50th Meeting

HHS Advisory Committee on Blood & Tissue Safety & Availability

April 15-16, 2019

Hubert H. Humphrey Building | Washington, DC

DTAC EXPERIENCE IN DISEASE TRANSMISSION AND OUTCOMES

CAMERON WOLFE, MBBS
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Transplant Infectious Disease

DTAC Experience in Disease Transmission and Outcomes

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Assoc Professor of Medicine
Infectious Diseases Division

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Organ Vigilance through DTAC:

- Aims:
  - Rapidly communicate unanticipated potential donor-derived issues to at-risk recipients
  - Evaluate epidemiologic trends; educate transplant community and public about risks/ mitigation
  - Provide a real time alert for CDC and public health about evolving issues
  - Inform policy and national guidelines surrounding transplant safety

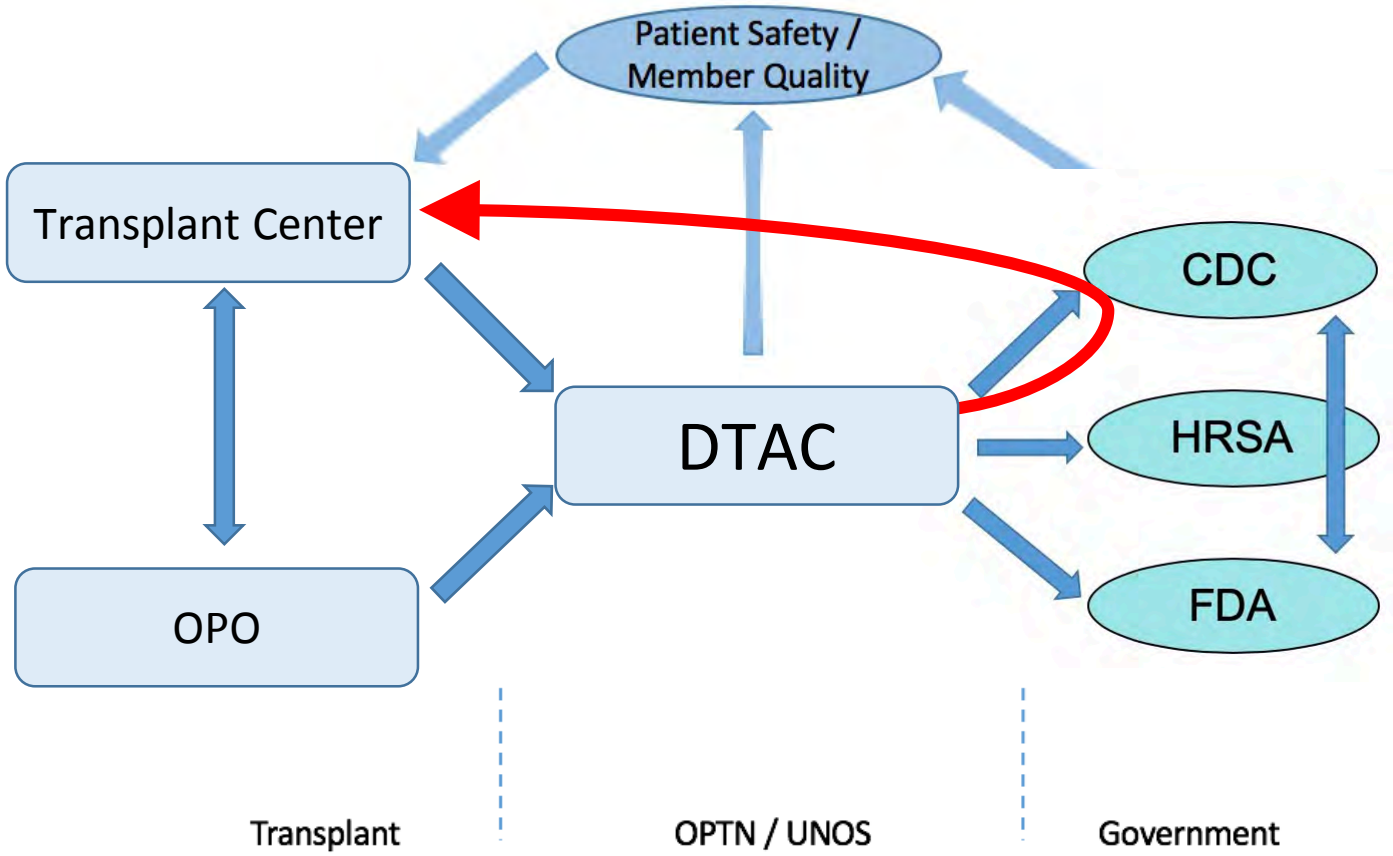
- Requirements for reporting disease:
  - OPO:
    - Urgent center notifications of high impact conditions identified post donation (eg: +BC's,)
    - General notifications of all microbiology, pathology and disease findings
    - Notification to DTAC of any "Pathogens of Special Interest"
  - Transplant Center:
    - Report to DTAC any unanticipated condition felt potentially donor-derived, esp if potental impact on other recipients exists (eg: TB, malignancy, HCV)

Organ Vigilance through DTAC:

Membership:

1 Tx hepatologist
2 Tx pathologist
1 Pulm. Crit Care
3 OPO directors
1 OPO lab director
12 Tx Infectious Dis
1 Tx Coordinator
2 Tx Surgeons

HRSA, CDC, FDA
non-voting members



For an extended description of this chart, please see the description on **page 211**.

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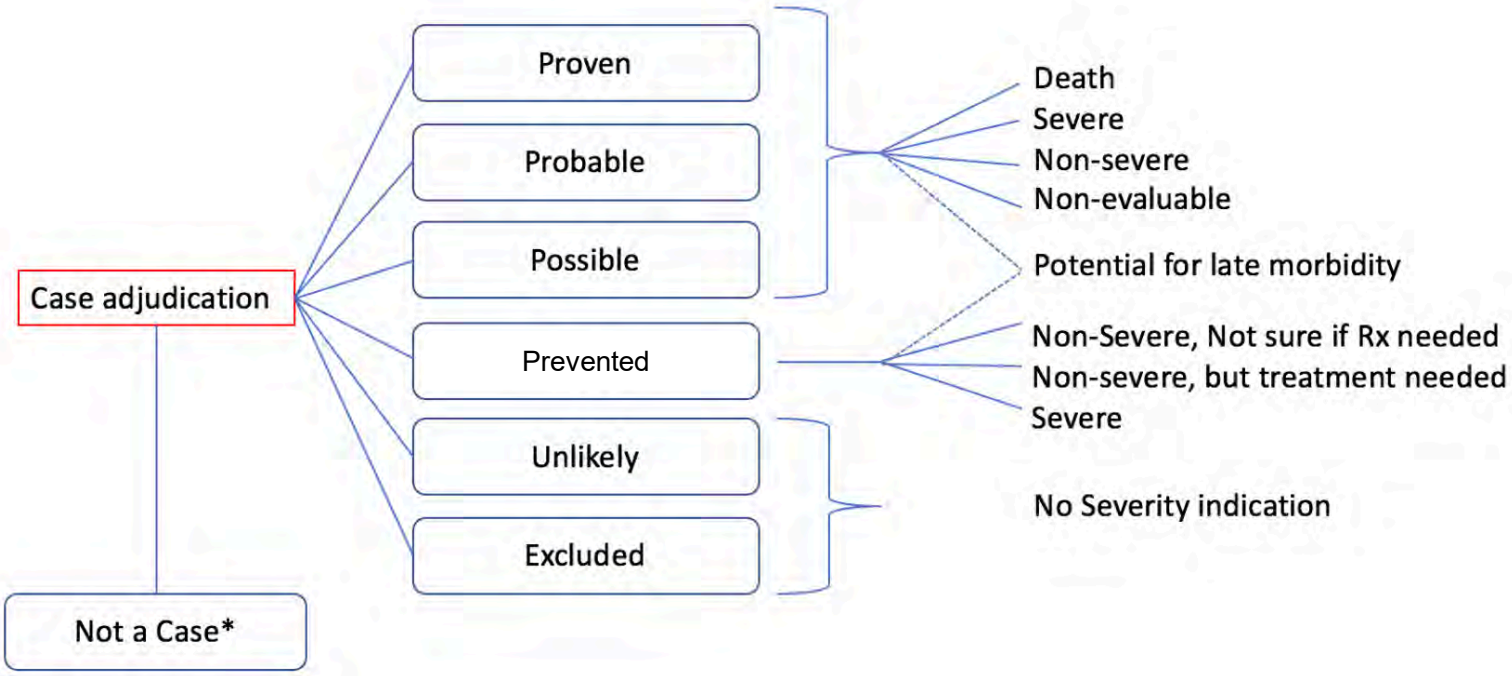
CDC – Public Health led investigations:

Notable Organ Transplant-Transmitted Infections
Investigated by Public Health Authorities, 1985 – 2017:

- 1985 - HIV
- 2000 - Hepatitis C (HCV)
- 2001 – Chagas Disease
- 2002 – West Nile Virus (WNV)
- 2003 – Lymphocytic Choriomeningitis Virus (LCMV)
- 2004 – Rabies
- 2005 – LCMV, WNV
- 2006 - Chagas
  2007 – HIV / HCV
- 2008 - Babesiosis
- 2009 - WNV
- 2010 – Zygomycosis, Coccidiodomycosis, TB
- 2011 – WNV, HCV (organ & tissue)
- 2012 - Microsporidium
- 2013 – Rabies, LCMV, MRSA
- 2014 - Microsporidium
- 2015 – M.tuberculosis, Hep A virus
- 2017 – Eastern Equine Encephalitis Virus (EEEV)

DTAC case evaluation:



For an extended description of this chart, please see the description on **page 211**.

Modified from Ison *et al*. ***Am J Transplant***. 2009; 9: 1929-1935.
Represented, modified: Wolfe *et al.* ATC, Jun 5, 2018, abstract 569

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Organ Specific Transmission Data: close up…

Table 1. Potential Donor-Derived Disease Transmission as Reported to the OPTN: 2005-2017

	Reports (Donors)	Recipients Potentially Involved°	Recipients with Proven/Probable Transmission	Donor-Derived Disease Attributable Deaths (Recipients)	Liver recipients° with proven or Probable transmissions	Heart recipients°	Kidney or Kidney/Panc recipients°	Lung or Heart/Lung recipients°
Malignancy	577	1,342	164	43	17	1	26	3
Viruses[∞]	463	1,463	216	27	26	6	41	14
Bacteria*	467	1,524	230	21	12	3	39	24
Fungi°	299	1043	179	26	10	5	18	15
Mycobacteria[§]	136	468	35	7	0	0	0	3
Parasites[†]	118	385	103	17	8	6	12	5
Other Disease	121	402	68	3	8	0	10	6
Total	**1,980**	**5,688**	**908 (15.9%)**	135	**81**	**21**	**146**	**70**

° Organ Specific numbers are only reflective of 2012-2017 data; organ-specific data was not effectively collected prior to this time point.

[∞] Viruses: Adenovirus, HBV, HCV, HEV, HHV-8, HIV, HTLV, Eastern Equine Encephalitis, herpes simplex, influenza, LCMV, Parainfluenza (PIV)-3, Parvovirus B19, rabies, West Nile Virus

* Bacteria: *Acinetobacter,* Brucella *Enterococcus* (including VRE), *Ehrlichia* spp, *E. coli, Enterobacter,* Gram Positive Bacteria, *Klebsiella*, Legionella, Listeria, Lyme Disease, Nocardia, *Pseudomonas*, Rocky Mountain Spotted Fever, *Serratia , S. aureus* (MRSA), Streptococcus spp, Syphilis, *Ureaplasma urealyticum, Veillonella*; bacterial meningitis & bacterial emboli

° Fungi: *Aspergillus* spp, *Candida* spp, *Coccidioides imitis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, Scopulariopsis, zygomyces

[§] Mycobacteria: Tuberculosis, Non-TB Mycobacteria

[†] Parasites: Babesia , *Balmuthia mandrillaris*, Chagas (*Trypanosoma cruzi*), *Naegleria fowleri*, schistosomiasis, strongyloides, Toxoplasma

Wolfe, Ison: *Clinical Transplantation*, 2019

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Wolfe, Ison: *Clinical Transplantation*, 2019

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Malignancy	43
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Wolfe, Ison: *Clinical Transplantation*, 2019

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Malignancy Transmissions over last 10 years:

Transmission	Type	Total Reports	Total Proven/Probable (P/P) Donors	Total Recipients from P/P Donors
Malignancy	Adenocarcinoma	36	6	14
	Breast	15	0	0
	Cholangiocarcinoma	3	2	2
	Hematological	14	2	7
	Kaposi's	12	1	5
	Liver	11	3	5
	Lung	21	2	2
	Melanoma	11	2	4
	Neuroendocrine	15	1	3
	Other Malignancy	94	5	13
	Renal	146	11	26
	Thyroid	28	0	0
	Urothelial	3	1	1
	Total Malignancy	409	36	82

Pending publication, 2019

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Zika:

Changing epidemiology meets variable risk tolerance

- Transplant Guidelines (HRSA/DTAC)
- At-risk Living donors:
  - Likely *defer* for at least 28d if not longer
  - Current guidance *does not preclude* using travelers or those living in endemic areas
  - If *proven infection* would *strongly suggest* 6 months *deferral*, akin to FDA tissue guidance
- At-risk Deceased donors:
  - Accepting an organ with a positive Zika test?
    - NAT: Should likely *defer*
    - IgM: less likely to be an issue, and unlikely to be done during donor evaluation
    - Accepting an organ from an asymptomatic recent traveler?
    - Cautiously *accept*, esp if > 28d

- Tissue/Blood Guidelines (FDA)
- Living donors:
  - *Ineligible* to donate if sick or travelled or lived in endemic area; or have male sexual partner with same risks – within 6 months.
- Deceased donors:
  - *Ineligible* to donate if diagnosed with zika within 6m

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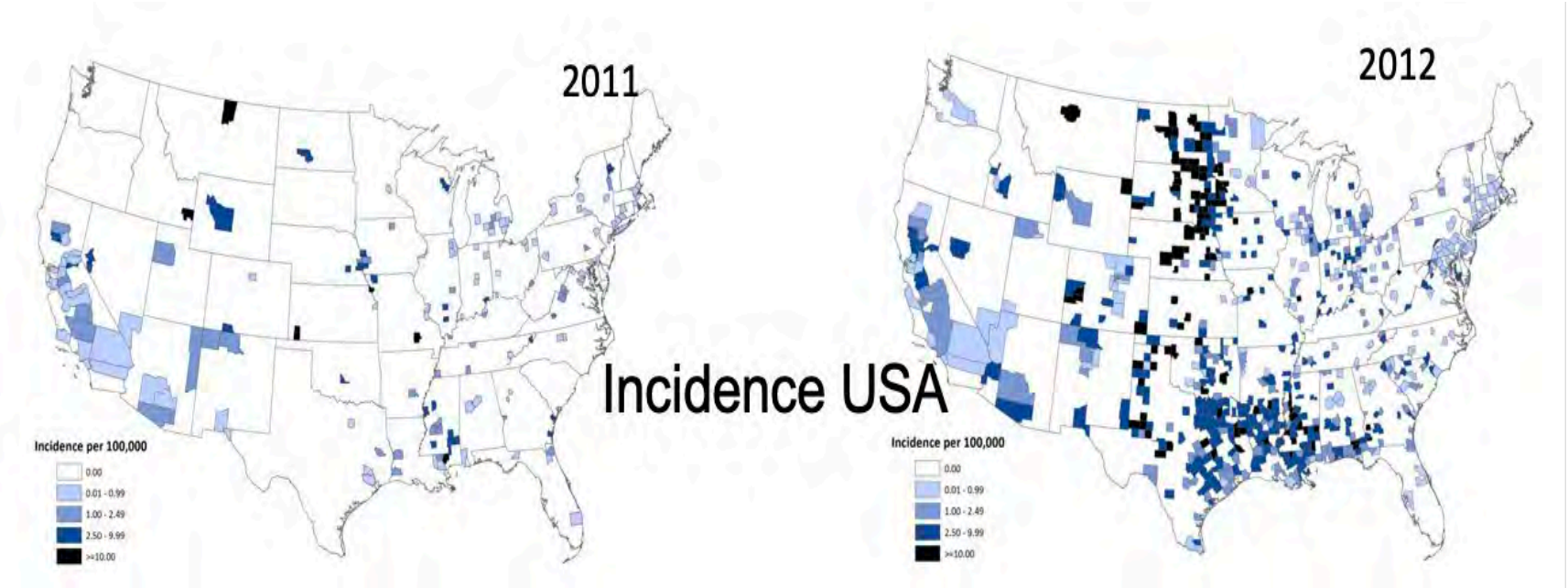
OPTN | UNOS

Chagas Disease / West Nile Virus: Emerging problems?



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For an extended description of these maps, please see the descriptions on **page 212** and **213**.

Learning to live with *some* risk:

1. Changing infectious epidemiology

Donor-Derived West Nile Virus Infection in Solid Organ Transplant Recipients: Report of Four Additional Cases and Review of Clinical, Diagnostic, and Therapeutic Features

Winston, Drew J.[1,12]; Vikram, Holenarasipur R.[2]; Rabe, Ingrid B.[3]; Dhillon, Gundeep[4]; Mulligan, David[2]; Hong, Johnny C.[1]; Busuttil, Ronald W.[1]; Nowicki, Marek J.[5]; Mone, Thomas[6]; Civen, Rachel[7]; Tecle, Selam A.[8]; Trivedi, Kavita K.[9]; Hocevar, Susan N.[10]; the West Nile Virus Transplant-Associated Transmission Investigation Team

2. Variable geographic risk

Donor-Related Coccidioidomycosis in Organ Transplant Recipients

Patty W. Wright[1,a], Demosthenes Pappagianis[2], Mark Wilson[1], Ana Louro[1], Stephen A. Moser[1], Kenneth Komatsu[3], and Peter G. Pappas[1]

3. Imperfect tests; window periods

HIV Transmitted from a Living Organ Donor --- New York City, 2009

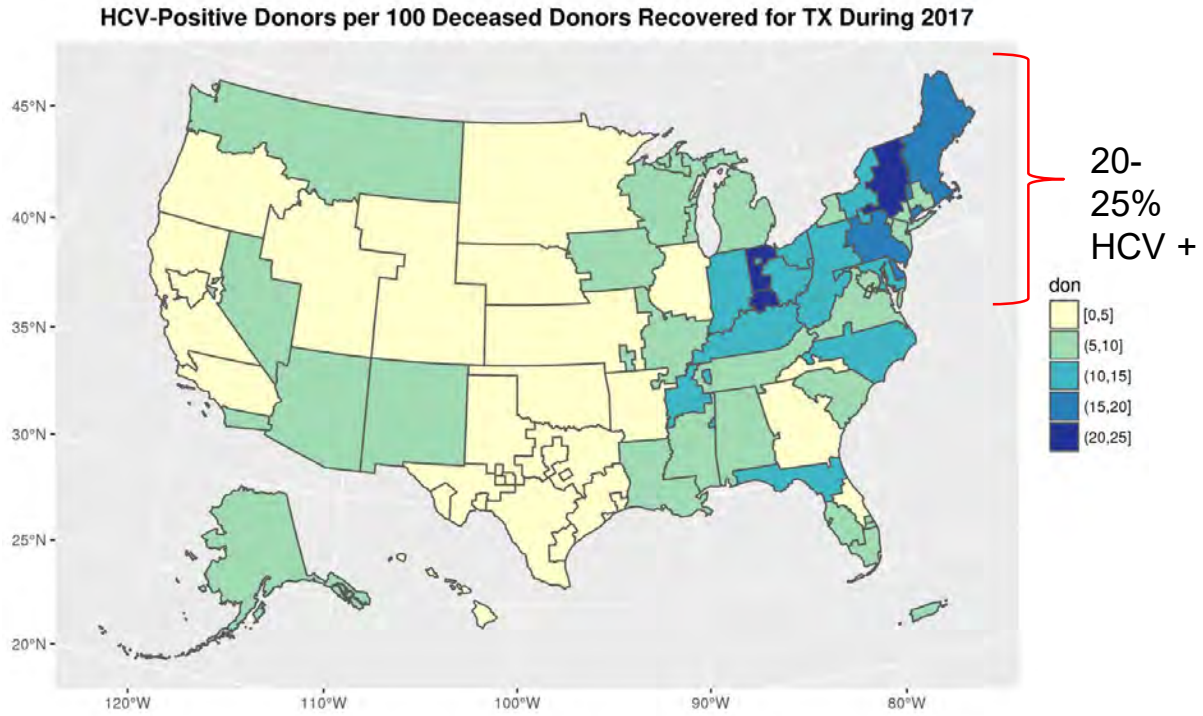
Weekly

March 18, 2011 / 60(10);297-301

4. Imperfect medical / social history

Raccoon Rabies Virus Variant Transmission Through Solid Organ Transplantation FREE

IVDU and HCV



For an extended description of the map, please see the description on **page 214**.

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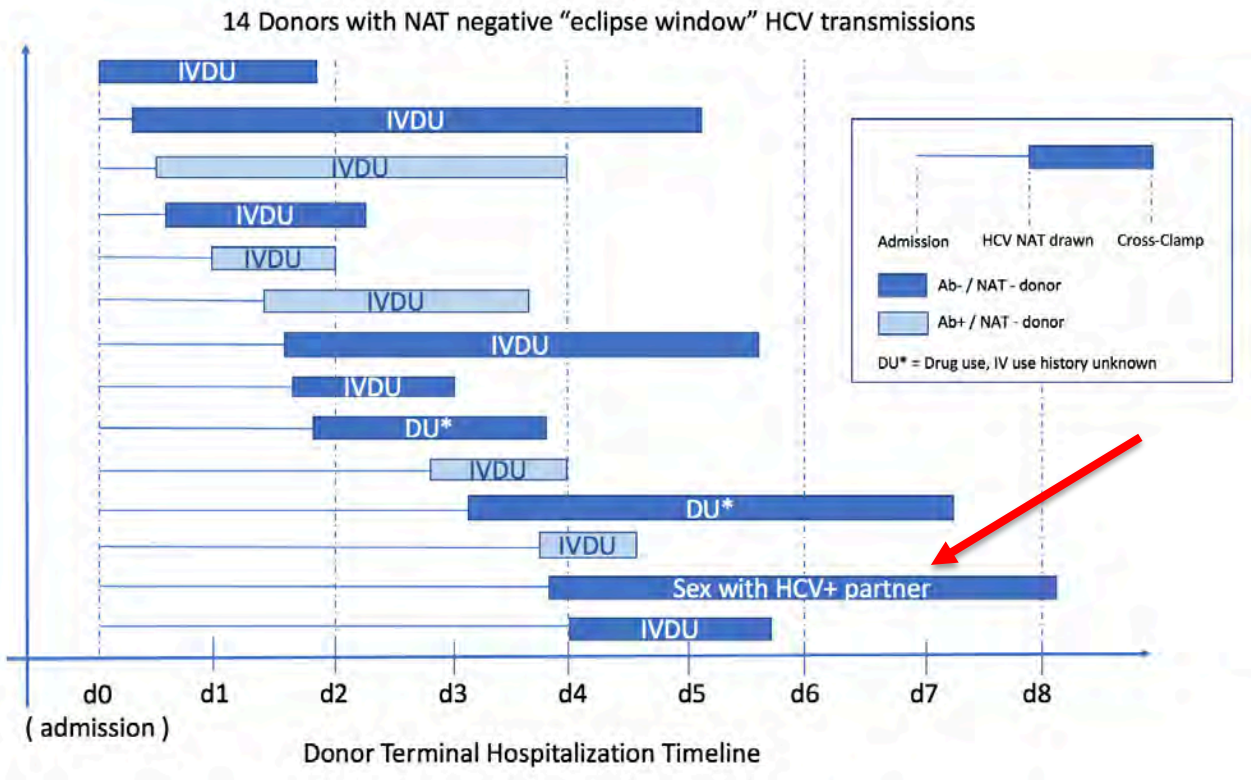
Donor testing timelines:

13 / 14 cases notable for IVDU or active reported drug use.



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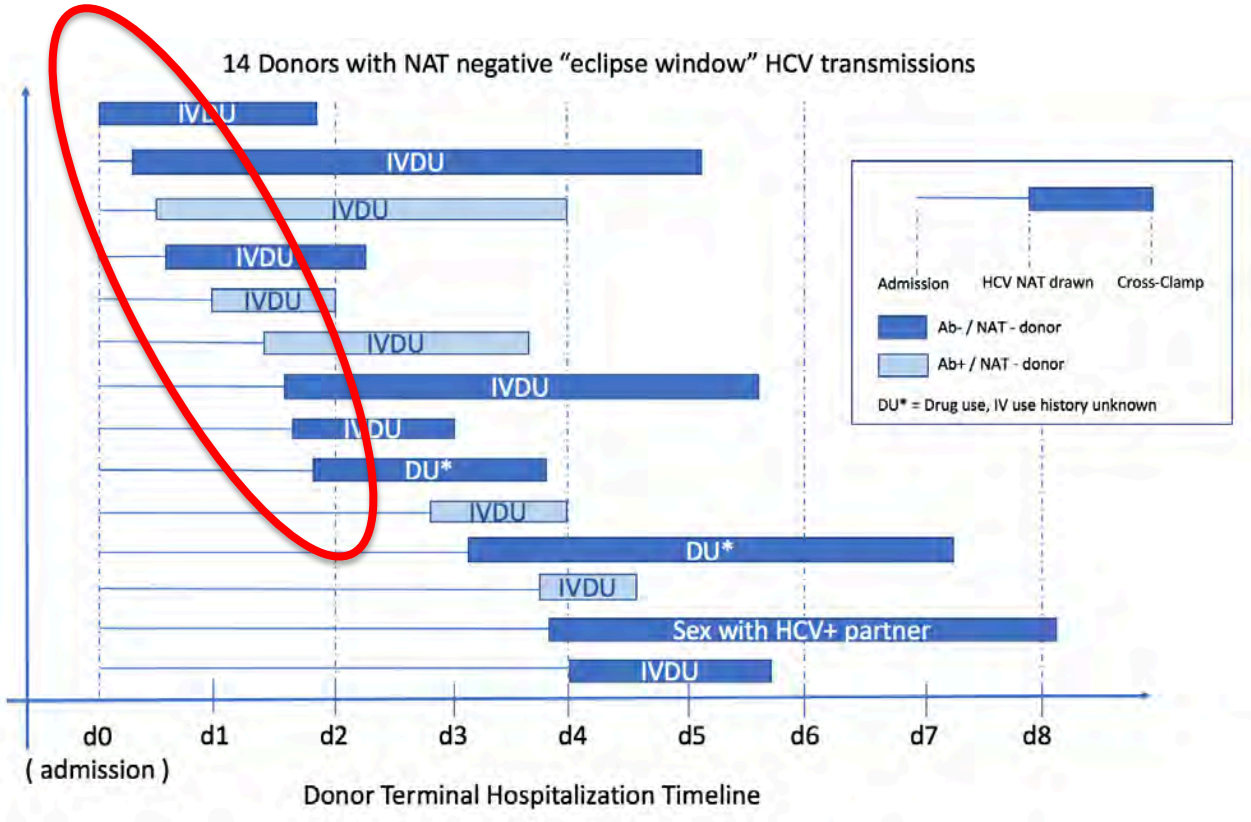
Donor testing timelines:

9 / 14 cases had HCV NAT drawn within a 48hr window of hospital arrival



Wolfe *et al.* ATC, Jun 5, 2018, abstract 569

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A therapeutic antiviral revolution:

HIV

HCV HBV

HIV / HCV / HBV transmissions in the US

HIV:

- No reported HIV transmissions in the US since 2009 living-donor transplant in NYC
- No reported HIV transmissions amongst deceased donors in the US since 2007, in Chicago

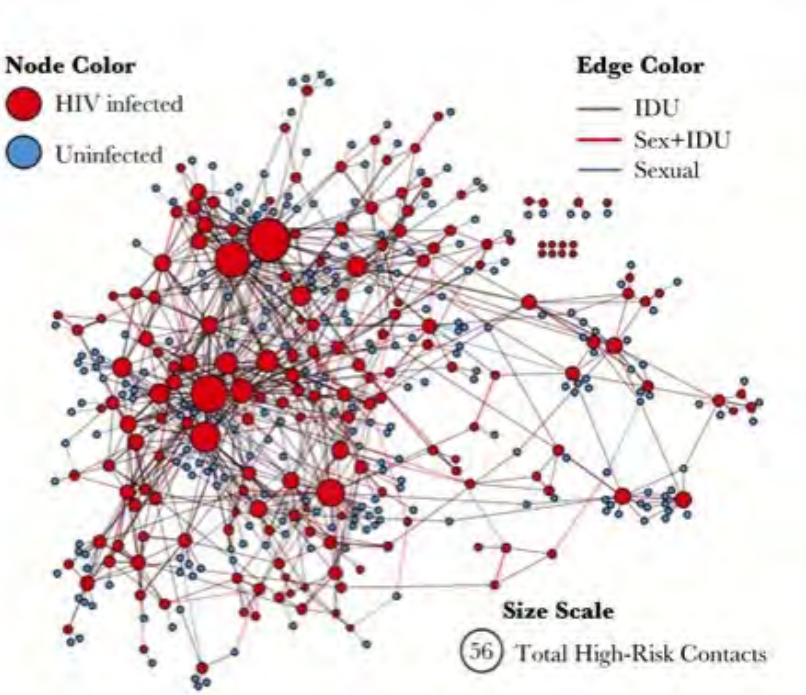
- Through the HOPE Act (transplantation of HIV+ donors into HIV+ recipients) risk has probably even gone *down further*
  - If donors with ?false-positive tests for HIV are found, they are transplanted safely into HIV +ve recipients.

- So current transplant management protocols appear SAFE in terms of detecting and managing HIV transmission risk

MMWR 2011 Mar 18;60(10):297-301
Am J Transplant. 2011 Jun;11(6):1218-25.

Less impact on HIV rates from opiate epidemic:

- But not zero…
  - Scott County, rural Indiana
  - Jan 2015 outbreak first recognized
  - By Sept 2016, 205 persons in community of 4,400 were diagnosed with HIV
  - Realistically community remains at a small risk of unanticipated HIV transmission



Campbell, *et al*; Detailed Transmission Network Analysis of a Large Opiate-Driven Outbreak of HIV Infection in the United States, *JID*, v216;9, 27 November 2017, 1053–1062

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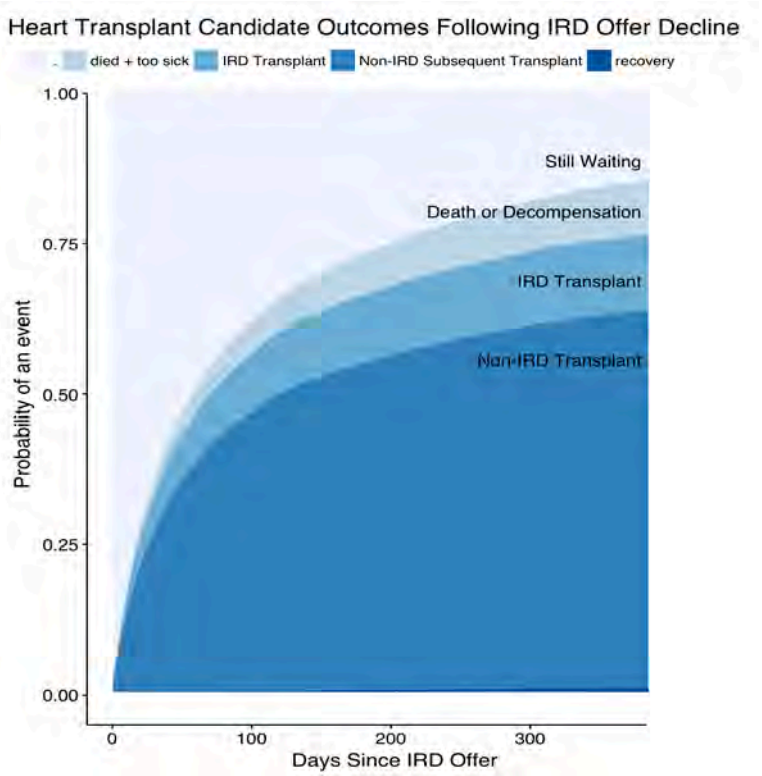
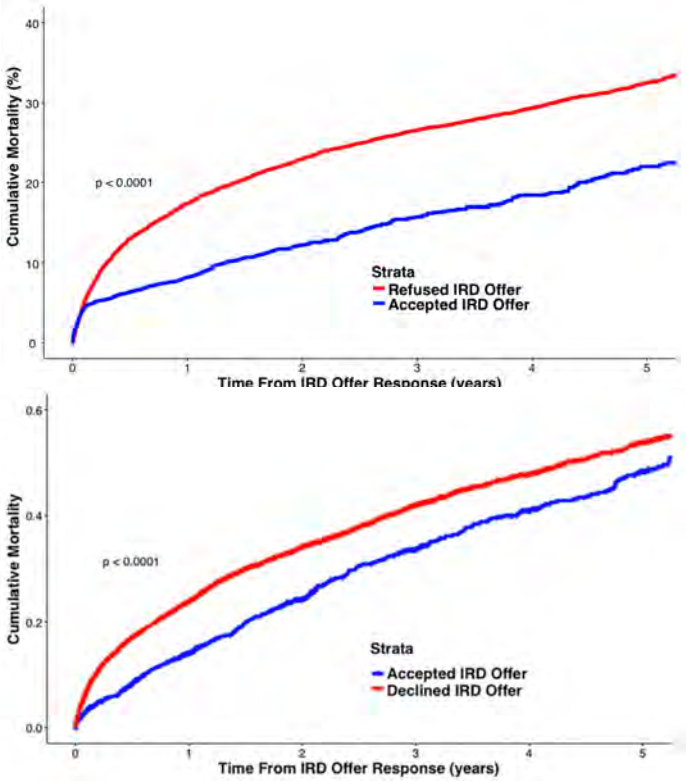
How do considerations of HCV / HIV impact the transplant community?

But what question does the patient face?





Heart Transplant

Lung Transplant

Mulvihil *et al*, J Am Coll Cardiol. 2018 Nov 6;72(19):2408-2409
M.Cox *et al,* J Heart Lung Transplant. 2019 Mar;38(3):295-305

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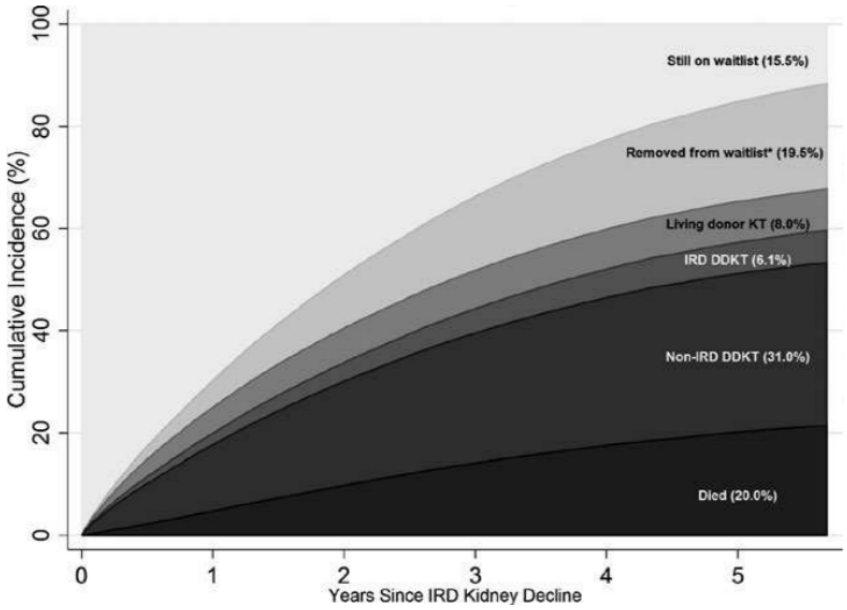
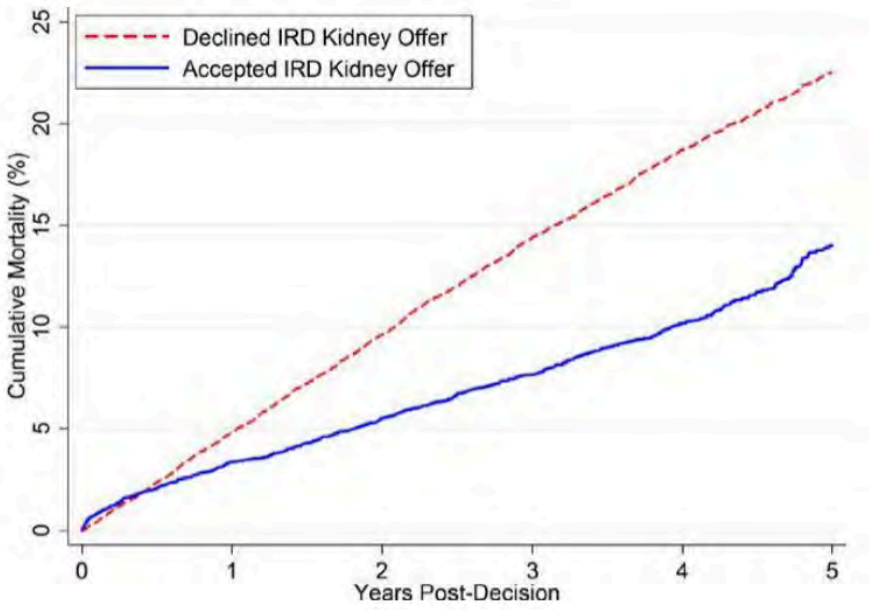
But what question does the patient face? (continued)

Kidney:





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Bowring et al, *Turn Down for What? Patient outcomes associated with declining increased infectious risk kidneys*, Am J Transplant. 2018;18:617–624.

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Conclusions:

- Donor-derived transmission events remain very rare in the US, although they can be significant.
- OPTN / DTAC can assess real-time changing trends in transplant, disease transmission, and helps explain and mitigate risk.
- Risk of the unknown is always balanced in solid organ transplant with the risk of doing nothing…

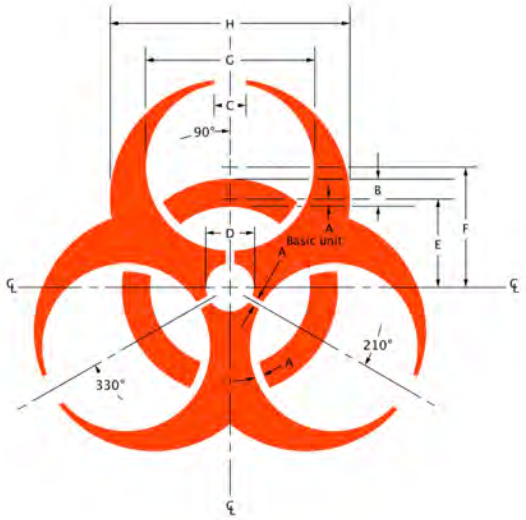
Questions?

Extra Slides if needed

Policies regarding Organ Vigilance:

- Required testing of donors:
  - Detailed NOK history, focusing on behavioural risks, geographic exposures
  - Required minimum standard testing:
    - HIV
    - HCV NAT
    - HBV serology
    - CMV, EBV, Syphilis
    - Toxoplasma IgG
    - Blood cultures
    - Urine cultures
    - Sputum / bronch cultures

  - Additional testing per OPO and transplant center negotiation
    - Strongyloides, Chagas, Coccidioides, West Nile Virus etc



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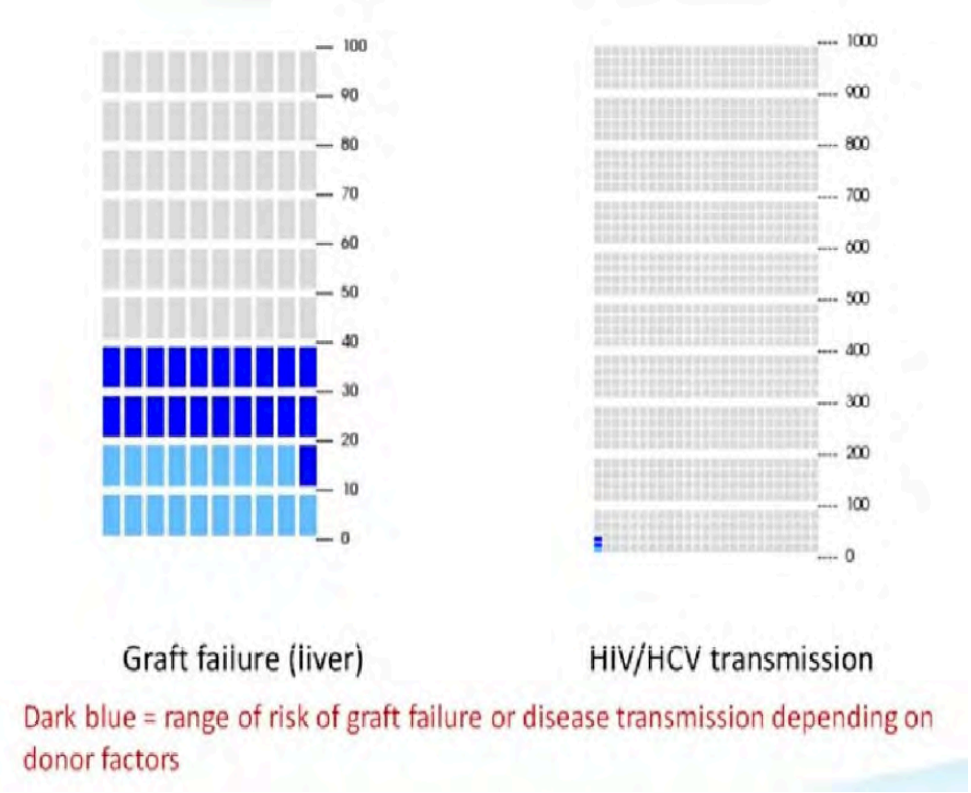
Increased Risk Donor issues vs Graft Issues:



For an accessible description of this image, please see the image description on **page 215**.

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The Antiviral Revolution:

Year	Trade Name	Generic Name	Genotypes	Success (SVR rate)
2013	Olysio	Simepravir	1	-
2013	Sovaldi	Sofosbuvir (+Sim)	1,2,3,4	95-97%
2014	Harvoni	Ledispasvir / sofosbuvir	1,4,5,6	93-100%
2014	Viekira Pak	Dasabuvir/ombitsavir/pariteprevir/ R	1	95-96%
2015	Technivie	Ombitsavir/paritaprevir/R	4	91-100%
2015	Daklinza	Daclatasvir	3	96-100% (not ESLD)
2016	Zepatier	Elbasvir/Grazoprevir	1,4	92-100% (inc HD/CKD)
2016	Epclusa	Sofosbuvir / velpatasvir	1,2,3,4,5,6	95-100%
2017	Vosevi	Sofosbuvir / velpatasvir/ voxilaprevir	1,2,3,4,5,6	96-98% (in Rx failures)
2017	Mavyret (8w)	Glecaprecvir / pibrentasvir	1,2,3,4,5,6	92-100% (inc HD/CKD)

Hepatitis C Ab+ donors: STILL underutilizing…

- 2015-2016: 9290 donors, 94% Ab-NAT-, ~2% Ab+/NAT-, remainder NAT+
  - 165 Ab+/NAT– donors = 134 livers, 80 kidneys, 1 lung, 0 hearts
  - 391 Ab+/NAT+ donors = 280 livers, 203 kidneys, 1 lung, 3 hearts

- Propensity score-matched model:
  - If we used Ab+/NAT-ve donors at the same pace as we do for Ab-/NAT- donors, we'd get an extra:
    - 48 kidney donors,
    - 37 hearts and
    - 15 more lung donors annually

	NAT+	NAT-
Ab+	474	272 False negative NAT? Spontaneously cleared? NAT below limit of detection?
Ab-	29 Infected recently, within serologic eclipse period? False positive NAT?	9,511 Infected recently, within NAT eclipse period?

US Deceased Donors 2017

Kling et al, AJT July 2017

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Pathogens of special interest- reportable for suspected or confirmed donor or recipient illness

Amebic encephalitis
Anaplasma or Ehrlichiosis
Anthrax
Babesiosis
Brucellosis
California Serogroup Virus Diseases
Chagas
Chikungunya Virus Disease
*Coccidioidomycosis/Valley Fever ** Specifically identified by autopsy, biopsy, or cultures. Exclude serology only*
Crimean-Congo Hemorrhagic Fever virus
Dengue virus infections
Eastern Equine Encephalitis Virus Disease
Ebola virus
Enterovirus D68
Hantavirus
Hepatitis A
Hepatitis C (acute, past or present)
HIV Infection
Influenza-associated pediatric mortality

Lassa virus
LCMV
Leptospirosis
Listeriosis
Lujo virus
Lyme disease
Malaria
Marburg virus
Measles/Rubeola
Microsporidia
MERS co-V
Mumps
New World Arenaviruses
Pandemic Influenza strains
Plague
Poliomyelitis, paralytic
Poliovirus infection, nonparalytic
Powassan Virus Disease
Q fever (acute, chronic)
Rabies, animal or human
Rubella/ German Measles
Severe Acute Respiratory Syndrome (SARS)-Associated Coronavirus Disease
• Smallpox/Variola

Spotted Fever Rickettsiosis (
St. Louis Encephalitis Virus Disease
Strongyloides
Tuberculosis (TB)
Tularemia
Varicella / Chickenpox
Viral Hemorrhagic Fever
West Nile Virus Disease
Western Equine Encephalitis Virus Disease
Yellow fever
Zika virus

OPTN/UNOS Disease transmission advisory committee

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DTAC PERSPECTIVE AND OPINIONS ON NECESSARY CHANGES TO THE PHS GUIDELINE RECOMMENDATIONS

MARIAN MICHAELS, MD, MPH
Professor Pediatrics and Surgery
UPMC Children's Hospital of Pittsburgh
Pediatric Infectious Diseases

PHS IRD Discussion: OPTN perspective

Marian G Michaels MD MPH
Chair, ad hoc OPTN DTAC
Professor of Pediatrics and Surgery
UPMC Children's Hospital of Pittsburgh

Acknowledgement

This analysis reflects, in part, work performed on behalf of the **OPTN.**

This work was supported wholly or in part by HRSA contract 234-2005-370011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of HHS, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government

Disclosures: No conflict of interest

Question 1: Is a new term needed to replace current term ‘PHS Increased Risk Donor’ ?

- Yes
  - Term PHS IRD has an unintended negative connotation
  - Although it is superior to prior term “High Risk Donor ”
- No consensus on specific new term
  - Recommend consultation with PR or behavioral psychologist
- OPTN DTAC member Informal discussion with psychologist
  - Lucy Cochran (lucy.m.cochran@gmail.com)
  - Cognitive biases may lead person to reject an organ despite probability of better outcome by accepting organ offer

Cognitive Biases

- Base Rate Fallacy:
  - Placing more emphasis on specific information versus general information
    - Focus on “increased risk” rather than on “good quality organ” is available
- Negativity Bias:
  - When all elements are equal, the potential negative outcome is given greater weight then potential positive or neutral outcome
- Stigma of Disease:
  - Perceived stigma of lifestyle leading to a risk for HIV, HCV, HBV
- Zero Risk Bias:
  - Preference to completely eliminate one risk (potential HIV,HCV,HBV) at the expense of not recognizing the greater risk (lack of organ availability)

Adapted from Lucy Cochran

Suggestions: Reframe the term and question

- Use more neutral term and offer more choices to make it less threatening
- Give 3 options rather than 2 options
  - **PHS A:** No further testing required based on PHS risk identification
  - **PHS B:** Further testing required based on identified possible risks
    - Behavioral risks or absence of adequate information
    - Equivalent to current PHS IRD
  - **PHS C:** Further testing/℞ required based on Positive donor test
    - Ex: Donor with Positive HCV NAT testing, or HOPE Act recipient

Question 2: Should donors continue to be identified based on risk factors for HIV, HBV, HCV?

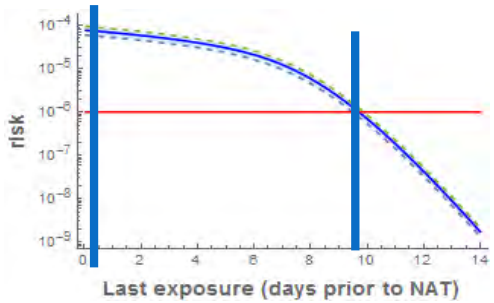
- Infections are a risk with transplantation
- OPTN supports education on donor transmission risks not just PHS IRD
  - OPTN Policy 15.3: Informed consent of transmissible disease risk
- However, OPTN also supports maintaining a classification specifically for HIV, HBV, and HCV:
  - To inform transplant center & recipient of need for follow-up testing
  - For transparency to the public

Question 3: Should time be shortened from 12 months?

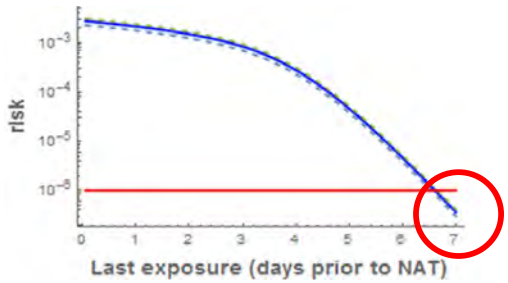
- **Yes**
  - We note that the 12 month period was a decrease from the 1994 guidelines which reviewed donor behaviors from the prior 5 years
- **Rationale:**
  - The 12 month period was instituted prior to all OPOs using nucleic acid tests (NAT)
  - NAT decreases the eclipse period substantially
  - By 2017 NAT used on >99.9% of donors - Abara et al MMWR Jan 2019
  - Accordingly, a protracted period of time no longer required
- **Based on data presented by CDC**
  - This window or eclipse period is < than 30 days for all three viruses and less than 10 days for HIV and HCV.

CDC data on risk of undetected virus based on time from behavior

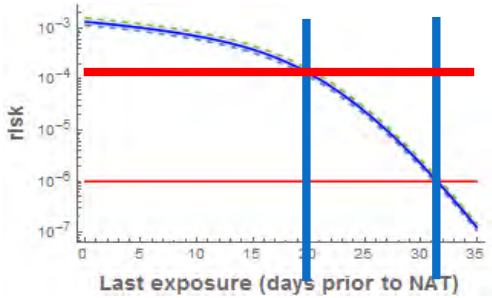
Risk of undetected HIV infection among PWID



Risk of undetected HCV infection among PWID with an HCV-positive injecting partner



Risk of undetected HBV infection among donors with 3x the incidence of HBV among MSM



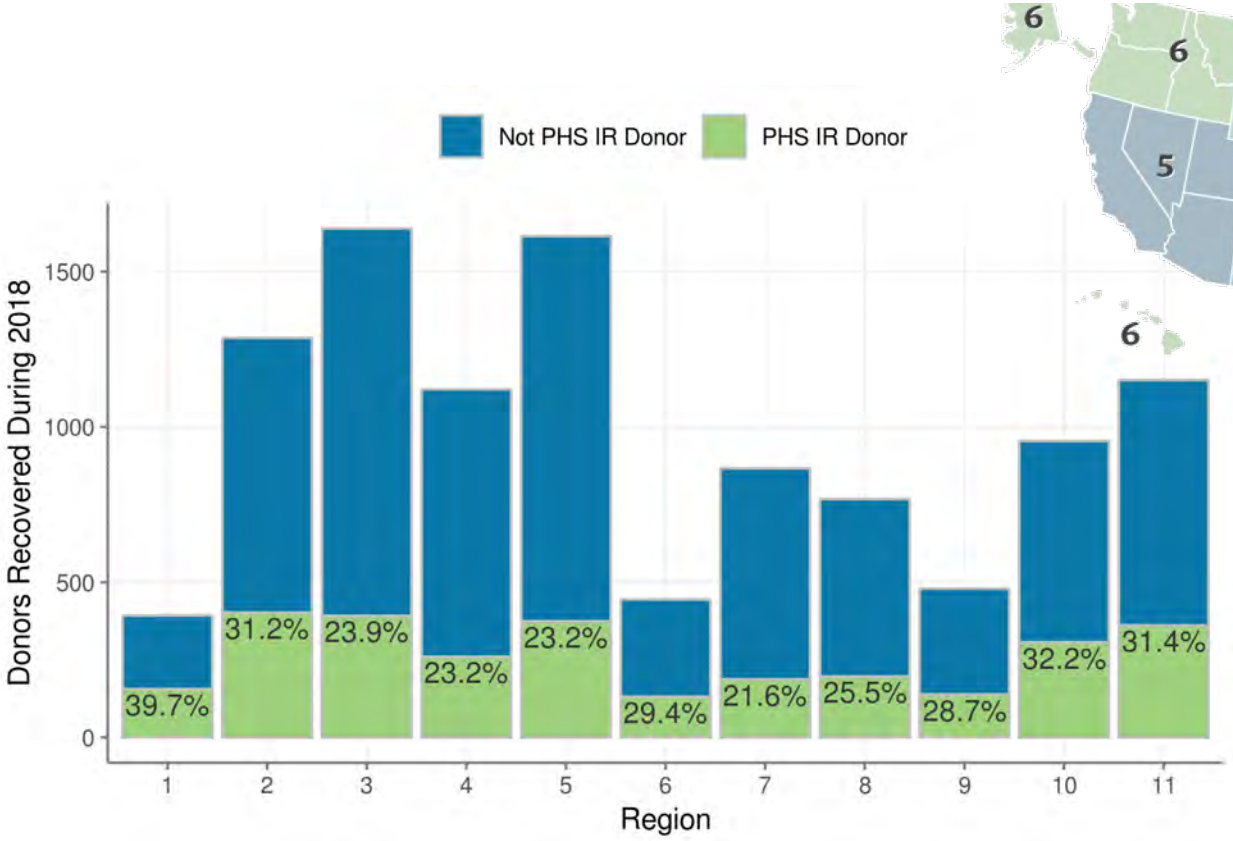
Eclipse period is < 30 days for all three viruses

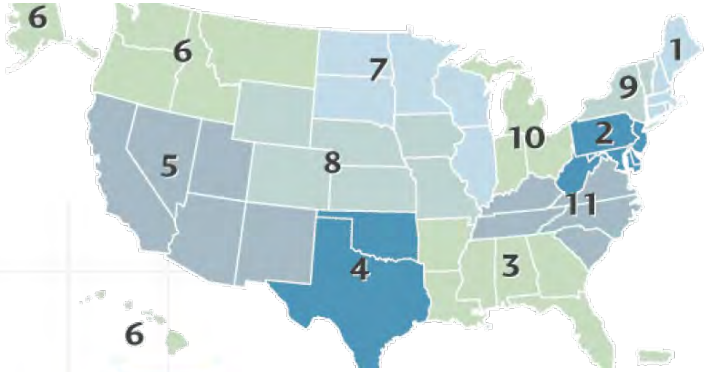
Question #4: Are there specific criteria which should be eliminated or revised?

OPTN Evaluation of PHIS IRD – 2018

- 2018: 2,904 donors classified as PHS IRD
  - 10% Donors Sampled: (N=290) to assess individual risks
  - Methods: used “free text” narratives provided in DonorNet:
    - Donor admission course
    - Donor highlights
    - Donor Medical/Social History
    - DRAI
  - Limitation: except for hemodilution or death by drugs could not tell the time of the risk behavior
  - 2 donors removed as not truly PHS IRD
    - Leaving Total Sample Size N= 288

Rates of PHS IRD By Region During 2018

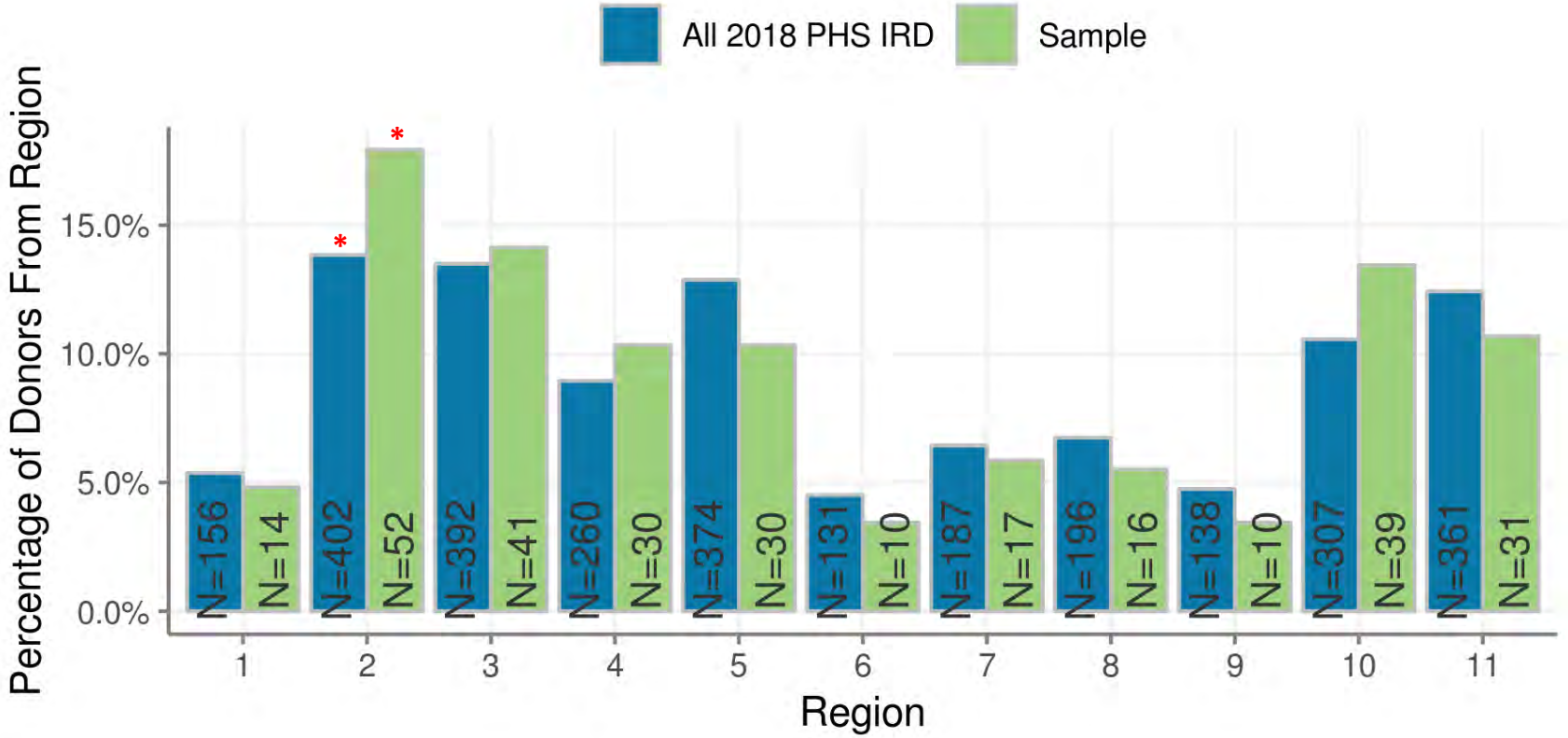




Regions

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

Rates of PHS IR Donors By Region 2018: All PHS IRD vs Sample



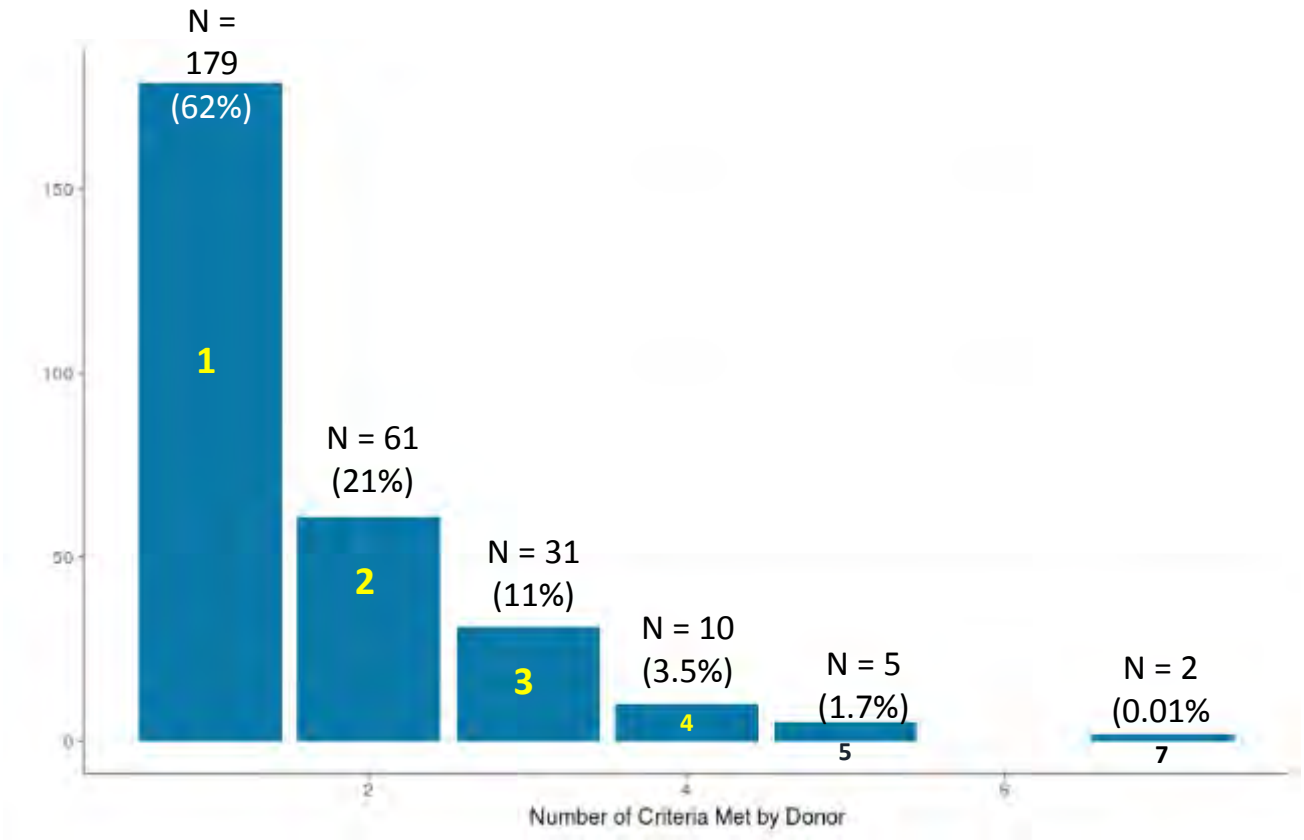
See map of regions on **page 42** to identify which States are located in each region.

PHS IR Donors Demographics: Sample vs Total

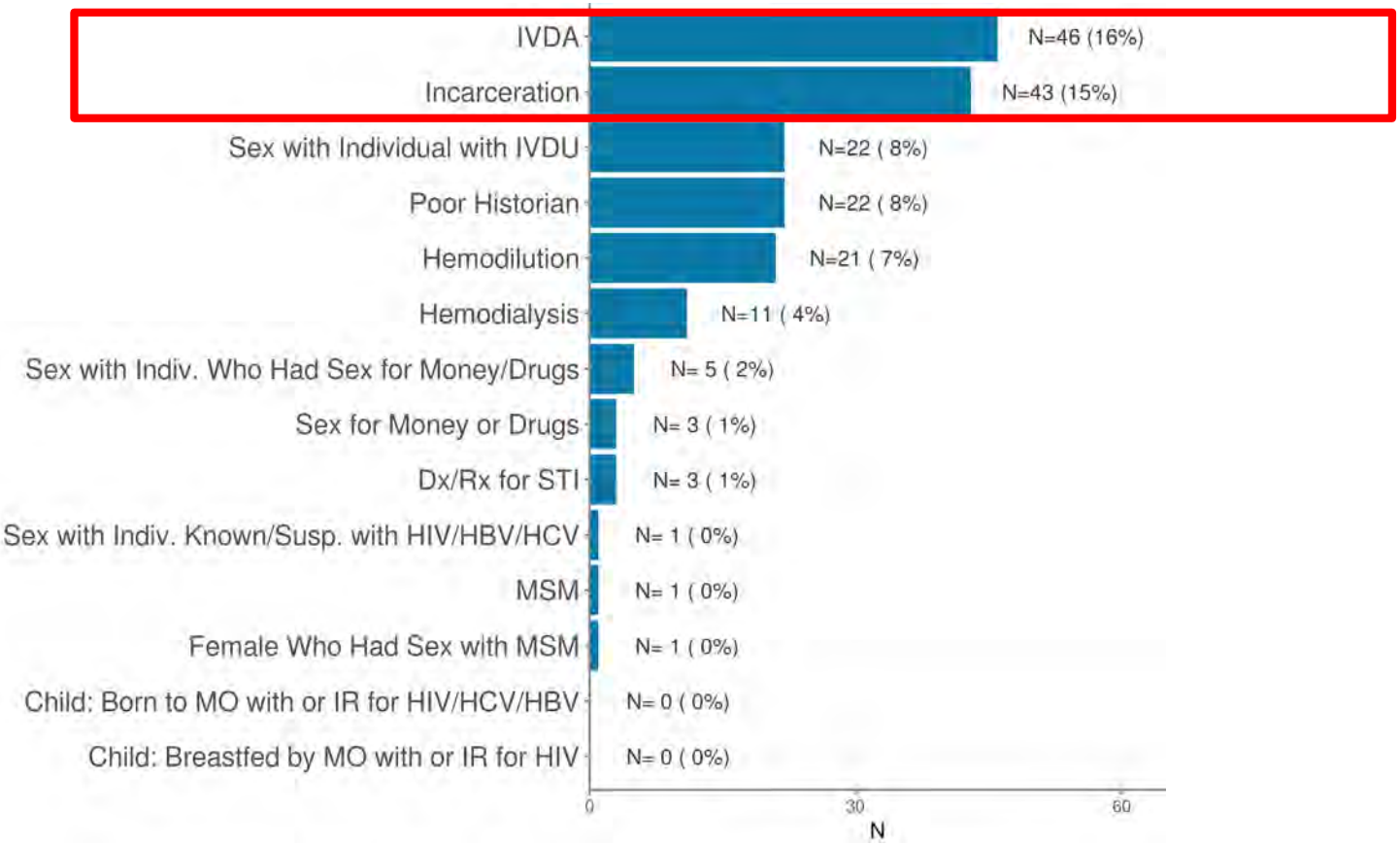
Description	Sample	All 2018 PHS IRD
N	288	2,904
Median Age (IQR)	36 (27 – 45)	35 (27—46)
Pediatric (<12 y.o.) Donors (%)	4 (1.4%)	47 (1.6%)
Female Donors (%)	92 (31.7%)	944 (32.5%)
Donor Ethnicity (%)		
White	211 (72.3%)	1995 (68.7%)
Black or African—American	39 (13.4%)	458 (15.8%)
Hispanic	33 (11.4%)	350 (12.1%)
Other/Multiracial	5 (1.7%)	101 (3.5%)

Results: PHS IRD Sample from 2018 (N= 288)

- Most deceased donors met only one criterion for increased risk:

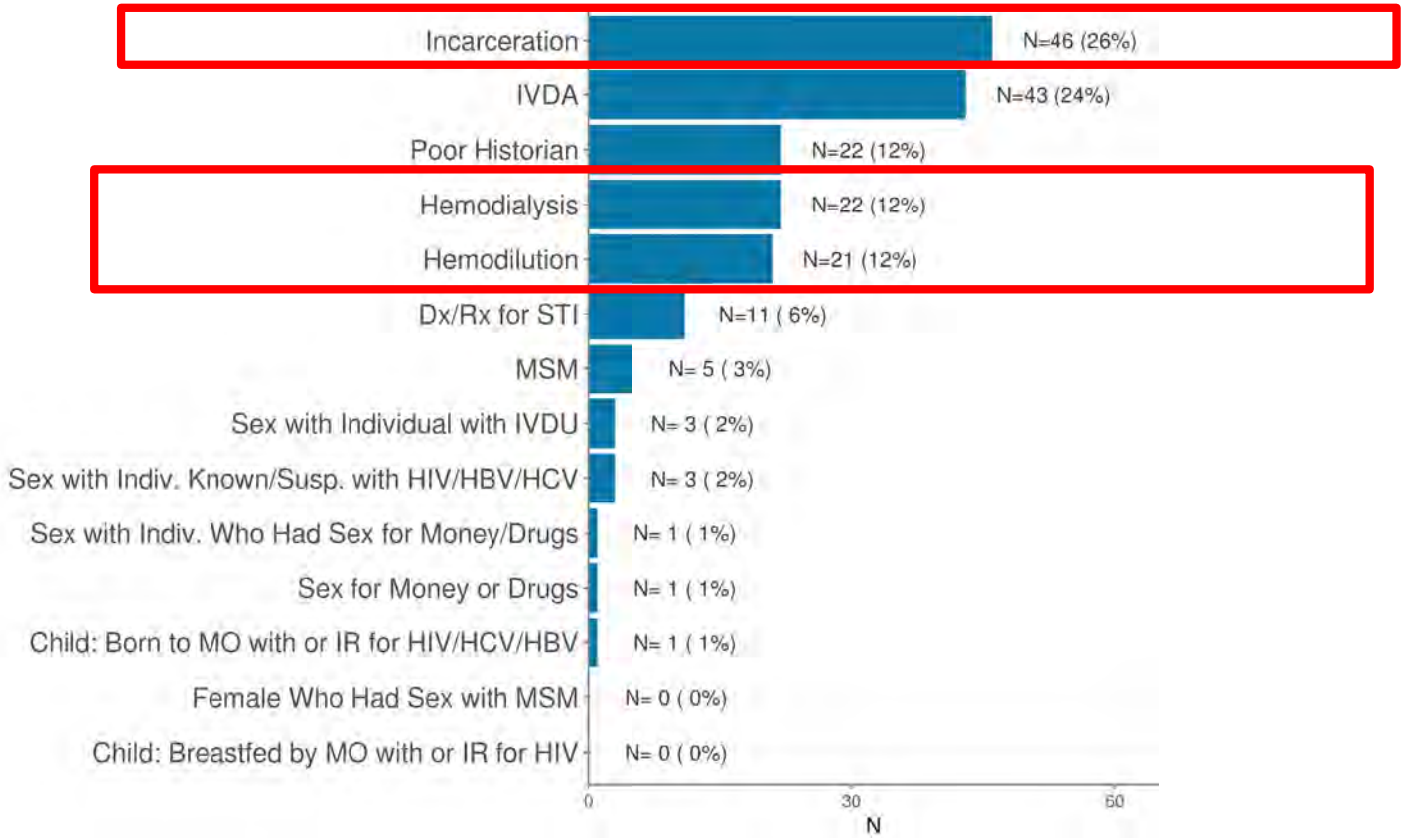


Results: Indication for PHS IR Designation N= 288



For an extended description of this chart, please see the description on **page 216**.

Results: N=179 donors with 1 Criterion only for PHS IRD



For an extended description of this chart, please see the description on **page 217**.

Hemodialysis and Hemodilution as risks

- Between 2008 and 2018 No transmissions of HIV, HCV, HBV due to hemodialysis or hemodilution as a risk factor
- Hemodilution was associated with transmission in very early transplant era using only Antibody testing not NAT
- Hemodialysis has been associated with confusion
  - Over 80% of dialysis centers test HCV annually and incidence decreased from 0.14 →0.08/100 person years
  - Accordingly, anticipate Donor testing by NAT identifying HCV infected donors who had been on routine hemodialysis

Pediatric Specific issue

- Looking at **all deceased donors** recovered in 2018
- 479 of 10,271 donors were less than 12 years of age
- Among these 479 pediatric donors:
  - 47 (10%) were PHS IRD
  - 28 /47 (60%) PHS IRD classification was due to hemodilution as sole criterion

OPTN Recommendations for Question #4:

- We believe the largest impact on decreasing the number of donors classified as PHS IRD will be based on changing 12 months to a shorter period of time
- Consider eliminating:
  - Hemodialysis
  - Hemodilution
    - Particularly for pediatric donor

OPTN Conclusions :

- Applaud PHS effort to consider changes to PHS IRD
- Believe there is worthiness to continue to have some assessment of risk for HIV, HCV and HBV
- Suggest changing the name to a more neutral term
- Recommend shortening the 12-month time period substantially
- Consider removal of hemodialysis and hemodilution particularly for pediatric population

HIV/HCV IN ORGAN TRANSPLANTATION: CLINICAL TRIALS AND OUTCOMES

CHRISTINE DURAND, MD

Associate Professor of Medicine and Oncology Johns Hopkins University, School of Medicine Division of Infectious Diseases, Transplant Oncology ID Group

JOHNS HOPKINS
MEDICINE

EPIDEMIOLOGY
RESEARCH GROUP IN
ORGAN TRANSPLANTATION

HIV and HCV in organ transplantation: clinical trials and outcomes

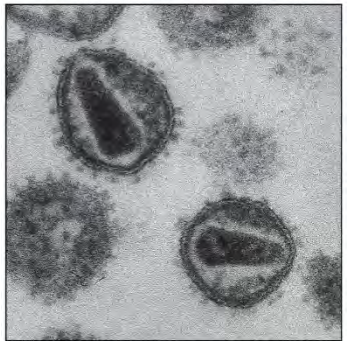
Christine M. Durand, MD
Associate Professor of Medicine, Transplant Infectious Diseases
HHS Advisory Committee on Blood & Tissue Safety and Availability
April 15, 2019

Outline

- HIV in organ transplantation
  - Biology and epidemiology
  - HIV- donor for HIV+ recipient (HIV D-/R+) transplantation
  - HIV+ donor for HIV+ recipient (HIV D+/R+) transplantation

- HCV in organ transplantation
  - Biology and epidemiology
  - HCV+ donor for HCV+ recipient (HCV D+/R+) transplantation
  - HCV+ donor for HCV- recipient (HCV D+/R-) transplantation

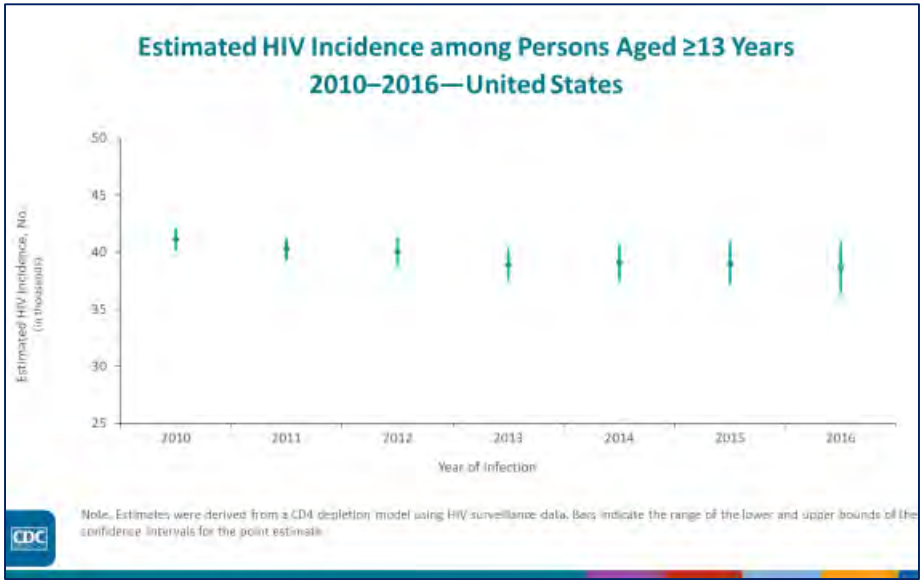
HIV

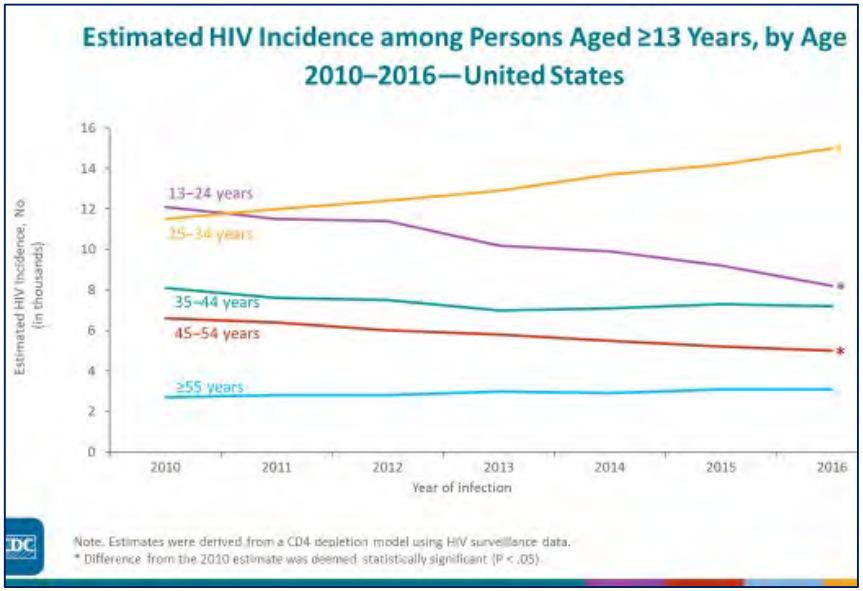


- Retrovirus, RNA virus, infects CD4 T cells
- Transmitted through blood or sexual contact
- Acute HIV
  - Flu like illness, can be severe with meningitis
  - Natural clearance or cure not reported
- Chronic HIV
  - If left untreated, over 5-15 years progression to AIDS
- Manageable condition with antiretroviral treatment near normal life expectancy

HIV epidemiology

- 1.1 million people with HIV in US
- Since 2012, incidence stable, with estimated 38,700 new cases in 2017





For an extended description of this charts, please see the descriptions on **page 218**.

Evolution of HIV treatment

7 drug classes, > 25 drugs

NRTI – nucleoside reverse transcriptase inhibitor
PI – protease inhibitor
NNRTI – non-nucleoside reverse transcriptase inhibitor
FI – Fusion inhibitor
CA – CCR5 antagonist
INSTI – integrase strand transferase inhibitor
PAI – post attachment inhibitor
FDC – Fixed dose combination

https://aidsinfo.nih.gov

For an extended description of this image, please see the descriptions on **page 219**.

Early experience of HIV transplant

- 1980's unintentional HIV D+ and HIV R+ transplants
  - n=18 (all organs) Univ Pittsburgh, 6 month survival 50%[1]
- 1988 National Organ Transplant Act amendment bans acquisition of organs from individuals with HIV
- 1990's intentional HIV D-/R+ transplants (pre-highly active antiretroviral therapy), inferior outcomes
  - n=32, kidney, SRTR, 3 yr survival 83%, graft survival 53% [2]
- HIV in a donor or a recipient was a contraindication

1. Dummer/Starzl, Transplantation 1989

2. Swanson/Abbott, Transpl Infect Dis 2002

HIV D-/R+ in era of effective ART

2003-2009 HIV Transplant Recipient (HIV TR) Study

HIV D-/R+ in era of effective ART

2003-2009 HIV Transplant Recipient (HIV TR) Study

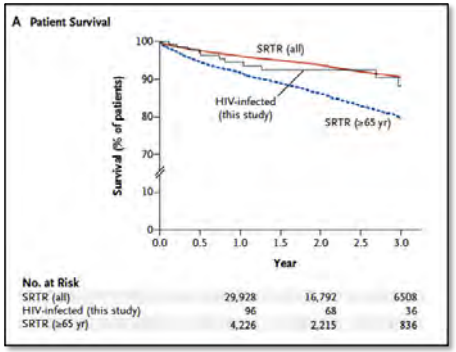
Kidney
n=150

ORIGINAL ARTICLE

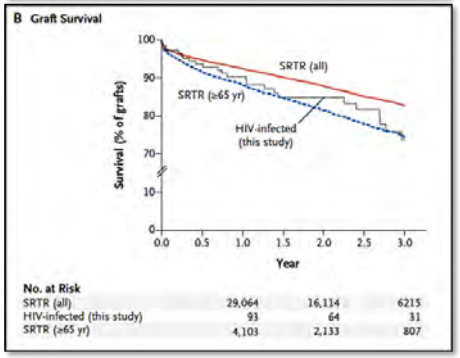
Outcomes of Kidney Transplantation in HIV-Infected Recipients

Peter G. Stock, M.D., Ph.D., Burc Barin, M.S., Barbara Murphy, M.D., Douglas Hanto, M.D., Ph.D., Jorge M. Diego, M.D., Jimmy Light, M.D., Charles Davis, M.D., Emily Blumberg, M.D., David Simon, M.D., Ph.D., Aruna Subramanian, M.D., J. Michael Millis, M.D., G. Marshall Lyon, M.D., Kenneth Brayman, M.D., Doug Slakey, M.D., Ron Shapiro, M.D., Joseph Melancon, M.D., Jeffrey M. Jacobson, M.D., Valentina Stosor, M.D., Jean L. Olson, M.D., Donald M. Stablein, Ph.D., and Michelle E. Roland, M.D. for the HIV-TR Investigators

Survival
1 yr: 95%
3 yr: 91%



Graft survival
1 yr: 90%
3 yr: 77%



For an extended description of these graphs, please see the descriptions on **page 220**.

Stock PG/Roland M NEJM 2010.

HIV D-/R+ in era of effective ART

2003-2009 HIV Transplant Recipient (HIV TR) Study

Kidney
n=150


ORIGINAL ARTICLE

Outcomes of Kidney Transplantation in HIV-Infected Recipients

Peter G. Stock, M.D., Ph.D., Burc Barin, M.S., Barbara Murphy, M.D., Douglas Hanto, M.D., Ph.D., Jorge M. Diego, M.D., Jimmy Light, M.D., Charles Davis, M.D., Emily Blumberg, M.D., David Simon, M.D., Ph.D., Aruna Subramanian, M.D., J. Michael Millis, M.D., G. Marshall Lyon, M.D., Kenneth Brayman, M.D., Doug Slakey, M.D., Ron Shapiro, M.D., Joseph Melancon, M.D., Jeffrey M. Jacobson, M.D., Valentina Stosor, M.D., Jean L. Olson, M.D., Donald M. Stablein, Ph.D., and Michelle E. Roland, M.D. for the HIV-TR Investigators

Survival
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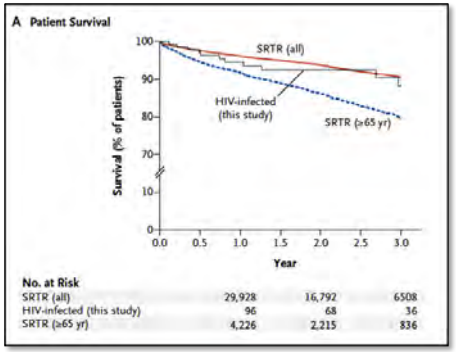
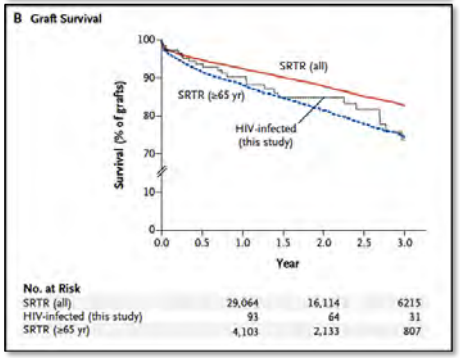
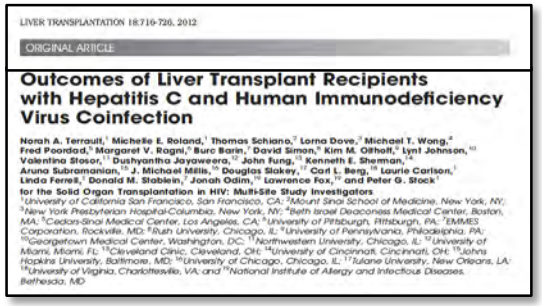


Graft survival
1 yr: 90%
3 yr: 77%



Stock PG/Roland M NEJM 2010.

Liver
HIV/HCV HCV
n=89 n=235

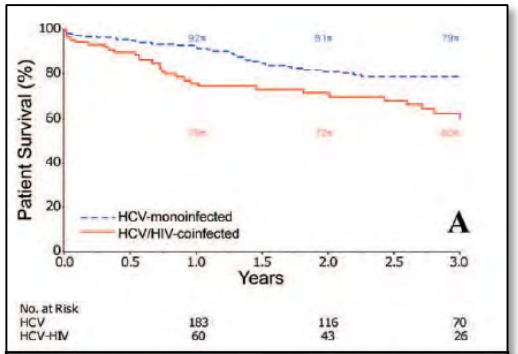

LIVER TRANSPLANTATION 18:716-726, 2012

ORIGINAL ARTICLE

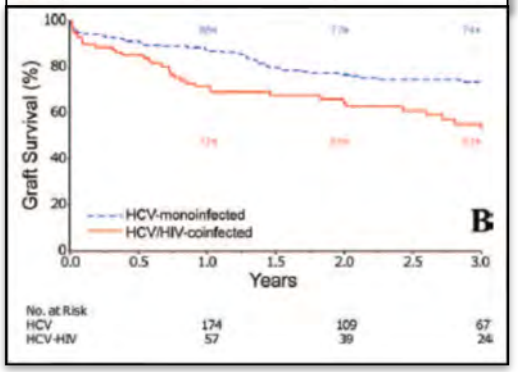
Outcomes of Liver Transplant Recipients with Hepatitis C and Human Immunodeficiency Virus Coinfection

Norah A. Terrault, Michelle E. Roland, Thomas Schiano, Lorna Dove, Michael T. Wong, Fred Poordad, Margaret V. Rogni, Burc Barin, David Simon, Kim M. Olthoff, Lynt Johnson, Valentina Stosor, Dushyantha Jayaweera, John Fung, Kenneth E. Sherman, Aruna Subramanian, J. Michael Millis, Douglas Slakey, Carl L. Berg, Laurie Carlson, Linda Ferrell, Donald M. Stablein, Jonah Odim, Lawrence Fox, and Peter G. Stock for the Solid Organ Transplantation in HIV: Multi-Site Study Investigators

Patient survival
1 yr: 76% 92%
3 yr: 60% 79%



Graft survival
1 yr: 72% 88%
3 yr: 53% 74%

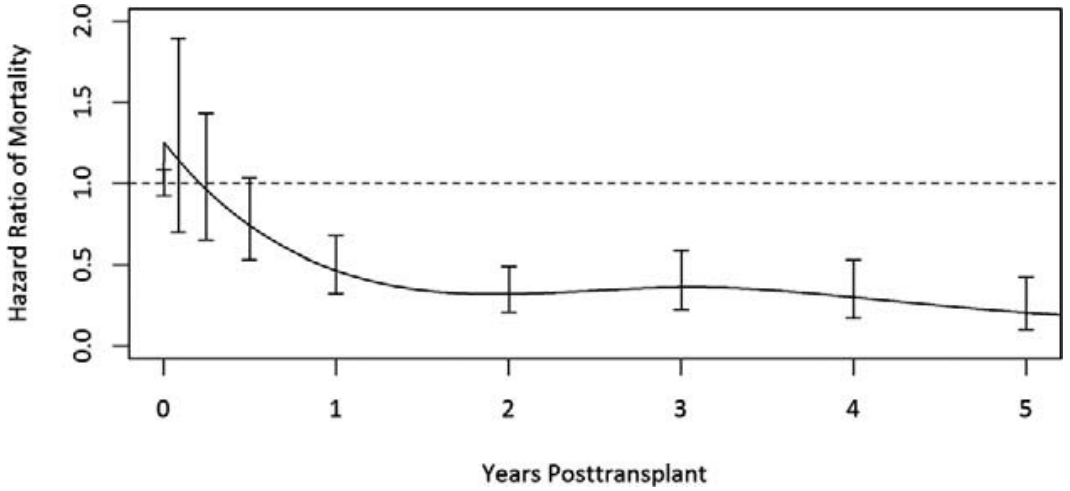


For an extended description of these graphs, please see the descriptions on **page 221**.

Terrault/Stock Liver Transp 2012

National real-world data confirms

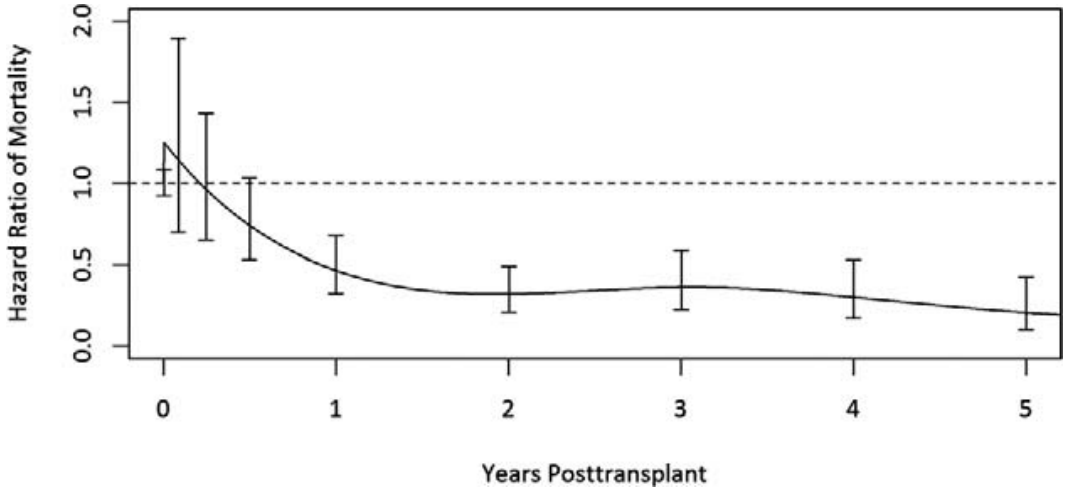
- 1431 HIV+ kidney transplant candidates 2001-2012
- Relative risk of mortality 79% lower for transplant vs dialysis



Locke JE/Segev DL. Ann Surgery, 2017

National real-world data confirms

- 1431 HIV+ kidney transplant candidates 2001-2012
- Relative risk of mortality 79% lower for transplant vs dialysis



Locke JE/Segev DL. Ann Surgery, 2017

- 180 HIV+ liver transplant recipients matched 1:10 HIV-
- HIV monoinfected recipients in modern era did not have increased hazard of death

Locke JE/Segev DL. Transplantation, 2016

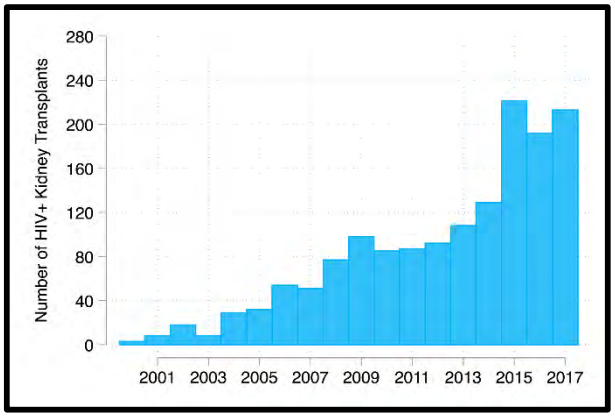
TABLE 4.

aHR by transplant Era and HCV status

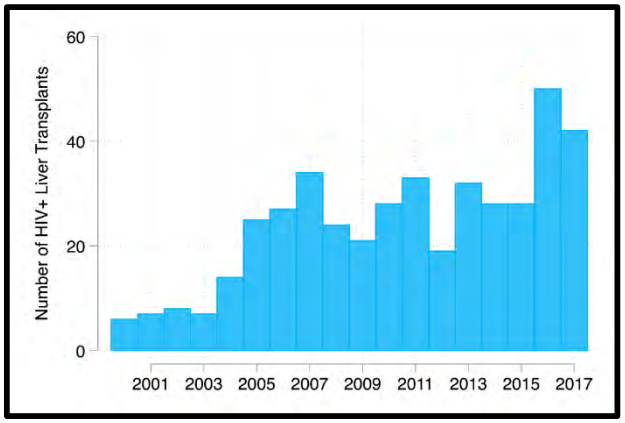
	Early (2002-2007), HR (95% CI)	Modern (2008-2011), HR (95% CI)
Graft loss		
All HIV+	1.86 (1.23-2.70)	1.58 (1.06-2.34)
All HIV−	ref	ref
Monoinfected (HIV+/HCV−)	3.26 (1.61-6.67)	0.89 (0.42-1.88)
No infection (HIV−/HCV−)	ref	ref
Coinfected (HIV+/HCV+)	1.56 (1.02-2.39)	2.07 (1.33-3.22)
HCV alone (HIV−/HCV+)	Ref	ref
Death		
All HIV+	1.66 (1.11-2.50)	1.88 (1.26-2.82)
All HIV−	ref	ref
Monoinfected (HIV+/HCV−)	3.58 (1.62-7.91)	1.11 (0.52-2.35)
No infection (HIV−/HCV−)	ref	Ref
Coinfected (HIV+/HCV+)	1.37 (0.86-2.19)	2.24 (1.43-3.53)
HCV alone (HIV−/HCV+)	ref	ref

Risk for graft loss and patient death for monoinfected patients have improved over time. However, outcomes among coinfected patients remain poor even in the modern transplant era.

HIV and transplant in modern era



Kidney > 200 transplants/year



Liver > 50 transplants/year

- National organ shortage remains
- HIV+ candidates on waitlist have disproportionate mortality compared to HIV-
- Novel donor sources needed

S Africa: HIV D+/R+ kidney transplant

The NEW ENGLAND JOURNAL of MEDICINE

Table1. Clinical Characteristics of HIV-Positive Recipients of a Transplant from an HIV-Positive Donor.

Characteristic	**Patient 1**	**Patient 2**	**Patient 3**	**Patient 4**
Age (yr)	47	56	37	29
Sex	Male	Male	Male	Female
Before transplantation				
Diagnosis on renal biopsy	HIV-associated nephropathy	HIV-associated nephropathy and hypertensive nephropathy	Malignant hypertension	HIV-associated nephropathy
Creatinine (liter)	678	582	1712	725
CD4 count (cells/mm)	288	258	132	147
HIV viral load (copies/ml)	<50	<50	<50	<50
Antiretroviral regimen	Tenofovir, lamivudine, and lopinavir-ritonavir	Stavudine, lamivudine, and efavirenz	Stavudine, lamivudine, and efavirenz	Zidovudine, lamivudine, and nevirapine

Muller/Mendelson, NEJM 2010

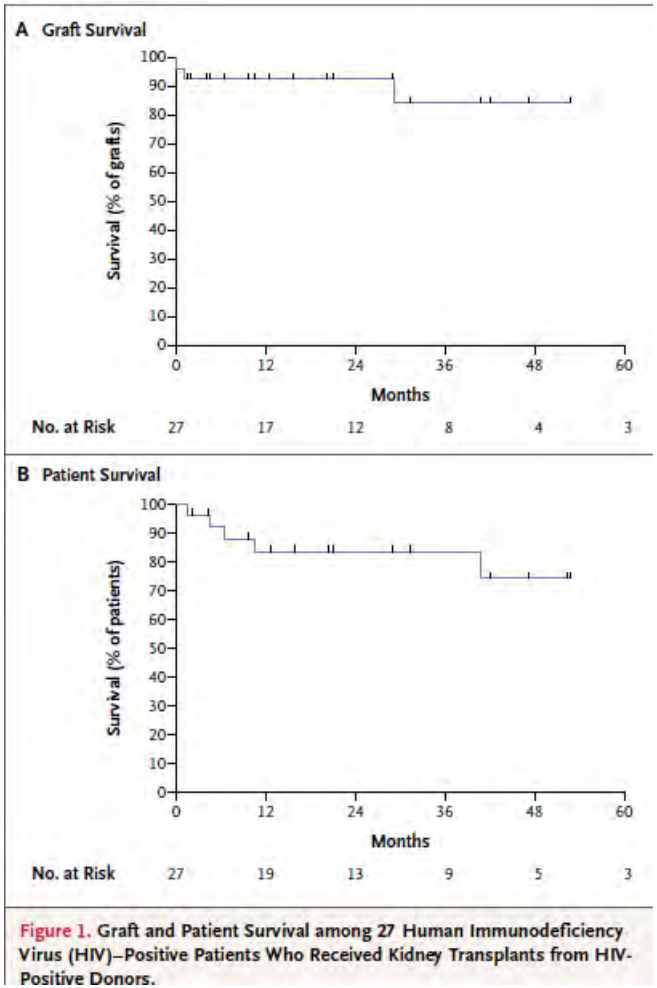


Figure 1. Graft and Patient Survival among 27 Human Immunodeficiency Virus (HIV)–Positive Patients Who Received Kidney Transplants from HIV-Positive Donors.

Muller/Kahn, NEJM 2015

Potential of HIV+ donor pool

American Journal of Transplantation 2011; 11: 1209–1217
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2011.03506.x

Estimating the Potential Pool of HIV-Infected Deceased Organ Donors in the United States

B. J. Boyarsky[a], E. C. Hall[a,b], A. L. Singer[a], R. A. Montgomery[a], K. A. Gebo[c,d,e] and D. L. Segev[a,d,*]

[a]Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD
[b]Department of Surgery, Georgetown University School of Medicine, Washington, DC
[c]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
[d]Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD
[e]HIV Research Network, Baltimore, MD
*Corresponding author: Dorry L. Segev, dorry@jhmi.edu

National Organ Transplant Act of 1984; OPTN, Organ Procurement and Transplantation Network; NIS, Nationwide Inpatient Sample; AHRQ, Agency for Healthcare Research and Quality; HCUP, Healthcare Cost and Utilization Project; CCS, Clinical Classification Software.

Received 03 December 2010, revised 24 January 2011 and accepted for publication 09 February 2011

Introduction

Due to superior medical management of human immuno-

An Assessment of HIV-Infected Patients Dying in Care for Deceased Organ Donation in a United States Urban Center

A. Richterman[1], D. Sawinski[1], P. P. Reese[1], D. H. Lee[2], H. Clauss[3], R. D. Hasz[4], A. Thomasson[1], D. S. Goldberg[1], P. L. Abt[5], K. A. Forde[1], R. D. Bloom[1], S. L. Doll[1], K. A. Brady[6] and E. A. Blumberg[1,*]

[1]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
[2]Department of Medicine, Drexel University, Philadelphia, PA
[3]Department of Medicine, Temple University, Philadelphia, PA
[4]Gift of Life Donor Program, Philadelphia, PA
[5]Department of Surgery, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

disease; GOL, Gift of Life; HAART, highly active antiretroviral therapy; HCVAb, hepatitis C virus antibody; HIV, human immunodeficiency virus; HIVDD, HIV-infected deceased donors; HOPE, HIV Organ Policy Act; KDPI, Kidney Donor Profile Index; KDRI, Kidney Donor Risk Index; LDRI, Liver Donor Risk Index; OI, opportunistic infection; PDPH, Philadelphia Department of Public Health; PVAMC, Philadelphia Veteran's Affairs Medical Center; VL, viral load

Received 17 December 2014, revised 05 February 2015 and accepted for publication 05 March 2015

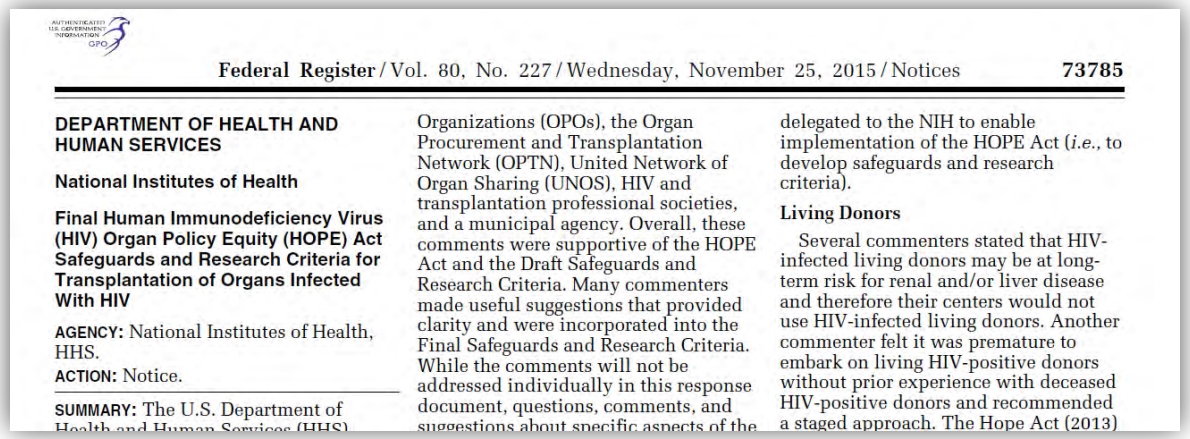
Introduction

- 300-500 potential HIV+ donors every year in US
- *Someone* on the waiting list is likely to benefit from them

HIV Organ Policy Equity Act 2013

HIV D+/R+: Research Only for Now

- Potential risks:
  - HIV superinfection from donor to recipient
  - HIV associated organ disease in allograft
  - Increased rejection
  - Increased infections
- NIH Safeguards and Research Criteria



Federal Register / Vol. 80, No. 227 / Wednesday, November 25, 2015 / Notices 73785

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Final Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act Safeguards and Research Criteria for Transplantation of Organs Infected With HIV

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The U.S. Department of Health and Human Services (HHS)

Organizations (OPOs), the Organ Procurement and Transplantation Network (OPTN), United Network of Organ Sharing (UNOS), HIV and transplantation professional societies, and a municipal agency. Overall, these comments were supportive of the HOPE Act and the Draft Safeguards and Research Criteria. Many commenters made useful suggestions that provided clarity and were incorporated into the Final Safeguards and Research Criteria. While the comments will not be addressed individually in this response document, questions, comments, and suggestions about specific aspects of the

delegated to the NIH to enable implementation of the HOPE Act (*i.e.*, to develop safeguards and research criteria).

Living Donors

Several commenters stated that HIV-infected living donors may be at long-term risk for renal and/or liver disease and therefore their centers would not use HIV-infected living donors. Another commenter felt it was premature to embark on living HIV-positive donors without prior experience with deceased HIV-positive donors and recommended a staged approach. The Hope Act (2013)

HIV D+/R+: Research Only for Now

- The HOPE Act states, “not later than 4 years after the date of enactment and annually thereafter, the Secretary shall review the results of scientific research in conjunction with the OPTN to determine whether the results warrant revision of the standards of quality.”
- IRB approved protocol
- Organ Procurement Transplantation Network - open variance and annual safety reports

HOPE IN ACTION

- Multicenter effort to determine if HIV D+/R+ transplantation in US is safe and effective
- Pilot/Parent kidney and liver study, opened in 2016
- NIH funded U01 trials for kidney and liver, opened in 2018 and 2019, respectively

Kidney: U01AI134591
NCT03500315

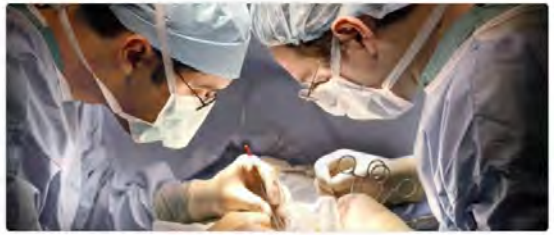
Liver: U01AI138897
NCT03408106

Johns Hopkins March 2016
First HIV D+/R+ kidney and liver transplants

CDC follows

Dr. Hazel Dean @DrDeanCDC · 2h
Great news! @HopkinsMedicine doctors performed 1st-ever liver **transplant** btwn **#HIV**+ patients 1.usa.gov/25KH8ab

ABC News @ABC · Mar 31
1st liver **transplant** between **HIV**-positive donor and recipient is milestone for **HIV** patients. abcn.ws/25yxvv3



Gizmodo @Gizmodo · Mar 31
Doctors successfully **transplant HIV**-infected organs in the US for the first time gizmo.do/dtetzER

AIDS.gov @AIDSgov · 41m
#DYK the HOPE Act is saving & improving lives, such as the 1st ever **#HIV**-positive to **HIV**-positive organ **transplant**?1.usa.gov/1q9wU2f

Christopher Anderson via **Los Angeles Times**
19 hrs ·

It's great to see that the HIV Organ Policy Equity Act (HOPE Act), which I introduced in the House and was signed into law, is working to save lives!

THE BALTIMORE SUN

BREAKING SPORTS MARYLAND POLITICS OPINION OBITS ENEWSPAPER ADVERTISING

Johns Hopkins performs first transplants between donors, recipients infected with HIV

The N

HEALTH

Hopkins Begins

By THE ASSOCIATED PRESS MARCH 30,

WASHINGTON — Surgeons in Baltimore for the first time have transplanted organs between an HIV-positive donor and HIV-positive recipients, a long-awaited new option for patients with the AIDS virus whose kidneys or livers also are failing.

Johns Hopkins University announced Wednesday that both recipients are recovering well after one received a kidney and the other a liver from a deceased donor — organs that ordinarily would have been thrown away because of the HIV infection.

Doctors in South Africa have reported successfully transplanting HIV-positive kidneys but Hopkins said the HIV-positive liver transplant is the first worldwide. Hopkins didn't identify its patients, but said the kidney recipient is recuperating at home and the liver recipient is expected to be

transplants from a donor infected with HIV to recipients also infected with the virus, a triumph for one of the transplant surgeons, who fought for six years for federal approval of the life-saving surgery.

People Magazine @people · Mar 31
Johns Hopkins performs first successful **HIV**-positive organ **transplant** peoplem.ag/YvMn3vR

Dorry Segev
59 mins · Baltimore, MD ·

We finally did it. We did the first HIV-to-HIV liver transplant in the world. This is the culmination of 6 years of research, writing and passing a congressional bill, setting up policy and safety protocols, and actually doing the thing. Press conference today at noon. Lesson: you can change the world, but it ain't easy. Or, in the words of Stephen Sondheim: wishes come true, not free.

STAT

For patients living with both HIV and end-stage organ disease… this could mean a new chance at life.

Dr. Dorry Segev, transplant surgeon

The White House OSTP @whitehouseostp
Great to see the HOPE Act beginning to save lives.

> **News from JHM** @HopkinsMedNews
> Today docs at Johns Hopkins share news of landmark surgeries that took place after the passage of HOPE Act. @WhiteHouse. #HopkinsGivesHOPE

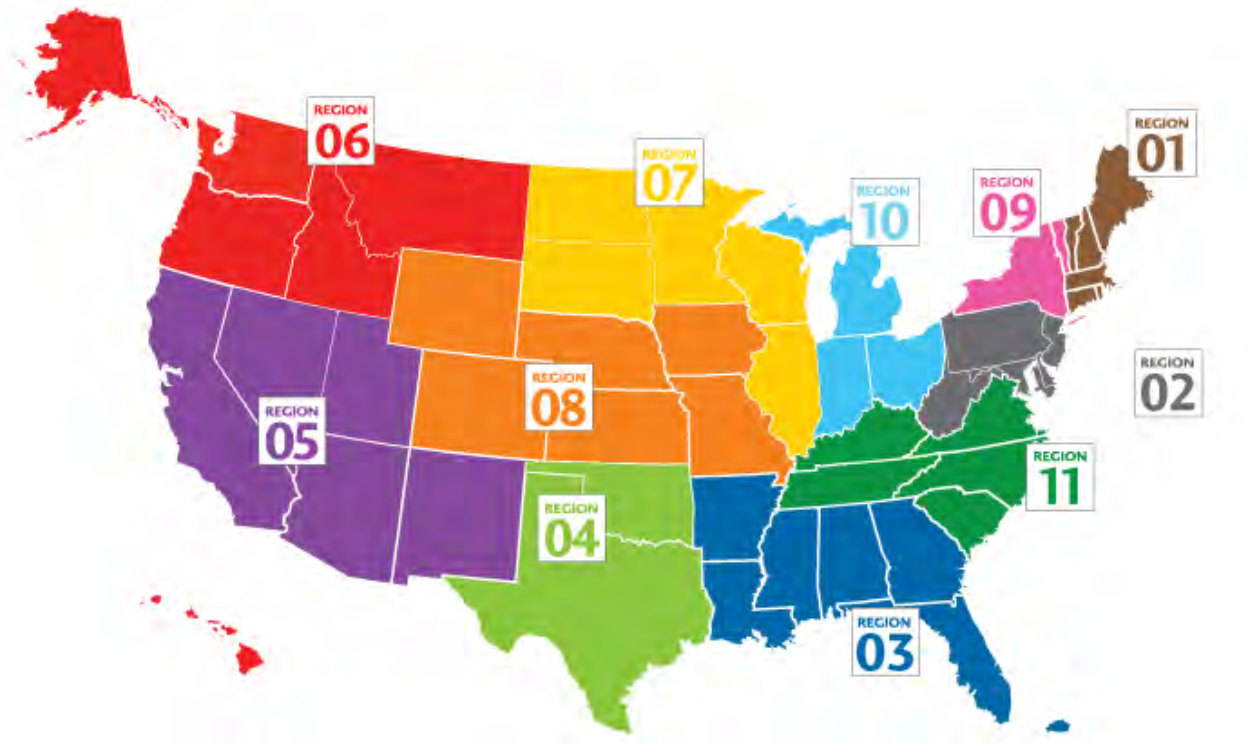
NPR Health News @NPRHealth · Mar 31
New Source Of **Transplant** Organs For Patients With **HIV**: Others With **HIV** n.pr/1RLlzxl

27 18 View summary

TIME.com @TIME · Mar 31
First ever **HIV**-to-**HIV** liver **transplant** performed in U.S. ti.me/1pMuWVe

First Transplant from HIV-Positive Donor Performed …

HOPE in 2019: 31 transplant centers



See map of regions on page 42 to identify which States are located in each region.

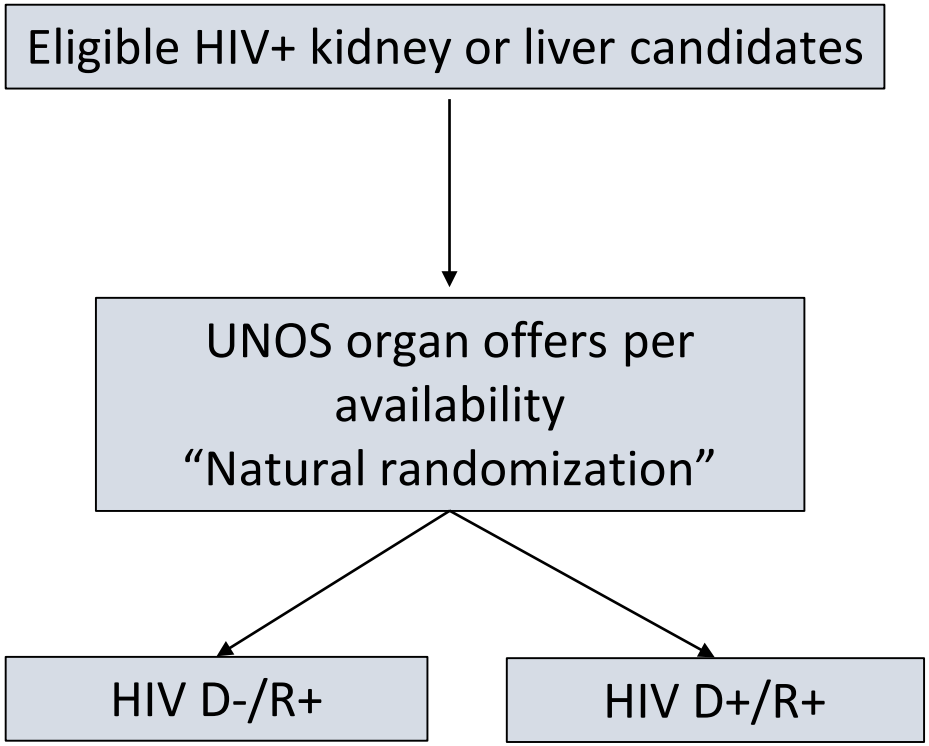
31 transplant centers

46/58 organ procurement organizations

Barnes Jewish Hospital, St Louis
Columbia University
Duke University
Emory University
Georgetown University
Hahnemann University
Indiana University Health
Jackson Memorial Miami
Johns Hopkins Hospital
Montefiore Medical Center
Mount Sinai Medical Center
Massachusetts General
Methodist Dallas Medical
Montefiore
New York University Medical
Northwestern Memorial
Ochsner Foundation Hospital
Rush University
Saint Barnabas Medical Center
University of Alabama
University of California SF
University of Cincinnati
University of Colorado
University of Illinois
University of Maryland
University of Minnesota
University of Pittsburgh
University of Virginia Medical Center
VCU Medical Center
Weill Cornell Medical Center
Yale New Haven Hospital

Study Design

HOPE IN ACTION



- HIV+ Candidate Criteria
  - No opportunistic infections
  - Kidney CD4 > 200 cells
  - Liver CD4 > 100 cells
- HIV+ Donor Criteria
  - No active opportunistic infections
  - Any HIV VL or CD4 count
  - Study team must describe effective ART for recipient

Federal Register / Vol. 80, No. 227 / Wednesday, November 25, 2015 / Notices

Received: 4 May 2018 | Revised: 15 June 2018 | Accepted: 18 June 2018
DOI: 10.1111/ajt.14993

BRIEF COMMUNICATION

AJT

Organs from deceased donors with false-positive HIV screening tests: An unexpected benefit of the HOPE act

HOPE IN ACTION

- Donors tested for both HIV antibody (Ab) and nucleic acid test (NAT)
- Designed to capture acute infection HIV Ab-/NAT+
- Assays have false positive rates Ab>NAT
- Screen > 20,000 donor/yr, false-positive rate 0.1-0.3%

→ ≈50-100 HIV false positive donors/year

Durand CM/Segev DL, AJT, 2018

Study Endpoints

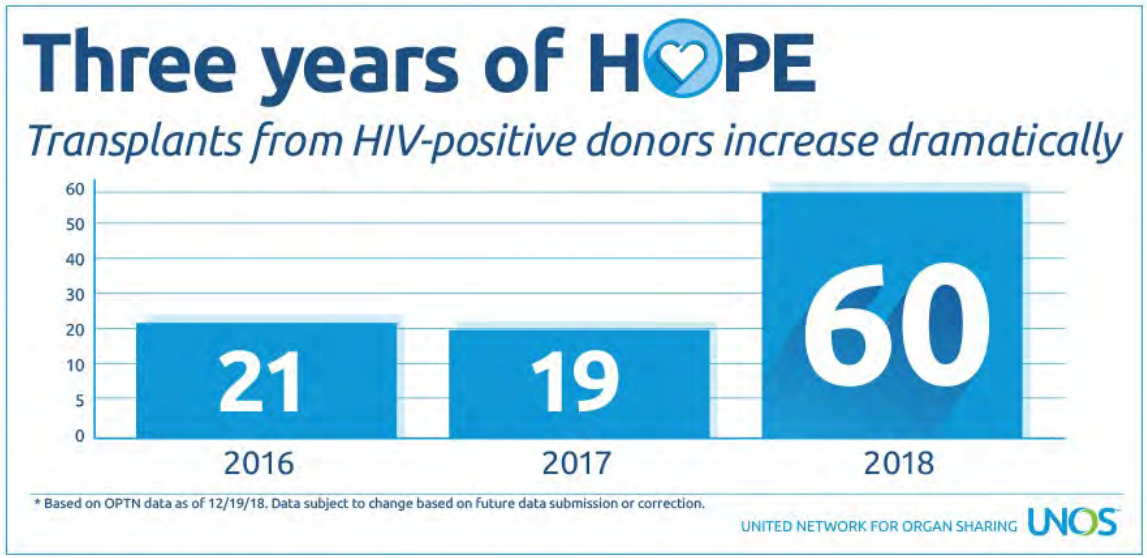
HOPE IN ACTION

- Patient survival
- Graft survival
- Rejection
- Graft function
- HIV related organ disease
- HIV breakthrough or failure
- HIV resistance
- Opportunistic infections
- Cancer incidence
- HIV superinfection in blood and tissues
- HIV anatomic sanctuaries
- HIV reservoirs over time
- Quality of life
- Patient reported outcomes

First three years of HOPE in Action

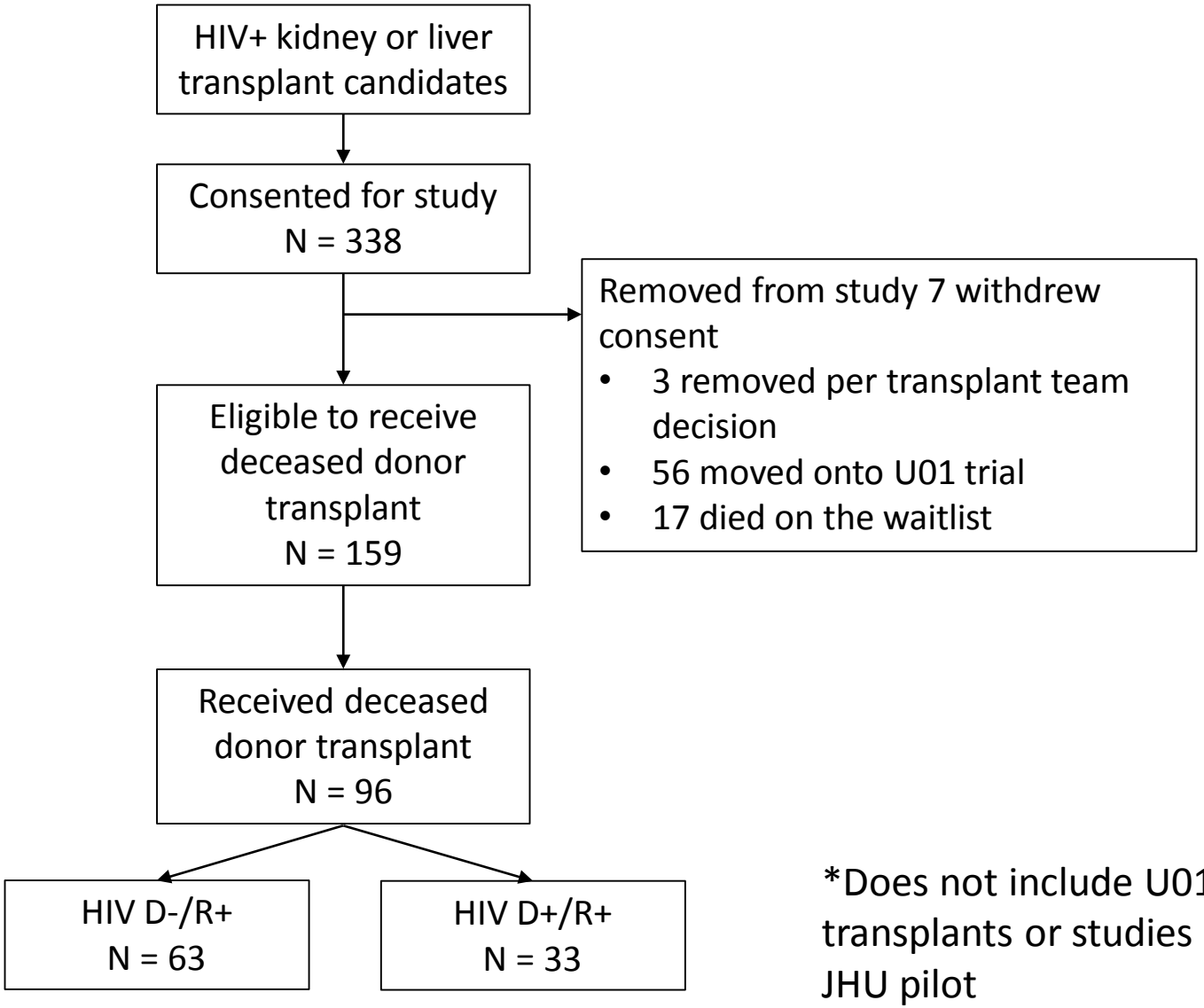
HOPE donors and transplants

Donor HIV	2016	2017	2018	2019	Total
True Positive	3	7	19	4	**33**
False Positive	6	2	14	1	**23**
Total	**9**	**9**	**33**	**4**	**56**



For an extended description of these graphs, please see the descriptions on **page 222**.

HOPE Pilot Study*



*Does not include U01 transplants or studies outside of JHU pilot

Consented candidates (N=338)

Characteristic	N (%)
Organ consented to receive	-
Kidney	273 (80.8%)
Liver	54 (16.0%)
Kidney/Liver	9 (2.7%)
Kidney/Pancreas	2 (0.6%)
Age at consent, median (IQR)	53 (44, 59)
Female	83 (24.6%)
Race	-
White/Caucasian	91 (26.9%)
Black/African American	241 (71.3%)
Asian	3 (0.9%)
American Indian	1 (0.3%)
Missing	2 (0.6%)
Ethnicity	-
Hispanic/Latino	37 (10.9%)
Non-Hispanic/Latino	299 (88.5%)
Missing	2 (0.6%)

HOPE deceased donors (N=71)

Factor	HIVD-	HIVFP	HIVD+	p-value
-	36	14	21	-
Organs used	-	-	-	<0.001
Kidney(s)-only	27 (75%)	6 (43%)	4 (19%)	-
Liver-only	5 (14%)	2 (14%)	6 (29%)	-
Both	4 (11%)	6 (43%)	11 (52%)	-
Age, median (IQR)	31.5 (27, 39.5)	29.5 (20, 41)	32 (27, 42)	0.7
Male sex	22 (61%)	9 (64%)	15 (71%)	0.8
Race	-	-	-	0.5
White/Caucasian	20 (56%)	7 (50%)	8 (38%)	-
Black/African American	12 (33%)	4 (29%)	11 (52%)	-
Asian	1 (3%)	0 (0%)	0 (0%)	-
Hawaiian	1 (3%)	0 (0%)	0 (0%)	-
Other	2 (6%)	3 (21%)	2 (10%)	-
Ethnicity	-	-	-	0.2
Hispanic/Latino	2 (6%)	3 (21%)	2 (10%)	-
Not Specified/Unknown	34 (94%)	11 (79%)	19 (90%)	-

HOPE deceased donors (N=71)

Factor	HIVD-	HIVFP	HIVD+	p-value
-	36	14	21	-
Organs used	-	-	-	<0.001
Kidney(s)-only	27 (75%)	6 (43%)	4 (19%)	-
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Hawaiian	1 (3%)	0 (0%)	0 (0%)	-
Other	2 (6%)	3 (21%)	2 (10%)	-
Ethnicity	-	-	-	0.2
Hispanic/Latino	2 (6%)	3 (21%)	2 (10%)	-
Not Specified/Unknown	34 (94%)	11 (79%)	19 (90%)	

HOPE deceased donors (N=71)

Factor	HIVD-	HIVFP	HIVD+	p-value
-	36	14	21	-
BMI, med (IQR)	25.7 (23.0, 30.0)	26.2 (22.1, 34.2)	23.1 (21.5, 26.0)	0.1
Donation after Cardiac Death	1 (3%)	3 (21%)	0 (0%)	0.03
Intravenous drug use	15 (42%)	1 (7%)	2 (10%)	0.01
Cause of Death	-	-	-	0.1
Anoxia	21 (58%)	3 (21%)	11 (52%)	-
Cerebrovascular/Stroke	4 (11%)	4 (29%)	4 (19%)	-
Head Trauma	11 (31%)	6 (43%)	6 (29%)	-
Other; specify	0 (0%)	1 (7%)	0 (0%)	-
History of hypertension	4 (11%)	4 (29%)	5 (24%)	0.3
History of cancer	0 (0%)	1 (7%)	1 (5%)	0.2
Creatinine (mg/dL), med(IQR)	1 (.75, 1.51)	.915 (.9, 1)	1 (.9, 1.3)	0.5
KDPI, median (IQR)	40.5 (29, 54)	30.5 (21, 73)	38 (28, 63)	0.5

KDPI; Kidney donor profile index; percentile score from 0-100

BMI; body mass index

Infectious disease characteristics of donors (n=71)

Factor	HIVD- (N=36)	HIVFP (N=14)	HIVD+ (N=21)	p-value
Anti-HIV I/II	-	-	-	<0.001
Negative	36 (100%)	1 (7%)	0 (0%)	-
Positive	0 (0%)	13 (93%)	21 (100%)	-
HIV NAT reactive	0 (0%)	1 (7%)	14 (67%)	<0.001
HIV viral load	-	-	-	-
Detectable	NA	-	11 (52%)	-
HIV viral load, med (range)	-	-	30220 (475-3074276)	-
CD4 count	-	-	-	-
Median (range)	-	-	293 (26-1683)	-
Not reported	-	-	2 (10%)	-
Anti-HCV	11 (31%)	0 (0%)	1 (5%)	0.008
HCV NAT	-	-	-	0.03
Negative	26 (72%)	14 (100%)	19 (90%)	-
Positive	10 (28%)	0 (0%)	2 (10%)	-
HBV NAT	-	-	-	0.2
Negative	36 (100%)	14 (100%)	20 (95%)	-
Positive	0 (0%)	0 (0%)	1 (5%)	-
Anti-HBcAb	3 (8%)	0 (0%)	2 (10%)	0.7

Infectious disease characteristics of donors (n=71)

Factor	HIVD- (N=36)	HIVFP (N=14)	HIVD+ (N=21)	p-value
Anti-HIV I/II	-	-	-	<0.001
Negative	36 (100%)	1 (7%)	0 (0%)	-
Positive	0 (0%)	13 (93%)	21 (100%)	-
HIV NAT reactive	0 (0%)	1 (7%)	14 (67%)	<0.001
HIV viral load	-	-	-	-
Detectable	NA	-	11 (52%)	-
HIV viral load, med (range)	-	-	30220 (475-3074276)	-
CD4 count	-	-	-	-
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HCV NAT	-	-	-	0.03
Negative	26 (72%)	14 (100%)	19 (90%)	-
Positive	10 (28%)	0 (0%)	2 (10%)	-
HBV NAT	-	-	-	0.2
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HIV viral load	-	-	-	-
Detectable	NA	-	11 (52%)	-
HIV viral load, med (range)	-	-	30220 (475-3074276)	-
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Median (range)	-	-	293 (26-1683)	-
Not reported	-	-	2 (10%)	-
Anti-HCV	11 (31%)	0 (0%)	1 (5%)	0.008
HCV NAT	-	-	-	0.03
Negative	26 (72%)	14 (100%)	19 (90%)	-
Positive	10 (28%)	0 (0%)	2 (10%)	-
HBV NAT	-	-	-	0.2
Negative	36 (100%)	14 (100%)	20 (95%)	-
Positive	0 (0%)	0 (0%)	1 (5%)	-
Anti-HBcAb	3 (8%)	0 (0%)	2 (10%)	0.7

HIV+ kidney-only transplant recipients (N=63)

Factor	HIVD-/R+	HIVD+/R+	p-value
N	46	17	-
Age at transplant, median (IQR)	52.5 (41, 56)	52 (45, 56)	0.5
Female sex	15 (33%)	4 (24%)	0.6
Race	-	-	0.08
Caucasian/White	3 (7%)	3 (18%)	-
African American/Black	43 (93%)	13 (76%)	-
Asian	0 (0%)	1 (6%)	-
Hispanic or Latino ethnicity	2 (4%)	1 (6%)	-
Primary cause of renal failure	-	-	0.1
HIV-Associated Renal Disease	17 (37%)	3 (18%)	-
Diabetes/Hypertension	18 (39%)	7 (41%)	-
Glomerulonephritis	0 (0%)	1 (6%)	-
IgA Nephrosclerosis	0 (0%)	1 (6%)	-
Other	11 (24%)	5 (29%)	-
Induction Immunosuppression	-	-	0.1
ATG	17 (37%)	2 (12%)	-
Basiliximab	27 (59%)	15 (88%)	-
Other	2 (4%)	0 (0%)	-

HIV+ kidney-only transplant recipients

Infectious disease characteristics

Factor	HIVD-/R+	HIVD+/R+	p-value
N	46	17	-
HIV RNA used for eligibility	-	-	-
Undetectable defined as < 200 copies	46 (100%)	17 (100%)	-
CD4 count used for eligibility, median (IQR)	506 (318, 667)	504 (409, 622)	0.90
HCV Ab+	12 (26%)	2 (12%)	0.3
Log_{10} HCV RNA (if detected), median (IQR)	5.7 (1.5, 6.6)	6.3 (6.3, 6.3)	0.5

HIV+ liver transplant recipients (N=33)

Factor	HIVD-/R+	HIVD+/R+	p-value
N	17	16	-
Age at transplant, median (IQR)	55 (46, 60)	61 (53, 63)	0.09
Female gender	5 (29%)	3 (19%)	0.7
Race	-	-	0.6
White/Caucasian	9 (53%)	11 (69%)	-
Black/African American	7 (41%)	5 (31%)	-
American Indian	1 (6%)	0 (0%)	-
Ethnicity	-	-	0.7
Hispanic or Latino	3 (18%)	4 (25%)	-
Not Hispanic or Latino	14 (82%)	12 (75%)	-
Indication for transplant	-	-	0.7
HCV	8 (47%)	10 (63%)	-
HCC alone	1 (6%)	1 (6%)	-
HepB	4 (24%)	1 (6%)	-
NASH	2 (12%)	1 (6%)	-
Other/Cryptogenic/Idiopathic	2 (12%)	3 (19%)	-

HIV+ liver transplant recipients

Infectious disease characteristics

Factor	HIVD-/R+	HIVD+/R+	p-value
N	17	16	-
HIV RNA used for eligibility	-	-	-
Undetectable	17 (100%)	16 (100%)	-
CD4 count used for eligibility, median (IQR)	314 (156, 461)	262 (154, 392)	0.6
HCV Ab+	9 (53%)	11 (69%)	0.5
Log10 HCV RNA (if detected), median (IQR)	1.2 (1.2, 7.1)	1.2 (1.2, 6.0)	0.3

HIV D+/R+ to date and future plans

HOPE in Action Pilot

- 63 deceased donor kidney and 33 liver transplants
- Excellent survival for those transplanted (deaths on waitlist)
- Excellent graft survival to date
- Rare HIV breakthroughs due to non-adherence
- Opportunistic infections in ≈20%, generally CMV and candida esophagitis
- Rejection common in kidney, associated with induction immunosuppression

HOPE in Action NIAID U01 trials

- Kidney: 40 transplants in year 1 (target 160 transplants over study)
- Liver: initiated in January 2019 (target 80 transplants over study)

Outline

- HIV in organ transplantation
  - Biology and epidemiology
  - HIV- donor for HIV+ recipient (HIV D-/R+) transplantation
  - HIV+ donor for HIV+ recipient (HIV D+/R+) transplantation

- HCV in organ transplantation
  - Biology and epidemiology
  - HCV+ donor for HCV+ recipient (HCV D+/R+) transplantation
  - HCV+ donor for HCV- recipient (HCV D+/R-) transplantation

Hepatitis C virus (HCV) biology

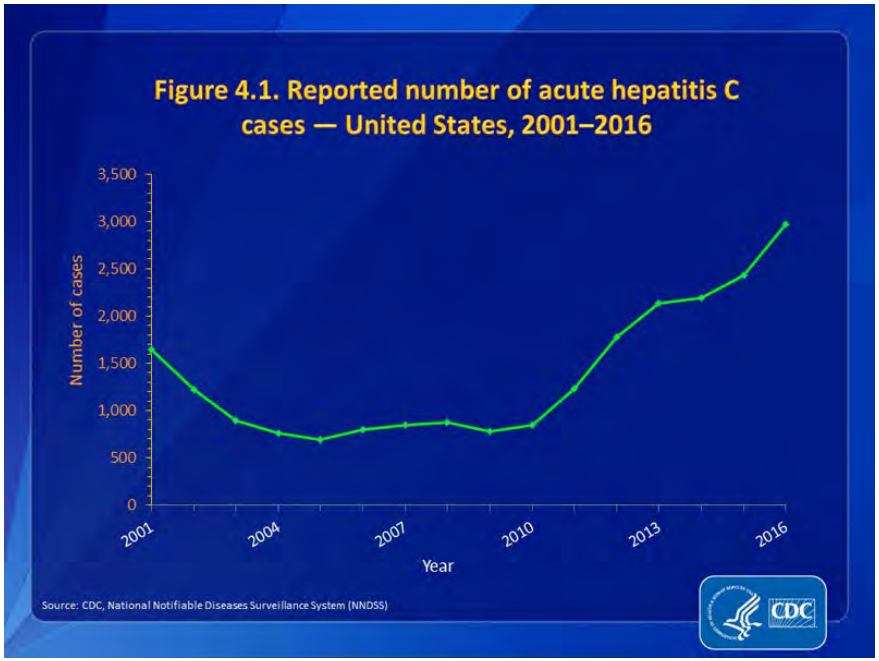
- RNA virus, infects liver hepatocytes
- Transmitted primarily through blood contact
- Acute HCV
  - Flu-like illness, rarely severe presentation
  - 2/3 individuals clear infection spontaneously
  - Can be severe in acute post-transplant setting, complications such as fibrosing cholestatic HCV
- Chronic HCV
  - 1/3 individuals develop chronic disease
  - Minimal symptoms over decades can progress to cirrhosis, liver failure, liver cancer

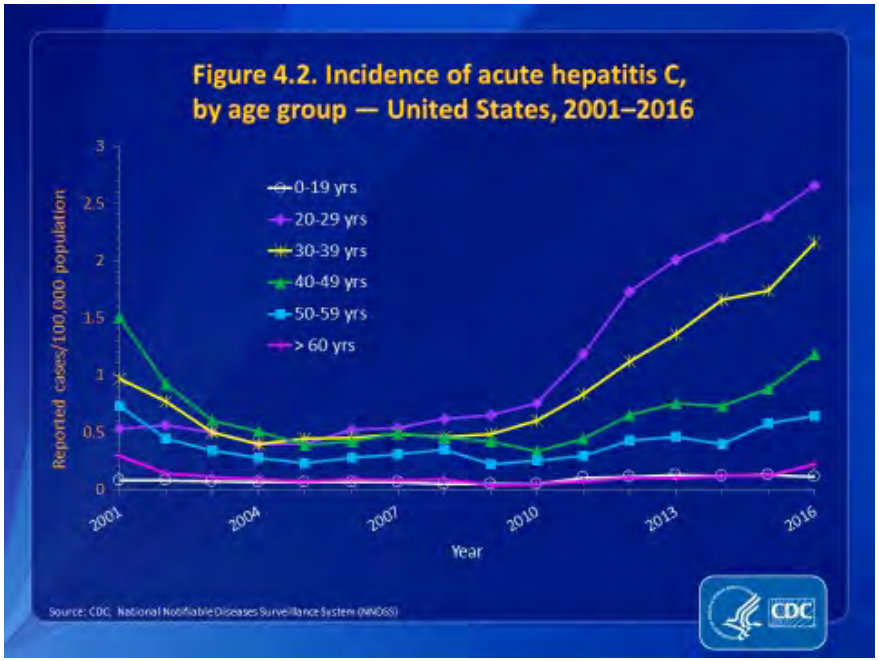
Hepatitis C virus (HCV) biology

- RNA virus, infects liver hepatocytes
- Transmitted primarily through blood contact
- Acute HCV
  - Flu-like illness, rarely severe presentation
  - 2/3 individuals clear infection spontaneously
  - Can be severe in acute post-transplant setting, complications such as fibrosing cholestatic HCV
- Chronic HCV
  - 1/3 individuals develop chronic disease
  - Minimal symptoms over decades can progress to cirrhosis, liver failure, liver cancer
- **Curable infection** (unlike CMV, EBV, HIV)

HCV epidemiology

- 2.4 million people living with HCV in US
- Since 2010, incidence continues to increase with estimated 41,200 new cases in 2016



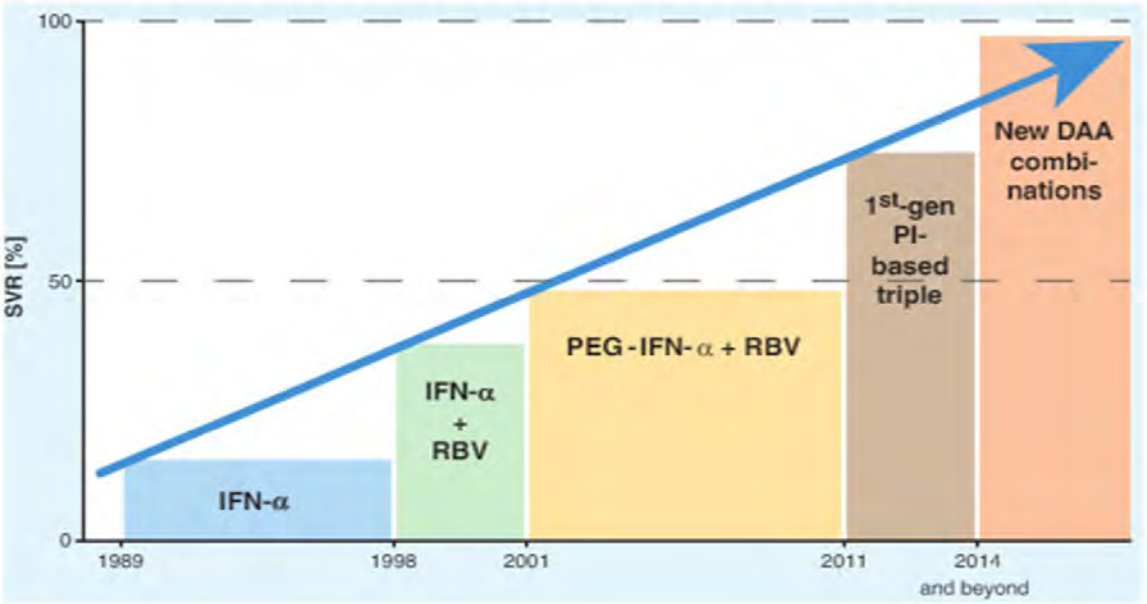


For extended description of these figures, please see the descriptions on **page 223**.

HCV treatment

- 1989: Injectable interferon (IFN)
- 1998: Oral ribavirin
- 2011: early direct acting antivirals (DAAs)
- 2014: all oral DAA combinations

- Cure = sustained virologic response (SVR) 12 weeks after treatment



For extended description of this chart, please see the descriptions on **page 224**.

HCV testing

- HCV antibody (Ab) – immune response to infection, persists after clearance or cure
- HCV nucleic acid test (NAT) – viral particles in blood, sign of active disease and transmission risk

- HCV Ab-/NAT- uninfected
- HCV Ab+/NAT+ chronic HCV infection
- HCV Ab+/NAT- cleared/cured HCV or false positive Ab
- HCV Ab-/NAT+ acute HCV or false positive NAT

DAAs in transplant recipients

Study	Study Design	Patient Population	Direct Acting Antiviral (DAA)	Genotype	SVR
MAGELLAN-2 Reau et al, 2018	Phase 3, open label, multicenter trial	N=100 Chronically infected HCV liver and kidney (N=20) TXP patients	Glecaprevir/pibrentasvir x 12 weeks	1-6	12 weeks: 99%
Colombo et al, 2016	Randomized, phase 2, open label, multicenter trial	N=114 Chronically infected HCV kidney TXP patients	Ledipasvir/sofosbuvir x 12 or 24 weeks	1 or 4	12 weeks: 100% 24 weeks: 100%
Saxena et al, 2017	Retrospective, multicenter, longitudinal treatment cohort	N=443 Chronically infected HCV liver, kidney (N= 60), and combined liver and kidney TXP patients	Ledipasvir/sofosbuvir ± ribavirin Sofosbuvir + Daclatasvir ± ribavirin Ombitasvir/ paritaprevir/ritonavir + dasabuvir ± ribavirin	1-6	12 weeks: Liver: 96.6% Kidney: 94.5% SLK: 90.9%

Reau N, et al. Hepatology 2018.
Colombo M,et al. Ann of Int Med. 2017.
Saxena V et al, Hepatology. 2017

TXP: Transplant
SVR: Sustained virologic response

HCV D+/R+ transplantation

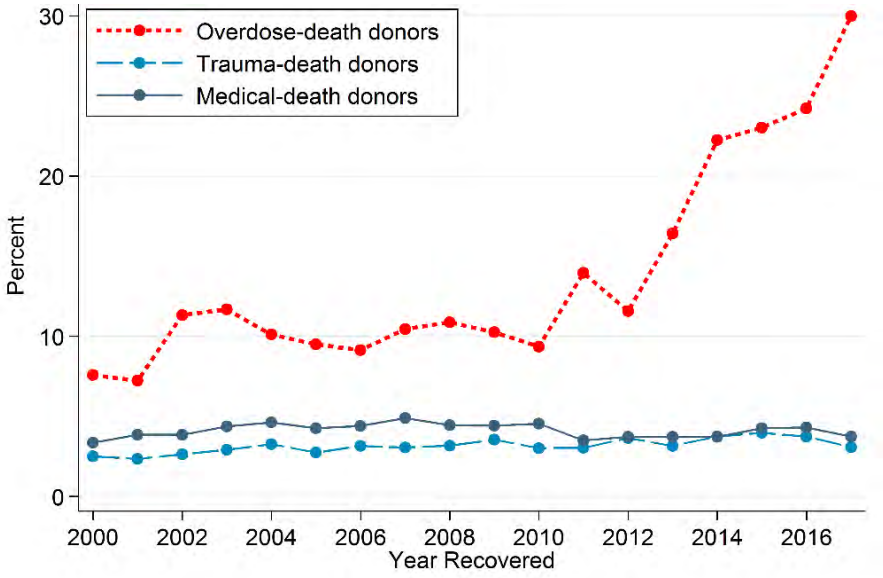
- HCV prevalence among transplant candidates:
  - Liver (≈ 40%)[1] > kidney (≈10%)[2] >> heart or lung
- HCV D+/R+ liver transplant common; many studies showing similar patient and graft survival[1,3]
- HCV D+/R+ kidney transplant common; studies showing survival benefit and shorter wait times[4]
- HCV D+/R+ rare in heart[4] and lung transplant due to decreased survival and coronary vasculopathy

1. Bowring/Durand, AJT 2017
2. Bowring/Durand, Transplantation 2018
3. Montenovo/Hansen, Ann Transp 2015
4. Bloom/Reddy, AJT 2005
5. Gasink/Lautenbach, JAMA 2006

Increasing number and quality of HCV+ donor organs over time

- Opioid overdose death donors now account for > 1 out of 8 deceased donors in US
- Over 30% of overdose donors were HCV Ab+ in 2017
- HCV Ab+ donors more likely to be younger with fewer comorbidities
- Outcomes of transplants from overdose death donor organs same or better than trauma death donors

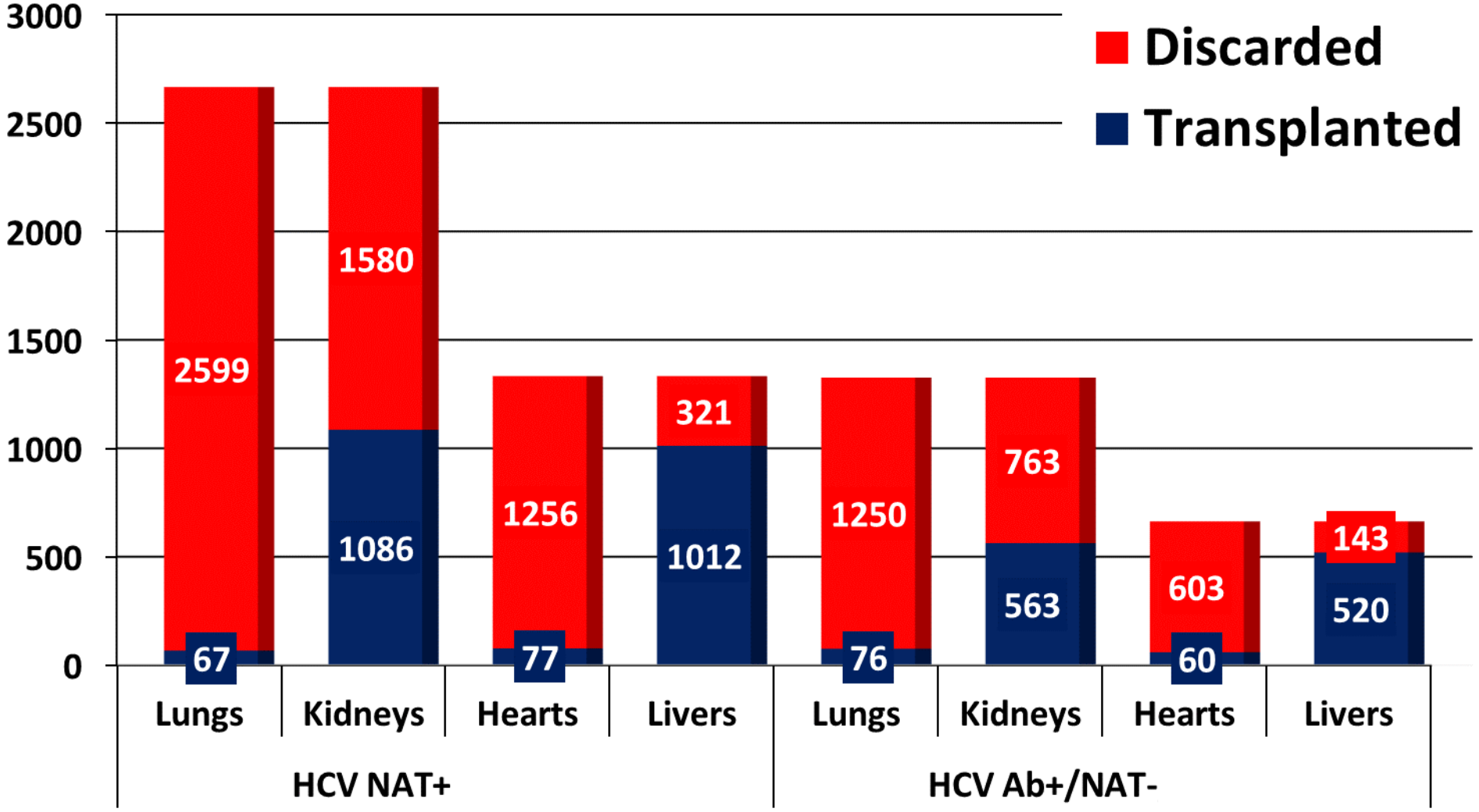
Prevalence of HCV+ donors (antibody)



For extended description of this chart, please see the descriptions on **page 225**.

Durand/Segev Ann of Intern Med 2018

But HCV+ organs remain underutilized 3/1/15-1/31/18



Slide courtesy of David Goldberg, OPTN data

True potential is likely larger

- “Donor” defined by UNOS as individual who had organs recovered for transplant
- Does not include donors not referred, not evaluated or not approached for donation
- Does not include donors after circulatory death
- Does not include single organ donors

HCV D+/R-: historical perspective

- Kidney: 118 HCV D+/R- (single center, 1991-2007)[1]
  - Select candidates with “poor life expectancy”
  - Median survival: 5.3 years, 10 year: 22.6%
  - 93 deaths: 24% cardiac, 16% nephropathy, 4% liver failure

1. Singh/Pirsch, Clin Transplant 2012

2. Gasink/Lautenbach, JAMA 2006

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  - Select candidates with “poor life expectancy”
  - Median survival: 5.3 years, 10 year: 22.6%
  - 93 deaths: 24% cardiac, 16% nephropathy, 4% liver failure
- Heart: 222 HCV D+/R- (multicenter, 1994-2003)[2]
  - National registry data, according to institutional standards
  - 2 fold higher risk of death
  - More likely to die of liver disease or coronary vasculopathy

1. Singh/Pirsch, Clin Transplant 2012

2. Gasink/Lautenbach, JAMA 2006

HCV D+/R-: in era of DAAs

The NEW ENGLAND JOURNAL of MEDICINE

Transplanting Hepatitis C–Positive Kidneys

Peter P. Reese, M.D., M.S.C.E., Peter L. Abt, M.D., Emily A. Blumberg, M.D., and David S. Goldberg, M.D., M.S.C.E.

The scarcity of kidneys for transplantation and high mortality among patients on the waiting list have led some patients to accept kidney transplants that carry elevated risks of transmitting infections or cancer. In certain cases, such as the transmission of cytomegalovirus, physicians can anticipate these events and insti-

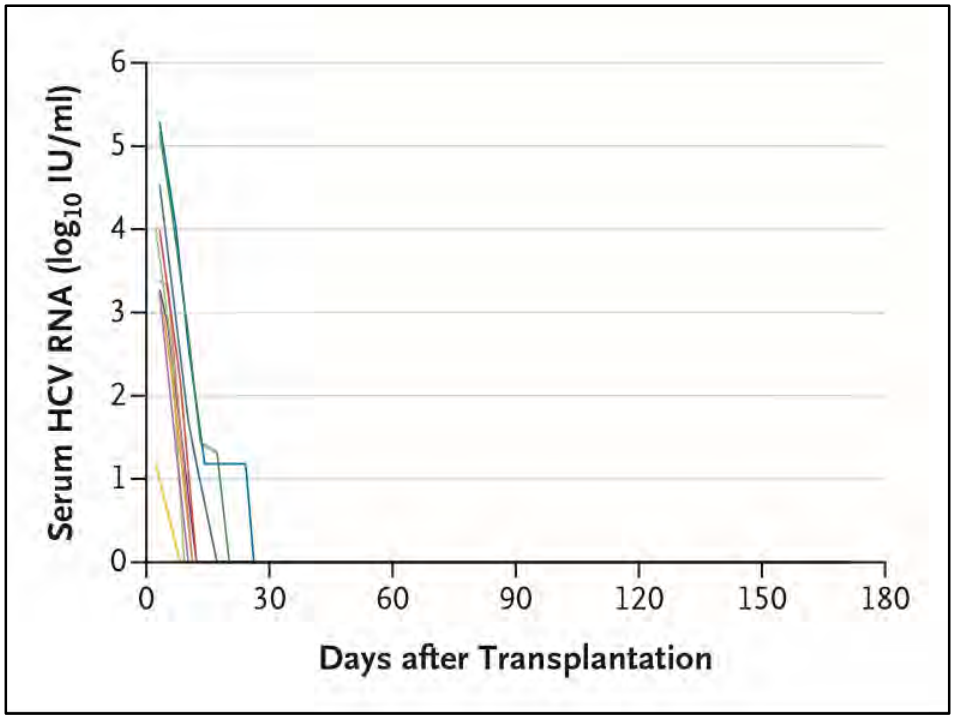
with long-term dialysis,[2] but it's available to an ever-smaller percentage of patients. In many regions of the United States, average waiting times for a kidney transplant exceed 5 years, especially for patients with blood type O or B, for whom there's a large imbalance between organ supply and demand. Average mor-

6546 kidneys, only 2402 (37%) were transplanted; 91% of the recipients had documented HCV infection. The other kidneys were discarded, although most were of good quality (according to the Kidney Donor Profile Index, a widely used transplant metric). These discarded kidneys could have benefited more than 4000

Reese/Goldberg, NEJM Perspective 2015

THINKER: Transmit and Treat

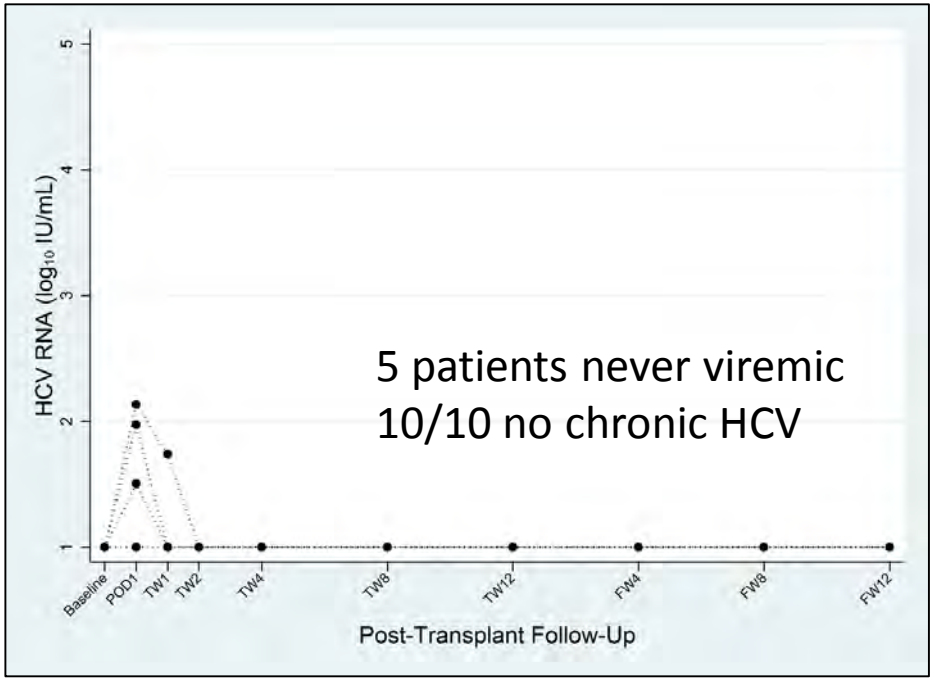
- HCV D+/R- kidney transplant, n=10
  - Genotype 1a only
- Treatment initiated if transmission: 100%
- Treated with GZR/EBR for 12 weeks
- All patients cured
- Median wait: 58 days



Goldberg/Reese NEJM 2017

EXPANDER: Prophylaxis

- HCV D+/R- kidney transplant n= 10
  - Genotypes 1a, 2, 3, mixed
- DAAs pre- and post-exposure prophylaxis
- Prophylaxis GZR/EBR +/- SOF for 12-16 weeks
- No chronic HCV
- Median wait: 30 days



Durand/Desai Ann Intern Med 2018

HCV D+/R- trials in heart and lung

USHER – Transmit and Treat

- n=10 heart transplants
- Treatment initiated if transmission: 100% day 3
- Treated with GZR/EBR for 12-16 weeks +/- RBV
- 9 patients cured, 1 died due acute rejection

ORIGINAL ARTICLE AJT

Transplanting hepatitis C virus–infected hearts into uninfected recipients: A single-arm trial

Rhondalyn C. McLean[1] | Peter P. Reese[2,3] | Michael Acker[4] | Pavan Atluri[4] | Christian Bermudez[4] | Lee R. Goldberg[1] | Peter L. Abt[4] | Emily A. Blumberg[5] | Vivianna M. Van Deerlin[6] | K. Rajender Reddy[7] | Roy D. Bloom[2] | Richard Hasz[8] | Lawrence Suplee[8] | Anna Sicilia[9] | Ashley Woodards[3] | Muhammad Nauman Zahid[10] | Katharine J. Bar[5] | Paige Porrett[4] | Matthew H. Levine[4] | Nicole Hornsby[1] | Caren Gentile[11] | Jennifer Smith[11] | David S. Goldberg[2,7]

Reese/Goldberg AJT 2018

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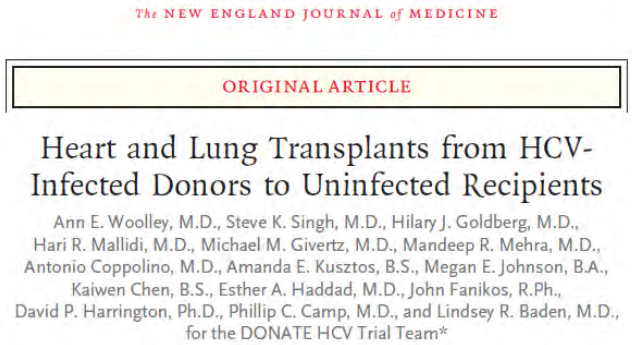
Reese/Goldberg AJT 2018

DONATE HCV – Post-prophylaxis

- n=36 lung, n=8 heart transplants
- 6 hours after transplant received post-exposure prophylaxis
- Prophylaxis SOF/VEL for 4 weeks
- No chronic HCV, increased rejection



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Heart and Lung Transplants from HCV-Infected Donors to Uninfected Recipients

Ann E. Woolley, M.D., Steve K. Singh, M.D., Hilary J. Goldberg, M.D., Hari R. Mallidi, M.D., Michael M. Givertz, M.D., Mandeep R. Mehra, M.D., Antonio Coppolino, M.D., Amanda E. Kusztos, B.S., Megan E. Johnson, B.A., Kaiwen Chen, B.S., Esther A. Haddad, M.D., John Fanikos, R.Ph., David P. Harrington, Ph.D., Phillip C. Camp, M.D., and Lindsey R. Baden, M.D., for the DONATE HCV Trial Team*

Wooley/Baden NEJM 2019

Moving into clinical practice

- Multiple observational studies of the “transmit and treat” approach
  - Schlendorf (Vanderbilt): 9 HCV D+/R- heart transplants[1]
  - Kwong (Stanford): 10 HCV D+/R- liver transplants[2]
  - Aslam (UCSD): 12 HCV D+/R- heart transplant[3]
  - Alonso (Utah): 10 HCV D+/R- liver transplants[4]

1. Schlendorf/Lindenfeld JHLT 2018
2. Kwong/Kwo AJT 2018
3. Aslam, abstract IHLTS 2018
4. Alonso, abstract ASTS 2017

Complications of HCV D+/R-

- Some reports suggest increased allograft rejection[1,2]
- HCV treatment failure
  - THINKER: n=1 viral breakthrough with initial therapy, required intensification of therapy and prolonged duration, cured
  - Toronto trial of HCV D+/R- lung transplant: 3/13 viral relapse, including severe case with fibrosing cholestatic HCV, on intensified treatment for prolonged duration, ongoing[4]
- Long term outcomes
- Logistical issues – insurance coverage of DAAs, administration via nasogastric tubes

1. Kwong/Kwo AJT 2018
2. Wooley/Baden NEJM 2019
3. Reese/Goldbert AJT 2018
4. Feld/Cyprel abstract AASLD 2018, updated data personal communication

Remaining questions

Prophylaxis vs Transmit and Treat

- Prevent any HCV related complications such as fibrosing cholestatic HCV, rejection
- Avoid any risk of transmission to others

- Ensure recipients can take oral medications, stable renal function
- More real-world for DAA coverage

Remaining questions

Prophylaxis vs Transmit and Treat

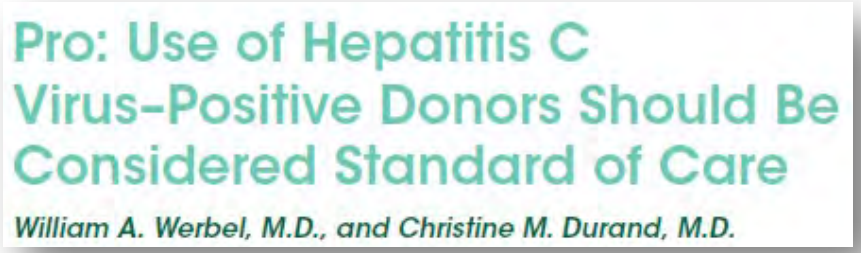
- Prevent any HCV related complications such as fibrosing cholestatic HCV, rejection
- Avoid any risk of transmission to others

- Ensure recipients can take oral medications, stable renal function
- More real-world for DAA coverage

Clinical care vs Research only

- Increased access to transplant
- Standard with CMV, HBV, EBV

- Guaranteed access to DAAs
- More rigorous consent process


Pro: Use of Hepatitis C Virus–Positive Donors Should Be Considered Standard of Care

William A. Werbel, M.D., and Christine M. Durand, M.D.


Con: Use of Hepatitis C Virus–Positive Donors Should Be Restricted to Research Protocols

Grace S. Lee, M.D., M.S.M.E.,* Judith A. Anesi, M.D.,† Behdad D. Besharatian, M.D.,† Therese Bittermann, M.D., M.S.C.E.,† Stephanie Hamel, Pharm.D.,‡ and David S. Goldberg, M.D., M.S.C.E.†

Summary

- Novel strategies to expand donor pool are needed
- Landscape of HIV and HCV treatment has evolved altering risk-benefit for those on the waitlist
- New frontiers of HIV D+/R+ transplant and HCV D-/R+ transplant are under investigation with encouraging early results

Thank you for your attention

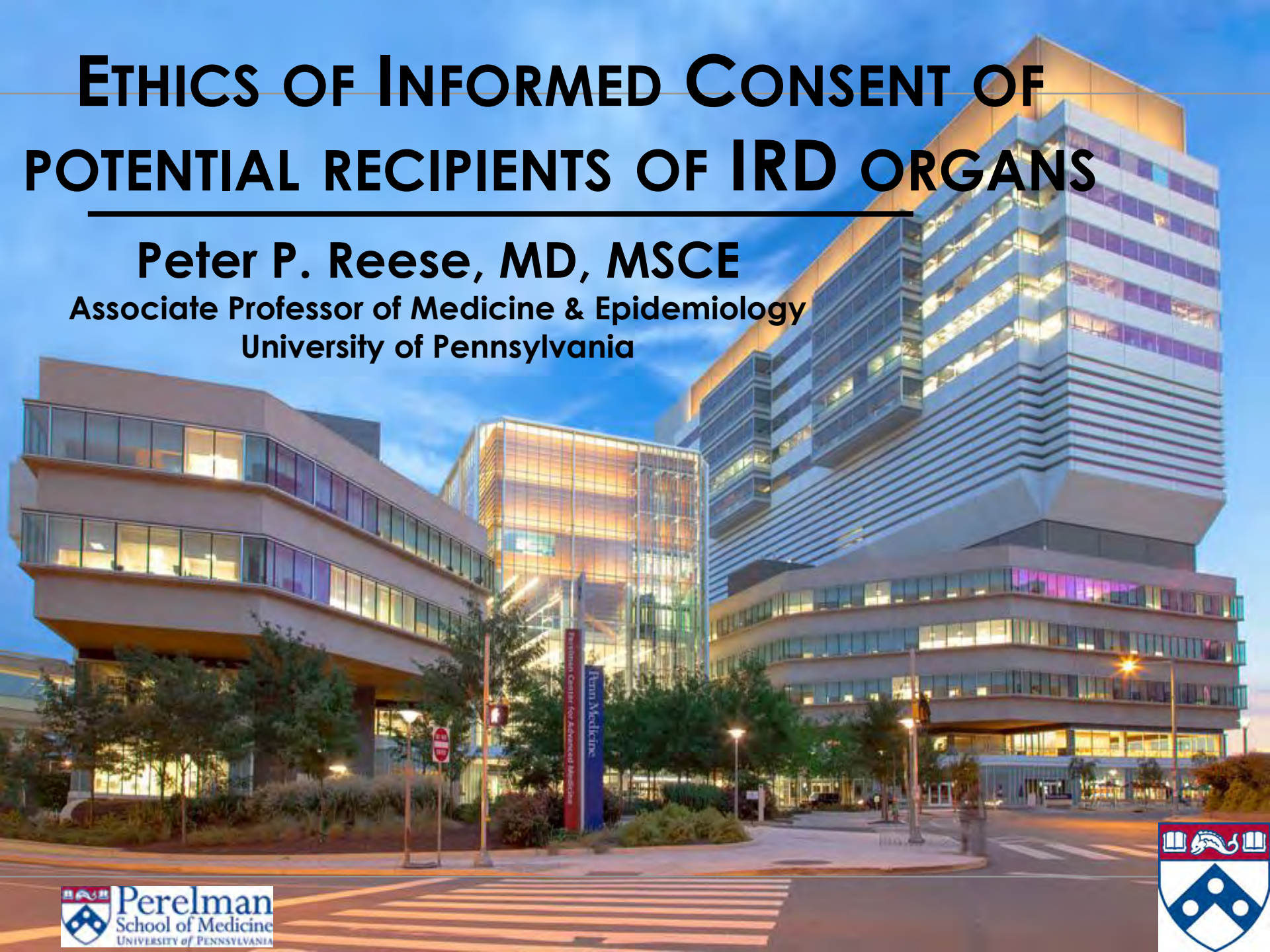
BREAK

Ethics of Informed Consent of recipients of IRD organs

PETER REESE, MD
Associate Professor of Medicine Center for Clinical Epidemiology and Biostatistics
University of Pennsylvania

Ethics of Informed Consent of potential recipients of IRD organs

Peter P. Reese, MD, MSCE
Associate Professor of Medicine & Epidemiology
University of Pennsylvania



Perelman School of Medicine
University of Pennsylvania

Ethical principles at the bedside: transplanting IRD organs

- **Beneficence:** Most organ transplant candidates have a substantial risk of death or other harms while on the wait-list
  - The physician's duty is to actively seek ways to improve patient health with guidance that balances potential risk and benefit
  - *"Do no harm" is an oversimplification that should be avoided*

- **Respect for Autonomy:** Patients deserve to be able to make decisions about transplantation consistent with their values
  - They need information presented in a way they can understand – thorough but not overwhelming
  - The setting of the decision ought to avoid coercion or other conditions that limit patient ability to make a decision

Bedside ethics: All organ transplants carry risks

- Those **risks** include disease transmission with infections and/or cancer, as well as harms from transplant medications and surgery

- **Informed consent** enables physicians to balance the duties of beneficence and respect for autonomy

- **What is ideal?**
  - Patients should have time to consider the decision and ask for clarification
  - A clinician should try to actively clear up misunderstanding
  - A clinician should elicit patient preferences where necessary
  - The main process of consenting should take place when patients are on the waiting list and when there is not the time pressure of an organ offer

Veatch R, Ross L. Transplantation Ethics. Georgetown University Press, 2015

Barriers to autonomy in current practice

- A long gap in time may elapse between patient education on the waiting list and organ offer
- Patient education on the waiting list may be overwhelming due to center interest in satisfying regulatory burden and legal concerns
- Organ offer
  - Specific education about IRD organs may be rushed and emotionally charged
  - Patients may feel that they have no real choice

- In some settings, the patient may be no longer able to make an informed decision and so surrogates must decide about organ acceptance
  - e.g., liver transplantation and hepatic encephalopathy

Ethics for policy-makers: Problems with the allocation of IRD organs

- **Utility**
  - On the one hand, these valuable IRD organs are at risk of discard
  - On the other, organ donation depends on public trust and disease transmission could undermine trust

- **Equity**
  - It is unclear that these organs are being allocated to patients in an equitable way

Serious utility problem: Many viable organs are declined or discarded

- **EXAMPLE: KIDNEYS**
- About 3,000 kidneys per year are discarded
- IRD status is associated with a greater probability of turning down a kidney offer
  - **Adjusted odds ratio for organ turndown: 2.49**
    - Cohen … Reese. *American Journal of Transplantation*. 2018
- Consequences of turning down a kidney offer
  - 43% of patients who turned down their first offer later got a transplant
  - Among those patients who get a transplant
    - Wait longer
    - 56% accept a kidney of **similar or lower quality** than the initial offer

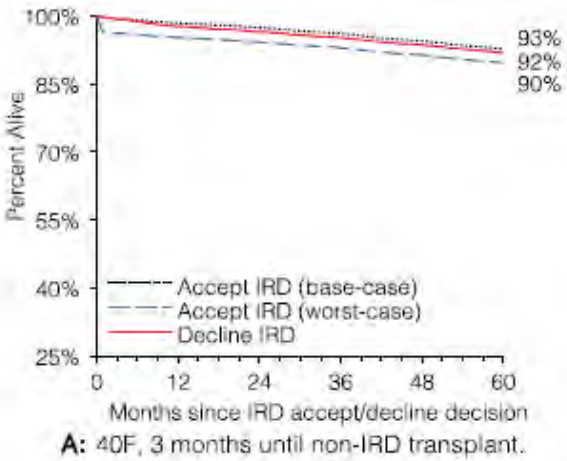
Cohen … Reese. *American Journal of Transplantation*. 2019

These rejected or lost organs would extend life for many patients

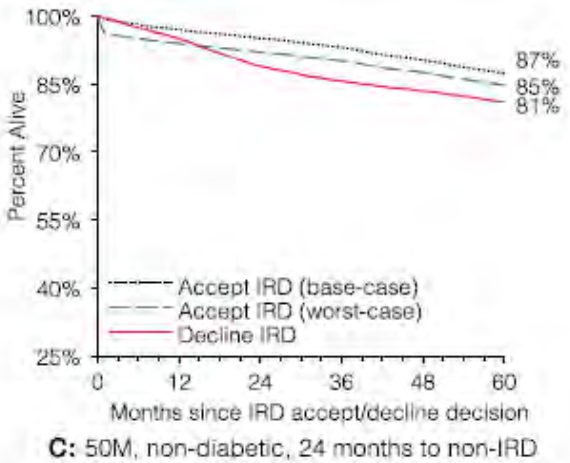
EXAMPLE: KIDNEYS

- Simulation of outcomes across the spectrum of kidney quality and patient characteristics
  - Chow … Segev. *American Journal of Transplantation*. 2013
- Model integrated death risks from dialysis, post-transplantation and related to rare complications of HIV and hepatitis C virus infection from transplantation
  - Notably, estimates of HCV infection risk would now be much lower if contemporary data were used because of better antiviral therapy
    - As a result: Outcomes for IRD transplant would be better today
  - Model integrates anticipated time until a non-IRD transplant

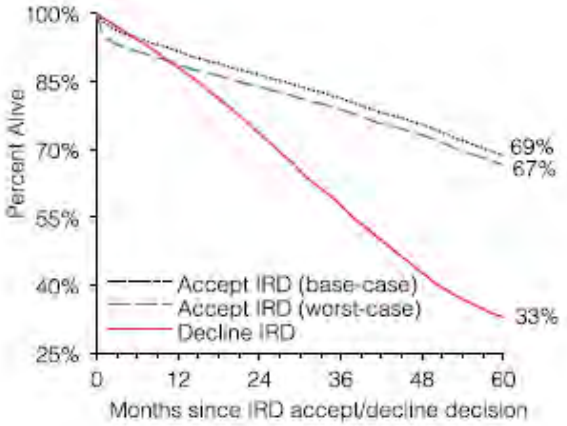
Survival outcomes for different recipients with IRD transplant



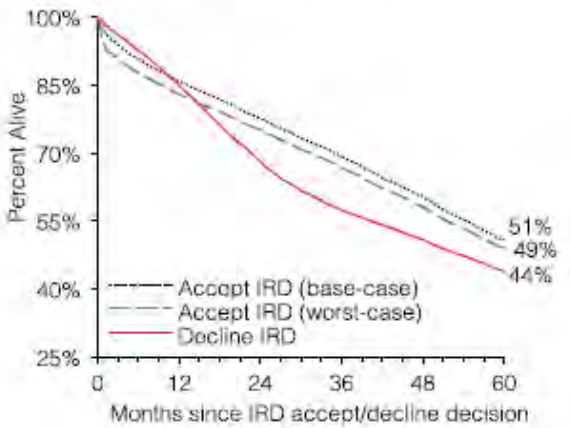
A: 40F, 3 months until non-IRD transplant.



C: 50M, non-diabetic, 24 months to non-IRD transplant.



B: 65F, diabetic, 60 months to non-IRD transplant.



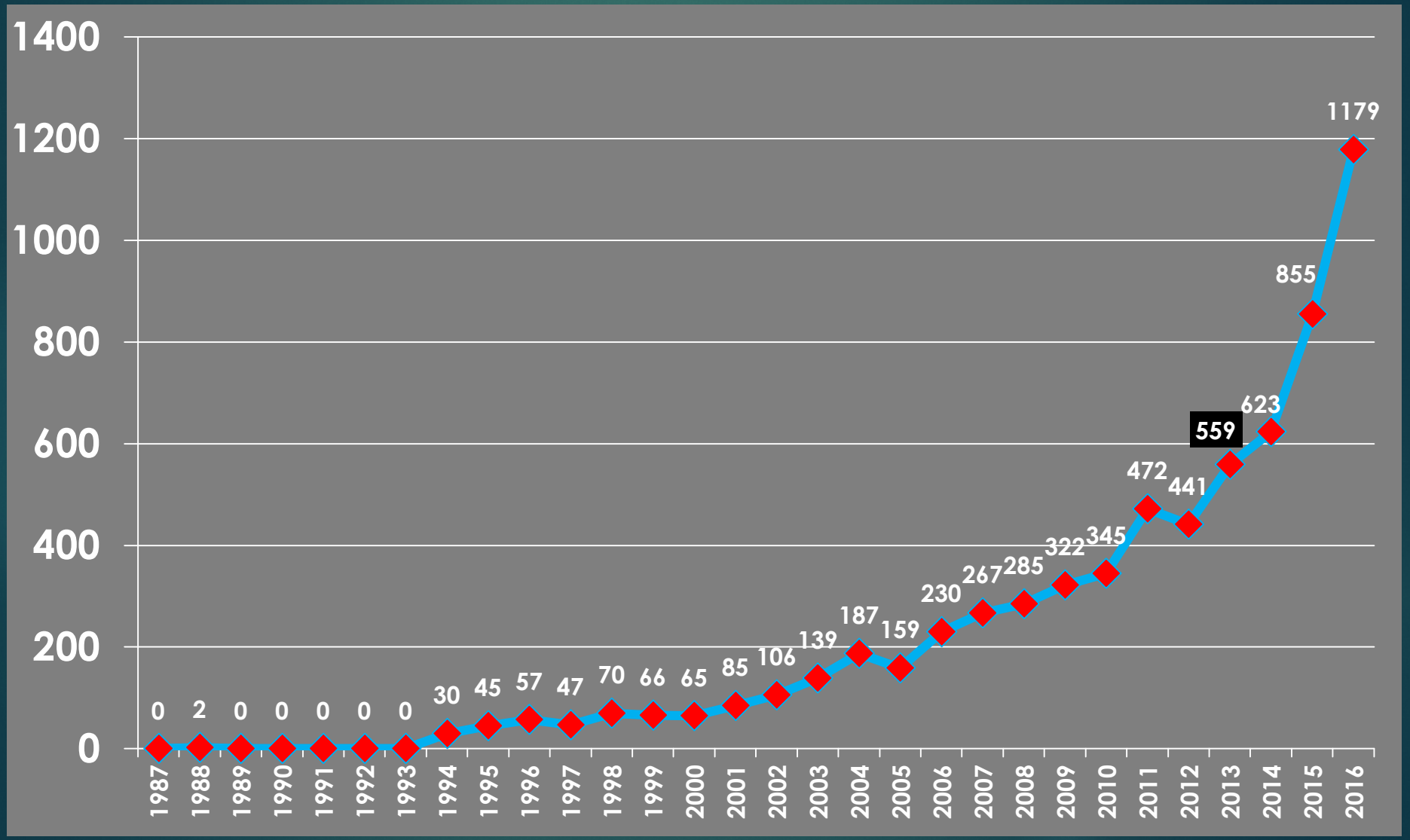
D: 75F, ABO AB, PRA 100, diabetic, 24 months to non-IRD transplant.

Figure 2: Predicted survival after accepting or declining IRD kidneys: Illustrative patient phenotypes. If not specified, the patient is Caucasian, non-diabetic, with a BMI of 25, PRA of 0, no previous transplants, and O blood type. M, Male, F, Female.

For an extended description of these chart, please see the image description on **page 226**

Contemporary relevance

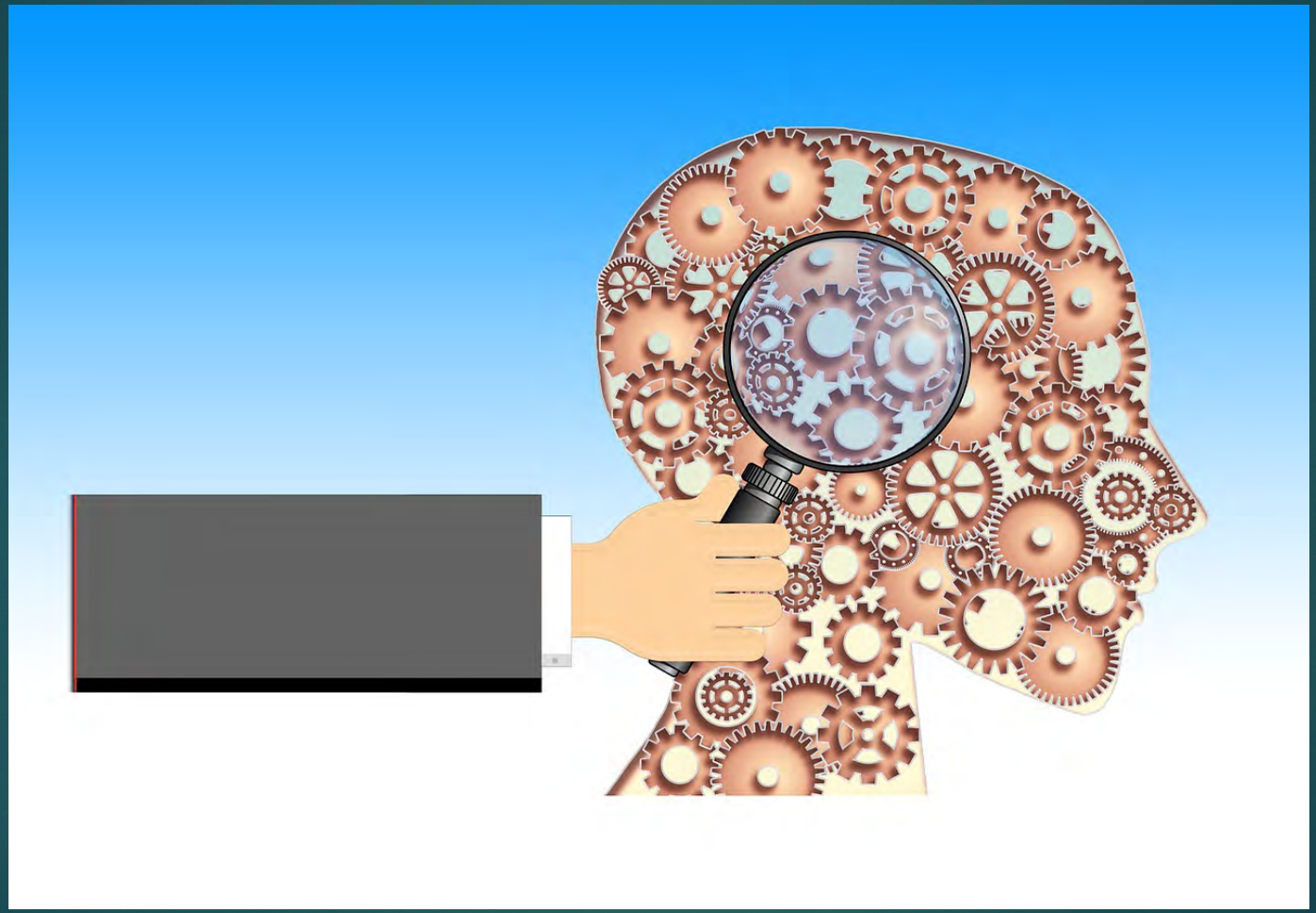
More and more organs from IRDs: Donor deaths to due opioid overdose



Other relevant considerations

- Hepatitis C virus infection is curable, even with transplant immunosuppression
- Donor derived, de novo hepatitis C virus infection (D+/R-)
  - 100% cure rates in the trial setting
    - THINKER (n=45) and EXPANDER (n=10) trials in 2018: kidney transplantation
    - USHER (n=10) and DONATE C (n=35) trials in 2019: thoracic transplantation
  - 100% cure reported with accidental transmission
    - Halleck et al. NEJM. 2017. German case series
- HCV transmission with transplant may less risky than CMV
- Donor-derived, de novo HIV infection could be emotionally devastating and impair quality of life
  - Yet, treatment outcomes for HIV-infected transplant recipients appear to be quite good
    - Stock et al. NEJM. 2010 Nov 18;363(21):2004-14
  - Achieving viral control generally feasible

Do cognitive biases cause transplant doctors to refuse IRD kidneys?



Do cognitive biases cause transplant doctors to refuse IRD kidneys?

- **Fear of sins of commission**
  - For many people, it feels worse to do something that leads to a bad outcome…
    - e.g., accept a kidney that has complications
    - Or "I gave that patient an infection"
  - … than to do nothing and have a bad outcome on the waiting list
    - e.g., refuse a kidney from an injection drug user for a wait-listed patient

- Yet, turning down organs needlessly (sin of omission) also harms the patient
  - Transplant physician still stands in the causal chain responsible for the death

Do cognitive biases cause transplant doctors to refuse IRD kidneys?

- Availability heuristic
  - Many transplant staff can picture the patient with a post-operative complication, but …
  - In some cases, they rarely see the patient who suffers on the waiting list
  - Therefore, it is harder for transplant staff to hold themselves as primarily responsible for the health outcomes of waitlisted patients …
    - … instead the primary medical physicians do, while rounding in dialysis unit or managing left ventricular assist devices for heart failure patients

Do cognitive biases cause doctors and patients to refuse kidneys?

- Overweighting small probabilities
  - Well described by cognitive psychologists
    - Tversky, A., & Kahneman, D. (1981). The Framing of Decisions and the Psychology of Choice. *Science*, 211 (4481), 453-458.
  - Some patients hear statistics about HIV transmission such as "1 in 1000" and worry much more than, say, the 5% risk of dying every year on dialysis
  - Transplant physicians may share this problem
- Cognitive flaw, not a preference

What do patients say about IRD organs?

- Qualitative study of 162 kidney transplant candidates at a single center
- Semi-structured interviews for patients returning to center for 1 and 3-year waiting list re-evaluation
  - Gordon et al. *Clinical Transplantation*. 2012
- Many patients believed that IRDs would be in poor health because of having chronic diseases such as diabetes, hypertension, or cancer (n = 71)
  - "I have been reading, I have more chance, am better off, if the donor don't smoke or drink."

  [African American man, 48 years old]
  - "I would assume some type of technical problems [with the organ] and that the organ might not last."

  [African American man, 37 years old]

How do patients weigh the importance of IRD status?

- Conjoint analysis – the goal is to figure out how important individual factors are to a decision; the factors are **CON**sidered **JOINT**ly.
- Cross-sectional study of adult kidney transplant candidates at the University of Pennsylvania.
- All candidates had undergone center education
- Participants considered 12 kidney offers in which we varied 3 things
  - Risk of HIV infection: 1/1500 vs. 1/10,000
  - Expected waiting time for a kidney: 1, 3 or 5 years
  - Donor age as a surrogate for kidney quality: 18 or 55 years

Reese PP …. Halpern SD. *Clinical Journal of the American Society of Nephrology*. 2012.

How do patients weigh the importance of IRD status?

- 24% rejected IRD kidneys under all circumstances
- 59% accepted IRD kidneys under some circumstances
- 17% always accepted IRD kidneys

Reese PP …. Halpern SD. *Clinical Journal of the American Society of Nephrology*. 2012.

Factors associated with accepting a kidney

Decision element	Odds Ratio	Confidence interval	P-value
5 year waiting time to transplant if this offer declined	4.20	2.97, 5.94	<0.01
3 year waiting time to transplant if this offer declined	3.50	2.57, 4.75	<0.01
Respondent on dialysis	2.88	1.71, 4.84	<0.01
Lower risk of HIV infection (1/10,000 vs. 1/1500)	2.12	1.61, 2.81	<0.01
Better kidney quality (18 year old vs 55 yo donor)	1.78	1.43, 2.23	<0.01
Participant older age	1.28	1.02, 1.63	0.04

Explanations for why tiny HIV transmission risks strongly influence decisions

- The problem of stigma associated with HIV
- Low understanding
  - Confusion of low quality organ with disease transmission
    - Gordon et al. *Clinical Transplantation*. 2012
- Cognitive bias
  - Overweighting small probabilities
- Patient preferences and judgments
  - Lack of trust in the medical system
  - Acceptable status quo
    - Example: Adaptation to dialysis

Potential areas to align ethics and practice

- Shift the burden of informed consent to the waiting list and away from the moment of organ offer
  - Informed consent should take place at regular intervals, not a 1-time event
  - At the time of organ offer, only minimal specific information about donor characteristics is necessary if a patient has prospectively agreed to accept an IRD organ
- Shift the language toward the most relevant comparison (no transplant) and away from the hypothetical ideal (a different, lower risk, better transplant)
  - "increased risk" is not optimal language

Potential areas to align ethics and practice

- Endorse best practices in patient education
  - Practices should address cognitive biases
- Regulations should transparently explain how change in practice aligns with ethical principles
- Endorse appropriate use of good tools in terms of patient and physician education
  - IRD organ risk calculator that predicts survival with accepting or rejecting an organ offer
  - http://transplantmodels.com/ird/
    - Chow…Segev. *American Journal of Transplantation*. 2013

Concerns about public trust

- A relevant issue for maintaining organ donation rates
  - Example: Germany's organ donation rate fell after physicians accused of manipulating waitlist priority
- Yet, robust informed consent at the time of wait-listing ought to be as good in maintaining public trust as consent in a hurry at the time of organ offer
- Similar surveillance for donor-derived blood borne viruses for all organ recipients would be simpler and logical, given that differences in risk are very small between IRD and non-IRDs

Proposals worthy of discussion

- Informed consent on the waiting list might also include informing patients (and referring doctors) about the number and quality of organs turned down for that candidate

- Goals
  - Promote patient autonomy
  - Better align physician and patient understanding about access to transplantation

- Potential risk
  - Patients might distrust physician decision-making

Conclusions

- Beneficence means integrating risks and benefits for each patient at the bedside
  - "Do no harm" is not a useful concept for waitlisted patients
- Informed consent for IRD organs is best implemented while the patient is on the waiting list, not at the time of organ offer
- Best practices for informed consent should address the following challenges
  - IRD organs may be declined due to patient preferences or lack of understanding
  - IRD organs may also be declined due to cognitive biases on the part of physicians or patients

Conclusions

- Ethics for policy-makers and transplant leaders
  - Organ discard and turndown rates are too high
  - The transplant community and policy-makers have a duty to maximize the benefits of the precious resource of IRD organs by reducing discards of viable organs

Acknowledgements

- HHS Advisory Committee on Blood & Tissue Safety & Availability for this invitation

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The Greenwall Foundation

NIH

OPO EXPERIENCE: HOW ARE IR DONORS IDENTIFIED, LIMITATIONS OF NEXT OF KIN INTERVIEW, TRANSMISSION OF INFORMATION TO RECIPIENT CENTERS

RICHARD HASZ, MFS
Vice President, Clinical Services
Gift of Life Donor Program

Heart Transplant Recipient , Hudson DeMartini (bottom left), with his family

HOPE ADVOCACY PASSION

One organ donor can save up to eight lives and one tissue donor can enhance the lives of more than 75 others. Register at **donors1.org**

DONATE LIFE
A Donate Life Organization

GIFT of LIFE DONOR PROGRAM

GIFT of LIFE DONOR PROGRAM

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

HHS Advisory Committee on Blood & Tissue Safety & Availability (ACBTSA)

OPO Experience with PHS Increased Risk Donors

Richard Hasz

VP, Clinical Services, Gift of Life Donor Program

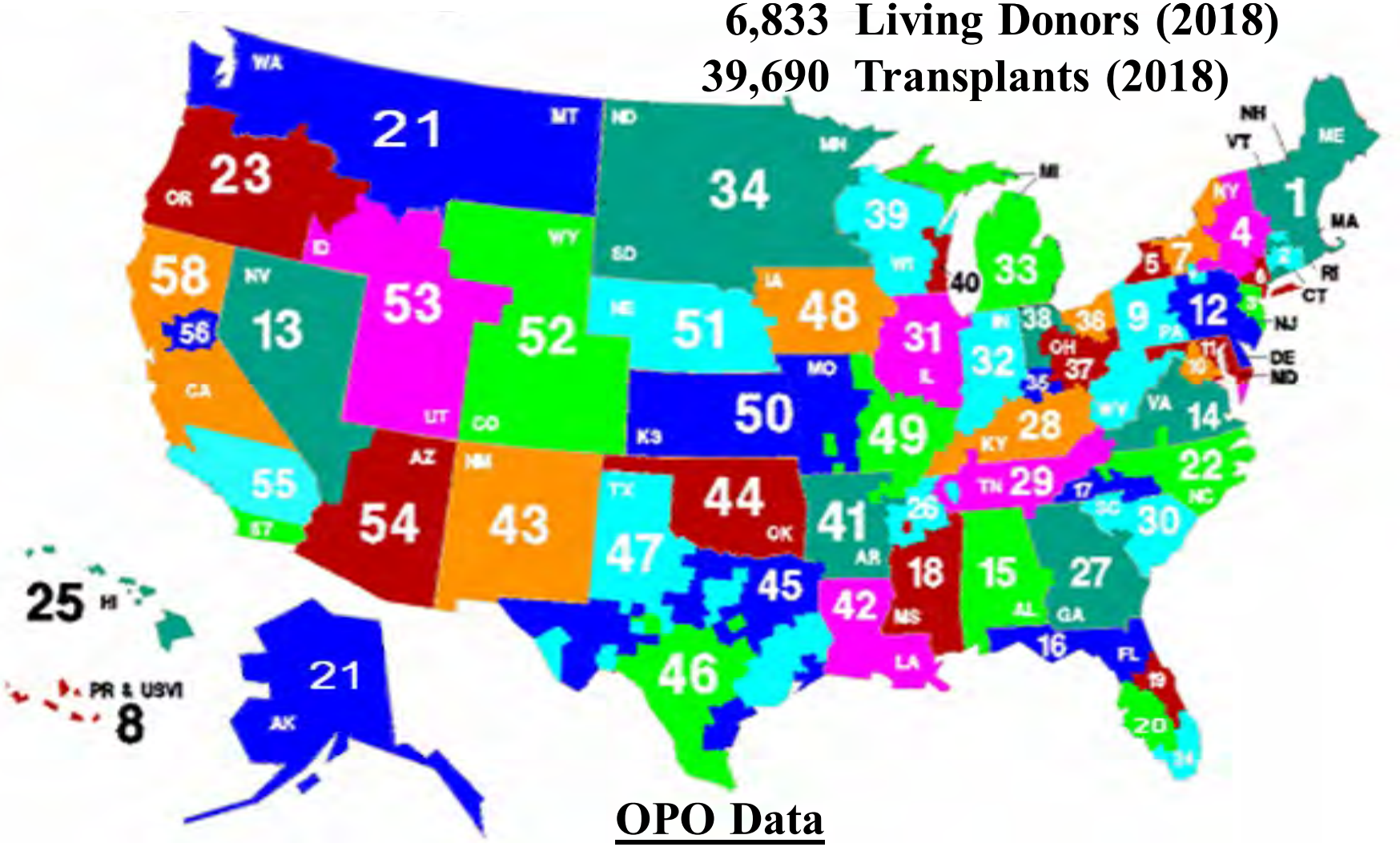
Gift of Life Donor Program

Philadelphia, Pennsylvania USA

- Non-Profit OPO/Tissue Recovery/Eye Bank
- Established in 1974
- Federally designated OPO (by Medicare) for eastern PA, Southern NJ & Delaware
  - 129 Acute Care Hospitals
  - 15 Transplant Centers, 43 Programs
  - 11 Million Population
- 615 organ donors in 2018, resulting in 1,671 transplants; highest volume in the U.S. – over 50 donors/MM; 1,368 bone recoveries; 2,173 cornea recoveries and 2,458 tissue recoveries
- Over 39,000 organs for transplantation and over 550,000 tissue allografts
- Accredited by: Association of Organ Procurement Organizations (AOPO); American Assoc. of Tissue Banks (AATB) & Eye Bank Assoc. of America (EBAA); UNOS/OPTN member OPO

58 OPO Donation Service Areas in the U.S.

326.9 million people – 10,721 Deceased Donors (2018)
6,833 Living Donors (2018)
39,690 Transplants (2018)



OPO Data

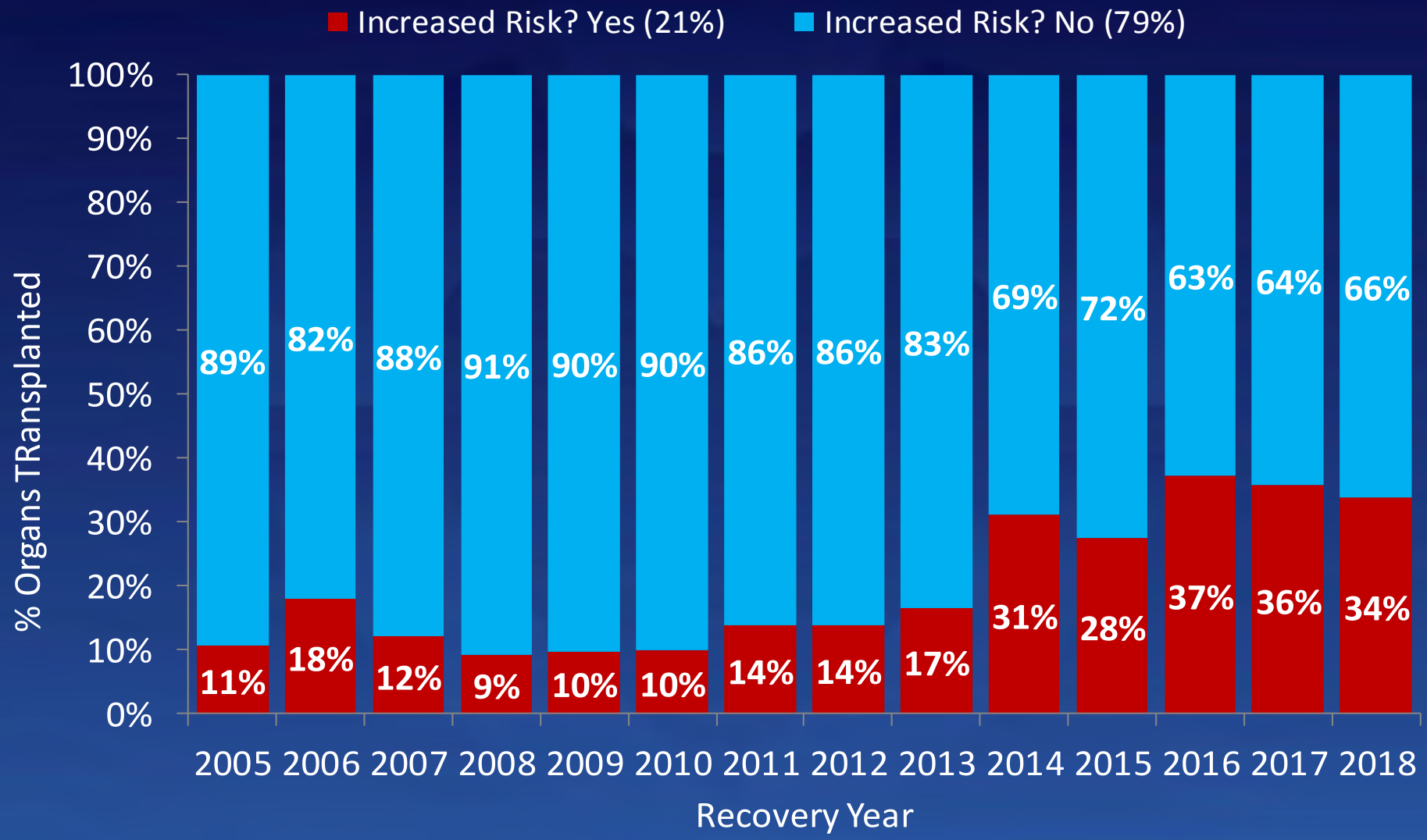
Population Bases from 1.4 Million to 19.5 Million
Deceased Donors Recovered ranged from 42 to 615 Donors
Donors per million (DPM) ranged from 20.0 to 59.1; U.S. Average 34.6

Gift of Life Donor Program

Organ Donor Experience

1974 – 2018

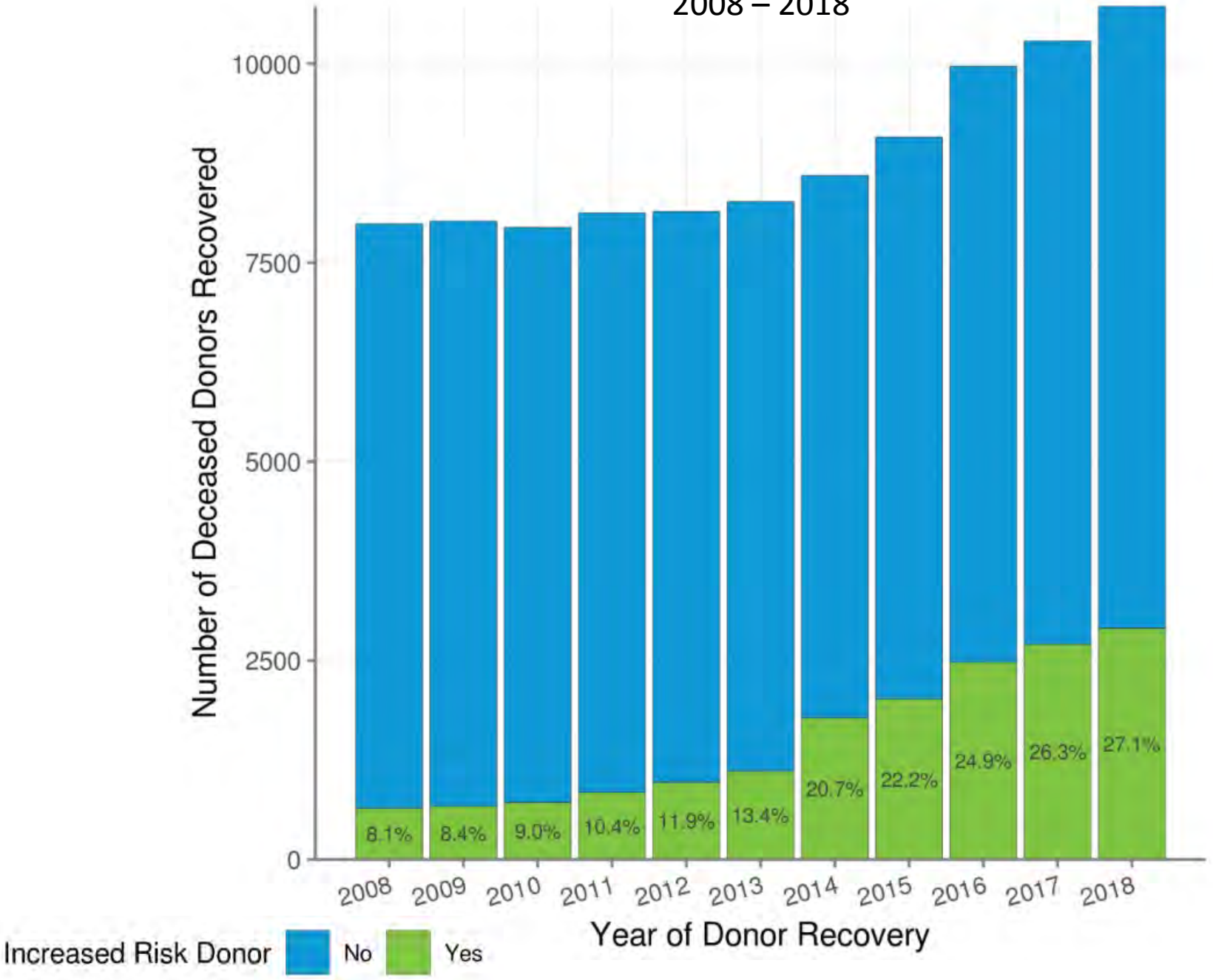
Organs Transplanted from GLDP PHS Increased Risk Organ Donors



GLDP PHS Increased Risk Organ Donors Recovered 2005 – 2018 By Cause of Death

Cause of Death	PHS Increased Risk?			
	Yes (n=1358)		No (n=5028)	
Anoxia	888	(65%)	1752	(35%)
Head Tauma	268	(20%)	1298	(26%)
CVA/Stroke	199	(15%)	1912	(38%)
CNS Tumor	0	(0%)	22	(0.4%)
Other	3	(0.2%)	44	(1%)
All COD	1358	(100%)	5028	(100%)

Number of Deceased Donors Recovered by Year and PHS Increased Risk Status 2008 – 2018



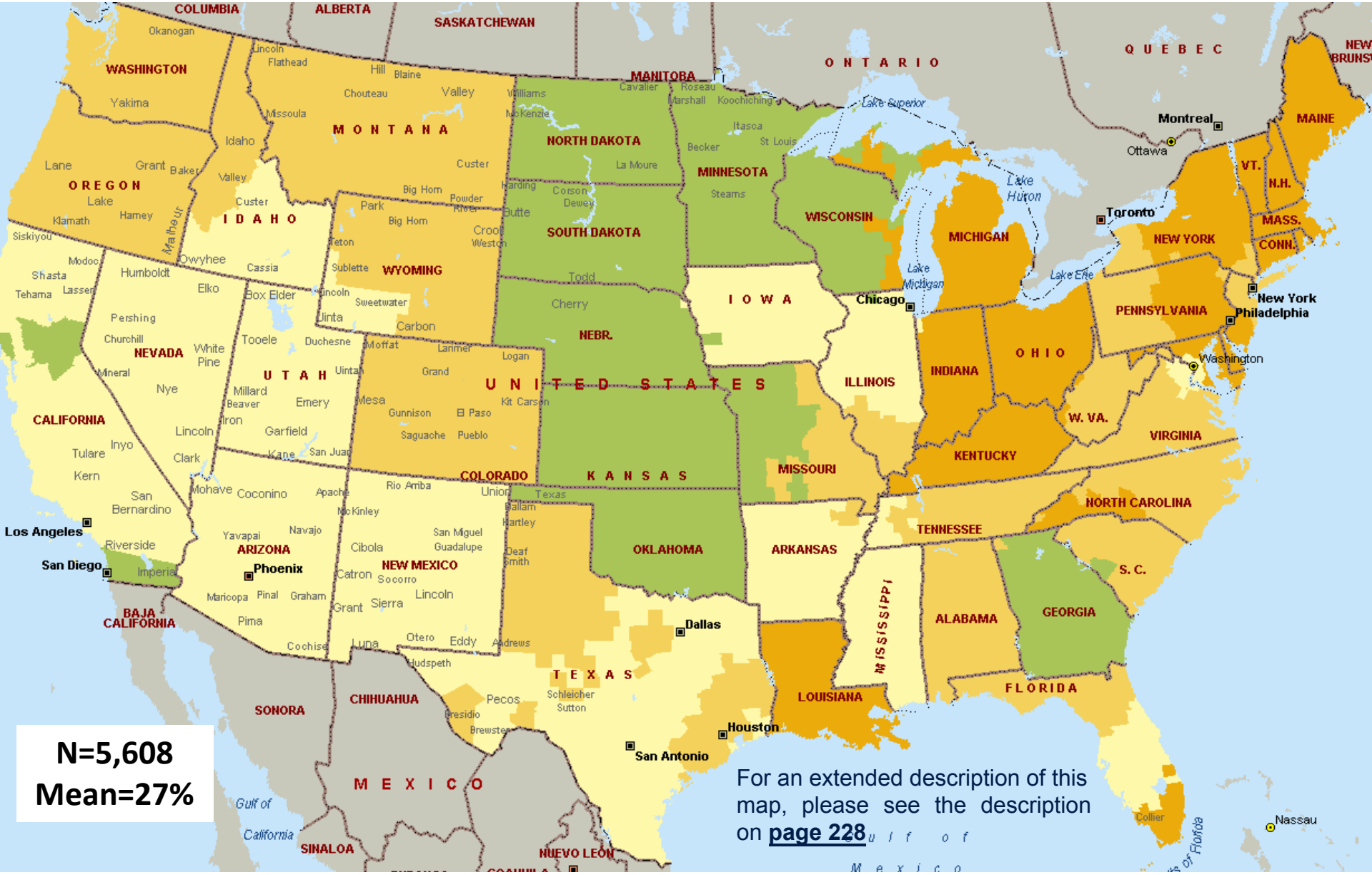
% PHS High Risk Donors by DSA 1/1/2015 – 12/31/2016

N=4,495
23.6%

For an extended description of this map, please see the description on page 227

30-40% 25-29% 20-24% 15-19% <15%

% PHS High Risk Donors by DSA 1/1/2017 – 12/31/2018

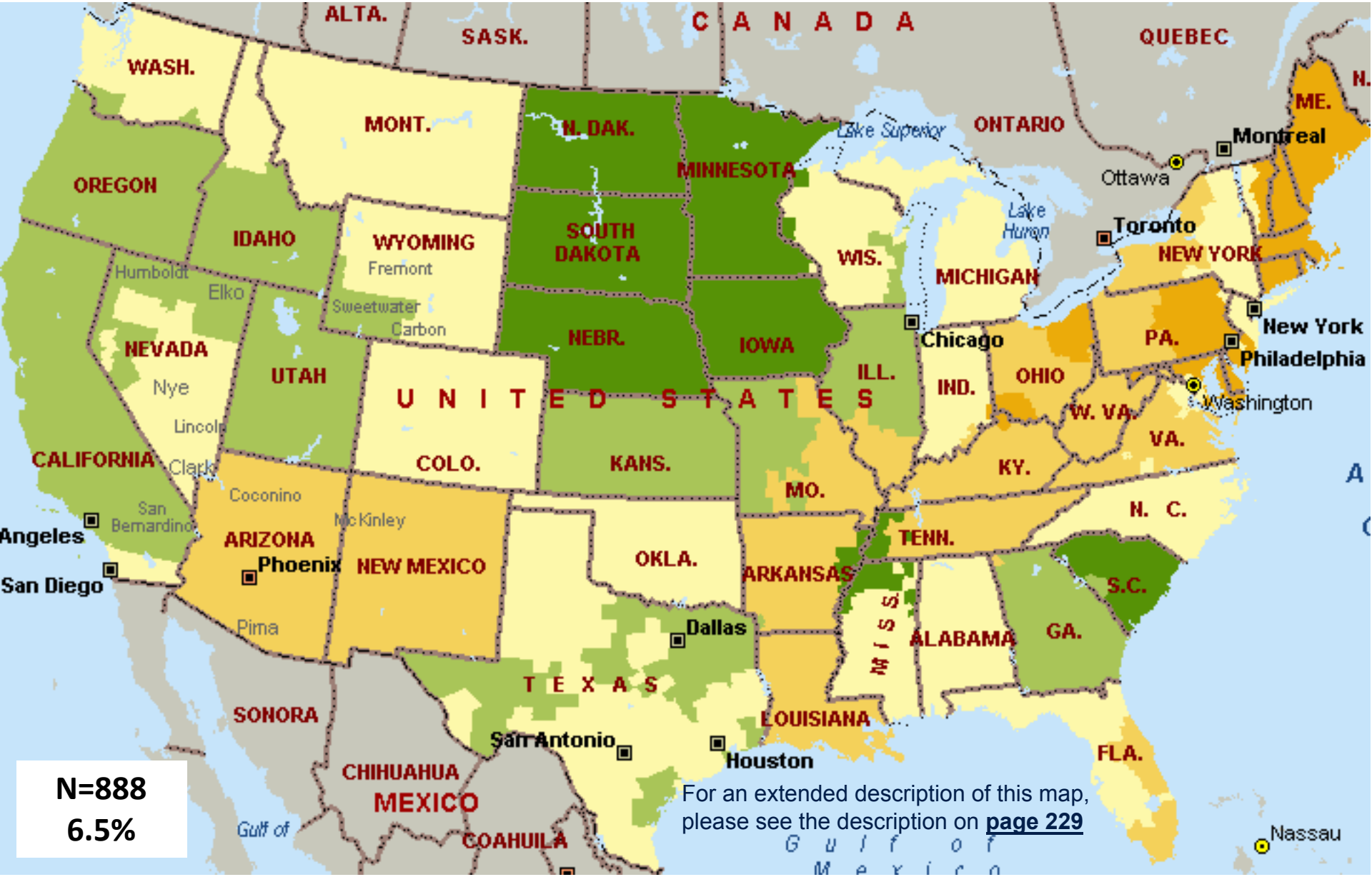


N=5,608
Mean=27%

For an extended description of this map, please see the description on **page 228**

30-42% **25-29%** **20-24%** **15-19%** **<15%**

% HCV Seropositive Donors by DSA 1/1/2015 – 12/31/2016

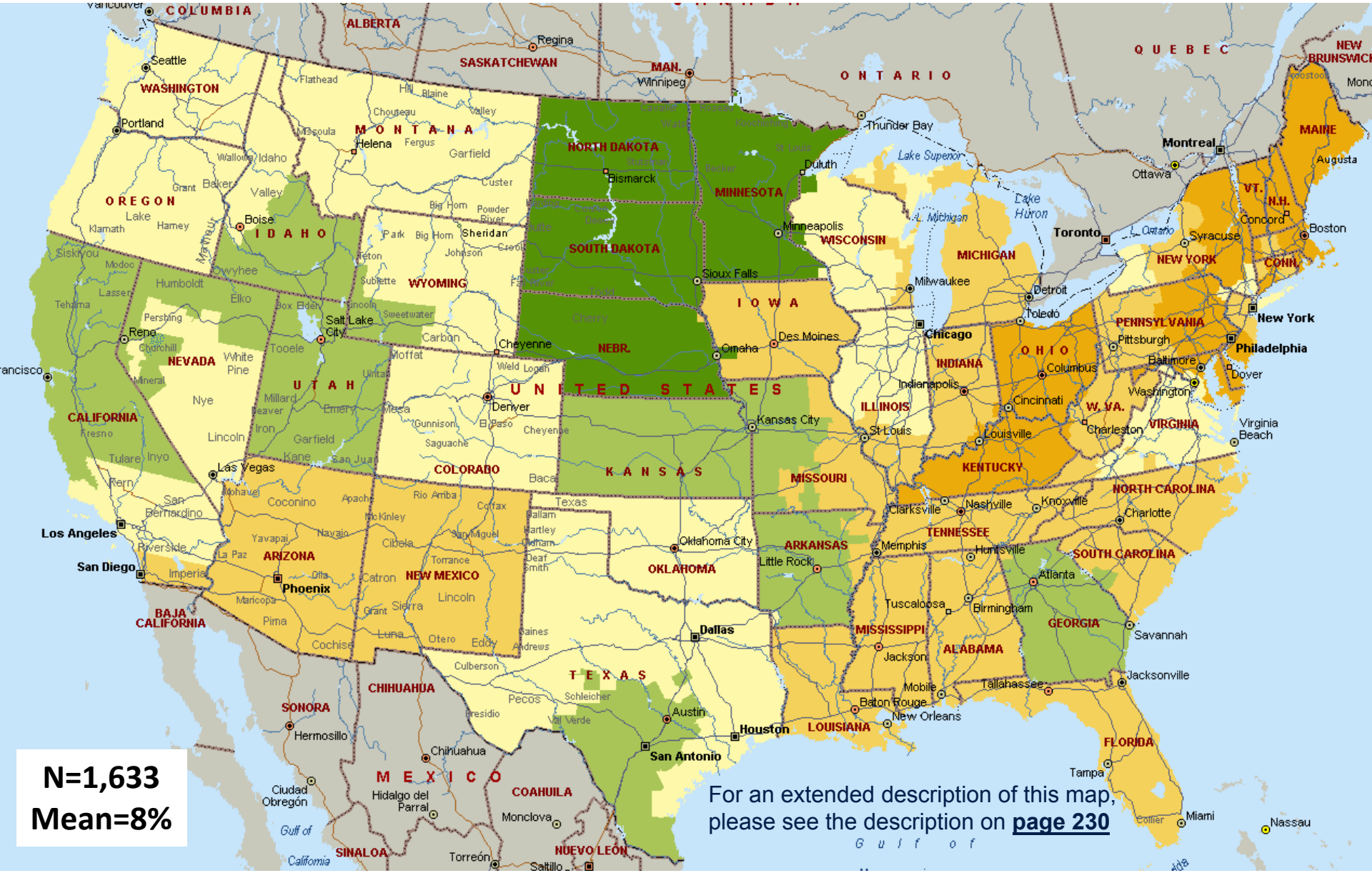


N=888
6.5%

For an extended description of this map, please see the description on **page 229**

12-16% | 7-11% | 4-6% | 2-3% | <2%

% HCV Seropositive Donors by DSA 1/1/2017 12/31/2018



N=1,633
Mean=8%

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

12-16% **7-11%** **4-6%** **2-3%** **<2%**

Determination of Increased Risk Donors

- Medical Social History Questionnaire
- Specimen Qualification
- Hemodialysis

Medical Social History Questionnaire

- Finding the right person to ask
- Reliability of the information provided
- Applying definitions correctly

GLDP Medical Social History Assessments

Prior to beginning the interview:

I want to advise you that some of the history questions are of a sensitive and personal nature. They are similar to those asked when someone donates blood and we are required to ask every question. For the purpose of this questionnaire, sexual activity is defined as any sexual contact including vaginal, anal, and oral sex. I will read each question, provide any explanations that you may need to thoroughly understand the question, and ask that you answer to the best of your knowledge with a "Yes" or "No."

Do you feel you know the deceased well enough to answer questions regarding the medical/social history? ◉ Yes ○ No

At the end of the interview:

50. Regarding these questions, are there other people, including healthcare professionals, who may provide additional information? ○ Yes ◉ No

50a. Name(s) and contact information:

After the interview:

Medical Social History Assessments

Date/Time Added	Person Interviewed	Relationship to Potential Donor	Status
02/19/2019 10:16:24 (756)	Carolyn Farmer	Mother	Complete - Full
02/19/2019 13:19:50 (757)			In Progress - Full

Add New Full Assessment | Add New Supplemental Assessment | Review Edited Questions | Review Yes Questions

SEXUAL HISTORY

Next, I will ask you about his sexual history. As a reminder, sexual activity refers to any method of sexual contact including vaginal, anal, and oral.

28. In the past 12 months has he been newly diagnosed or been treated for syphilis, gonorrhea, chlamydia, or genital ulcers? ○ Yes ◉ No

If 28. is yes, donor is PHS high risk.

28a. Which one was it?

28b. When?

28c. Was it treated? ○ Yes ○ No

29. In the past **5 years** was he sexually active, even once? ○ Yes ◉ No

***If no**, proceed to question 30.*
***If yes**, complete the following questions (29a. to 29g.)*

29a. In the past **5 years**, did he have sex in exchange for money or drugs? ○ Yes ○ No

***If no**, proceed to question 29b.*

If yes, **29a(i).** Did he have sex in exchange for money or drugs in the preceding **12 months**? ○ Yes ○ No

***If 29a(i). is yes, donor is PHS high risk**, complete question 29a(ii).*

29a(ii). When?

☐ *(N/A) Donor is Female*

29b. MALE DONOR only: In the past **5 years**, did he have sex with another male? ○ Yes ○ No

***If no or N/A**, proceed to question 29c.*

***If yes**, **29b(i).** Did he have sex with another male in the preceding **12 months**? ○ Yes ○ No

***If 29b(i). is yes, donor is PHS high risk**, complete question 29b(ii).*

29d. In the preceding **12 months**, did he have sex with a person who has had sex in exchange for money or drugs? ○ Yes ○ No

***If no**, proceed to question 29e.*

If yes, **29d(i).** Did that sexual partner have sex in exchange for money or drugs in the past **5 years**? ○ Yes ○ No

***If no**, proceed to question 29e.*

If yes, **29d(ii).** Did that sexual partner have sex in exchange for money or drugs in the preceding **12 months?** ○ Yes ○ No

If 29d(ii). is yes, donor is PHS high risk.

29e. In the preceding **12 months**, did he have sex with a person who injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons? ○ Yes ○ No

***If no**, proceed to question 29f.*

If yes, **29e(i).** Did that sexual partner inject drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the past 5 years? ○ Yes ○ No

***If no**, proceed to question 29f.*

If yes, **29e(ii).** Did that sexual partner inject drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the preceding 12 months? ○ Yes ○ No

If 29e(ii). is yes, donor is PHS high risk

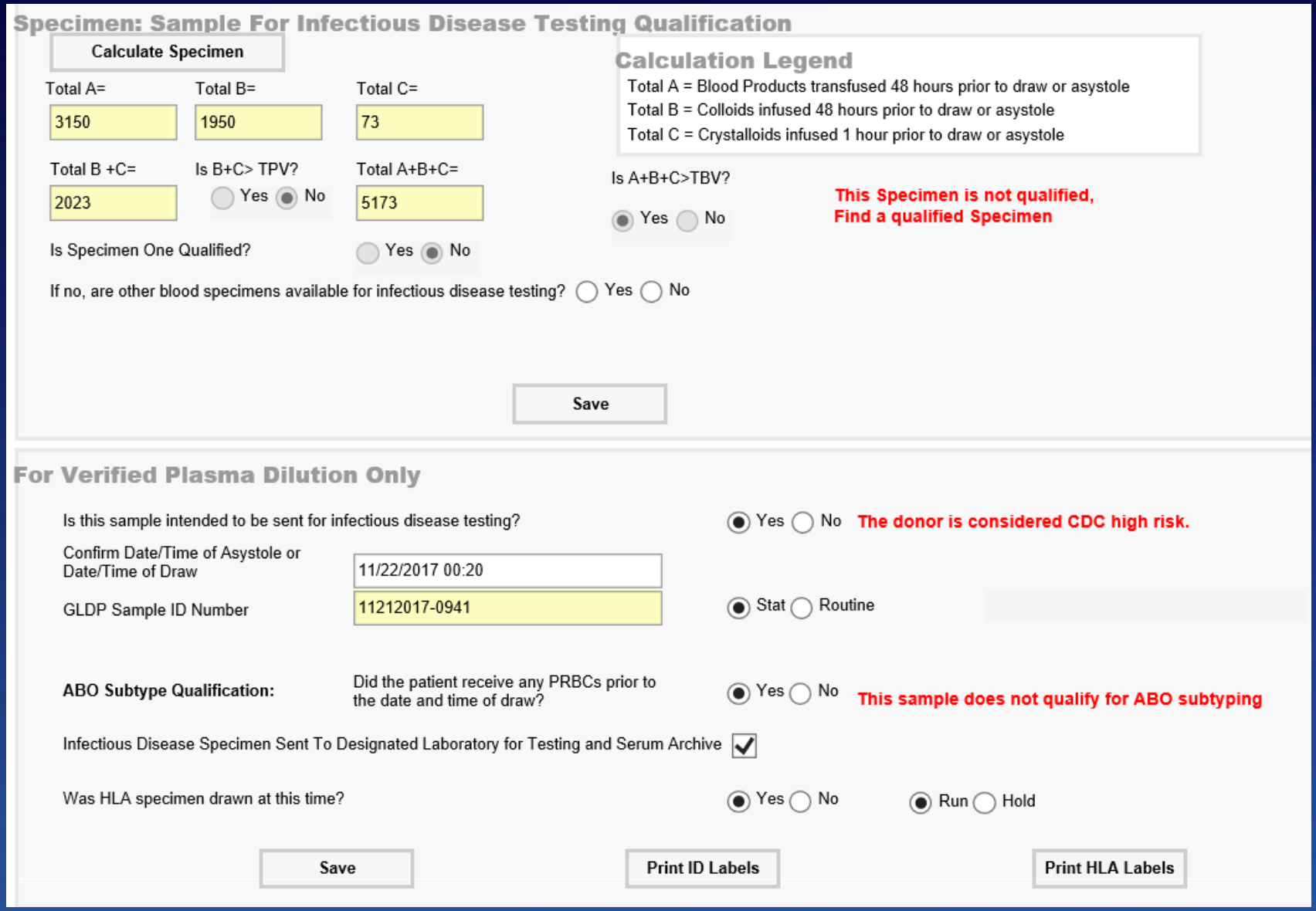
GLDP PHS Increased Risk Organ Donors Recovered 2005 - 2018

Med Soc Interview w/	PHS Increased Risk?			
	Yes (n=1358)		No (n=5028)	
Parents	735	54%	1644	33%
Spouse	178	13%	1749	35%
Children	164	12%	879	17%
Sibling	159	12%	479	10%
Other	122	9%	277	6%
All	1358	100%	5028	100%

Specimen Qualification

- Hemodilution Calculation
- Timing of Specimen Collection

GLDP PHS Increased Risk System Alerts



GLDP PHS Increased Risk System Alerts

22. Did she EVER use or take drugs, such as steroids, cocaine, amphetamines, or anything NOT prescribed by her doctor?

◉ Yes ○ No

***22a. If yes**, document details of all non-medical drug use in the grid below and complete question 22b.*

Non-Medical Drugs

Drug Name	Duration of Use?	When Last Used?	Method of Use					
			Inhaled	Smoked	Orally	Snorted	Injected	Comments
cocaine	2 yrs	today	☐	☐	☐	☑	☐	
heroin	2 yrs	today	☐	☐	☐	☑	☑	

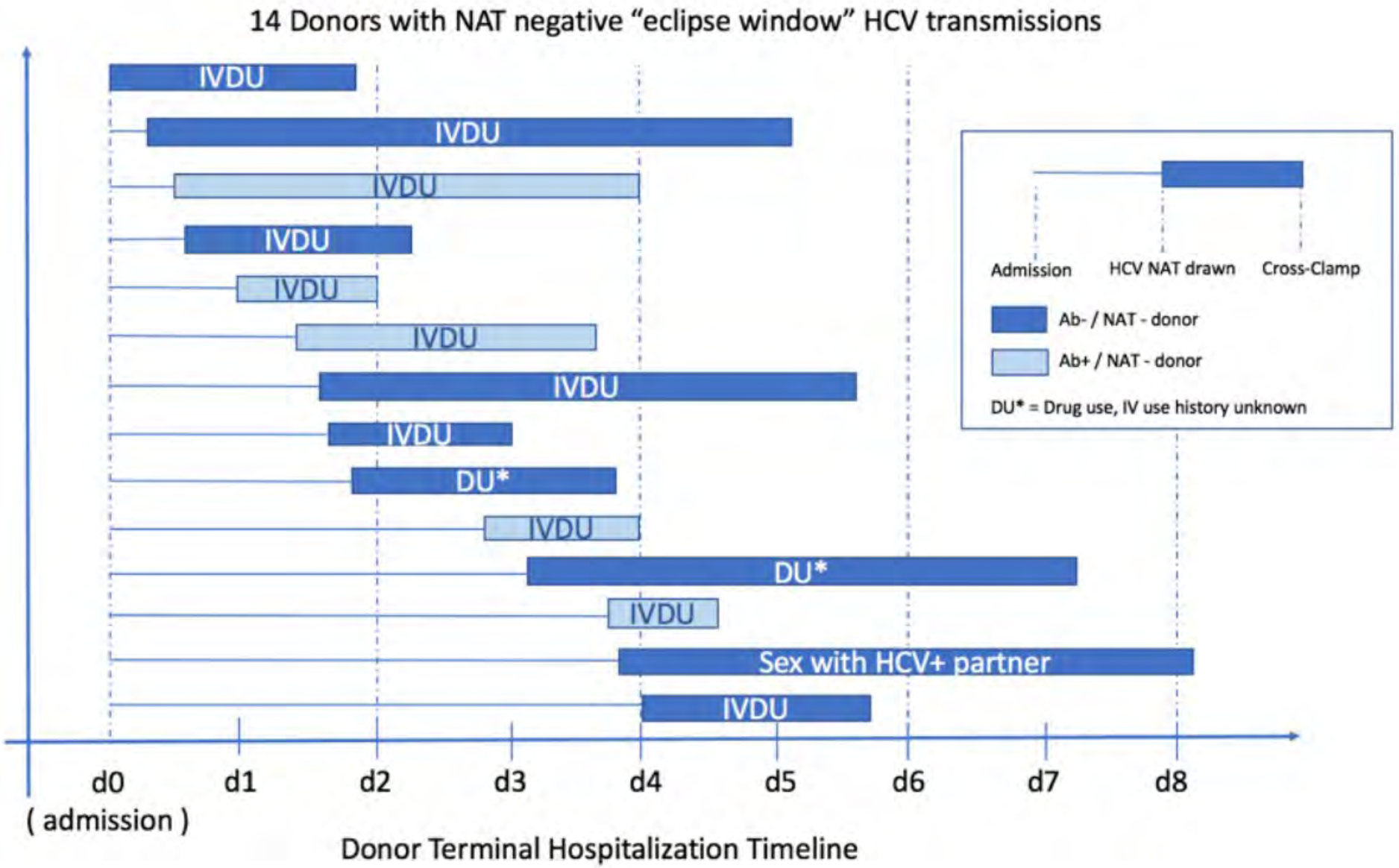
22b. In the past **five years**, did she inject drugs by intravenous, intramuscular, or subcutaneous route for non-medical reasons? ◉ Yes ○ No

***22b(i). If yes,** document all in the table above*

22b(ii). If yes, was it in the preceding 12 months? ◉ Yes ○ No

If 22b(ii). is yes, donor is PHS high risk.

Unanticipated donor-derived transmissions 2013-2017



15d. Dialysis? ○ Yes ◉ No *If yes to dialysis*, **15d(i).** check type(s). ☐ Hemodialysis ☐ Peritoneal Dialysis

15d(i)a. If hemodialysis, did this occur in the preceding **12 months**? ○ Yes ○ No

If 15d(i)a. is yes, donor is PHS high risk.

15d(ii). Explain why and how long he received dialysis treatment

27. In the past 12 months was he in lockup, jail, prison, or any juvenile correctional facility for more than 72 consecutive hours? ◉ Yes ○ No

If 27. is yes, donor is PHS high risk.

27a. How long? 1.5 weeks

27b. Where? Juvenile Corrections

PHS Increased Risk

AOC

Date/Time Discussed with AOC

- [ ] No Increased Risk Categories Identified

Check all that apply

- [ ] In the absence of a medical history & behavioral risk assessment interview, the donor will be considered to be in an increased risk category. Authorization for donation is included in the donor record.
- [ ] When a deceased potential organ donor's blood specimen is hemodiluted, the donor should be considered at increased risk for HIV, HBV, and HCV infection because the donor's risk for infection is unknown.

This donor has been determined by medical history & behavioral risk assessment to meet one or more of the PHS criteria for increased risk (See item(s) below):

- [ ] People who have had sex with a person known or suspected to have HIV, HBV, or HCV infection in the preceding 12 months
- [ ] Men who have had sex with men (MSM) in the preceding 12 months
- [ ] Women who have had sex with a man with a history of MSM behavior in the preceding 12 months
- [ ] People who have had sex in exchange for money or drugs in the preceding 12 months
- [ ] People who have had sex with a person who had sex in exchange for money or drugs in the preceding 12 months
- [ ] People who have had sex with a person who injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the preceding 12 months
- [ ] A child who is ≤18 months of age and born to a mother known to be infected with, or at increased risk for, HIV, HBV, or HCV infection
- [ ] A child who has been breastfed within the preceding 12 months and the mother is known to be infected with, or at increased risk for, HIV infection
- [ ] People who have injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the preceding 12 months
- [ ] People who have been in lockup, jail, prison, or a juvenile correctional facility for more than 72 consecutive hours in the preceding 12 months
- [ ] People who have been newly diagnosed with, or have been treated for, syphilis, gonorrhea, Chlamydia, or genital ulcers in the preceding 12 months

Donors who meet the following criterion should be identified as being at increased risk for recent HCV infection only:

- [ ] People who have been on hemodialysis in the preceding 12 months

GLDP Donors by PHS Categories Donors Recovered 2017 - 2018

PHS Increased Risk Category	2017		2018	
No Increased Risk Categories Identified	363	(64%)	406	(66%)
People who have injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the preceding 12 months	125	(22%)	116	(19%)
People who have been in lockup, jail, prison, or a juvenile correctional facility for more than 72 consecutive hours in the preceding 12 months	84	(15%)	75	(12%)
People who have had sex with a person who injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical	72	(13%)	48	(8%)
People who have had sex with a person who had sex in exchange for money or drugs in the preceding 12 months	33	(6%)	27	(4%)
People who have had sex in exchange for money or drugs in the preceding 12 months	29	(5%)	20	(3%)
People who have had sex with a person known or suspected to have HIV, HBV, or HCV infection in the preceding 12 months	22	(4%)	13	(2%)
People who have been on hemodialysis in the preceding 12 months	18	(3%)	13	(2%)
Blood specimen is hemodiluted	6	(1%)	18	(3%)
People who have been newly diagnosed with, or have been treated for, syphilis, gonorrhea, Chlamydia, or genital ulcers in the preceding 12	15	(3%)	7	(1%)
Men who have had sex with men (MSM) in the preceding 12 months	10	(2%)	2	(0%)
Absence of a medical history & behavioral risk assessment interview	3	(1%)	4	(1%)
Women who have had sex with a man with a history of MSM behavior in the preceding 12 months	2	(0%)	2	(0%)
All Donors	**565**		**615**	

GLDP Donor Demographic Profile Donors Recovered 2005 - 2018

Demographic	PHS Increased Risk?	
	Yes (n=1358)	**No (n=5028)**
Average Age (Yrs)	36	45
Race	75% White	74% White
Sex	68% Male	58% Male
Cause of Death	65% Anoxia	38% CVA
Manner of Death	42% Drug OD	40% Stroke
Med Soc By	54% Parents	35% Spouse

Communication with Transplant Centers

- DonorNet
- Pre-recovery time out
- Organ offer (3rd party screeners)

Donor Highlights:

PHS High risk criteria MET due to track marks seen on physical assessment. Patient has had 2 exams and CBF c/w brain death Family requested OR no sooner than 3/30/2019 1200

Admission course comments:

Initial Referral Information: Patient admitted 03/27, was found down with bags of heroin around him. EMS gave Narcan, epi x 5, CPR and shocked. Appears areflexic, CTH pending, PMH: unknown, however, patient has old sternotomy scar, MD believes he can hear a valve click, and they have seen pacer spikes. Full code. Wife NOK, apparently she is in jail and pregnant. Admission Comments:3/27/19 Pt admitted on 3/27/19 after being found down, unresponsive, and surrounded by drug paraphernalia (small plastic bags) and an almost empty bottle of gabapentin (had been full the previous day), EMS called. No bystander CPR. Per ER records, EMS arrived in 30 mins, pt was in asystole, CPR initiated, Epi x5, shock x1 for VF with ROSC achieved in the field. No documentation of CPR time, or total DT. Initial CTH showed diffuse cerebral edema consistent with anoxic injury. HTP initiated @2100. Past Medical History:Congenital bicuspid aortic valve, Endocarditis (2011), Severe aortic stenosis (2014), CHB secondary to AVR (2014), HTN, anxiety, Bipolar, GERD, high triglycerides Past Surgical History: Mechanical AVR (2007), Redo AVR (porcine) secondary to endocarditis @PATJ (2011), Redo AVR (mechanical) with aortic root repair, secondary to severe AS and paravalvular leak (2/2 presumed latent/indolent endocarditis 2014), CHB post-op and had PPM placed, Cardiac Cath (2014) Past Social History: Smoker, Opiate abuse, on suboxone, heroin abuse, on Methadone, marijuana use, EtOH use Any Documented Allergies: Benadryl Clinical Course Procedures: Date/Time:03/27/2019 18:50; Procedure:Head CT; Comment:Despite motion, findings highly suspicious for anoxic brain injury/diffuse cerebral edema, Date/Time:03/29/2019 21:16; Procedure:Head CT; Comment:Worsening cerebral edema and findings of anoxic brain injury CPR/Downtime: Total Downtime - >30, CPR (>30), Defibrillation, Found in asystole, 30 mis of DT prior to CPR, Epi x5, shock x1 for VF with ROSC. CPR/DT not clearl

ICOM STUDIES

here are no DICOM images associated with this donor >

EDICAL & SOCIAL HISTORY

History of diabetes:	NO
History of cancer:	NO
History of hypertension:	YES, 0-5 YEARS
Compliant with treatment:	YES
History of coronary artery disease (CAD):	NO
Previous gastrointestinal disease:	NO
Chest trauma:	NO
Cigarette use (>20 pack years) ever:	YES
And continued in last six months:	YES
Heavy alcohol use (2+ drinks/daily):	NO
I.V. drug usage:	YES
According to the OPTN policy in effect on the date of referral, does the donor have risk factors for blood-borne disease transmission:	YES

Medical & social history comments:

Smoked 1ppd 25 yrs never quit. Drank beer couple times/yearly @ events for 10 years. Smoked marijuana for 25 years last used 3/27. High cholesterol for unk years, treated. Saw PCP in March for a regular visit to check coumadin levels and cardiac. Sexually active- no high risk. Had open heart surg X3 PATJ 2007, Aortic valves replacement PATF 2009, Foot Fx and surg 2014; 2005. Had heart valve replacement X3 due to congenital heart defect. Valve replaced. Maternal GM had CAD, PVD recently dx - no treatment. Father had DM, Had scar on chest and foot from surg. Worked in sales. Born Philadelphia, Had Tattoos or R arm and leg professionally >12 months ago. 2007 heart valve replaced w/ pig valve. Travel to Bahamas 2012 for 7 day vacation. Coumadin unk dose 14yrs - compliant Lipitor unk dose, unk how long - compliant Xanax unk dose for 2 years - compliant Suboxone - unk dose - 2 years - compliant

GIFT OF LIFE DONOR PROGRAM
REVIEW AND RECEIPT OF DONOR INFORMATION

Patient Name _____ UNOS# AGDA213

By affixing my signature in the space provided, I am certifying in good faith that I have reviewed and agree with the documentation for this organ donor. I understand that the documentation and information includes, but is not limited to:

1. Donor UNOS ID
2. Donor blood type, and subtype if used for allocation
3. Intended Recipient blood type and subtype as indicated on Organ Donor Verification Form, except for kidneys.
4. Recipient known compatibility or incompatibility as indicated on Organ Donor Verification Form, except for kidneys.
5. Pronouncement of Death (except for DCD donor)
6. Authorization for Donation and Medical-Social History
7. Infectious Disease profile results

(If a single surgeon is to recover multiple organs, please indicate by marking "same as _____" for each recovered organ.)

Heart Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

R-Lung Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

L-Lung Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

Liver Surgeon S. M Rudich A Rudich Date 04/02/2019 Time 21:19
Printed Name Signature

Segmented Liver Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

Pancreas Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

Intestine Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

Right Kidney Surgeon " " Date 04/02/19 Time 21:19
Printed Name Signature

Left Kidney Surgeon " " Date 04/02/19 Time 21:19
Printed Name Signature

VCA Surgeon _____ Date ___/___/___ Time ___:___
Printed Name Signature

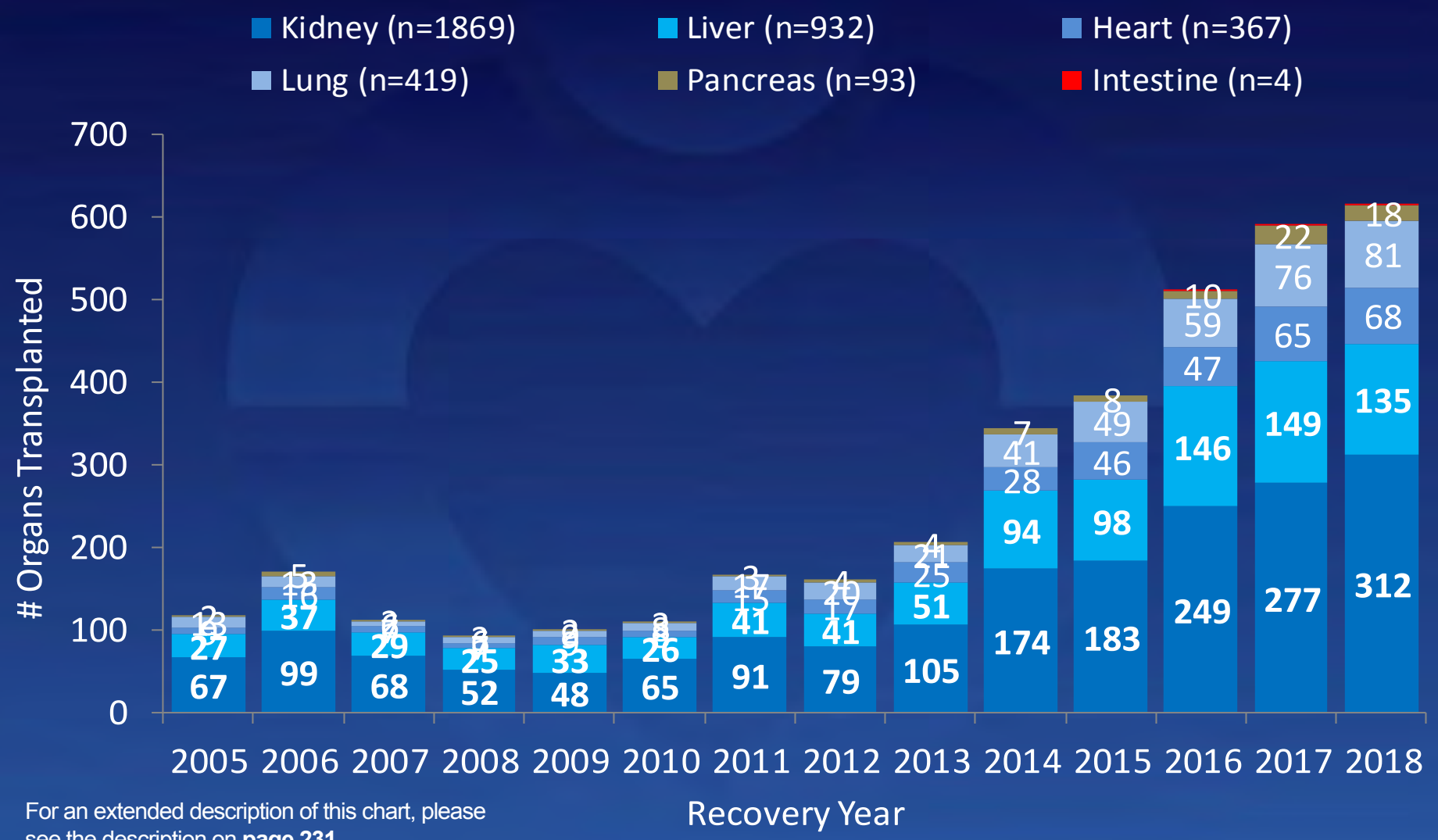
☒ **Credentials verified for all surgeons* performing recovery.**
*** (Credentialed surgeons are qualified healthcare professionals for blood type reporting and verification.)**

☒ **All perfusion solution lot # and expiration dates used during case have been given to the GLDP Perfusionist.**

As the responsible primary OPO coordinator, I have provided said documentation explained above for receipt and/or review by aforementioned surgeons who have attached their signatures.

OPO Coordinator _____ Date 4/2/19 Time 21:20

3684 Organs Transplanted from 1358 GLDP PHS Increased Risk Organ Donors 2005-2018

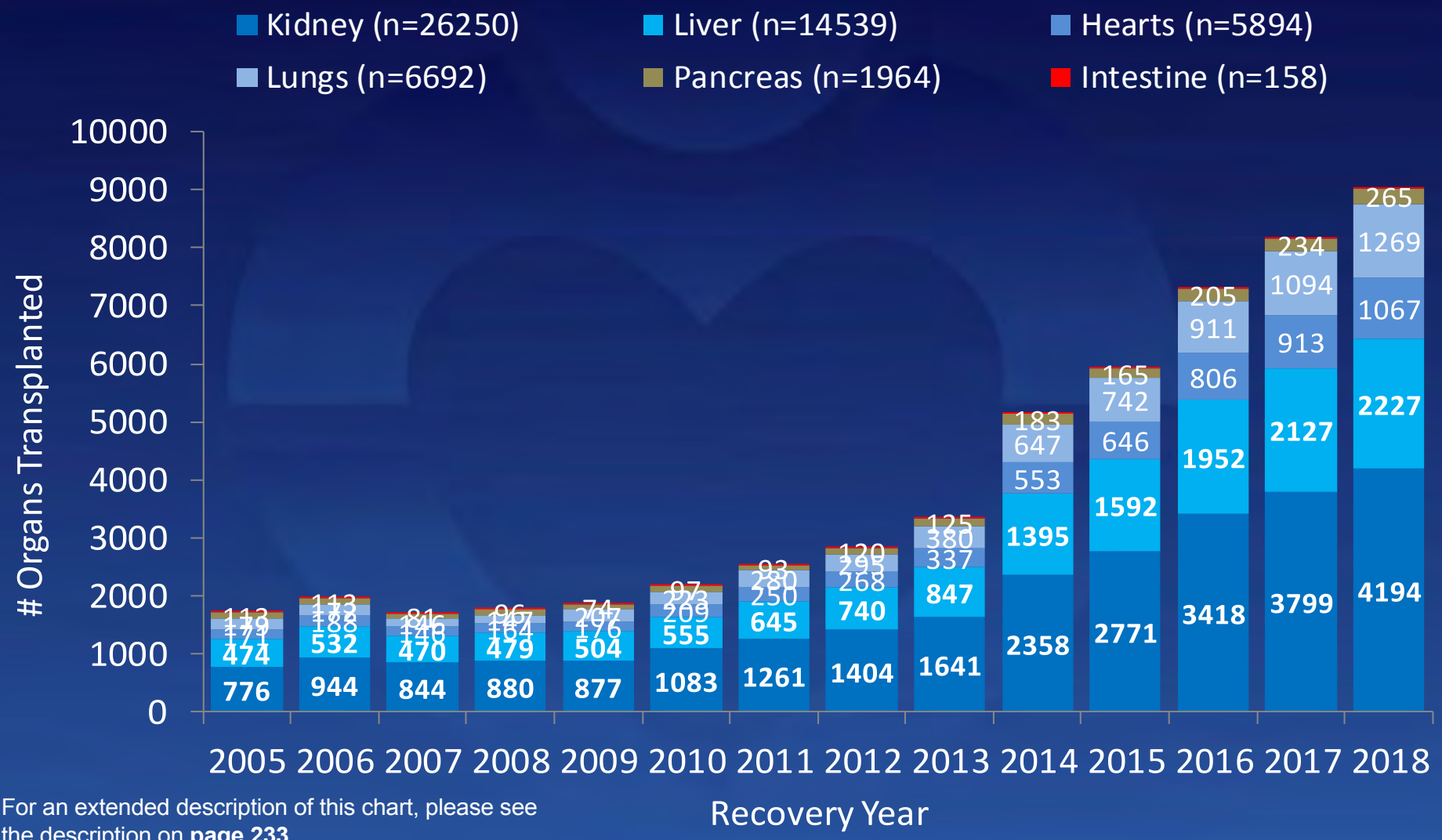


For an extended description of this chart, please see the description on **page 231**

Organ Discard Rates from GLDP PHS Increased Risk Organ Donors

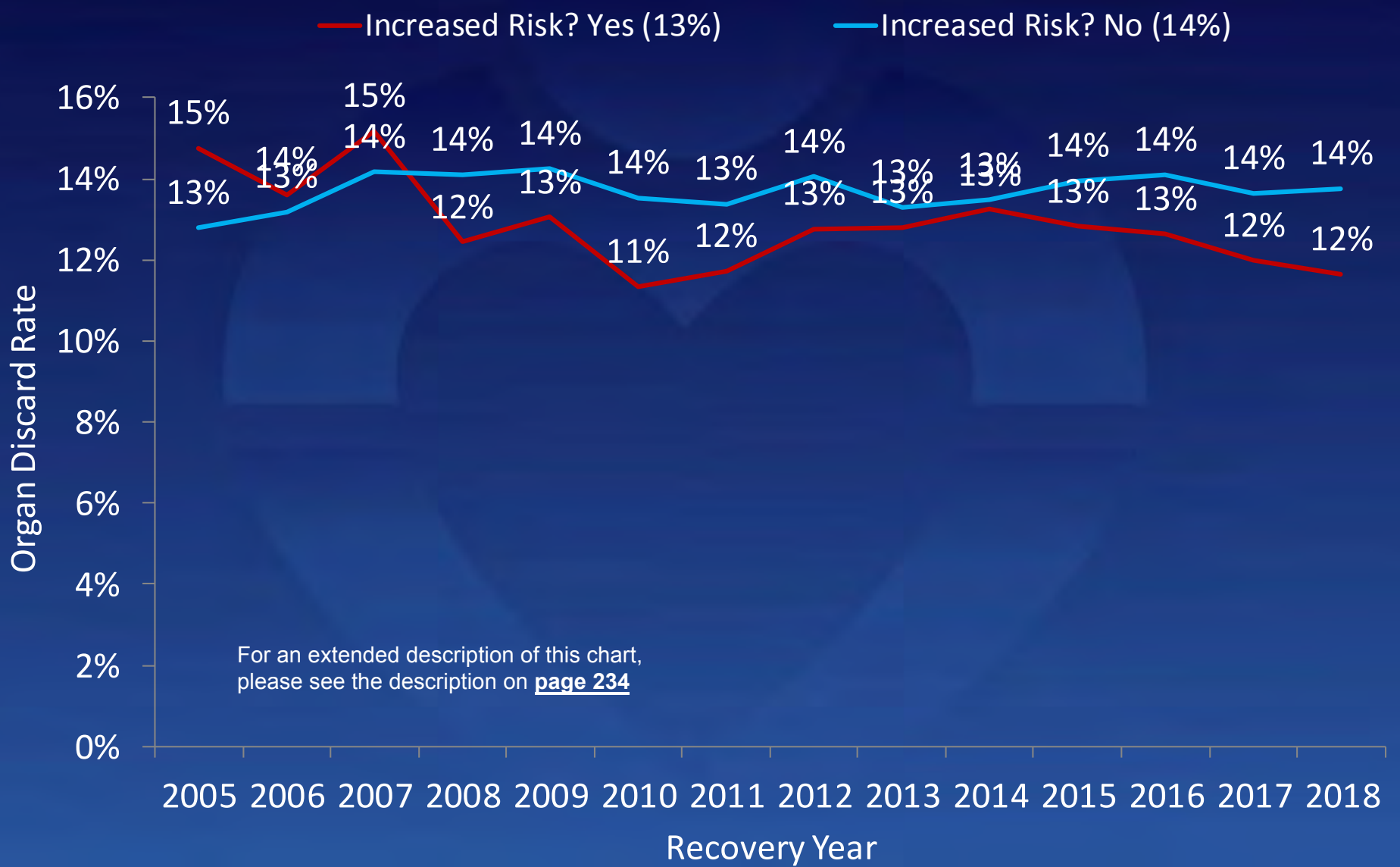
For an extended description of this chart, please see the description on **page 232**

55,497 Organs Transplanted from U.S. PHS Increased Risk Organ Donors 2005-2018



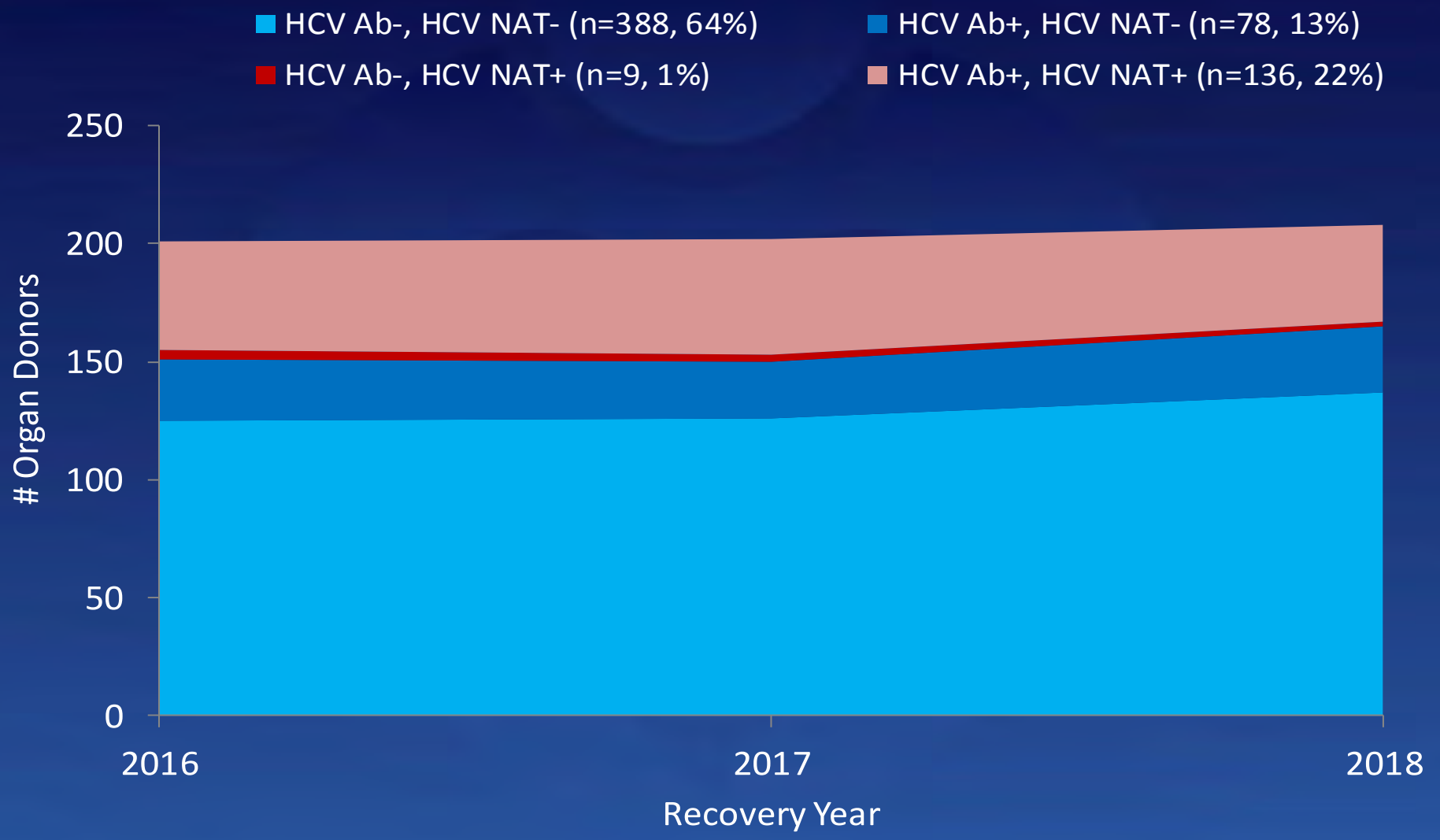
For an extended description of this chart, please see the description on **page 233**

Organ Discard Rates from U.S. PHS Increased Risk Organ Donors

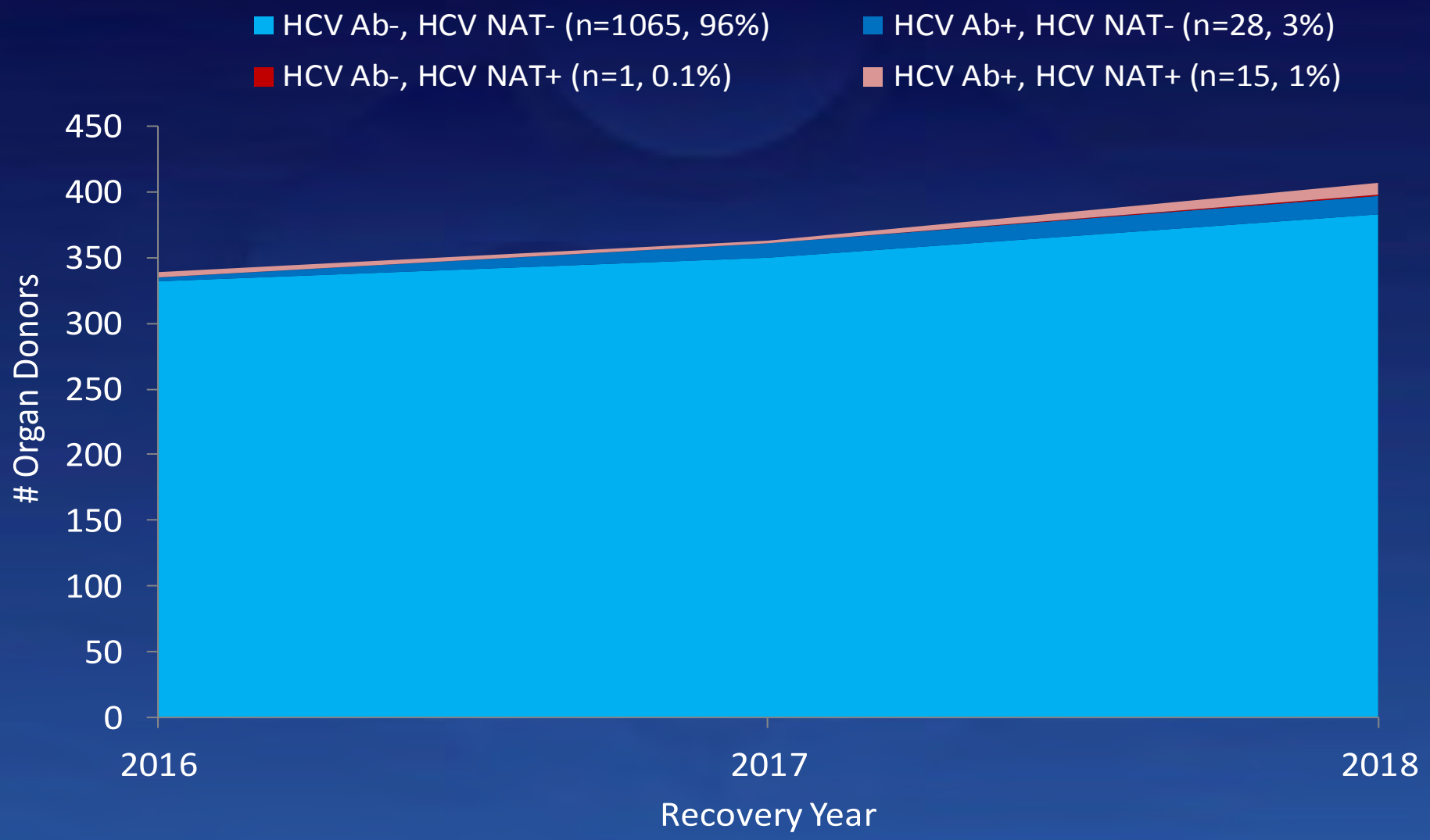


For an extended description of this chart, please see the description on **page 234**

611 GLDP PHS Increased Risk Organ Donors 2016 – 2018 by HCV Ab / HCV NAT Results



1109 GLDP Organ Donors NOT Identified as High Risk 2016 – 2018 by HCV Ab / HCV NAT Results



Summary

- Significant increase in the number of PHS Increased Donors and organ utilization since 2014
- Medical Social History Questionnaire is increasingly complex
- Routine availability of NAT testing pre-recovery

ASTS PERSPECTIVE ON PROPOSED REVISION TO GUIDELINE RECOMMENDATIONS

DIXON KAUFMAN, MD
Chairman, Division of Transplantation
University of Wisconsin

AST COMMENT ON PROPOSED REVISION TO GUIDELINE RECOMMENDATIONS

NICOLE TURGEON, MD

Professor of Surgery, Division of Transplantation, Department of Surgery, Emory University School of Medicine

Director, Clinical Islet Transplant Program, Emory Transplant Center

Director of Pancreas Transplantation, Emory Transplant Center

Surgical Director, Living Donor Kidney and Living Donor Pancreas Transplant Programs, Emory Transplant Center

Director, Kidney Transplant Program, Children's Healthcare of Atlanta

American Society of Transplantation Comment on Increased Risk Donor Definitions

Dr. Nicole Turgeon
AST Councilor-at-Large
April 15-16, 2019

American Society of Transplantation

- Founded in 1982
- Largest transplant organization in North America, with over 4,000 members representing the comprehensive transplant team:
  - physicians and surgeons across all organ specialties, infectious disease experts, pharmacists, advanced practice providers, basic/clinical/translational researchers, psychosocial professionals, transplant administrators, etc.

Risk is Relative…

The comparative risk of transplant versus the small risk of HIV, HBV, and HCV transmission- particularly in the era of treatment- must be considered

- Long waits for organs for many
  - Risk tolerance feels different as illness progresses and a candidate remains on the wait list
  - Other risks besides infectious disease (e.g. donor age, organ quality, cold ischemic time)

Put into Perspective - Comparative risks

Risk factor	Per 10,000
Being struck by lightning in your lifetime (80 yrs)	1
Dying in a plane crash in your lifetime	2
Dying in a car accident	125
Dying crossing the street	16
Missing HIV with NAT[1,2]	0.04-5
Missing HCV with NAT[1,2]	0.03-32
Dying if no liver transplant in next 3 months with MELD 20-29	2,000
Dying on kidney transplant waitlist in next year	900
Acquiring HCV per year of hemodialysis[3,4]	37

Courtesy of Peter Chin-Hong, MD, UCSF

1. Kucirka L et al. ***Am J Transplant*** 2011;11(6):1188-200.
2. Kucirka L et al. ***Am J Transplant*** 2011;11(6):1176-87.
3. Patel RR et al. ***Am J Kidney Dis*** 2010;56(2):371-8.
4. Kalantar-Zadeh K et al. ***J Am Soc Nephrol*** 2007;18(5):1584-93.

HCV Antiviral Revolution for Adults

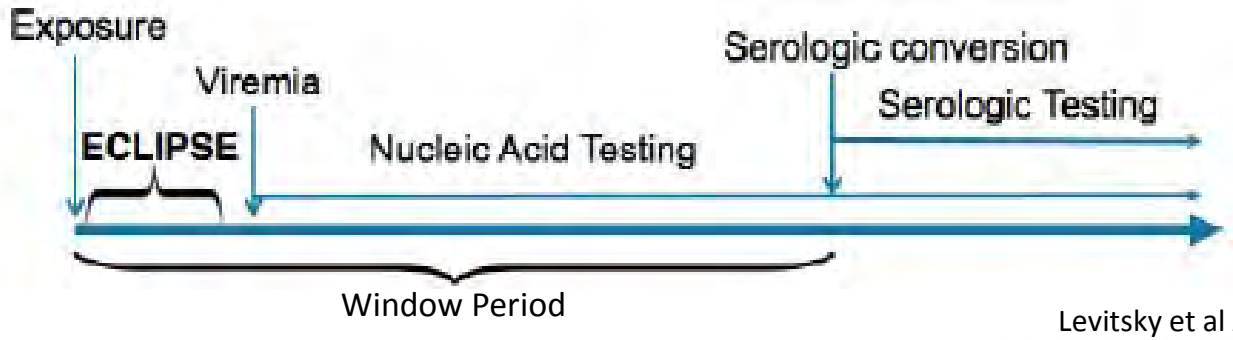
Year	Trade Name	Generic Name	Genotypes	Success (SVR rate)
2013	Olysio	Simepravir	1	
2013	Sovaldi	Sofosbuvir (+Sim)	1,2,3,4	95-97%
2014	Harvoni	Ledispasvir / sofosbuvir	1,4,5,6	93-100%
2014	Viekira Pak	Dasabuvir/ombitsavir/pariteprevir/ R	1	95-96%
2015	Technivie	Ombitsavir/paritaprevir/R	4	91-100%
2015	Daklinza	Daclatasvir	3	96-100% (not ESLD)
2016	Zepatier	Elbasvir/Grazoprevir	1,4	92-100% (inc HD/CKD)
2016	Epclusa	Sofosbuvir / velpatasvir	1,2,3,4,5,6	95-100%
2017	Vosevi	Sofosbuvir / velpatasvir/ voxilaprevir	1,2,3,4,5,6	96-98% (in Rx failures)
2017	Mavyret (8w)	Glecaprecvir / pibrentasvir	1,2,3,4,5,6	92-100% (inc HD/CKD)

Question 1: Is a new term needed to replace current term 'PHS Increased Risk Donor' ?

- Yes, this term can be confusing to transplant candidates!
  - Emphasizes the negative (though clearly more neutral than previous terminology!)
  - Can leave candidate with more questions than answers
    - Window periods
    - False positives
  - No specific term suggestion, but recommend working with psychosocial professionals to develop a new term

HCV "Positive" Donor - definitions

HCV Ab	HCV NAT	Means	Transmit
+	+	Active infection	Yes
+	-	Cleared Treated False +	None documented
-	+	WP infection False +	Yes



Levitsky et al AJT 2017

Risk of HIV, HCV window period infection by CDC risk factor: Serology (ELISA) vs NAT Testing

Risk per 10,000 donors	HIV ELISA	HIV NAT	HCV ELISA	HCV NAT
Men who have sex with men	10.2	4.2	32.5	3.5
IV Drug Users	12.1	4.9	300.6	32.4
Hemophiliacs	0.086	0.035	0.26	0.027
Commercial sex worker	6.6	2.7	114.9	12.3
Sex with a partner in above categories	0.7	0.3	114.9	12.3
Blood product exposure	1.5	0.6	4	0.4
Incarceration	2.3	0.9	7.2	0.8

American Journal of Transplantation 2011; 11: 1176–1187

False Negatives

- Window Phase by Donor Serologic and Nucleic Acid Testing (NAT)

Virus	Serology	4th gen Ag/Ab	NAT
HIV	17-22 days	~7-16 days	5-9 days
HBV	35-44 days		20-22 days
HCV	~66 days	40-50 days	3-7 days

Humar *et al*. ***Am J Transplant***. 2010; 10: 889-899. ; Orlowski *et al*. ***Am J Transplant***. 2009; 9: 555.
Thedoropoulos *et a*l. ATC 2012. Abstract LB17. Michael Ison, MD. Northwestern Univ

Question 2: Should donors continue to be identified based on risk factors for HIV, HBV, HCV?

- High profile diseases with long-standing implications- inadvertent transmission could certainly affect trust in the system
- Continued transparency and understanding anticipated risks based upon donor behavior must be communicated to recipients
  - Enhanced communication about other infectious and non-infectious risks should not be sacrificed by these higher profile infections
  - Education to communicate both anticipated and unanticipated transmission for donors need to be explained to candidates.

Question 2: Should donors continue to be identified based on risk factors for HIV, HBV, HCV?

- The AST supports continued identification based on HIV/HBV/HCV risk and suggests adding it in the context of all transmission potential as part of the routine education of candidates.

Question 3: Should time be shortened from 12 months?

- Data is not publicly available yet to make a determination here; however,
  - The AST's Infectious Disease Community of Practice is supportive of a significant shortening of this time period based on the best evidence available to substantially mitigate risk
  - We also support the collection of information about timing of risk, if possible, so that this time period can be further honed to most accurate time period.

Question #4: Are there specific criteria which should be eliminated or revised?

- We've received minimal feedback from our membership on this due to the limits of the published data available.
- We believe that lower risk events could be safely eliminated:
  - Hemodialysis
  - Blood product exposure (i.e. hemodilution)

Thank you

The American Society of Transplantation appreciates this opportunity to provide input on this topic that is so important to our patients and our profession.

AOPO COMMENT ON PROPOSED REVISION TO GUIDELINE RECOMMENDATIONS

Diane Brockmeier, BSN, MA
President and CEO
Mid-America Transplant Services (MTS)

aopo

association of
organ procurement organizations®

HHS Advisory Committee on Blood & Tissue Safety & Availability

Diane Brockmeier
AOPO President

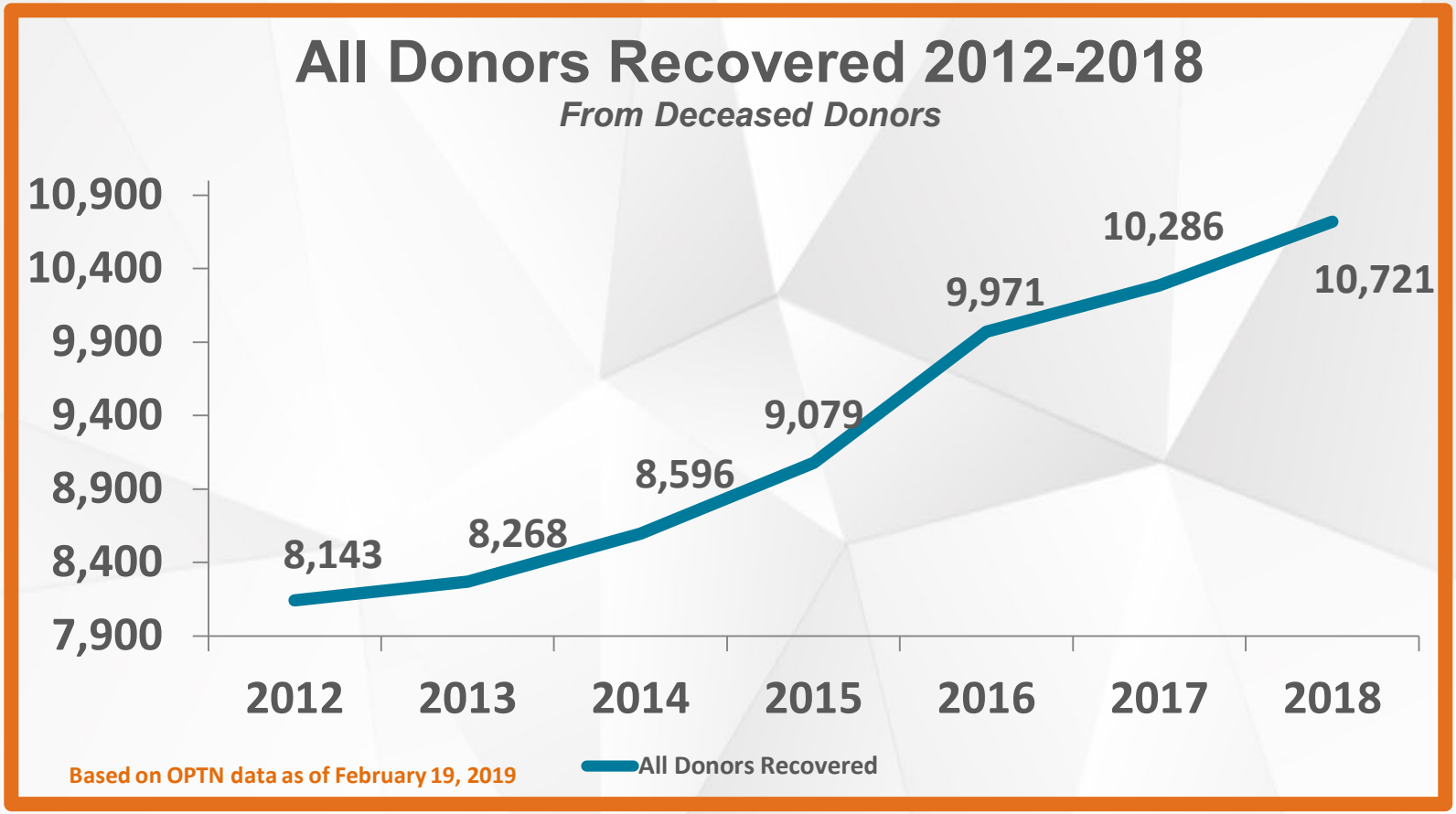
Association of Organ Procurement Organizations – AOPO

- Incorporated in 1984
- AOPO is a non-profit organization acting as the unified voice for all of the 58 federally designated organ procurement organizations (OPOs) in the US
- OPOs are the primary organizations responsible for the identification of donors and the safe and timely recovery, preservation and transportation of organs for transplant

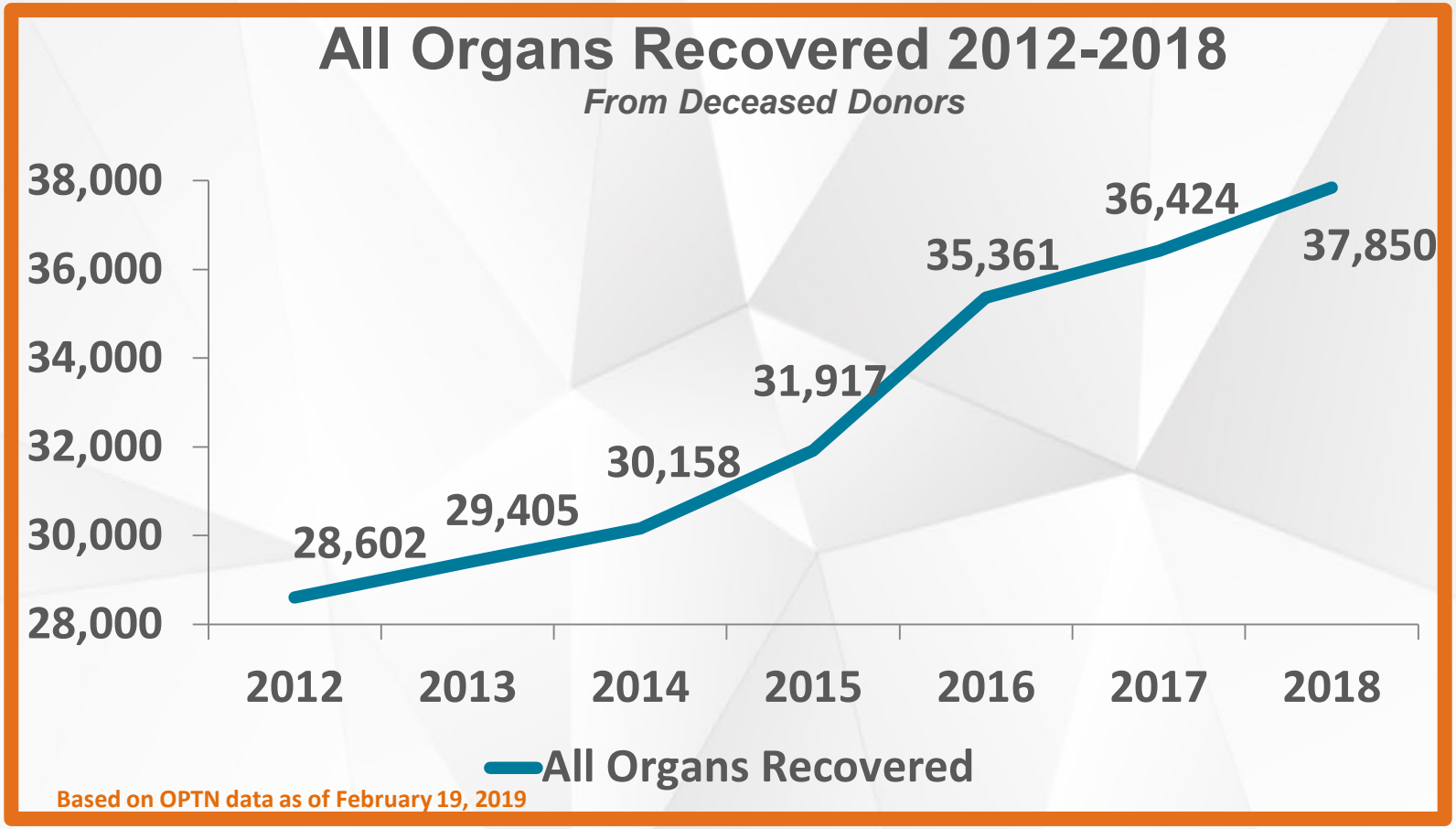
AOPO's Mission and Vision

MISSION: To help member OPOs maximize the availability of organs and tissues for transplantation and enhance the quality, effectiveness and integrity of the donation process.

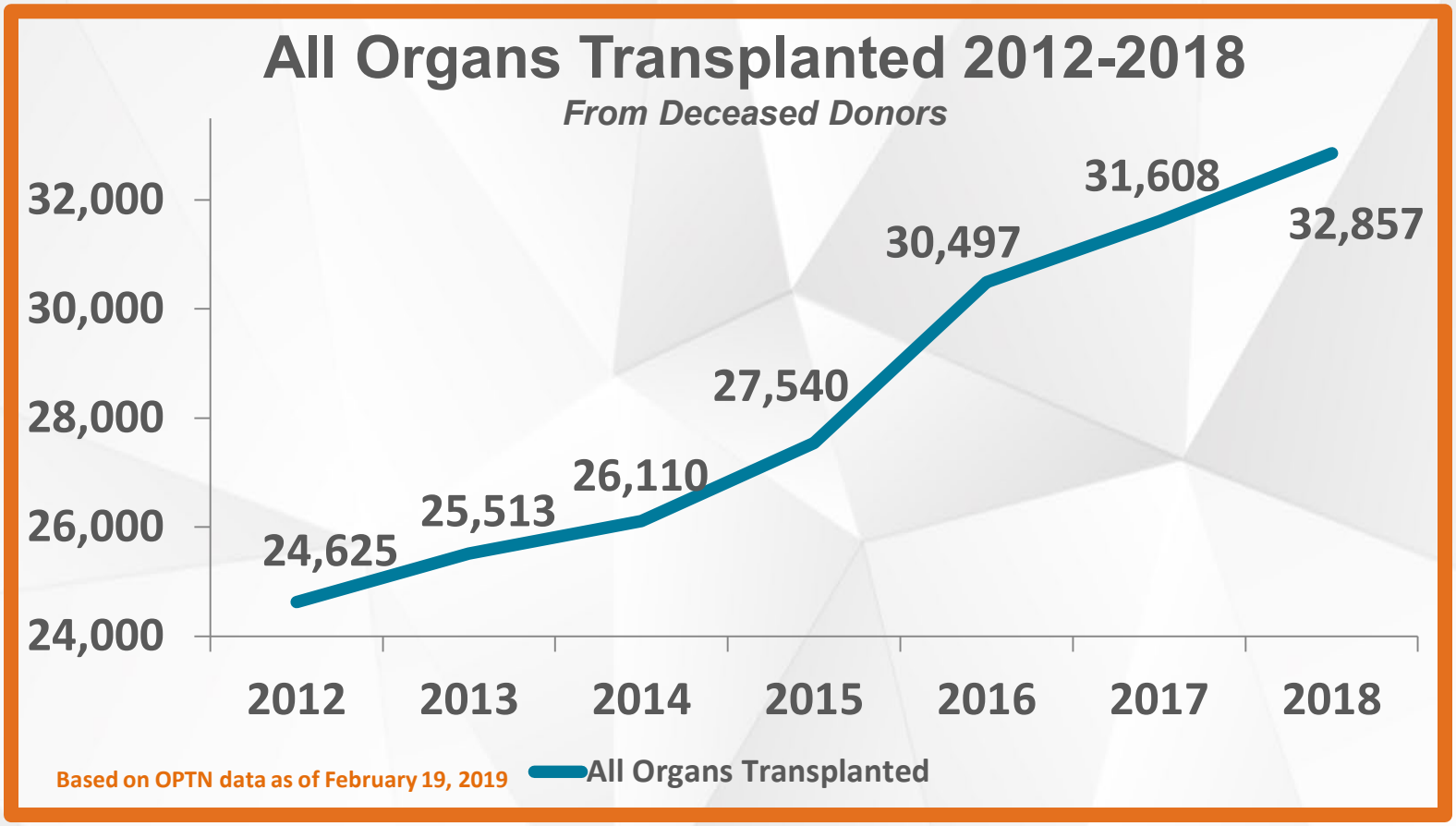
VISION: Those in need of a transplant receive donated organs or tissues in a timely manner in order to end deaths on the waiting list.



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



For an extended description of this chart, please see the description on **page 236**



aopo association of organ procurement organizations®

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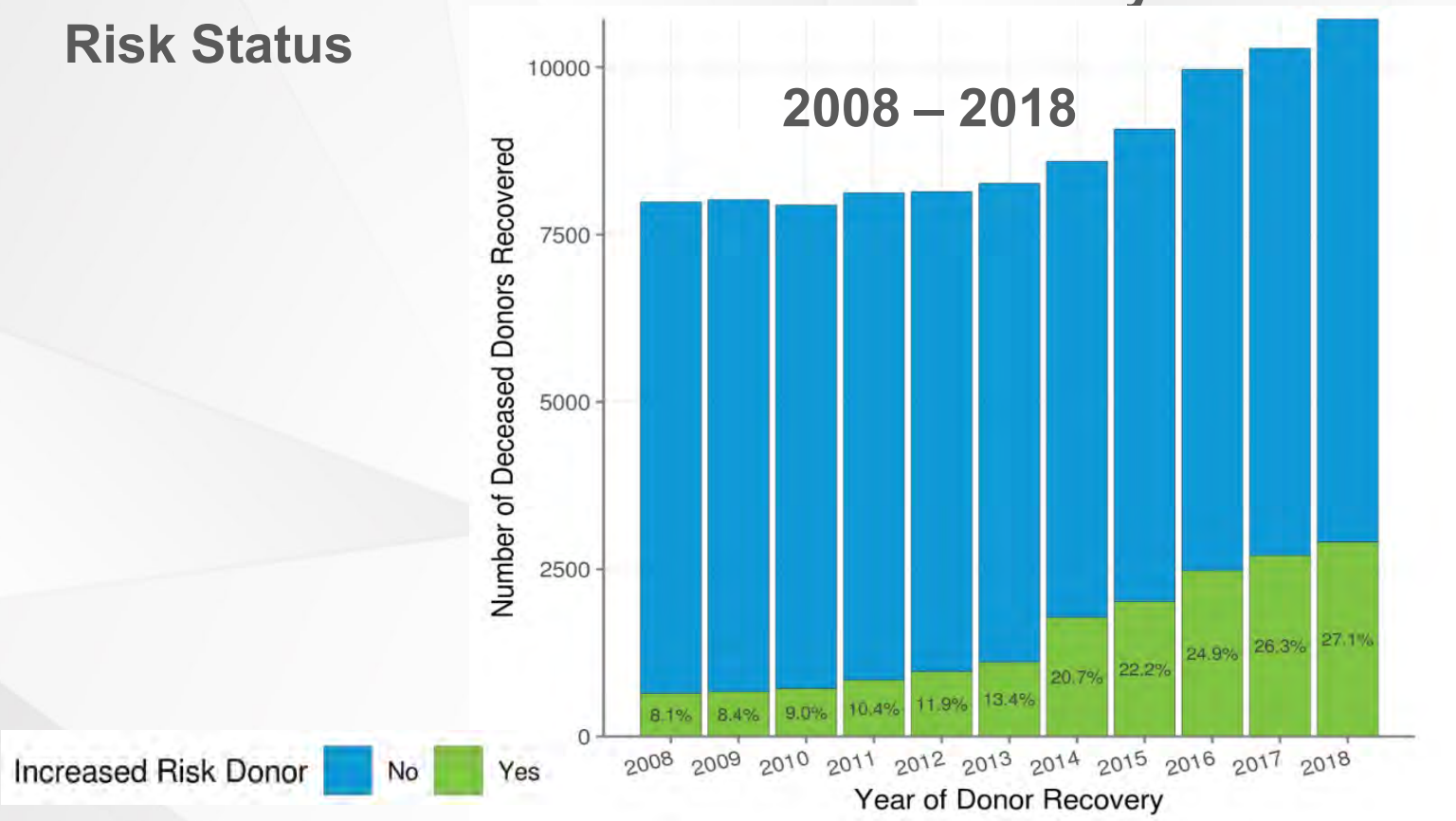
For an extended description of this chart, please see the description on **page 237**

Number of Deceased Donors Recovered by Year and PHS Increased Risk Status



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

% PHS High Risk Donors by DSA 1/1/2017 – 12/31/2018

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For an extended description of this map, please see the description on **page 228**

AOPO Conclusions

- Appreciative of effort to consider changes to PHS IRD
- IR donors identified through extensive interviews/serological testing
- Medical-Social Questionnaire “accuracy” limited by the reliability of the historian
- Transmission of information to transplant centers
  - Documentation includes Donor Net
  - Pre-recovery time-out and disclosure signed by recovery surgeon

AOPO Conclusions *(cont'd)*

- Does the available information support a reduction of the current 12 month risk behaviors time frame?
  - Would defer to our medical colleagues as this is a medical decision
  - For consideration, NAT testing in routinely available in real-time for all OPOs

- Is there a more appropriate term than "increased risk donor" to designate donors with risk factors for undetected HIV, HBV, or HCV infection?
  - Yes: Suggest changing the name to a more neutral term
  - High risk verbiage negatively perceived by donor families

- Should some criteria for increased donors be modified?


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PHS Guidelines for Reducing HIV, HCV, and HBV Through Organ Transplantation

- Does the available information support a reduction of the current 12-month risk behaviors time frame for determining Increased Risk Donor designation?
- Is there a more appropriate term than "Increased Risk Donor" to designate donors with risk factors for undetected HIV, HBV, or HCV infection?
- Should some criteria for Increased Risk Donors be modified (e.g., hemodilution of specimen used for HIV, HBV, or HCV testing, history of STD, or outpatient hemodialysis)?

Recap Day One

ADJOURNMENT
DAY ONE

Extended Descriptions

Organ Vigilance through DTAC

The chart shows the flow of communication within an organ vigilance system through DTAC that involves transplant centers, OPOs, OPTN/UNOS, and government agencies (CDC, HRSA, and FDA). On the left side of the chart are Transplant Centers and OPOs. On the right side of the chart are CDC, HRSA, and FDA. On the top of the chart (above DTAC) is Patient Safety/Member Quality. There is a two-way arrow between Transplant Centers and OPOs. There are two one-way arrows pointing from Transplant Centers and OPOs to DTAC. There are three one-way arrows pointing from DTAC to CDC, HRSA, and FDA. There is a two-way arrow between CDC and FDA. There is one curved arrow pointing from DTAC to Transplant Centers, and a one-way arrow pointing from DTAC to Patient Safety/Member Quality. There is a one-way arrow pointing from CDC to Patient Safety/Member Quality, and another one-way arrow pointing from Patient Safety/Member Quality to Transplant Centers. Go back to **page 5**

DTAC case evaluation

The left-to-right flow chart shows DTAC's case evaluation and adjudication process. On the left side of the chart are Case adjudication and Not a Case. In the middle of the chart are categories of the cases determined by DTAC, including Proven, Probable, Possible, Prevented, Unlikely, or Excluded. On the right of the chart are severity indexes associated with different cases. Cases that are proven, probable, or possible may have an severity index of death, severe, non-severe, non-evaluable, or potential for late morbidity. Cases that are classified as prevented may have an severity index of potential for late morbidity; non-severe, not sure if Rx needed; non-severe but treatment needed; or severe. Cases that are considered unlikely or excluded have an severity index of no severity indication.

There is a line between Case adjudication and Not a Case, and a line between Case adjudication and each of the case categories. There are also arrows and lines pointing from the case categories to the severity indexes. There is a star on the top-right corner of Not a Case. Go back to **page 7**

Chagas Disease / West Nile Virus: Emerging problems?

2011 Incidence in US

Incidence per 10,000	States
0.00	Washington, Oregon, South Dakota, New Hampshire, Maine
0.01 - 0.99	California, Nevada, Arizona, New Mexico, Colorado, Kansas, Texas, Minnesota, Missouri, Louisiana, Mississippi, Georgia, Florida, South Carolina, North Carolina, Tennessee, Kentucky, Illinois, Indiana, Ohio, Michigan, Maryland, Delaware, New Jersey, Pennsylvania, New York, Connecticut, Rhode Island, Massachusetts
1.00 - 2.49	California, Utah, Arizona, New Mexico, Texas, Nebraska, Iowa, Arkansas, Louisiana, Mississippi, Florida, Tennessee, Kansas, Virgina, West Virgina, New York
2.50 - 9.99	California, Nevada, Wyoming, Colorado, North Dakota, Nebraska, Iowa, Missouri, Oklahoma, Mississippi, Georgia, Tennessee, Illinois, Indiana, Michigan, Vermont
> = 10.00	Idaho, Montana, Kansas, Missouri, Mississippi

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Chagas Disease / West Nile Virus: Emerging problems?

2012 Incidence in US

Incidence per 10,000	States
0.00	Oregon
0.01 - 0.99	Washington, Idaho, California, Nevada, Utah, Arizona, New Mexico, Colorado, Nebraska, Kansas, Oklahoma, Texas, Minnesota, Michigan, Missouri, Arkansas, Louisiana, Mississippi, Georgia, Florida, South Carolina, North Carolina, Tennessee, Kentucky, Illinois, Indiana, Ohio, West Virginia, Maryland, Delaware, New Jersey, Pennsylvania, New York, Connecticut, Rhode Island, Massachusetts, Vermont, New Hampshire, Maine
1.00 - 2.49	California, Utah, Arizona, New Mexico, Texas, Nebraska, Iowa, Arkansas, Louisiana, Mississippi, Florida, Tennessee, Kansas, Virgina, West Virgina, New York
2.50 - 9.99	California, South Dakota, Nevada, Wyoming, Colorado, North Dakota, Nebraska, Iowa, Missouri, Oklahoma, Mississippi, Georgia, Tennessee, Illinois, Indiana, Michigan, Vermont
> = 10.00	Idaho, Montana, North Dakota, South Dakota, Colorado, Nebraska, Kansas, Oklahoma, Texas, Mississippi, Louisiana, Alabama, Georgia, Minnesota, Iowa, Missouri, Arkansas, Illinois, Indiana, West Virgina

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IVDU and HCV

The U.S. map shows the percentage of HCV-positive donors (per 100 deceased donors recovered for TX) varies across the country. In 2017, up to 25% of deceased donors were HCV positive, with the highest percentages (15-20, and 20-25%) reported in the northeastern parts of the country, and lower percentages in the middle and west parts of the country.

Donors	States
[0, 5]	Hawaii, Oregon, California, Idaho, Nevada, Utah, Colorada, North Dakaota, South Dakota, Minnesota, Nebraska, Kansas, Oklahoma, Texas, Missouri, Arkansas, Illinois, Georgia, North Carolina, Florida
(5,10)	Alaska, Washington, Idaho, Montana, Nevada, California, Arizona, New Mexico, Wisconsin, Michigan, Iowa, Missouri, Alabama, Tennessee, Illinois, South Carolina, Virginia, Washington D.C., New Jersey, New York, Connecticut, Massachusetts, Florida
(10,15)	Florida, Missouri, Arkansas, Tennessee, Kentucky, Indiana, Ohio, Pennsylvania, West Virginia, Maryland, North Carolina, New York
(15, 20)	Pennsylvania, Delaware, Connecticut, Massachusetts, Vermont, New Hampshire, Maine
(20, 25)	Ohio, New York

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Increased Risk Donor issues vs Graft Issues:

Two graphs demonstrating the risk of liver graft failure (left graph) is much lower than the risk of HIV/HCV transmission (right graph) from increased risk donors. On the bottom of the graphs is a notation for dark blue, which indicates the range of risk of graft failure or disease transmission depending on donor factors.

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Results: Indication for PHS IR Designation

The Bar graph shows IVDA (16%) and incarceration (15%) as main indications for PHS IR designation (N=288)

Indication	Number (%)
IVDA	46 (16)
Incarceration	43 (15)
Sex with Individual with IVDU	22 (8)
Poor Historian	22 (8)
Hemodilution	21 (7)
Hemodialysis	11 (4)
Sex with Indiv. Who Had Sex for Money/Drugs	5 (2)
Sex for Money or Drugs	3 (1)
Dx/Rx for STI	3 (1)
Sex with Indiv. Known/Susp. With HIV/HBV/HCV	1 (0)
MSM	1 (0)
Female Who Had Sex with MSM	1 (0)
Child: Born to MO with or IR for HIV/HCV/HBV	0 (0)
Child: Breastfed by MO with or IR for HIV	0)0)

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Results: N=179 donors with 1 Criterion only for PHS IRD

Bar chart highlighting among donors who met only one criterion for PHS IRD, incarceration is the most common reason (N=179)

Indication	Number (%)
Incarceration	46 (26)
IVDA	43 (24)
Poor Historian	22 (12)
Hemodialysis	22 (12)
Hemodilution	21 (12)
Dx/Rx for STI	11 (6)
MSM	5 (3)
Sex with Individual with IVDU	3 (2)
Sex with Indiv. Known/Susp. With HIV/HBV/HCV	3 (2)
Sex with Indiv. Who Had Sex for Money/Drugs	1 (1)
Sex for Money or Drugs	1 (1)
Child: Born to MO with or IR for HIV/HCV/HBV	1 (1)
Female Who Had Sex with MSM	0 (0)
Child: Breastfed by MO with or IR for HIV	0 (0)

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HIV epidemiology (extended description)

Left: The bar graph shows estimated HIV incidences among persons aged at least 13 years remained stable (around 40,000) in the U.S. between 2010 and 2016. Note: The estimates were derived from a CD4 depletion model using HIV surveillance data. Bars indicate the range of the lower and upper bounds of the confidence intervals for the point estimate.

Right: The multiple-line graph demonstrates the trends in estimated HIV incidences in different age groups in the U.S. between 2010 and 2016. The incidence slightly reduced in the 13-24-year group, increased in 25-34-year group, and remained relatively stable for other age groups (35-44, 45-54, and 55 years and older). In 2010, the incidence was highest in the 13-24-year group, followed by 25-34, 35-44, 45-54, and 55 and above groups. From 2011 to 2016, the incidence was highest in the 25-34-year group, followed by 13-24, 35-44, 45-54, and 55 and above groups.

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Evolution of HIV treatment (extended description)

1987 - Zidovudine (NRTI)
1991 - Didanosine (NRTI)
1992 - Zalcitabine (NRTI) *
1994 - Stavudine (NRTI) *
1995 - Lamivudine (NRTI), Saquinavir (PI)
1996 - Indinavir (PI)*, Nevirapine (NNRTI), Ritonavir (PI)
1997 - Combivir (FDC), Delavirdine (NNRTI)*, Nelfinavir (PI)*
1998 - Abacavir (NRTI), Efavirenz (NNRTI)
1999 - Amprenavir (PI)*
2000 - Didanosine EC (NRTI), Kaletra (FDC), Trizivir (FDC)
2001 - Tenofovir DF (NRTI)
2003 - Atazanavir (PI) Emtricitabine (NRTI) Enfuvirtide (FI) Fosamprenavir (PI)
2004 - Epzicom (FDC), Truvada (FDC)
2005 - Tipranavir (PI)
2006 - Atripla (FDC), Darunavir (PI)
2007 - Maraviroc (CA,) Raltegravir (INSTI)
2008 - Etravirine (NNRTI)
2011 - Complera (FDC), Nevirapine XR (NNRTI), Rilpivirine (NNRTI)
2012 - Stribild (FDC)
2013 - Dolutegravir (INSTI)
2014 - Cobicistat (PE), Elvitegravir (INSTI), Triumeq (FDC)
2015 - Evotaz (FDC), Genvoya (FDC), Prezcobix (FDC)
2016 - Descovy (FDC), Odefsey (FDC)
2017 - Juluca (FDC)
2018 - Biktarvy (FDC), Cimduo (FDC), Delstrigo (FDC), Doravirine (NNRTI), Ibalizumab (PAI), Symfi (FDC), Symfi Lo (FDC,) Symtuza (FDC)

* *No longer available*

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HIV D-/R+ in era of effective ART (extended description)

A Survival

The statistical curves compare the patient survival of HIV-infected kidney transplant patients with the U.S. Scientific Registry of Transplant Recipients (SRTR) data for all kidney-transplant recipients and SRTR data for kidney-transplant recipients 65 years of age or older. Patient survival rates at 1 year and 3 years were about 95% and 91%, respectively. Patient survival rates were generally between those reported in the SRTR database for kidney-transplant recipients 65 years of age or older and for all kidney-transplant recipients.

B Graft survival

The statistical curves compare the graft survival of HIV-infected kidney transplant patients with the U.S. Scientific Registry of Transplant Recipients (SRTR) data for all kidney-transplant recipients and SRTR data for kidney-transplant recipients 65 years of age or older. Graft survival rates at 1 year and 3 years were about 90% and 74%, respectively. Graft survival rates were generally between those reported in the SRTR database for kidney-transplant recipients 65 years of age or older and for all kidney-transplant recipients.

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HIV D-/R+ in era of effective ART (continued)

2003-2009 HIV Transplant Recipient (HIV TR) Study

Patient survival:
The statistical curves show that the 1-year, 2-year, and 3-year patient survival rates (95% CI) were 76%, 72%, and 60% in HCV/HIV-coinfected patients; and 92%, 81%, and 79% in HCV mono-infected patients.

Graft survival:
The statistical curves show that the 1-year, 2-year, and 3-year graft survival rates (95% CI) were 72%, 65%, and 53% in HCV-HIV-coinfected patients; and 88%, 77%, and 74% in HCV mono-infected patients.

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HOPE donors and transplants (extended description)

The top-to-bottom flow chart shows the donor and recipient selection process in the HOPE IN ACTION study. On the top of the chart is “eligible HIV positive kidney or liver candidates.” In the middle of the chart is “UNOS organ offers per availability ‘Natural randomization’.” On the bottom of the chart are “HIV negative donor/positive recipient” and “HIV positive donor/positive recipient.”

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HCV epidemiology (extended description)

Figure 4.1

Reported number of acute hepatitis C cases – United States, 2001-2016
The line graph shows that the number of acute hepatitis C cases reported to CDC dropped between 2001 (around 1,600 cases) and 2004 (around 700 cases), remained relatively stable between 2004 and 2010, but drastically increased between 2010 and 2016 (more than 3,000 cases).
Source: CDC, National Notifiable Diseases Surveillance System (NNDSS). CDC logo, DEPARTMENT OF HEALTH AND HUMAN SERVICES. USA

Figure 4.2

Incidence of acute hepatitis C, by age group – United States, 2001-2016
The multiple-line graph shows the changes in the number of acute hepatitis C cases (per 100,000 population) reported to CDC in different age groups between 2001 and 2016.

Between 2001 and 2004, the numbers of reported cases dropped in the 40-49, 30-39, and 50-59 years groups; the numbers remained relatively stable in the other age groups. During this period, the number of reported cases was highest in the 40-49 years group, followed by 30-39, 20-29, 50-59, 60 and older, and 0-19 years groups.

Between 2004 and 2010, the numbers remained relatively stable in all age groups.

Between 2010 and 2016, the numbers increased drastically in the 20-29 and 30-39 years groups. During the same period, the reported cases moderately increased in the 40-49 and 50-59 years groups, and remained relatively stable in the 60 years and older as well as 0-19 years groups. Overall, the number of reported cases was highest in the 20-29 years group, followed by 30-39, 40-49, 50-59, 60 and older, and 0-19 years groups.

Source: CDC, National Notifiable Diseases Surveillance System (NNDSS). CDC logo, DEPARTMENT OF HEALTH AND HUMAN SERVICES. USA

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HCV treatment (extended description)

The bar chart shows that advancements in HCV treatment (1989 to 2014) has drastically increased patient survival rates (SVR; %). Between 1989 and 1998, IFN-alpha was the only treatment option, and the survival rate was around 20%. Between 1998 and 2001, treatment options included IFN-alpha and RBV, and the survival rate was around 40%. Between 2001 and 2011, treatment options included PEG-IFN-alpha and RBV, and the survival rate was close to 50%. Between 2011 and 2014, treatment options included 1st generation PI-based triple, and the survival rate was around 75%. Since 2014, new DAA combinations became available, and the survival rate has increased to close to 100%.

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Increasing number and quality of HCV+ donor organs over time (extended description)

The multiple-line graph shows the prevalence (percent) of HCV positive donors (identified based on antibody) between 2000 and 2016. The percentage of deceased donors who died of opioid overdose and were HCV positive remained relatively stable between 2000 and 2010 (around 10%); however, the percentage drastically increased from 2010 to 2016 (near 30%). In contrast, the percentage (less than 5%) of deceased donors who died of trauma or other medical conditions remained relatively stable from 2000 to 2016.

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Survival outcomes for different recipients with IRD transplant (extended description)

The figure contains four multiple-line graphs (A, B, C, and D), showing predicted survival outcomes for different recipients after accepting or declining an IRD kidney. The graphs show that the percentage of patients alive after transplant decreases as time goes on, and that overall accepting an IRD kidney appears to be associated with increased survival benefit. The following table shows the percent of patients alive 60 months after transplant.

Figure	Percent Alive (%)		
	Accepted IRD (base-case)	**Accepted IRD (worst-case)**	**Declined IRD**
A: 40 F, 3 months until non-IRD transplant	**93**	**90**	**92**
B: 65F, diabetic, 60 months to non-IRD transplant	**69**	**67**	**33**
C: 50 M, non-diabetic, 24 months to non-IRD transplant	**87**	**85**	**81**
D: 75 F, ABO, AB, PRA 100, diabetic, 24 months to non-IRD transplant	**51**	**49**	**44**

If not specified, the patient is Caucasian, non-diabetic, with a BMI of 25, PRA of 0, no previous transplants, and O blood type. M, male; F, female.

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% PHS High Risk Donors by DSA 1/1/2015 – 12/31/2016 (extended description)

Percentages	States
30-40%	New Mexico, Kentucky, Ohio, Pennsylvania, New York, Delaware, New Jersey, Connecticut, Rhode Island, Massachusetts, Vermont, New Hampshire, Maine
25-29%	Arizona, Texas, Louisiana, Alabama, Florida, Missouri, Illinois, Indiana, Michigan, Wisconsin, Virginia, Maryland, Connecticut, Massachusetts
20-24%	Washington, Oregon, Idaho, Montana, Wyoming, Colorado, Utah, Nevada, California, Texas, Arkansas, Mississippi, Tennessee, North Carolina, Virgina, West Virginia, Washington, DC, Ohio, Illinois, Pennsylvania, New Jersey, New York, Vermont
15-19%	California, Nevada, North Dakota, South Dakota, Nebraska, Wisconsin, Kansas, Oklahoma, Texas, Missouri, Mississippi, Georgia, South Carolina, Florida
<15%	Iowa, South Carolina

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% PHS High Risk Donors by DSA 1/1/2017 – 12/31/2018 (extended description)

Percentage	States
30-42%	Michigan, Wisconsin, Indiana, Ohio, Kentucky, Louisiana, Florida, North Carolina, West Virginia, Maryland, Delaware, Pennsylvania, New Jersey, Connecticut, Rhode Island, Massachusetts, New York, Vermont, New Hampshire, Maine
25-29%	Washington, Oregon, Idaho, Montana, Wyoming, Colorado, Texas, Missouri, Arkansas, Tennessee, Alabama, Florida, South Carolina, North Carolina, Virgina, West Virgina, Pennsylvania, New Jersey, New York
20-24%	California, Nevada, Idaho, Utah, Wyoming, Arizona, New Mexico, Texas, Iowa, Illinois, Arkansas, Mississippi, Florida, Virginal, Washington DC, Maryland
15-19%	California, North Dakota, South Dakota, Nebraska, Kansas, Oklahoma, Minnesota, Wisconsin, Missouri, Georgia
<15%	-

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% HCV Seropositive Donors by DSA 1/1/2015 – 12/31/2016 (extended description)

Percentages	States
12-16%	Ohio, Maryland, Delaware, New Jersey, Pennsylvania, Connecticut, Rhode Island, Massachusetts, Vermont, New Hampshire, Maine
7-11%	Arizona, New Mexico, Missouri, Arkansas, Louisiana, Florida, Tennessee, Kentucky, Illinois, Ohio, West Virginia, Virginia, Pennsylvania, New York
4-6%	Washington, Idaho, Montana, Wyoming, California, Nevada, Colorado, Texas, Oklahoma, Wisconsin, Michigan, Indiana. Mississippi, Alabama, Florida, North Carolina, Virgina, Washington DC, New Jersey, New York, Vermont
2-3%	Oregon, Idaho, California, Nevada, Utah, Wyoming, Texas, Kansas, Missouri, Illinois, Wisconsin, Georgia
<2%	North Dakota, South Dakota, Minnesota, Iowa, Nebraska, Arkansas, Tennessee, Mississippi, South Carolina

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% HCV Seropositive Donors by DSA 1/1/2017 12/31/2018 (extended description)

Percentages	States
12-16%	Kentucky, Ohio, Maryland, Delaware, New Jersey, Pennsylvania, New York, Connecticut, Rhode Island, Massachusetts, Vermont, New Hampshire, Maine
7-11%	California, Arizona, New Mexico, Iowa, Missouri, Arkansas, Louisiana, Mississippi, Alabama, Florida, South Carolina, North Carolina, Virgina, West Virgina, Tennessee, Illinois, Indianan, Wisconsin, Michigan, Pennsylvania, New York, New Jersey, Connecticut, Massachusetts
4-6%	Washington, Oregon, Idaho, Montana, Wyoming, California, Nevada, Colorado, Texas, Oklahoma, Wisconsin, Michigan, Illinois, Virgina, New York
2-3%	California, Nevada, Utah, Idaho, Wyoming, Texas, Kansas, Missouri, Arkansas, Georgia
<2%	North Dakota, South Dakota, Minnesota, Nebraska

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3684 Organs Transplanted from 1358 GLDP PHS Increased Risk Organ Donors 2005-2018

(extended description)

The stacked bar graph shows an overall increase in the number of organs transplanted from GLDP PHS increased risk organ donors each year from 2005 to 2018.

Recovery Year	Number of Organs Transplanted					
	Kidney (1869)	**Liver (932)**	**Heart (367)**	**Lung (419)**	**Pancreas (93)**	**Intestine (4)**
2005	67	27	9	13	2	0
2006	99	37	16	13	5	0
2007	68	29	7	6	2	0
2008	52	25	7	6	3	0
2009	48	33	9	9	2	0
2010	65	26	8	8	3	0
2011	91	41	15	17	3	0
2012	79	41	17	20	4	0
2013	105	51	25	21	4	0
2014	174	94	28	41	7	0
2015	183	98	46	49	8	0
2016	249	146	47	59	10	1
2017	277	149	65	76	22	2

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Organ Discard Rates from GLDP PHS Increased Risk Organ Donors

(extended description)

Recovery Year	Organ Discard Rate	
	Increased Risk	Non-increased Risk
2005	14%	14%
2006	24%	17%
2007	24%	23%
2008	25%	23%
2009	22%	25%
2010	16%	22%
2011	22%	26%
2012	24%	31%
2013	24%	27%
2014	25%	28%
2015	22%	27%
2016	20%	28%
2017	20%	24%
2018	19%	27%

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55,497 Organs Transplanted from U.S. PHS Increased Risk Organ Donors 2005-2018

(extended description)

Recovery Year	Number of Organs Transplanted					
	Kidney (26250)	**Liver (14539)**	**Heart (5894)**	**Lungs (6692)**	**Pancreas (1964)**	**Intestine (158)**
2005	776	474	171	179	113	2
2006	944	532	188	172	113	6
2007	844	470	146	146	81	6
2008	880	479	164	147	96	9
2009	877	504	176	207	74	8
2010	1083	555	209	223	97	14
2011	1261	645	250	280	93	7
2012	1404	740	268	295	120	8
2013	1641	847	337	380	125	11
2014	2358	1395	553	647	183	20
2015	2771	1592	646	742	165	14
2016	3418	1952	806	911	205	14
2017	3799	2127	913	1094	234	21
2018	4194	2227	1067	1269	265	18

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Organ Discard Rates from U.S. PHS Increased Risk Organ Donors (extended description)

Recovery Year	Organ Discard Rate	
	Increased Risk	Non-increased Risk
2005	15%	13%
2006	14%	13%
2007	15%	14%
2008	12%	14%
2009	13%	14%
2010	11%	14%
2011	12%	13%
2012	13%	14%
2013	13%	13%
2014	13%	13%
2015	13%	14%
2016	13%	14%
2017	12%	14%
2018	12%	14%

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All Donors Recovered 2012-2018 From Deceased Donors

Year	Number of donors recovered
2012	8,143
2013	8,268
2014	8,596
2015	9,079
2016	9,971
2017	10,286
2018	10,721

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All Organs Recovered 2012-2018
From Deceased Donors

Year	Number of donors recovered
2012	28,602
2013	29,405
2014	30,158
2015	31,917
2016	35,361
2017	36,424
2018	37,850

Based on OPTN data as of February 19, 2019

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All Organs Transplanted 2012-2018 From Deceased Donors

Year	Number of donors recovered
2012	24,625
2013	25,513
2014	26,110
2015	27,540
2016	30,497
2017	31,608
2018	32,857

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Number of Deceased Donors Recovered by Year and PHS Increased Risk Status

Year of Donor Recovery	Number of Deceased Donors Recovered	Percent of Increased Risk Donors (%)
2008	Between 7,500 and 10,000	8.1
2009	Between 7,500 and 10,000	8.4
2010	Between 7,500 and 10,000	9.0
2011	Between 7,500 and 10,000	10.4
2012	Between 7,500 and 10,000	11.9
2013	Between 7,500 and 10,000	13.4
2014	Between 7,500 and 10,000	20.7
2015	Between 7,500 and 10,000	22.2
2016	About 10,000	24.9
2017	More than 10,000	26.3
2018	More than 10,000	27.1

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