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# Impact Of Donor Smoking History On Post Heart Transplant Outcomes: A Propensity Matched Analysis Of The ISHLT Registry

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# Disclosures



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- None

# Background



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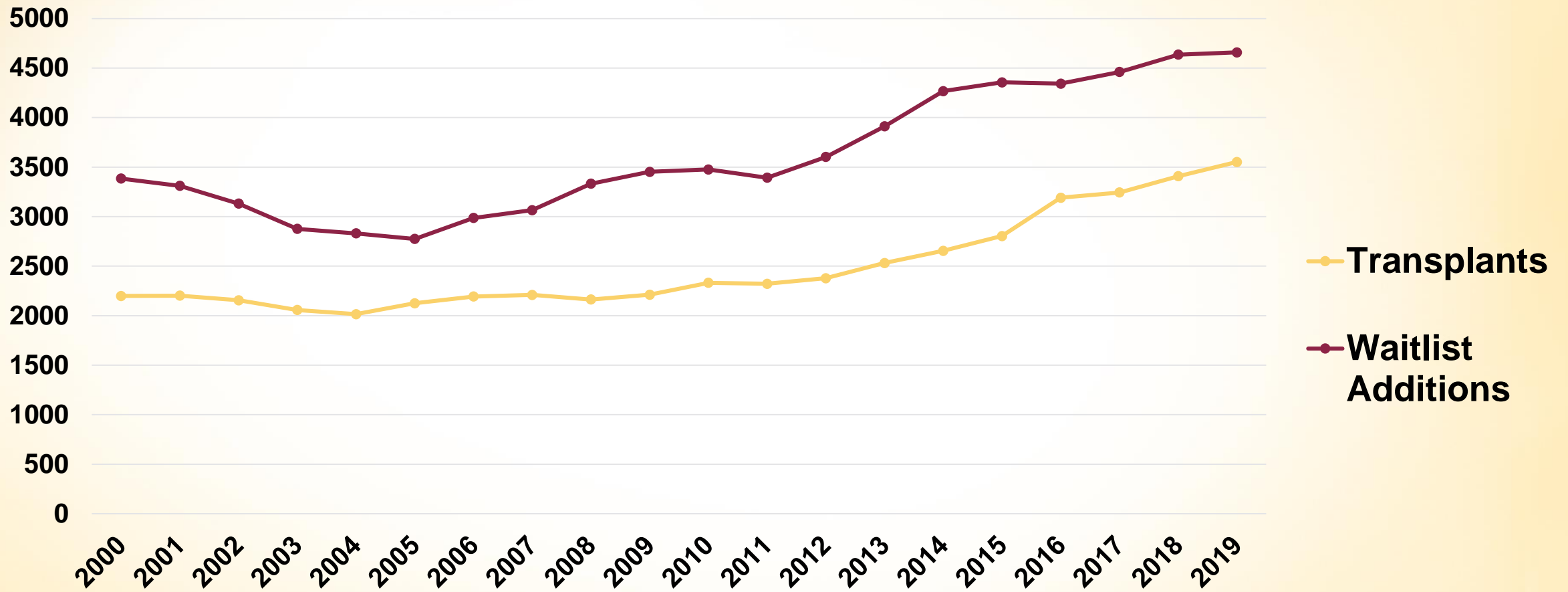
- Orthotopic heart transplant (OHT) remains the treatment of choice for patients with end stage heart failure
- Median survival is now 11-13 years
- Organ allocation remains a significant issue

Lund LH, Edwards LB, Kucheryavaya AY, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirtieth Official Adult Heart Transplant Report--2013; focus theme: age. *J Heart Lung Transplant.* 2013;32(10):951-964

# Heart Transplants United States



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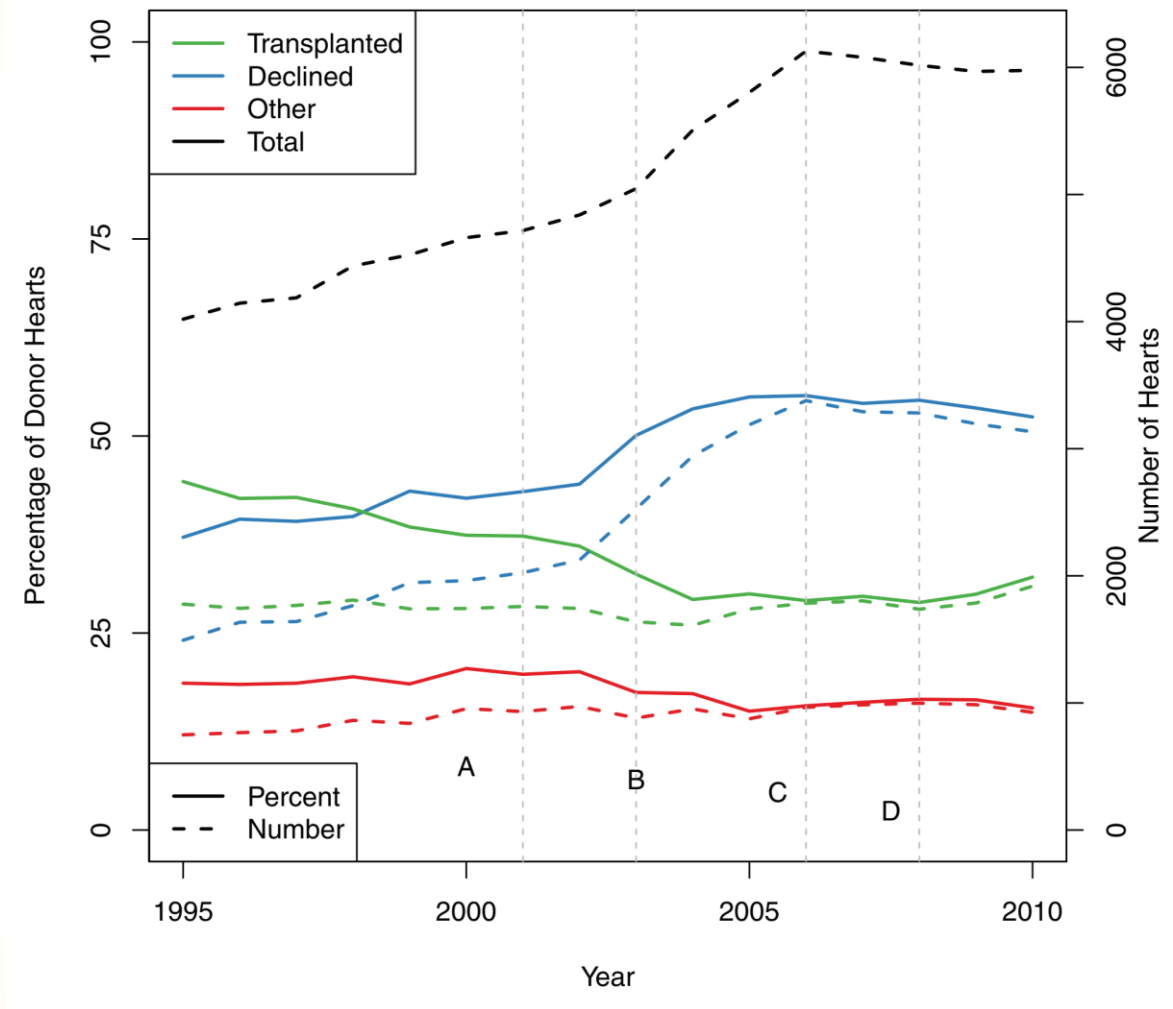
<https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/>

# Background

- Despite increasing need for organs
- 52% of organs were declined in 2010



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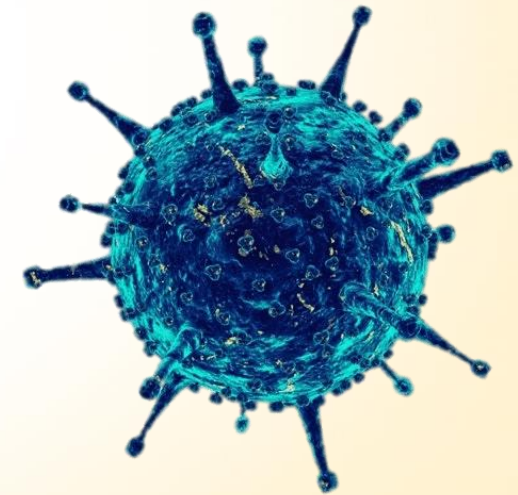


Khush KK, Zaroff JG, Nguyen J, Menza R, Goldstein BA. National decline in donor heart utilization with regional variability: 1995-2010. *Am J Transplant.* 2015;15(3):642-649.

# High Risk Donors?



- Traditional donor inclusion criteria
  - Age <55 years old
  - No cardiac history
  - Normal ECG, echocardiogram, coronary angiogram
  - Ischemic time > 4 hours
- Mismatch
- CDC High Risk Donors
  - Hepatitis B+, Hepatitis C+, HIV+
- Alcohol use, Cocaine





# What about smoking?

Though there is perceived increased risk with donor smokers,  
little data exists to quantify this risk.

# AIM



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- Investigate the impact of donor tobacco smoking on post-heart transplant outcomes



# Methods



- International Society for Heart and Lung Transplantation (ISHLT) registry.
- Registry reports donor smoking history as:
  - non-smoker
  - current smoker (within past 6 months)
  - past smoker
- We classified donors as smokers (current and past) and non-smokers.

# Methods



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- Primary Outcome
  - Transplant Survival
- Secondary Outcomes
  - Acute rejection
  - Cardiac allograft vasculopathy
  - Graft failure

# Study Population



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- Adult HTx recipients (age  $\geq 18$  years)
- ISHLT registry - January 1, 2005 through December 31, 2016.
- Patient records with missing survival data or missing information regarding the primary variables of interest (donor history of cigarette smoking, high risk donor status) were excluded.

# Analysis



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- We derived propensity score matching to reduce bias using a greedy algorithm to identify a matched cohort with no history of donor smoking.
- Hazard ratios for post-transplant outcomes for the propensity matched sample were estimated from separate Cox proportional hazard models using robust sandwich covariance matrix estimates.

# Results



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**26390 pts**

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Documented donor smoking status

**4667 pts**

Any history of smoking

**3432 (73.6%)**

Active

**1235 (26.3%)**

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Past

**4572**

Matched pairs for analysis

Median follow-up duration 4 years

# Recipients

- Recipients from donor smokers were more likely to be female and have HTN
- Otherwise no significant differences

	Overall n=26,390	Donor: history of smoking n=4,664	Donor: no history of smoking n=19,915 (81.1%)	p-value
Recipient age	52.5 (12.7)	52.8 (12.4)	52.4 (12.7)	0.053
Recipient Female	6560 (24.9)	1103 (23.6)	5457 (25.1)	0.035
Gender mismatch	6642 (25.2)	1219 (26.1)	5423 (25.0)	0.093
Recipient BMI (n=26321)	27 (4.9)	26.8 (4.7)	27 (4.9)	0.004
Inotropes at transplant (n=25767)	9809 (38.1)	1626 (37.6)	8183 (38.2)	0.51
Support at transplant				
Life support (n=25537)	18748 (73.4)	2915 (68.1)	15833 (74.5)	<0.001
IAPB (n=25766)	1574 (6.1)	294 (6.8)	1280 (6.0)	0.037
ECMO (n=25769)	199 (0.8)	46 (1.1)	153 (0.7)	0.016
VAD (n=25044)	9432 (37.7)	1380 (34.1)	8052 (38.4)	<0.001
Ventilator (n=25766)	533 (2.1)	122 (2.8)	411 (1.9)	<0.001
Recipient comorbidities				
Diabetes (n=26049)	6823 (26.2)	1101 (24.5)	5722 (26.6)	0.004
Hypertension (n=20782)	10063 (48.4)	1697 (43.9)	8366 (49.5)	<0.001
PVD (n=19775)	623 (3.2)	115 (3.1)	508 (3.2)	0.83
COPD (n=18383)	899 (4.9)	140 (4.6)	759 (4.9)	0.49
H/O malignancy (n=26089)	1978 (7.6)	323 (7.2)	1655 (7.7)	0.26
Recipient creatinine (n=26054)	1.2 (1.0-1.5)	1.2 (1.0-1.5)	1.2 (0.9-1.5)	0.022
Recipient dialysis (n=24924)	1021 (4.1)	149 (3.8)	872 (4.2)	0.27
Pre-transplant amiodarone (n=18346)	6018 (32.8)	980 (32.4)	5038 (32.9)	0.64
Positive CMV (n=24908)	15242 (61.2)	2375 (60.4)	12867 (61.4)	0.24
PRA > 0 (n=22730)	7466 (32.8)	1123 (32.0)	6343 (33.0)	0.23

# Donor Characteristics



- Donor smokers were older, had more HTN, DM2, cocaine use, longer ischemic time
- These differences were eliminated in the matched analysis

	Overall n=26,390	Donor: history of smoking n=4,664	Donor: no history of smoking n=19,915 (81.1%)	p-value
Donor age (n=26389)	32.3 (12)	40.2 (10.4)	30.7 (11.6)	0.000
Donor BMI (n=26276)	27 (5.7)	27 (5.5)	27 (5.7)	0.749
Donor LVEF (%) (n=24323)	61.6 (7.1)	61.7 (6.9)	61.6 (7.1)	0.229
Donor Cause of death (n=26366)				
Anoxia	5113 (19.4)	766 (16.5)	4347 (20.0)	<0.001
Cerebrovascular/stroke	5577 (21.2)	1347 (28.9)	4230 (19.5)	
Head trauma	13624 (51.7)	1746 (37.5)	11878 (54.7)	
Other	2052 (7.8)	795 (17.1)	1257 (5.8)	
Ischemic hours (n=24674)	3.2 (1.1)	3.3 (1.1)	3.2 (1.1)	0.019
Donor diabetes (n=25962)	822 (3.2)	197 (4.4)	625 (2.9)	<0.001
Donor hypertension (n=26032)	3797 (14.6)	1047 (23.3)	2750 (12.8)	<0.001
Donor cocaine use (n=24481)	3845 (15.7)	1043 (27.8)	2802 (13.5)	<0.001
Donor high risk behavior (n=24791)	3457 (13.9)	572 (15.0)	2885 (13.8)	0.044

# Results



	Overall survival	Graft failure	CAV	Acute rejection
No. patients	9144	9144	6290	7174
Donor smoking history				
No cigarette use	1 (Reference)	1 (Reference)	1 (Reference)	1 (Reference)
Cigarette use	1.11 (1.03-1.20)	1.11 (1.03-1.20)	0.95 (0.87-1.04)	1.05 (0.97-1.13)
p-value	0.009	0.005	0.24	0.22

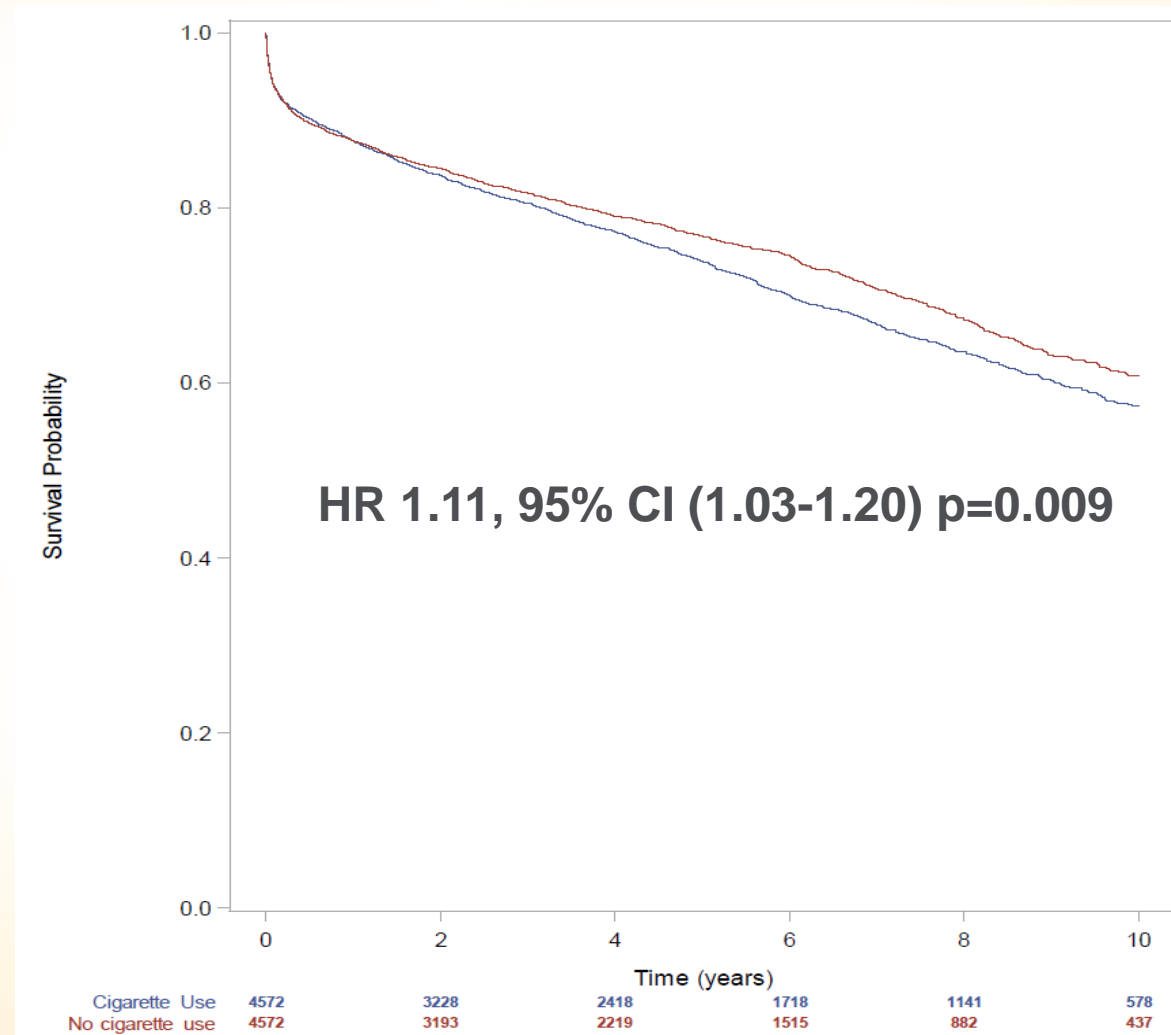
- Donor smokers had worse survival (HR 1.11, p=0.009)
- Donor smokers had more graft failure (HR 1.11, p=0.005)
- No statistical difference was seen with CAV or acute rejection



# Kaplan Meier Curve for Survival



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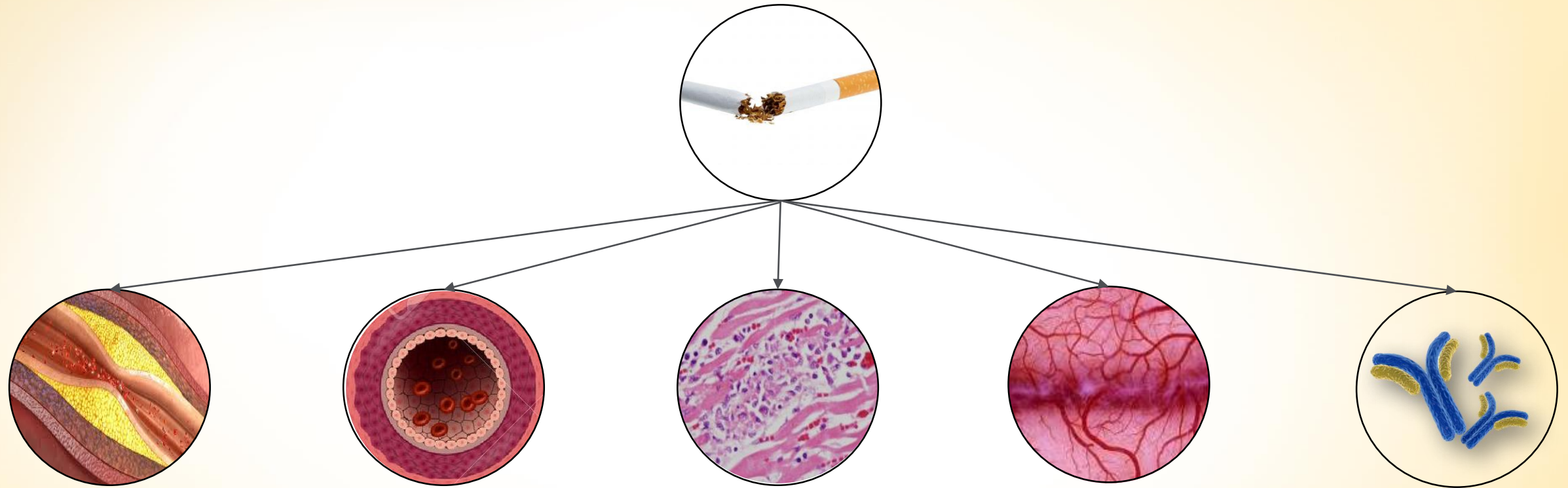


Median follow-up 4 years

# Potential Mechanisms



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**Atherogenesis**

**Vascular Injury**

**Inflammation**

**Microvascular  
Constriction**

**Immunogenicity**

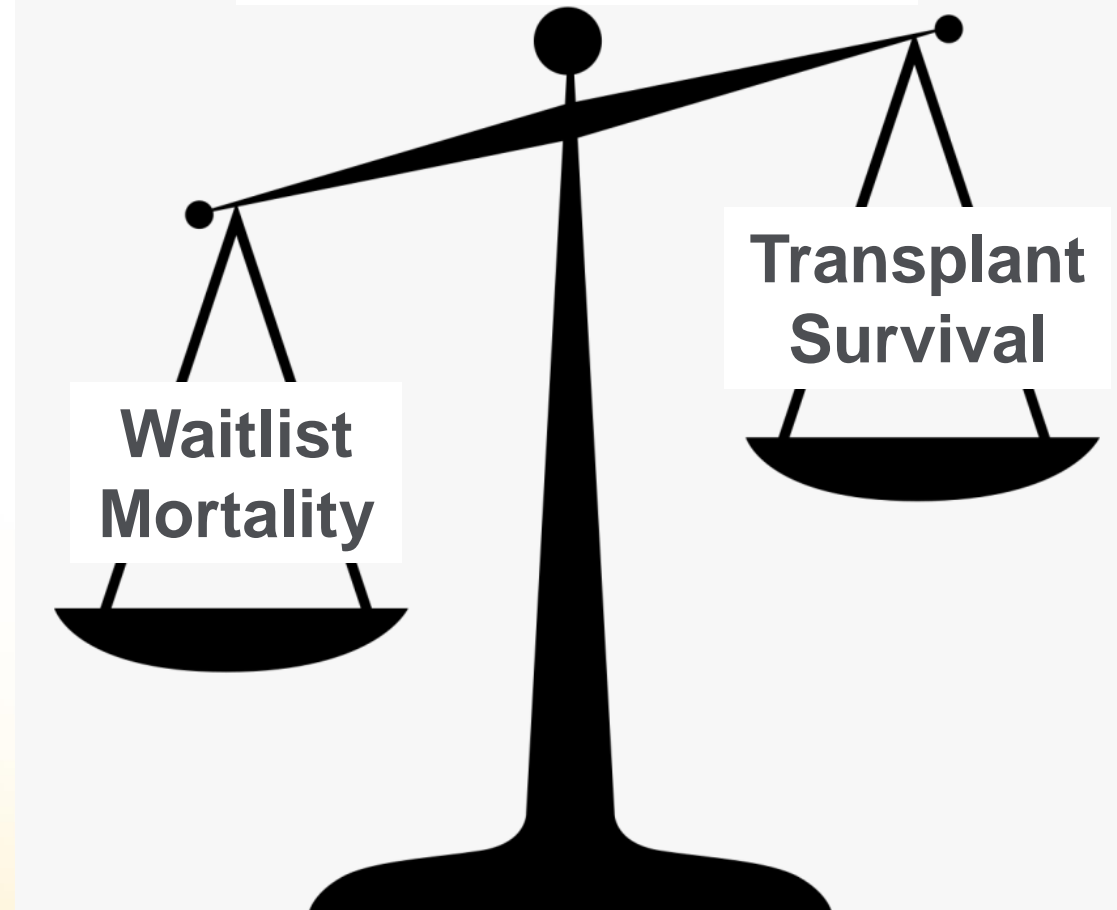
1. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: An update. *J Am Coll Cardiol.* 2004;43(10):1731-1737.
2. Leone A, Landini L. Vascular pathology from smoking: look at the microcirculation! *Curr Vasc Pharmacol.* 2013;11(4):524-530.
3. Corbett C, Armstrong MJ, Neuberger J. Tobacco smoking and solid organ transplantation. *Transplantation.* 2012;94(10):979-987.

# Clinical Implications



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## Organ Allocation



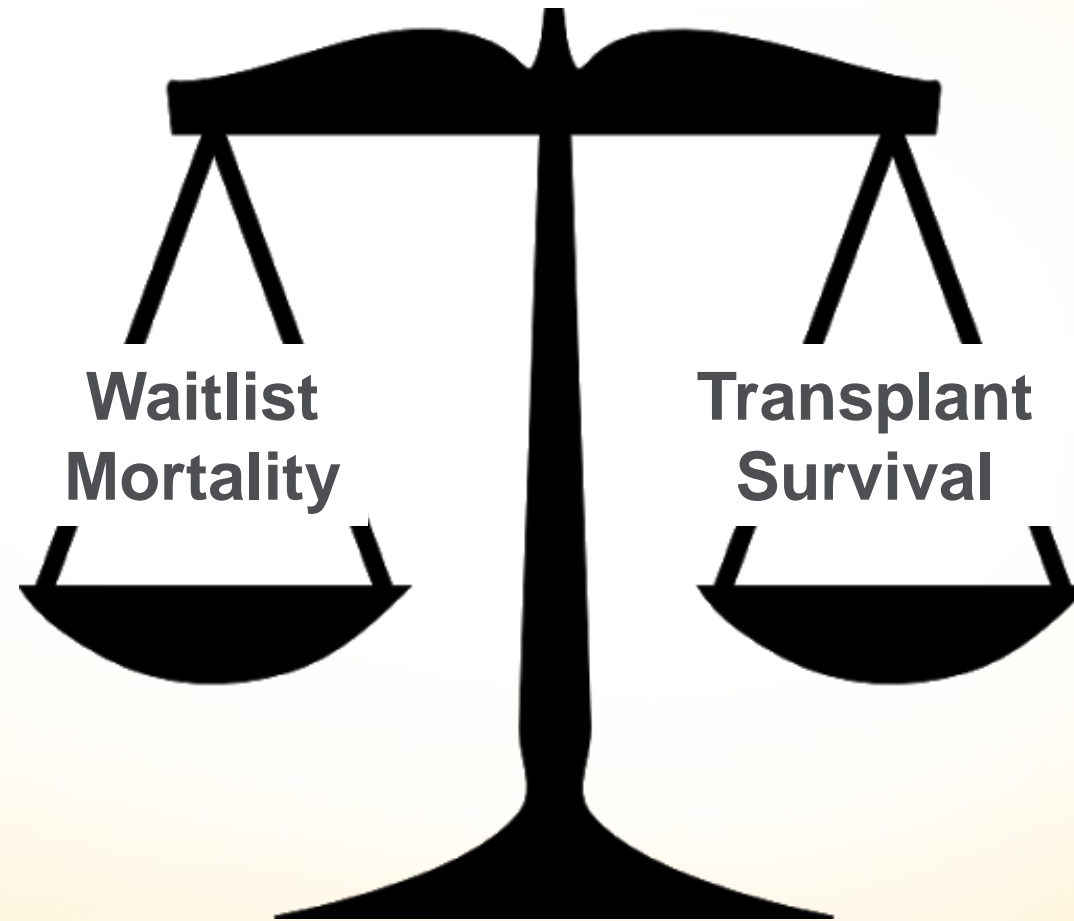
Current US  
allocation  
system

# Clinical Implications



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## Organ Allocation



Current US  
allocation  
system

New donor risk  
score focusing  
on transplant  
outcomes

# Clinical Implications



- Risk scores incorporating post transplant survival already exist in other solid organ transplants
  - Donor Risk Index
  - Kidney Profile Risk Index
- Multiple risk scores for heart transplantation have been proposed
- Donor smoking should be included in future risk scores

# Limitations



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- Registry study
  - Unlisted confounders
- Graft failure was not defined in the registry
  - More difficult to elucidate a mechanism

# Conclusions



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- Donor smoking is an independent marker of increased transplant mortality
- This information can help guide organ selection and should be included in any modelling involving transplant mortality