

Solid organ transplant and HIV: The HOPE Act

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2023-4-5

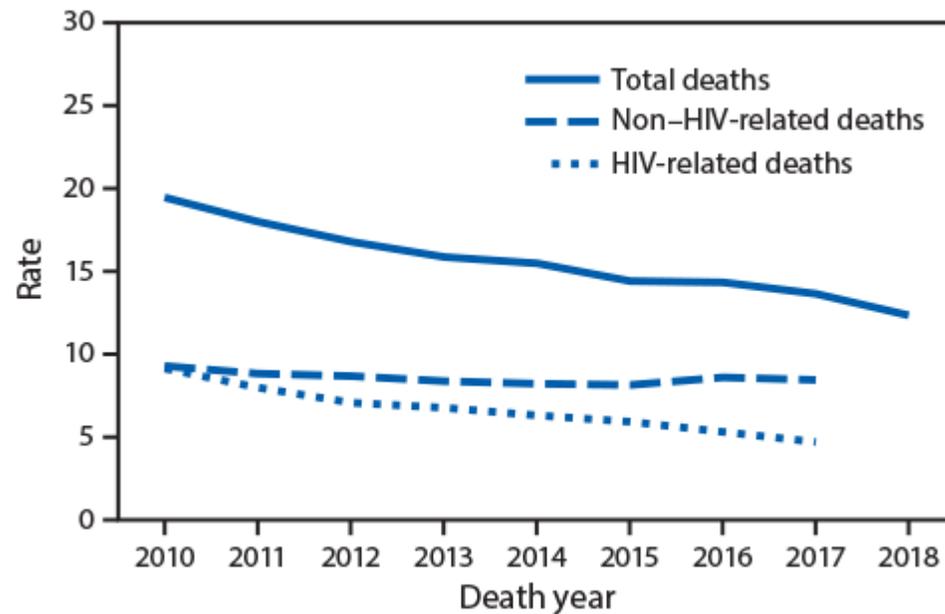
NASSAU/SUFFOLK CARE COORDINATION NETWORK

Disclosures

- Research funding from Merck to study pneumococcal vaccine response in LVAD recipients

Introduction

- Antiretrovirals have transformed HIV into a chronic disease
- In the modern era, the majority of people living with HIV die from non-HIV comorbidities



MMWR Morb Mortal Wkly Rep 2020;69:1717–1724.

HIV and end-organ disease

Kidney disease	<ul style="list-style-type: none">• Direct effects of HIV• Older antiretrovirals (TDF)	900 new dialysis patients/year
Liver disease	<ul style="list-style-type: none">• Hepatitis B/C• Alcohol• Older antiretrovirals	~15% of deaths in people with HIV
Cardiac disease	<ul style="list-style-type: none">• Direct effects of HIV• Inflammation→increased risk of myocardial infarction• Smoking• Abacavir	~2400 people with HIV with advanced heart failure
Lung disease	<ul style="list-style-type: none">• HIV-associated pulmonary hypertension• Smoking• Prior infection (pneumocystis)• Independent effect of HIV?	Unknown

J Heart Lung Transplant. 2014 Sep;33(9):924-30.
Clin J Am Soc Nephrol. 2017 Mar 7; 12(3): 467–475.
Arch Intern Med. 2006 Aug;166(15):1632-41.

HIV and end-organ disease

- People with HIV are *more* likely to die once they develop end organ disease
- They are *less* likely to be:
 - Referred to a transplant center by their providers
 - Listed for transplant once referred
 - Transplanted once listed

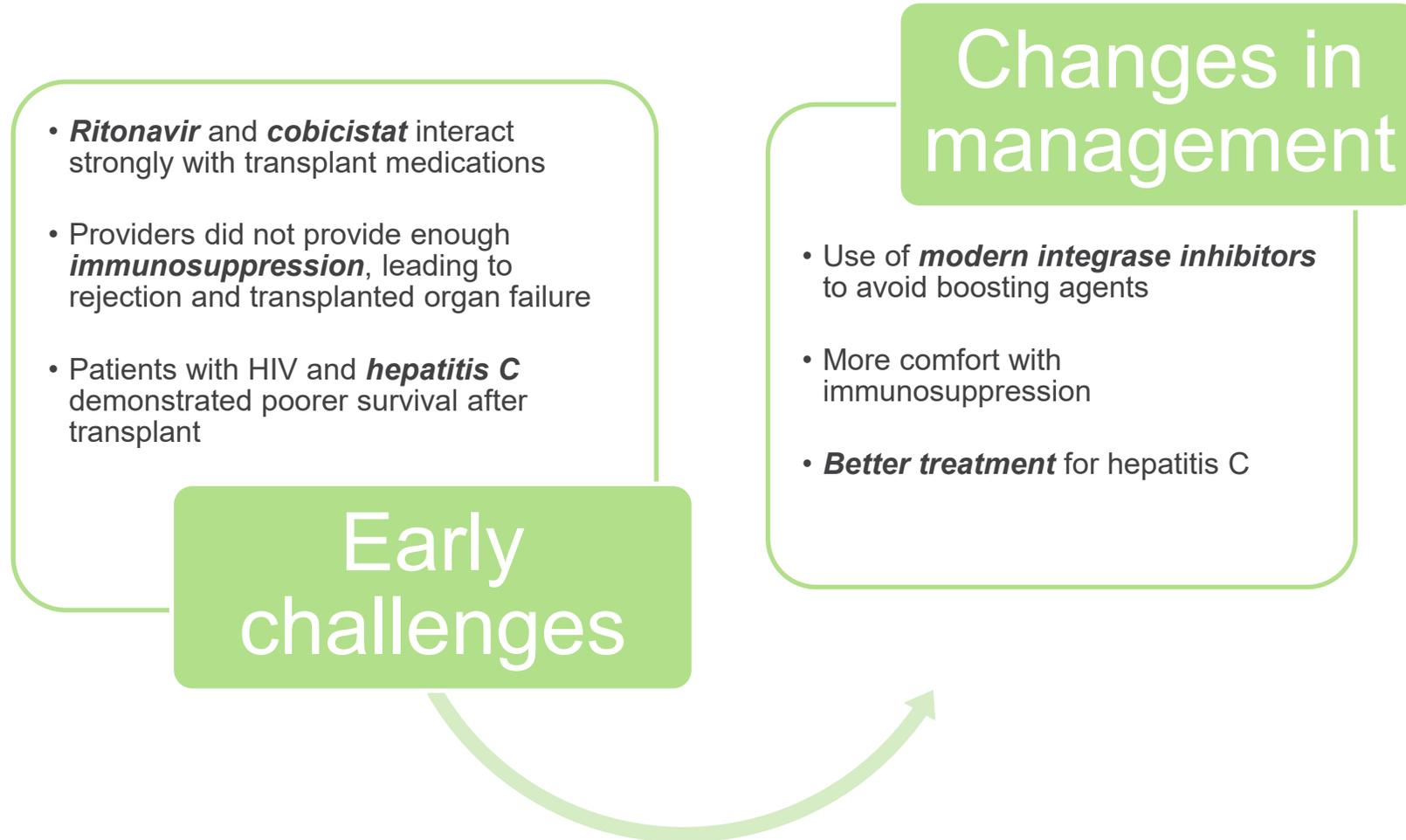
Early experience with HIV and transplant

- Studies in the early 2000s demonstrated that people living with HIV could safely receive kidney and liver transplants under select conditions:
 - CD4 count 200+ cells/uL for kidney, 100+ for liver
 - Viral load under 75 copies/mL (except for “blips”). Note: this requirement can be waived under appropriate circumstances.
 - No history of opportunistic infection for which prophylaxis does not exist (e.g. PML)

Ann Surg. 2016 Mar;263(3):430-3.

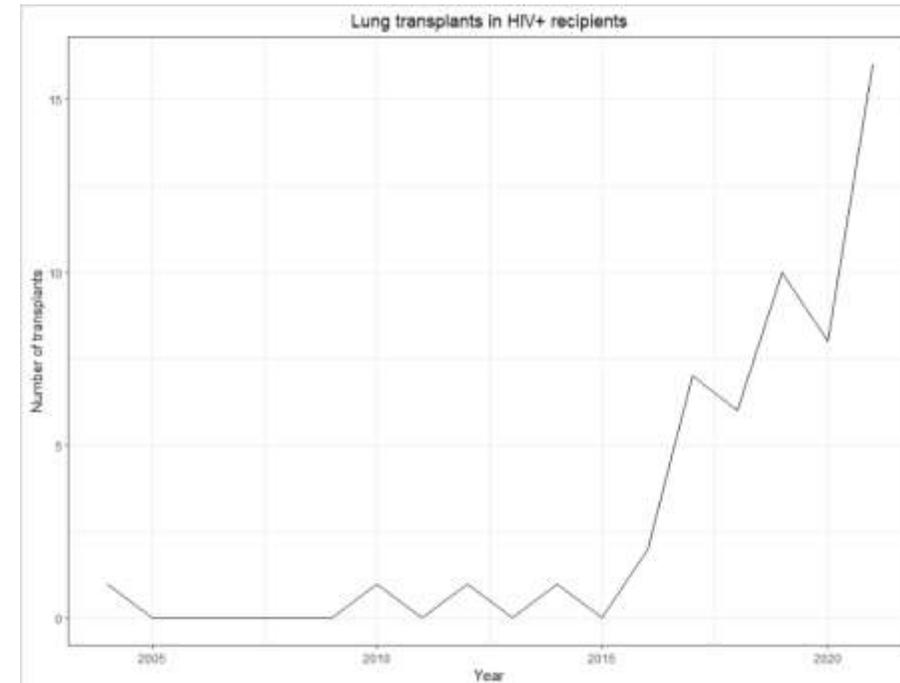
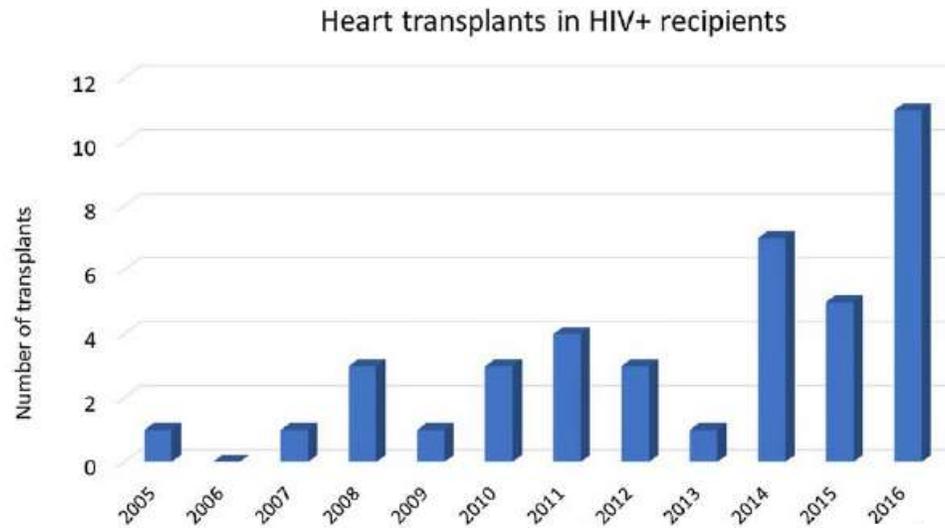
N Engl J Med. 2010 Nov 18; 363(21): 2004–2014.

Early experience with HIV and transplant



HIV and thoracic transplant

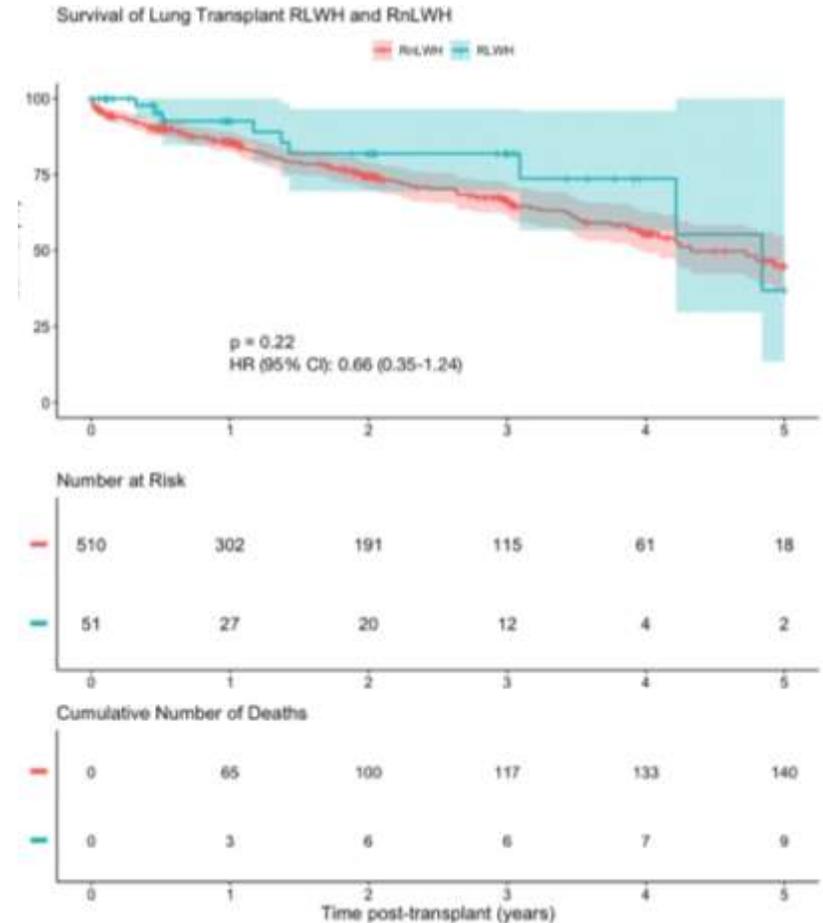
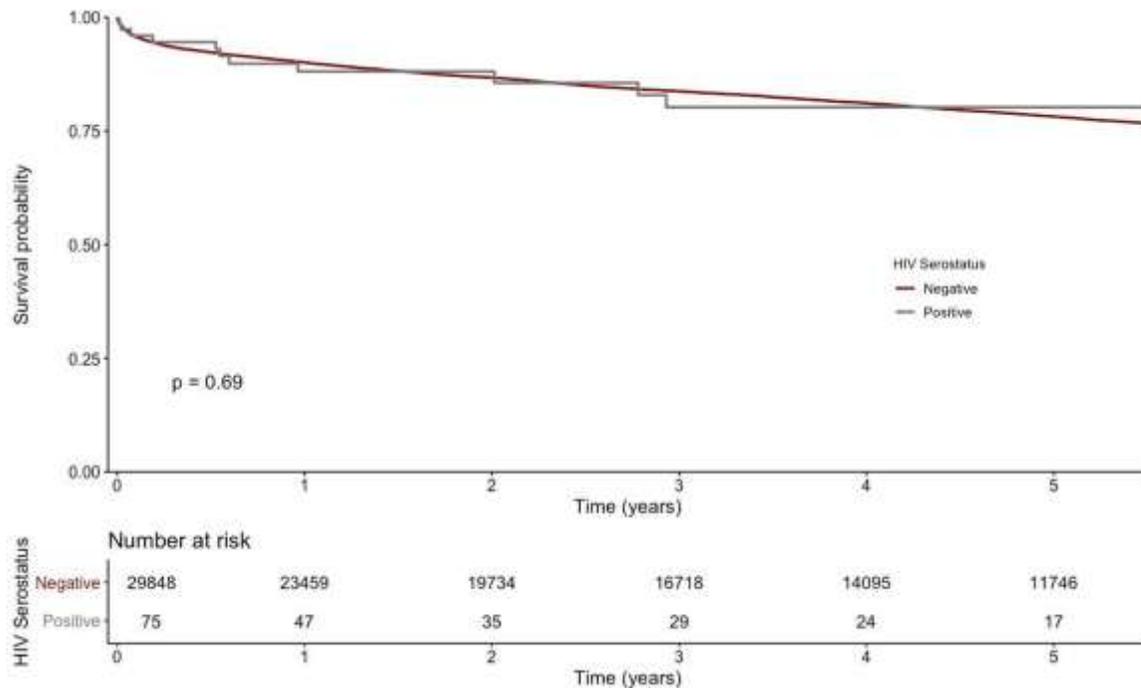
However, until recently, *very* few centers were willing to offer heart or lung transplant to patients living with HIV



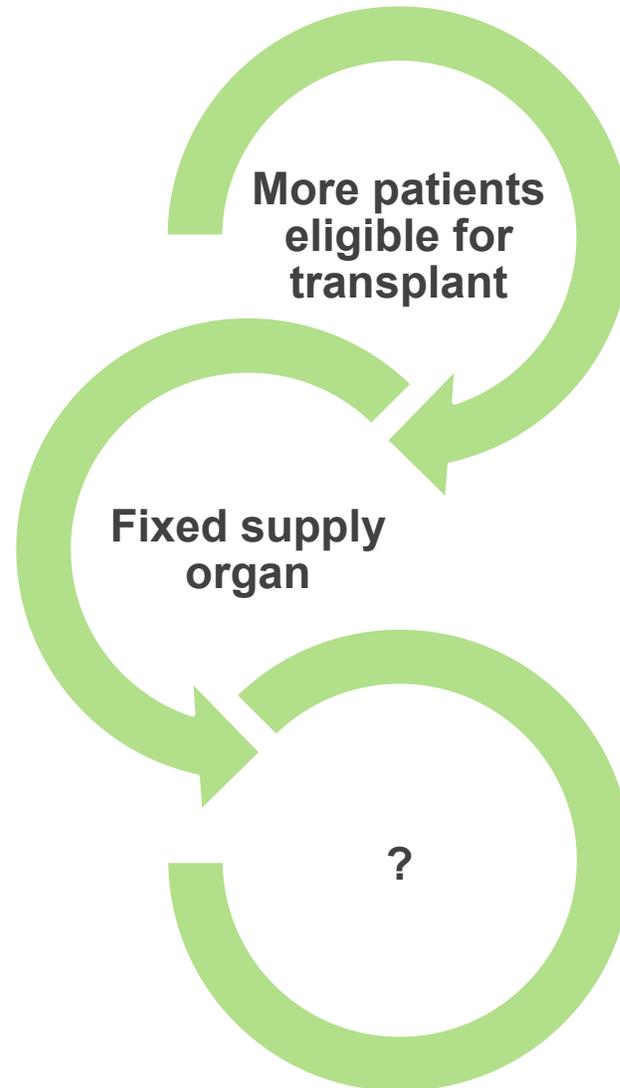
Am J Transplant. 2019 May;19(5):1529-1535.
Personal research (unpublished).

HIV and thoracic transplant

- Recent data has suggested that patients with HIV can safely receive heart and lung transplants.

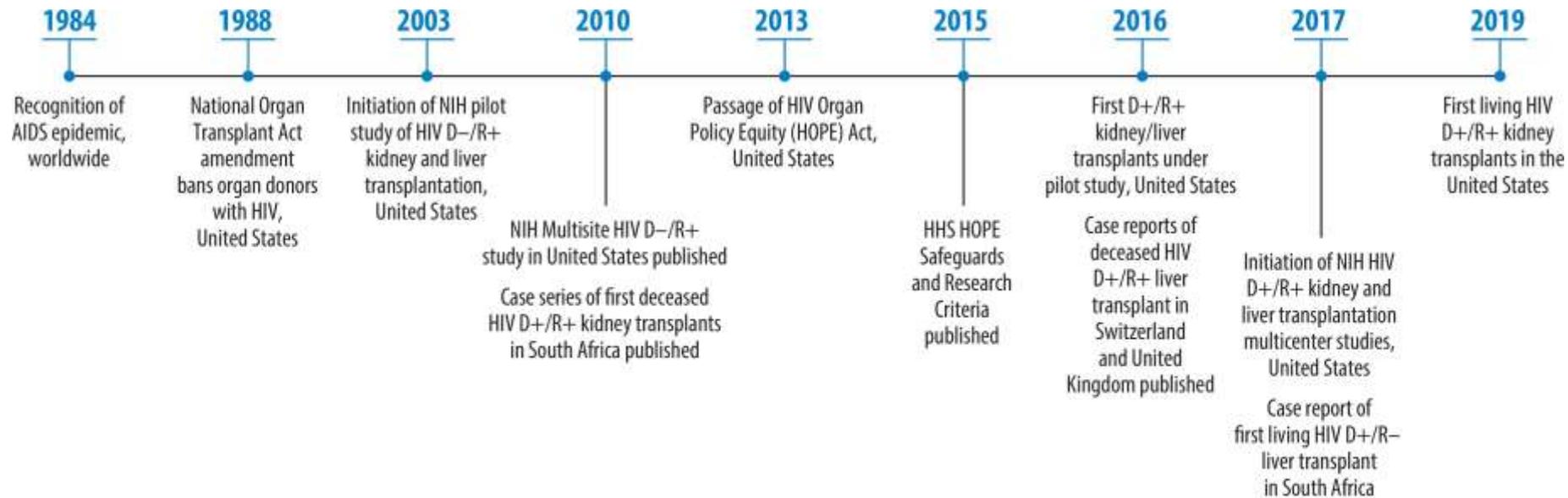


Increasing the donor supply



Federal law

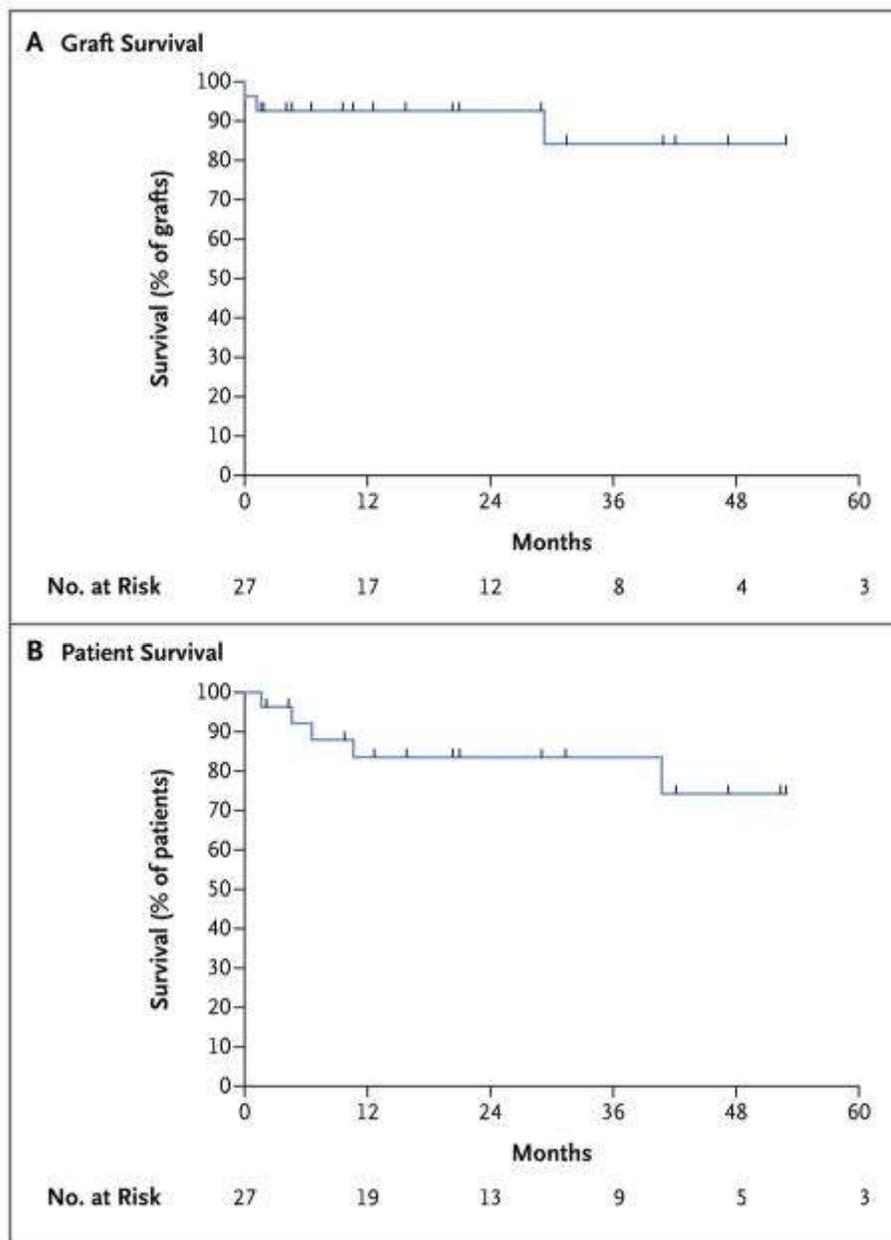
- Transplantation of organs from donors who test positive for HIV was banned by the National Organ Transplant Act amendment (NOTA) Act of 1988, which reflected the poor outcomes of transplant-associated HIV in an era without effective treatments for HIV



First HIV-to-HIV transplants

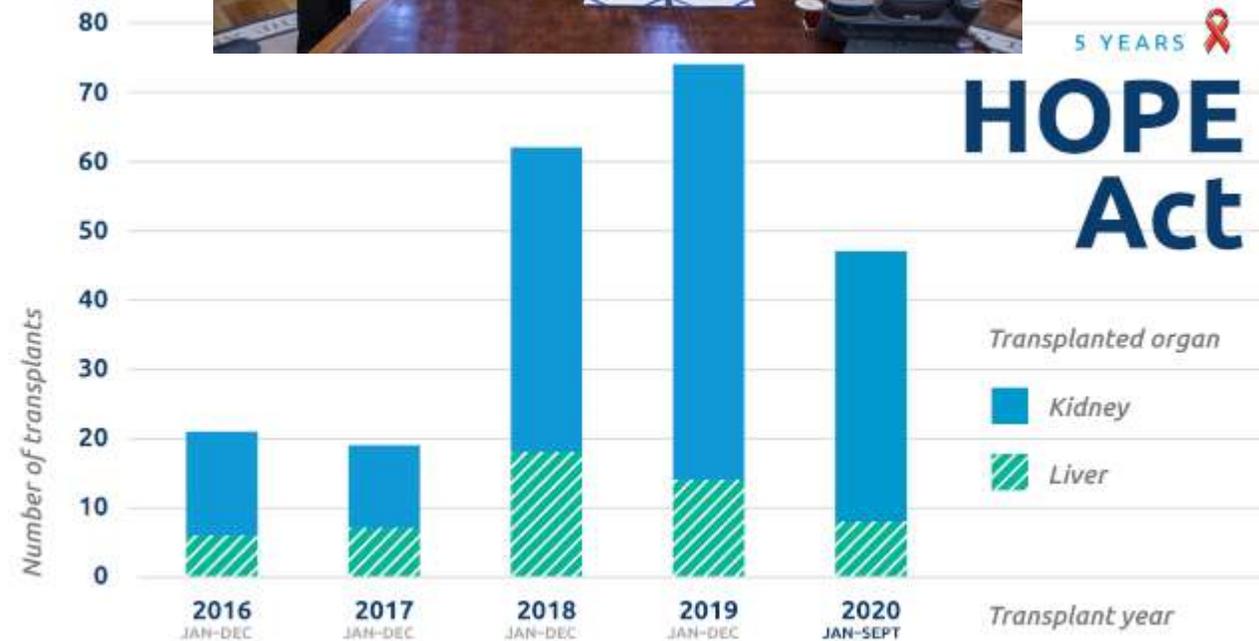
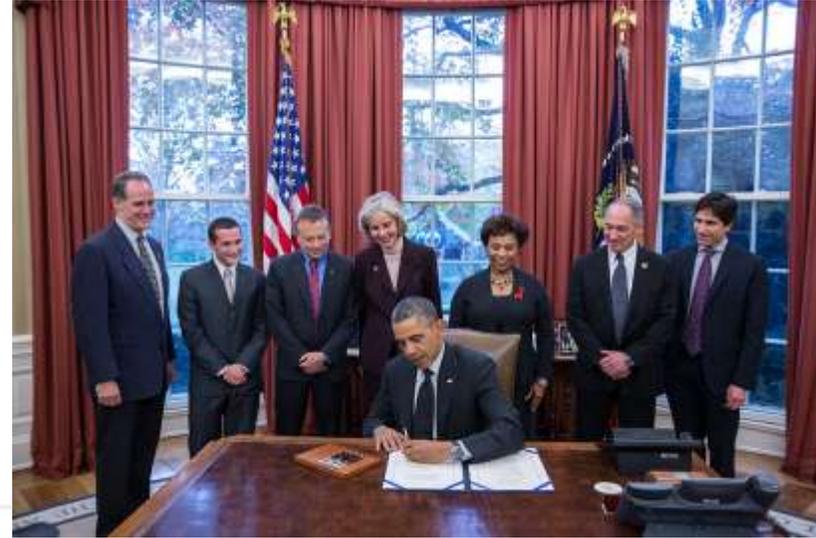
- The first study of HIV D+/R+ transplant was done in South Africa
 - Limited access to dialysis
 - High prevalence of HIV

N Engl J Med. 2010 Jun 17; 362(24): 2336–2337.
N Engl J Med. 2015 Feb 12; 372(7): 613–620.



The HIV Organ Policy Equity Act (the HOPE Act)

- Federal law signed 21 Nov 2013
- Permits transplantation of kidneys and livers from HIV+ donors (D+) into HIV+ recipients (R+) *under research protocols*
- On 7 Jun 2020 amended to include other organs
- Program must have organ-specific experience with 5³HIV D-/R+ to perform D+/R+



Based on OPTN data as of Nov. 13, 2020. Data subject to change based on future data submission or correction.

Why is HIV D+/R+ different? What were the concerns?

Resistance

Infection

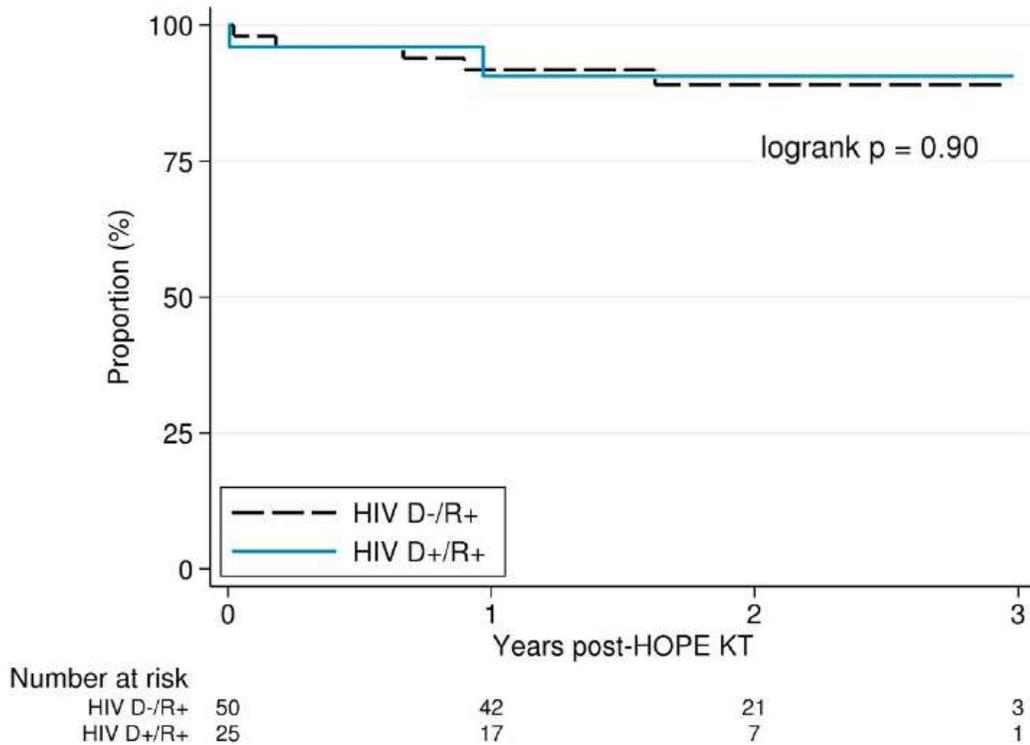
Malignancy
(especially
lymphoma)

Rejection

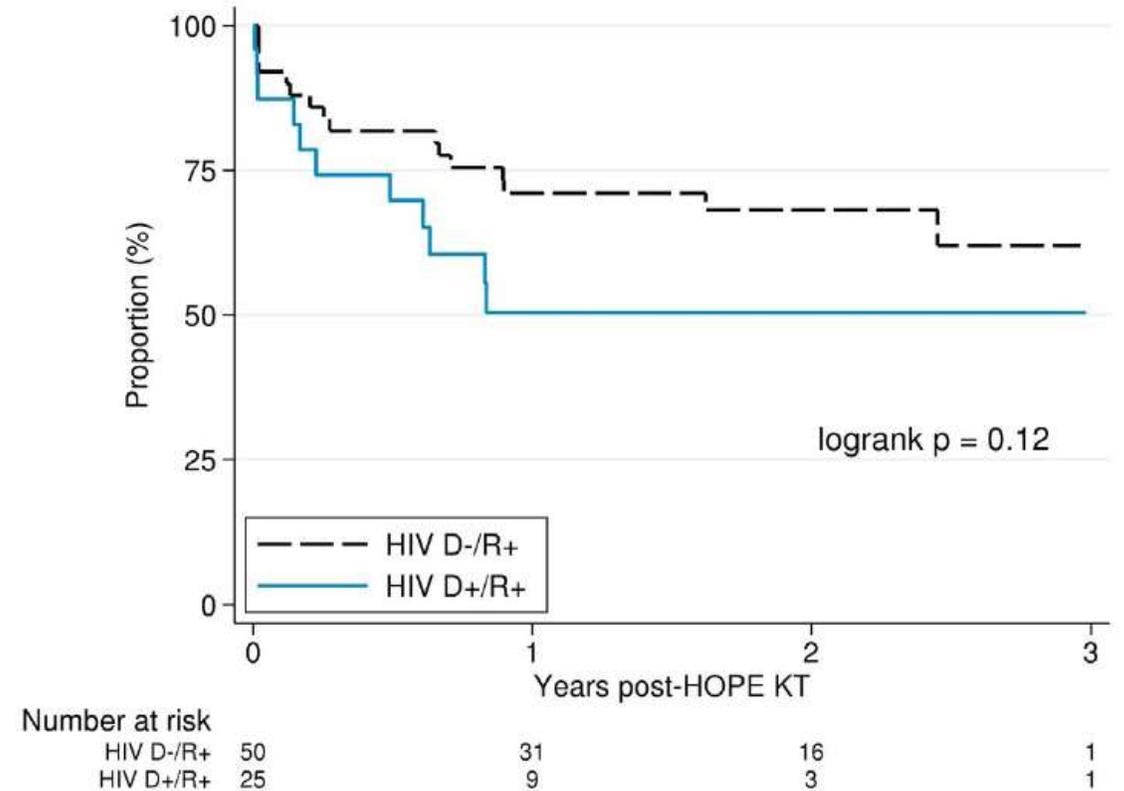
Of note, only rejection has been an issue in actual practice.

Outcomes in kidney transplant patients under the HOPE Act

A Graft survival by donor HIV status

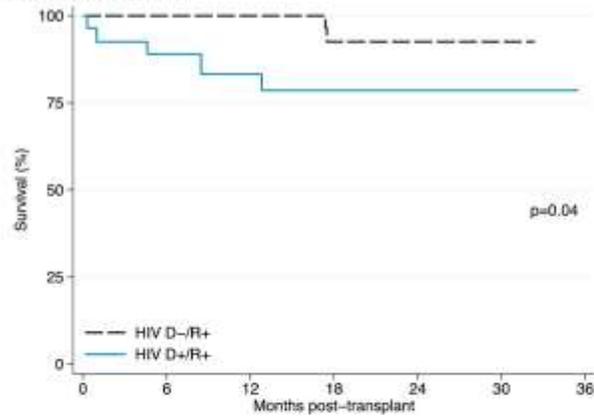


B Rejection-free survival by donor HIV status

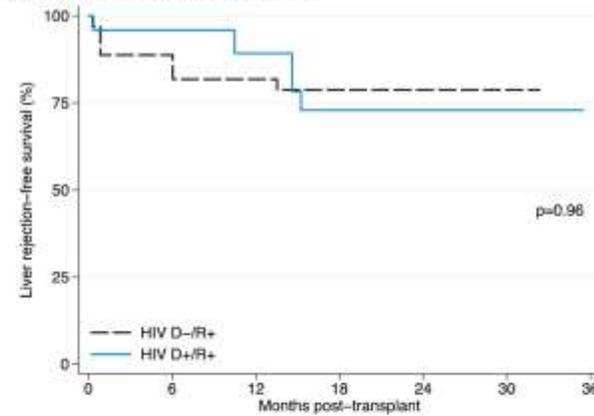


Outcomes in liver transplant patients under the HOPE Act

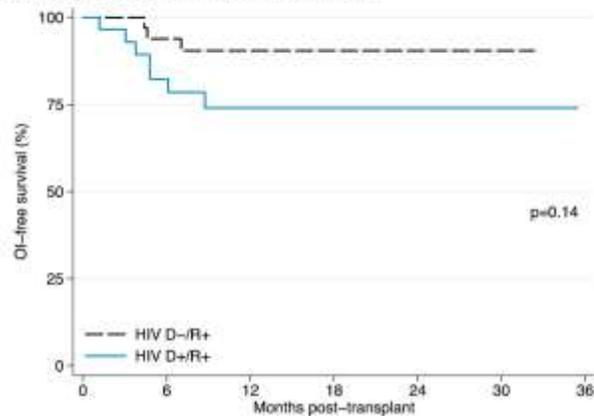
(A) Overall survival



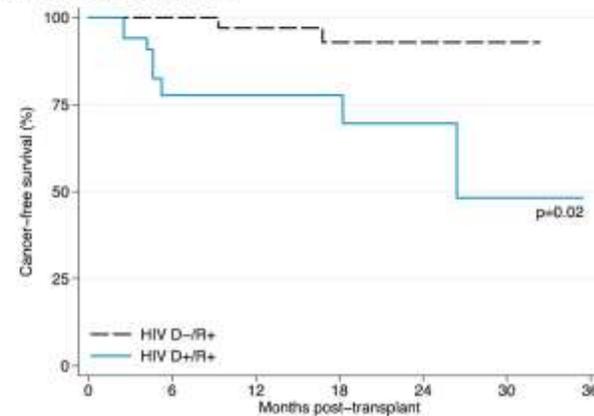
(B) Liver rejection-free survival



(C) Opportunistic infection-free survival

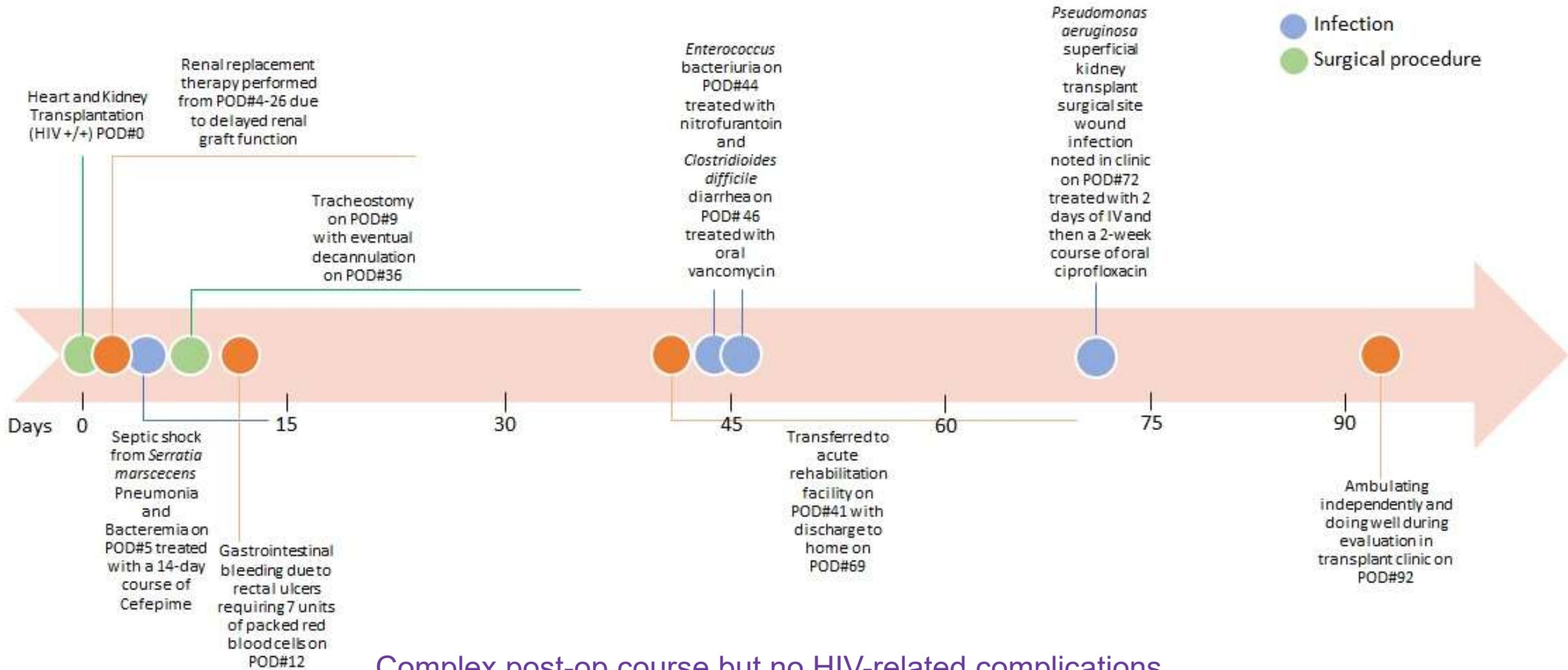


(D) Cancer-free survival



- So far, 24 HIV D+/R+ transplants done to date
- Survival numbers acceptable but liver may have more infections and cancer, which needs to be balanced against risk of dying on liver transplant list

HIV D+/R+ Cardiac Transplant: Post Transplant Course



Complex post-op course but no HIV-related complications
 Normal renal and cardiac function > 180 days post-transplant
J Heart Lung Transplant, online 24 Nov 2022

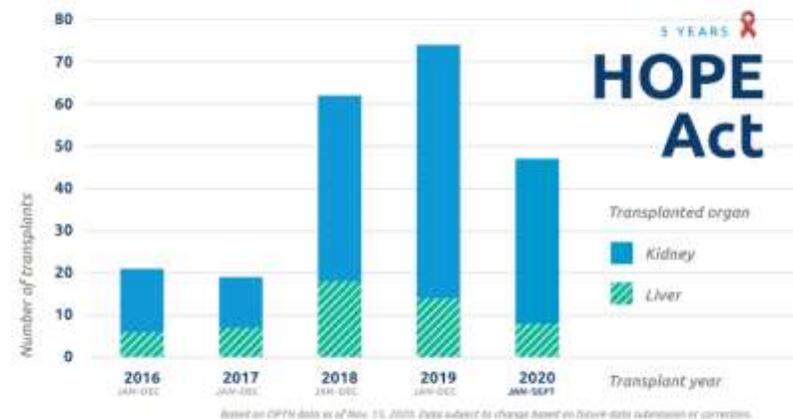
HOPE Act

Nevertheless, volumes to date have been less than anticipated

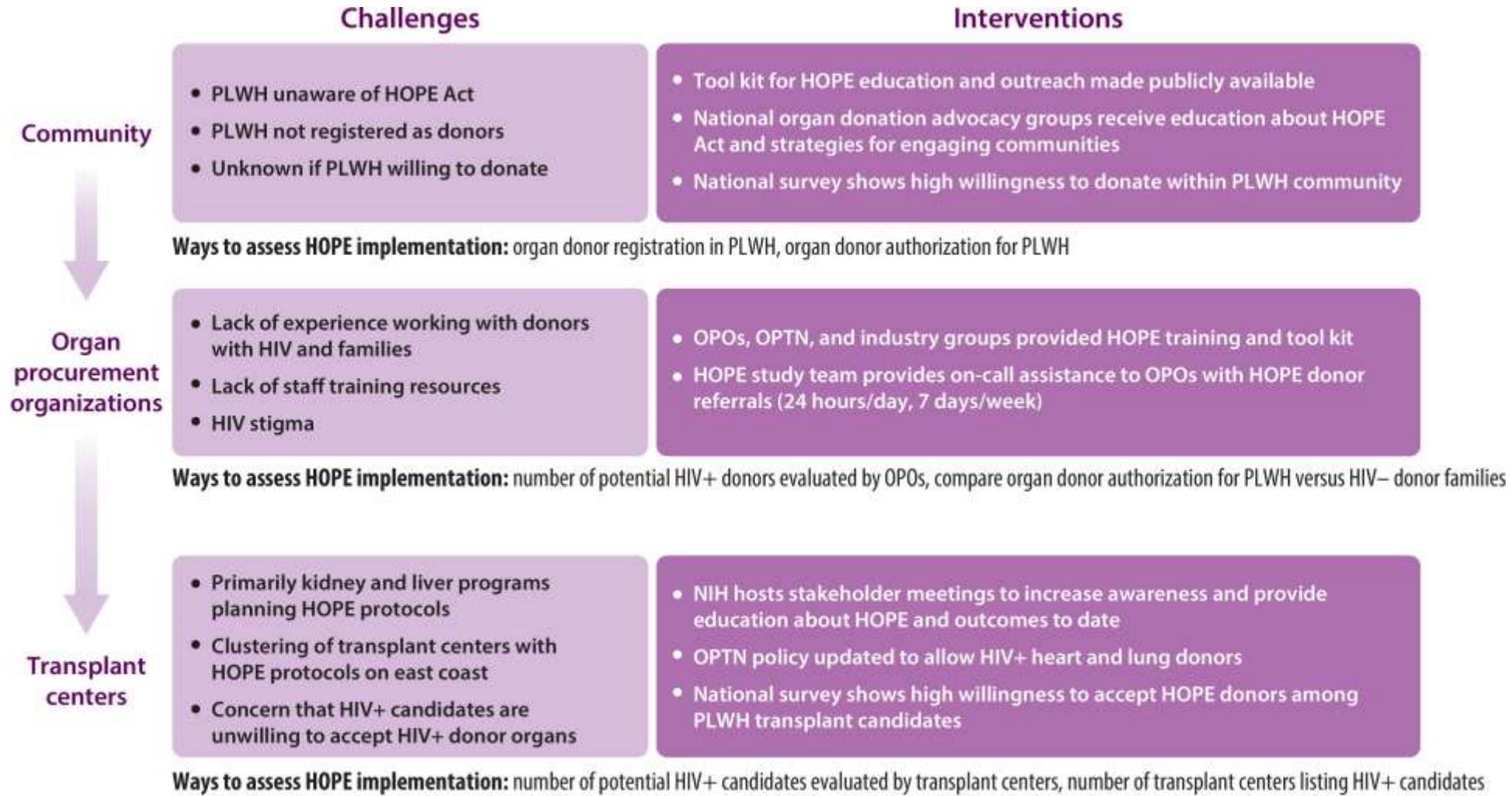
Anticipated volume:

500-600
transplants/year

Actual volume:



Many barriers exist to HIV D+/R+ transplant



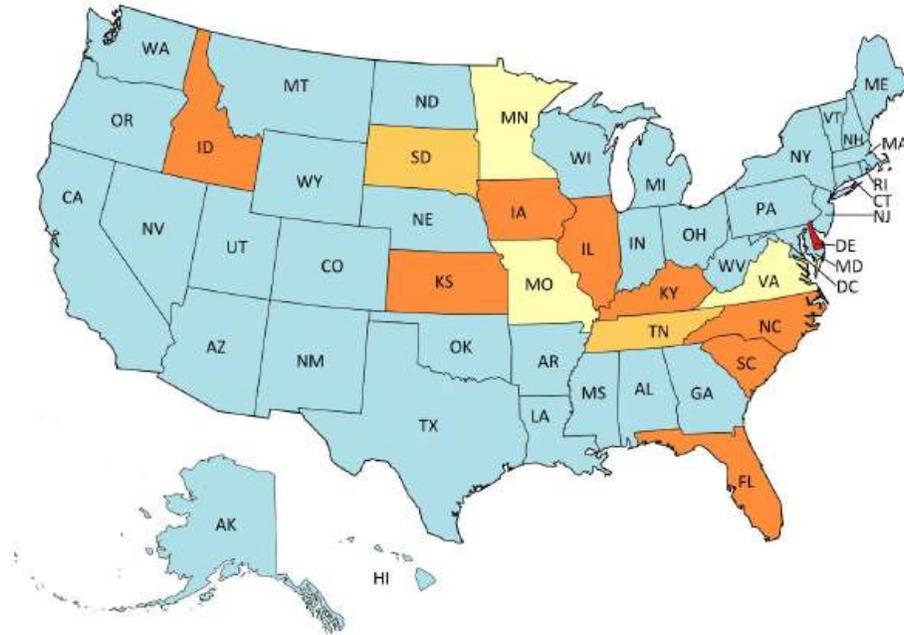
Referral patterns

- There is no organized system to guide patients with HIV and advanced organ failure to centers experienced with their care
- It's up to patients (and their providers) to navigate the system, find an appropriate transplant center, and navigate the transplant cascade of care



Legal barriers

Figure 1:



Type of legal Prohibition	States	Applies to OPOs and transplant center?	Applies to deceased or living donors?	Interpretation
<p>■ Law prohibits transfer or use of organs from HIV+ individuals</p>	Delaware	Yes	Living and Deceased	<ul style="list-style-type: none"> • HIV+ to-HIV+ donation and transplantation is prohibited • Revision to state law required in order to facilitate HOPE Act protocols
<p>■ Law prohibits HIV+ individuals from donating organs.</p> <p>■ Law prohibits HIV+ individuals from donating but permissible with consent</p>	Florida Idaho Illinois Iowa Kansas Kentucky North Carolina South Carolina <i>Permissible with consent:</i> South Dakota Tennessee	No	Living	<ul style="list-style-type: none"> • "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
<p>■ Law allows for HIV+ organ donation for "medical research."</p>	Minnesota Missouri US VI Virginia	No	Living and Deceased	<ul style="list-style-type: none"> • 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
<p>■ Laws don't directly implicate organ donation</p>				

Availability of HOPE act centers nationally



Map Legend	
+	HOPE Approved Transplant Center(s)

Are patients with HIV willing to accept HIV positive organs?

- Most pts willing to accept:
 - HIV+ living donor organs (87%)
 - HIV+ deceased donor organs (84%)
 - Increased infectious risk donor organs (70%)
- Thirty percent of patients expressed concerned about HIV superinfection and transmitted resistance, but even a majority (71%) of these pts would accept an HIV offer
- Other concerns that led them to decline enrollment:
 - HIV D+/R+ transplantation was safe (45% vs. 77%, $P = 0.02$),
 - HIV D+ organs would work similar to HIV D- organs (55% vs. 77%, $P = 0.04$)
 - Would receive an infection other than HIV from an HIV D+ organ (64% vs. 13%, $P < 0.01$).

J Acquir Immune Defic Syndr. 2020 Sep 1;85(1):88-92.

False positive HIV tests

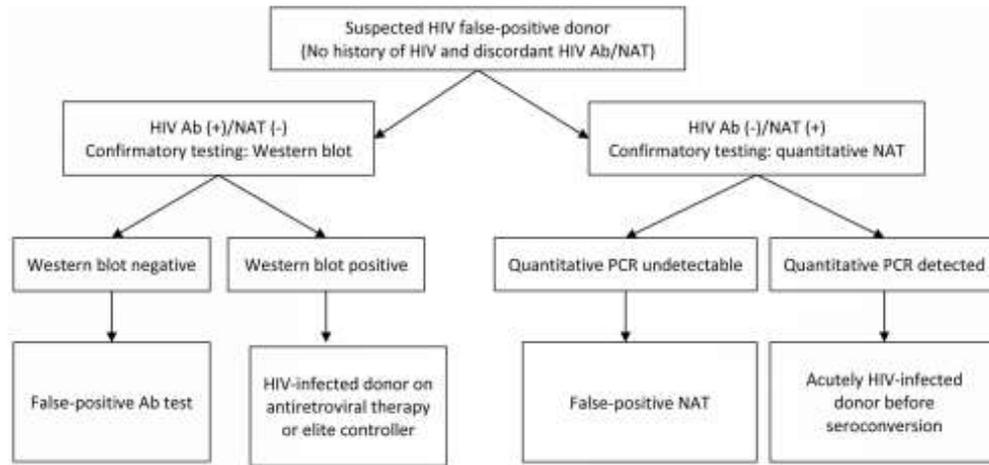


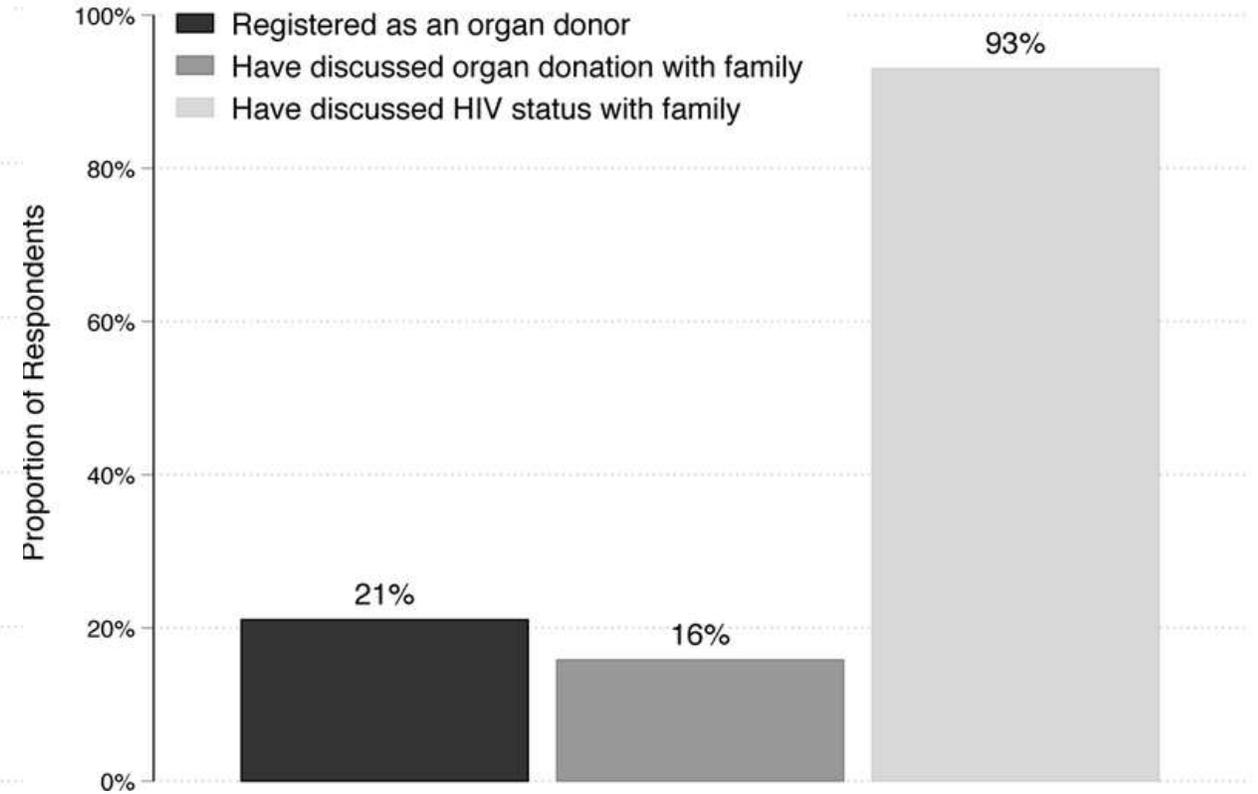
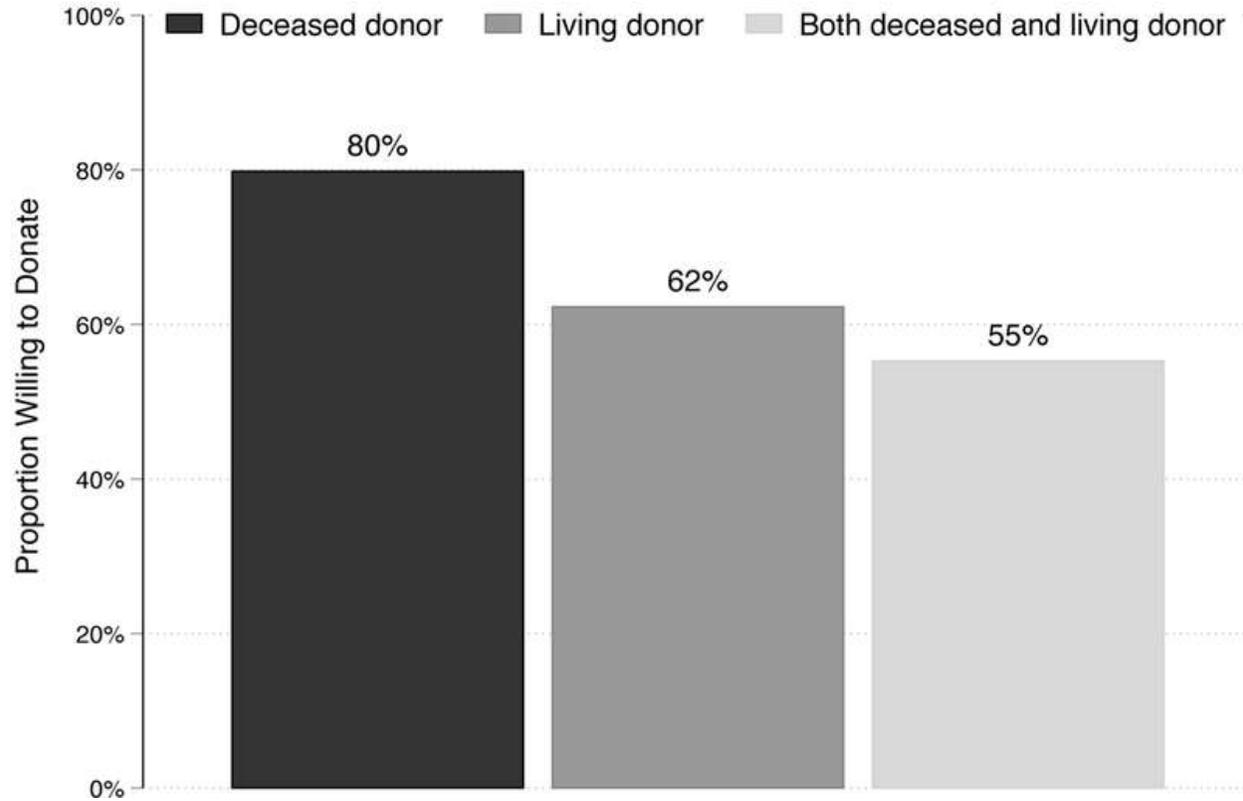
Figure 1. Suspected False-positive Donor Algorithm

Potential explanations for discordant HIV Ab and NAT testing in a potential donor with no prior history of HIV per the medical record or family history. In cases of a reactive Ab test (left), a Western blot or HIV Ag/Ab combination assay would be the preferred next test. If the Western blot is negative, this confirms result was a false-positive. If the Western blot is positive, the donor could be HIV-infected and taking effective antiretroviral therapy or have an effective immune response (i.e. elite controller). In cases of a nonreactive Ab test and a positive qualitative NAT (right), a quantitative viral PCR would be the preferred next test. If the quantitative PCR is undetectable, this confirms the qualitative NAT was a false-positive. If the quantitative PCR is positive this indicates the donor was recently HIV-infected and has not yet

Typically, organs from potential donors with suspected false positive HIV testing were discarded, but the HOPE act means that these organs can now be used.

These donors have reflected ~1/3 of organs transplanted under the HOPE Act.

Are people with HIV willing to sign up for organ donation?



Encouraging organ donation in primary care

I CAN'T REGISTER AS AN ORGAN DONOR WITHOUT SHARING MY HIV STATUS.

You never have to share your HIV status when registering to save lives as an organ donor...just say "YES"! Everyone can register. Everyone can save lives.



PEOPLE LIVING WITH HIV CANNOT RECEIVE ORGAN TRANSPLANTS.

Research shows that people living with HIV wait longer to receive a life-saving organ transplant. But YOU can change that. Living with HIV? Register as an organ donor. Be a hero to someone waiting.



DEAR TEAM HOPE, I'M LIVING WITH HIV. HOW CAN I REGISTER AS AN ORGAN DONOR?

Great question! Registering to be an organ donor is the same for everyone, HIV+ or HIV-. Take your pick from options 1, 2, or 3. Remember, you are **not** required to disclose your status to register:

- ONLINE AT REGISTERME.ORG
- AT YOUR LOCAL DMV WHEN YOU GET YOUR DRIVERS LICENSE
- ON YOUR IPHONE IN THE HEALTH APP



CELEBRATE WORLD AIDS DAY... BY REGISTERING AS AN ORGAN DONOR!

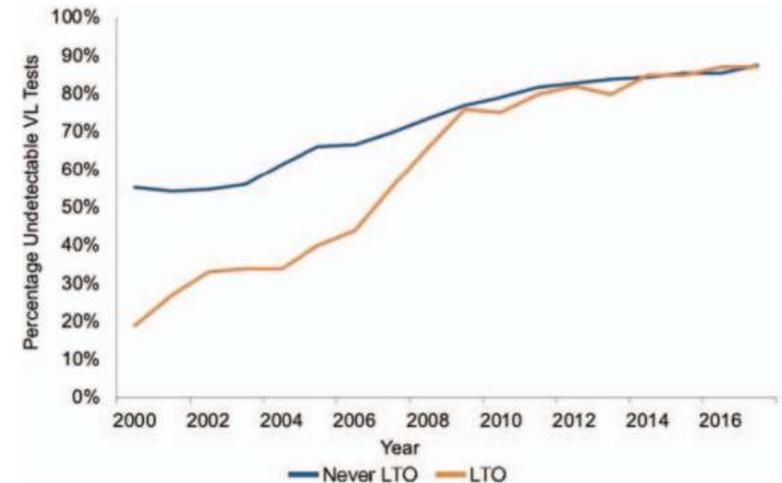
Living with HIV? You can register as an organ donor! The HOPE Act of 2013 made HIV-HIV transplants legal in the U.S.

DON'T LET HIV STOP YOU FROM BEING A HERO... REGISTER TODAY AT REGISTERME.ORG!



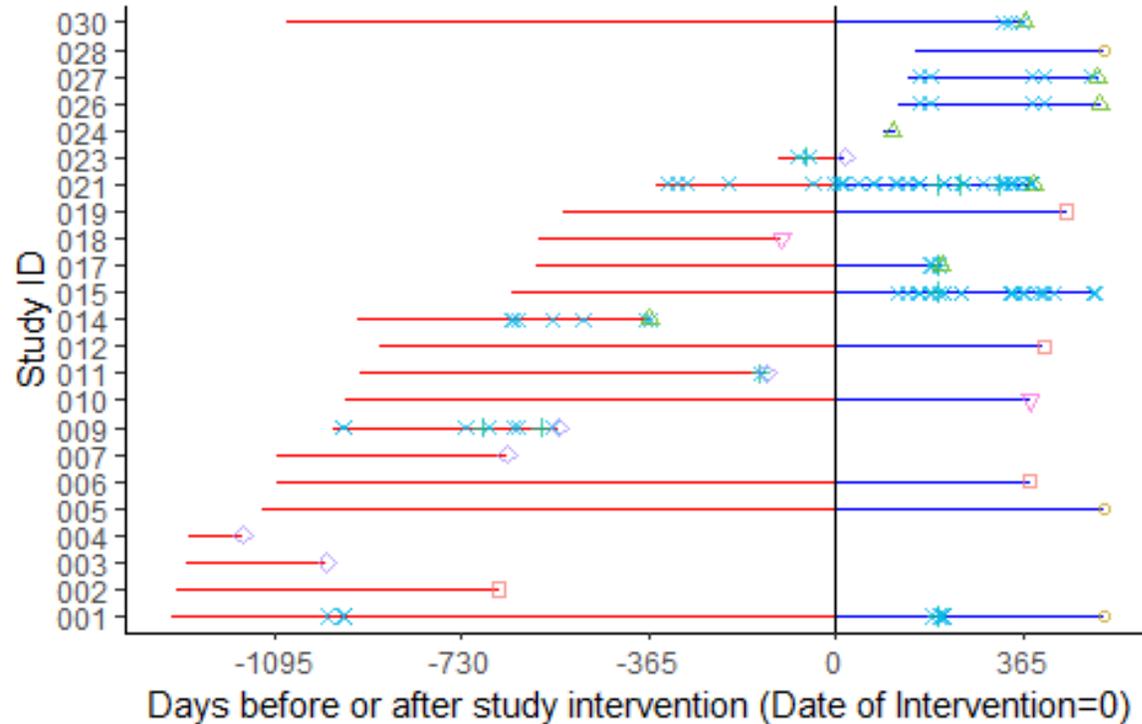

Resistance is not a problem anymore

- The rate of prevalent resistance in ARV-naïve patients in the modern era is negligible and fewer than 1% of all patients with HIV in the modern era meet criteria for having limited treatment options (LTO).
- Pts with LTO in recent years have the same outcomes as pts with susceptible virus
- In fact, many clinics don't even check resistance genotypes before starting ARVs anymore (*same-day initiation*).



AIDS. 2020 Nov 15;34(14):2051-2059.

Benefits of receiving an organ from a donor with HIV



△ HIV offer accepted and transplanted × HIV offer declined
+ HIV offer accepted, but not transplanted ◇ Non-HIV offer accepted and transplanted

- Our own internal data demonstrate that kidney patients were transplanted much faster once we started more aggressively accepted HOPE offers

IDWeek 2022.

So, as a practical matter, what do we do when we get called about a potential HIV-seropositive donor?

Resistance

- Prior HIV genotypes
- Treatment history

Opportunistic infection

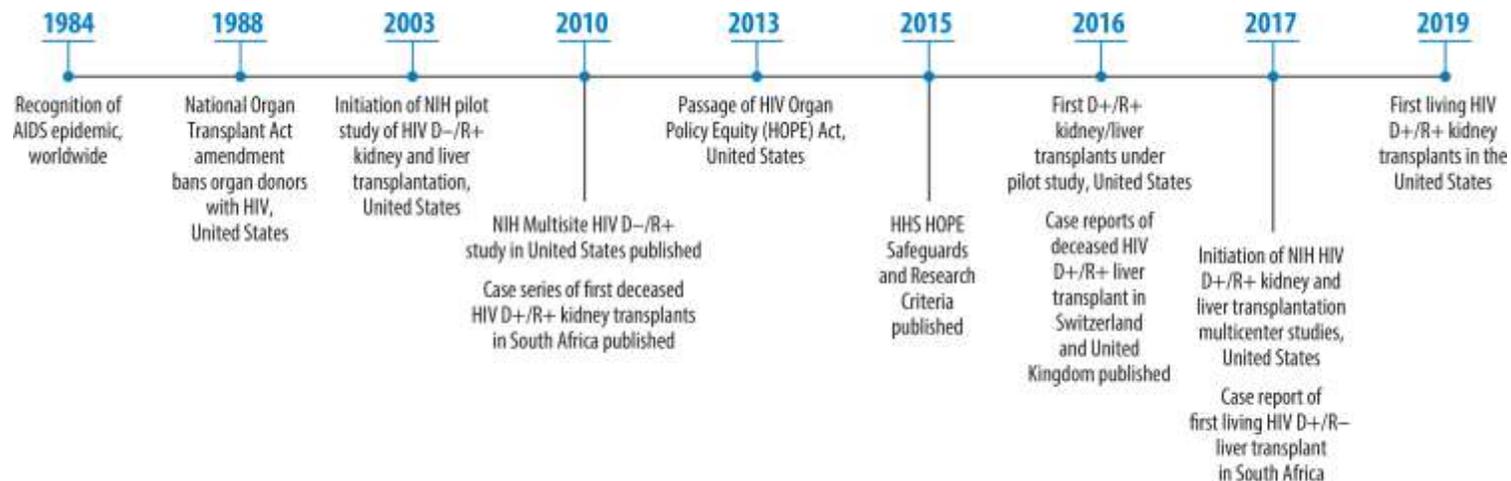
- CD4+ count
- Viral load
- Medical records

Malignancy

- Medical records

What does the future hold?

- Kidney and liver transplant likely no longer to be considered experimental → more centers to offer
- Other organs will require that HOPE transplants will continue to be done under research protocols *with removal of the volume requirement*
 - More centers to offer heart transplant
 - HOPE lung and pancreas transplants?



Thank you!

Montefiore



Albert Einstein College of Medicine

