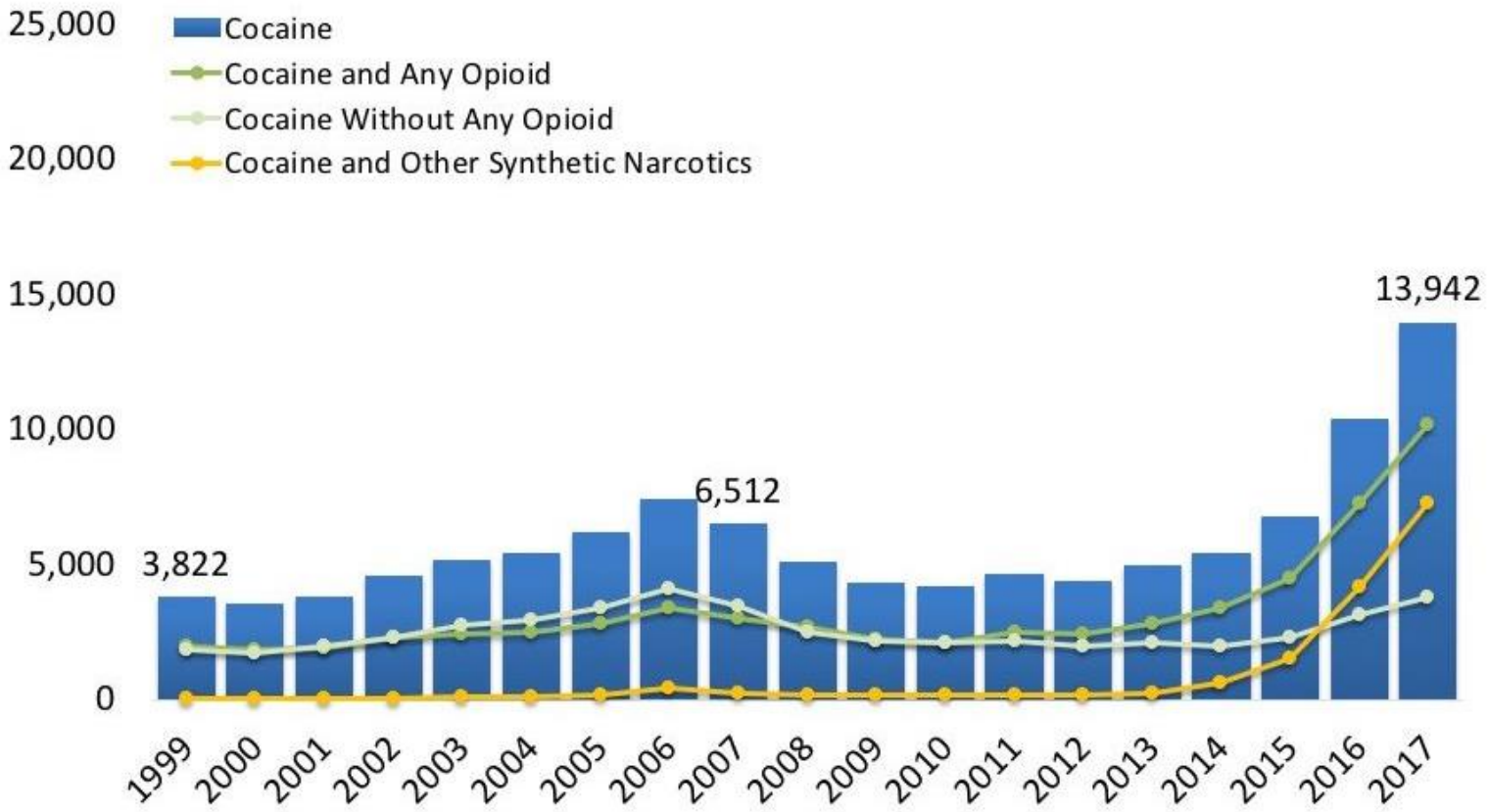
Cocaine Use in Organ Donors and Long-term Outcome After Heart Transplantation: *An ISHLT Registry Analysis*

Jefferson L Vieira MD, PhD, Wida S Cherikh PhD, Kelsi Lindblad PhD, Josef Stehlik MD, MPH, and Mandeep R Mehra MD, MSc

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

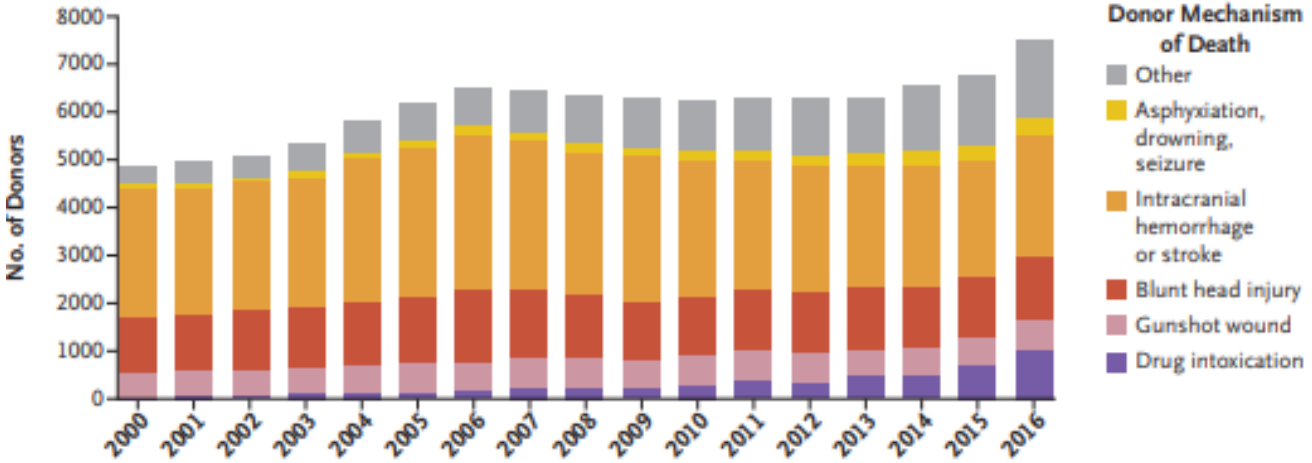
MAGNET RECOGNIZED
AMERICAN NURSES CREDENTIALING CENTER

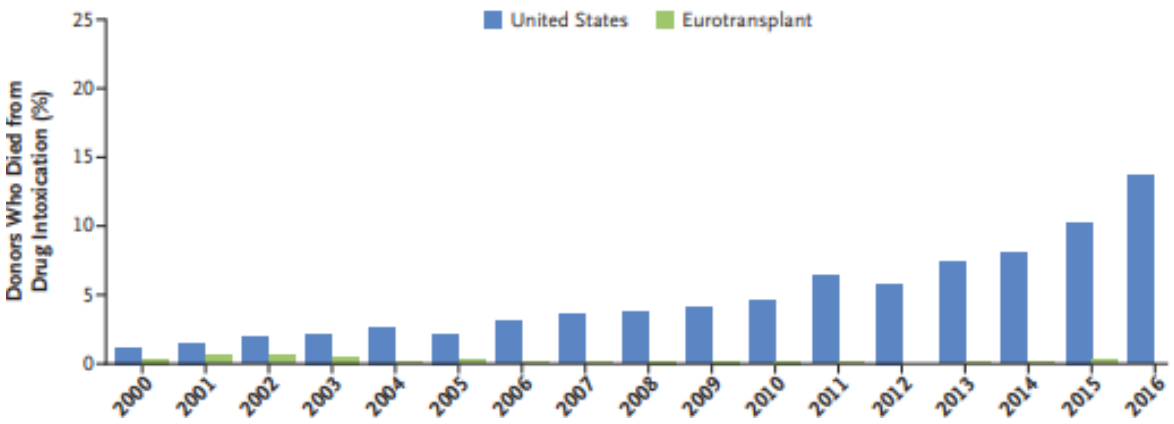
The number of overdose deaths involving cocaine has been increasing steadily since 2014



CDC, WONDER Online Database
Scholl L et al. MMWR Morb Mortal Wkly Rep. 2018

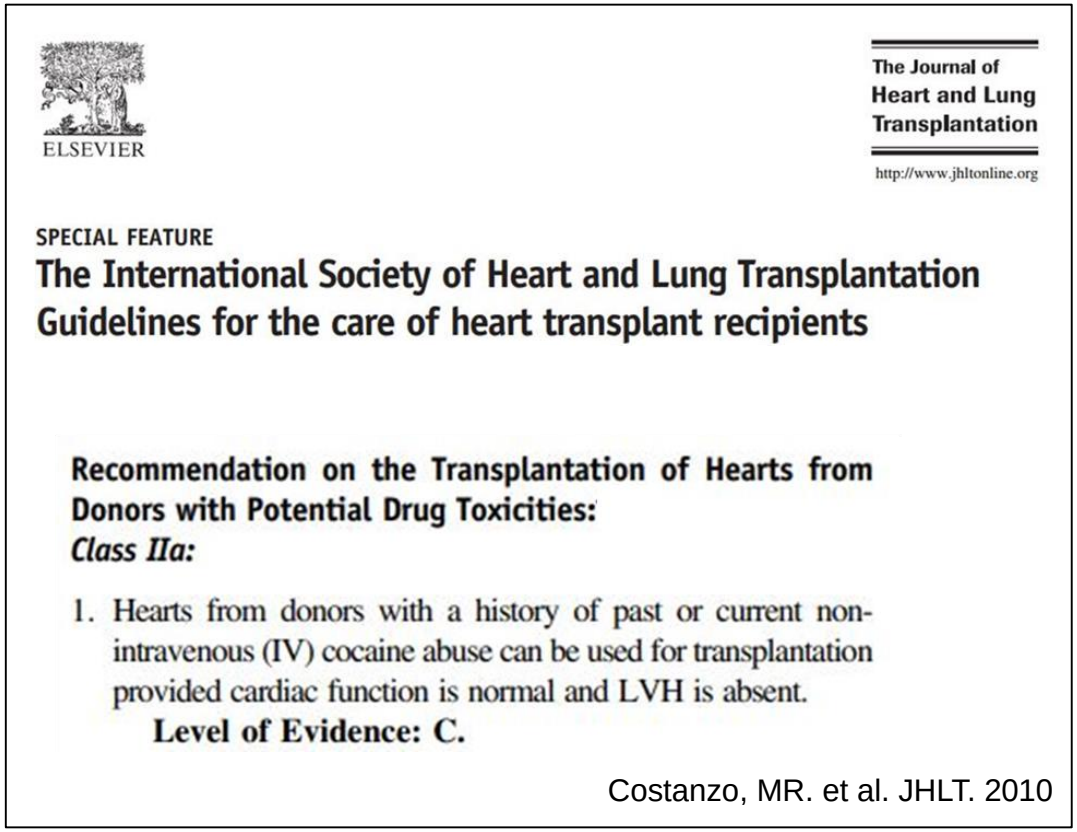
Drug-overdose donation increased from 59 (1.2%) in 2000 to 1,029 (13.7%) in 2016





Mehra M et al. NEJM 2018

Current guidelines do not consider donor cocaine use as a contraindication for Heart Transplantation…



ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

SPECIAL FEATURE

The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients

Recommendation on the Transplantation of Hearts from Donors with Potential Drug Toxicities:
Class IIa:

1. Hearts from donors with a history of past or current non-intravenous (IV) cocaine abuse can be used for transplantation provided cardiac function is normal and LVH is absent.
   Level of Evidence: C.

Costanzo, MR. et al. JHLT. 2010

… however, overdose-death donors are more likely to be discarded than trauma-death donors

Discard of Overdose-Death vs. Trauma-Death Donor Organs (aRR*)

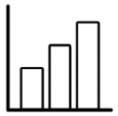
Organ		P-value
Kidneys	1.15 (1.10-1.22)	<0.001
Livers	1.13 (1.02-1.25)	0.02
Hearts	1.50 (1.21-1.86)	<0.001
Lungs	1.50 (0.91-2.48)	0.10

*aRR adjusted Relative Rate

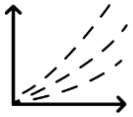
Bowring, M. et al. Am J Transplant. 2017

Gaps in the literature

Prior studies used **OPTN-based registries** (UNOS and SRTR) , without international data (**ISHLT TTX Registry**)



Data on **long-term rates of CAV and AR** using hearts from donors with a history of cocaine abuse



Predictors and influence of **CAV** and **AR** in **long-term survival** using hearts from donors with a history of cocaine abuse

Organ decline rates by centers according to the history of donor cocaine use

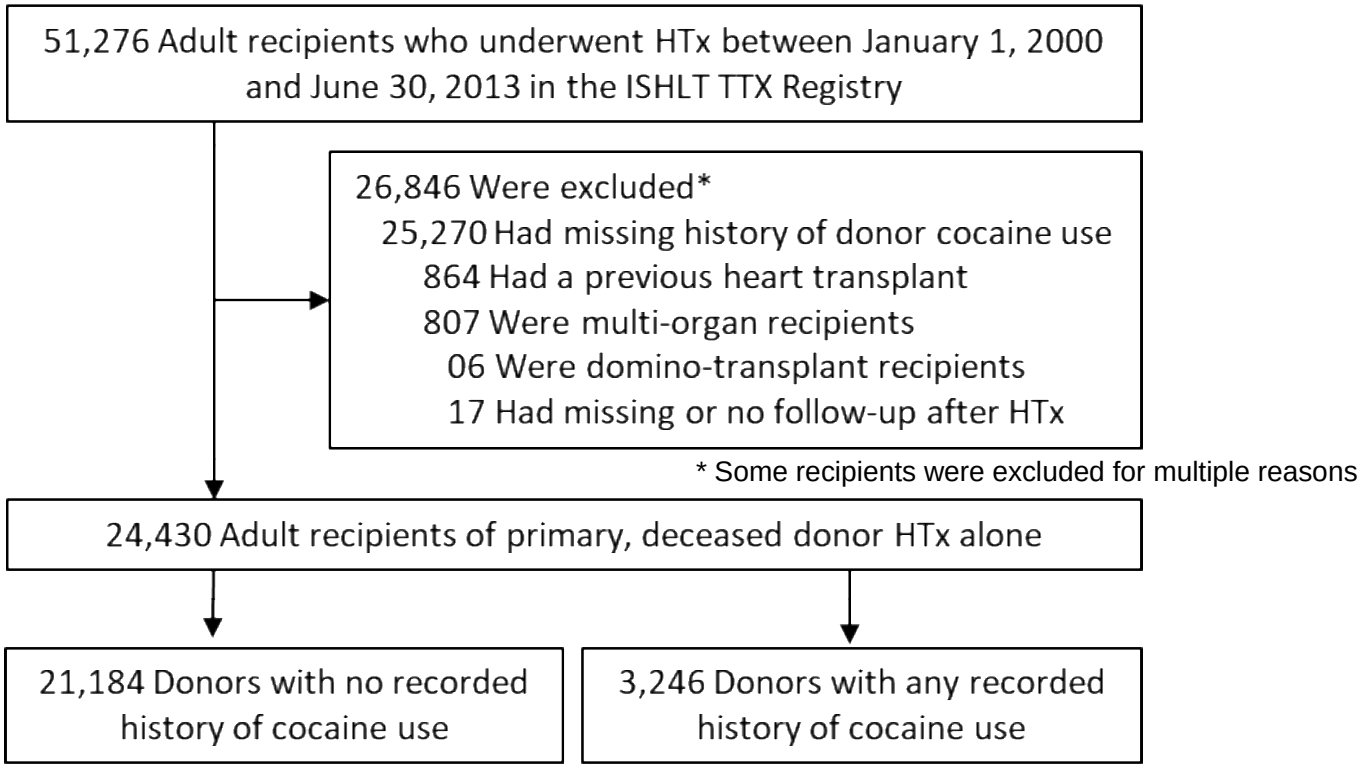
Cocaine Use in Organ Donors and Long-Term Outcomes After Heart Transplantation: An ISHLT Registry Analysis

Retrospective cohort study using the **International Thoracic Organ Transplant Registry**

Population: Adult recipients of primary, heart-alone transplants

Objective: What is the impact of donor cocaine abuse on heart transplant outcomes?

N = 24,430



Analysis

Categorical variables were compared with the $\chi 2$ or Fisher's Exact test
Continuous variables were compared with the Kruskal Wallis test p-value

Cardiac Allograft Vasculopathy at 5 years, Acute Rejection at 5 years, and Survival at 10 years were tabulated by donor cocaine use and compared using the Chi-square test

Outcomes were estimated using the **Kaplan-Meier method**, stratified by donor cocaine use and compared using the **log-rank test**

Cox regression models were developed to assess the association of donor cocaine use with outcomes of interest in the presence of established risk factors for poor HTx outcomes

Iterative backward selection method determined which risk factors to retain in the final model

Statistical analyses were performed with SAS v9.3 (SAS Institute) and R v3.5.0 (https://www.R-project.org/)

Demographics

Donors

	Donor Cocaine Use		
	Any Exposure (N = 3,246)	Non-User (N = 21,184)	P-value
Donor			
Age (Years)	33 ± 10	32 ± 13	<0.001
Male Sex	2574 (79%)	14786 (70%)	<0.001
Weight (kg)	81 ± 17	81 ± 18	0.016
Height (cm)	176 ± 9	174 ± 10	<0.001
Diabetes	94 (3%)	548 (3%)	0.30
Smoking	1234 (38%)	4262 (20%)	<0.001
Hypertension	452 (14%)	2727 (13%)	0.09
Malignancy	40 (1%)	388 (2%)	0.016
Cause of Death			<0.001
Anoxia	661 (20%)	2520 (12%)	
Cerebrovascular	632 (19%)	5550 (26%)	
Head Trauma	1852 (57%)	12448 (59%)	
Other	99 (3%)	646 (3%)	
Coronary Angiography	918 (28%)	4540 (22%)	<0.001
Abnormal	58 (2%)	305 (2%)	0.72

Recipients

	Donor Cocaine Use		
	Any Exposure (N = 3,246)	Non-User (N = 21,184)	P-value
Recipient			
Age (Years)	53 ± 13	52 ± 12	0.023
Male Sex	2553 (79%)	15951 (75%)	<0.001
Weight (kg)	82 ± 17	81 ± 17	<0.001
Height (cm)	174 ± 10	173 ± 10	<0.001
Diabetes	807 (25%)	4962 (24%)	0.08
Smoking	1146 (51%)	6741 (49%)	0.07
Pre-op Malignancy	214 (7%)	1315 (6%)	0.42
PVR (Woods)	1.9 [0.0 - 5.2]	1.9 [0.0 - 5.2]	0.08
PRA (%)	0.0 [0.0 - 54.0]	0.0 [0.0 - 52.0]	0.35
Creatinine (mg/dl)	1.3 ± 0.5	1.3 ± 0.5	0.47
Diagnosis Category			0.06
Ischemic	1513 (47%)	9874 (47%)	
Non-ischemic	1456 (45%)	9555 (45%)	
Other	277 (9%)	1726 (8%)	
Pre-op Inotropes	1423 (44%)	8956 (42%)	0.10
Pre-op IABP	200 (6%)	1142 (5%)	0.07
Pre-op Ventilator	74 (2%)	584 (3%)	0.12
Pre-op MCS Device	792 (30%)	4915 (30%)	0.78

Demographics

Heart Transplantation

	Donor Cocaine Use		
	Any Exposure (N = 3,246)	Non-User (N = 21,184)	P-value
Transplant			
D/R Sex Match			<0.001
Female-Female	316 (10%)	2816 (13%)	
Female-Male	355 (11%)	3583 (17%)	
Male-Female	379 (12%)	2415 (11%)	
Male-Male	2196 (68%)	12370 (58%)	
HLA Mismatch			0.13
0-1	24 (1%)	108 (1%)	
2-4	1137 (41%)	7175 (40%)	
≥ 5	1628 (58%)	10589 (59%)	
Ischemic Time (Hours)	3.3 ± 1.1	3.2 ± 1.1	0.006
Induction Therapy	1569 (50%)	10425 (51%)	0.24

	Donor Cocaine Use		
	Any Exposure (N = 3,246)	Non-User (N = 21,184)	P-value
Immunosuppressive Therapy at Discharge			
Calcineurin Inhibitor			<0.001
Tacrolimus	1924 (62%)	11731 (58%)	
Cyclosporine	1070 (34%)	7720 (38%)	
None	108 (3%)	712 (3%)	
Antimetabolite	2819 (89%)	18123 (88%)	0.11
mTOR Inhibitor	109 (3%)	839 (4%)	0.09
Steroid Use at One Year			0.007
No	409 (14%)	2249 (13%)	
Yes	2411 (85%)	15496 (87%)	

Organ Decline Rates

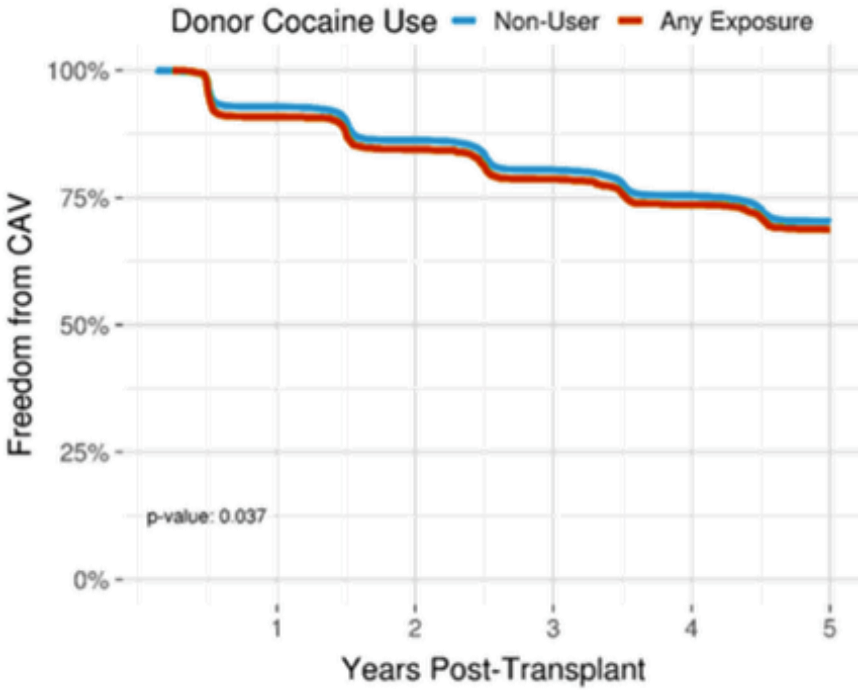
Organs from donors with a history of cocaine use were transplanted at a higher sequence number

Offer Accept **Sequence Number** for Adult Heart Transplants Performed in US (2000-2013) By Donor History of Cocaine Use

	Donor Cocaine Use		
	Any Exposure (N = 3,096)	Non-User (N = 19,630)	P-value
Offer Accept Sequence Number			
Mean ± SD	16.1 ± 55.6	11.5 ± 38.2	<0.001
Median [IQR]	3 [1 to 11]	3 [1 to 8]	<0.001

Based on OPTN data as of October 4, 2019

Kaplan-Meier Estimates of Freedom from Cardiac Allograft Vasculopathy within 5 Years

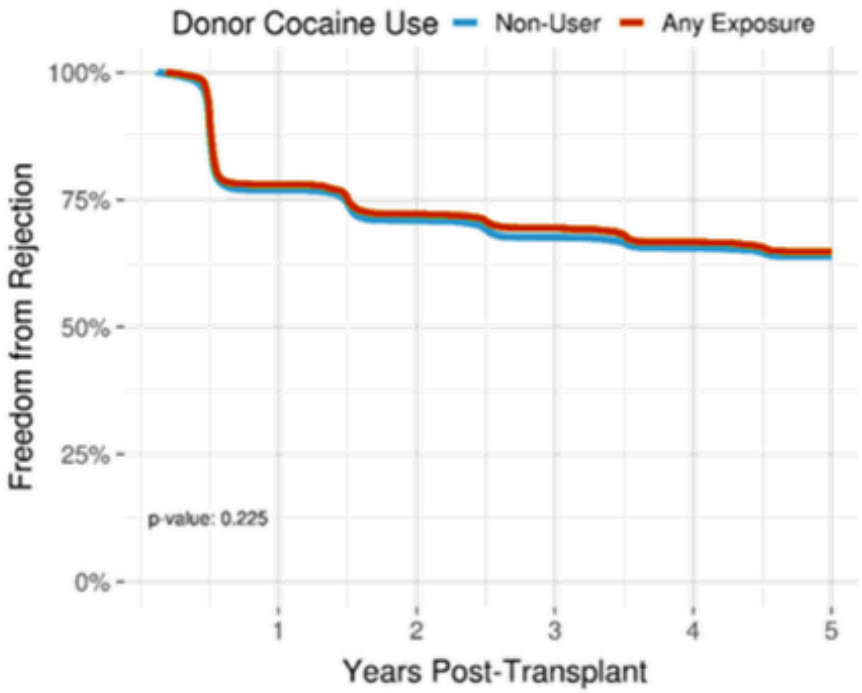


Unadjusted log-rank test
P = 0.037

Multiadjusted
HR, 1.02 (0.94 to 1.11)
P = 0.56

	Non-User		Any User	
Year	Number at Risk	Survival (95% CI) (%)	Number at Risk	Survival (95% CI) (%)
1	14444	92.85 (92.45, 93.24)	2269	90.88 (89.72, 91.92)
2	11941	86.26 (85.71, 86.8)	1900	84.49 (83.01, 85.85)
3	10090	80.46 (79.8, 81.09)	1618	78.62 (76.91, 80.21)
4	8587	75.37 (74.64, 76.08)	1372	73.64 (71.77, 75.41)
5	7073	70.35 (69.55, 71.13)	1121	68.72 (66.70, 70.65)

Kaplan-Meier Estimates of Freedom from Treatment for Acute Rejection within 5 Years

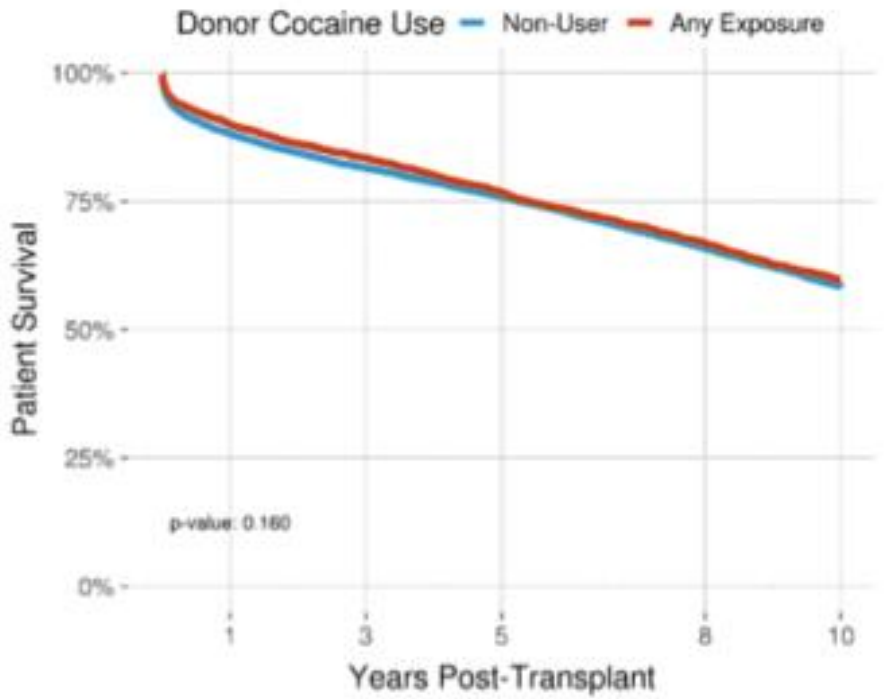


Unadjusted log-rank test
P = 0.22

Multiadjusted
HR, 0.98 (0.92 to 1.05)
P = 0.61

	Non-User		Any User	
Year	Number at Risk	Survival (95% CI) (%)	Number at Risk	Survival (95% CI) (%)
1	13426	76.89 (76.27, 77.5)	2150	77.96 (76.4, 79.44)
2	11724	70.93 (70.26, 71.59)	1891	72.14 (70.44, 73.75)
3	10648	67.61 (66.91, 68.3)	1735	69.41 (67.66, 71.09)
4	9761	65.55 (64.83, 66.25)	1571	66.61 (64.81, 68.34)
5	4681	63.91 (63.18, 64.62)	687	64.73 (62.88, 66.5)

Kaplan-Meier Estimates of Survival within 10 Years

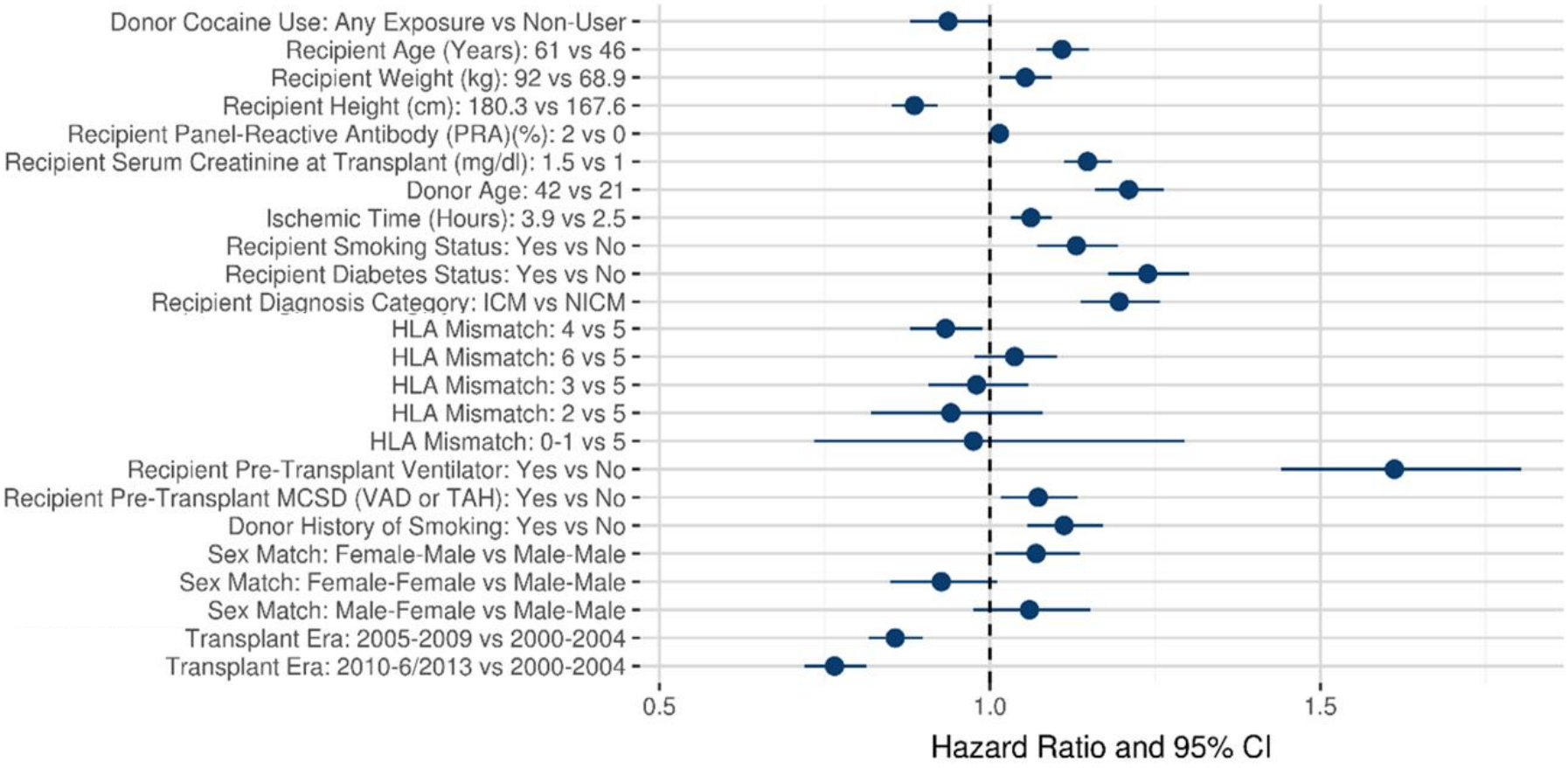


Unadjusted log-rank test
P = 0.16

Multiadjusted
HR, 0.94 (0.88 to 1.00)
P = 0.050

	Non-User		Any User	
Year	Number at Risk	Survival (95% CI) (%)	Number at Risk	Survival (95% CI) (%)
1	18327	88.14 (87.7, 88.57)	2892	89.99 (88.91, 90.98)
3	16663	81.51 (80.97, 82.03)	2640	83.39 (82.06, 84.63)
5	14941	75.83 (75.24, 76.4)	2333	76.74 (75.23, 78.17)
8	9639	65.8 (65.13, 66.47)	1463	66.74 (65.01, 68.42)
10	6660	58.46 (57.71, 59.2)	988	59.66 (57.74, 61.52)

Risk Factors for Mortality within 10 Years



Limitations

Observational study

Cohort selection was limited to collectives and centers that provided data on donor cocaine use, predominantly from North America

Past and current cocaine users were combined into one group, which might have biased the “any cocaine exposure” group toward the null

Lack of information on donors with a history of cocaine use that were offered for HTx but were not accepted and subsequently discarded

Conclusions

The use of **well-selected heart donors** with a history of cocaine use does not have an adverse impact on long-term **mortality**, **CAV** or **acute rejection** among HTx recipients

These findings indicate an opportunity to improve the **organ recovery process**