

# Evidence to Inform Transplant Policy and Practice

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# Disclosures

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- **Treasurer – American Society of Transplantation**
  - ◆ **Opinions do not necessarily reflect official policy of the AST**
- **Grant Support – Astellas**
- **Consultant – Astellas**
- **Consultant – Sanofi**
- **Canadian**
- **Nephrologist**

# Overview

Issue	Policy / Practice
Cessation of coverage for immunosuppressant drugs	“Immuno- Bill”
Fragmentation of dialysis and transplant care	Patients Demonstration Act
Access to transplantation	Referral for kidney transplantation
Care of wait-list patients	Screening for coronary artery disease

# Cessation of coverage for immunosuppressant drugs

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- For patients insured by ESRD Medicare
  - ◆ Immunosuppressant drug coverage ceases three years after transplantation
  - ◆ Cessation of drug coverage is associated with transplant failure

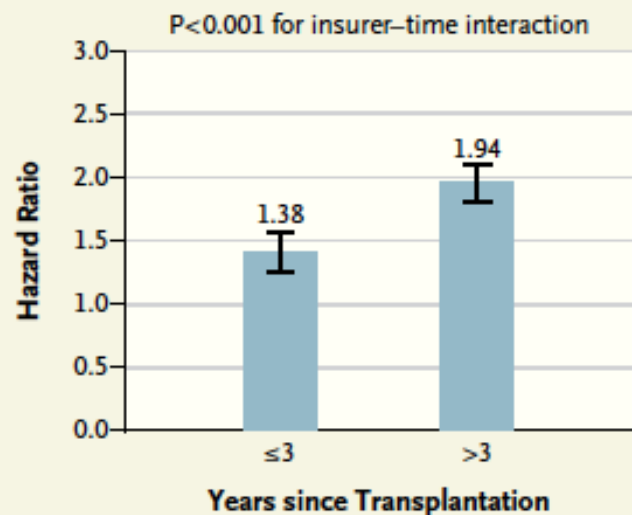
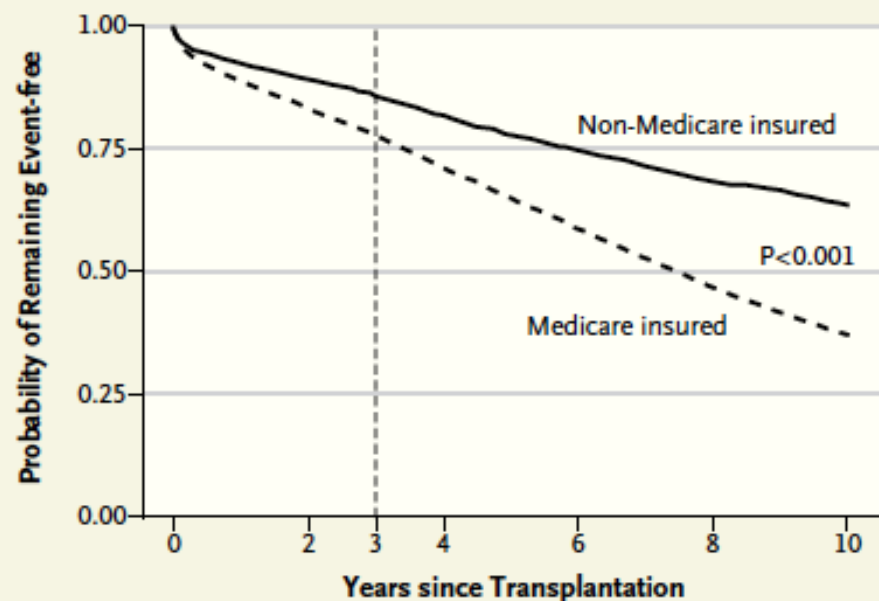


# The NEW ENGLAND JOURNAL of MEDICINE

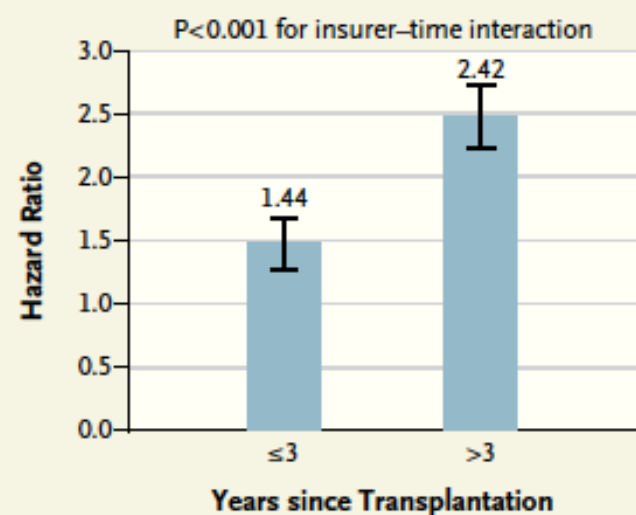
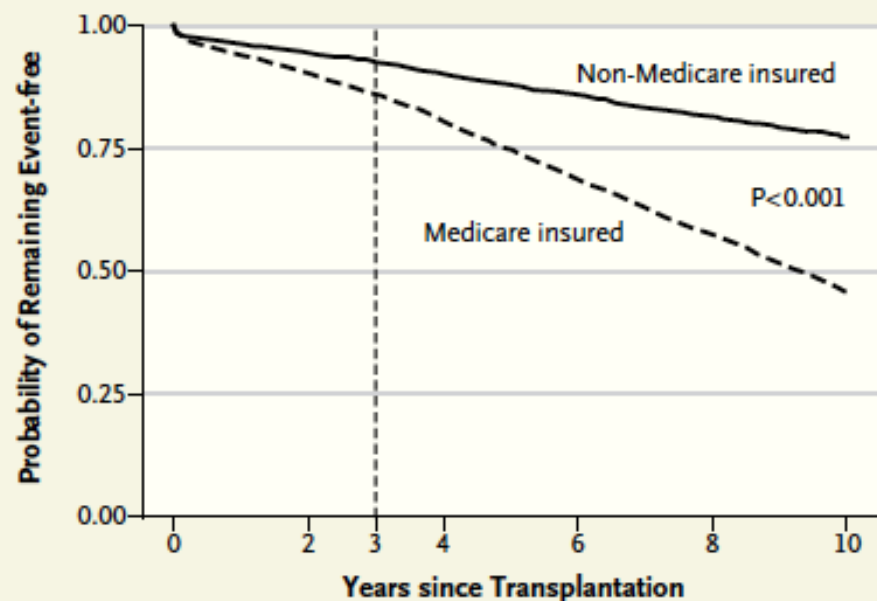
## Kidney-Transplant Survival and Immunosuppressive Coverage Policies for Selected Countries (for Recipients of a First Kidney-Only Transplant from a Deceased Donor).\*

Country	5-Yr Survival	10-Yr Survival	Government-Funded Immunosuppressive Coverage
	<i>percent</i>		
Australia	81	59	Lifetime for all recipients
Canada	80	58	Lifetime for all recipients
United Kingdom	78	56	Lifetime for all recipients
United States	69	43	Lifetime for recipients >65 yr of age or with work-related disability; 3 yr for all other recipients

**A Deceased-Donor Graft Loss from Any Cause**



**B Living-Donor Graft Loss from Any Cause**



# The Washington Post

*Democracy Dies in Darkness*

Opinions

## Our Medicare policy for kidney transplants is totally irrational



Doctors perform a kidney transplant. (Linda Davidson/The Washington Post)

By **Marcello Tonelli** and **John Gill**  
December 6, 2017

*Marcello Tonelli is associate vice president of research at the University of Calgary. John Gill is a clinician scientist and professor of medicine at the University of British Columbia and a member of the board of directors for the American Society of Transplantation. They are both former presidents of the Canadian Society of Nephrology.*



# *ASPE*

## *ISSUE BRIEF*

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### **ASSESSING THE COSTS AND BENEFITS OF EXTENDING COVERAGE OF IMMUNOSUPPRESSIVE DRUGS UNDER MEDICARE**

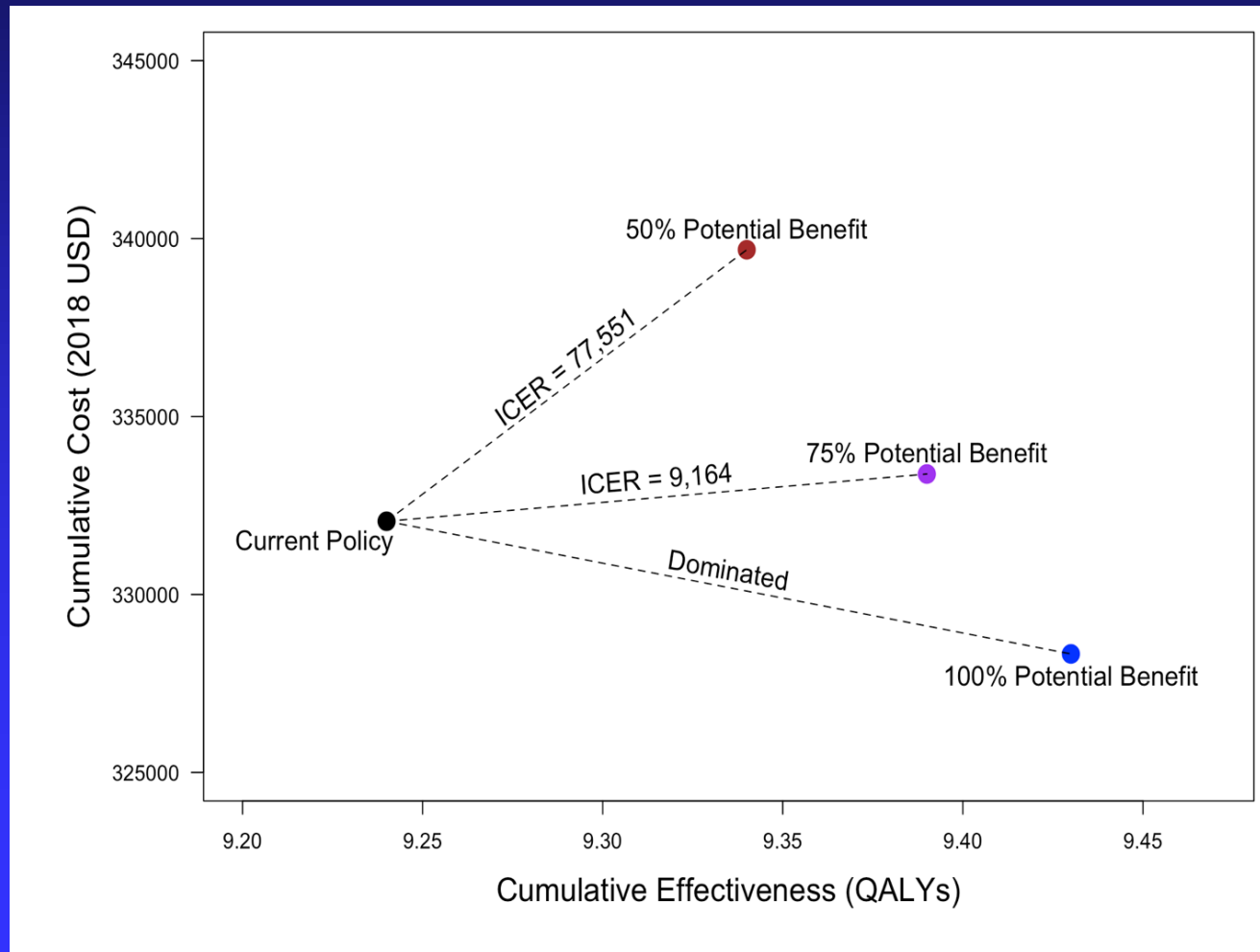
May 10, 2019

**Estimated 10 year cost savings of \$73 million**



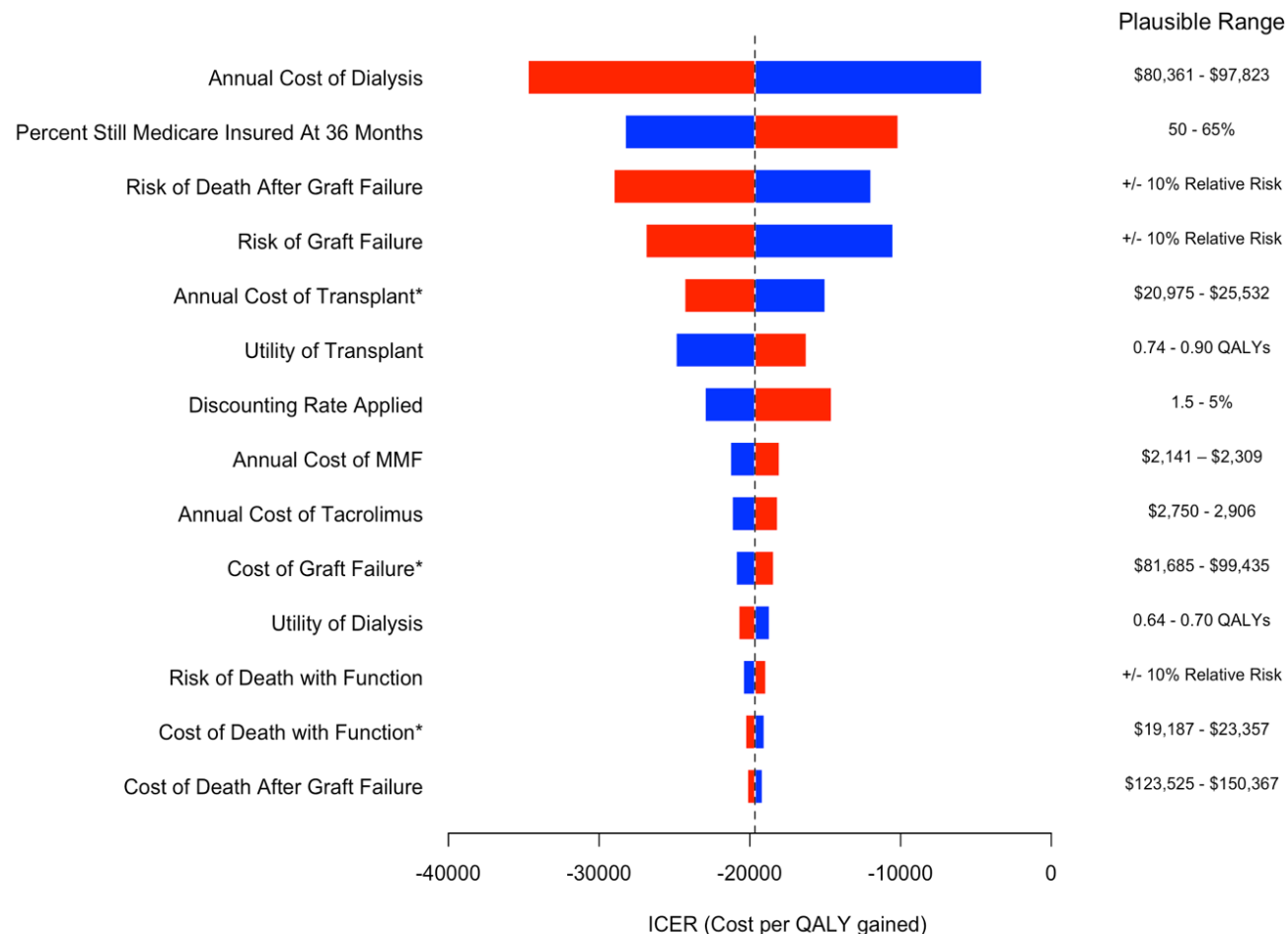
# Extending Immunosuppressant Coverage is likely cost saving but definitely cost-effective

Kadatz and Gill – manuscript under review



# Varying factors that could affect cost within a plausible range did not alter cost savings

Kadatz and Gill manuscript under review

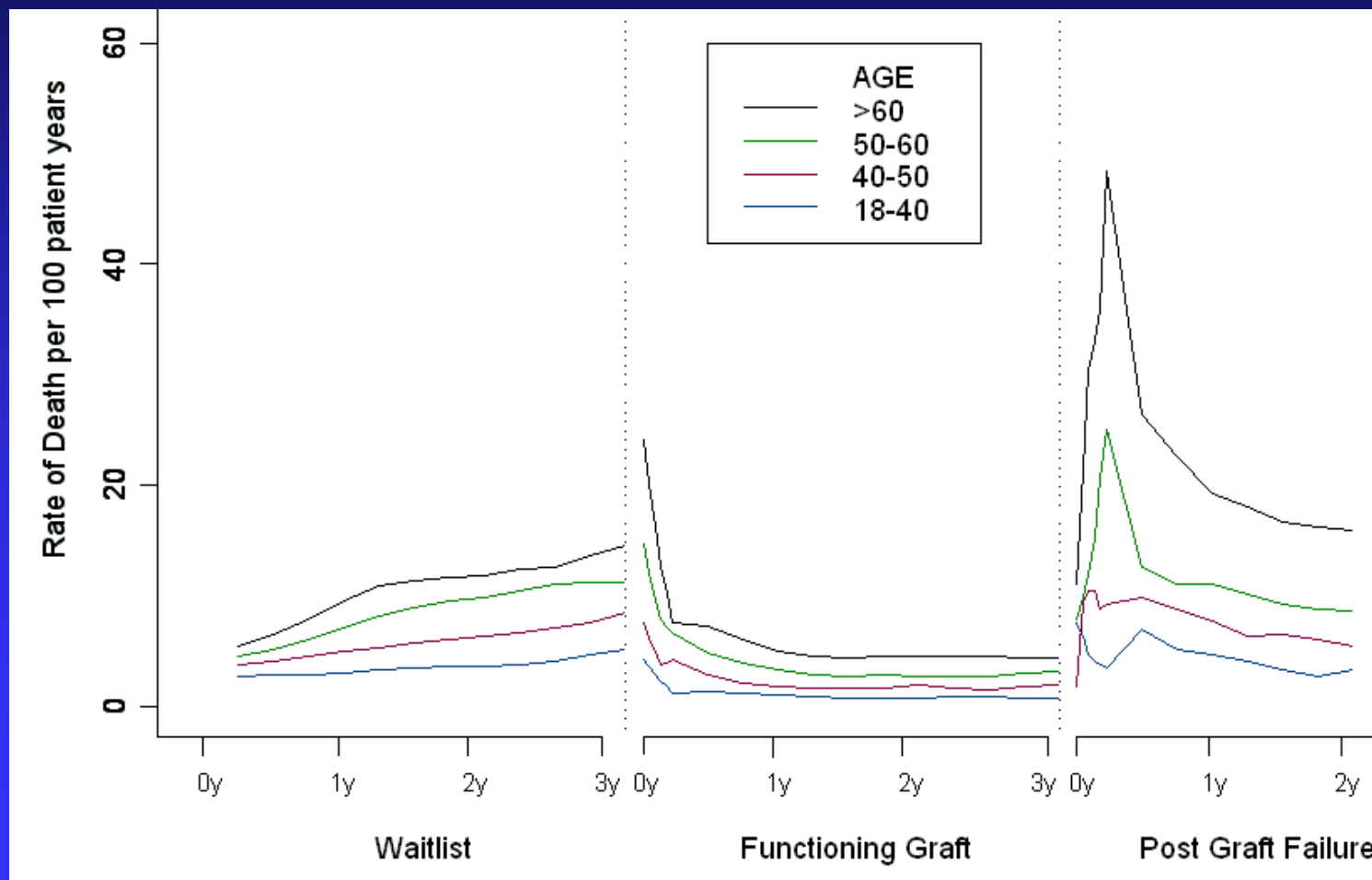


# Fragmentation of Dialysis and Transplant Care

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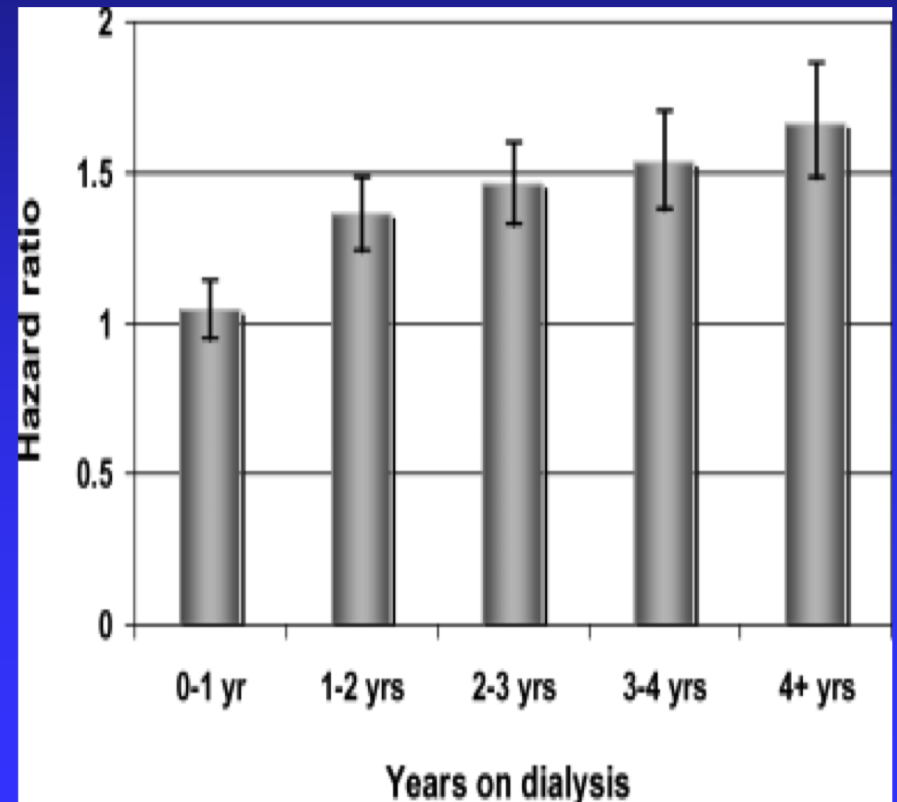
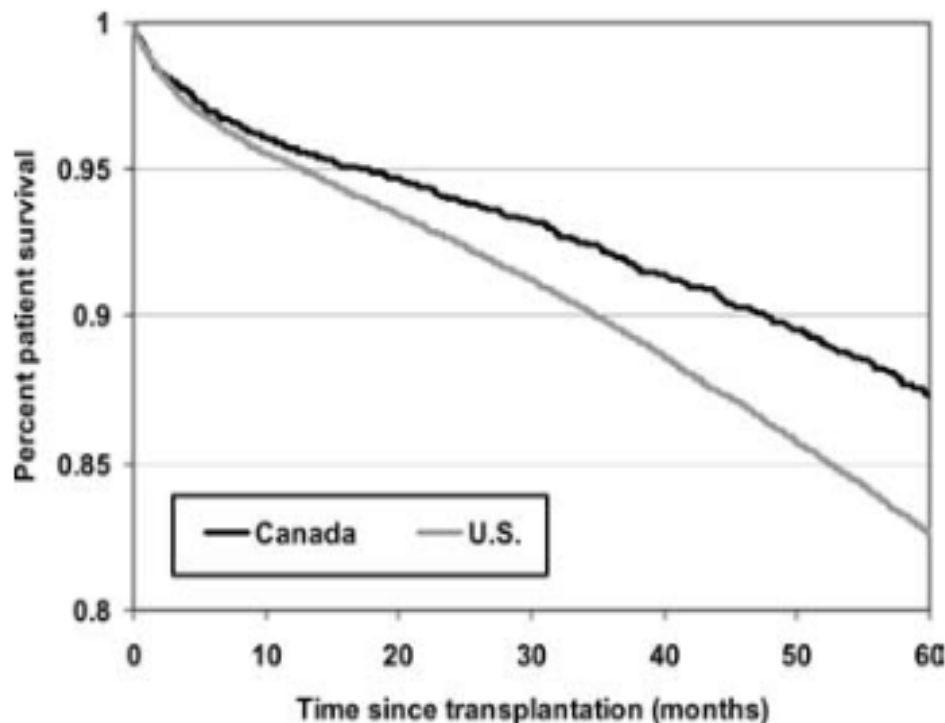
# Transitions Between Dialysis and Transplantation and Risk of Death



# Post-transplant Patient Survival In Canada and United States

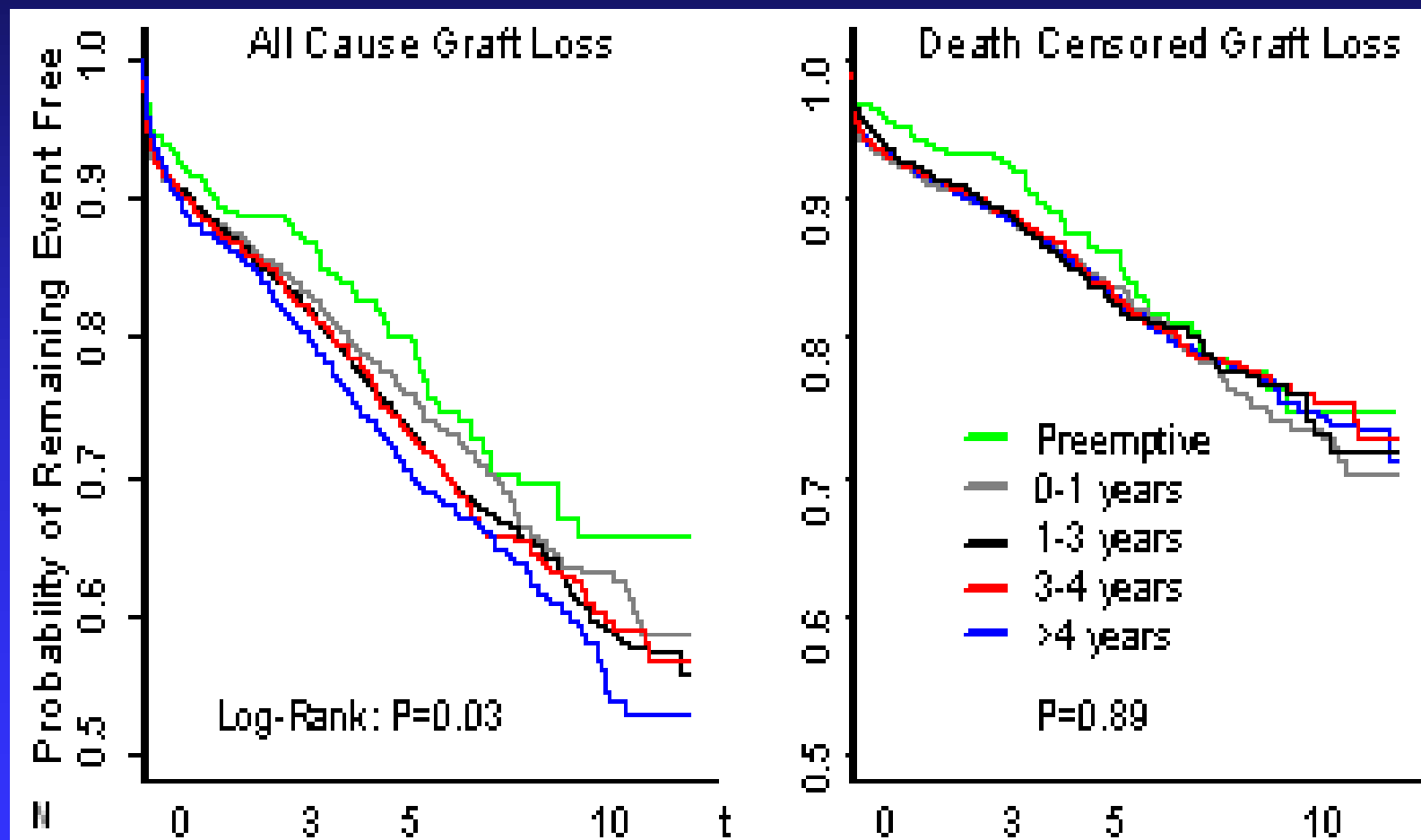
Patient Survival > Canada

Higher risk of death in U.S. patients related to duration of dialysis before transplant



# Dialysis Exposure and Kidney Transplant Survival In Canada

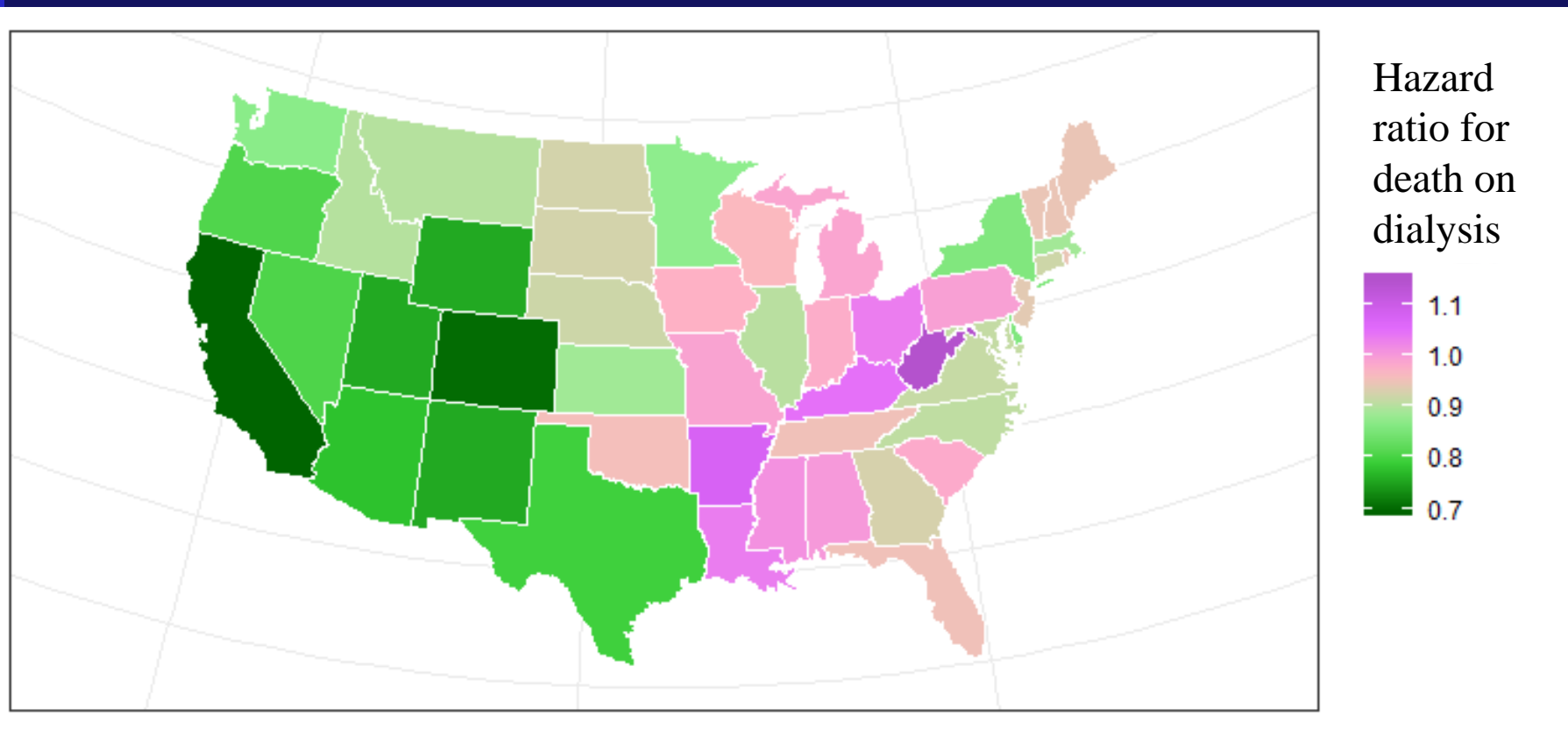
ATC 2010



N = 6191 Adult First Deceased Donor Kidney Transplant Recipients 95-05

# Geographic variation in dialysis mortality in United States

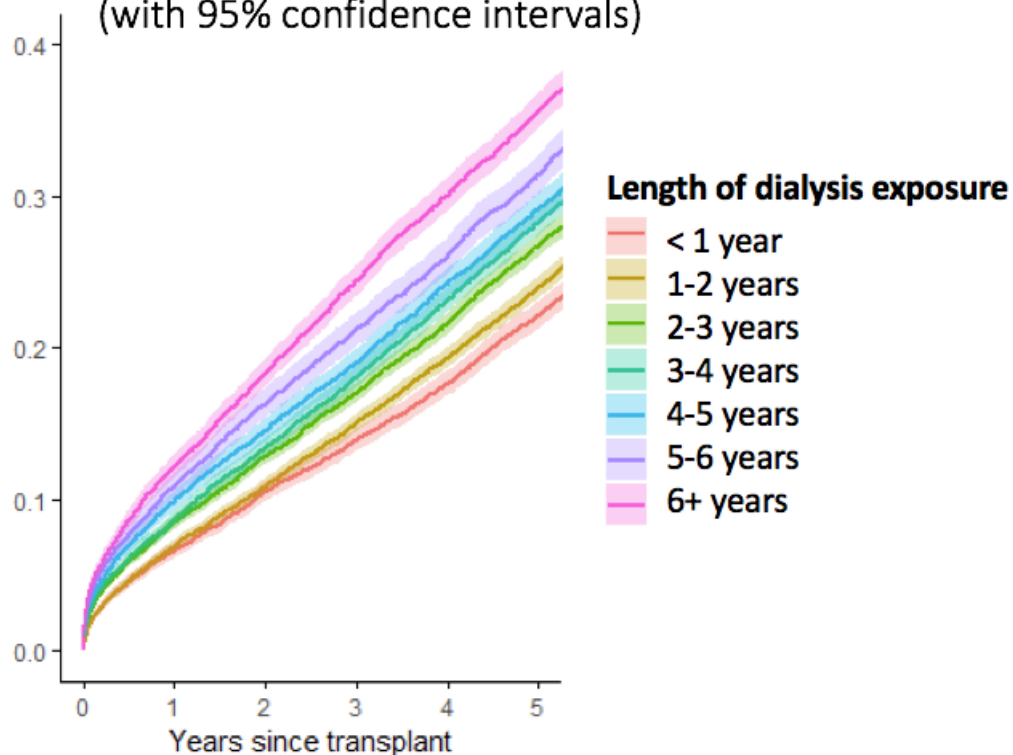
( hazard ratio for death on dialysis, 2010-2014)



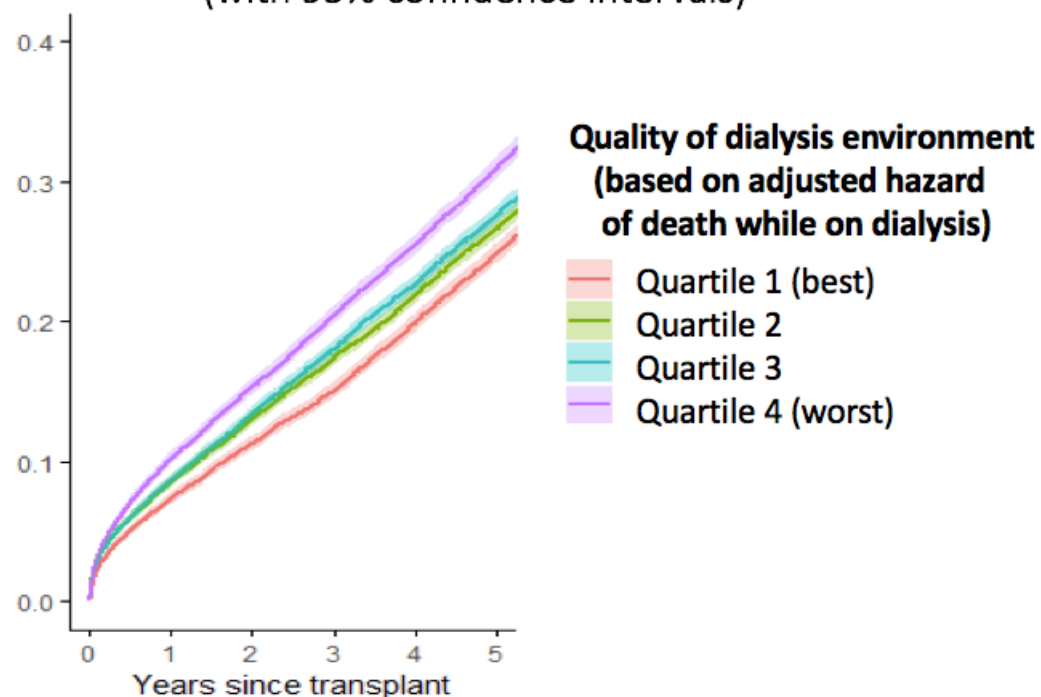
Cox model output, adjusted for: age (18-49 or 50+), gender, race, cause of ESRD, and dialysis vintage (<2, 2-5, or >5 years).

# Post-Transplant Survival Associated with Duration of Pre-transplant Dialysis and Death rate on dialysis in state of residence

Cumulative incidence of graft loss  
(with 95% confidence intervals)

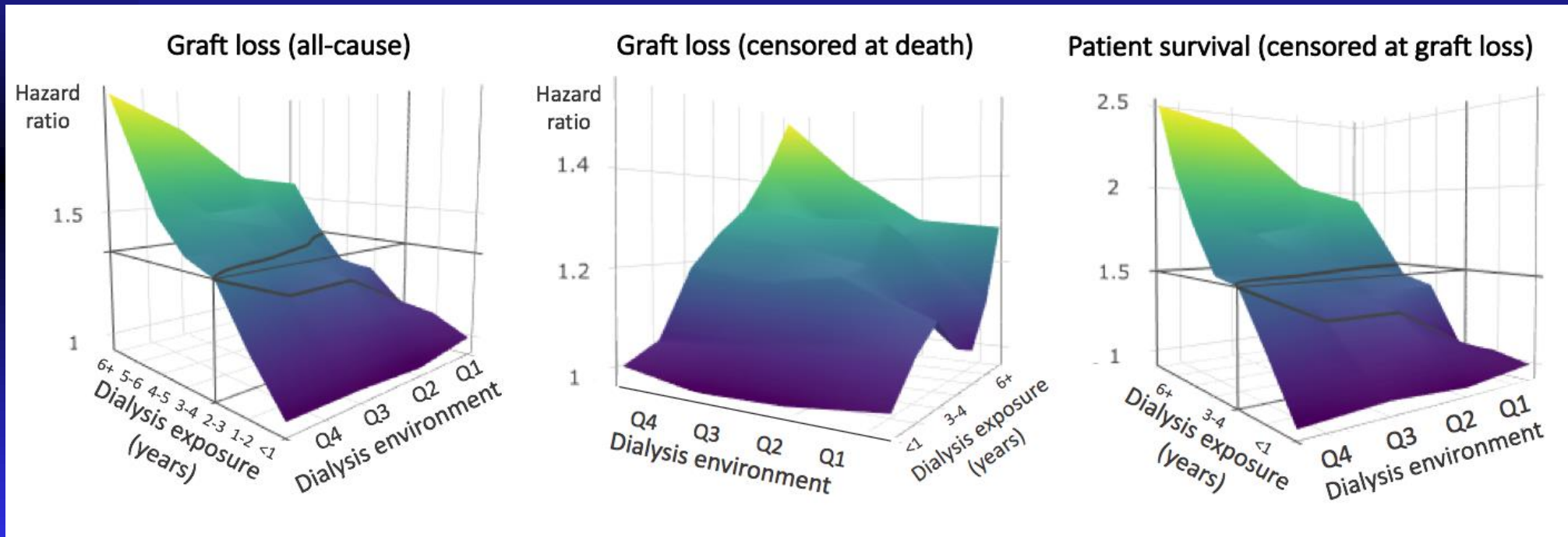


Cumulative incidence of graft loss  
(with 95% confidence intervals)





# The impact of longer pre-transplant dialysis exposure was greater in regions with higher dialysis mortality



Cox model adjusted for: Age, gender, cause of ESRD, race, BMI, year of transplant, PRA, PVD, CHF, CVA, ASHD, diabetes, non-ambulatory state, COPD and tobacco use

# Policy Implications

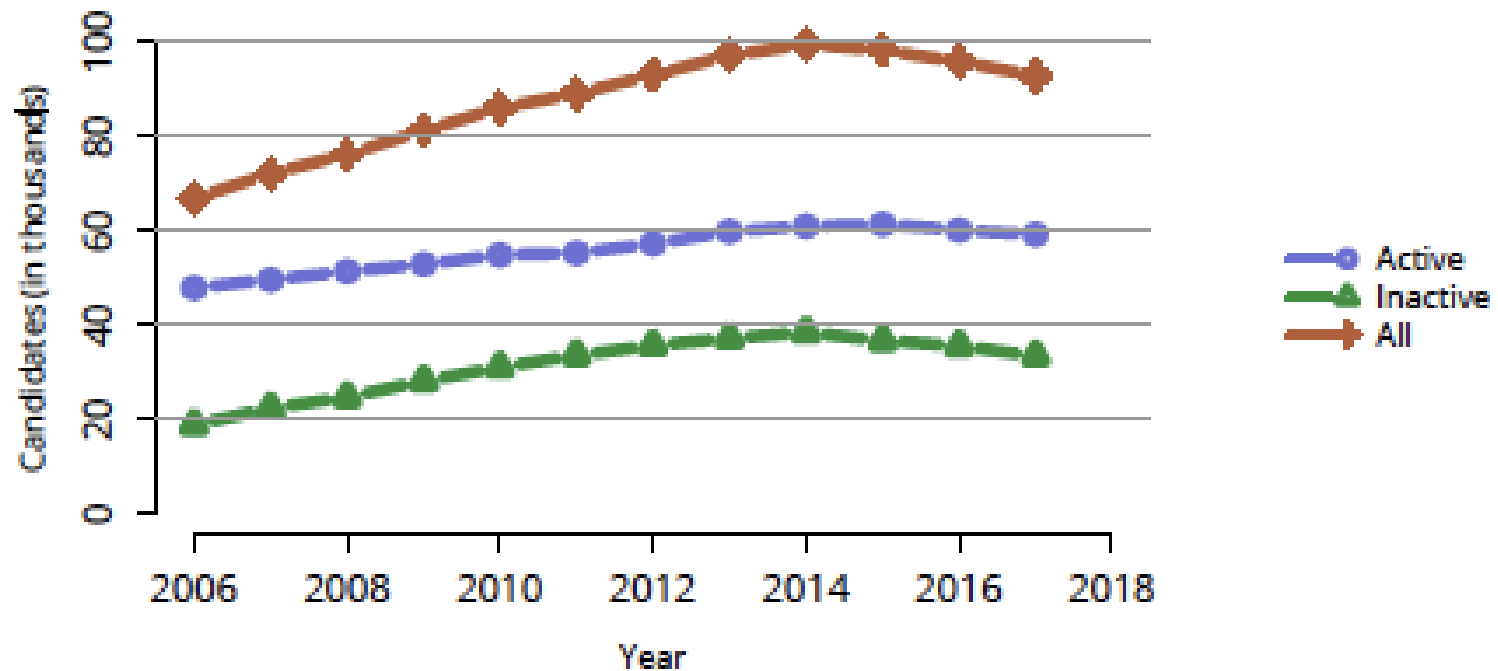
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- **Post transplant dialysis outcomes are impacted by pre-transplant dialysis care**
- **Silos of care are inappropriate**
- **Integrated care models including dialysis and transplantation are needed to ensure optimal patient outcomes**



# Access to kidney transplantation

## Kidney Transplant Wait-List Is Shrinking



# Why is the waiting-list decreasing ?

Waiting list state	2015	2016	2017
Patients at start of year	99,322	98,018	95,658
Patients added during year	30,215	30,854	30,918
Patients removed during year	31,466	33,167	33,891
Patients at end of year	98,071	95,706	92,685

Removal reason	2015	2016	2017
Deceased donor transplant	12,279	13,501	14,077
Living donor transplant	5331	5334	5536
Transplant outside US	49	77	67
Patient died	4983	4862	4414
Patient refused transplant	518	471	524
Improved, transplant not needed	208	193	212
Too sick for transplant	4078	4345	4505
Other	4020	4384	4556

# Why is the waiting-list decreasing ?

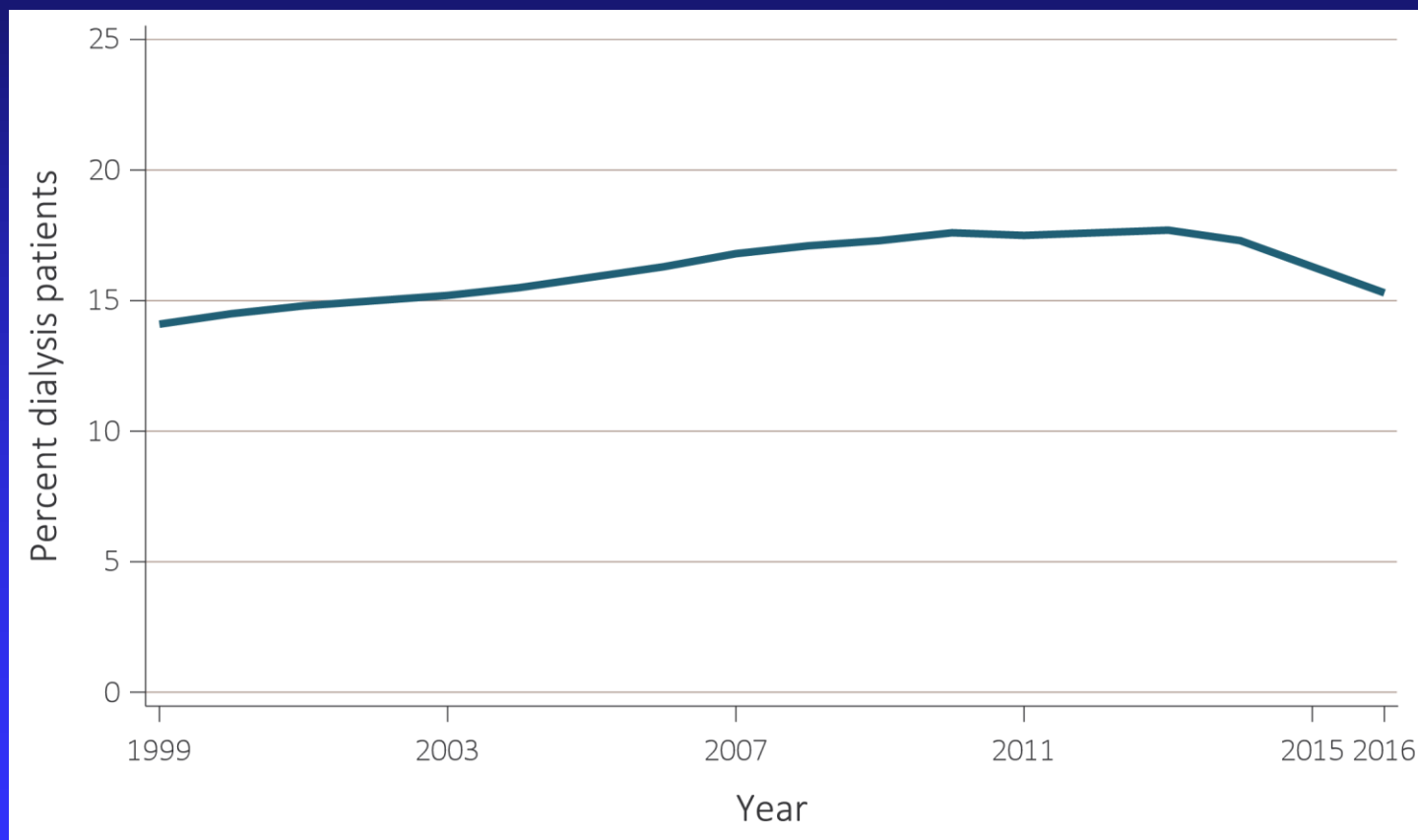
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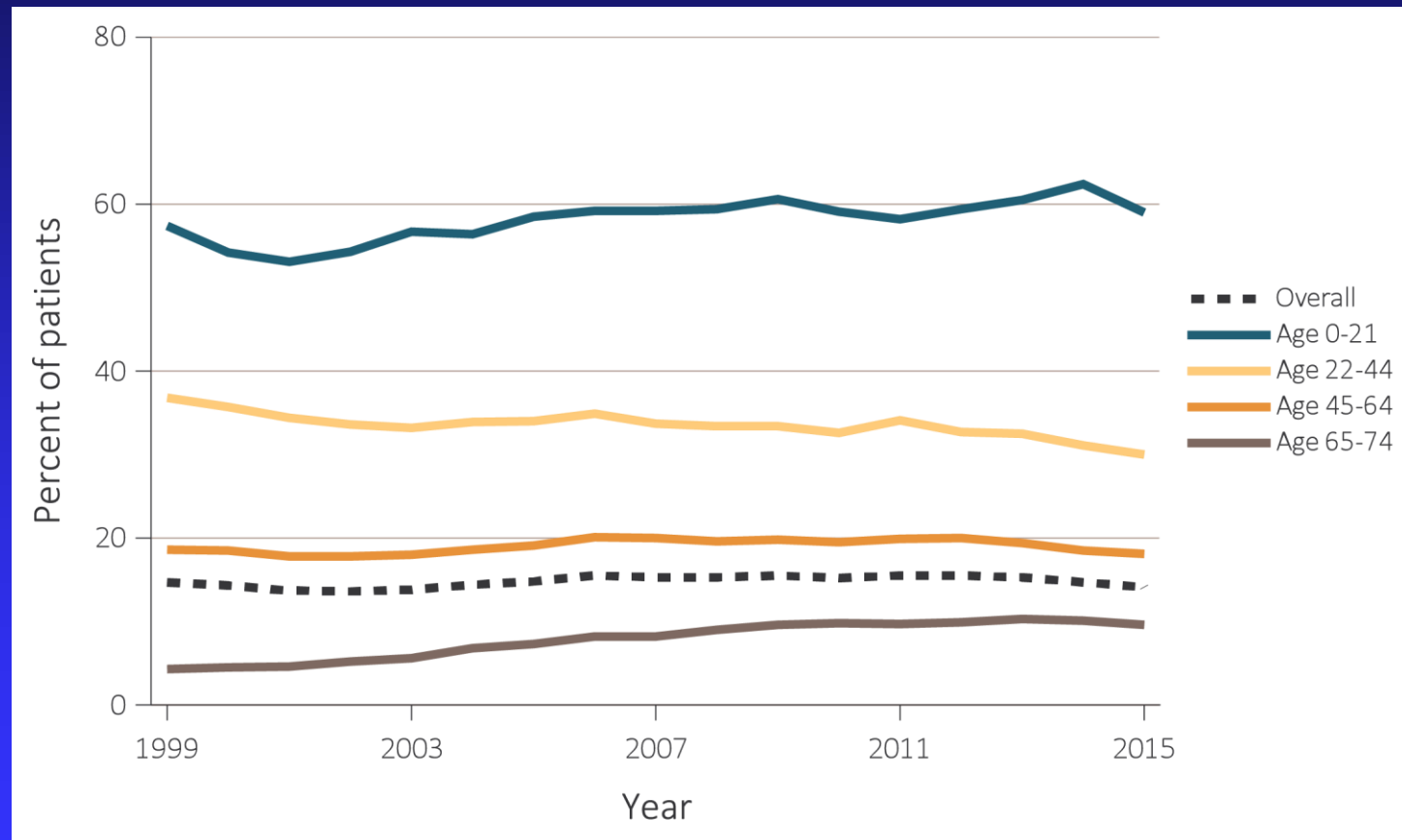
# Access to transplantation

## Percentage of dialysis patients who were wait-listed

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# Proportion of incident dialysis patients who were wait-listed or received a kidney transplant within one year



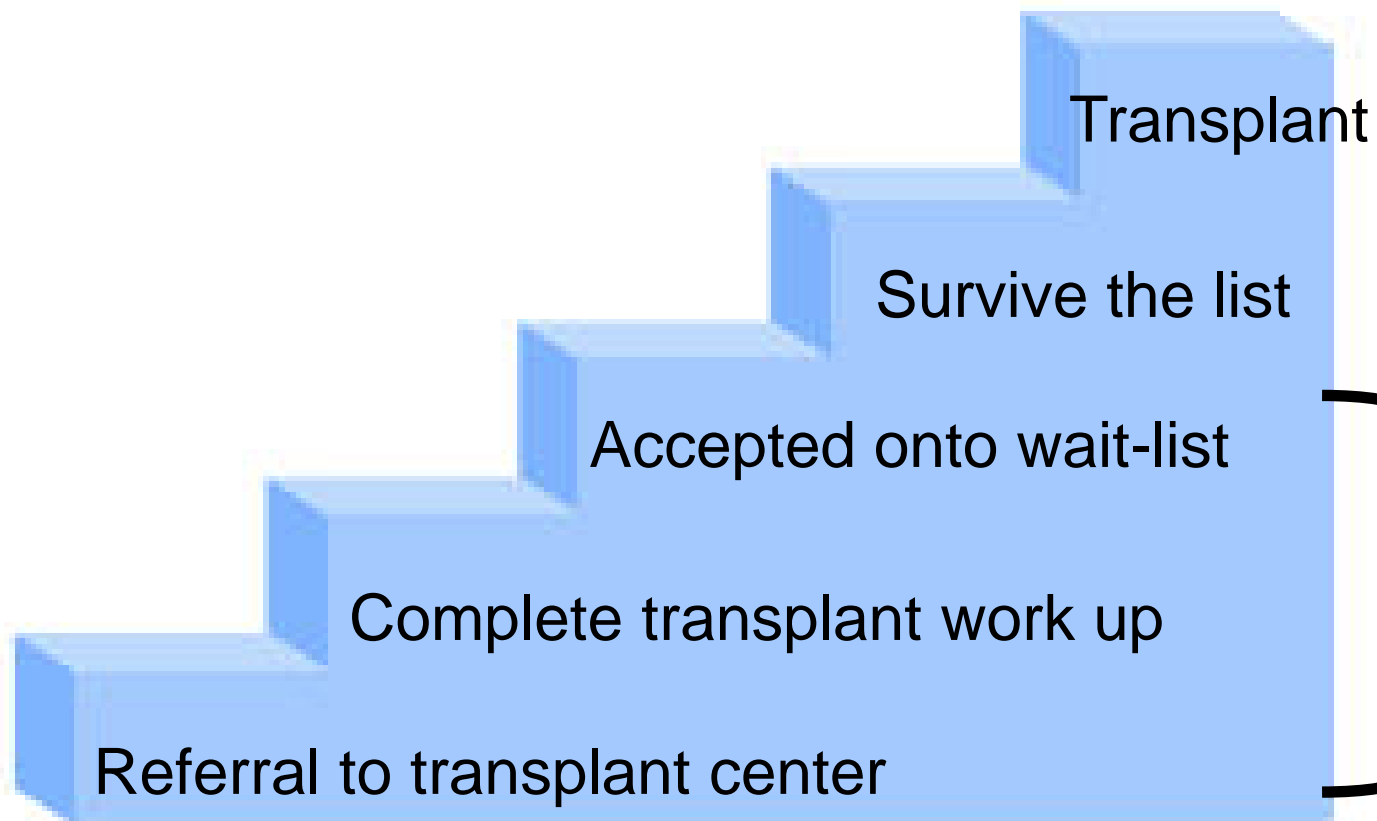
# **Wait-list provides an incomplete picture of the need for transplantation**

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# Steps to access transplantation



**No National  
Data**

# Referral for kidney transplantation in Canadian provinces

## METHODS

Prospective ascertainment of referral for transplantation in 12 Transplant Centers



Linked to national data (Canadian Organ Replacement Register) on incident dialysis patients to determine incidence of referral



Outcome: Referral for kidney transplantation (per 100 patient years of dialysis)



**CONCLUSION** : Referrals varied more than 3 fold between provincial regions in which deceased donor kidneys are routinely shared suggesting the need for standardization of referral practices and national reporting of referral

doi: 10.1681/ASN. Kim SJ\*, Gill JS\*, Knoll G, Campbell P, Cantarovich M, Cole EH, Kiberd B. (co-first authors)

# Implications – policy and practice

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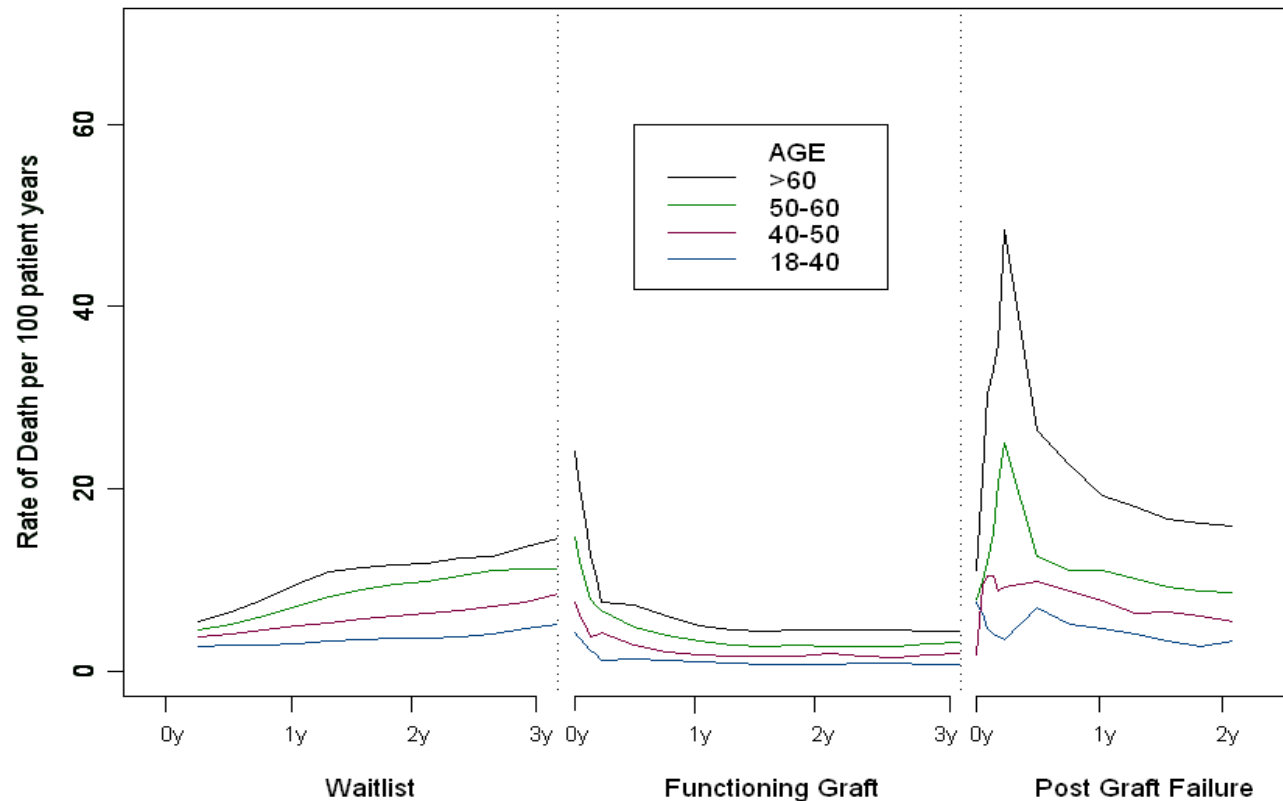
- **National reporting of referral for transplantation is needed**
- **Standardization of referral is needed**

# Management of wait-listed patients

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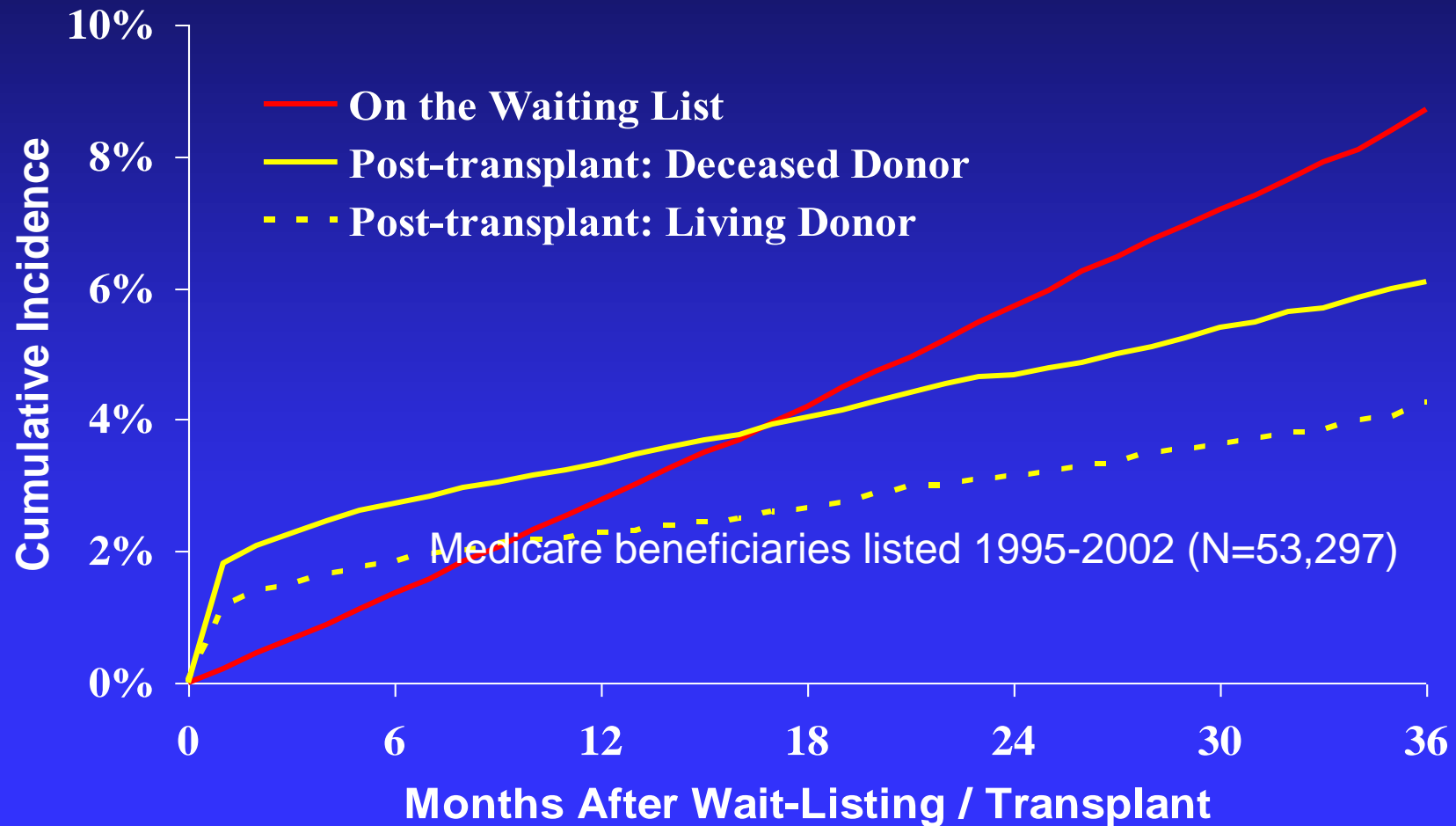
# When Do Our Patients Die ?

Gill et al KI 2007; 71(5): 442-7



# Incidence of Myocardial Infarction

Kasiske et al, *JASN* 2006; 17:900



# Transplant Guidelines

## What are we supposed to be doing?

### Before Listing

#### AST 2001

High-risk → stress test

Diabetes

Prior IHD

≥2 traditional risk factors

Positive test → anigography

Critical lesions → revascularize

*Am J Transplant 2001;1:S3*

### During Wait-listing

#### KDOQI 2005

Annual stress tests in wait-listed patients who have:

Diabetes

Prior IHD, PVD or EF≤40%

≥2 traditional risk factors

*Am J Kidney Dis 2005;45:S1*

# Transplant Guidelines differ from General Guidelines

## AST 2001

High-risk → stress test  
Diabetes  
Prior IHD  
≥2 traditional risk factors  
Positive test → anigography  
Critical lesions → revascularize

*Am J Transplant 2001;1:S3*

## KDOQI 2005

Annual stress tests in wait-listed patients who have:  
Diabetes  
Prior IHD, PVD or  $EF \leq 40\%$   
≥2 traditional risk factors

*Am J Kidney Dis 2005;45:S1*

## AHA/ACC 2007

Intermediate Risk Surgery  
≥1 Risk Factor

No Symptoms  
Functional Capacity ≥4 METS

Yes  
Proceed to Surgery

No/Unknown  
Surgery with HR Control  
Stress testing “if it will change management” (Class IIb)

*J Am Col Cardiol 2007;50:1707*



# Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates

A Scientific Statement From the American Heart Association and the American College of Cardiology Foundation

*Endorsed by the American Society of Transplant Surgeons,  
American Society of Transplantation, and National Kidney Foundation*

Krista L. Lentine, MD, MS, Co-Chair; Salvatore P. Costa, MD, Co-Chair;  
Matthew R. Weir, MD, FAHA; John F. Robb, MD, FAHA; Lee A. Fleisher, MD, FAHA;  
Bertram L. Kasiske, MD; Robert L. Carithers, MD; Michael Ragosta, MD; Kline Bolton, MD;  
Andrew D. Auerbach, MD; Kim A. Eagle, MD, FAHA, Chair; on behalf of the American Heart  
Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease

JACC Vol. 60, No. 5, 2012  
July 31, 2012:434–80

# What did AHA recommend for screening after wait-listing?

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- The usefulness of periodically screening asymptomatic WL patients for myocardial ischemia while on the transplant waiting list to reduce the risk of MACEs is uncertain
- Class IIB Level C

# Now What?

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# Is a trial of screening ethical ?

**Strategy of testing/ intervention is not risk free/ and may be harmful**

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- Risk of loss of residual renal function with angiography
- Risk of In hospital mortality following coronary revascularization is about 3 times higher in dialysis patients vs non-ESRD
- Risk of blood transfusion and CVA in ESRD patients
- Abnormal screening tests may unnecessarily delay transplantation or exclude patients from consideration of transplantation

**CARSK**

**Canadian Australasian Randomized Trial of Screening  
Kidney Transplant Candidates for Coronary Artery Disease**

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# Hypothesis

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- After screening for wait list entry, non use of cardiac screening tests is non-inferior versus the current standard care which is screening all asymptomatic wait-listed patients for coronary artery disease (CAD) at regular intervals
- We will also compare the benefits and costs of screening and subsequent treatment versus not screening from a health system perspective

Inclusion Criteria:  
At least 18 years of Age  
No symptoms of active cardiac disease  
Actively Wait-listed For Kidney Only Transplant  
No previous extra-renal transplant  
Anticipated date of transplantation > 12 months from date of enrollment  
Anticipated to require cardiac screening before transplantation\*

Informed Consent

Randomization

Regular Screening  
During Wait-listing

No Screening after  
Wait-listing

Note patients in both groups may be investigated for symptoms

Annual from date  
of last test  
-Diabetes  
Angiographic  
CAD not  
revascularized  
-PTCA  
Incomplete CABG  
CABG > 3 yrs ago

Every 24 months  
for all others

Management of a positive non-invasive test irrespective of whether it was  
done for screening or symptoms will be managed as per center protocol

# It's a trial about "NOTHING"

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**SEINFELD** says it's the "show

**about nothing."**

**So I watch it with the t.v. off.**

ICANHASCHEEZBURGER.COM



# Expected Outcomes

## Practice Implications

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- The trial will enroll 3300 patients in Canada, Australasia, Spain, Germany (trial results will be disseminated to US transplant physicians in a knowledge translation partnership with United Health Group)
- Irrespective of the outcome – the trial will either
  - a) make better use of scarce deceased donor kidneys by informing better management of wait-list patients (n = 175,000 world-wide),
  - and/or b) save valuable resources (estimated \$300 million/year) by averting needless and potentially harmful tests.

# Summary

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Issue	Policy / Practice
Cessation of coverage for immunosuppressant drugs	“Immuno- Bill”
Fragmentation of dialysis and transplant care	Patients Demonstration Act
Access to transplantation	Referral for kidney transplantation
Care of wait-list patients	Screening for coronary artery disease

# Thank You !

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- Please address any questions to
  - ◆ [jgill@providencehealth.bc.ca](mailto:jgill@providencehealth.bc.ca)