



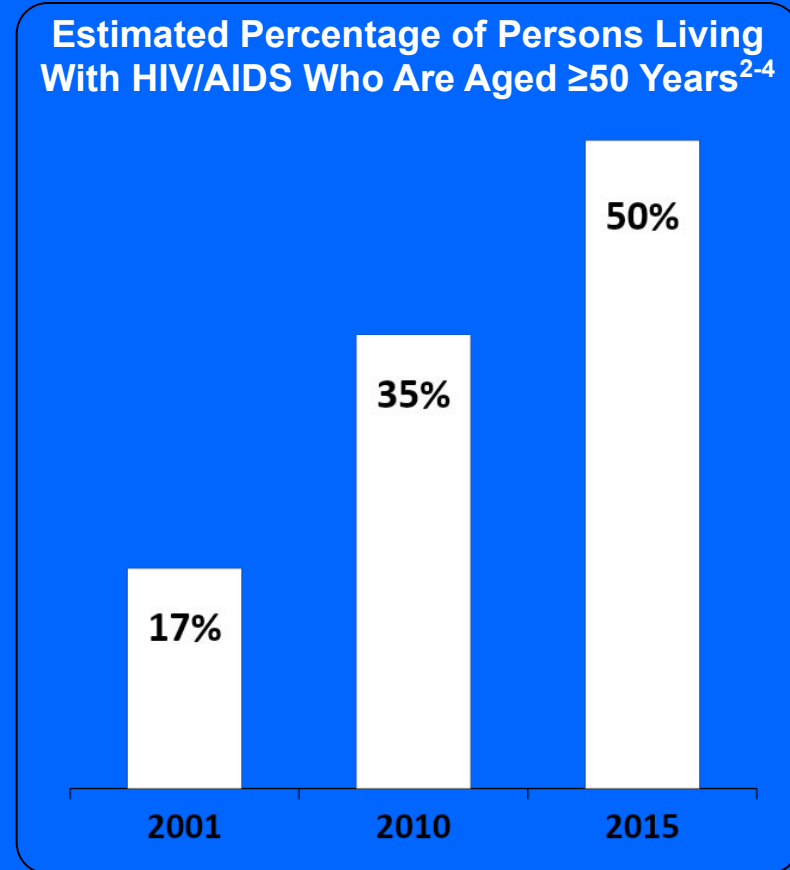
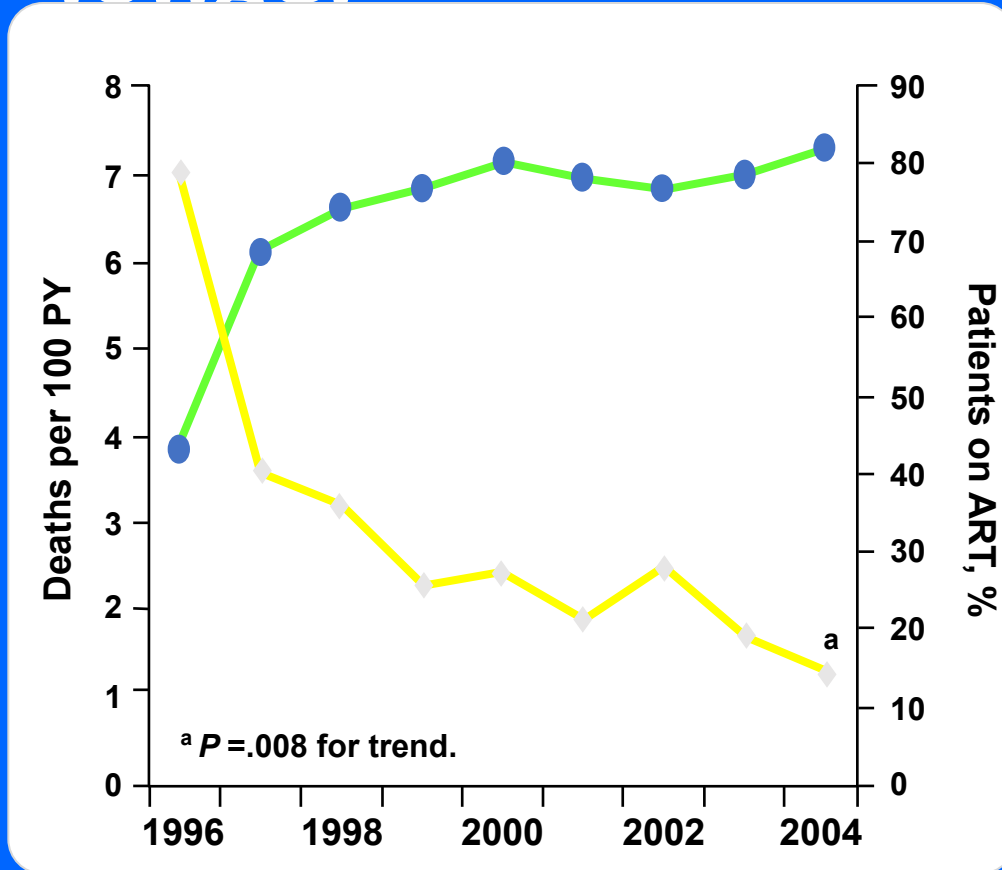
HIV Positive Organs HIV Positive Recipients

How Did We Get Here?

Alan Taege, M.D.

**Assistant Professor of Medicine
Department of Infectious Disease**

HIV-positive Patients are living longer



- In the United States, a 20-year-old HIV-positive patient can now expect to live into his/her early 70s⁵

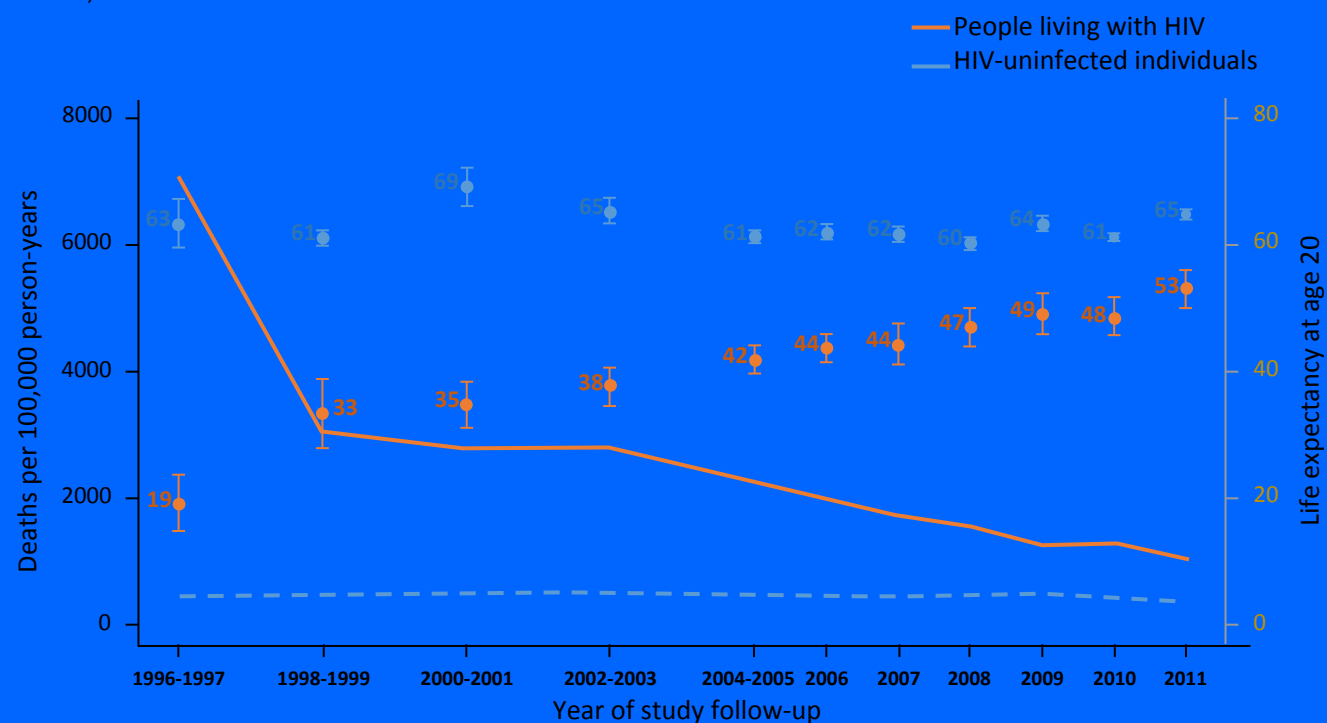
ART, antiretroviral therapy; PY, person years.

¹ Palella FJ, et al. *J Acquir Immune Defic Syndr*. 2006;43:27-34; ² Centers for Disease Control and Prevention (CDC). *HIV/AIDS Surveillance Report: Cases of HIV Infection and AIDS in the United States and Dependent Areas*. 2005; ³ CDC. *Diagnoses of HIV Infection in the United States and Dependent Areas*. 2011; ⁴ Effros RB, et al. *Clin Infect Dis*. 2008;47:542-553; ⁵ Samji H, et al. *PLoS ONE* 2013; 8:e81355.



People ARE LIVING LONGER with HIV

Age-adjusted mortality rates and life expectancy at age 20 for people living with HIV and HIV-uninfected individuals^{a,b} (Kaiser Permanente, 1996-2011)



- In a large cohort study, age-adjusted mortality rates decreased while life expectancy at age 20 rose for people living with HIV
 - In 1996-1997, 20-year-olds living with HIV had a life expectancy of 19.1 years
 - In 2008, life expectancy for a 20-year-old living with HIV more than doubled to 47.1 years
 - In 2011, life expectancy in a 20-year-old living with HIV increased to 53.1 years

^aKaiser Permanente cohort study of 24,768 people living with HIV and 257,600 HIV-uninfected individuals to estimate expected years of life remaining (“life expectancy”) at age 20.

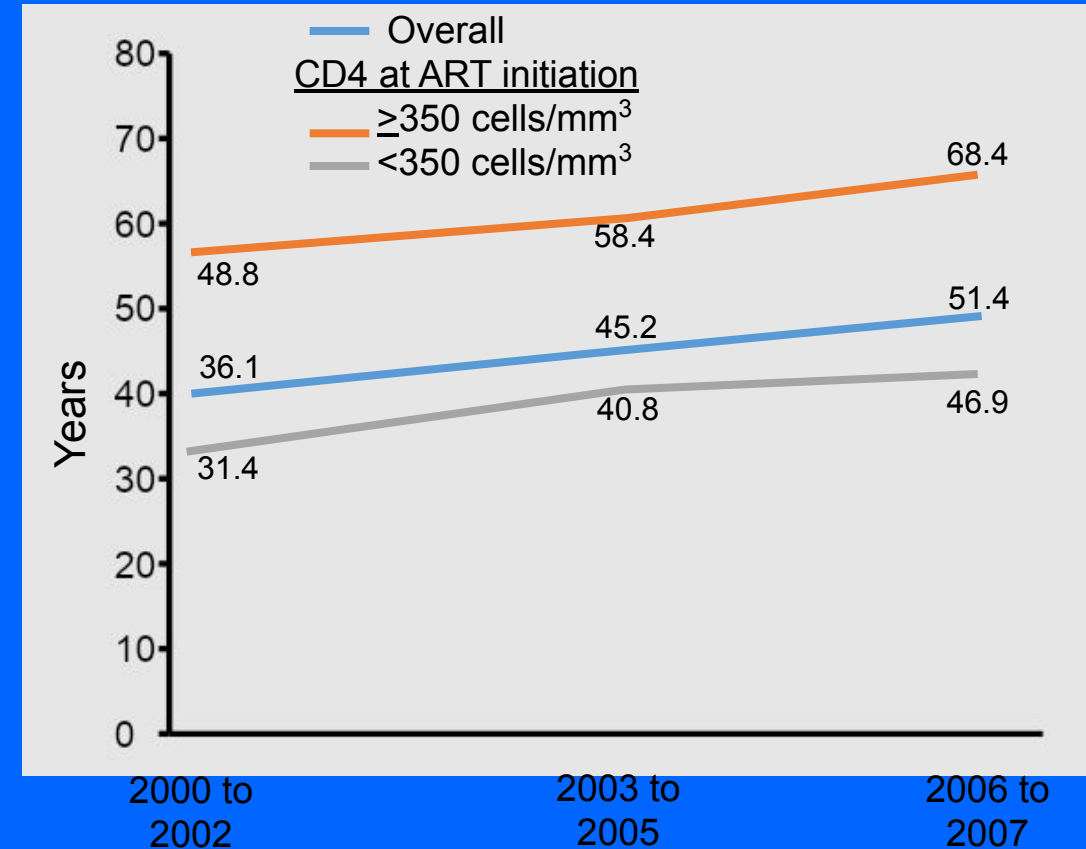
^bAge-adjusted mortality rates for HIV-uninfected individuals showed no trend over time ($P=0.43$), whereas rates decreased for people living with HIV ($P<0.001$). Change in life expectancy at age 20 for HIV-uninfected individuals was not statistically significant overall. In contrast, increases in survival for people living with HIV were observed across all gender, race/ethnicity, and HIV-transmission risk groups from 1996–2007 to 2008–2011 ($P<0.001$ for all increases).

Marcus JL, et al. *J Acquir Immune Defic Syndr.* 2016;73:39-46.

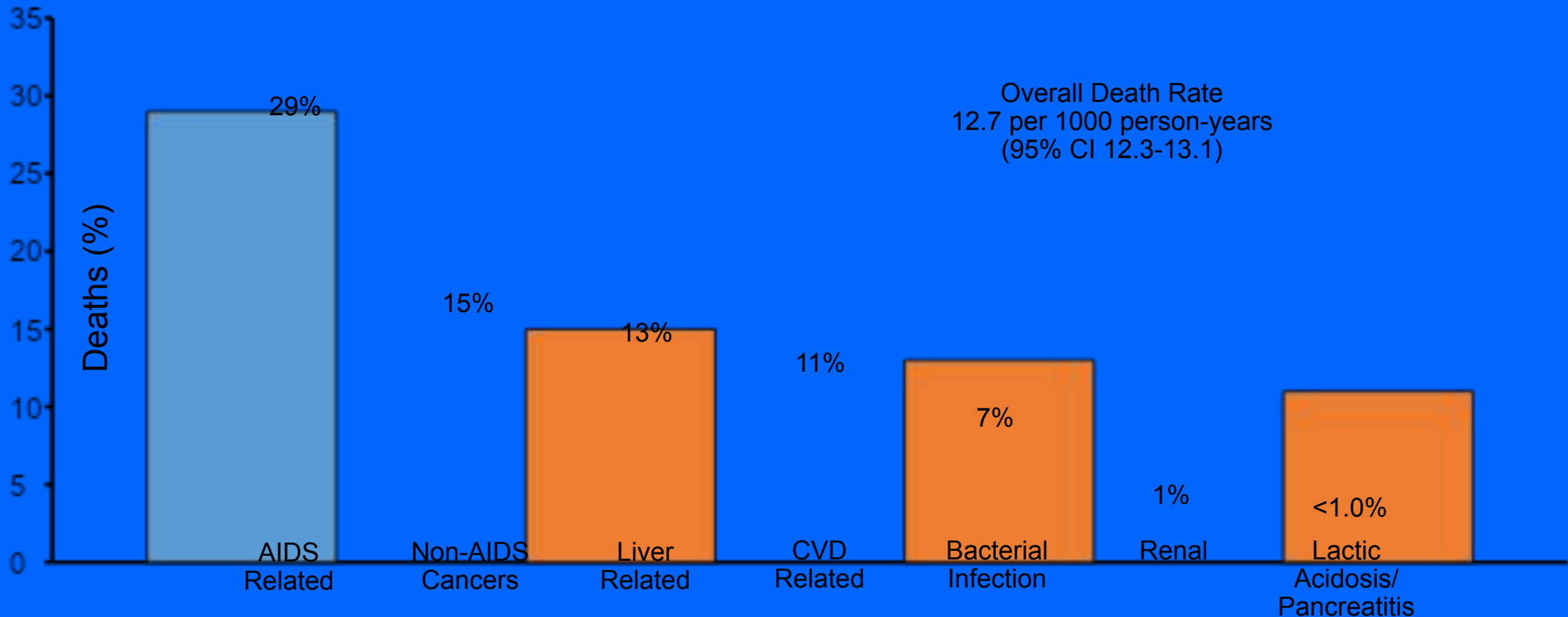
Life Expectancy Among Treated HIV Patients in the US and Canada (2000-2007)

- NA-ACCORD participants ≥ 20 years of age (n=22,937)
 - Treatment-naïve before initiating ART
- Crude mortality rate (2000-2007)
 - 19.8 per 1000 person-years (n=1622 deaths)
- Life expectancy at 20 years of age
 - Increased from 36.1 to 51.4 years from 2000-2002 to 2006-2007
- **A 20-year-old HIV-positive person is expected to live into their early 70s**

Life Expectancy Estimates

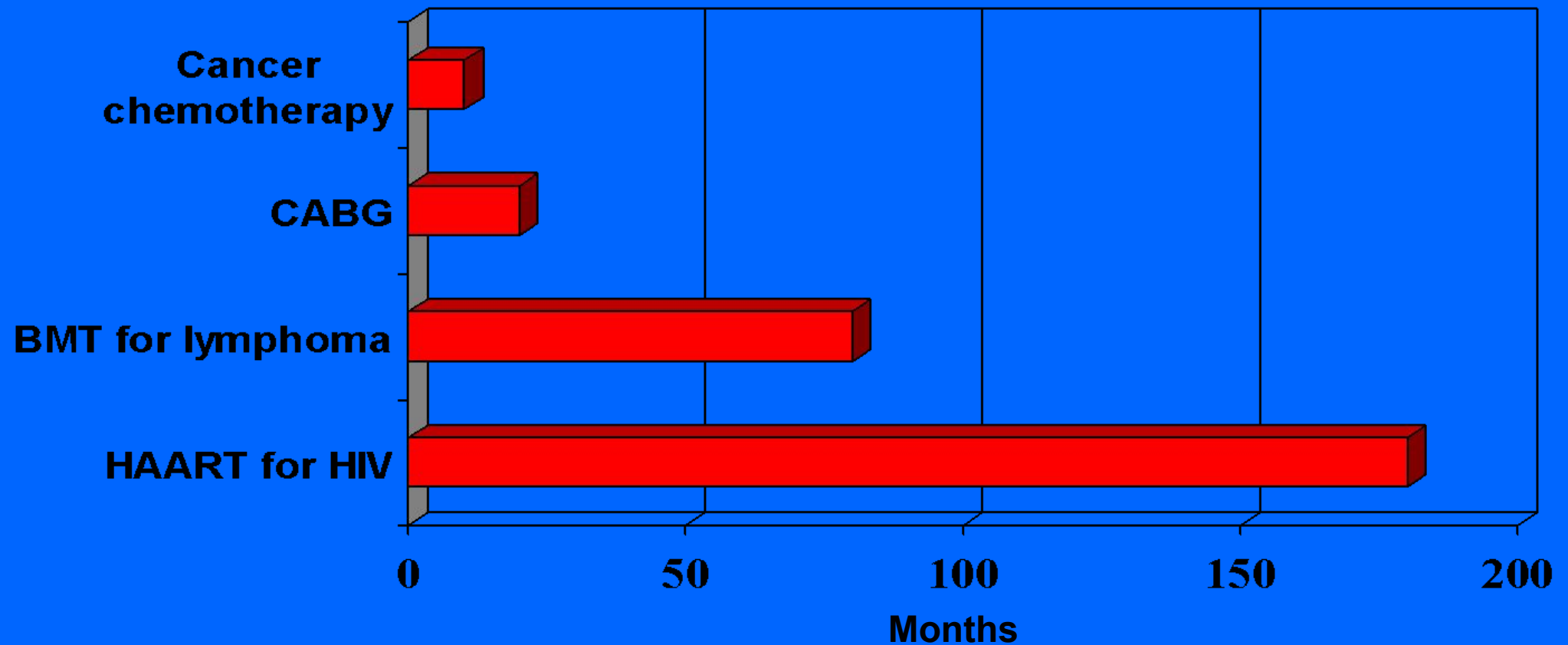


D:A:D Study (1999-2011): Underlying Causes of Death in HIV Patients



n=49,731 HIV-infected patients (1999-2011).
A total of 3909 deaths over 308,719 person-years of follow-up.

Per-Person Survival Gains



Should solid organ transplantation be considered in HIV+ patients in this era of HAART?

Current considerations of efficacy in organ allocation can be summarized as follows. We have substantial evidence of diminished survival among HCV-positive patients, patients with diabetes, black patients, and patients requiring retransplantation, yet we do not prevent transplantation in these groups. In contrast, we have no evidence of poorer survival among otherwise healthy HIV-positive patients who are receiving antiretroviral therapy, yet both overt and covert barriers to transplantation remain. This contra-

“On ethical grounds alone, there is no justification for providing organs to these groups of patients but not to patients infected with HIV.”



ACS statement on the Surgeon and HIV infection

(Revised May 2004)

- **Surgeons have the same ethical obligations to render care to HIV-positive patients as they have to care for other patients**
- Surgeons should utilize the highest standards of infection control, involving the most effective known sterile barriers, universal precautions, and scientifically accepted infection control practices. This practice should extend to all sites where surgical care is rendered and to all patients who receive surgical care.
- Postexposure prophylaxis with antiretroviral chemotherapy is recommended.



2003 (2007)
NIAID

Survival in HIV-positive transplant recipients compared with transplant candidates and with HIV-negative controls (HIVTR)

Table 3. Impact of liver transplantation on mortality comparing HIV-infected transplant candidates and recipients

Multivariate predictors	HR	(95% confidence interval)	P value
Transplantation with MELD >15a	0.1	(0.05, 0.1)	<0.0001
Transplantation with MELD<15a	0.7	(0.3, 1.8)	0.43
Most recent MELD pretransplanta	1.1	(1.1, 1.2)	<0.0001
HCV-infected	3.7	(2.0, 6.9)	<0.0001
Age (by decade)	1.4	(1.1, 1.9)	0.02

Table 4. Impact of kidney transplantation on mortality comparing HIV-infected transplant candidates and recipients

Multivariate predictors	HR	(95% confidence interval)	P value
Transplantationa	0.6	(0.3, 1.4)	0.23
Age (by decade)	1.7	(1.2, 2.3)	0.001
BMI at enrollment (<21)	2.6	(1.2, 5.7)	0.02

Conclusion: Kidney transplantation should be standard of care for well managed HIV-positive patients.

Liver transplant in candidates with high MELD confers survival benefit; transplant is a viable option in selected candidates. The increased mortality risk compared with HIV-negative recipients was modest.

Motivation/Significance

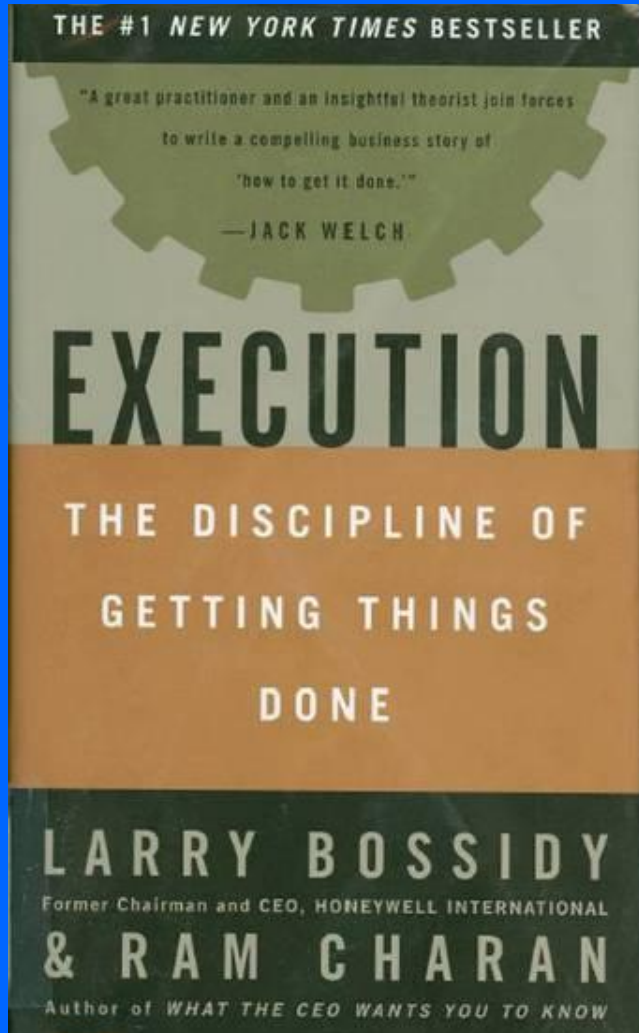
- **Prevalence of end stage kidney and liver disease in HIV+ increasing (Lucas CID 2014; Smith Lancet 2014)**
- **HIV+ candidates have higher waitlist mortality compared to HIV- (Trullas AIDS 2011, Ragni Liver Transpl 2005)**
- **Excellent outcomes with HIV- organs for HIV recipients (HIV D-/R+) (Roland AIDS 2016, Locke JASN 2015; Locke Transplantation 2016)**

The Problem

- Shortage of organs
- Many die while waiting on transplant list

Vision without Execution is Hallucination

Thomas Edison

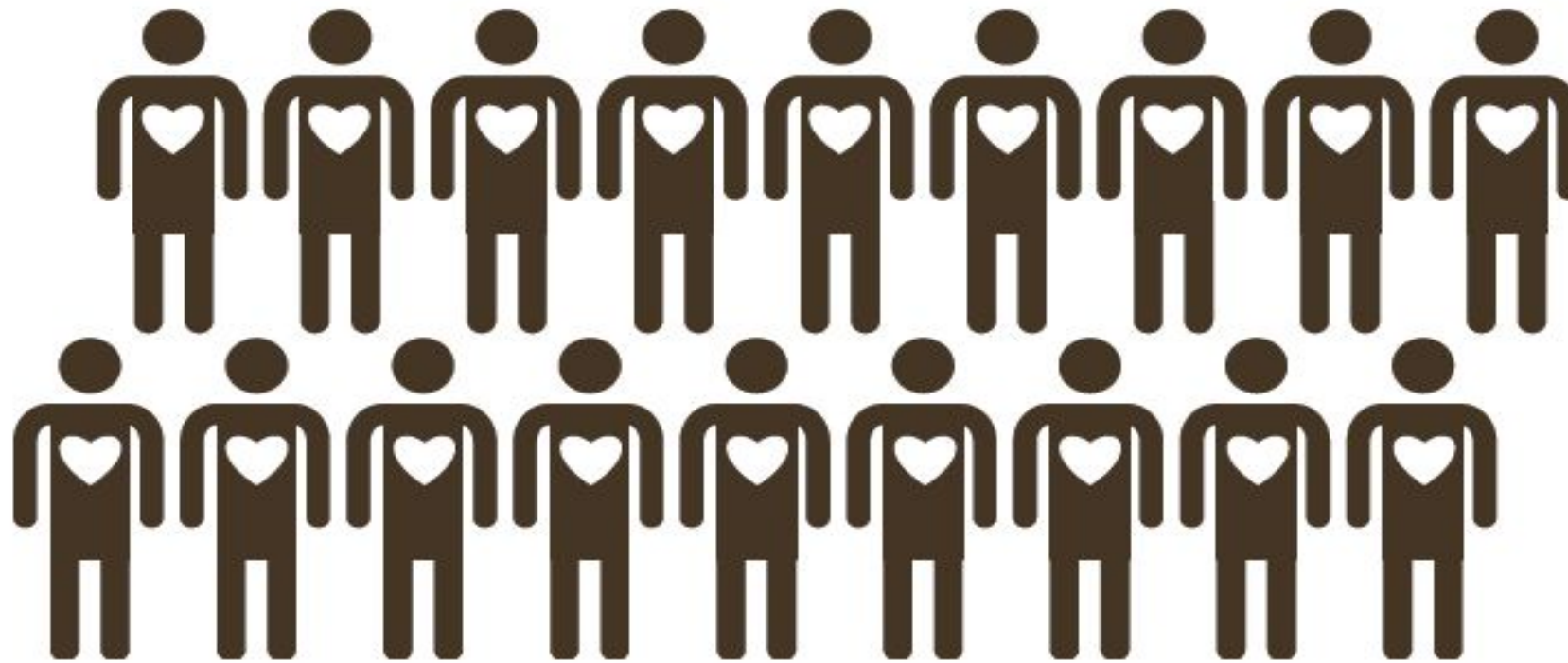


Tenets of Getting Things Done

1. Execution is a discipline
2. Execution is the major job of leadership
3. Execution must be core element of an organization's culture

"We believe that, in the modern era of HIV care, a universal ban on transplants from HIV-infected donors may no longer be justified."

Joint statement from four groups involved with transplantation issues



Donation dilemma

Should the ban on HIV-positive organ transplants be lifted?

ANGELA TOWNSEND | *Plain Dealer Reporter*

As of Aug. 29, nearly 112,000 people in the United States are on the waiting list for an organ

Estimating the Available Pool

- Estimate - conservative
- Nationwide Inpatient Sample (NIS), HIV Research Network, UNOS.
- 20 donors discarded annually – unexpectedly HIV +
- Estimated 500-600 potential HIVDD (481-652)
 - ~63 kidney only
 - ~221 liver only
 - ~250 multiple organ donors
- Potential to help 1000 patients!
- Untapped potential - - - shorten waiting list for HIV and other patients
- Feasible?
- Has it been done?

Roadblocks

- National Organ Transplant Act 1984 section 273 forbids:
“shall adopt and use standards of quality for the acquisition and transportation of donated organs, including standards for preventing the acquisition of organs that are infected with the etiologic agent for acquired immune deficiency syndrome” **An absolute contraindication to donation.**
- OPTN Final Rule – HIV infection is an absolute contraindication to deceased organ donation in the United States.
- Public opinion
- Centers willing to perform – harvest/transplantation?
- Should medical decision making be governed by law?

2007 Charlie Norwood Amendment

- CONGRESS
- BILLS
- H.R. 710 (110TH)

H.R. 710 (110th): Charlie W. Norwood Living Organ Donation Act

110th Congress, 2007–2009

An Act to amend the National Organ Transplant Act to provide that criminal penalties do not apply to human organ paired donation, and for other purposes.

Introduced:

Jan 29, 2007

Sponsor:

Rep. Charles “Charlie” Norwood [R-GA10, 2007-2007]

Status:



Broadening Pool of Donors ...for HIV infected recipients

- HIV infected donors?
 - Use of HIV infected donors was illegal
 - Estimated 500 additional donors/yr, 1000 kidneys
- Renal transplantation: HIV+ donors and HIV+ recipients
 - Muller, et al. NEJM 2010
 - South Africa!
 - Caveat: low rates of ARV resistance

S Africa: HIV D+/R+ Kidney Transplant

The NEW ENGLAND JOURNAL of MEDICINE

Renal Transplantation between HIV-Positive Donors and Recipients



Table 1. 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 ($\mu\text{mol/liter}$)	678	582	1712	725
CD4 count (cells/ mm^3)	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 nevirapine	Zidovudine, lamivudine, and nevirapine

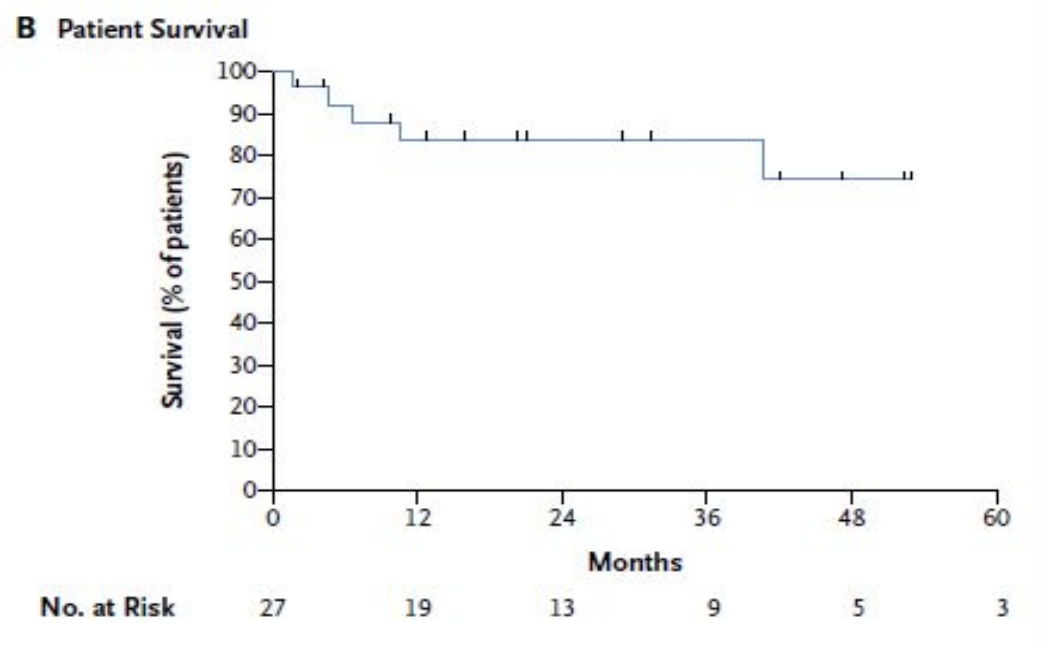
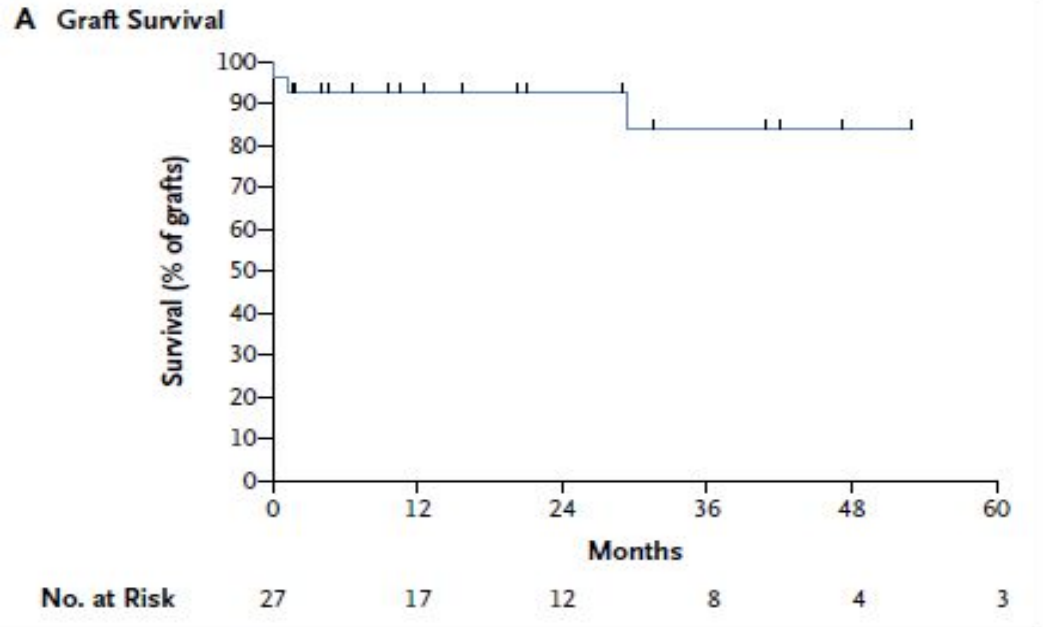
From Cape Town to the U.S.

- NEJM letter: 4 kidney recipients from HIV+ donors in 2008
- Great deal of debate in U.S. transplant community:
 - Benefits: increasing donor pool for everyone
 - Risks: super-infection, HIV + cadaveric donors risk of developing renal disease, surgical risk

Background and details

- South Africa
- Resource limited
- Limited ability to use dialysis
- Renal failure – often sent home to die
- Four renal transplants 2008:
 - HIV + organs to HIV + patients

HIV Positive to Positive Kidney Transplants 3-5 Years



N = 27

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

November 2013

HIV Organ Policy Equity (HOPE) Act

Legalized positive to positive donation in research setting



Protocol and Pilot Study

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/25yxwv3



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 NEWSPAPER ADVERTISING

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

PHOTO GALLERY



The Baltimore Sun

HEALTH

Hopkins Begins

By THE ASSOCIATED PRESS MARCH 31

WASHINGTON — Johns Hopkins University doctors performed the first liver transplant between two HIV-positive patients in the United States, a triumph for recipients, a long-sought goal for donors whose kidneys or livers were otherwise discarded because of the HIV infection.

Johns Hopkins University doctors performed the first liver transplant between two HIV-positive patients in the United States, a triumph for recipients, a long-sought goal for donors whose kidneys or livers were otherwise discarded 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

January 2016, Pilot protocol (NCT02602262)
 March 2016, First in US HIV D+/R+ kidney and liver transplants

People Magazine @people · Mar 31
 Johns Hopkins performs first successful HIV-positive organ transplant peoplemag.com/YVMn3vR



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

Read more at statesnews.com

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

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 ...

Johns Hopkins performed the first ever HIV-to-HIV liver

HOPE **TO DATE**

IN ACTION →

HIV-to-HIV Transplants Save Lives

LIVES SAVED BY
TRANSPLANT **26**

11 ORGAN DONOR
HEROES

TRANSPLANT
CENTER **18**
PARTNERS

12 ORGAN
PROCUREMENT
ORGANIZATIONS

Visit transplantepi.org for more about HOPE
Register to be an organ donor at registerme.org

Minireview

Challenges and Clinical Decision-Making in HIV-to-HIV Transplantation: Insights From the HIV Literature

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Biologic risks

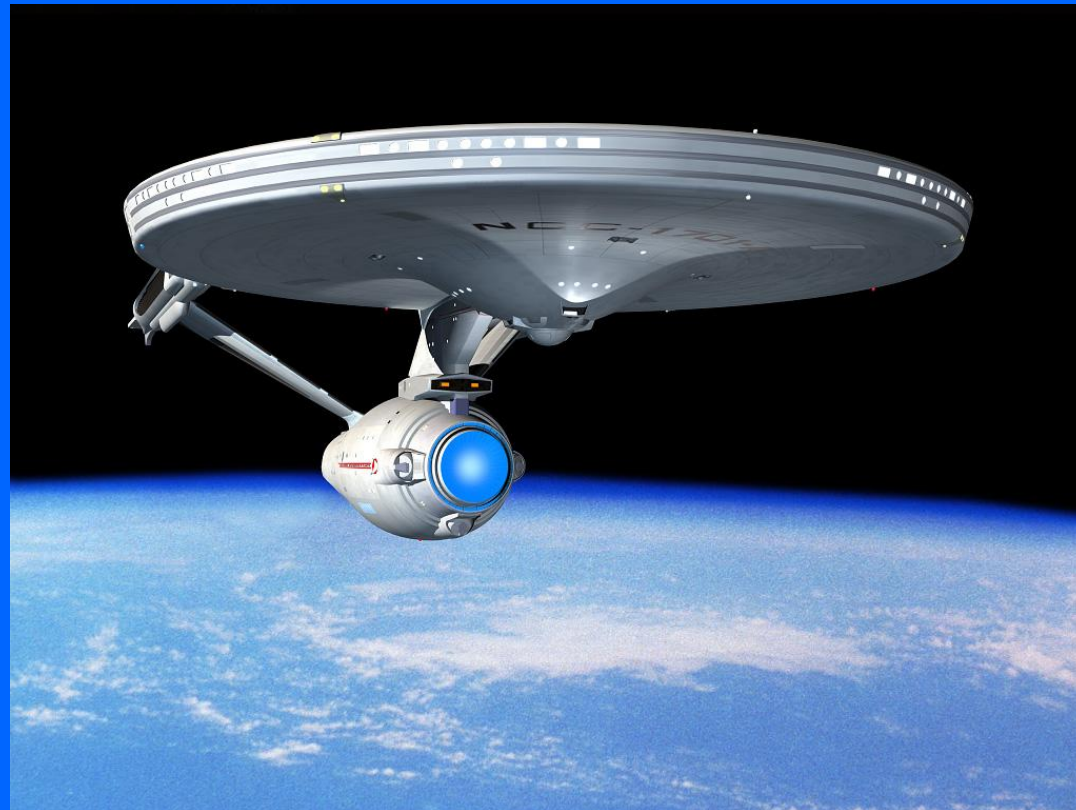
- HIV superinfection
- HIV nephropathy
- Donor derived infections
- Rejection

The Way Forward

- Tragedy does not have to end in total loss – Drug Epidemic/donation
- Stay ahead of the virus – new drugs: ART, Immunosuppression
- Understand rejection more completely; new and better approaches
- Continue innovating
- HCV+ HIV+ organ donation?

Go Boldly Where No Man Has Gone Before

Captain James Kirk
Starship Enterprise





Thus in silence in dreams' projections,
Returning, resuming, I thread my way through the hospitals;
The hurt and wounded I pacify with soothing hand,
I sit by the restless all dark night - some are so young;
Some suffer so much - I recall the experience sweet and sad...

Walt Whitman, *Leaves of Grass*, 1876