HIV and lung transplantation

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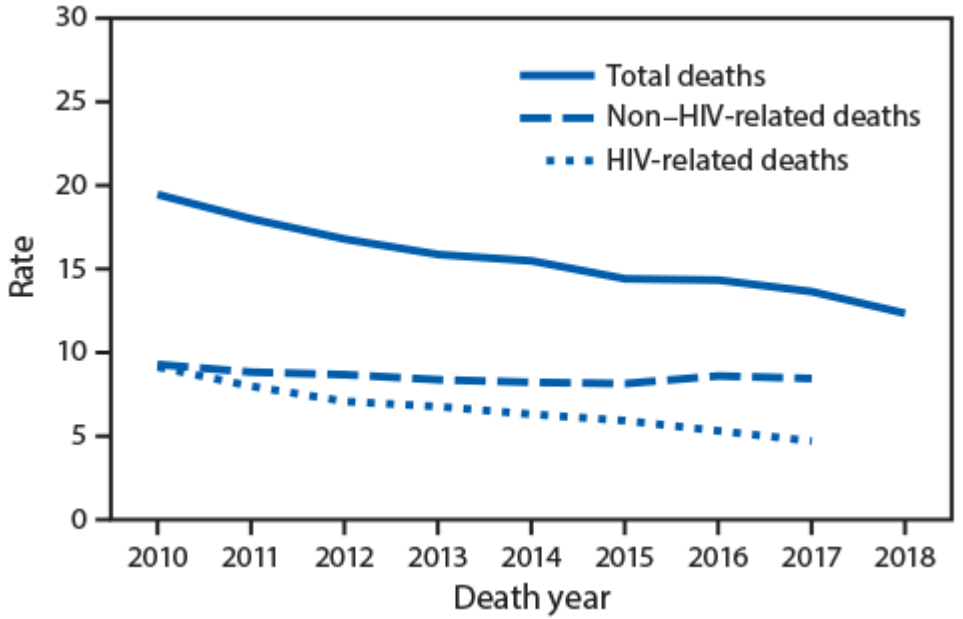
Disclosures

- 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.

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HIV and end-organ disease

Kidney disease	• Direct effects of HIV • Older antiretrovirals (TDF)	900 new dialysis patients/year
Liver disease	• Hepatitis B/C • Alcohol • Older antiretrovirals	~15% of deaths in people with HIV
Cardiac disease	• Direct effects of HIV • Inflammation→increased risk of myocardial infarction • Smoking • Abacavir	~2400 people with HIV with advanced heart failure
Lung disease	• 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

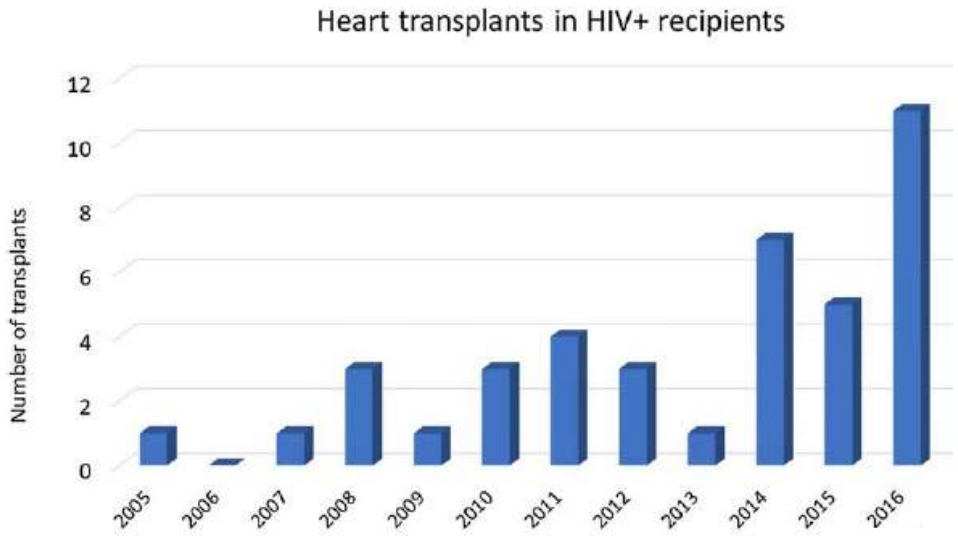
- People with HIV are *more* likely to die once they develop end organ disease

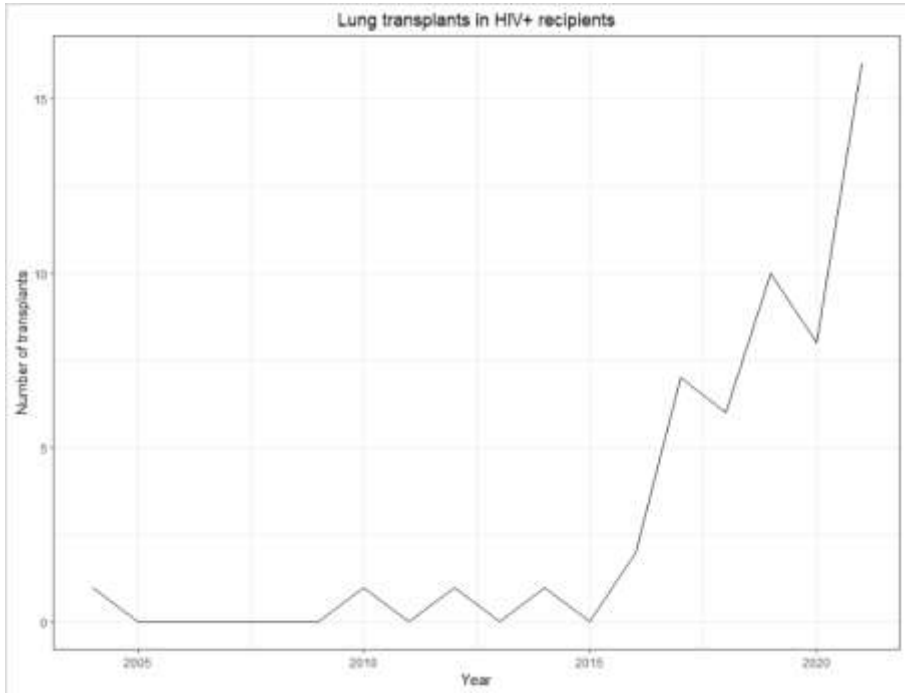
- They are *less* likely to be:
  - Referred to a transplant center by their providers
  - Listed for transplant once referred
  - Transplanted once listed

Clin J Am Soc Nephrol. 2017 Mar 7;12(3):467-475.

HIV and thoracic transplant

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Personal research (unpublished).

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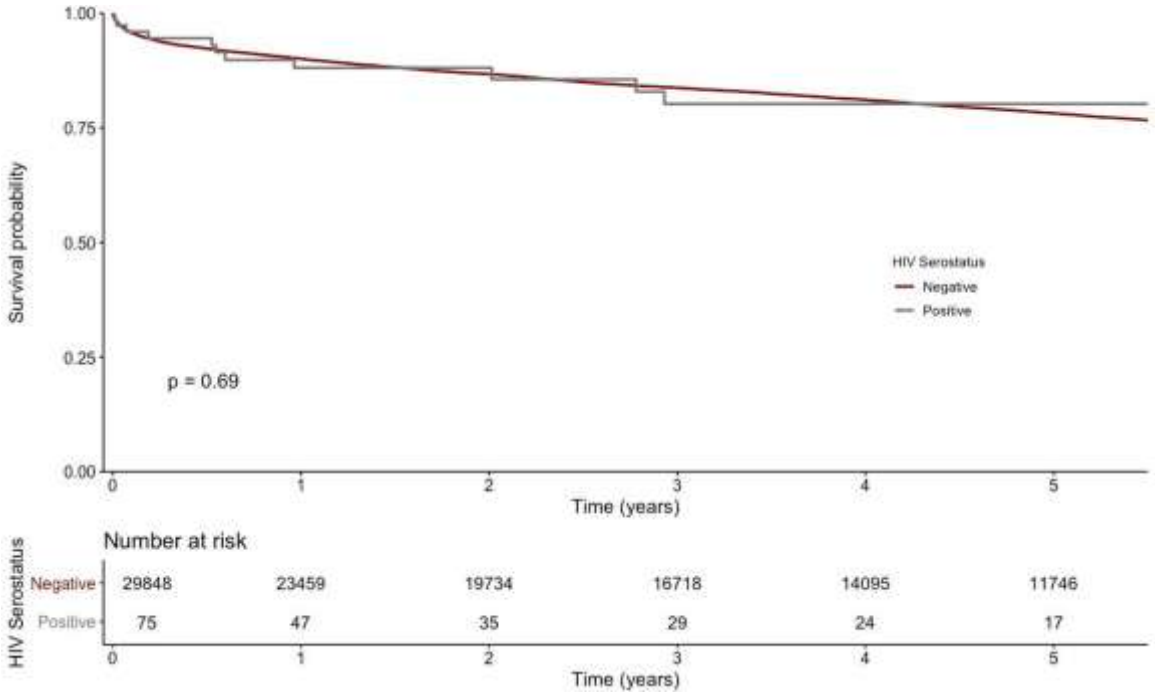
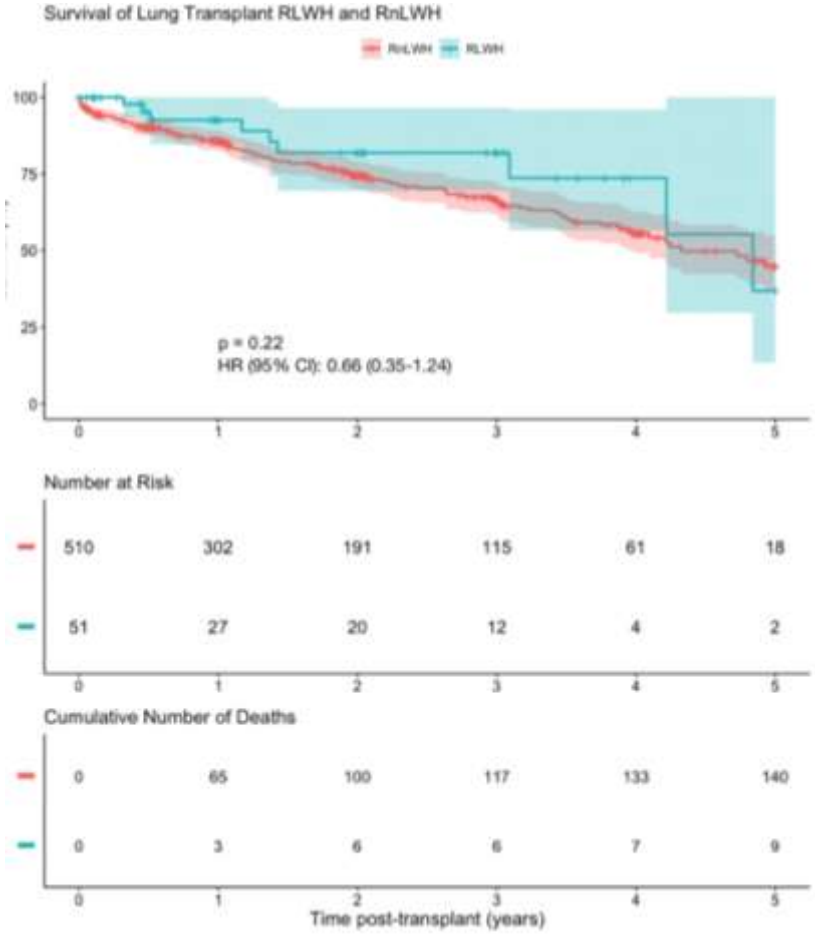
HIV and thoracic transplant

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





Ann Thorac Surg. 2021 May; 111(5): 1465–1471.

ATC 2022.

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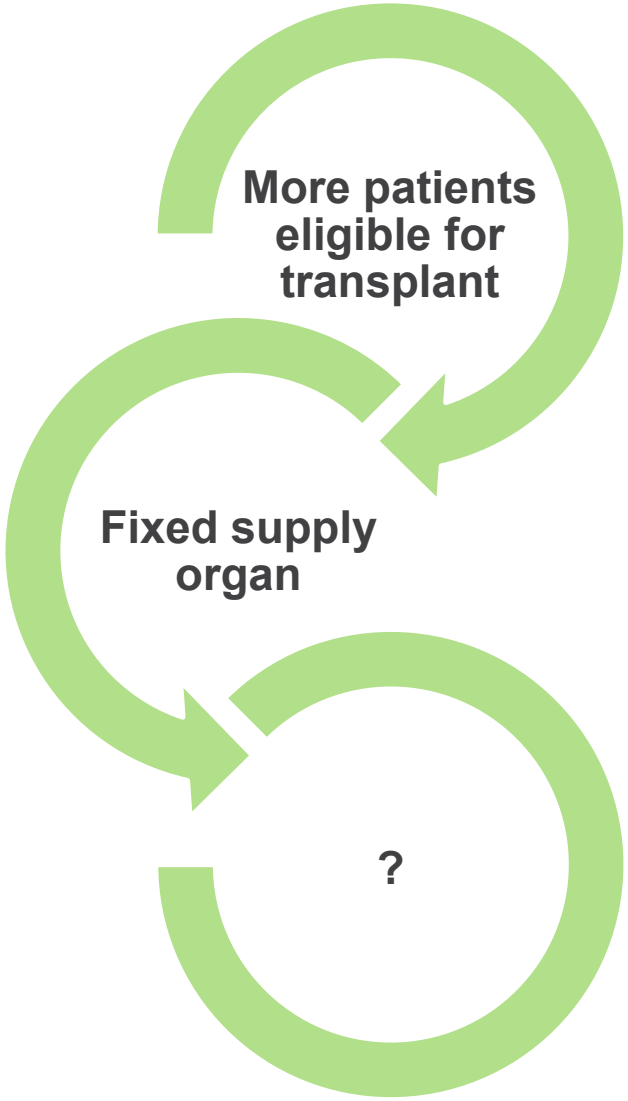
Increasing the donor supply



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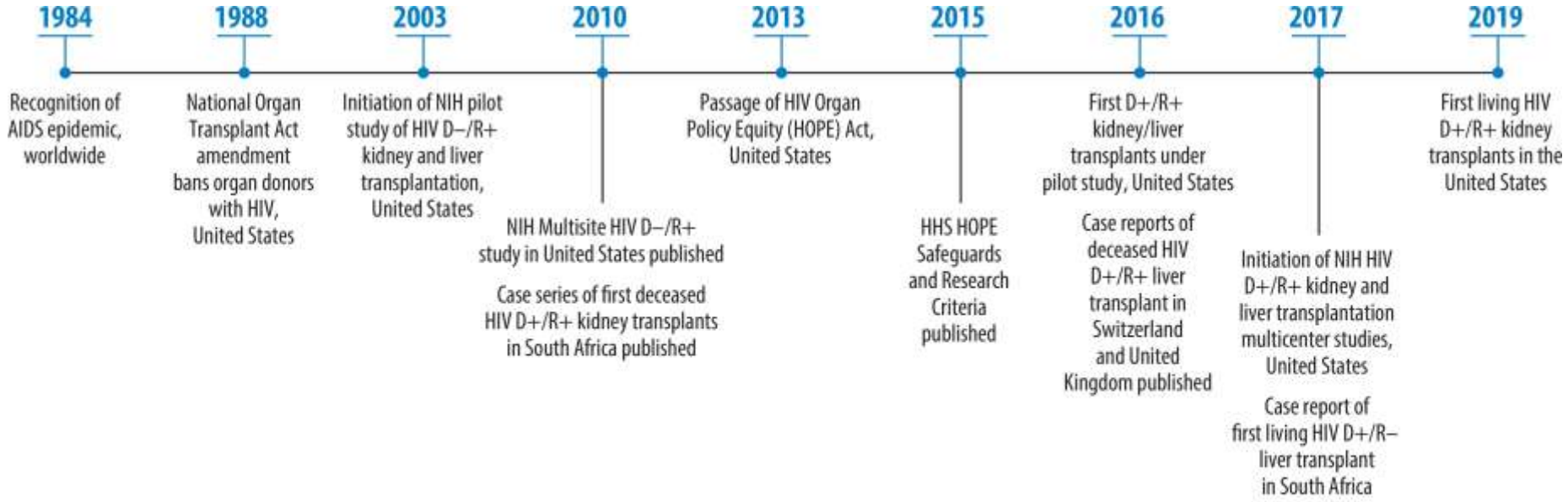
Federal law

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



Nambiar PH, et al. 2021
Annu. Rev. Med. 72:107–18

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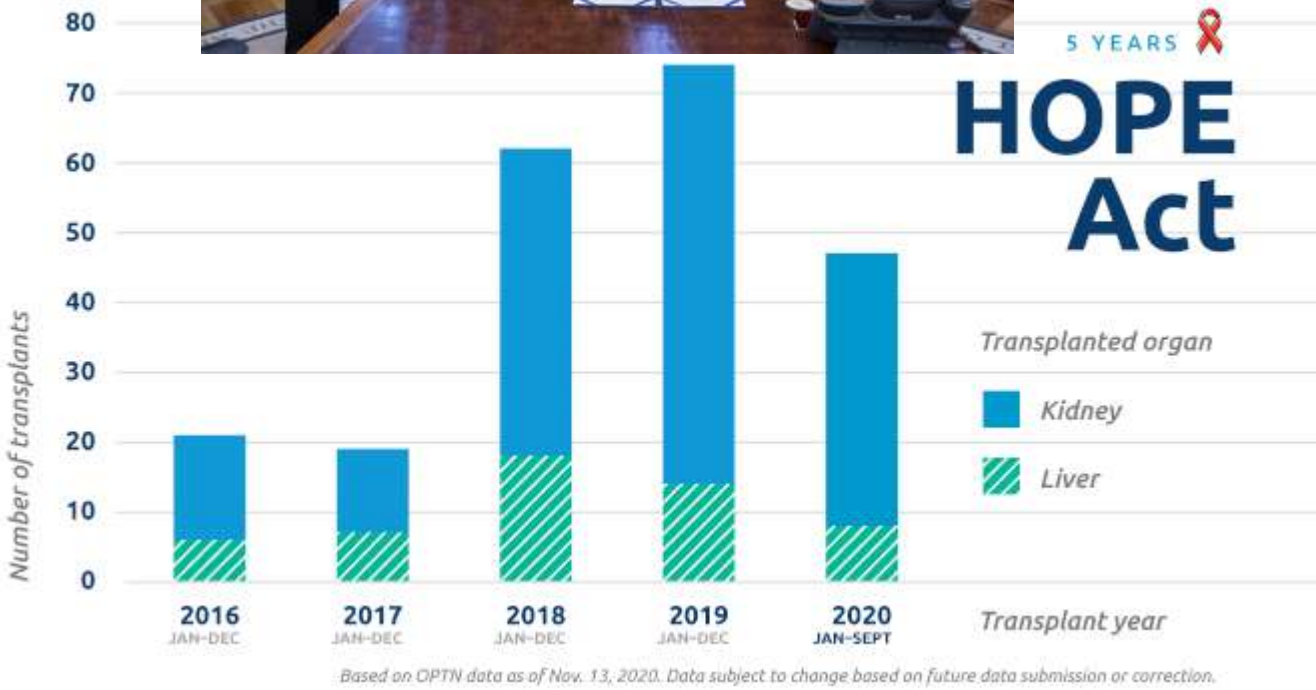
The HIV Organ Policy Equity Act (the HOPE Act)

- 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

- Regulations amended in 2024 to eliminate volume requirements



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.

Pre-transplant process

- ID evaluation of potential recipient
- Consent pt for study (Harith Raees is coordinator)
- Must mark patient in UNOS as willing to accept HIV D+ organ

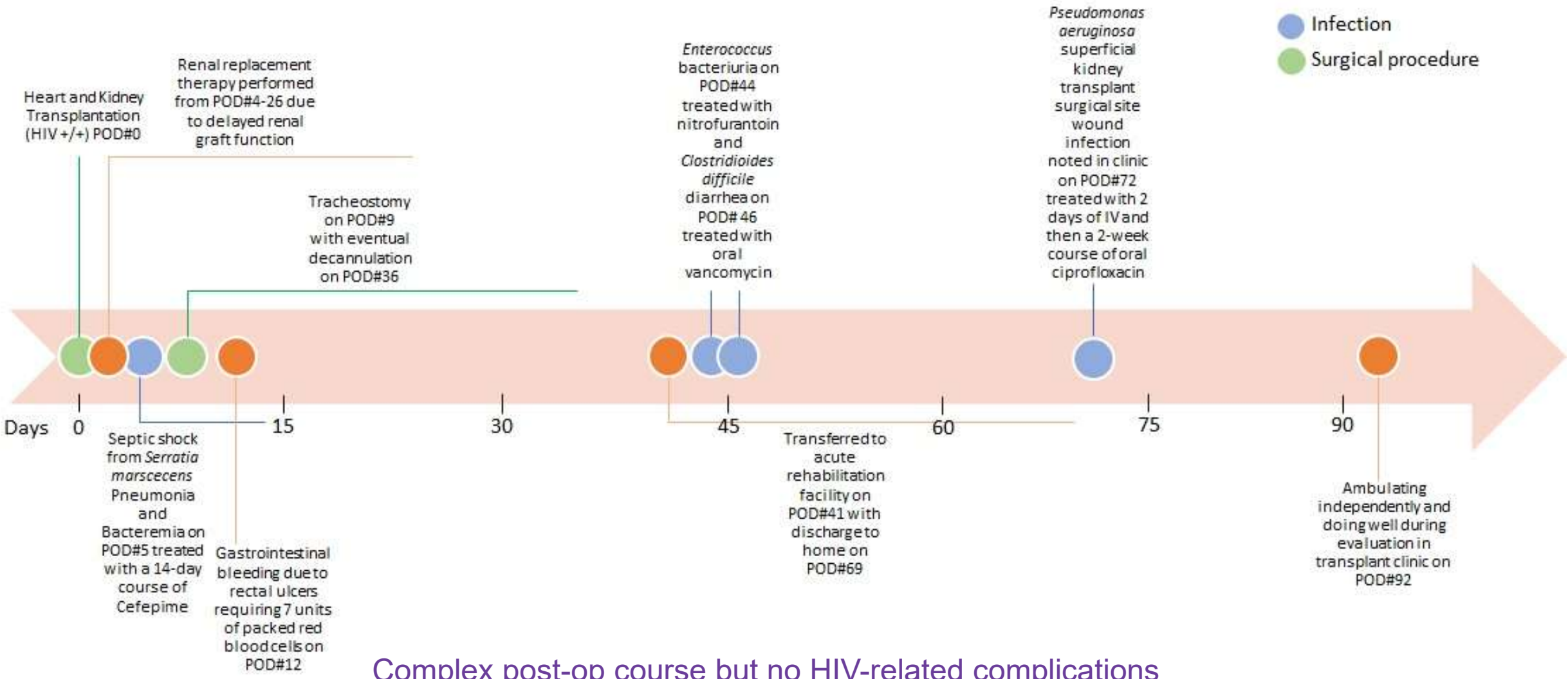
So, as a practical matter, what needs to happen for an HIV-positive donor?

- Organ offer received
- ID contacted EARLY IN THE PROCESS
- ID to reach out to Hopkins (either via email or cell phone)
  - OPO is supposed to reach out to Hopkins, but frequently this does not happen
- Hopkins dedicated HOPE act coordinator can obtain pharmacy records and clinic notes (note, this typically has to happen during waking hours)
- Detailed review of all medical records and multidisciplinary discussion leading to decision to accept or reject
  - Much of this area is a completely evidence-free zone, so we frequently find ourselves hitting the “phone a friend” button

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

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



Complex post-op course but no HIV-related complications
Normal renal and cardiac function 1.5 years post-transplant
J Heart Lung Transplant, online 24 Nov 2022

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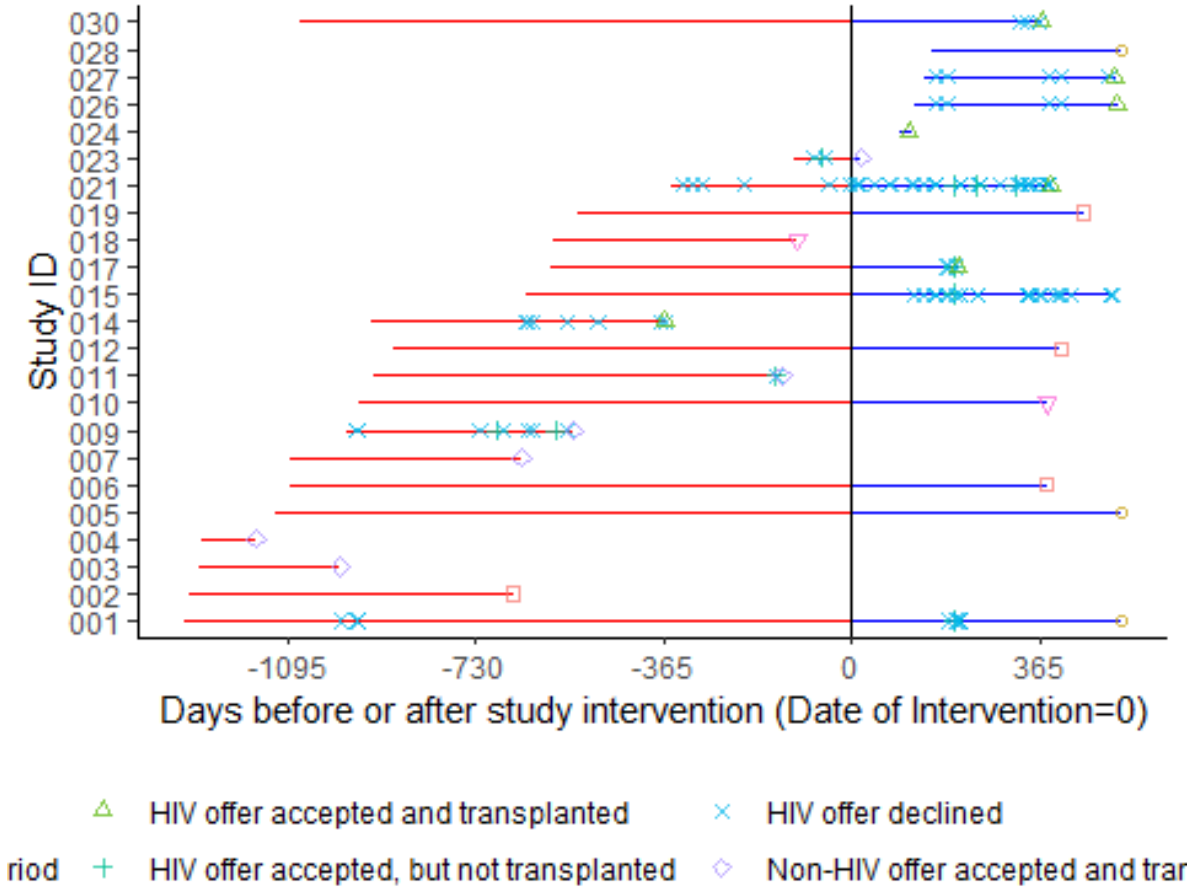
Benefits of receiving an organ from a donor with HIV



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

IDWeek 2022.

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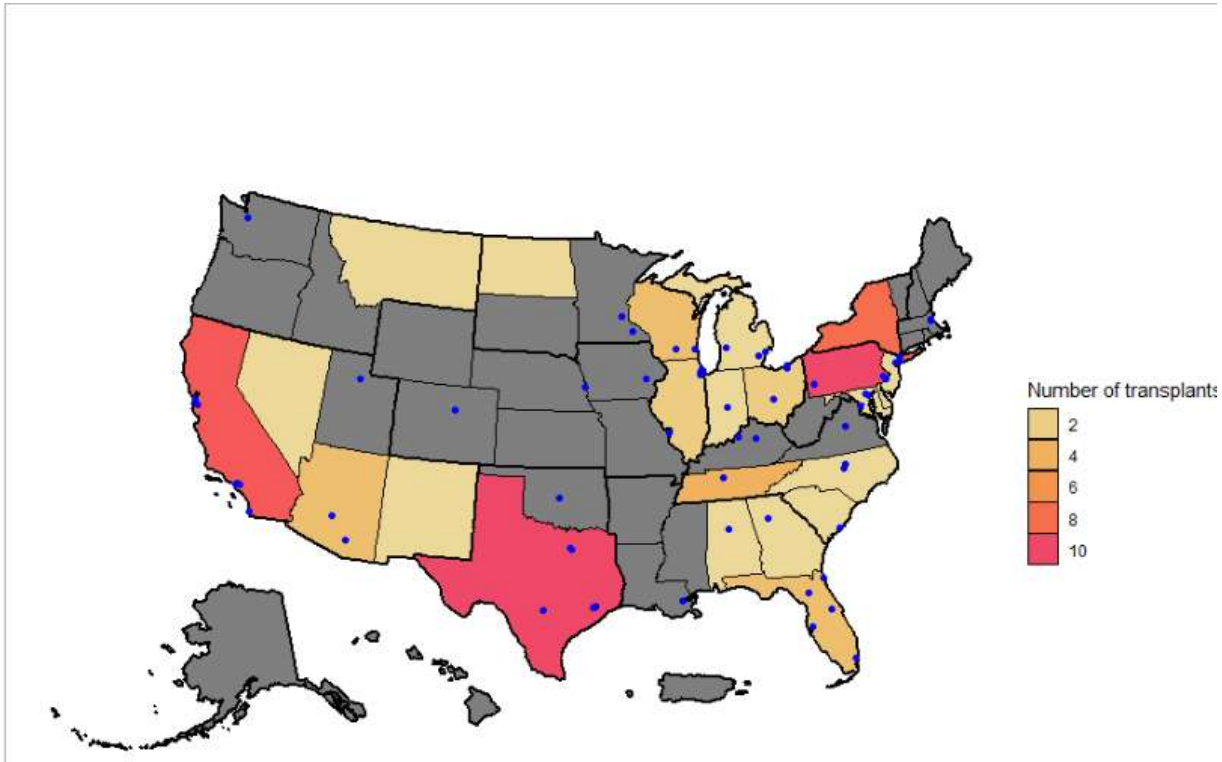
HIV D+/R+ lung transplant not yet performed to date



ATC 2023, abstract 279

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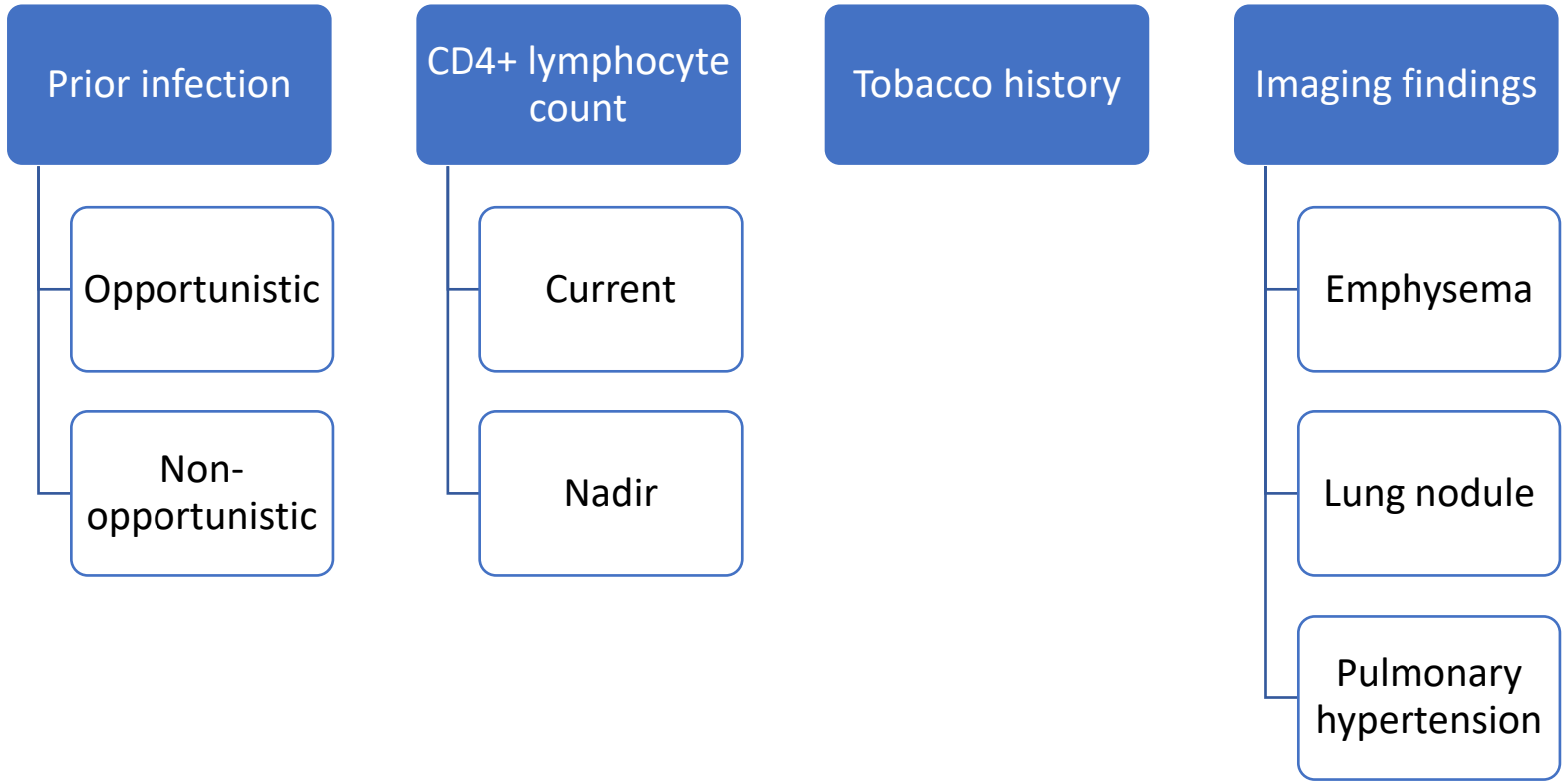
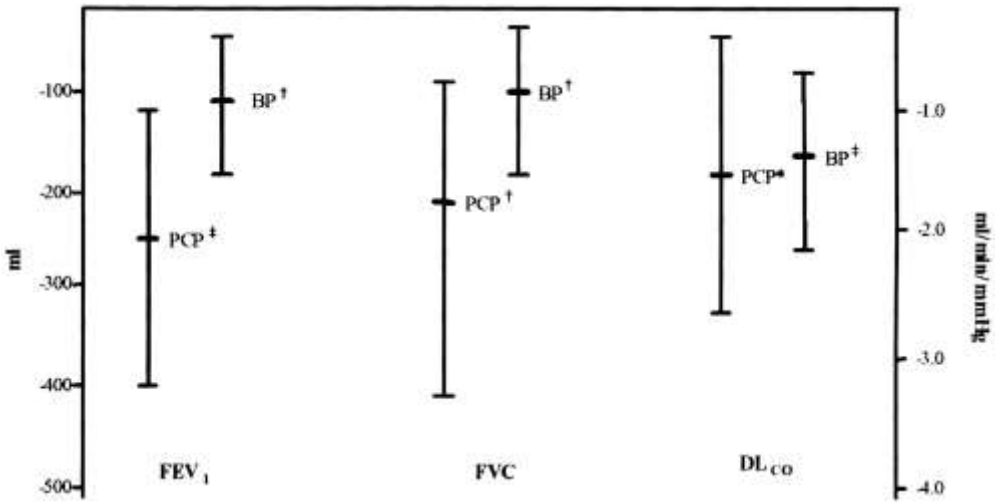
HIV D+/R+ lung transplant will pose unique challenges

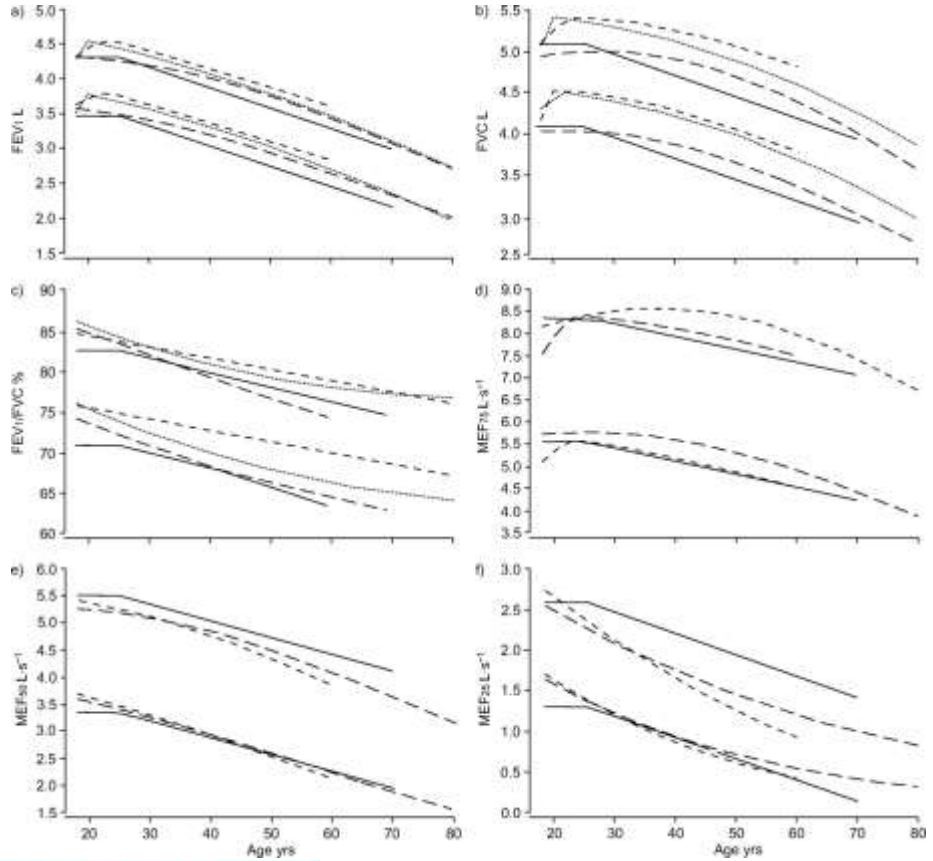
- Effects on the lung that may not show up on
  - Pre-transplant laboratory testing
  - Imaging
  - Biopsies
- Hidden opportunistic infections
  - PJP (?mitigated by prophylaxis?)
  - *Mycobacterium avium* complex
  - Tuberculosis
  - Endemic fungi

Evaluating the HIV D+ lung donor



Long-term effects of pneumonia





- FEV_1 decrease after PJP the equivalent of aging ~8 years
- Decreases did not resolve with time in this pre-HAART era study

Am J Respir Crit Care Med. 2000 Aug;162(2 Pt 1):612-6.
European Respiratory Journal 2008; 31: 860-868.

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People with HIV are more likely to smoke and more likely to experience medical complications from smoking

- High prevalence of smoking
- 2-5 fold higher rates of lung cancer; association persists after controlling for smoking rates (VACS study 1.5-1.7 IRR).
- Again cumulative time with low CD4+ lymphocyte count may be predictive

Clin Infect Dis. 2013 Mar;56(5):727-34.
Curr Opin HIV AIDS. 2017 Jan; 12(1): 31–38.
AIDS. 2012 May 15; 26(8): 1017–1025.

Nodules are common in smokers with HIV

Table 2 Baseline results of selected American low-dose computed tomography lung cancer screening trials and the IELCAP trial

Variables	NLST (28,29)	ELCAP (30)	IELCAP (6)	Mayo[†] (31)	PLuSS[†] (5,32)
Participants					
Received CT screening	26,309	1,000	31,567	1,520	3,642
Age, mean (SD)[‡] or median (IQR)[§]	NA	67 (NA)[§]	62 (NA)[§]	59 (NA)[‡]	59 (NA)[‡]
Pack years, mean (SD)[‡] or median (IQR)[§]	NA	45 (NA)[§]	30 (NA)[§]	45 (NA)[§]	47 [33–62][§]
Nodule detection limit	≥4 mm	None reported[¶]	≥5 mm	None reported	None reported
Participants with lung cancer	270/26,309 (1.0%)[††]	27/1,000 (2.7%)	405/31,567 (1.3%)	31/1,520 (2.0%)	53/3,642(1.5%)
Participants with NCNs	7,041/26,309 (26.8%)	233/1,000 (23.3%)	4,186/31,567 (13.3%)	780/1,520 (51.3%)	1,477/3,642 (40.6%)

Transl Lung Cancer Res. 2017 Feb;6(1):42-51.

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•. 2017 Sep 10;31(14):1973-1977.

CD4 count and viral load are likely associated with chest CT findings

- EXHALE study (part of the VACS study):
  - noncalcified nodule>=4 mm in 55% of patients with CD4+ lymphocyte count<200/µL
  - 25% if CD4+ lymphocyte 200/µL or greater
- COCOMO study:
  - $CD4^+$ T lymphocyte count under 500 cells/µl and $CD4^+$ T lymphocyte nadir less than 200 cells/µl were each associated with increased odds of a positive image (OR) 2.32 (95% CI: 1.01–5.13, *P* = 0.04)
  - Previous history of PCP [OR 4.32 (95% CI: 1.34–11.9), *P* = 0.01] independently associated with abnormal CT chest

AIDS 2014, 28: 1007–1014.
AIDS 2017, 31: 1973-1977.

Accelerated COPD development in PLWH

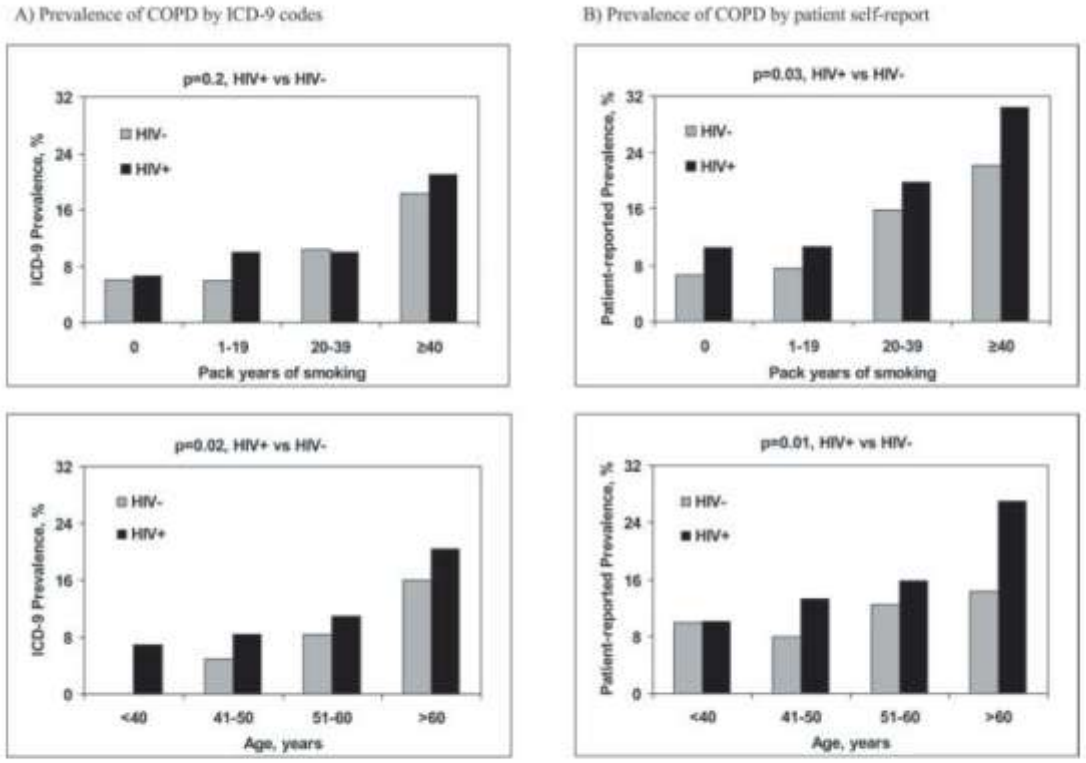

FIGURE 1. Prevalence of COPD among HIV-positive and HIV-negative subjects stratified by number of pack-years of smoking or age. *Left top* and *bottom*, *A*: the prevalence of COPD as diagnosed by ICD-9 codes. *Right top* and *bottom*, *B*: the prevalence of COPD as diagnosed by patient self-report. The p values are given for the likelihood of COPD in HIV-positive subjects vs HIV-negative subjects adjusted for either age or smoking group. HIV+ = HIV-positive; HIV− = HIV-negative.

- Younger age
- Lower pack-year history

Table 3—*Predictors of COPD in HIV-Positive and HIV-Negative Subjects

Predictors	COPD Diagnosis	
	ICD-9 Codes	Patient Self-Report
HIV status	1.47 (1.01–2.13)†	1.58 (1.14–2.19)†
Age, per 10 yr	1.57 (1.29–1.87)†	1.17 (1.00–1.37)
Black	0.77 (0.53–1.13)	0.63 (0.46–0.87)†
Hispanic	1.13 (0.67–1.90)	0.80 (0.50–1.27)
Smoking, per 10 pack-yr	1.12 (1.07–1.18)†	1.16 (1.11–1.22)†
IDU	1.44 (0.99–2.12)	1.56 (1.13–2.16)†
Alcohol abuse	2.24 (1.54–3.25)†	1.52 (1.09–2.12)†

*Values are given as the OR (95% CI).
†Significant at $p \leq 0.05$.

CHEST 2006; 130:1326 –1333.

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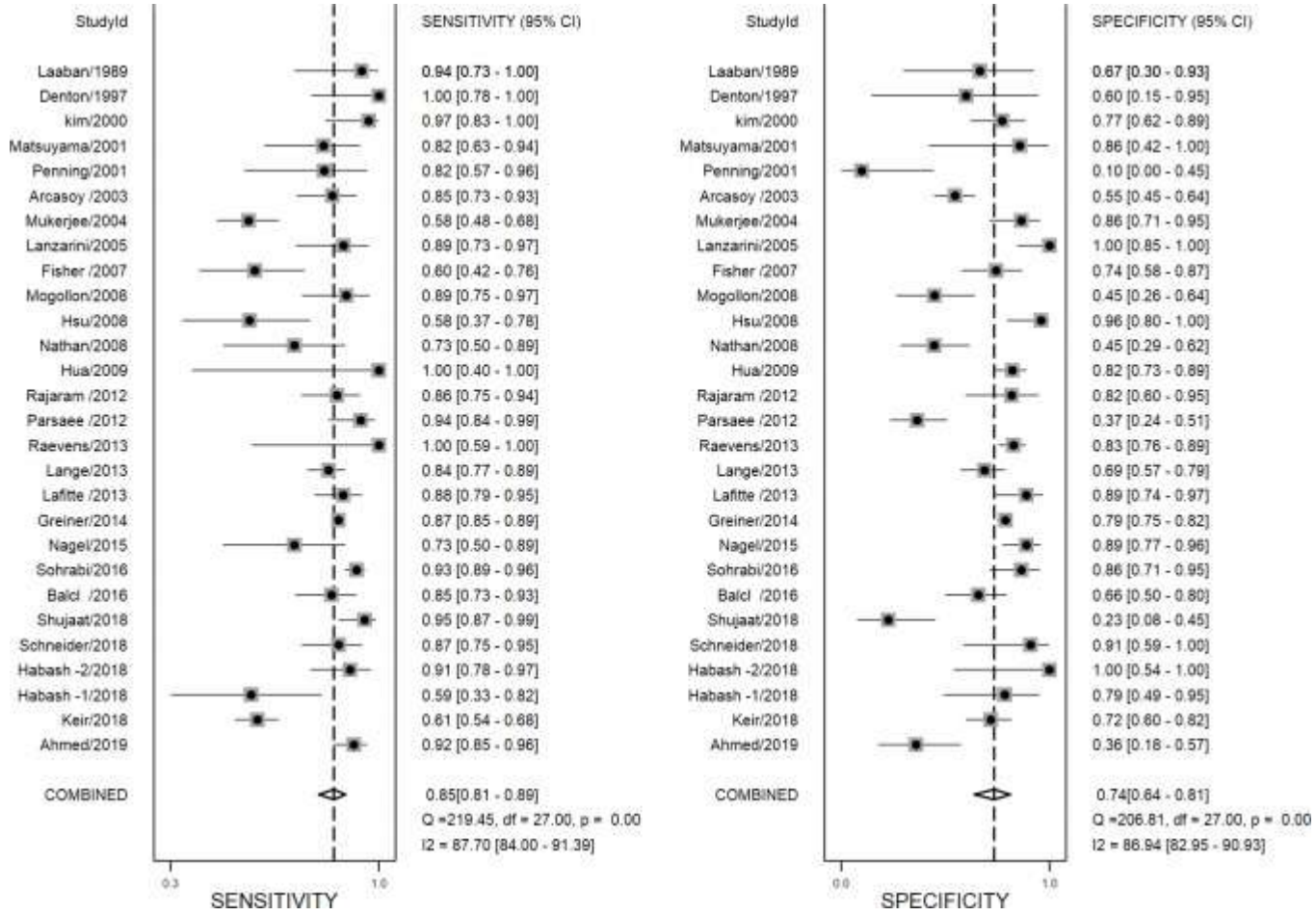
Pulmonary hypertension and HIV

- Ten-fold higher prevalence in people with HIV
- Sensitivity of echocardiography for diagnosing pulmonary hypertension ~80%.



Lancet Healthy Longev. 2021 Jul;2(7):e389-e390.
BMJ Open. 2019 Dec 22;9(12):e033084.

- Traditional vs. extended criteria for the lung donor without HIV.

Table 1
Criteria used to assess donor lung suitability, defining a "standard lung donor"

Traditional Criteria (Standard Donor)	Extended Criteria (Marginal Donors)
Age ≤55 y	Age >70 y
Clear chest X-ray	Minor diffuse and moderate focal chest radiograph changes acceptable
Pao_2 ≥300 on Fio_2 = 1.0 and positive end-expiratory pressure (PEEP) 5 cm H_2O	Pao_2/Fio_2 <300 mm Hg on PEEP 5 cm H_2O
Tobacco history ≤20 pack yr	Tobacco history <40 pack yr
Absence of chest trauma	Chest trauma not relevant if good pulmonary function
No history of primary pulmonary disease or active pulmonary infection	
No evidence of aspiration/sepsis	Aspiration/sepsis acceptable if good, stable/improving pulmonary function
Absence of pulmonary secretions at bronchoscopy	Purulent secretions not relevant if good, stable/improving pulmonary function
No evidence for human immunodeficiency virus, hepatitis B, hepatitis C, or any other relevant viral disease	
No history or evidence of malignant disease	
ABO compatibility	
Sputum Gram stains: absence of organisms	

Anesthesiology Clin 2019; 37:639–660.

Questions for the future

- What is an acceptable treatment history for the HIV D+ lung donor?
- When should opportunistic infections exclude lung donation?
- What smoking history is acceptable?
- Single vs double?

False positive HIV tests

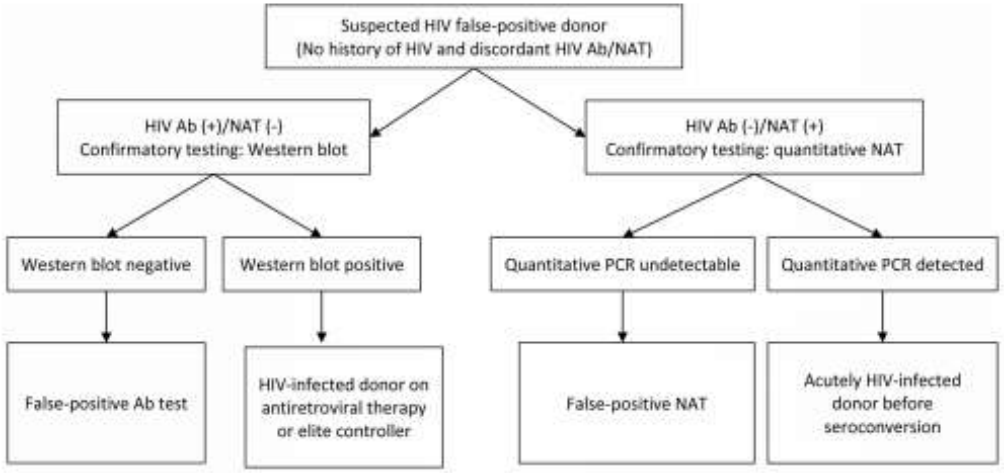


Figure 1. Suspected False-positive Donor Algorithm
Potential explanations for discordant HIV Ab and NAT testing in a potential donor with no prior history of HIV per the medical record or family history. In cases of a reactive Ab test (left), a Western blot or HIV Ag/Ab combination assay would be the 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.

Am J Transplant. 2018 Oct;18(10):2579-2586.

Thank you!

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