed Revised Policy
  - Requirement of special informed consent
  - Subsequently requirement to perform testing: Still not optimal
- Testing: Recognition of potential value of NAT
  - Increased NAT capacity at OPOs around the US
  - Debate about optimal role of NAT for donor screening
- Calls for updating PHS Definitions of Increased Risk Donors
- Enthusiasm and interest in Disease Transmission Data

Formation of DTAC

- In response to HIV/HCV Transmission event, enhanced focus on DTAG and work it was doing
- Recognition that there was a need to develop and invest in the process
  - Significant effort and time (esp after hours; 22-33 hours) utilized for cases
- DTAG became the *Ad Hoc* Disease Transmission Advisory Committee
  - Remove requirement for regional representation
  - Independent from Operations (although kept members for linkage)
  - Allowed flexible membership to reflect content knowledge
  - Had to remain a "closed" committee because of medical peer review
  - Commitment to increase support for the Committee
    - Increased number of and support for coordinators
    - Develop components of Patient Safety portal
    - Enhance Sharepoint utility

Formation of DTAC

- Initial charge
  - Determine current understanding of the risk of donor disease transmission through solid organ transplantation [Patient Safety]
  - Evaluate current status of screening and diagnostic testing for donor disease transmission, and recommend appropriate evidenced-based OPTN policy concerning donor testing and screening for transmissible disease [Patient Safety]
  - Develop plans to address risk of donor disease transmission through collaborative consensus conference (AST, ASTS, AOPO, SRTR, etc.) [Patient Safety]
  - Collaborate with other Committees
    - Operations: Work with DTAC to address safety of donor organ supply
    - Organ Availability Committee: Work with Operations Committee, DTAC and OPO Committee to identify and address issues pertaining to safety of the donor organ supply
    - Organ Procurement Committee: Work with Operations Committee, DTAC, and Organ Availability Committee to identify and address issues pertaining to safety of the donor organ supply

DTAG: *Accomplishments*

- Formalization of Group Structure and Function
  - Draft Charter: pending Operations approval
  - Monthly Calls, Annual Meeting
  - Formal numbering system
- Partnering with Other Experts
  - American Organ Procurement Organization
    - Standardized donor questionnaire
    - Collecting data on NAT as implemented regionally
  - Israel Penn International Transplant Tumor Registry
  - Living Donor Committee
  - Centers for Disease Control & Prevention
    - Enhancing and simplifying the flow of information to and from CDC to help inform DTAG decisions

Establishing a US Organ Vigilance System: *DTAC*

- Organ Procurement & Transplant Network Policy Creates the Reporting Requirement
  - OPTN Policy 15.4: Requires reporting of any suspected or proven disease transmission to the OPO, all transplant centers and the OPTN within 24 hours of first becoming aware of the potential transmission
  - An Electronic Reporting Portal Created: *Patient Safety System*
  - Creation of Review Committee of Experts: *Disease Transmission Advisory Committee*
  - Developed a case review process
    - Patient Safety Staff prepare summary of event with identifiers redacted
    - Key materials are uploaded to SharePoint Server and shared with members
    - E-mail based discussion
    - Day 45 Follow-up Reports submitted
    - Handling of Special Cases: CDC, Required Calls and MPSC
  - Monthly conference calls
  - Bi-Annual Meeting
- Establish an internationally agreed upon definition of imputibility

http://optn.transplant.hrsa.gov/ContentDocuments/OPTN_Policies.pdf
Ison *et al*. ***Am J Transplant***. 2009; 9: 1929-1935.
Ison & Nalesnik. ***Am J Transplant***. 2011; 11: 1123–1130.

Establishing a US Organ Vigilance System: *DTAC*

Proven	• Donor plus one recipient
Probable	• One or more recipients with suggestive data
Possible	• Evidence to suggest but not prove transmission
Intervention without Documented Transmission (IWDT)	• No transmission because antimicrobials were used (or for RCC, affected KI discarded or tumor excised)
Unlikely	• Limited evidence to suggest transmission could have occurred, but no transmission documented
Excluded	• No evidence of transmission

Garzoni C, Ison MG. ***Transplantation***. 2011; 92: 1297-1300
Ison et al. ***Am J Transplant***. 2009; 9: 1929-1935.
Green *et al*. ***Transplantation***. 2015;99:282-287.

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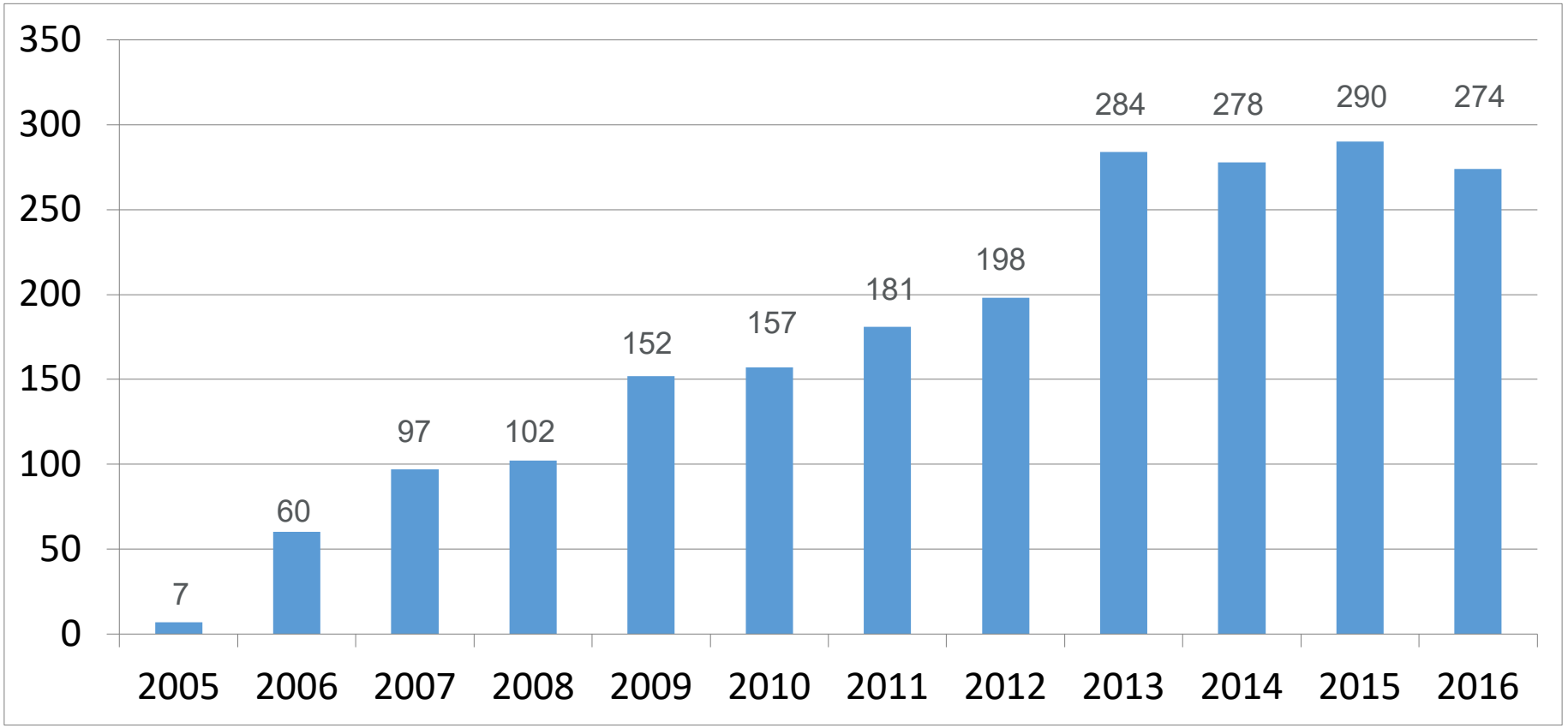
Potential Donor Derived Transmission Events (PDDTE)



*Additional reports are submitted, but not reviewed by full DTAC (duplicates, expected transmissions and other unnecessary reporting, etc).

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For an extended description of this chart, please see the description on **page 237**.

Organ Vigilance Systems Develop Real-Time Guidelines

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Guidance: *HTLV Testing in the US*

- Setting: 2009, manufacturers of HTLV testing in the US announced they were discontinuing production of assays
  - OPTN Policy required HTLV testing
  - Few HTLV positive organs were being used
  - Options: Research only reagents, develop a new assay, allow retrospective testing or drop requirement for testing

- OPTN/DTAC Develop a plan for addressing
  - Collect real data on organ usage
  - Collect data on positivity (only available on patients with organs used)
  - Provide guidance to the community on next steps

Kaul *et al*. ***Am J Transplant***. 2010;10: 207-213.

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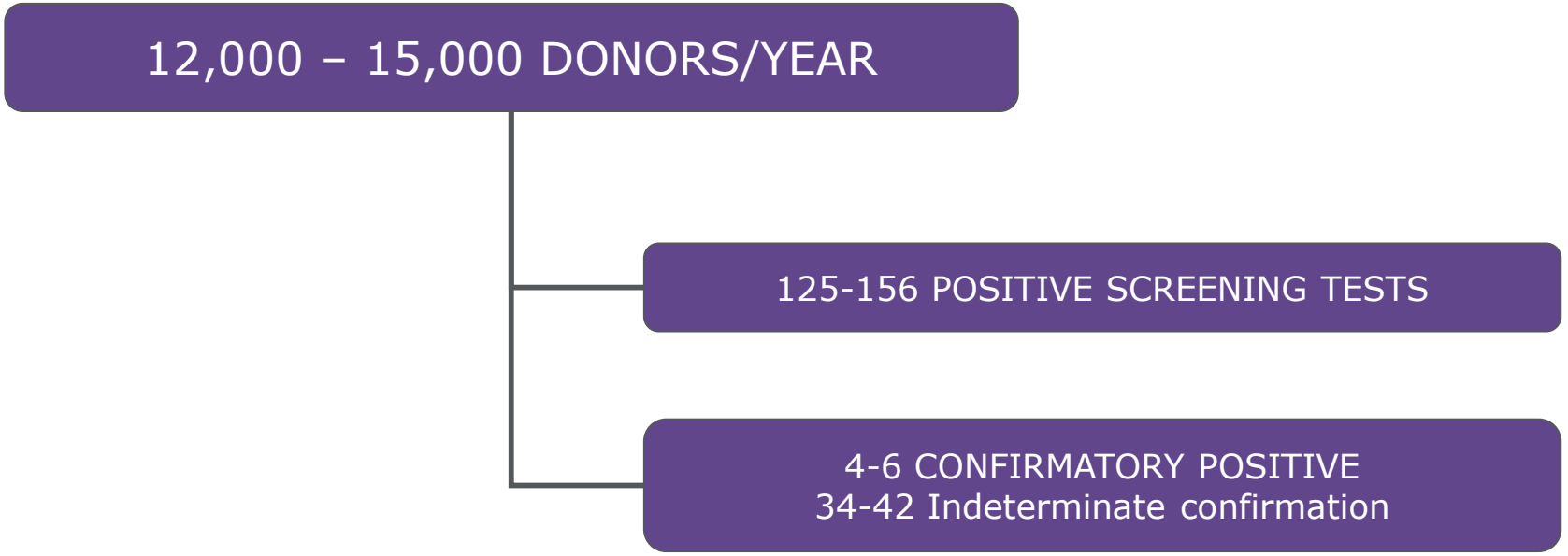
Guidance: *HTLV Testing in the US*



Estimated that 83-114 donors lost per year from false positive screen or HTLV-2 infection.

Kaul *et al.* ***Am J Transplant***. 2010;10: 207-213.

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Guidance: *HTLV Testing in the US*

- Outcome
  - OPTN Policy changed to no longer require HTLV testing
  - Few OPOs doing HTLV testing
  - Feedback from community: Appreciated the education and wished they had used more HTLV+ organs in the past
  - No reports of HTLV-associated disease transmission in the 10 years since removing the requirement for testing

Kaul *et al*. ***Am J Transplant***. 2010;10: 207-213.

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DTAC: *Challenges & Opportunities*

- Interface between OPTN/UNOS DTAC and Public Health
  - Multiple pinch points and conflicts led to the need for formal agreements
  - HRSA coordinated a series of calls and meetings to develop ground rules
  - Clear delineation of roles of Public Health and DTAC
  - It is in everyones best interest to have significant data sharing in collaborative cases
- AATB: Uniform Donor Health Questionnaire
- AOPO: Understanding donor screening used by OPOs in the US
- Specific Donor Risk Issues
  - Chagas, Dengue, Endemic Mycoses, Hemodilution
  - Vessels, NAT

Revision of PHS Increased Risk Guidelines

- DTAC was invited to provide advice and contributed to knowledge for the 2013 revision of PHS Increased Risk Guidelines
  - Work on issues related to vessels, living donors, collection of data not currently on forms
  - Survey of serologic and NAT use at OPOs nationally
  - Co-Organized the "OPTN/UNOS DTAC and AST IDCoP Infectious Risk Ad Hoc Committee"
    - Identify banks of serum from "high risk" donors who were screened but not accepted, to determine frequency of sero-negative and NAT positive for the agents of interest
    - Could also look at data in which high risk patients were turned down for by some centers but accepted by others or in which some organs were accepted and others were rejected – what is the rate of transmission.
    - Review of current data from those conducting NAT: How many tests are done and how many are serology negative, NAT positive; if possible, would stratify by 1994 PHS Guideline High Risk positive or negative and optimally also by high risk criteria.
    - Review the current data on high risk donors and the rate of transmission of disease (mostly focus on limitation of post-transplant testing).
    - Review Available literature
- Implementation of revised guidelines into OPTN policy

DTAC: Major Accomplishments 2005-2010

- Established the epidemiology of donor-derived disease transmission
- Increased organ availability
  - HTLV review and policy change
  - Malignancy Donor Guidance
- Provided guidance on key issues
  - H1N1, Dengue, West Nile Virus
  - Vessel policy proposal
  - Donor screening, UDHQ
- Education
  - 2 Publications (***American Journal of Transplantation***)
  - 8 Meeting Abstracts
  - 31 Meeting presentations
- Development of collaborations with key transplant players
- Established the importance of ID expertise within UNOS
  - But please don't forget about malignancies!

The Biggest Accomplishment of DTAC

- DTAC is the Gold Standard for Organ Vigilance Systems in the World
  - Led to EU law requiring all member states to develop organ vigilance systems
  - Led to establishment of the Australian vigilance system
- New programs consistently want to learn from OPTN/UNOS DTAC
- Our presentations and publications generated enthusiasm and demonstrated value for organ vigilance
- Open and free sharing of our vigilance data is essential
  - Need to ensure that key lessons learned continue to be shared
  - Review limits placed on communication to ensure they are needed
  - Need a public forum for presenting up-to-date data generated from DTAC

The Initial Work Took an Army

- To the entire committee
  - Michael Nalesnik, Vice-Chair
  - Rick Hasz – the true partner in getting this all started with Operations Committee
  - 4,250 e-mails (~1000/year)
- To our coordinators
  - Joyce Hager
  - Vipra Ghimire
  - Shandie Covington
  - Kimberly Taylor
  - Kimberly Parker
  - Susan Tlusty
- To our research support: Sarah Taranto

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Questions?

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Feedback from transplant community: need for guideline recommendation revision; data gathering and analyses to inform current revision efforts; aspects of recs amenable to revision

SRIDHAR BASAVARAJU, MD
Acting Director, Office of Blood, Organ, and Other Tissue Safety
Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

The 2013 PHS Guideline to Reduce the Risk of Unintended HIV/HBV/HCV Transmission Through Organ Transplantation: Opportunities for Improvement

Sridhar V. Basavaraju, MD
CDR-U.S. Public Health Service
Director - CDC Office of Blood, Organ, and Other Tissue Safety
Division of Healthcare Quality Promotion
National Center for Emerging and Zoonotic Infectious Diseases
CDC

Background

Summary of 2013 PHS Guideline recommendations: deceased donors

- Guideline goal is to reduce the risk of unintended HIV, HBV, or HCV transmission through transplantation
- All donors tested by HIV, HBV, HCV serology and HCV NAT
- Increased risk donors (IRD) tested by either HIV NAT or p24 antigen
  - No recommendation for HBV NAT
- Donors classified as IRD if having ≥ 1 of 12 medical/social risk factors for undetected HIV, HBV, or HCV infection or unknown medical/social history or hemodiluted blood sample used for testing
- No donor exclusion is recommended
  - Specific informed consent for recipients of IRD organs
  - Post-transplant testing of IRD organ recipients for HIV, HBV, and HCV

Community feedback about 2013 PHS Guideline- since implementation in 2014

- Too many donors are being designated as IRD
- Organs are underutilized from IRD
- Risk designation of donors is not necessary because all donors screened with NAT and effective treatment available
- Given universal adoption of NAT, evidence for 12 month timeframe is lacking
  - "Increased risk" nomenclature does not accurately portray risk of morbidity and mortality of accepting IRD organs
- Not all 12 + 2 IRD criteria increase the risk of transmission of viral bloodborne pathogens
- Request for data from CDC on HBV or HCV transmissions and outcomes

PHS response to address community feedback:

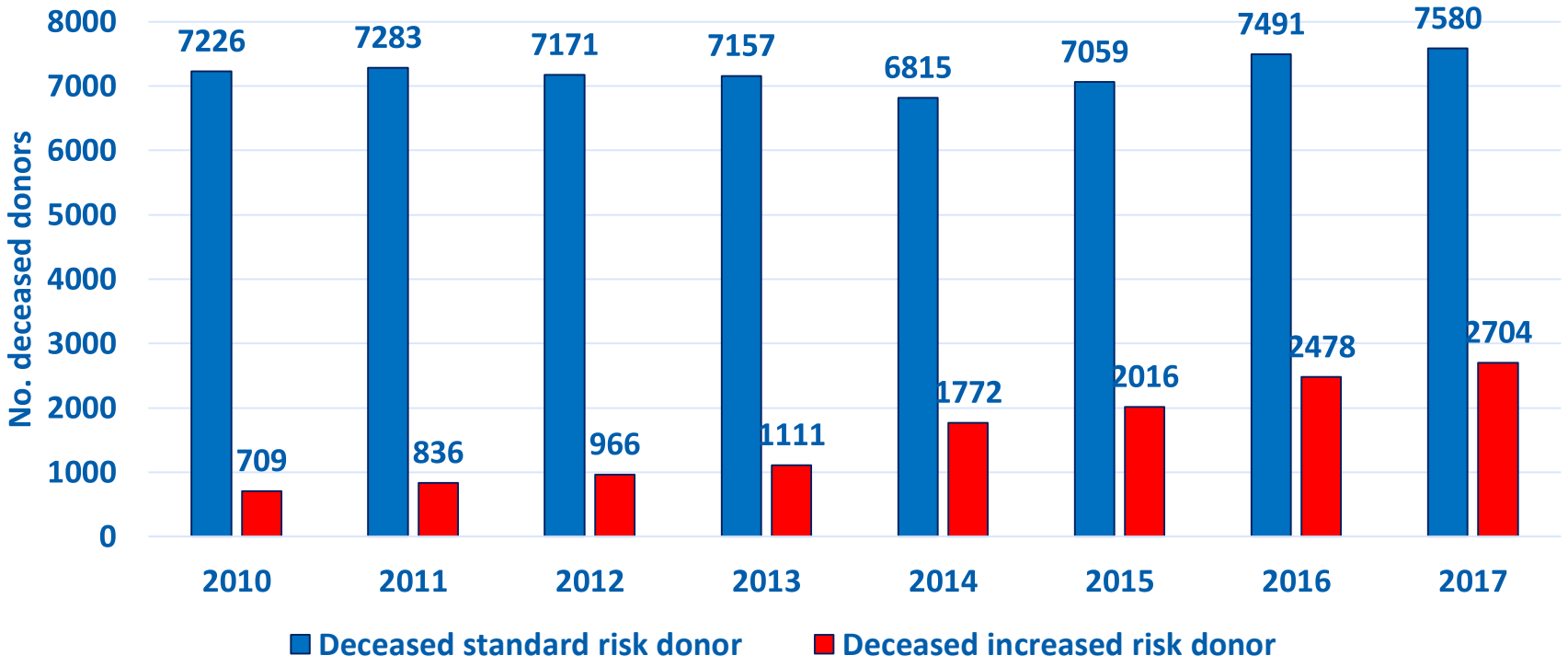
- Four analytic projects:
  - Donor characteristics and screening test results of IRD compared to standard risk donors
  - CDC-led outbreak investigations (2014-2017) of HBV/HCV transmission through transplantation
  - Impact of IRD designation on organ utilization
  - Mathematical model of risk of undetected HIV/HBV/HCV infection among IRD from time of risk behavior to negative NAT
- Ongoing engagement with stakeholders
- Present findings at Advisory Committee on Blood and Tissue Safety and Availability in April 2019
- Draft revised recommendations and post in federal registry for public comment during 2019
- Publish revised recommendation during 2020

Analytic Project 1:

Trends in deceased solid organ donor characteristics and hepatitis B, C, and HIV screening results—United States, 2010–2017

*Abara et al. Characteristics of deceased solid organ donors and screening results for Hepatitis B, C, and Human Immunodeficiency Viruses - United States, 2010-2017. MMWR Morb Mortal Wkly Rep. 2019

Deceased organ donors in the United States by increased risk status* 2010–2017 (N = 70,414)

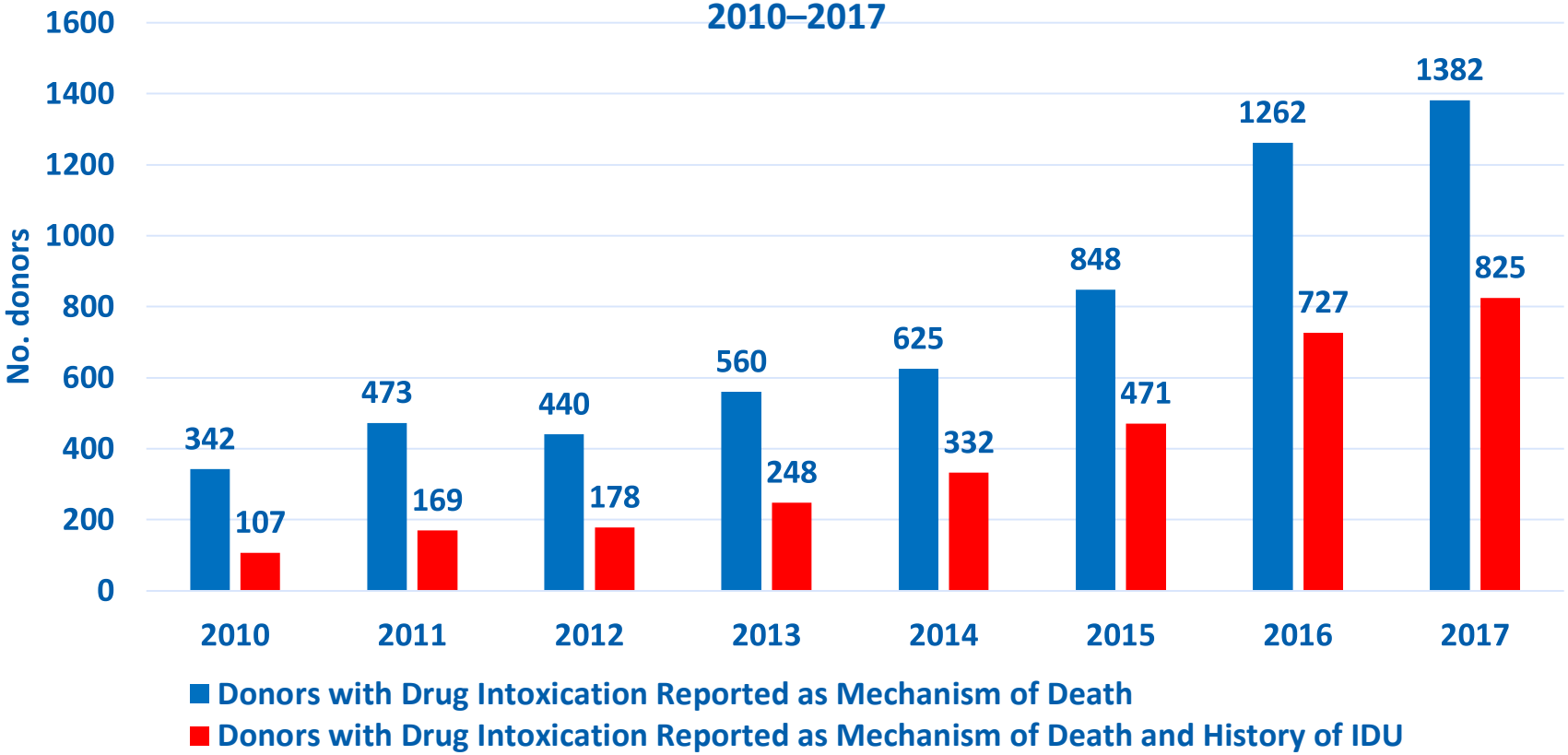


Data source: Organ Procurement and Transplantation Network

*Increased risk for HIV, Hepatitis B Virus, or Hepatitis C Virus

For an extended description of this chart, please see the description on **page 238**.

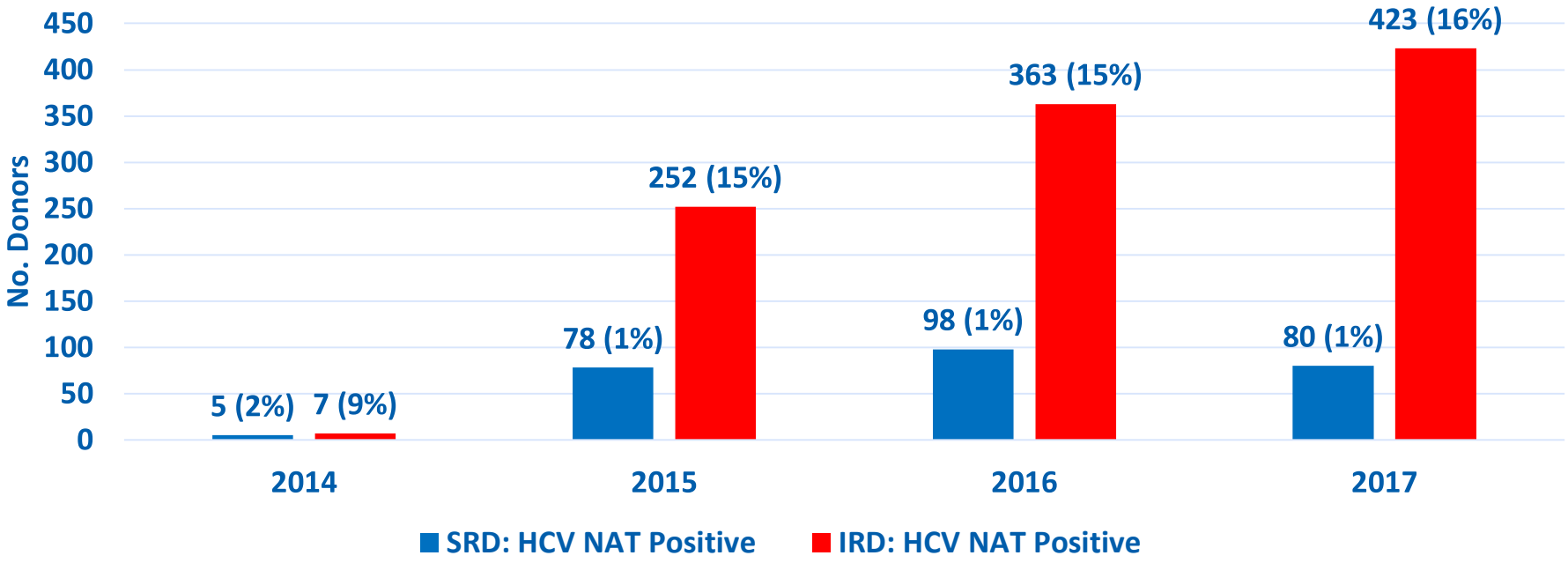
Number of deceased organ donors who died from drug intoxication and those dying from drug intoxication + history of intravenous drug use United States, 2010–2017



Data source: Organ Procurement and Transplantation Network

For an extended description of this chart, please see the description on **page 239**.

Number and percent of donors with a reactive Hepatitis C Virus nucleic acid test result by increased risk status* — United States, 2014–2017



*Increased risk for HIV, Hepatitis B Virus, or Hepatitis C Virus;
% of donors tested for HCV by NAT: 2014: 5%, 2015:86%, 2016:100%, 2017:100%
Data source: Organ Procurement and Transplantation Network

For an extended description of this chart, please see the description on **page 240.**

As a result of opioid epidemic, number of IRD increasing.

In 2017, IRD had ~ 16 times the prevalence of detectable hepatitis C virus compared to standard risk donors.

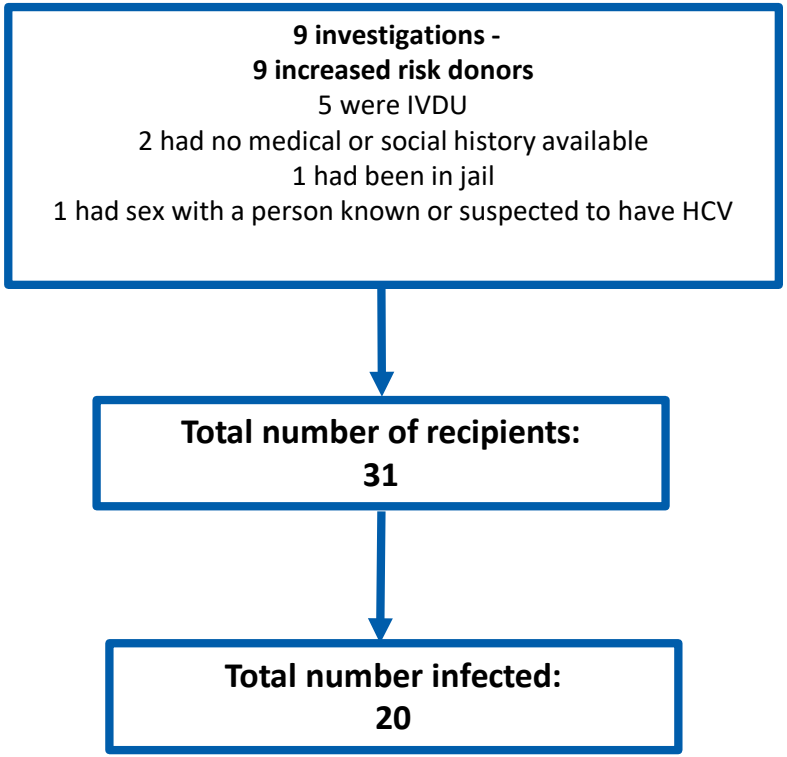
$$\frac{HCV\ NAT\ Prevalance\ Among\ IRD}{HCV\ NAT\ Prevalance\ Among\ SRD} = \sim 16$$

Analytic Project 2:

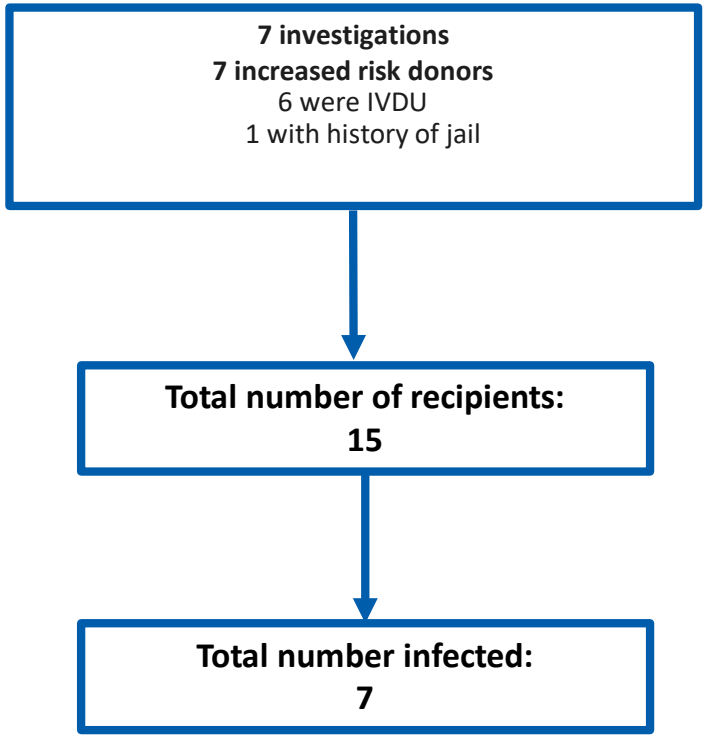
Description of all CDC-led outbreak investigations (2014-2017) of HBV/HCV transmission through transplantation

*Bixler et al. Hepatitis B and C virus infections transmitted through organ transplantation investigated by CDC, United States, 2014-2017. Am J Transplant. 2019.

HCV transplant-associated transmissions — United States, 2014–2017



HBV transplant-associated transmissions — United States, 2014—2017

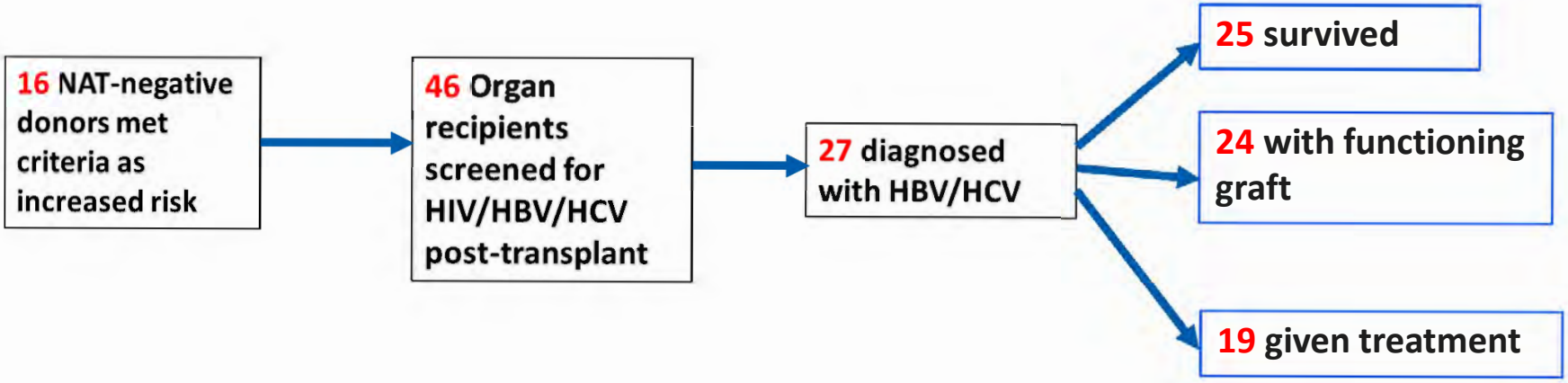


Outcomes within 3-18 months after transplantation among organ recipients with transplant-associated HBV — United States, 2014–2017

Organ Transplanted	Total Recipients	HBV NAT (+) Recipients	HBV NAT (+) Recipients Who Survived	Outcomes Among Survivors		
				Graft Functioning	Clinically stable	Started on Treatment for HBV
Bilateral Lungs	1	0	–	–	–	–
Kidney	7	1	1	1	1	1
Liver	6	5	5	5	5	4
Pancreas	1	1	0	–	–	–
TOTAL (%)	**15**	**7 (47)**	**6 (86)**	**6 (100)**	**6 (100)**	**5 (83)**

Outcomes within 3-18 months after transplantation among organ recipients with transplant-associated HCV — United States, 2014–2017

Organ Transplanted	Total Recipients	HCV NAT (+) Recipients	HCV NAT (+) Recipients Who Survived	Outcomes Among Survivors		
				Graft functioning	Clinically stable	Started on Treatment for HCV
Heart	5	2	2	2	2	1
Kidney	16	8	8	8	8	7
Kidney/pancreas	1	1	1	1	1	1
Liver	5	5	5	5	4	4
Lung	4	4	3	2	1	1
TOTAL (%)	**31**	**20 (65)**	**19 (95)**	**18 (95)**	**16 (84)**	**14 (74)**



- Transmission of HBV and HCV from test-negative donors occurs
  - All donors met criteria as IRD
- Post-transplant screening of IRD organ recipients led to early identification and treatment
- Risk of death and graft failure was likely reduced

Analytic Project 3:

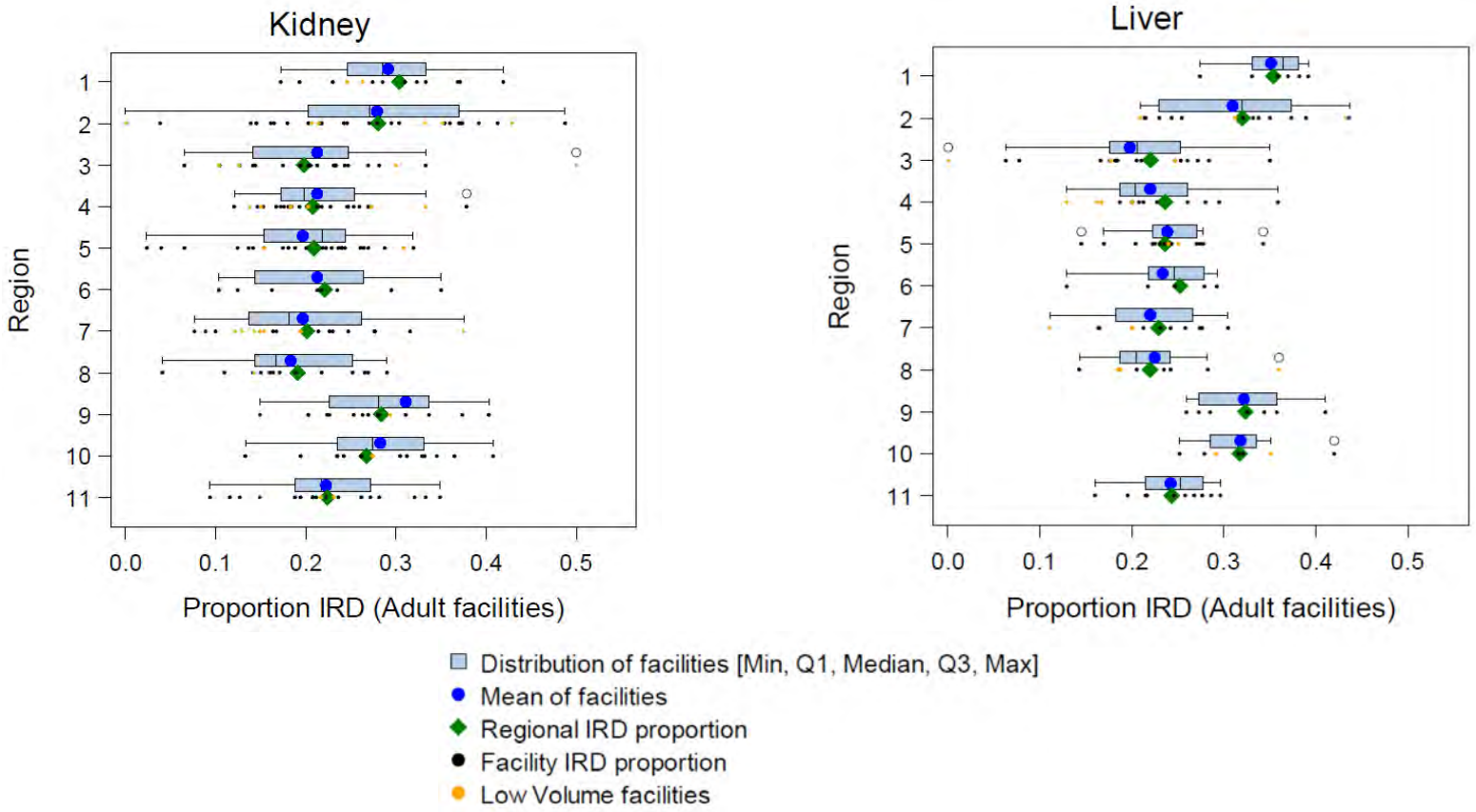
Impact of public health service increased risk deceased donor designation on organ utilization – analyzing data from the Organ Procurement and Transplantation Network

*Sapiano et al. Impact of U.S. Public Health Service Increased Risk Deceased Donor Designation on Organ Utilization. Am J Transplant 2019.

Utilization rate after excluding HBV/HCV-positive donors (2014-2017)

Recipient age group	Organ	Number of organs	Utilization rate		P-value*	Organs underutilized, per year
			Not IRD	IRD		
Adults	Heart	31,216	31.84%	31.51%	0.4548	7.6
	Kidney	64,299	76.58%	73.17%	<.0001	148.3
	Liver	31,531	74.58%	74.09%	0.2199	10.9
	Lung	31,686	25.14%	23.83%	0.0024	33.5
Pediatrics	Heart	3,848	46.16%	36.52%	<.0001	11.7
	Kidney	2,837	69.60%	65.66%	0.0744	4.2
	Liver	3,069	64.31%	62.73%	0.4041	1.6
	Lung	4,042	4.51%	3.62%	0.3311	1.2

Boxplots of distribution of facility-level proportion IRD organ transplants



Tabular summary of results

*	No difference in utilization
◘	Difference in utilization between IRD and non-IRD appears to be due to subset of facilities
◆	Difference in utilization between IRD and non-IRD appears to be widespread

Organ	Adult	Pediatric
Heart	No difference in utilization due to IRD, after excluding HBV/HCV positive donors *	Significant difference in utilization between IRD and non-IRD (11.7 hearts per year) ◆
Kidney	Significant difference in utilization between IRD and non-IRD (148.3 kidneys per year) Under-utilization driven by a subset (41/208) of facilities under-utilization ◘	No difference in utilization due to IRD, after excluding HBV/HCV positive donors *
Liver	No difference in utilization due to IRD *	No difference in utilization due to IRD *
Lung	Significant difference in utilization between IRD and non-IRD (33.5 lungs per year). More generalized under-utilization, nationally ◆	No difference in utilization due to IRD, after excluding HBV/HCV positive donors *

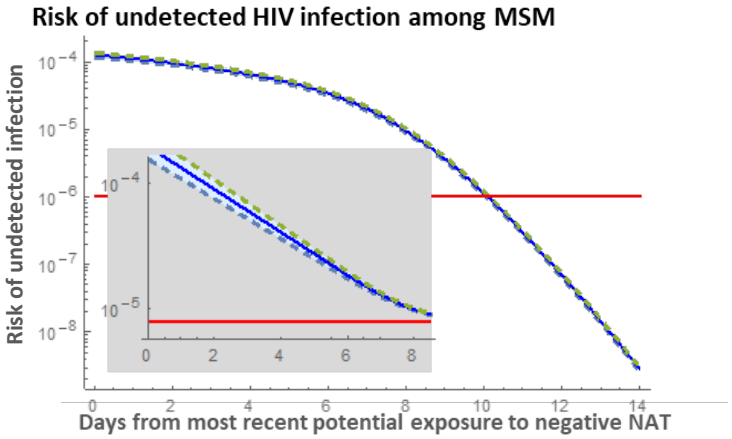
- **No difference between risk-adjusted utilization rates of IRD and non-IRD organs for most organ types**
- **IRD is associated with underutilization of**
  - **Adult kidneys (148/year)**
  - **Adult lungs (34/year)**
  - **Pediatric hearts (12/year)**
- **Subset of facilities contribute to underutilization of adult kidneys**

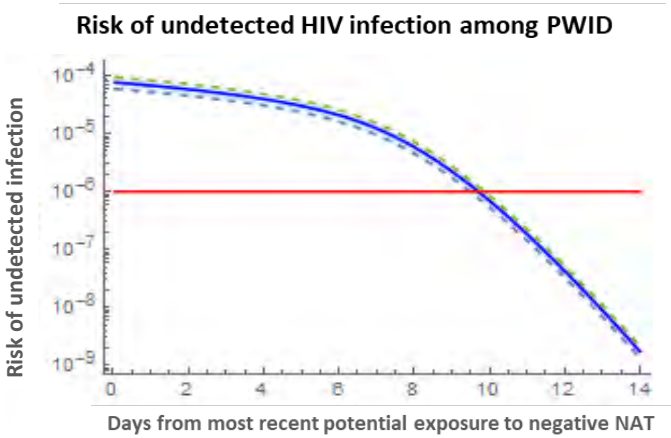
Analytic Project 4:

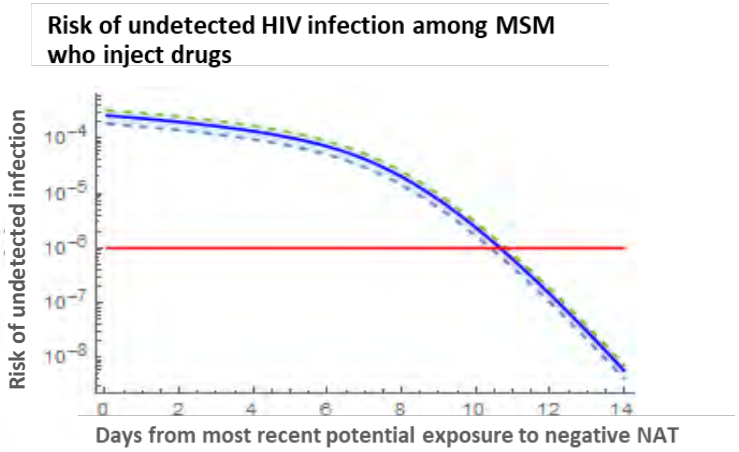
Model to describe risk of undetected HIV, HBV, and HCV infection among Public Health Service increased risk donors with negative NAT result

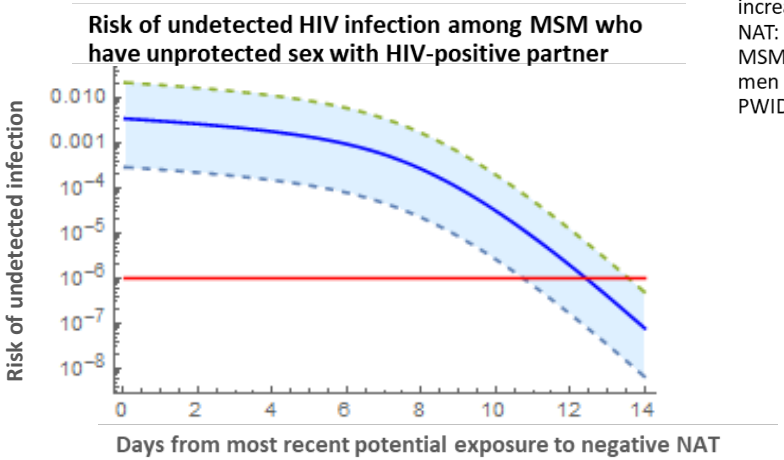
*Jones et al. Quantifying the Risk of Undetected HIV, Hepatitis B Virus, or Hepatitis C Virus Infection in Public Health Service Increased Risk Donors. Am J Transplant 2019. (in press)

Risk of undetected HIV infection among PHS IRD with negative NAT by risk behavior and time of NAT from most recent potential exposure





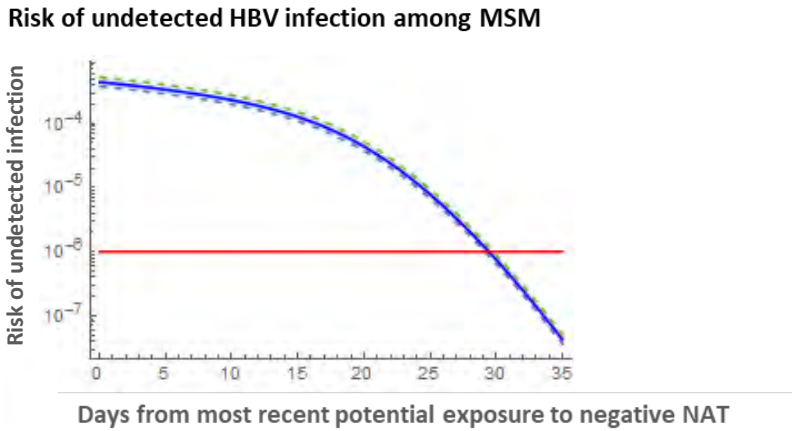


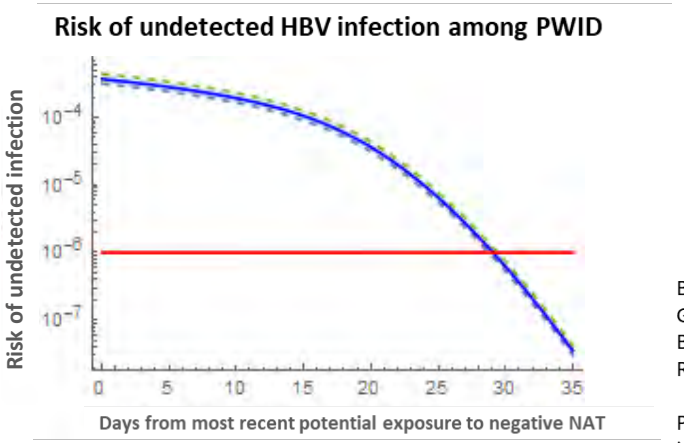


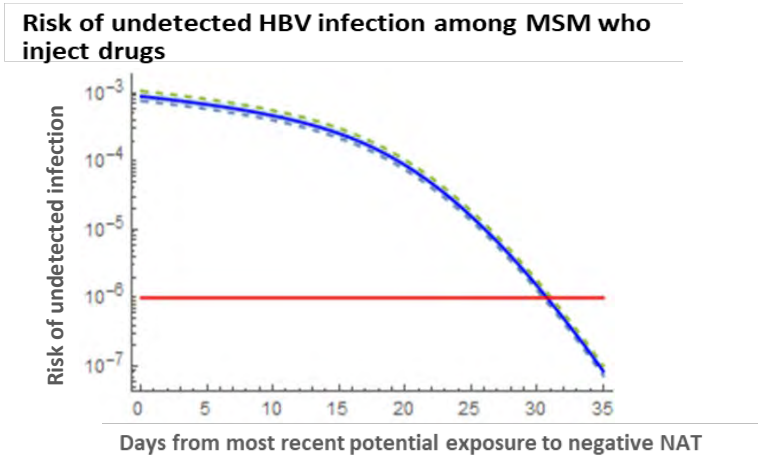
Blue line: Mean risk
Green dashed line: Upper 95% CI
Blue dashed line: Lower 95% CI
Red line: 1/1,000,000 risk

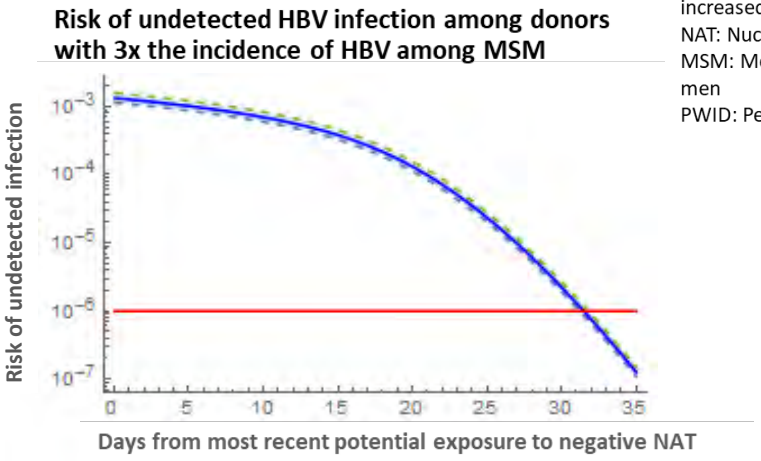
PHS IRD: Public Health Service increased risk donor
NAT: Nucleic acid test
MSM: Men who have sex with men
PWID: People who inject drugs

Risk of undetected HBV infection among PHS IRD with negative NAT by risk behavior and time of NAT from most recent potential exposure









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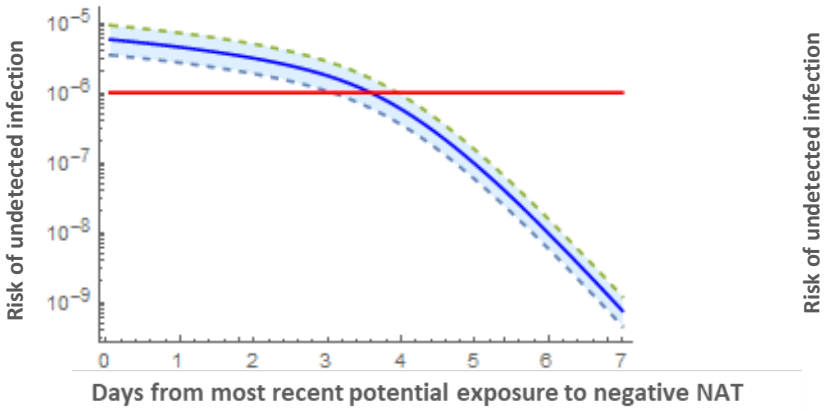
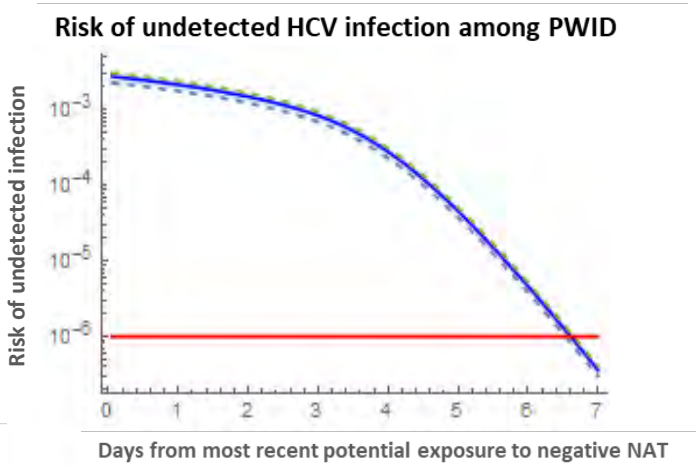
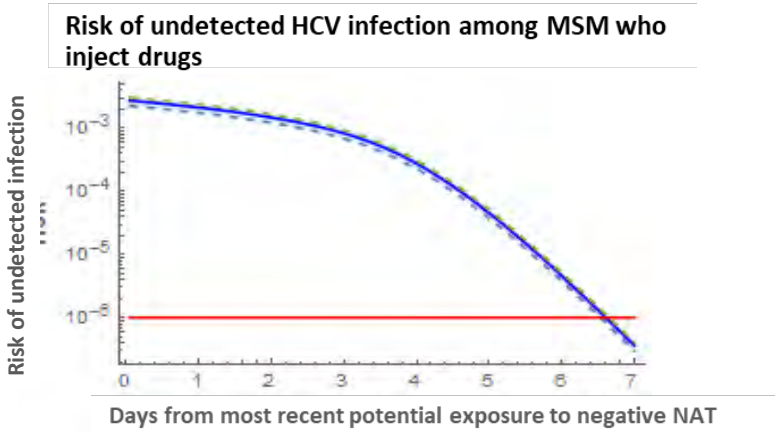
Green dashed line: Upper 95% CI
Blue dashed line: Lower 95% CI
Red line: 1/1,000,000 risk

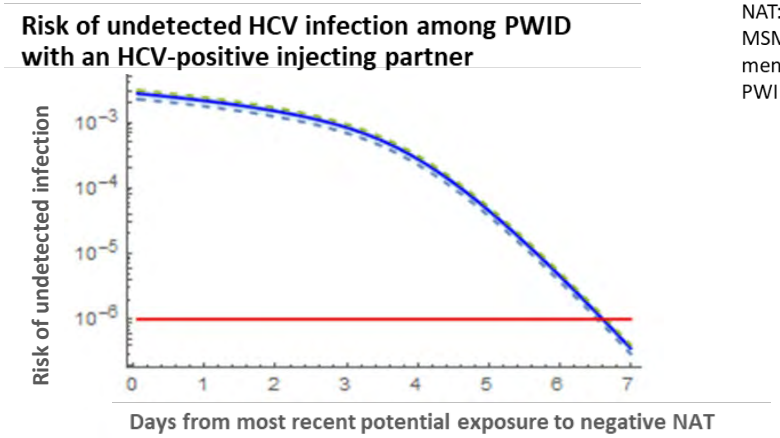
PHS IRD: Public Health Service increased risk donor
NAT: Nucleic acid test
MSM: Men who have sex with men
PWID: People who inject drugs

Risk of undetected HCV infection among PHS IRD with negative NAT by risk behavior and time of NAT from most recent potential exposure





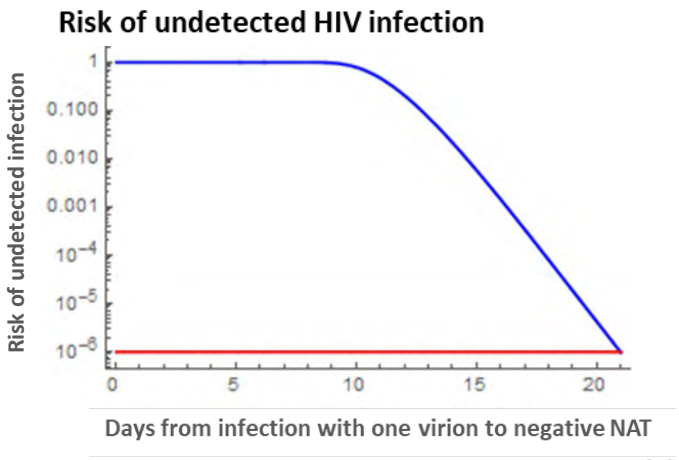


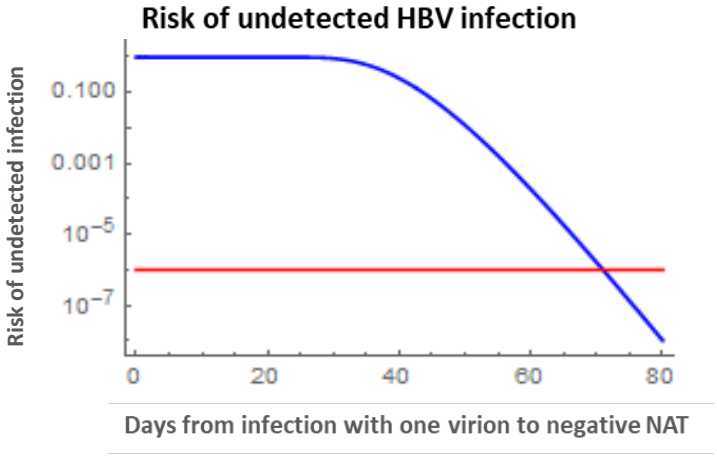


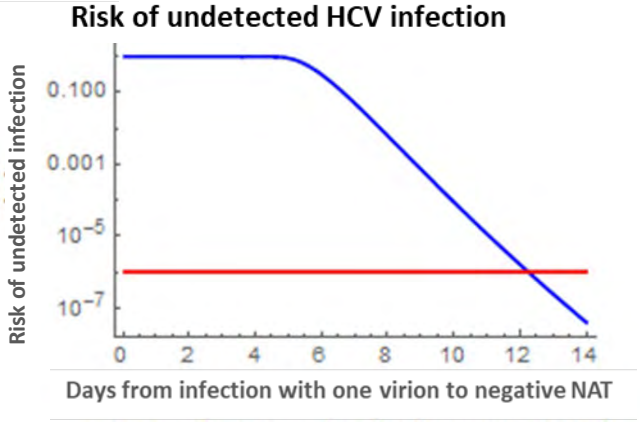
Blue line: Mean risk
Green dashed line: Upper 95% CI
Blue dashed line: Lower 95% CI
Red line: 1/1,000,000 risk

PHS IRD: Public Health Service increased risk donor
NAT: Nucleic acid test
MSM: Men who have sex with men
PWID: People who inject drugs

Risk of undetected HIV, HBV, and HCV infection among persons with negative NAT infected with one virion from time of infection







Blue line: Mean risk
Red line: 1/1,000,000 risk

NAT: Nucleic acid test

- For **IRD**, the risk of undetected infection is < 1/1,000,000 for
  - HIV, HCV: > 2 weeks after most recent exposure
  - HBV: > 5 weeks after most recent exposure

- Even if donor **infected with one virion** (highly unlikely scenario), the risk of undetected infection is < 1/1,000,000 for
  - HIV, HCV: > 3 weeks after infection
  - HBV: > 10 weeks after infection

- Period during which reported donor risk behaviors result in IRD designation can be safely shortened

Evaluation of criteria resulting in deceased donor IRD designation

Increased risk donor (IRD) designation criteria

- Medical/social criteria resulting in IRD designation
  - Sex with a person known or suspected to have HIV, HBV, or HCV infections
  - Men who have had sex with men (MSM)
  - Women who have had sex with a man with a history of MSM behavior
  - Sex in exchange for money or drugs
  - Sex with a person who had sex in exchange for money or drugs
  - Sex with a person that has injected drugs by IV, IM, or subQ route
  - Injected drugs by IV, IM, or subQ route for nonmedical reasons
  - Incarceration for > 72 hours
  - Newly diagnosed or have been treated for syphilis, gonorrhea, Chlamydia, or genital ulcers
  - Child (age ≤18 months) born to a mother known to be infected with, or at increased risk for HIV, HBV, or HCV
  - Child breastfed within the preceding 12 months by mother known to be infected with, or at increased risk for HIV infection.
  - Hemodialysis (only increased risk for HCV)
- Other criteria resulting in IRD designation
  - Unknown medical/social history
  - Hemodiluted blood specimen used for infectious disease testing

Transplant-transmissions from deceased IRD: 2008-2018*

	HCV	HBV	HIV
Transplant Transmissions (Adjudicated as Proven/Probable)	23	14	0
Criteria resulting in IRD designation			
Sex with a person known or suspected to have HIV, HBV, or HCV infections	2	-	-
MSM	-	-	-
Sex with MSM (women)	-	-	-
Sex in exchange for money or drugs	4	1	-
Sex with a person who had sex in exchange for money or drugs	2	4	-
Sex with PWID	4	5	-
PWID	19	10	-
Incarceration	10	8	-
Newly diagnosed/treated STD	-	1	-
Child (age ≤18 months) born to a mother known/suspected for HIV, HBV or HCV	-	-	-
Breastfed child by mother known/suspected for HIV, HBV, or HCV	-	-	-
Hemodialysis	-	-	-
Other Criteria resulting in IRD designation			
Unknown medical/social history	2	1	-
Hemodiluted blood specimen used for infectious disease testing	-	-	-

*Includes all DTAC and CDC led investigations with Adjudication of Proven or Probable
Note: Ongoing investigations on three 2018 cases

Transplant- transmissions* with only one IRD criteria identified in the deceased donor: 2008-2018

	HCV	HBV	HIV
Transplant Transmissions (Adjudicated as Proven/Probable)	10	6	0
Criteria resulting in IRD designation	-	-	-
Sex with a person known or suspected to have HIV, HBV, or HCV infections	-	-	-
MSM	-	-	-
Sex with MSM (women)	-	-	-
Sex in exchange for money or drugs	-	-	-
Sex with a person who had sex in exchange for money or drugs	-	-	-
Sex with PWID	-	-	-
PWID	8	3	-
Incarceration	-	1	-
Newly diagnosed/treated STD	-	-	-
Child (age ≤18 months) born to a mother known/suspected for HIV, HBV or HCV	-	-	-
Breastfed child by mother known/suspected for HIV, HBV, or HCV	-	-	-
Hemodialysis	-	-	-
Other Criteria resulting in IRD designation	-	-	-
Unknown medical/social history	2	1	-
Hemodiluted blood specimen used for infectious disease testing	-	-	-

*Includes all DTAC and CDC led investigations with Adjudication of Proven or Probable
Note: Ongoing investigations on three 2018 cases

Criteria implicated in transmission* (Published/DTAC)

- Medical/social criteria resulting in IRD designation
  - **Sex with a person known or suspected to have HIV, HBV, or HCV infections**
  - **Men who have had sex with men (MSM)**
  - Women who have had sex with a man with a history of MSM behavior
  - **Sex in exchange for money or drugs**
  - **Sex with a person who had sex in exchange for money or drugs**
  - **Sex with a person that has injected drugs by IV, IM, or subQ route**
  - **Injected drugs by IV, IM, or subQ route for nonmedical reasons**
  - **Incarceration for > 72 hours**
  - Newly diagnosed or have been treated for syphilis, gonorrhea, Chlamydia, or genital ulcers (2019)
  - Child (age ≤18 months) born to a mother known to be infected with, or at increased risk for HIV, HBV, or HCV
  - Child breastfed within the preceding 12 months by mother known to be infected with, or at increased risk for HIV infection.
  - Hemodialysis (only increased risk for HCV)
- Other criteria resulting in IRD designation
  - **Unknown medical/social history**
  - **Hemodiluted blood specimen used for infectious disease testing**

* Includes all DTAC and CDC led investigations with Adjudication of Prov or Probable

Criteria Considered for Removal

- Medical/social criteria resulting in IRD designation
  - Sex with a person known or suspected to have HIV, HBV, or HCV infections
  - Men who have had sex with men (MSM)
  - Women who have had sex with a man with a history of MSM behavior
  - Sex in exchange for money or drugs
  - Sex with a person who had sex in exchange for money or drugs
  - Sex with a person that has injected drugs by IV, IM, or subQ route
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- Other Criteria resulting in IRD designation
  - Unknown medical/social history
  - **Hemodiluted blood specimen used for infectious disease testing**

Sexually Transmitted Disease (STD)

Evaluation of STD as an IRD criteria

- Does a person with a newly diagnosed or receiving treatment for syphilis, gonorrhea, chlamydia, or genital ulcers in the last 12 months have a higher risk of acquiring a newly diagnosed HIV infection?
- Literature review
  - MSM & STD
    - Many publications describing risk of HIV among MSM with STD
    - MSM are classified as IRD regardless of STD status
  - Non-MSM & STD
    - Is there a significant risk of acute HIV infection if **non-MSM** (male or female) person had an STD diagnosis within the previous 12 months?
    - Focus on US studies
  - Which STDs confer a risk for acute HIV?

    a. Syphilis

    b. Gonorrhea

    c. Chlamydia

    d. HSV/genital ulcer

Risk of HIV among women following STD diagnosis

- Surveillance data to estimate risks of HIV acquisition
  - Florida STD and HIV surveillance: 2000-2009
  - HIV rate among 13–59-year-old women following a diagnosis of syphilis, gonorrhea or chlamydia compared to women with no reported STD.
  - Among 328,456 women with reported STD and 2,221,944 PY's of follow-up
    - Syphilis (n=3325), gonorrhea (n=67,784) or chlamydia (n=257,347)
    - 2118 women diagnosed with HIV
  - Among 5,582,148 women with no reported STD and 64,763,832 PY's of follow-up
    - 19,531 women diagnosed with HIV

Petermen et al. Risk for HIV following a diagnosis of syphilis, gonorrhea or chlamydia: 328,456 women in Florida, 2000–2011. International Journal of STD & AIDS, 2014.

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Risk of HIV among women following STD diagnosis

Table 1. Rate of HIV diagnosis for 13–59 year-old women in Florida 2000–2011, comparing women with and without a history of a preceding sexually transmitted infection in 2000–2009.

No sexually transmitted infection reported 2000–2009				
			Reported with HIV	
Characteristic	*n*	Person-years	*n*	Rate[b]
Total	5,582,148	64,763,832	19,531	30.2

Sexually transmitted infection reported 2000–2009					
			Reported with HIV		
Characteristic	*n*	Person-years	*n*	Rate[b]	Relative rate[a]
Total	328,456	2,221,944	2,118	95.3	3.2
Syphilis	3,325	24,251	145	597.9	19.8
Gonorrhoea	67,784	490,929	841	171.3	5.7
Chlamydia	257,347	1,706,764	1,132	66.3	2.2

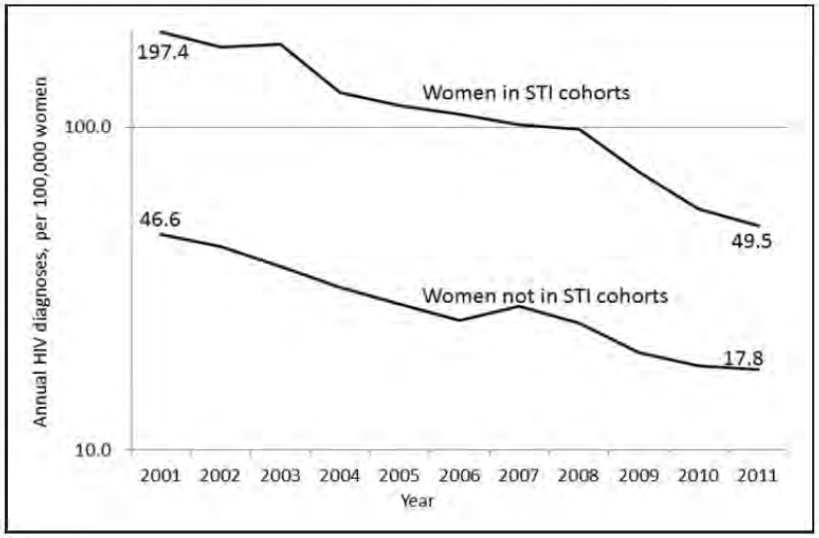

Figure 2. Annual HIV diagnosis rates for 13–59 year-old women in the STI cohorts and women not in the STI cohorts, Florida, 2001–2011 (log scale).

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Subsequent HIV diagnosis rate was higher for women diagnosed with Syphilis, gonorrhea, or chlamydia than with no STD

Figure 2. Annual HIV diagnosis rates for 13–59 year-old women in the STI cohorts and women not in the STI cohorts, Florida, 2001–2011 (log scale).

Petermen et al. Risk for HIV following a diagnosis of syphilis, gonorrhea or chlamydia: 328,456 women in Florida, 2000–2011. International Journal of STD & AIDS,2014.

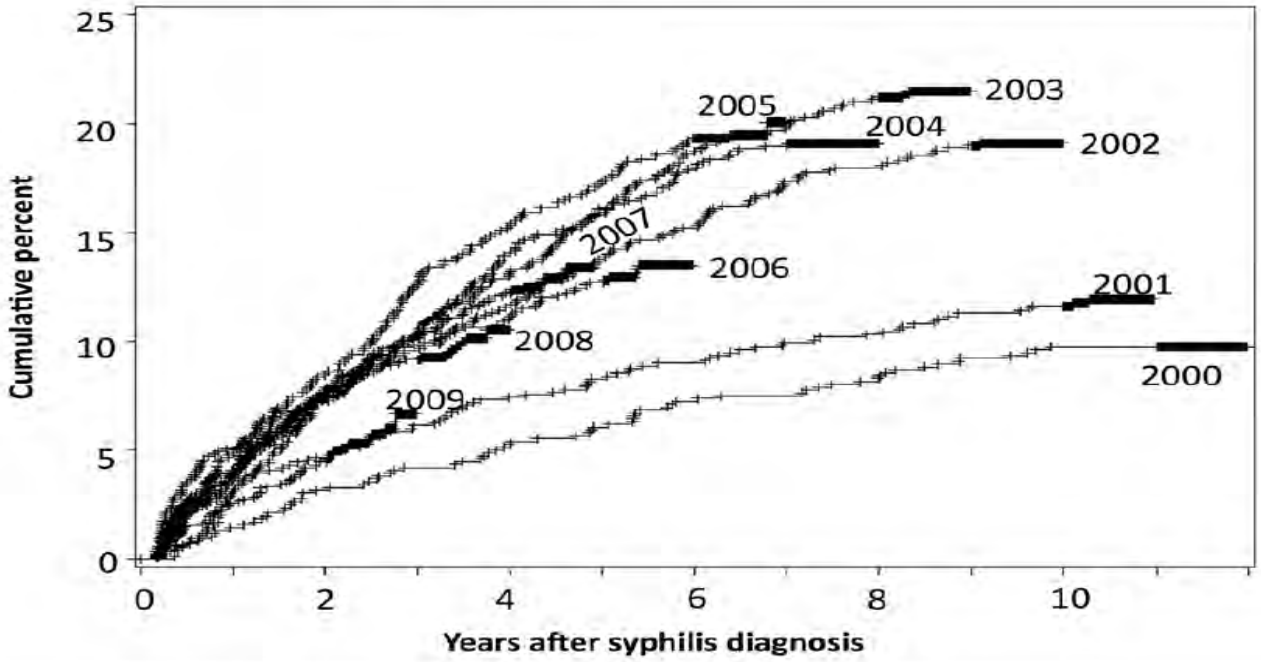
Risk of HIV among men following syphilis diagnosis

- 9,512 men with syphilis were followed by health department
  - 27% of men self-identified as heterosexual
  - 1,323 were subsequently diagnosed as having HIV infection 60–3,753 days after their syphilis diagnosis
- The risk of a subsequent diagnosis of HIV infection was 3.6% in the first year after syphilis was diagnosed and reached 17.5% 10 years after a syphilis diagnosis
- Of men diagnosed with syphilis in 2003, 21.5% were reported as having a new HIV diagnosis by December 31, 2011.

Petermen et al. High Risk for HIV following a diagnosis of syphilis, men living in Florida, 2000-2011. Public Health Reports, 2014.

Risk of HIV among men following syphilis diagnosis

Figure. Cumulative percent of men aged 13–59 years with newly reported HIV infection following syphilis diagnosis,[a] by year of syphilis diagnosis: Florida, 2000–2011



[a]Syphilis diagnosed from 2000 to 2009
HIV = human immunodeficiency virus

Petermen et al. High Risk for HIV following a diagnosis of syphilis, men living in Florida, 2000-2011. Public Health Reports, 2014.

Risk of HIV among men following syphilis diagnosis

- Risk of HIV infection after syphilis infection was 3.6% in the first year
  - 17.5% at 10 years after a syphilis diagnosis.
- Men who acquire syphilis are at high risk of HIV infection.

Petermen et al. High Risk for HIV following a diagnosis of syphilis, men living in Florida, 2000-2011. Public Health Reports, 2014.

Risk of HIV among men and women following any STD

- Retrospective cohort of heterosexual men and women with repeat HIV tests between January 1990 and April 1998 in New Orleans STD clinic
- Cox hazard survival analysis used to examine risk factors for HIV seroconversion

Hanson et al. Assessment of sexually transmitted diseases as risk factors for HIV seroconversion in a New Orleans sexually transmitted disease clinic, 1990-1998. Annals of Epidemiology, 2005.

Risk of HIV among men and women following any STD

TABLE 3. Cox's proportional hazards ratios for HIV seroconversion (with 95% confidence intervals) with time-dependent covariates for STD exposure: Overall models comparing STD diagnosis to no STD diagnosis during preceding intervals of 2 and 1 years

Characteristic	With interval of previous 2 years		With interval of previous 1 year	
	Hazard ratio	95% CI	Hazard ratio	95% CI
Men (n = 8044 repeat testers, 106 seroconverters)				
Age at first clinic visit	1.0	1.0, 1.0	1.0	1.0, 1.0
Male sex with male	3.3	2.0, 5.3	3.3	2.1, 5.4
Injecting drug use	0.9	0.4, 2.0	0.9	0.5, 2.0
Sex with IDU	0.7	0.3, 1.7	0.8	0.3, 2.0
Exch. money/drugs for sex	1.5	1.0, 2.3	1.6	1.0, 2.4
STD history within interval (compared to no STD exposure during interval)				
Non-ulcerative STD*	0.9	0.6, 1.3	1.4	0.9, 2.3
Any syphilis or GUD	4.2	2.4, 7.2	4.7	2.1, 10.2
Women (n = 2679 repeat testers, 29 seroconverters)				
Age at first clinic visit	1.0	1.0, 1.1		
Sex with HIV+ partner	9.5	2.1, 42.5		
Injecting drug use	0.7	0.1, 3.6		
Sex with IDU	2.0	0.6, 7.2		
Exch. money/drugs for sex	1.5	0.5, 4.6		
STD history within interval (compared to no STD exposure during interval)				
Non-ulcerative STD*	0.9	0.3, 3.1		
Any syphilis or GUD	5.0	1.9, 13.0		

*Non-ulcerative STD includes gonorrhea and chlamydia diagnoses for both men and women and NGU diagnosis for men only.

- Syphilis and genital ulcer disease most associated with HIV infection
- Other non-ulcerative STDs might be associated

Hanson et al. Assessment of sexually transmitted diseases as risk factors for HIV seroconversion in a New Orleans sexually transmitted disease clinic, 1990-1998. Annals of Epidemiology, 2005.

Risk of HIV after HSV-2 seroconversion

- Systematic review and meta-analysis of longitudinal studies.

- Of 19 eligible studies identified, 8 described incident HSV-2 seroconversion and risk of HIV acquisition
- Most HIV seroconversions occurred during same period as HSV-2 seroconversion
- Only 2 studies in U.S.

Source	Recent HSV-2 seroconverters who converted to HIV[a]	RR (unadjusted or adjusted)[b]
Ramjee *et al.* 2005 [19]	F: 11	F: 6.0 (2.6–14.0)
Todd *et al.* unpublished data 2005	F: 6 M: 9	F: 4.3 (1.1–17.6) M: 6.2 (1.7–21.9)
Renzi *et al.* 2003 [24]	M: 5	M: 2.00 (0.51–6.92)
Reynolds *et al.* 2003 [25]	M and F: 20 remote and 8 recent[d]	F: 1.0 (0.31–3.26)[d] M: 1.8(0.96–3.2)[d] M: 5.2 (2.5–11.1)[e]
McFarland *et al.* 1999 [27]	M: 22	M: 4.94 (2.99–8.17)
Nelson *et al.* 1997 [30]	M: 8	M: 1.8 (0.55–6.1)
Keet *et al.* 1990 [33]	M: 3	M: 2.2 (0.4–12.1)
Holmberg *et al.* 1988 [32]	M: 11	M: 4.4 (1.1–18.8)

Freeman et al. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. AIDS, 2006.

Risk of HIV after HSV-2 seroconversion

- Prevalent HSV-2 infection: 3-fold increased risk of HIV

- Recent HSV-2 seroconversion: Higher risk of HIV than prevalent HSV-2 infection (range: 1- to 6-fold)
  - Might be less in the United States

Freeman et al. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. AIDS, 2006.

STD and increased risk for HIV transplant-transmission

- Available data from US studies suggest that STD is a risk factor for HIV infection
  - Risk of subsequent HIV infection persists for up to 10 years following STD diagnosis
- Highest risk for HIV infection is with recent syphilis or new genital ulcer
  - In females, chlamydia and gonorrhea confer risk for HIV infection

Hemodialysis

Hemodialysis and the risk of undetected HCV infection

- Hemodialysis numbers
  - Persons on hemodialysis in 2016: 450,887
  - Patients beginning hemodialysis 2016: 108,895
- Incidence of Hepatitis C in general population is unknown
  - High rates of asymptomatic infection
  - Testing not mandated
    - Among dialysis patients, testing recommended but not required and practices vary
  - Reporting not universal
- Data sources
  - DTAC data
  - CDC outbreak reports
  - National Healthcare Safety Network Outpatient Dialysis Center Practices Survey
  - Dialysis Outcomes and Practice Patterns Study (DOPPS)

https://www.usrds.org/2018/view/Default.aspx

Transmission of HCV associated with hemodialysis

- No reported transmission from a donor with history of hemodialysis (from either DTAC data or publications in scientific literature)

- CDC Outbreak Investigations
  - During 2008-2018, 21 outbreaks in hemodialysis settings reported to CDC
  - 102 outbreak-associated cases of HCV
  - 3,026 persons notified for screening
- DOPPS
  - HCV incidence decreasing in patients on hemodialysis (1996-2015)

Source: UNITED STATES RENAL DATA SYSTEM https://www.usrds.org/2018/view/Default.aspx

National Healthcare Safety Network — HCV prevalence and incidence (preliminary data)

- Over 80% of dialysis centers test for HCV at least annually

Year	Prevalence of HCV (per 100 person years)	Incidence of HCV (per 100 person years)
2014	5.70	0.14
2015	5.31	0.11
2016	5.38	0.19
2017	5.27	0.08

DOPPS – HCV prevalence

	DOPPS Phase						
Region/Country	1	2	3	4	5		p-value
United States	**11.5 (3215)**	**9.6 (2240)**	**6.6 (1804)**	**6.5 (4430)**	**6.9 (6228)**		**<.01**
All DOPPS countries	14.3 (7894)	10.4 (8858)	8.3 (8320)	9.5 (11790)	9.9 (14771)		
DOPPS 1+ countries	14.3 (7894)	12.1 (6682)	9.5 (6245)	9.4 (8617)	8.4 (10042)		<.01

HCV prevalence, by DOPPS region/country and study phase, in initial cross-sections of study patients in each phase.

- HCV prevalence by phase shown as % (n patients) weighted by facility sampling fraction; n=51,633 patients
- DOPPS Phase 1 (1996-2001 in the United States, 1998-2001 in Europe/Japan); Phase 2 (2002-2004); Phase 3 (2005-2008); Phase 4(2009-2011); Phase 5 (2012-2015) excluding facilities who did not accept HCV+ patients;

Jadoul et al. Prevalence, incidence, and risk factors for hepatitis C virus infection in hemodialysis patients. Kidney Int 2019.

DOPPS – HCV incidence per 100 patient years

	DOPPS Phase					
Region/Country	**1**	**3**	**4**	**5**		**P-value**
United States	**3.5(3.1,4.1) [184/4033]**	**2.5(1.7,3.6) [27/937]**	**1.0(0.7,1.5) [23/2537]**	**0.8(0.6,1.1) [44/4680]**		**<.01**
All DOPPS countries	2.9(2.6,3.2) [339/9584]	2.0(1.8,2.3) [229/7817]	1.9(1.6,2.1) [214/9660]	1.2(1.0,1.4) [159/10744]		-
DOPPS 1+ countries	2.9(2.6,3.2) [339/9584]	2.2(1.9,2.5) [180/5568]	1.9(1.6,2.2) [174/7473]	1.2(1.0,1.4) [138/8473]		<.01

HCV incidence per 100 patient years, by DOPPS region/country and phase

- Restricted to patients with at least two HCV antibody measurements and in whom the initial HCV antibody measurement was negative
- HCV incidence by phase shown as rate per 100 patient years (95% CI) [n HCV patients/N patients total]; restricted to facilities accepting HCV+ patients;
- HCV antibodies not collected longitudinally in DOPPS phase 2 and China DOPPS phase 4; DOPPS phase 1 (1996-2001 in the United States, 1998-2001 in Europe/Japan); phase 3 (2005-2008); phase 4(2009-2011); phase 5 (2012-2015)

Jadoul et al. Prevalence, incidence, and risk factors for hepatitis C virus infection in hemodialysis patients. Kidney Int 2019.

Hemodialysis and IRD designation

- Outpatient hemodialysis confers a small risk of HCV infection
- Due to improving infection control practices, the risk has declined since 2001
- Likelihood of acute, undetected HCV infection resulting from most recent outpatient dialysis exposure is low

Hemodilution

FDA tissue hemodilution guidelines

- Cannot use sample for infectious disease screening of tissue donors if
  - Blood and colloid (e.g., plasma, platelets, albumin) transfused in previous 48 hrs + crystalloid transfused in previous 1 hour > patient blood volume

    OR
  - Colloid transfused in previous 48 hrs + crystalloid transfused in previous 1 hr > patient plasma volume

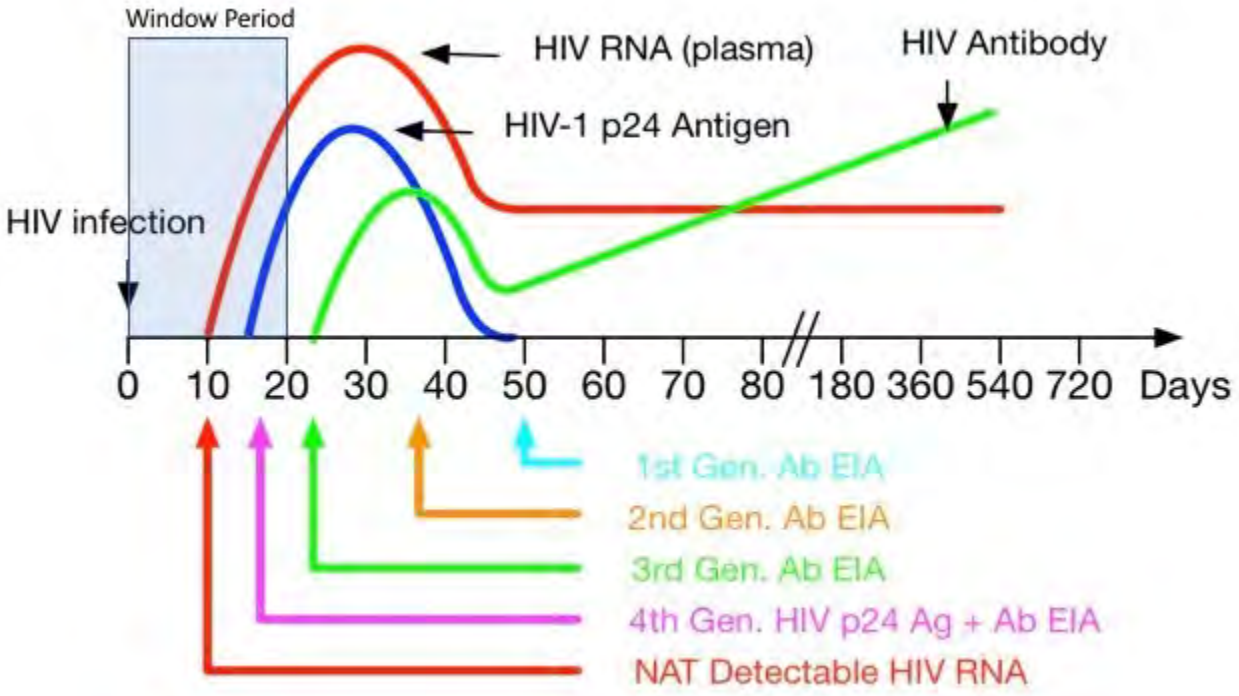
Hemodilution can result in false-negative test

- Organ donors can receive multiple blood transfusions and fluid prior to HIV/HBV/HCV screening, resulting in hemodilution
- Hemodilution can potentially result in a false negative result
- In 1986, an organ donor tested negative for anti-HIV antibodies by EIA after receiving 56 units of blood components
  - HIV transmission to 2 recipients
  - Pre-transfusion donor blood samples tested positive by EIA, suggesting initial test was false negative because of hemodilution

https://www.cdc.gov/mmwr/preview/mmwrhtml/00019010.htm

Improvements in HIV screening diagnostics

- Should donor sample hemodilution continue to result in increased risk designation in era of universal donor NAT?

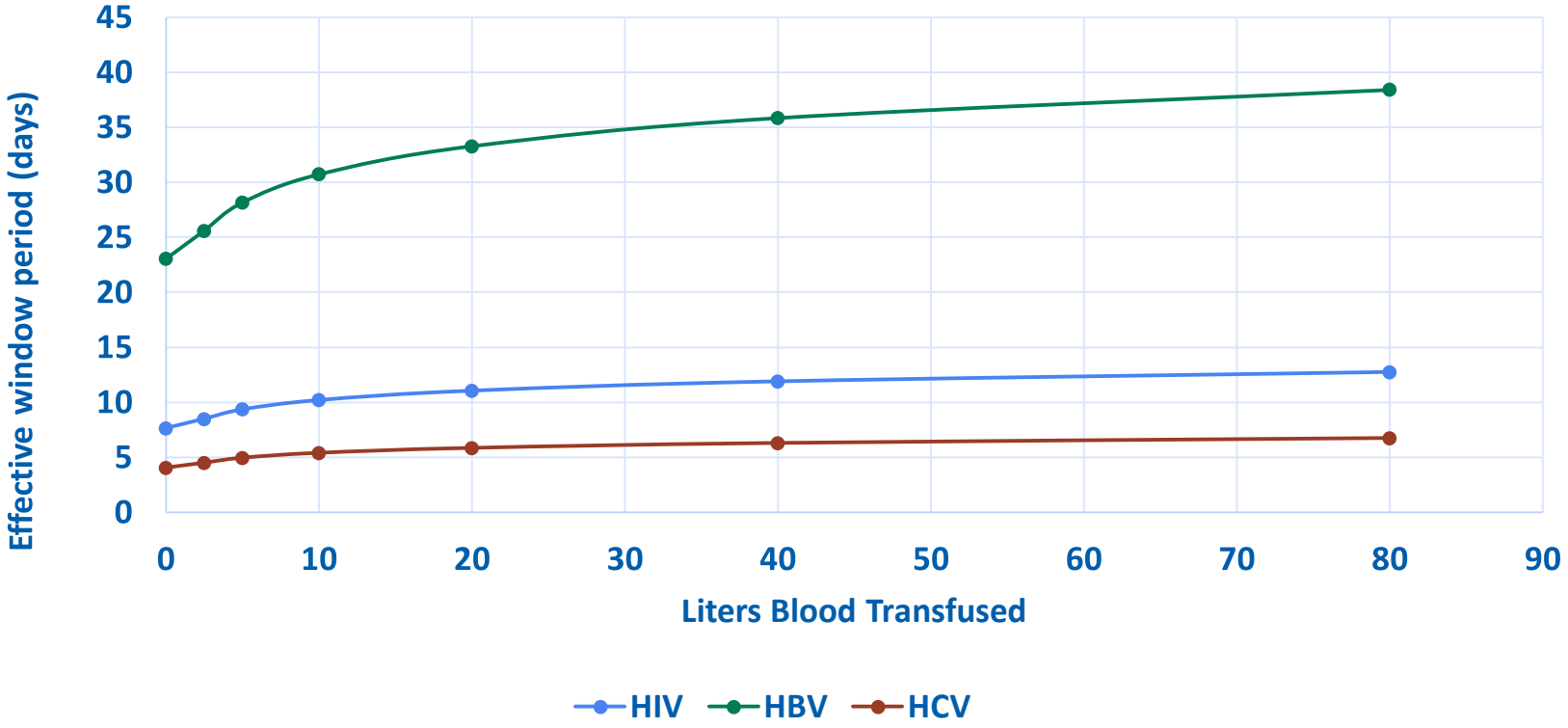


https://blog.ucdmc.ucdavis.edu/labbestpractice/index.php/2017/09/15/best-practices-for-hiv-12-screening-when-to-test-and-what-to-test/

What is effect of hemodilution on NAT?

- Model generated to illustrate effect on NAT window period during early infection
- Assumptions include
  - 50% blood loss in average-sized donor (2.5L remaining blood volume)
  - Equal mixing (2.5L of blood would result in 1:1 dilution of sample)
  - Number of initial virions that establish infection, viral doubling time, and test limit of detection based on recent CDC modelling paper

Model of effective window period length after hemodilution from blood transfusion — HIV, HBV, and HCV



Hemodilution resulting in increased risk designation

- Model suggests hemodilution can lengthen window period by >40%
- If even mixing not assumed, risk of false negative higher
- If the time between infection and the NAT is shortly after standard NAT window period and the donor receives a large amount of blood/fluids prior to NAT testing, then hemodilution can result in false negative testing

Manufacturer studies on hemodilution - HIV

Table 33a. Procleix System - Detection of HIV-1 WHO Standard in Analytical Sensitivity Panels with the Procleix HIV-1 Discriminatory Assay

HIV-1 WHO (97/656) IU/mL	Number of reactive/ tested*	% Positive	95% Confidence Limits		Average S/CO	%CV
			Lower	Upper		
600	119/119	100	97	100	23.48	13
200	120/120	100	97	100	22.58	12
60	119/119	100	97	100	20.56	17
20	110/118	93	87	97	14.28	43
6	73/120	61	52	70	11.17	57
0	0/120	0	0	3	0.10	59

- Untreated persons can have high viral load (>100,000 copies/mL)
- Certain patients can chronically have low viral loads

https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-bio-gen/documents/document/ucm335285.pdf

Manufacturer studies on hemodilution - HBV

Procleix Ultrio Assay						
HBV WHO (97/746) IU/mL	Number of reactive/ tested*	% Positive	95% Confidence Limits		Average S/CO	%CV
			Lower	Upper		
45	120/120	100	97	100	14.27	7
15	119/120	99	95	100	13.91	12
5	89/120	74	65	82	11.18	36
1.67	48/120	40	31	49	11.89	32
0.56	22/119	19	12	27	9.95	48
0	0/119	0	0	3	0.12	73

- Wide variety of viral load depending on progression of disease
- Asymptomatic chronic infections can have low levels of viremia

https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-bio-gen/documents/document/ucm335285.pdf

Manufacturer studies on hemodilution - HCV

Procleix Ultrio Assay						
HCV WHO (96/790) IU/mL	Number of reactive/ tested*	% Positive	95% Confidence Limits		Average S/CO	%CV
			Lower	Upper		
100	118/118	100	97	100	7.45	5
30	119/119	100	97	100	7.32	5
10	119/120	99	95	100	7.10	8
3	109/120	91	84	95	6.52	19
1	77/120	64	55	73	5.80	28
0	0/120	0	0	3	0.09	52

- Chronic disease usually have higher viral load
  - Can have nadirs <1,000 IU/mL

https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-bio-gen/documents/document/ucm335285.pdf

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2741541/

Hemodilution and IRD designation

- Hemodilution of sample tested by HIV, HBV, or HCV NAT can result in undetected infection
- The effect on NAT detection is most likely to occur during early infection and will result in prolonged window period

Summary of CDC Analyses

- IRD more likely to be infected with HCV than non-IR donors
- Transmissions of HBV and HCV from recently infected IRD to organ recipients continue to occur
  - As a result of opioid epidemic, might be occurring with greater frequency
  - Post-transplant screening of IRD organ recipients led to early identification and treatment
  - Risk of death and graft failure was likely reduced
- IRD designation is associated with underutilization of adult lungs and kidney and pediatric hearts
  - Magnitude of under utilization is lower than previous estimates
  - ~200 organs underutilized per year, small proportion of total unmet need
- Period during which reported donor risk behaviors result in IRD designation can be safely shortened
- Hemodialysis can be removed as IRD criteria while preserving safety

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Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

LUNCH

Potential Donor Derived Transmission Events (extended description)

Year	Number of PDDTE reviewed by DTAC
2005	7
2006	60
2007	97
2008	102
2009	152
2010	157
2011	181
2012	198
2013	284
2014	278
2015	290
2016	274
2017	272

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Updated Potential Donor Derived Transmission Events (extended description)

Year	Total PDDTE	DTAC cases	Proven/Probable Transmissions
2011	212	180	31
2012	241	198	33
2013	392	284	32
2014	452	278	35
2015	407	290	38
2016	430	274	42
2017	368	272	47
2018	382	276	26*

*Many cases reported in 2018 are under ongoing investigation; 26 proven or probable transmissions have been identified as of Jan 15, 2019

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More Donors at "Increased Risk" (extended description)

Year	Number of Deceased Donors Recovered	Percent of Deceased Donors with PHS Identified Risk (%)
2005	587	7.7
2006	672	8.4
2007	607	7.5
2008	617	7.7
2009	638	8.0
2010	709	8.9
2011	836	10.3
2012	966	11.9
2013	1,110	13.4
2014	1,772	20.6
2015	2,016	22.2
2016	2,478	24.9

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Discard rate trends – kidney (extended description)

Year	Recovered Kidney Volume	Observed Kidney Discard Rate (%)
1987	1816*	6.8
1988	7,705	5.1
2000	10,909	14.9
2009	14,394	19.2
2010	2,641	N/A
2011	2,646	N/A
2012	2,763	N/A
2013	2,734	N/A
2014	2,888	N/A
2015	3,157	19.2
2016	3,629	20.0

* Data collection began 10/1/87

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Graft Survival and Discard Rates by KDPI(extended description)

KDPI	2-year Graft Survival Rate (%)	Discard Rate (%)
0-5	95.0	1.1
21-25	91.7	5.1
46-50	90.3	11.1
71-75	87.2	27.0
96-100	78.8	75.1

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Deceased Organ Donors in the United States by PHS Increased Risk Status

(extended description)

Year	Number of Deceased Standard Risk Donors	Number of Deceased Increased Risk Donors
2010	7226	709
2011	7283	836
2012	7171	966
2013	7157	1111
2014	6815	1772
2015	7059	2016
2016	7491	2478
2017	7580	2704

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Survival Benefit of IRD Livers(extended description)

Time After Offer (months)		0	12	24	36	48	60
Number at Risk	Declined	56,106	34,641	24,595	18,664	14,308	10,801
	Accepted	9851	6620	4762	3554	2749	2071

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Potential Donor Derived Transmission Events (PDDTE) (extended description)

Year	Number of PDDTE reviewed by DTAC
2005	7
2006	60
2007	97
2008	102
2009	152
2010	157
2011	181
2012	198
2013	284
2014	278
2015	290
2016	274

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Deceased organ donors in the United States by increased risk status* 2010–2017 (extended description)

Year	Number of Deceased Standard Risk Donors	Number of Deceased Increased Risk Donors
2010	7226	709
2011	7283	836
2012	7171	966
2013	7157	1111
2014	6815	1772
2015	7059	2016
2016	7491	2478
2017	7580	2704

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Number of deceased organ donors who died from drug intoxication and those dying from drug intoxication + history of intravenous drug use United States, 2010–2017 (extended description)

Year	Number of Donor with Drug Intoxication Reported as Mechanism of Death	Number of Donor with Drug Intoxication Reported as Mechanism of Death and History of IDU
2010	342	107
2011	473	169
2012	440	178
2013	560	248
2014	625	332
2015	848	471
2016	1262	727
2017	1382	825

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Number and percent of donors with a reactive Hepatitis C Virus nucleic acid test result by increased risk status — United States, 2014–2017 (extended description)

Year	Number of IRD (HCV NAT Positive) Donors (percent)	Number of SRD (HCV NAT Positive) Donors (percent)
2014	7 (9%)	5 (2%)
2015	252 (15%)	78 (1%)
2016	363 (15%)	98 (1%)
2017	423 (16%)	80 (1%)

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