Kidney Transplantation: Overview of Health and Function

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General Thoughts

- Many people with CKD and ESRD
- Heterogenous population and outcomes:
  - CKD/ESRD
  - KT candidates
  - KT recipients
  - Donors
- More frailty, disability, dependence, cognitive decline, than one might imagine

Absolute Contraindications

- Active malignancy, except skin ca
  - 2-3 year wait after adequate treatment for most
- Acute infection--osteomyelitis, line sepsis
- Clinically active SLE or vasculitis

Courtesy of Dan Brennan, MD

Relative Contraindications

- Advanced cardiopulmonary disease
- Extensive peripheral vascular disease
- Severe chronic liver disease
- Morbid obesity
- Uncontrolled psychiatric disorder
- Intact parathyroid > 800 off cinacalcet

Courtesy of Dan Brennan, MD

Surgical Complications

- Urologic (< 7%): urine leaks or obstruction
- Vascular: renal artery/vein thrombosis (2%); renal artery stenosis (10%)
- Fluid collections (20%)
  - Lymphoceles (15%):
  - Urinoma 2%
  - Seroma (215%
- Wound infections (< 5%)

Courtesy of Dan Brennan, MD

Medical Complications

- Hypertension
- Anemia
- Hyperkalemia
- Hypercalcemia
- Hypophosphatemia
- Diabetes
- Dyslipidemia

- Acute rejection
- Chronic rejection
- Calcineurin Toxicity
- Infection
- Recurrent disease
- Bone disease
- Malignancy
- Drug interactions

Courtesy of Dan Brennan, MD

Causes of Death

- Cardiovascular 30-40%
  - Cytomegalovirus
  - Hypercholesterolemia
  - Hypertension
  - Left ventricular hypertrophy
  - Diabetes
- Infection 20-30%
  - Viral
  - Fungal
  - Bacterial
- Malignancy 20-30%
  - PTLD
  - Solid Organ
  - Skin
- Liver Disease 5-20%
  - Hepatitis B
  - Hepatitis C

Courtesy of Dan Brennan, MD

The Estimated Post Transplant Survival (EPTS) score is a numerical measure used to allocate some kidneys in the new kidney allocation system. Every adult patient on the kidney waitlist receives an EPTS score for use in the kidney allocation system.

EPTS scores range from 0% to 100%. Candidates with a lower EPTS score are expected to experience more years of graft function from high-longevity kidneys compared to candidates with higher EPTS scores.

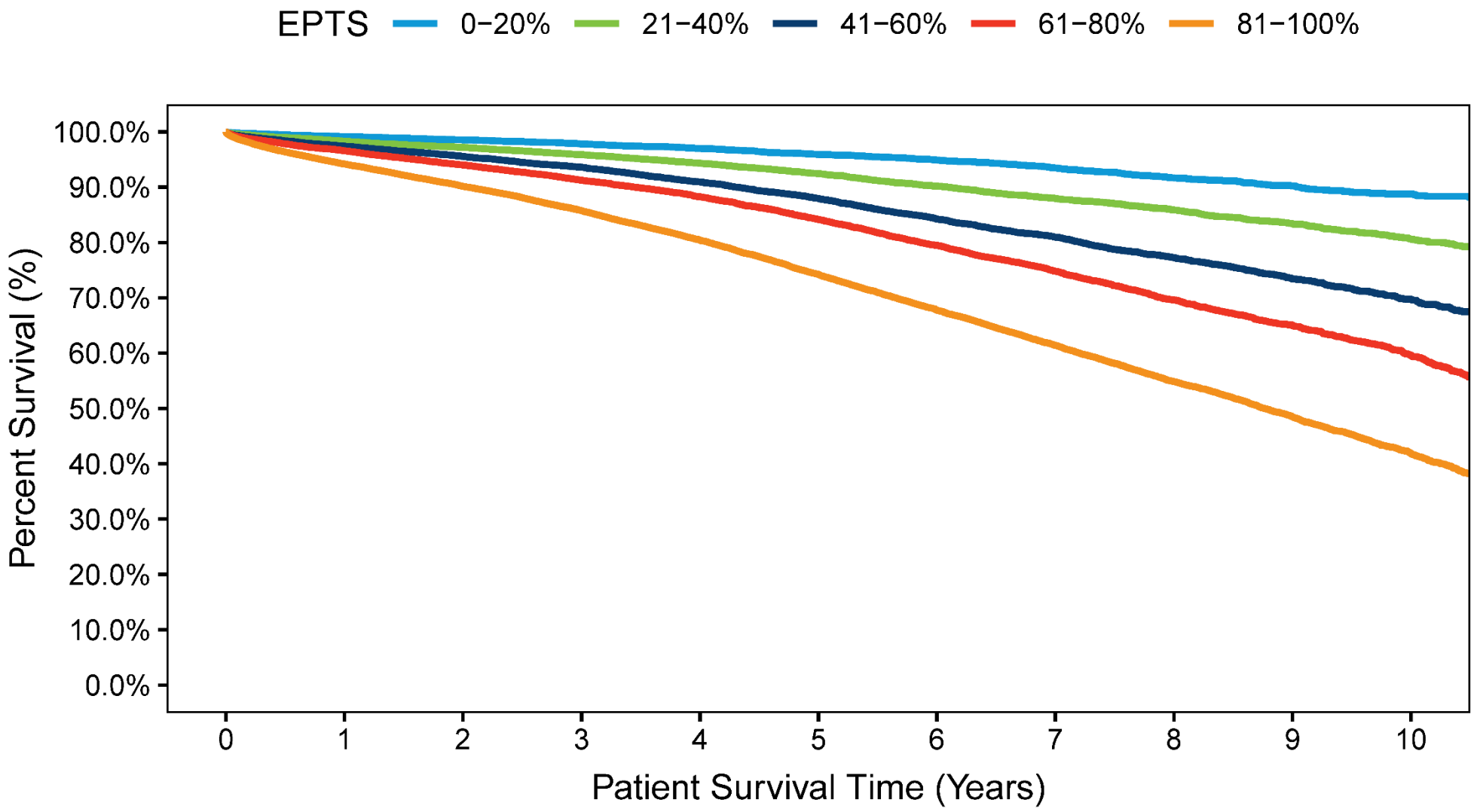
Per OPTN policy, the EPTS score is derived from the following formula:

$$
\begin{aligned}
\text{Raw EPTS} \; = \; & 0.047 * max(\text{Age} - 25, 0) - 0.015 * \text{Diabetes} * max(\text{Age} - 25, 0) \\
& + 0.398 * \text{Prior Solid Organ Transplant} - 0.237 * \text{Diabetes} * \text{Prior Organ Transplant} \\
& + 0.315 * log(\text{Years on Dialysis} + 1) - 0.099 * \text{Diabetes} * log(\text{Years on Dialysis} + 1) \\
& + 0.130 * (\text{Years on Dialysis} = 0) - 0.348 * \text{Diabetes} * (\text{Years on Dialysis} = 0) + 1.262 * \text{Diabetes}
\end{aligned}
$$

The factors included in the formula are the candidate's age in years, duration on dialysis in years, current diagnosis of diabetes, and whether the candidate has had a prior solid organ transplant.

The raw EPTS is converted to an EPTS score by using the EPTS mapping table, which is updated annually.

Figure 1. Kaplan−Meier Patient Survival Curves by EPTS Score for Deceased Donor, Adult, Kidney−Alone Transplants Performed During 2008−2018



Based on OPTN data as of April 17, 2020.

Calculating and Interpreting the Kidney Donor Risk Index (KDRI)

The KDPI is derived from the Kidney Donor Risk Index (KDRI)[1]. Consequently, to determine a donor's KDPI, the first step is to calculate the donor's KDRI.

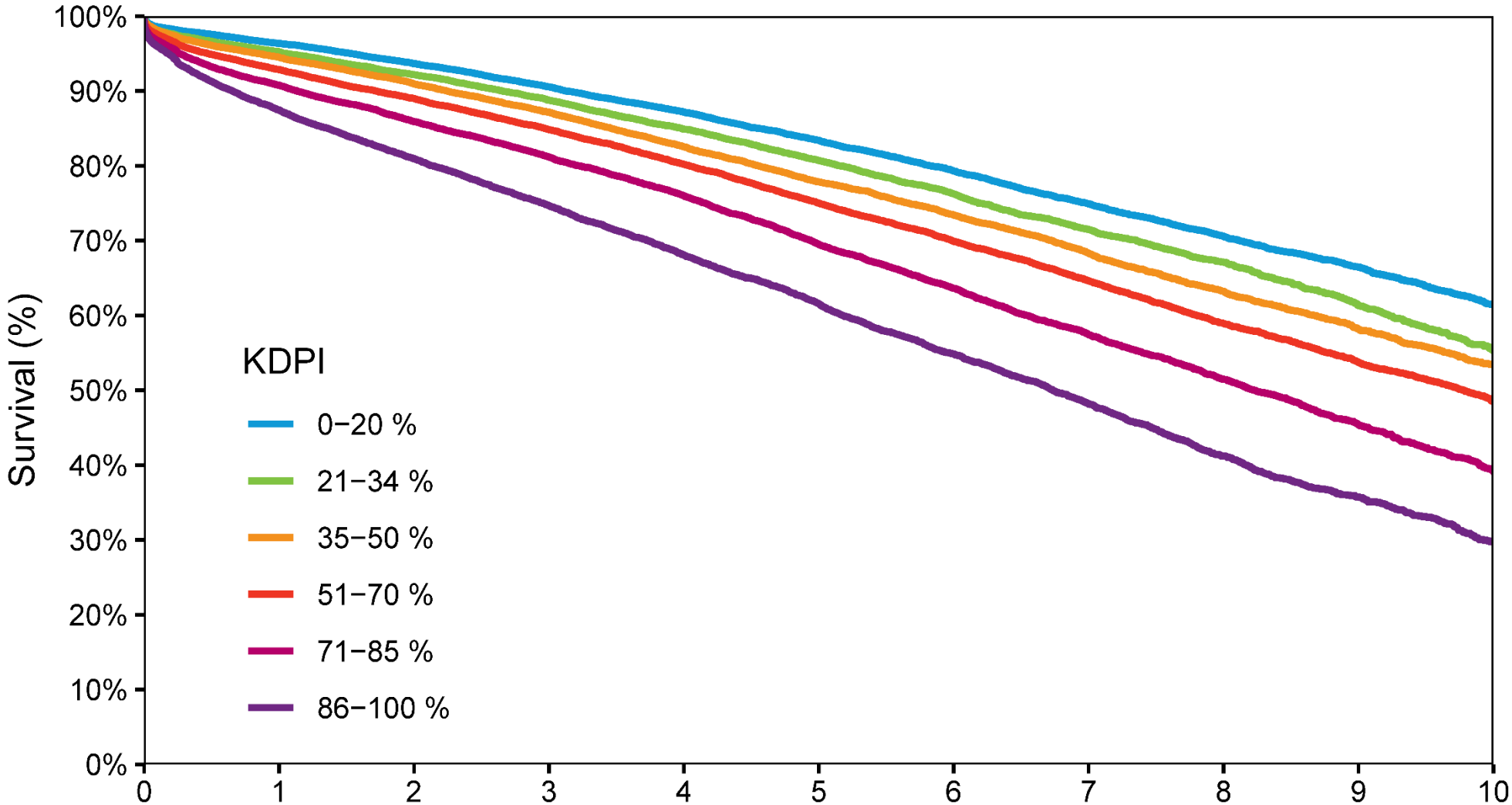
The KDRI displayed in DonorNet® and referenced in this document is the *scaled, donor-only* version of the KDRI. As explained in Rao, et al[1], several factors pertaining to the recipient and/or transplant procedure (cold ischemic time, degree of HLA mismatching, single vs. double vs. en-bloc kidneys) can also be used to calculate a "full" KDRI.

Since these factors are generally not known at the time offers are made or are candidate-specific, the donor-only KDRI was implemented.

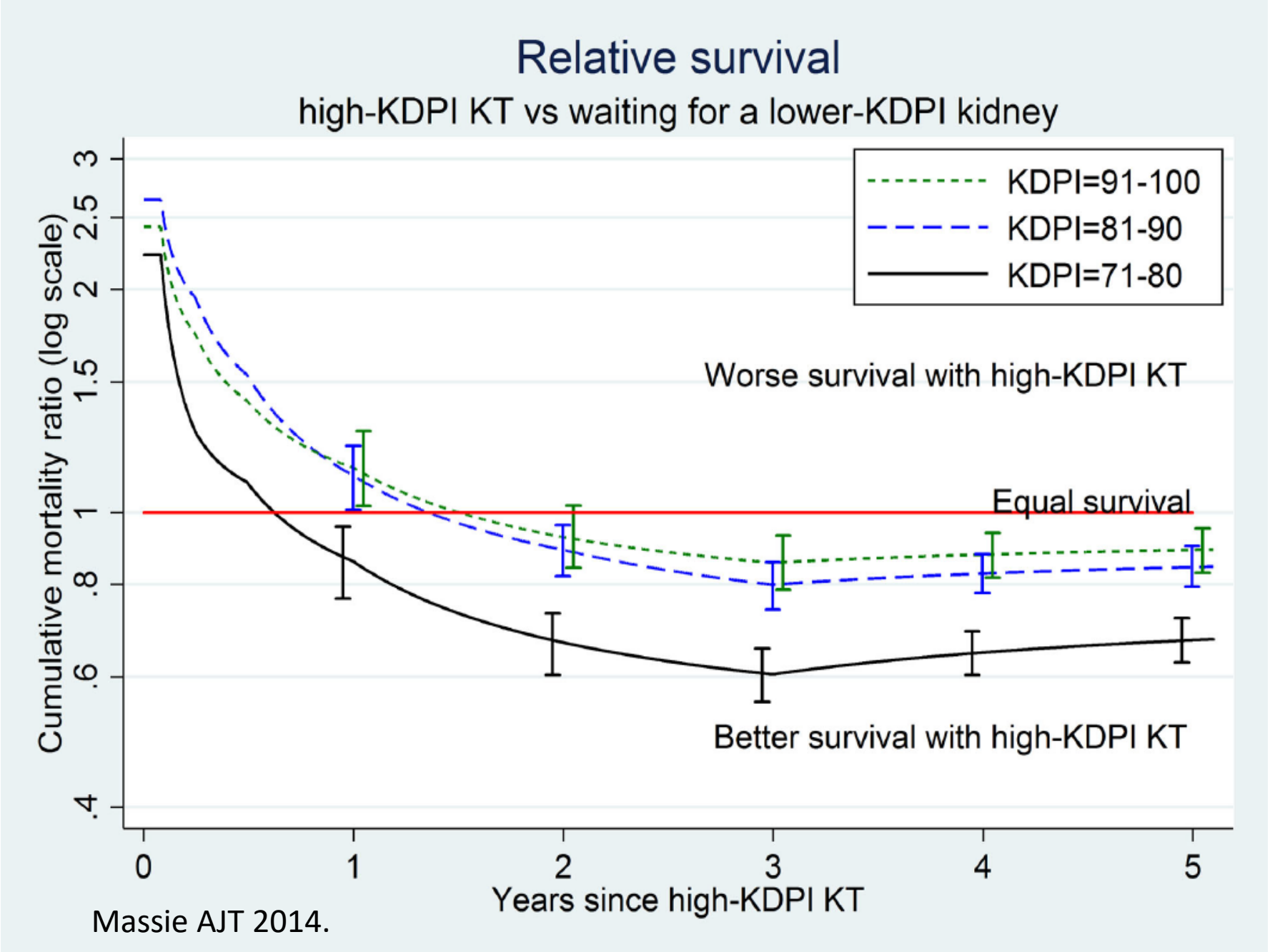
The following donor characteristics are used to calculate the KDRI:

- ✓ Age
- ✓ Height
- ✓ Weight
- ✓ Ethnicity
- ✓ History of Hypertension
- ✓ History of Diabetes
- ✓ Cause of Death
- ✓ Serum Creatinine
- ✓ Hepatitis C Virus (HCV) Status, from serological or NAT testing
- ✓ Donation after Circulatory Death (DCD) Status

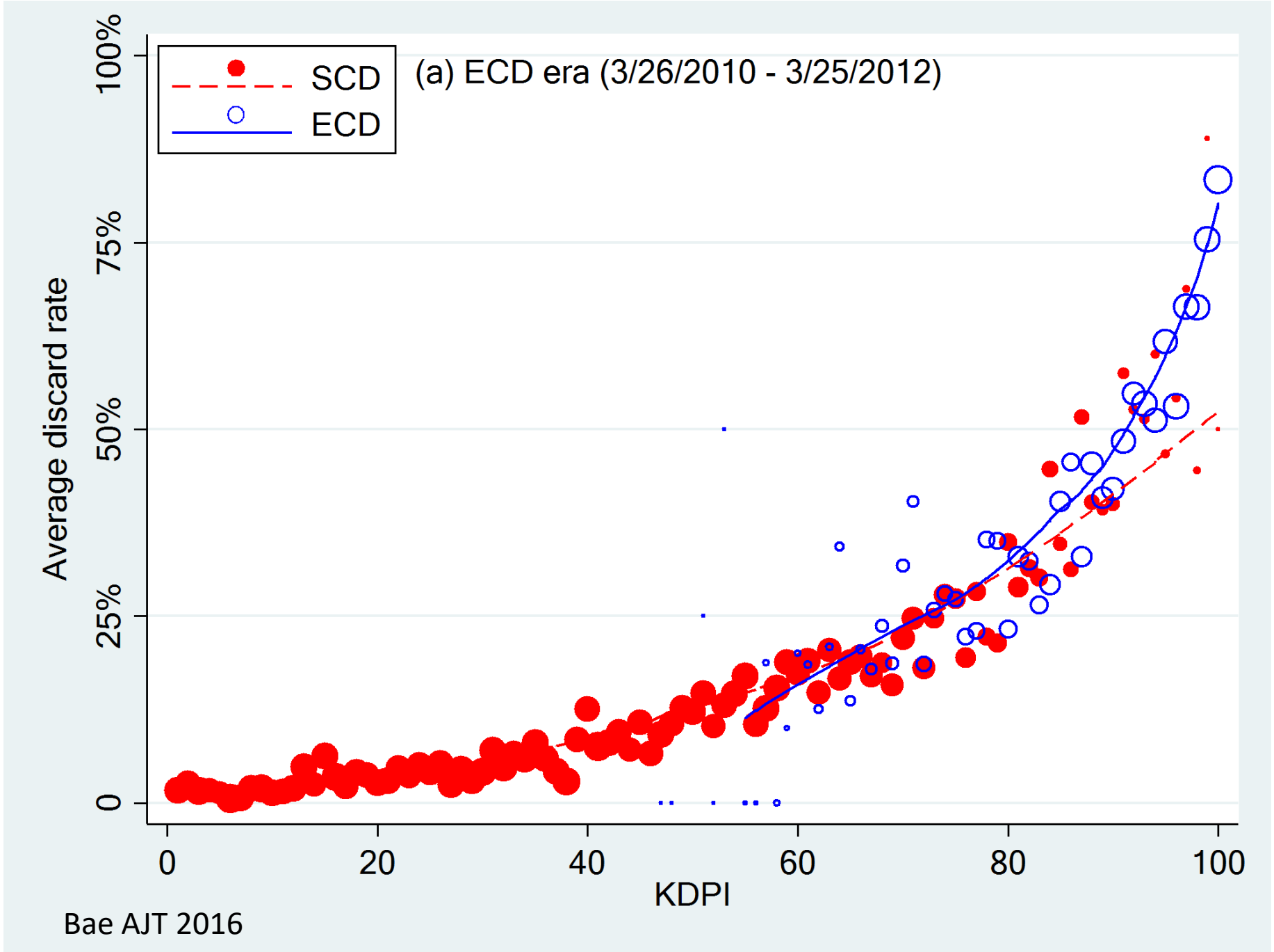
Figure 1. Kaplan−Meier Graft Survival Estimates for Adult, Deceased Donor, Kidney−Alone Transplants During 2008−2018 by KDPI



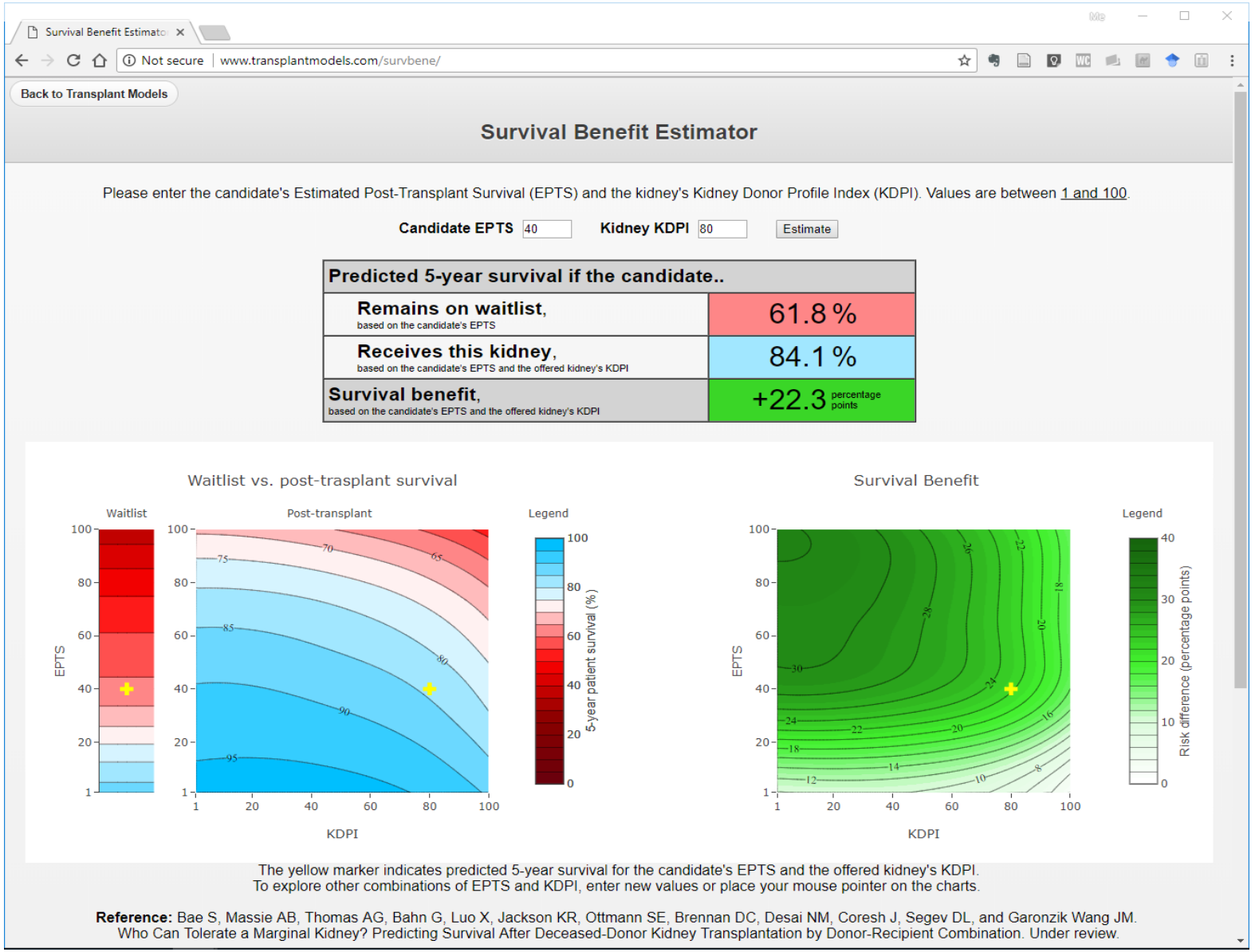
Based on OPTN data as of March 20, 2020.



Massie AJT 2014.


SCD
ECD
(a) ECD era (3/26/2010 - 3/25/2012)
Average discard rate
0
25%
50%
75%
100%
0
20
40
60
80
100
KDPI
Bae AJT 2016

www.transplantmodels.com/KDPI-EPTS



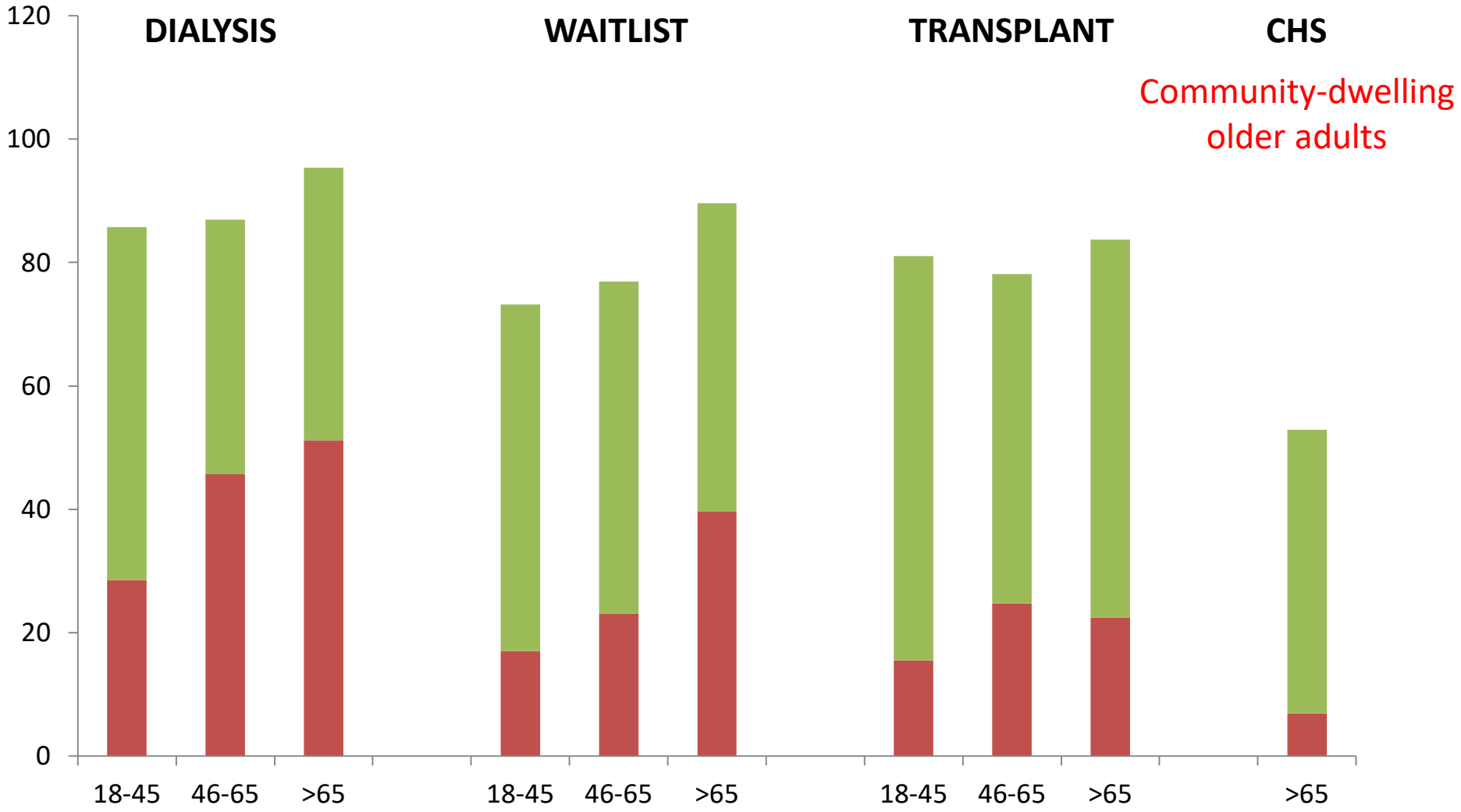
"There should be no absolute upper age limit for excluding patients whose overall health and life situation suggest that transplantation will be beneficial"

—the American Society of Transplantation

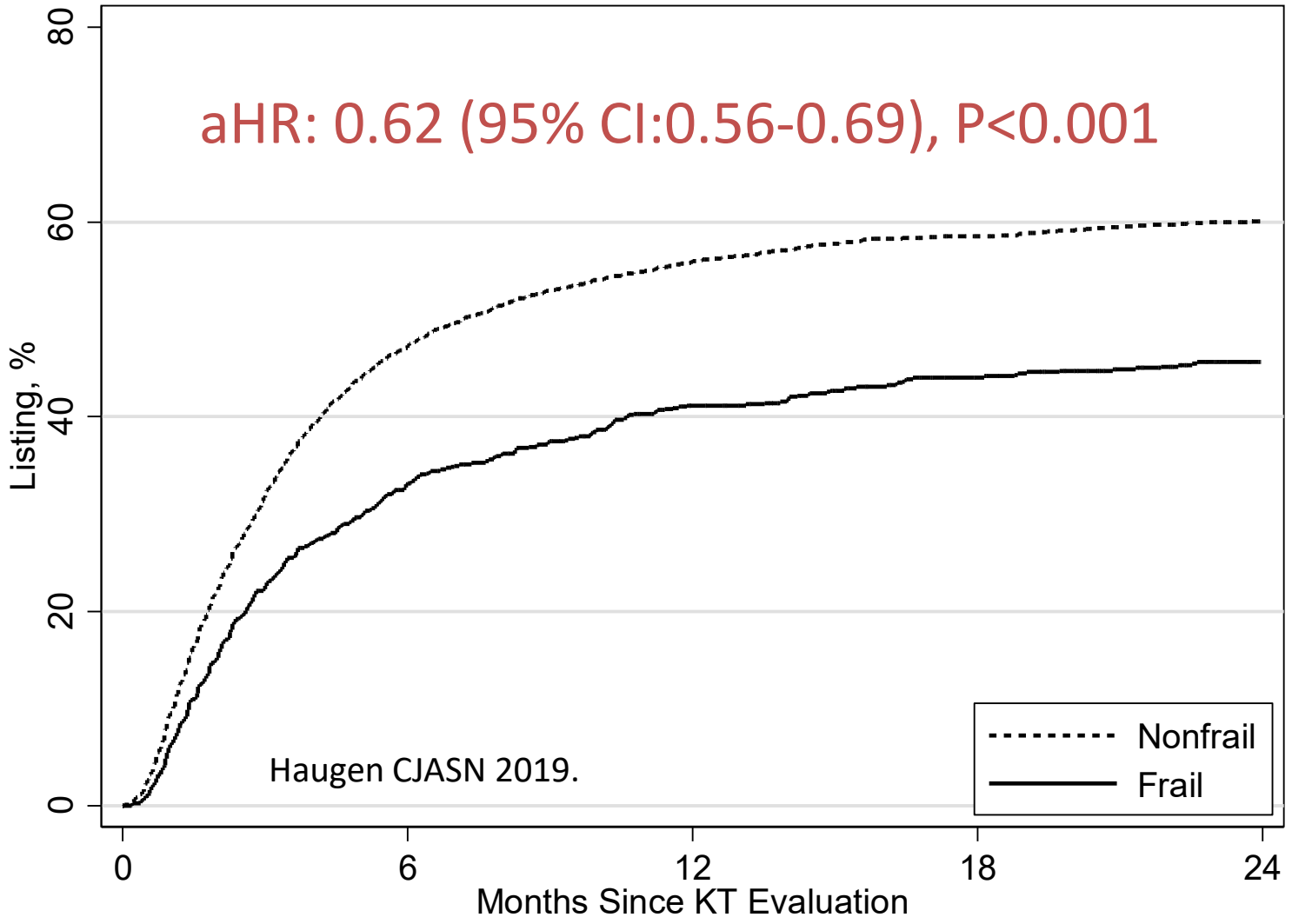
- Among KT candidates and recipients: frailty, disabilities, and dependence are highly prevalent and associated with poor outcomes, but are not routinely measured.

McAdams-DeMarco 2012. McAdams-DeMarco 2013.
Haugen 2019. Chu 2019.

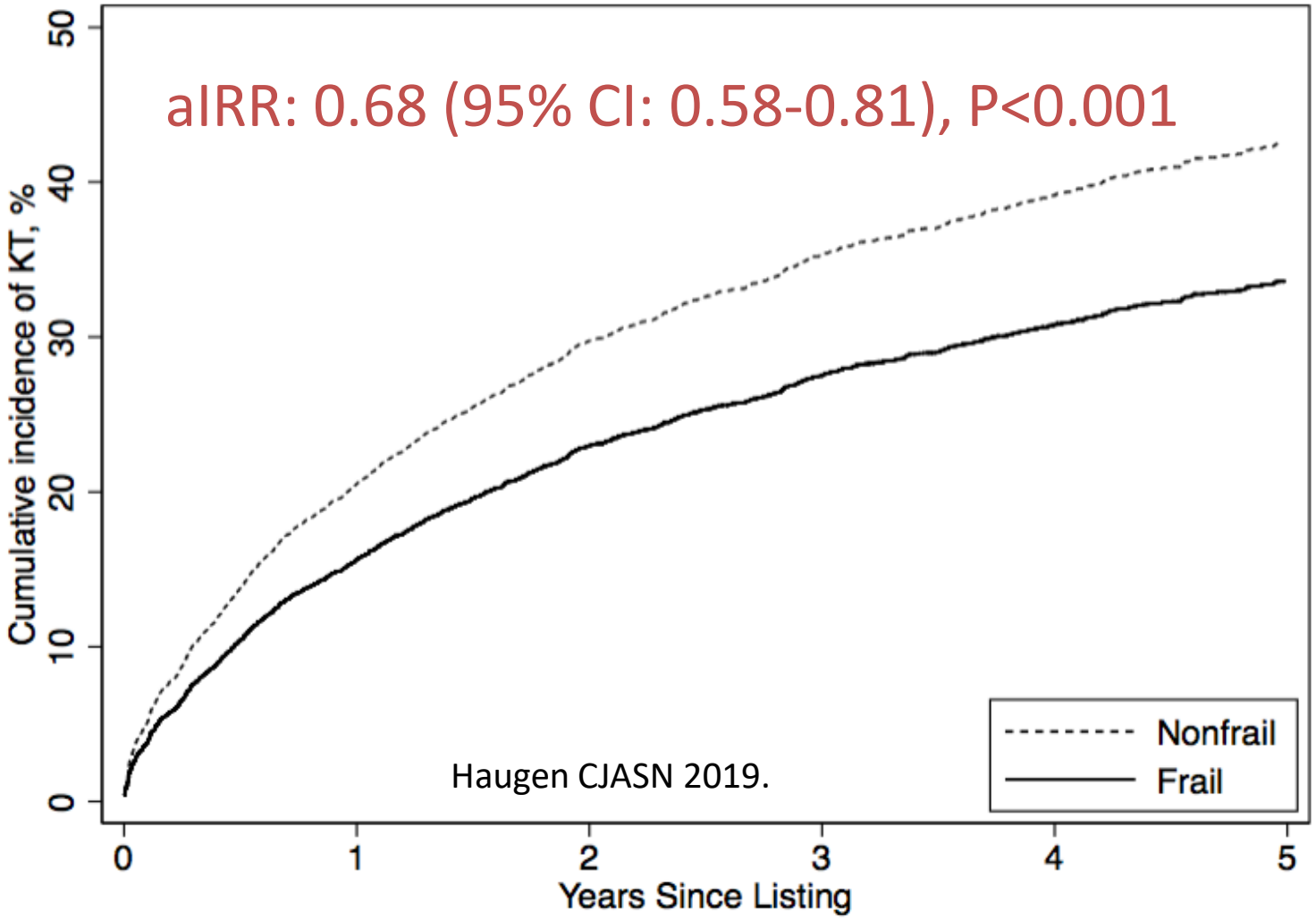
Frailty Prevalence: By Cohort, By Age



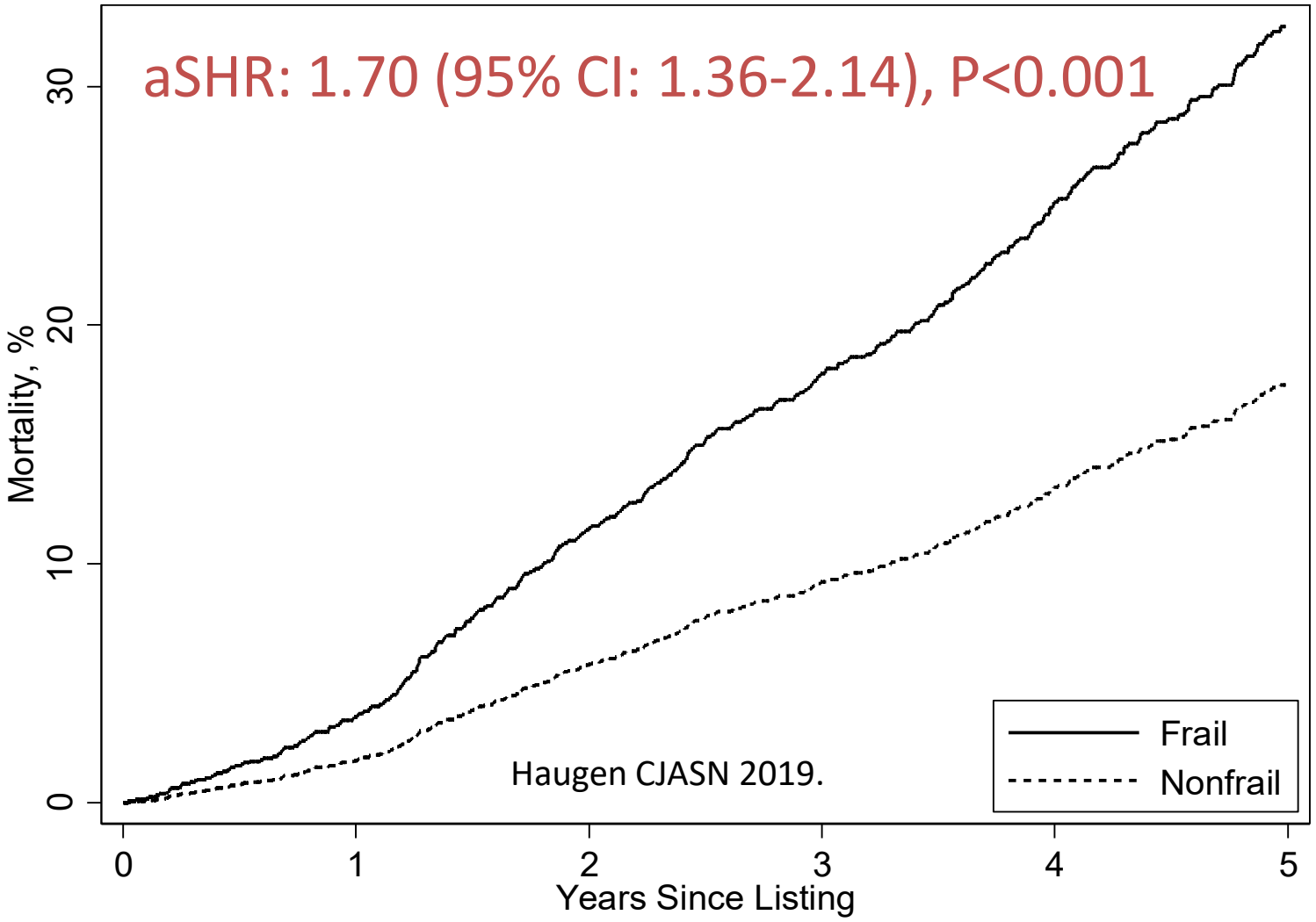
Frailty: decreased listing for transplantation



Frailty: decreased transplantation



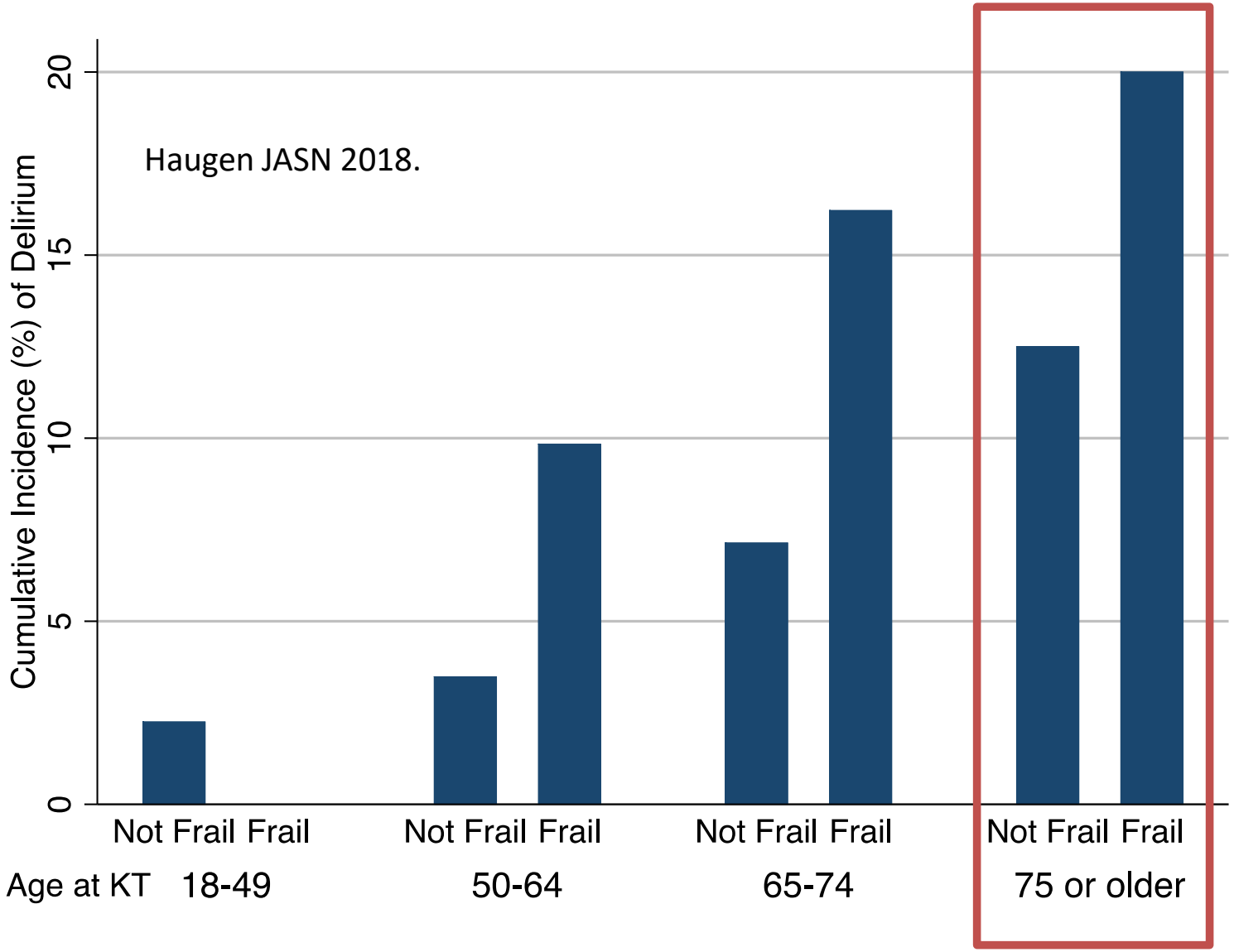
Frailty: increased waitlist mortality



Frailty: worse post-transplant outcomes

- 1.57-times the odds of 2-week or longer **KT length of stay**
  - McAdams-DeMarco/Segev, Ann Surgery 2016
- 1.61-fold increased risk of **early hospital readmission**
  - McAdams-DeMarco/Segev, AJT 2013
- 1.94-fold increased risk of **delayed graft function**
  - Garonzik-Wang/Segev, JAMA Surgery 2012
- 2.19-fold increased risk of **mortality**
  - McAdams-DeMarco/Segev, AJT 2013

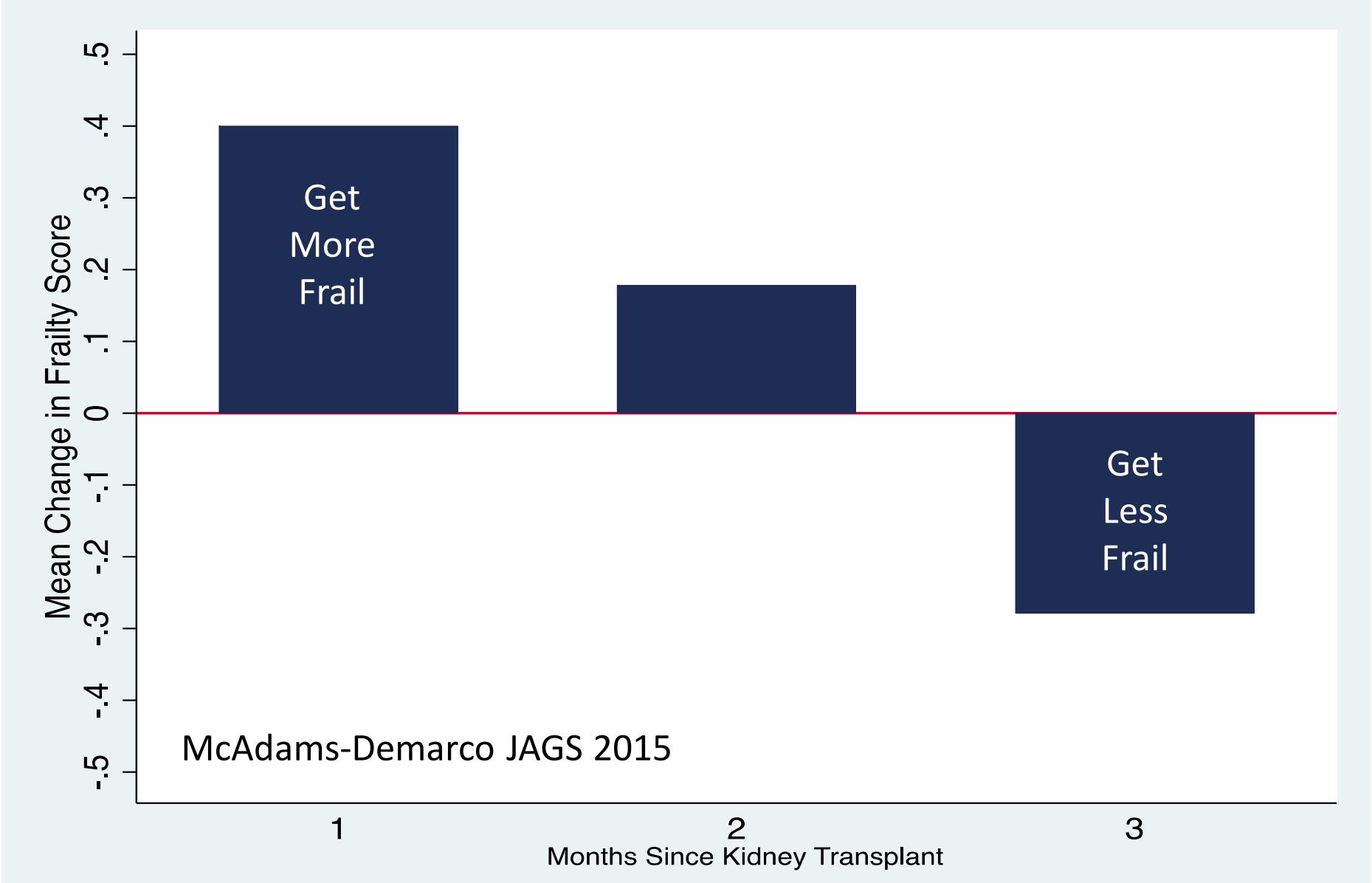
Frailty: higher post-KT delirium



Post-KT delirium: adverse outcomes

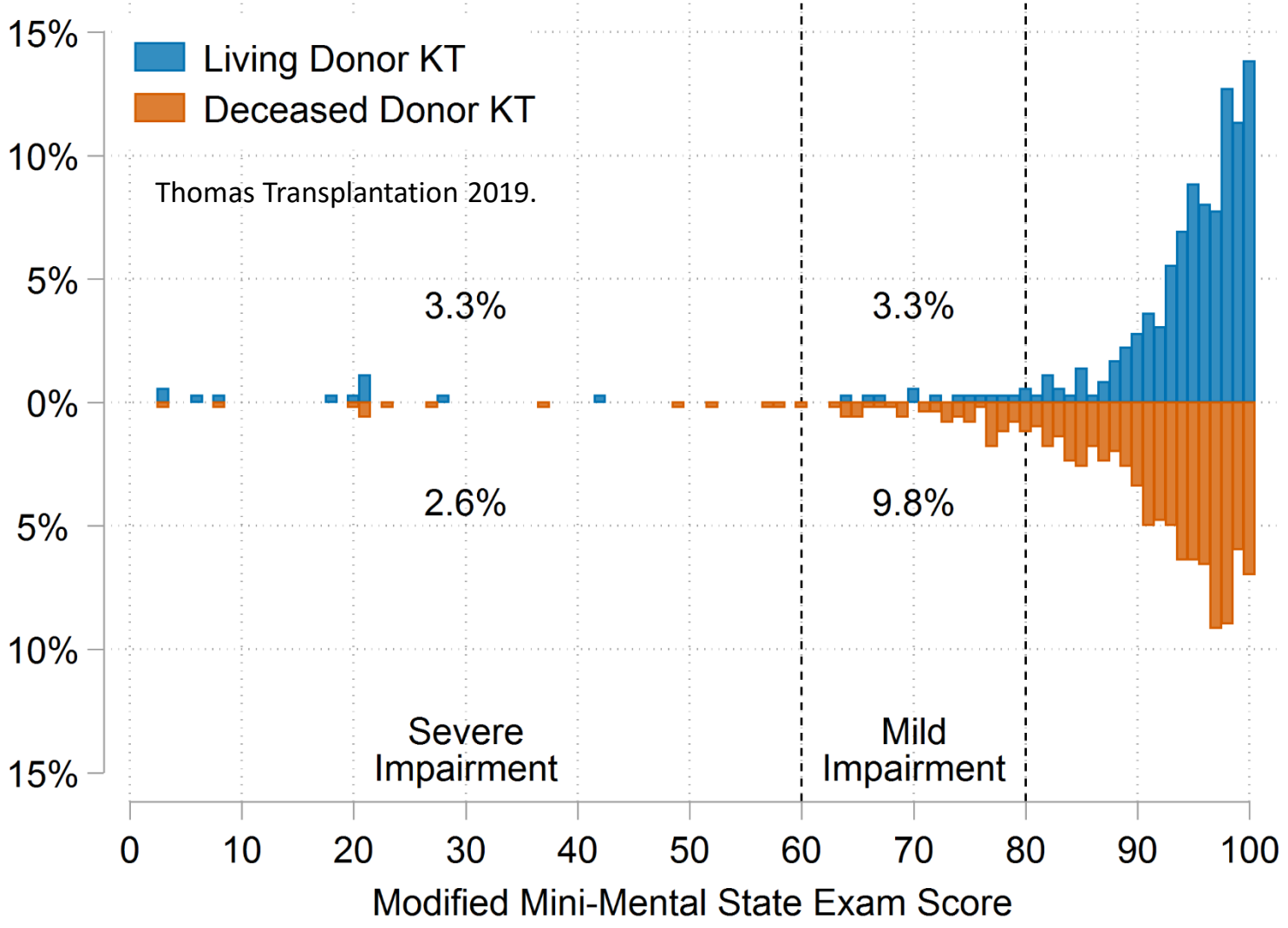
	Adjusted
Length of Stay	
Days (RR, 95% CI)	2.49 (2.13-2.91)
2-week or longer length of stay (OR, 95% CI)	5.42 (2.76-10.66)
Institutional Discharge (OR, 95% CI)	22.41 (7.85-63.98)
Death-Censored Graft Loss (HR, 95% CI)	2.73 (1.14-6.53)
Mortality (HR, 95% CI)	3.12 (1.76-5.54)

Change in Frailty after KT

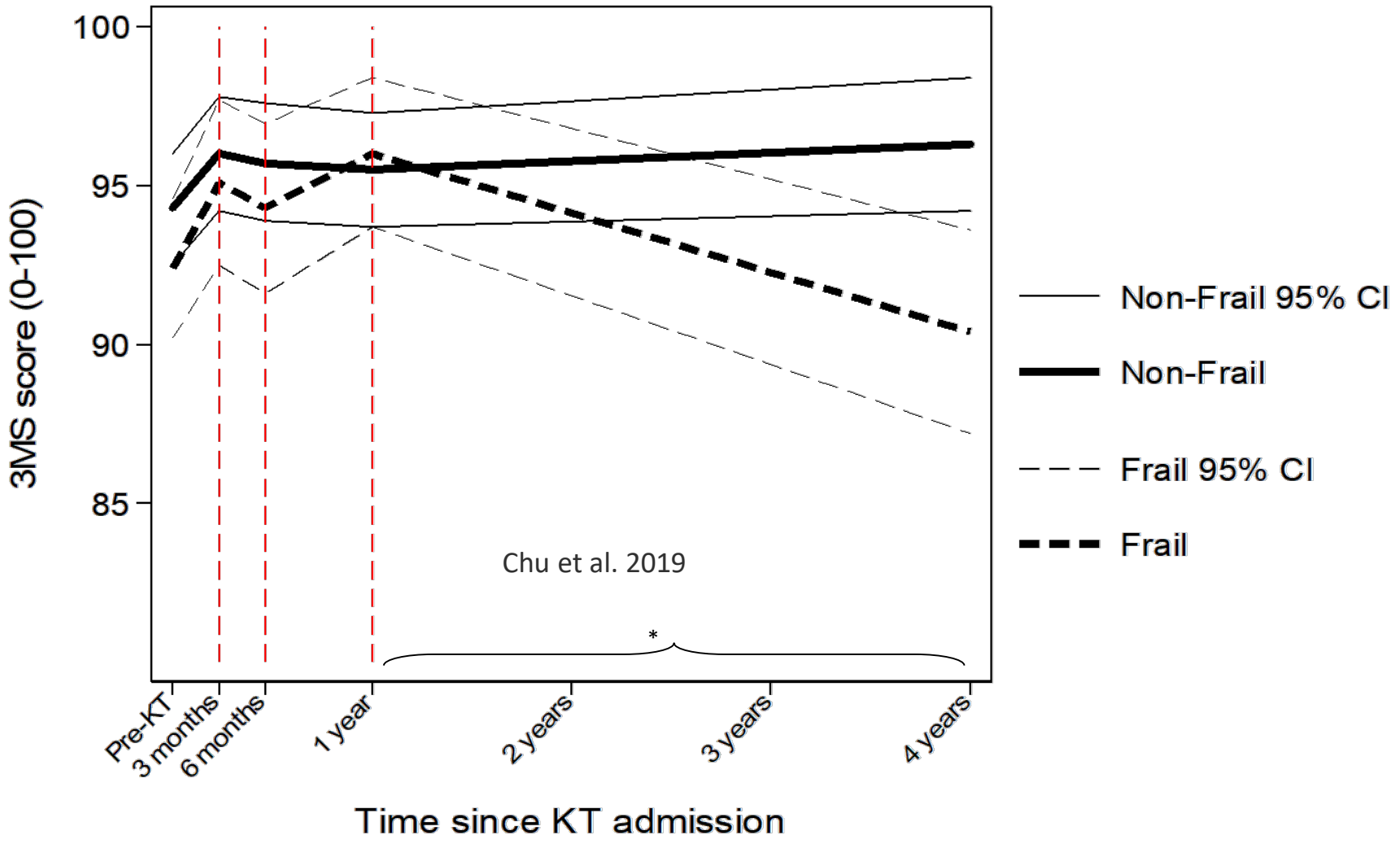


Cognitive Impairment at Admission for KT

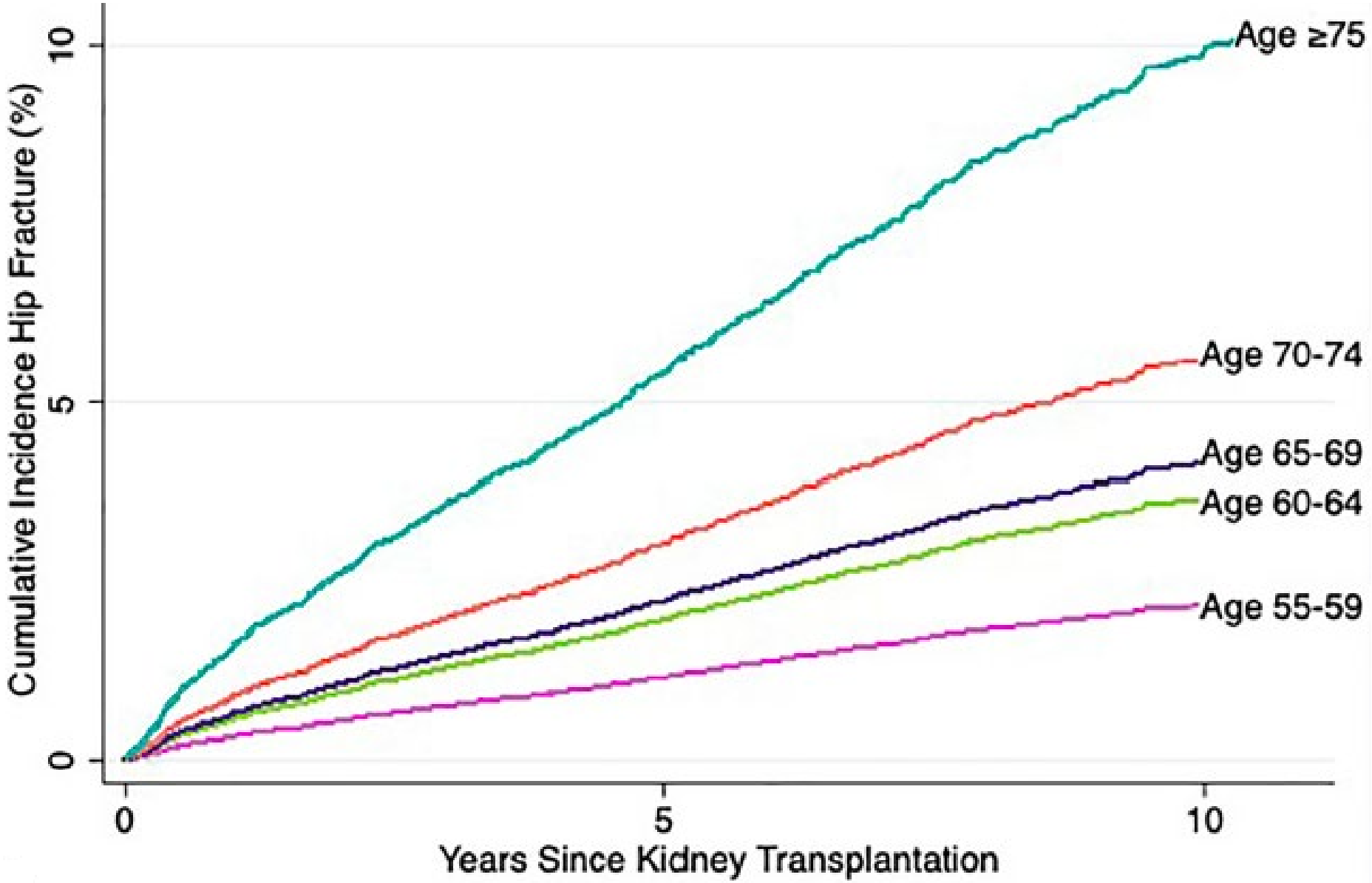
→ Higher graft loss, mortality



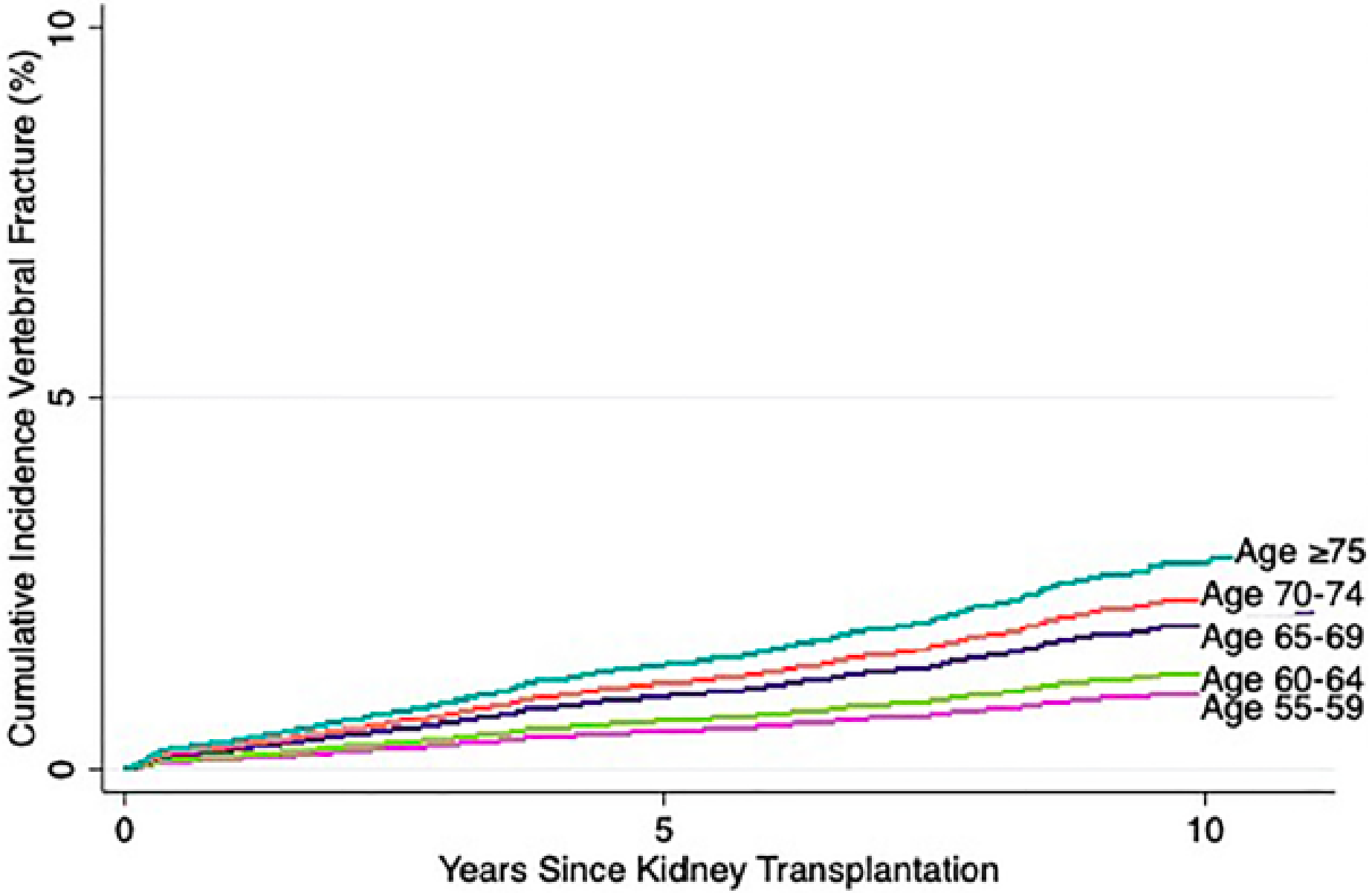
Cognitive function improves for all patients post-KT, but frailty is associated with greater cognitive decline in the long-term.



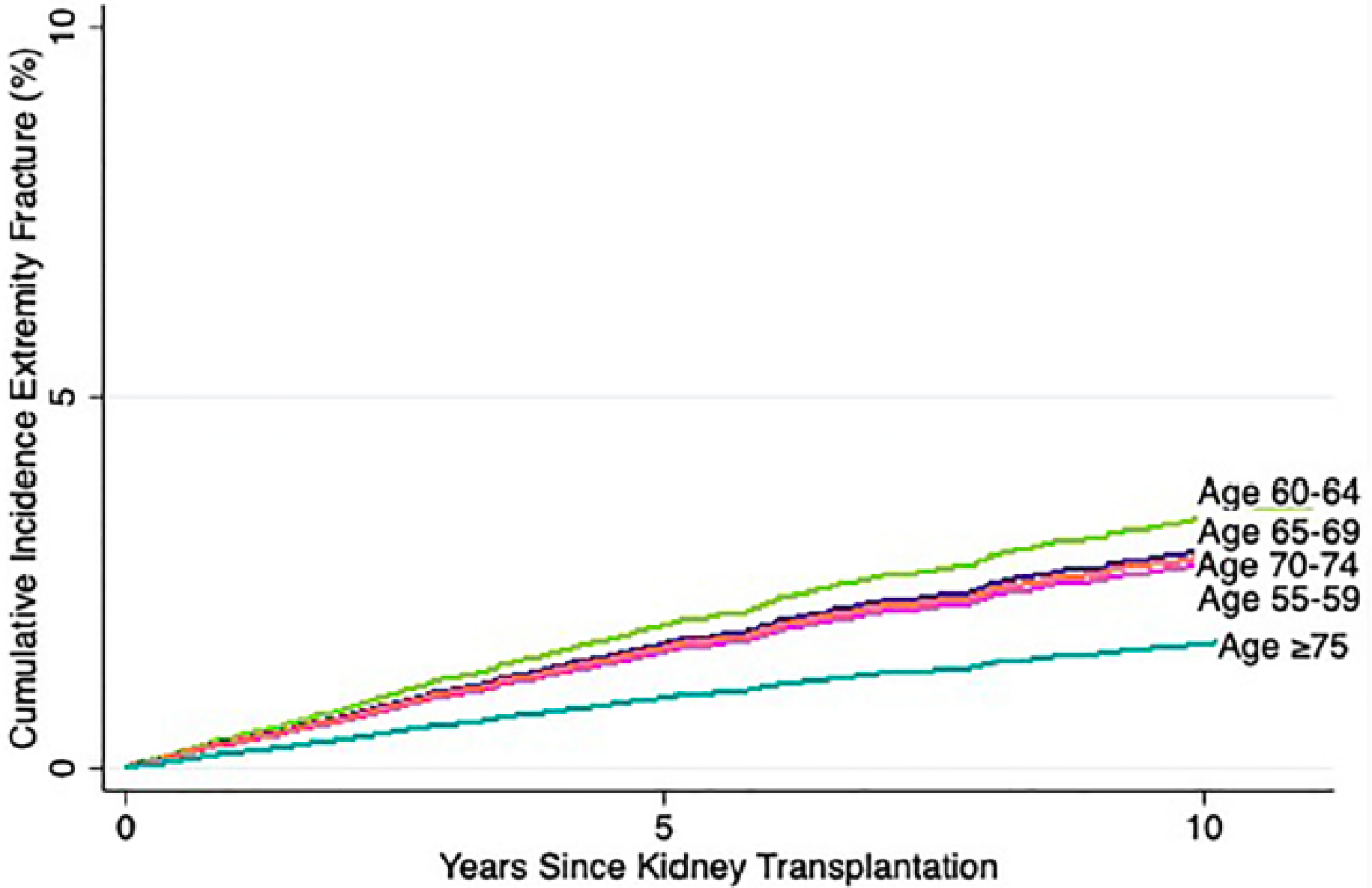
Hip Fracture



Vertebral Fracture



Extremity Fracture



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