AETC AIDS Education & Training Center Program Southeast

The HOPE Act: Organ Donation for Persons Living with HIV

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Disclosures:

- In the last 24m, I have received research and DMSB funding from:
  - Consultancy:
    - Chimerix (Antivirals);
    - Cellerant (Heme/onc);
    - PWN Health (ID diagnostics)
    - Paratek (Antibiotics)
    - Abbott (ID diagnostics)
  - DSMB:
    - Visterra, Janssen, Cellerant, Merck

None of these will be discussed during this talk!

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Outline:

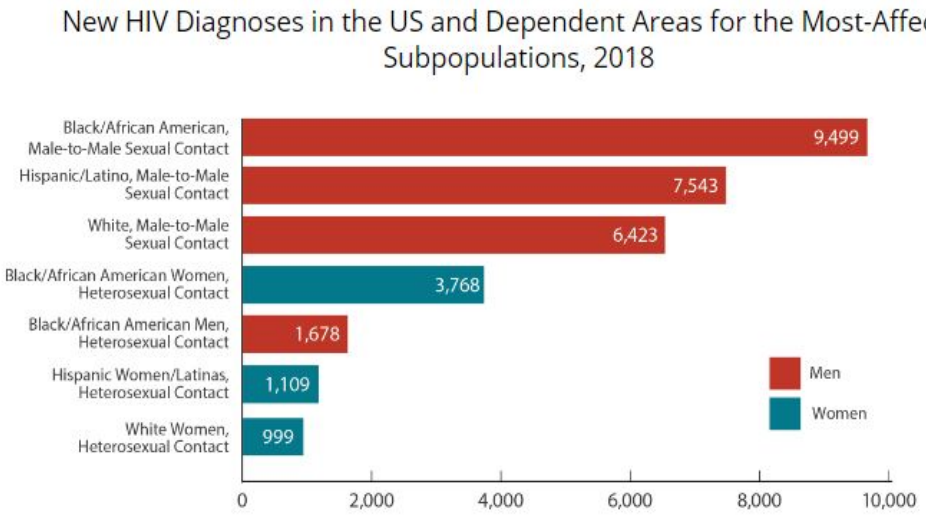
- (1) End stage organ disease for people living with HIV in the US
- (2) What current options for transplantation exist in the US? What are their success rates?
- (3) Legal framework and operational logistics behind the HOPE Act
- (4) What has transpired so far in the US and beyond?
- (5) outline the options for patients and their caregiving teams to facilitate organ donation, both living and deceased

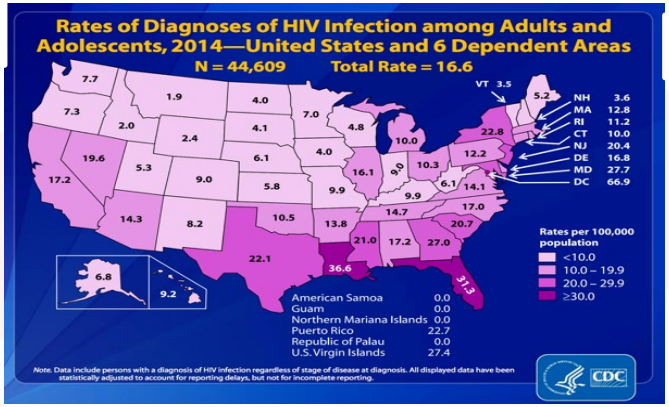

This is Gary.
Gary is HIV+
and living a full, happy life
after a liver transplant.
This is...
HOPE
IN ACTION
Living with HIV?
You can be an organ donor.
You can receive a transplant.

HIV for the non-ID provider

- Background US epidemiology
  - >1.1milion infections (>13yrs) in the
  - 1 in 7 (15%) HIV+ patients don't kno
- ~39,000 new infections every year
- Not evenly distributed:
  - Socioeconomically variable
  - Racially variable
  - Geographically variable

Yet people living longer, and healthier





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Chronic liver and renal disease:

- 1 in 5-10 people with HIV will be at risk of chronic liver disease
  - D:A:D cohort 13% of deaths were liver related;
  - 15% of the Swiss HIV Cohort Study, increased to 18% if you included HCC)
- Prevalence of CKD in HIV population – between 2.5 % in Europe to 7.4% in North America.
- Once CKD has commenced for someone with HIV, the likelihood of developing ESRD is 2- to 20-fold greater compared to the uninfected counterpart.
- The increased susceptibility related to:
  - Things encountered in general population: age, hypertension and diabetes.
  - Also things unique to HIV: AIDS status, hepatitis B and C coinfection, low CD4 nadir, lipodystrophy and ART.
- Patients of African descent 18 to 50% higher risk of developing HIV-related ESRD compared to white

Genetic renal predisposition in AA?

- High risk alleles found for APOL1, a gene sited on chromosome 22, have been strongly associated with the development of the most severe form of HIV-associated glomerulonephrites such as focal segmental glomerulosclerosis (FSGS) and HIV-associated nephropathy (HIVAN).

- Because up to 20–30% of patients of African origin have no APOL1 risk alleles, other variables may contribute

Revolution #1: Simple, effective, and safe antivirals!

HIV HCV HBV

Circa 2005

2019

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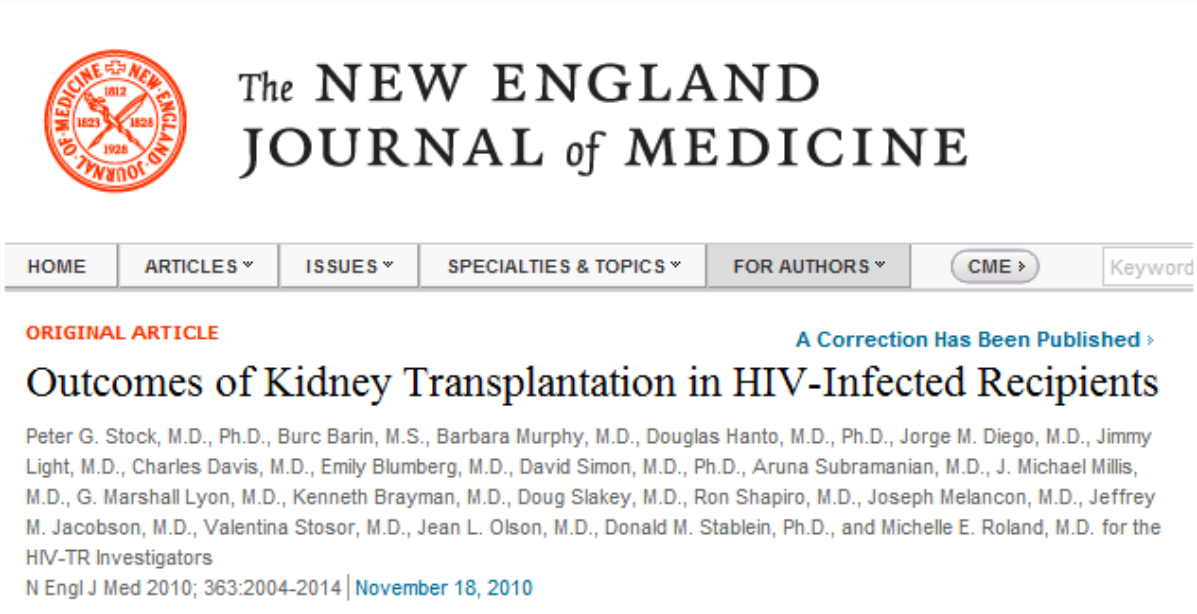
Revolution #2: We had experience with *old* ART



The NEW ENGLAND JOURNAL of MEDICINE

HOME | ARTICLES | ISSUES | SPECIALTIES & TOPICS | FOR AUTHORS | CME | Keyword

ORIGINAL ARTICLE

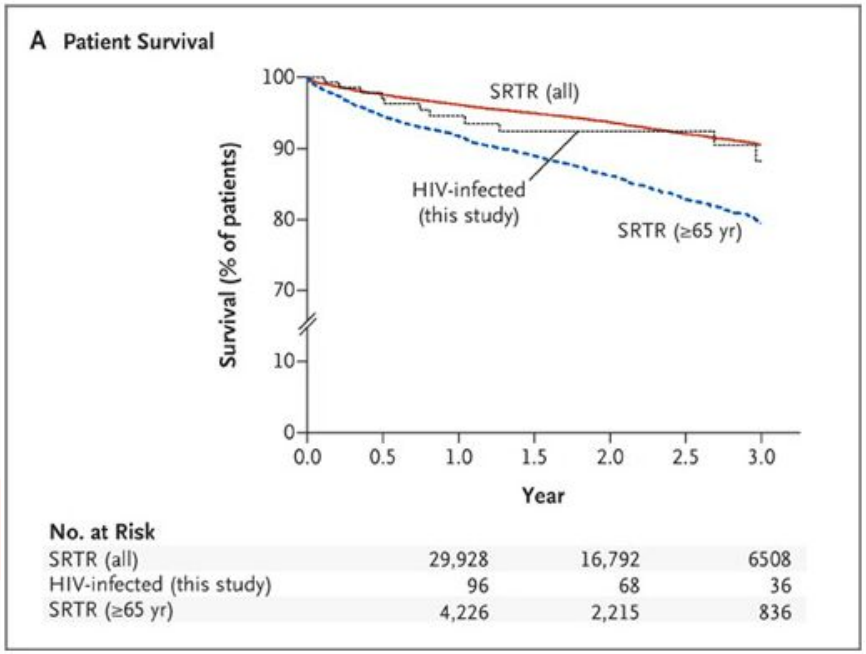
A Correction Has Been Published

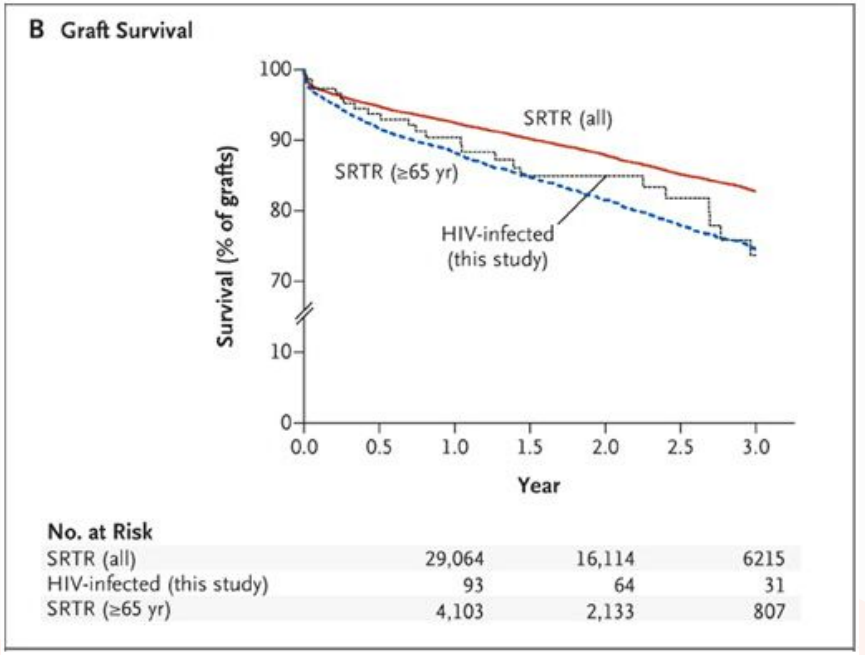
Outcomes of Kidney Transplantation in HIV-Infected Recipients

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

N Engl J Med 2010; 363:2004-2014 | November 18, 2010

Study period 2003-2009, US data





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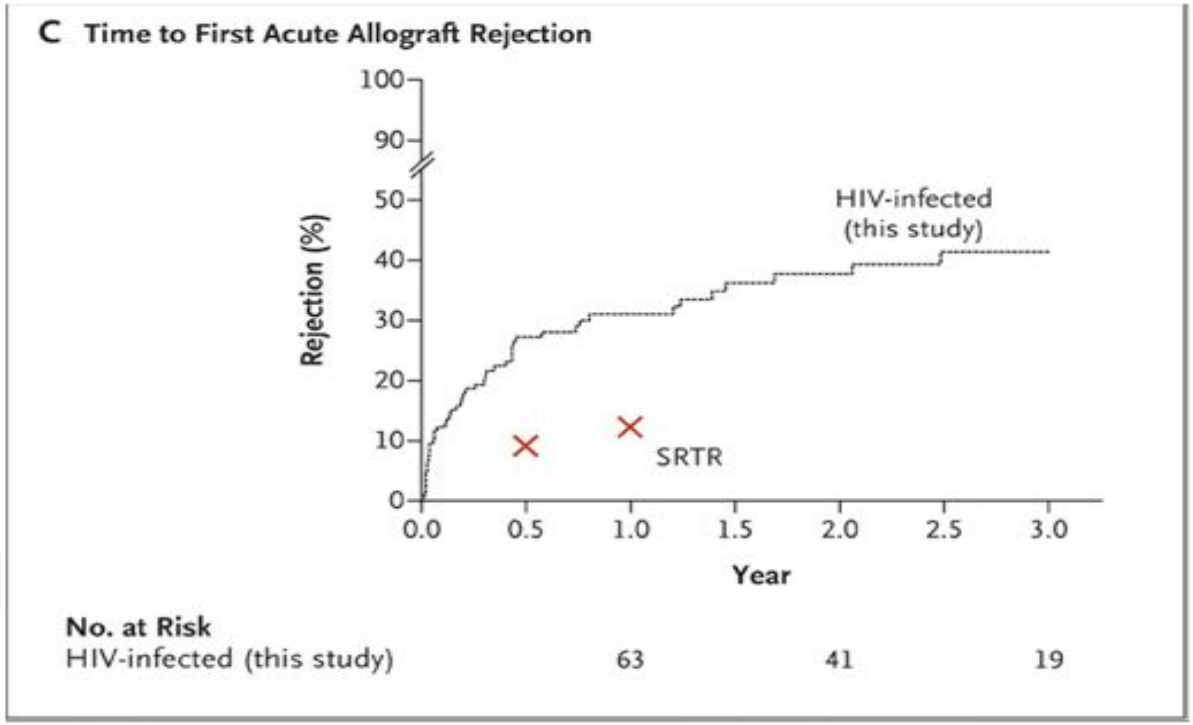
Stock et al, 2010

Word of caution:



? Secondary to under-dosing immunosuppression through fear of OI's?

? Secondary to inadevertent subtherapeutic calcinuerin levels of I/S due to interactions with protease inhibitors

? Due to something unique about the HIV+ transplant recipient?

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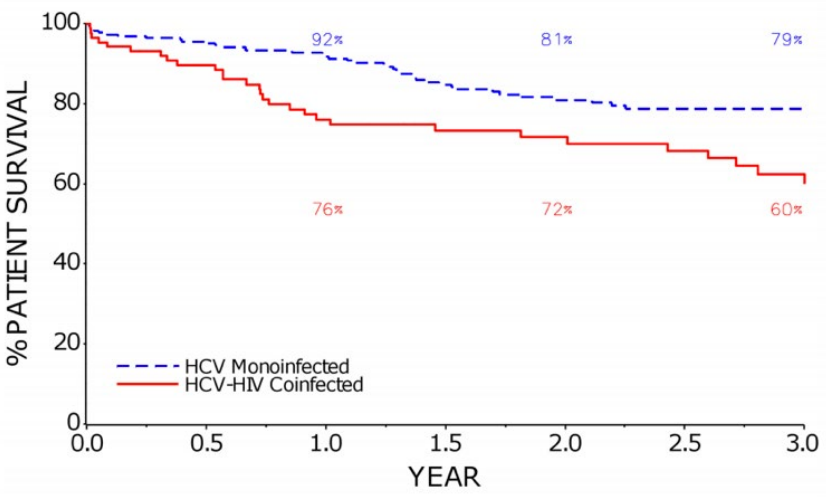
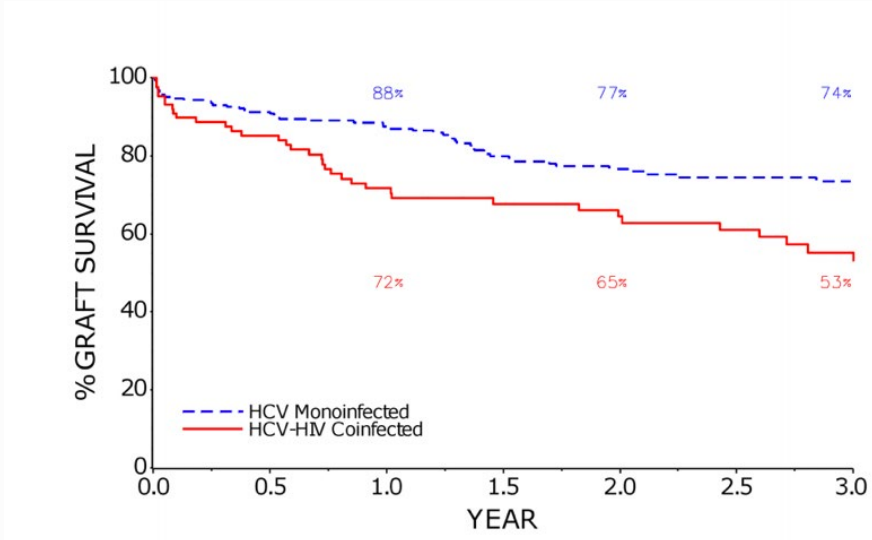
Infectious and Neoplastic Complications

Ciclosporin	Tacrolimus
HIV Viral Load	
• Viral load blips (50 – 139 cps/mL) [n=4]	HIV VL control in all patients (<50 cps/mL)
Tumour/Neoplasms	
• Kaposi's sarcoma (n=2) • Bowen's disease (n=1) • Melanoma (n=1)	• Basal cell carcinoma (n=1) • Bowen's disease (n=1)
Latent Viral Reactivation (LVR)	
N=22	**N=12**
• LVR preceding allograft rejection (n=9)	• LVR preceding allograft rejection (n=1)
• CMV Infection (n=13) • CMV prophylaxis (n=9)	• CMV Infection (n=7) • CMV prophylaxis (n=23)
• Herpes simplex (n=4)	Herpes simplex (n=2)
• Epstein-Barr Virus (n=0)	Epstein-Barr Virus (n=2)
• BK viraemia/nephropathy (n=5)	BK viraemia/nephropathy (n=1)

HIV+ liver transplant outcomes, USA:



No. at Risk			
HCV	183	116	70
HCV-HIV	60	43	26



No. at Risk			
HCV	174	109	67
HCV-HIV	57	39	24

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HIV+ liver transplant outcomes, USA:

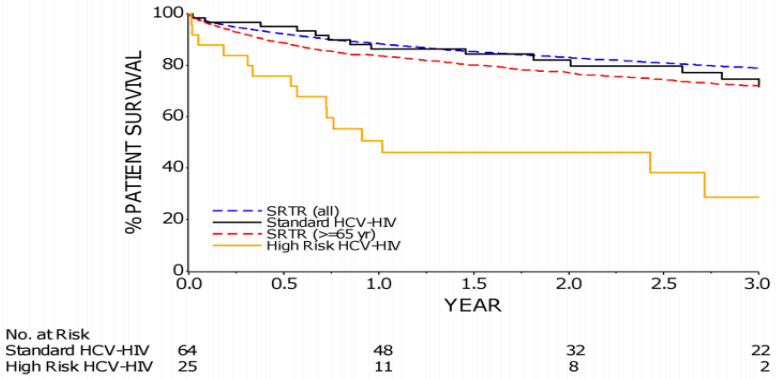

Figure 1D

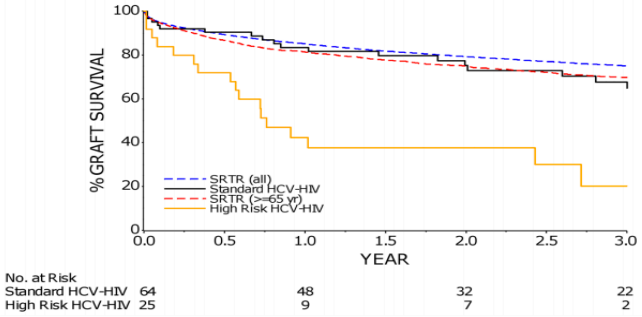

Figure 1.
1A: Kaplan–Meier Estimates of Patient Survival in HCV-HIV and HCV Liver Transplant Recipients
The 1 and 3 year patient survival rates (95% CI) were 76% (66–84%) and 60% (47–71%) in HCV-HIV, and 92% (87–95%) and 79% (72–84%) in HCV ($p<0.001$).
1B: Kaplan–Meier Estimates of Graft Survival in HCV-HIV and HCV Liver Transplant Recipients

"High Risk HCV+/HIV+" included one or more of:

(a) BMI < 21
(b) Combo liver / renal Trx
(c) HCV+ donor

Acute rejection:

(a) 1.6x higher in HIV+ group, (39% vs 24%)
(b) 54% of these episodes occurred in the first 21d

Again, all data collected pre effective HCV DAA therapy

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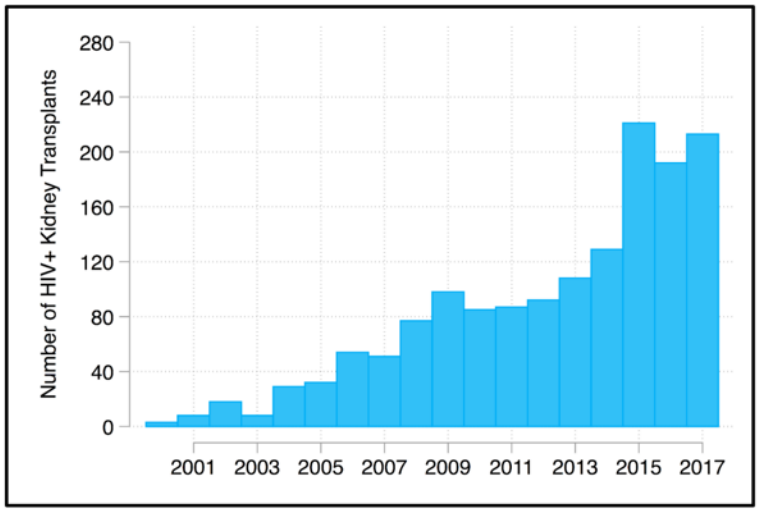
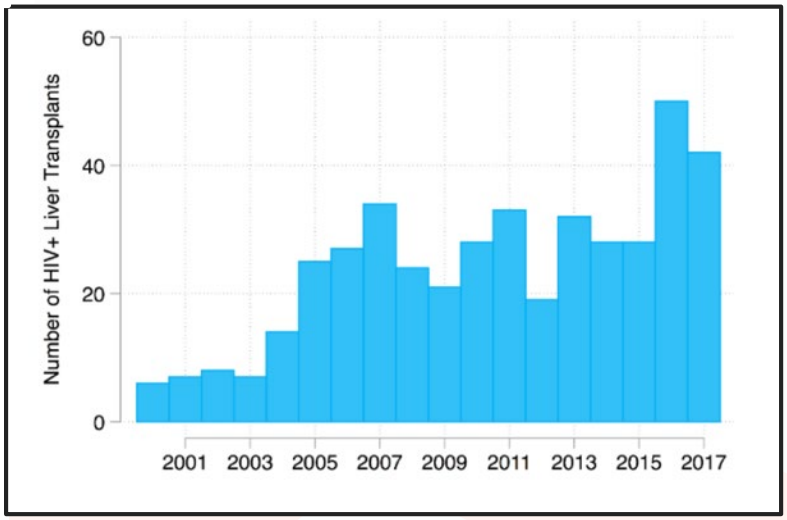
HIV for the non-ID provider





UNOS data, courtesy A.Wilk,
personal communication, May 2018

Revolution #3: someone just started….
10+ years of HIV+ SOT donors

"I started to realize I am so often refusing organs from a patient because they have HIV. Then I thought this doesn't make sense because we have patients with HIV who we can't give dialysis to. So this was a simple way of solving the problem." –Dr. Muller

HIV+/+ kidney transplantation
Results at 3 to 5 years

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Elmi Muller, M.B., Ch.B., M.Med., Zunaid Barday, M.B., Ch.B., Marc Mendelson, M.D., Ph.D., and Delawir Kahn, M.B., Ch.B., Ch.M.

First D+/R+ kidney transplant Sept 2008, still alive at 10 years.

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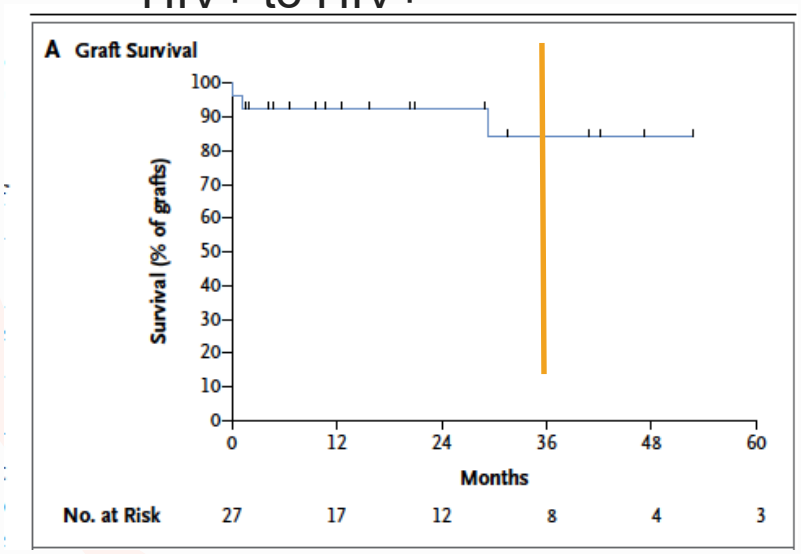
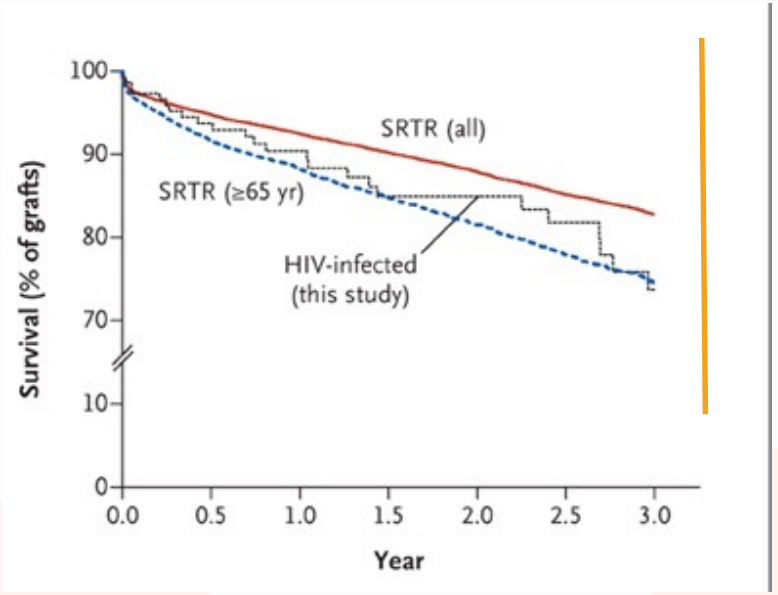
HIV+/+ positive kidney transplantation
Results at 3 - 5 years

HIV+ to HIV+



Rejection: 8% at 1 yr, 22% at 3 yrs
6/8 treated successfully, 2 developed graft failure

HIV- to HIV+ (Stock et al., NEJM 2010)



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Should we believe it's the same in USA?

- Epidemiologic differences:
  - HIV prevalence (17.8 in South Africa versus 0.6% in the United States)
  - Annual HIV deaths (310,000 in South Africa versus 17,000 in the United States)
  - Transmitted resistance (<5% in South Africa versus 10–18% in the United States)
- Logistical / Health care difference:
  - Dialysis not really an option for most in S. Africa

In a US Context? Potential Organ Availability

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*

- **2000-2008**
- **2 national registries (NIS, HIVRN)**
- **Excluded those with missing data and medical contraindication**
- **500-600 donors per year**

How many organs are we talking about?

- Blumberg et al:

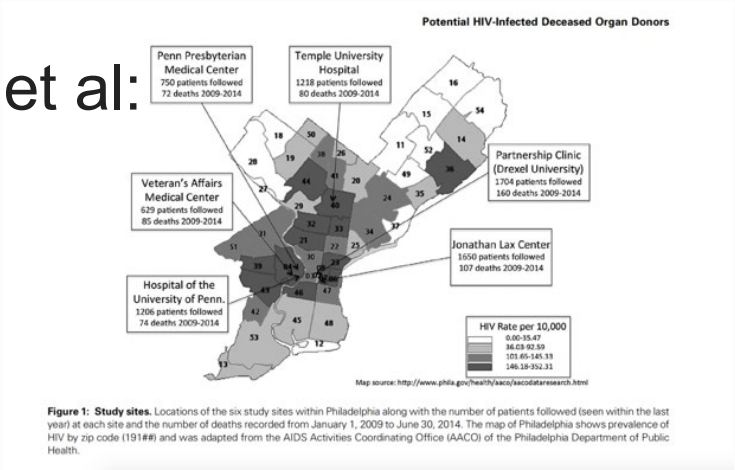
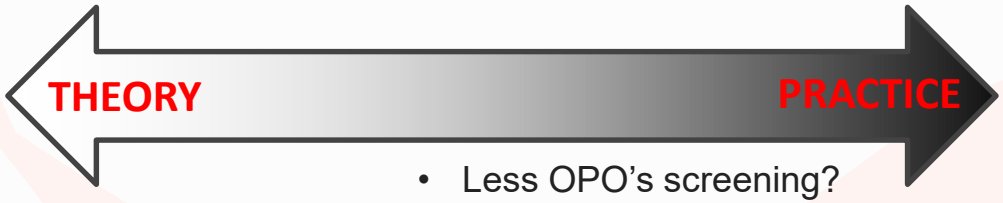
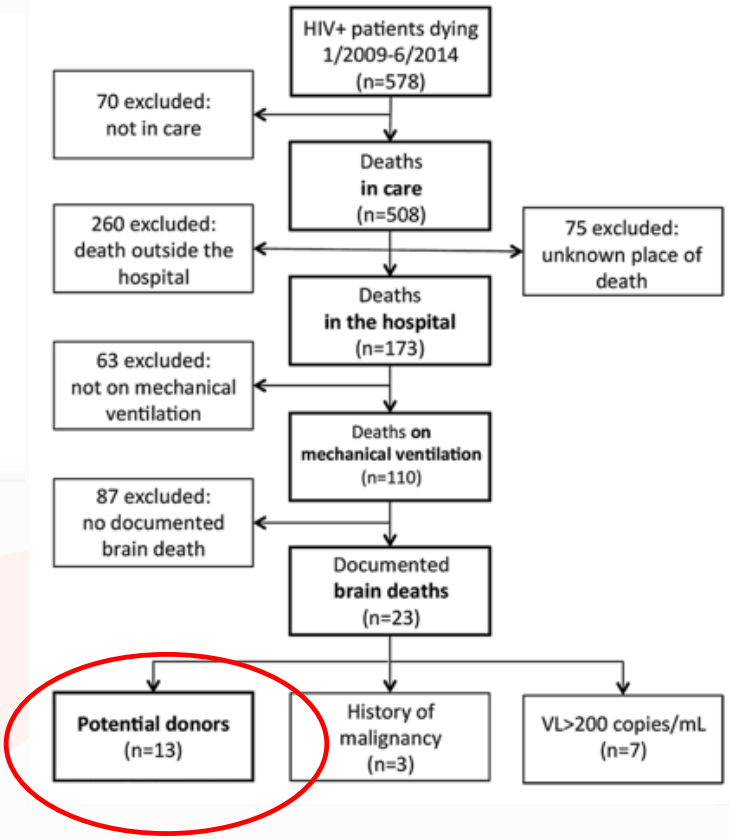


Figure 1: Study sites. Locations of the six study sites within Philadelphia along with the number of patients followed (seen within the last year) at each site and the number of deaths recorded from January 1, 2009 to June 30, 2014. The map of Philadelphia shows prevalence of HIV by zip code (191##) and was adapted from the AIDS Activities Coordinating Office (AACO) of the Philadelphia Department of Public Health.



- Less OPO's screening?
- Donor center reluctance?
- Donor family reluctance?
- Financial or logistical constraints?
- Recipient center caution?



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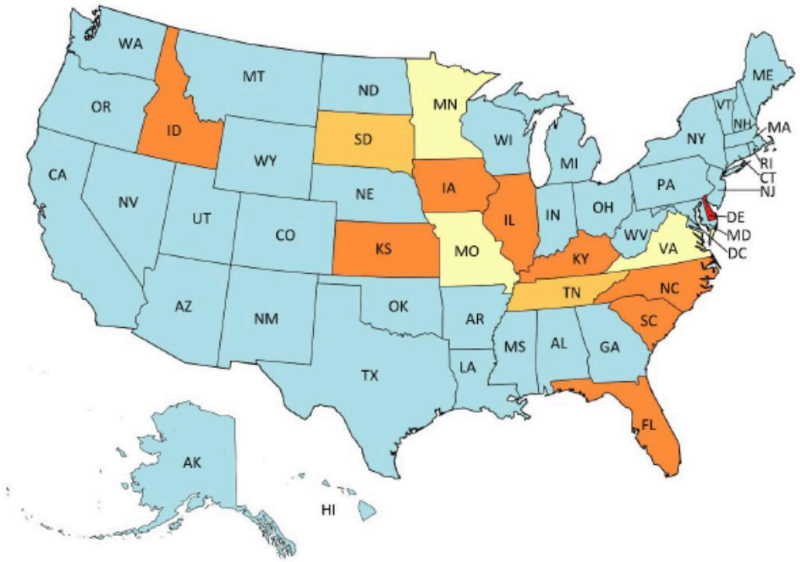
The HOPE Act

- HIV Organ Policy Equity Act was enacted on November 21, 2013
- People with HIV (PWH) Organ Donation allowed under the HOPE Act since 2015

Federal Law is not enough…



Type of legal Prohibition	States	Applies to OPOs and transplant center?	Applies to deceased or living donors?	Interpretation
Law prohibits transfer or use of organs from HIV+ individuals	Delaware	Yes	Living and Deceased	• HIV+-to-HIV+ donation and transplantation is prohibited • Revision to state law required in order to facilitate HOPE Act protocols
Law prohibits HIV+ individuals from donating organs. Law prohibits HIV+ individuals from donating but permissible with consent	Florida Idaho Illinois Iowa Kansas Kentucky North Carolina South Carolina *Permissible with consent:* South Dakota Tennessee	No	Living	• "Individuals" is interpreted as a living person • The state cannot prosecute a decedent. • Participation in deceased donor HOPE Act research protocols should not be impacted • Living HIV+ donors are implicated and revision to these state laws is necessary to enable HIV+ living donor transplantation. • For 2 states living donation is nonetheless permissible with living consent
Law allows for HIV+ organ donation for "medical research."	Minnesota Missouri US VI Virginia	No	Living and Deceased	• HIV+-to-HIV+ transplants should be permissible in these states as they are currently limited to research protocols • If HIV+-to-HIV+ transplantation becomes standard of care, it will be prohibited in these states
Laws don't directly implicate organ donation				

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NC Department of Health 'Control Act':
Duke granted research exemption in 2017, Eventually statewide modification in 2018

Currently Active HOPE Act Centers

As of Jan 16th, 2020:

177 transplants
132 kidney (inc 2 living)
45 livers (all deceased)

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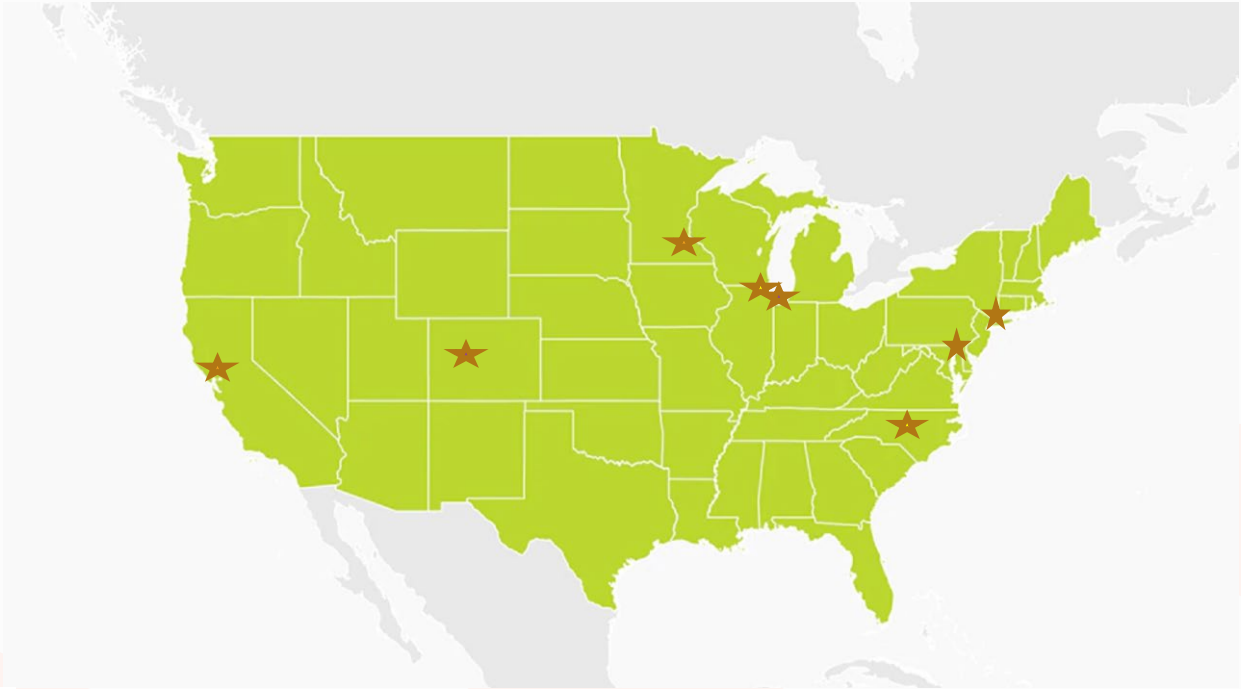
Active Living Donor HOPE Act sites:



- Living Liver
- Living Kidney
- Both kidney/liver

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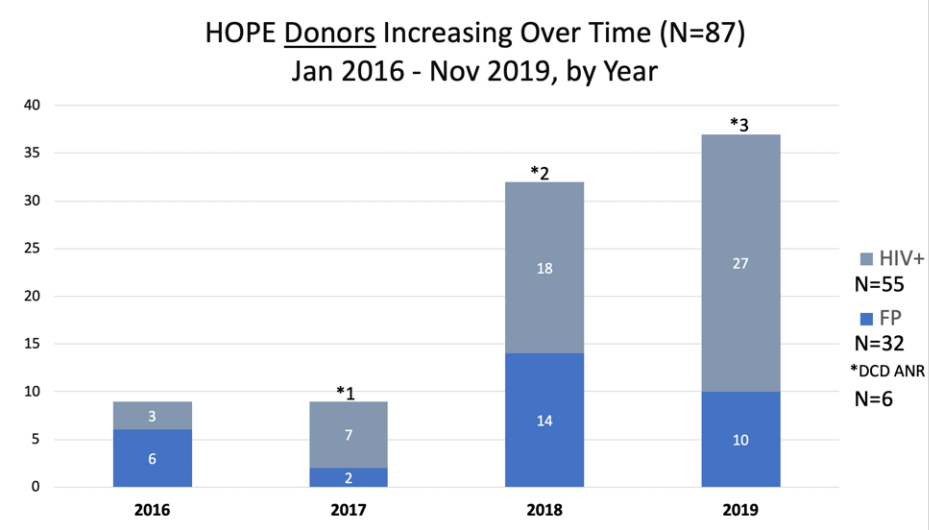
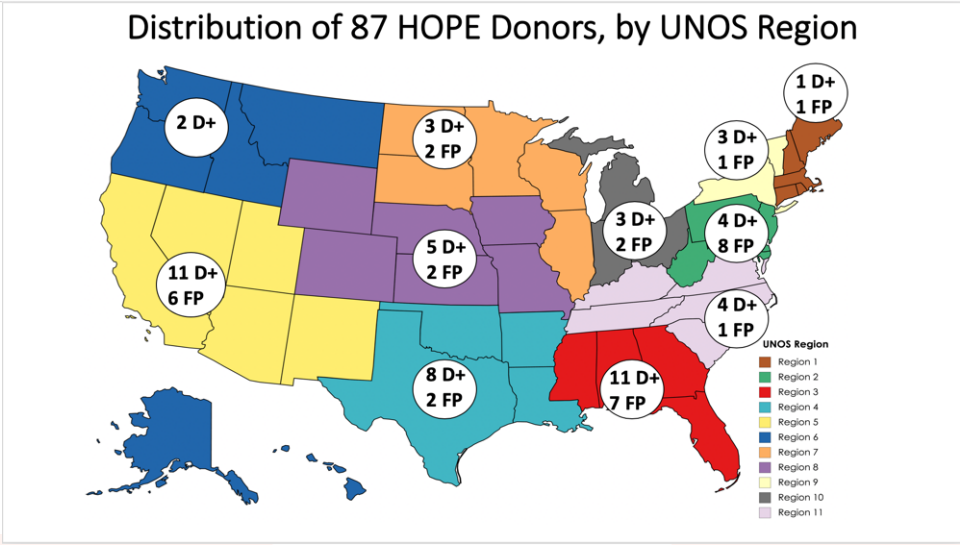
HOPE Donors – what do they look like?





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Current baseline stipulations?

Recipient Eligibility	CD4+ T-cell count ≥200/μL (kidney)
	CD4+ T-cell count ≥100 μL (liver) within 16 weeks prior to transplant and no history of opportunistic infection (OI); or ≥200 μL if history of OI is present.
	HIV-1 RNA <50 copies/mL and on a stable antiretroviral regimen.
	No evidence of active opportunistic complications of HIV infection.
	No history of primary central nervous system (CNS) lymphoma or progressive multifocal leukoencephalopathy (PML).

Additional stipulations at most centers:

- All routine transplant hurdles must be passed, first
- All patients to be accepted onto HIV- list

- Clinical review by TxID faculty before hand to evaluate ART
  - Compliance (>16wk undetectable), drug interactions (ritonavir, cobi, TDF) , OI history etc

- >18yrs only (to date, no pediatrics, no that we can't!)

- TxID actively involved in donor selection

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Risks – donor kidney as "Trojan horse"

- The donor kidney may super-infect the recipient
  - Either a *recombinant* form of virus or with virus of a *different clade*
  - Relies on blood (if viraemic), archived genotype data, podocyte or urine infection
- The donor kidney may transmit drug-resistant virus
- The donor kidney may transmit other infectious diseases / malignancy
- High background rate of HIV-associated renal and liver disease make *living* donation challenging

- Ethically appropriate for pt. with HIV to be *positively* discriminated against?

Outcomes to date:

- 132 kidney transplants and 45 liver recipients
- No significant viral rebound (no donor, or mixed strain virus)
- Typical infectious and surgical complications for transplant
  - 2 graft thrombosis (2,10 days); 1 primary kidney failure (90d), 4 chronic rejection
  - Comparable graft survival between D+ and D- recipients

- Of note – almost twice the rejection at 1 year mark… *why??*

More detailed results in publication… stay tuned!!

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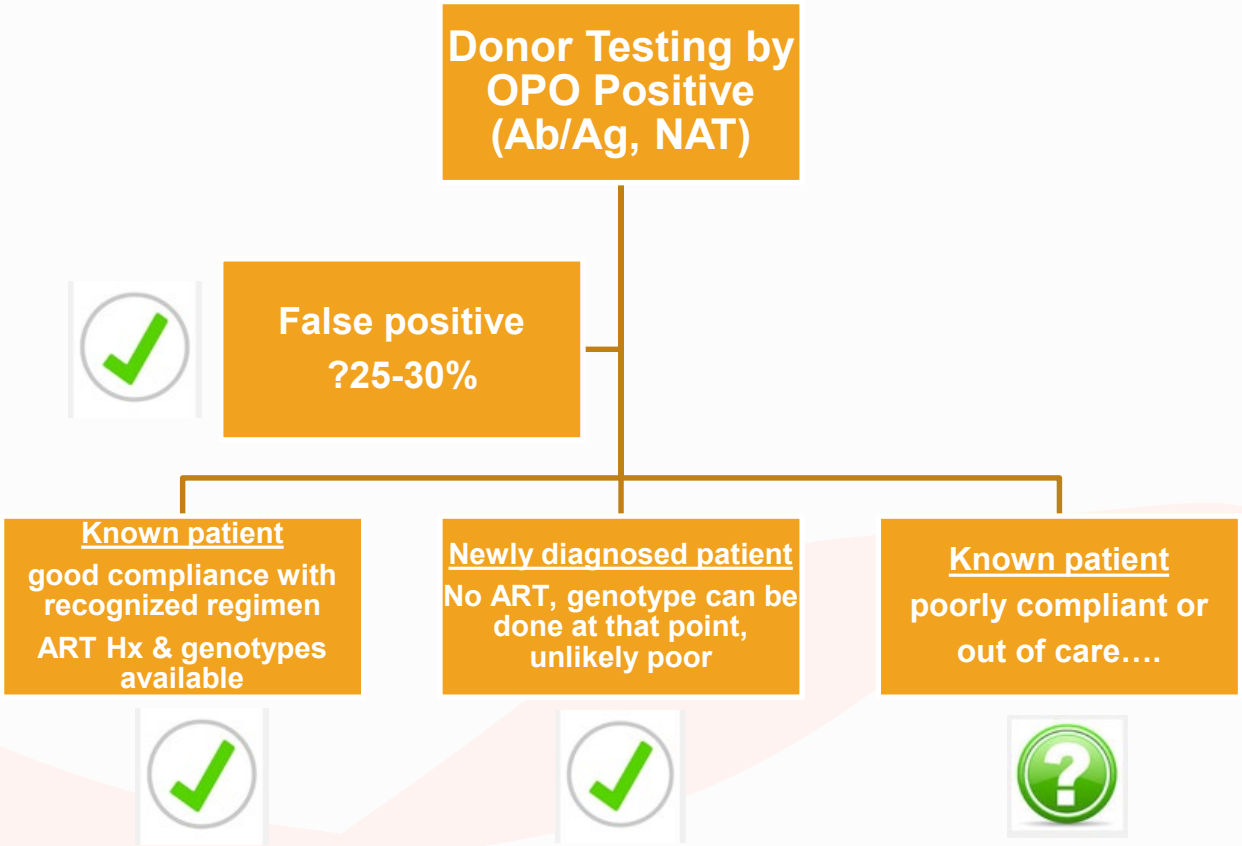
How can an HIV+ donor present?



Personal experience recently:

- 23yr white male, MSM, rural NC, dies of opiate overdose
- Cr 0.7, GFR >100
- HIV Ab and HIV-1 NAT qualitative positive. Not previously known positive

- Family remember he was “using PrEP” in the last 12 months..
- Our recipient on - ABC / 3TC / DOL

- Rilpivirine added peri-transplant to ‘reinforce’ Triumeq in case of 184v /65R?
- Ultimately posthumous donor genotype = K103N

Personal experience recently:

- 49yr old woman, died of seizures and anoxic brain injury
- HIV identified during donor evaluation, no previous documented +'s
- No history of taking ARV's
- CrCl > 100, good UO; synthetic liver function excellent
- Psych history of some depression / bipolar

- More history – well until 3 weeks prior had first seizure. CT brain normal. Then fell at home, fractured ankle, ORIF, sent to rehab.
- In rehab becomes somnolent over some days, found "arrested" in bed one morning, ?aspirated. WCC 1.6, lymphopaenic

- CrAg + 1:640, LP = CrAg positive, pressure elevated. Organs declined

Heart and/or Lung Transplant if you're HIV positive?

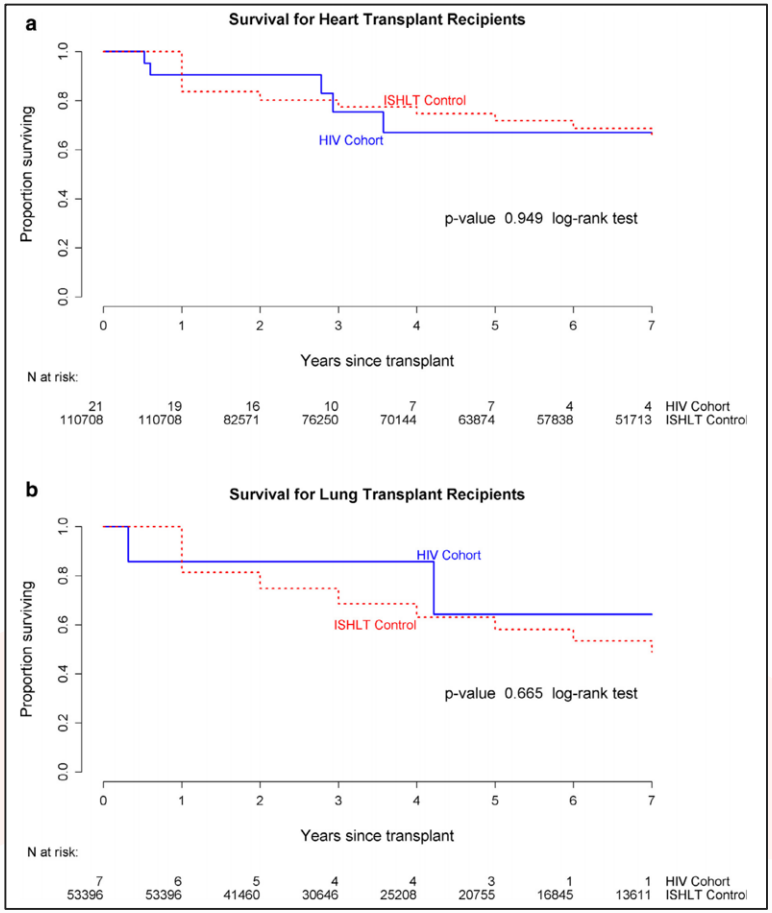
The Journal of Heart and Lung Transplantation
The Official Publication of the International Society for Heart and Lung Transplantation

Heart or lung transplant outcomes in HIV-infected recipients

Christine E. Koval, MD,[a] Maryjane Farr, MD,[b] Jill Krisl, PharmD,[c] Ghady Haidar, MD,[d] Marcus R. Pereira, MD,[e] Nabin Shrestha, MD,[a] Maricar F. Malinis, MD,[f] Nicolas J. Mueller, MD,[g,h] Margaret M. Hannan, MD,[i] Paolo Grossi, MD,[j] and Shirish Huprikar, MD[k]

OUTCOMES

	Heart N=21 (%)	Lung N=7 (%)	Heart Lung N=1*
Patient Survival			
1 Year	19 (90)	6 (86)	1
3 year, heart N=15, lung 5	11 (73)	4 (80)	NA
5 Year, heart N=11, lung 4	7 (64)	3 (75)	NA
Functional Status 1 yr N=17,7,1*			
Acute care	0	1 (14)	0
Home, not working for income	10 (59)	4 (57)	0
Home, working for income	5 (29)	1 (14)	1
Died	2 (10)	1 (14)	0



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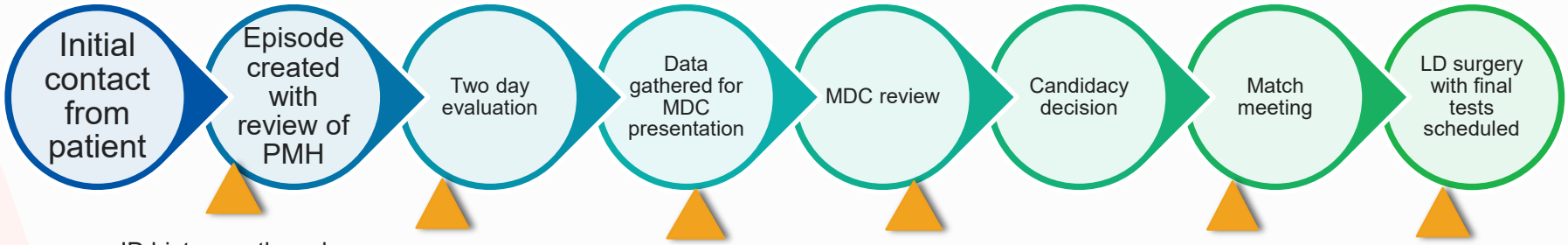
Challenges that remain?

- HIV – especially poorly controlled HIV - remains associated with a number of other conditions that can impact transplant:
  - Psychiatric illness
  - Substance abuse
  - Higher rates of liver and kidney disease
  - Accelerated cardiovascular / cerebrovascular disease
  - Stigma - hence loved ones may not know status; hard to approach
  - Co-infection (hepatitis C, syphilis especially)
  - Is there a different standard to measure suitability for living donation?

Living Donors with HIV?

Evaluation Process

Evaluation Process



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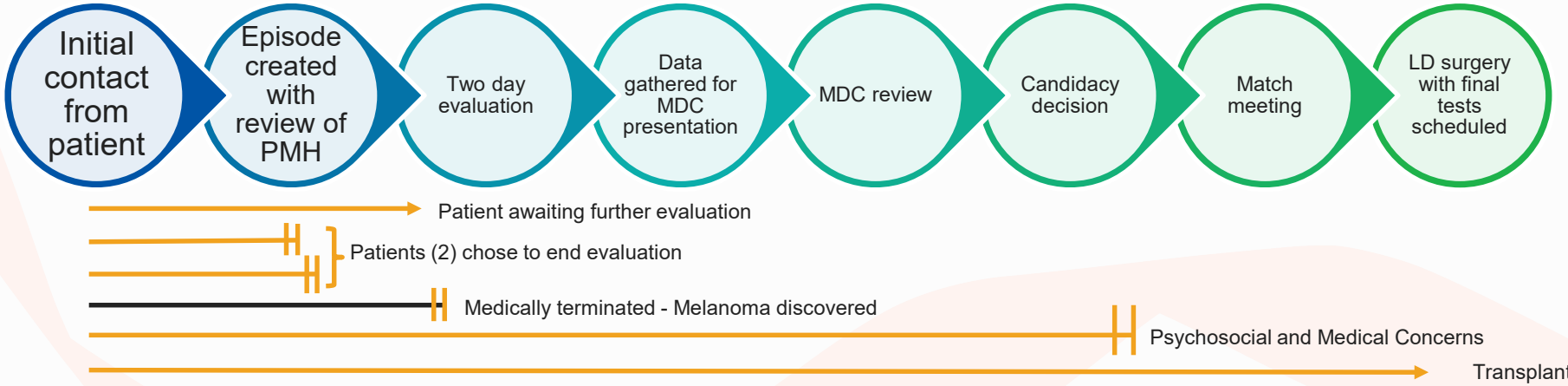
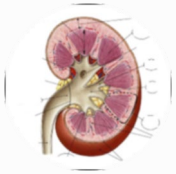
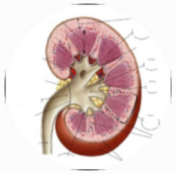
Evaluation Process



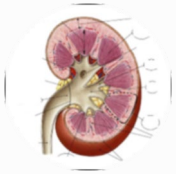
Case Study of Potential NDD



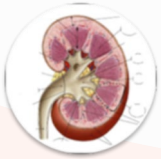
Transplant Professional, Early 50s, Caucasian, Male



Current smoker with history of hypertension, recent 50lbs weight loss with discontinuation of HTN medications

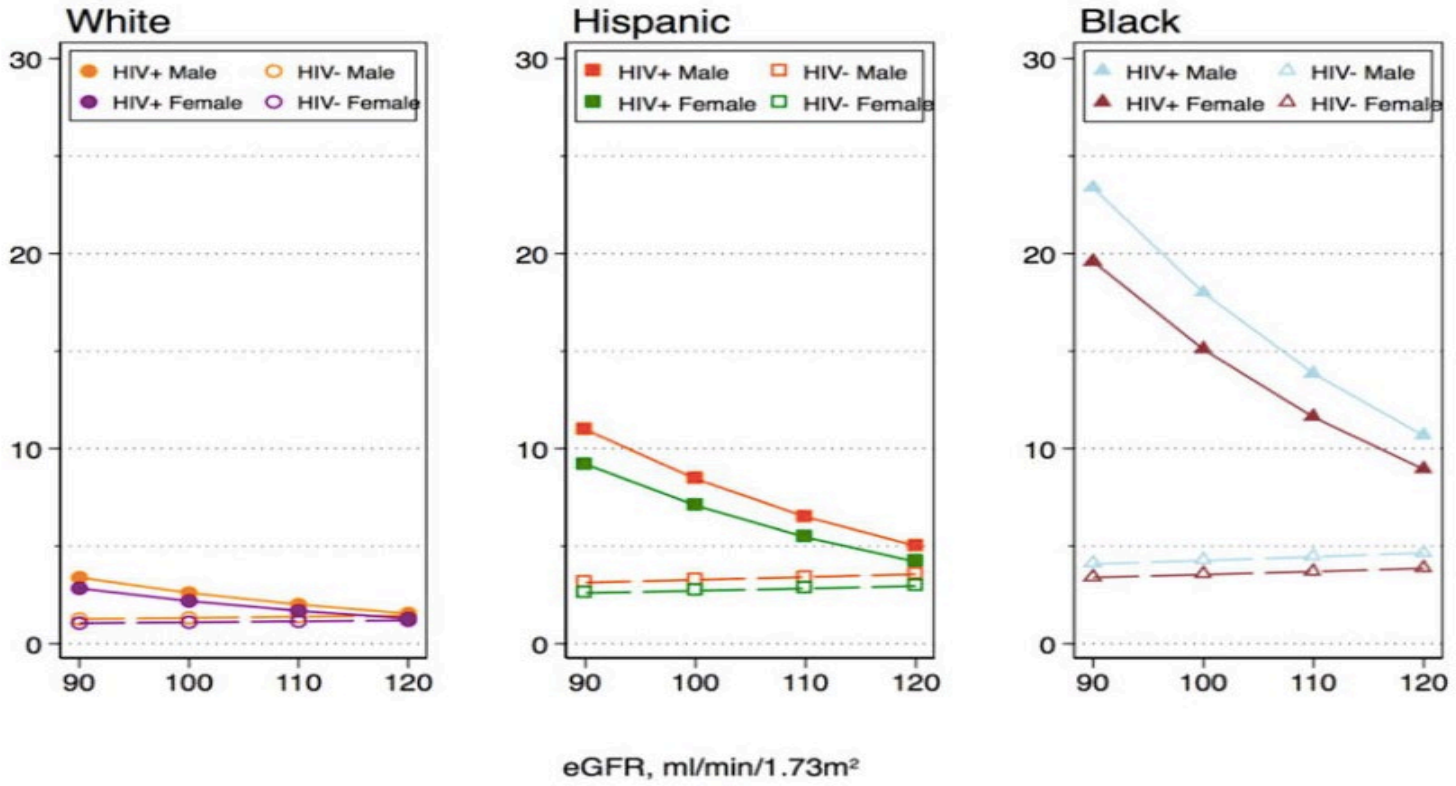


HIV+ for 10 years, non-viremic, CD4 counts >500, and on Atripla (TDF / FTC / EFV) medication regimen



Evaluation found elevated microalbuminuria level

9-Year Cumulative Incidence, per 10,000



Am J Transplant. 2017 Jul;17(7):1823-1832. doi: 10.1111/ajt.14235. Epub 2017 May 12.

Risk of End-Stage Renal Disease in HIV-Positive Potential Live Kidney Donors.

Muzaale AD[1], Althoff KN[2], Sperati CJ[3], Abraham AG[2], Kucirka LM[1,2], Massie AB[1,2], Kitahata MM[4], Horberg MA[5], Justice AC[6], Fischer MJ[7], Silverberg MJ[8], Butt AA[9,10,11], Boswell SL[12], Rachlis AR[13], Mayor AM[14], Gill MJ[15], Eron JJ[16], Napravnik S[16], Drozd DR[17], Martin JN[18], Bosch RJ[19], Durand CM[3], Locke JE[20], Moore RD[3], Lucas GM[3], Segev DL[1,2].

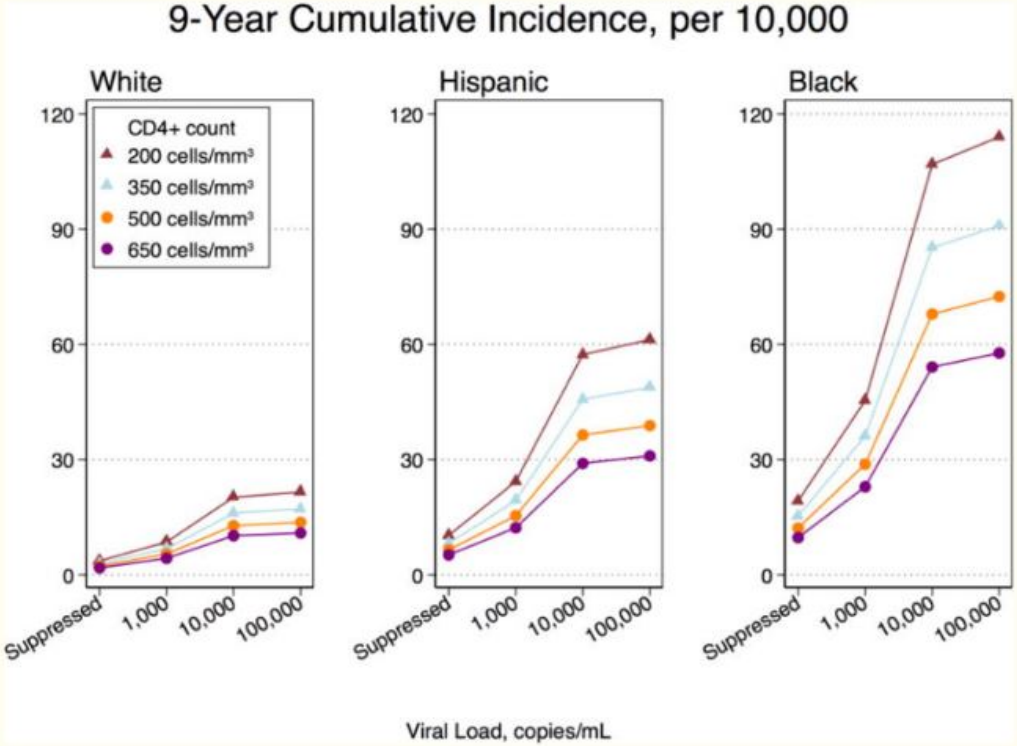


Figure 1

Estimated 9-year cumulative incidence of ESRD among HIV-positive participants of the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) according to HIV viral load and CD4+ cell count for the hypothetical profile of a 40-year-old male with no diabetes, no hypertension, no HCV co-infection, and expected eGFR by age and race/ethnicity (95, 95, and 105 ml/min/1.73m^2 for white, Hispanic, and black individuals).

Scenarios including suppressed viral load and CD4+ count >500 cells/μL meet the Department of Human and Health Services criteria for well-controlled HIV infection in a HIV-positive potential live kidney donor (5)

Estimated 9-year cumulative incidence of ESRD among other hypothetical HIV-positive and HIV-negative populations[a]

					9-year risk[b]		
#	Age	Race	eGFR[c]	Hypertension	HIV-positive	HIV-negative	Risk Increase[d]
1	40	White	95	No	3.0	1.3	1.7
2	40	Black	105	No	15.8	4.4	11.4
3	**40**	**White**	**90**	**No**	**3.4**	**1.3**	**2.1**
4	**40**	**Black**	**90**	**No**	**23.4**	**4.1**	**19.3**
5	50	White	90	No	1.8	1.6	0.1
6	50	Black	100	No	9.5	5.5	4.0
7	50	White	90	Yes	4.8	1.7	3.1
8	50	Black	100	Yes	25.5	5.6	19.9
9	30	White	105	No	4.3	1.0	3.3
10	30	Black	115	No	23.0	3.5	19.5

“ Like many 20 year old gay men in the 80’s, one of things in the forefront of my mind was staying alive. Now 30 years later as a healthy undetectable HIV + transplant coordinator, I have the ability to help someone else worried about staying alive. Donation was not a difficult decision to make. “

- Karl

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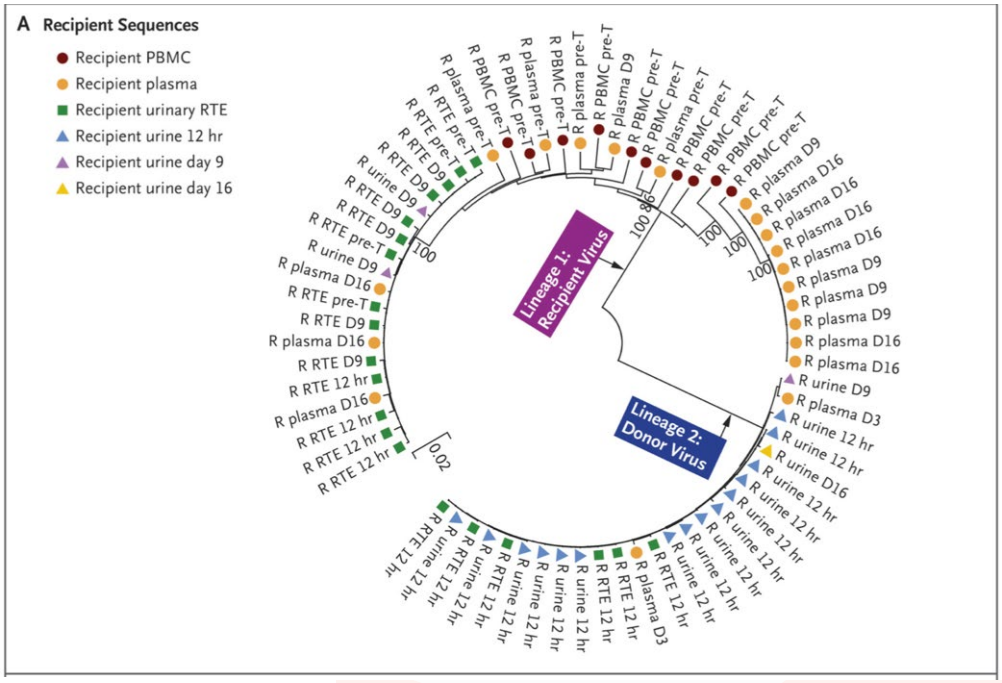
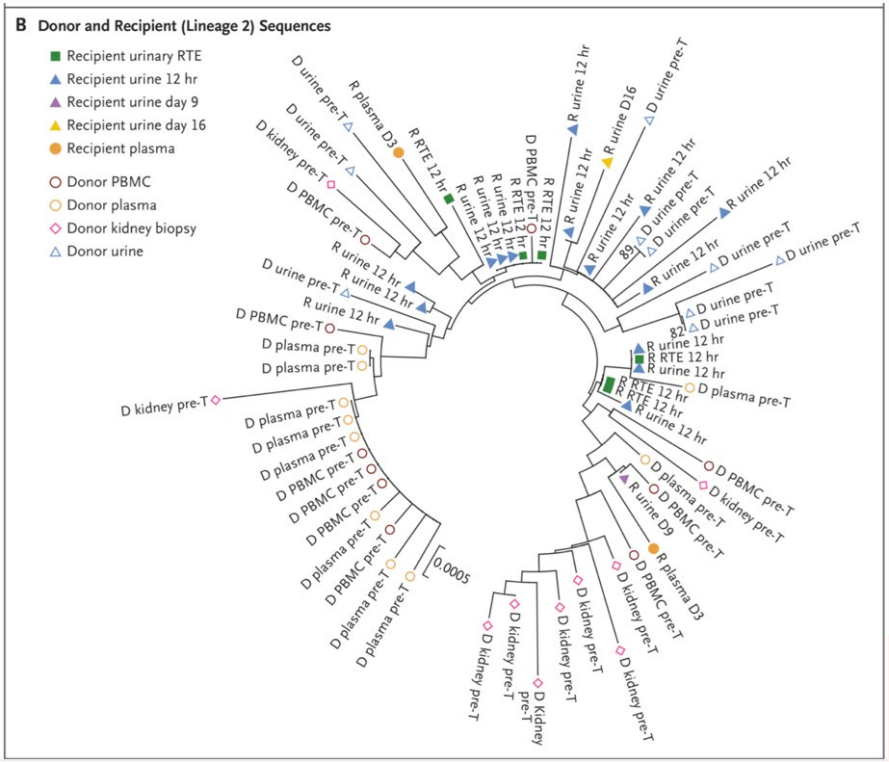
The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med. 2020 Jan 9;382(2):195-197. doi: 10.1056/NEJMc1910189.

Detection of Donor's HIV Strain in HIV-Positive Kidney-Transplant Recipient.

Blasi M[1], Stadtler H[1], Chang J[1], Hemmersbach-Miller M[1], Wyatt C[1], Klotman P[2], Gao F[3], Wolfe C[3], Klotman M[3].





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AETC AIDS Education & Training Center Program Southeast

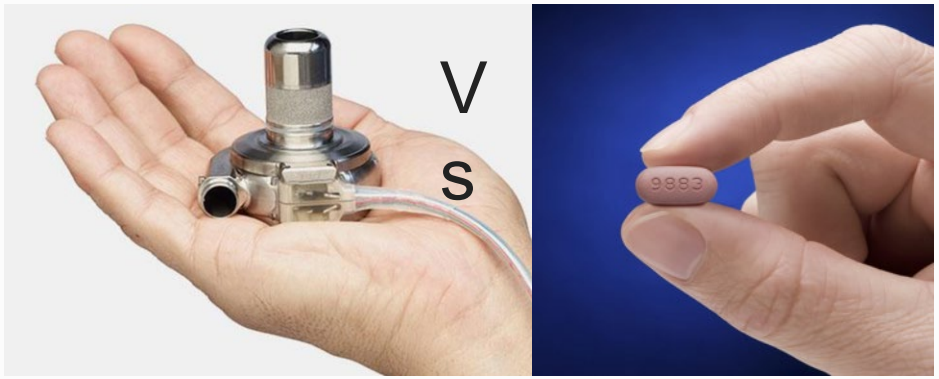
Horizon? D+/R- HIV transplant: A bridge too far?

AIDS
An official International AIDS Society Journal

HIV solid organ transplantation: looking beyond HOPE

Kolber, Michael A.

AIDS: August 24, 2018 - Volume 32 - Issue 13 - p 1733–1736



Outcomes of Solid Organ Transplantation from an HIV Positive Donor to Negative Recipients.

S.-N. Lin,[1] M.-K. Tsai,[1] C.-Y. Luo,[2] C.-Y. Lee,[1] R.-H. Hu,[1] J.-M. Lee,[1] H.-S. Lai.[1]

[1]Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan
[2]Department of Surgery, National Cheng Kung University Hospital, Tainan, Taiwan.

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Horizon? D+/R- HIV transplant: A bridge too far?

HIV positive mom's liver transplanted into HIV negative child

NEWS / 4 OCTOBER 2018, 1:37PM / TEBOGO MONAMA

Minister of Health Aaron Motsoaledi at the Wits Donald Gordon Medical Centre. Picture: Karen Sandison/African News Agency(ANA)

Johannesburg- In what is believed to be the first in the world, researchers at Wits University have transplanted a liver from an HIV positive mother to her HIV negative child.

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Questions?

www.donatelife.net