UNC KIDNEY CENTER

The Kidney Allocation System Changed in a Substantive Way on December 5, 2014

Your Patients Have Been, and Will Be, Affected by These Changes

The New Kidney Allocation System
Terms of Importance

- Pediatric
- Zero HLA Mismatch = 0 ABDR MM
- CPRA = Calculated Panel Reactive Antibody
  - 100 %
  - 99 %
  - 98%
- EPTS Score = Estimated Post Transplant Survival
  - Top 20
  - Bottom 80
- KDPI = Kidney Donor Profile Index
- KDRI = Kidney Donor Risk Index

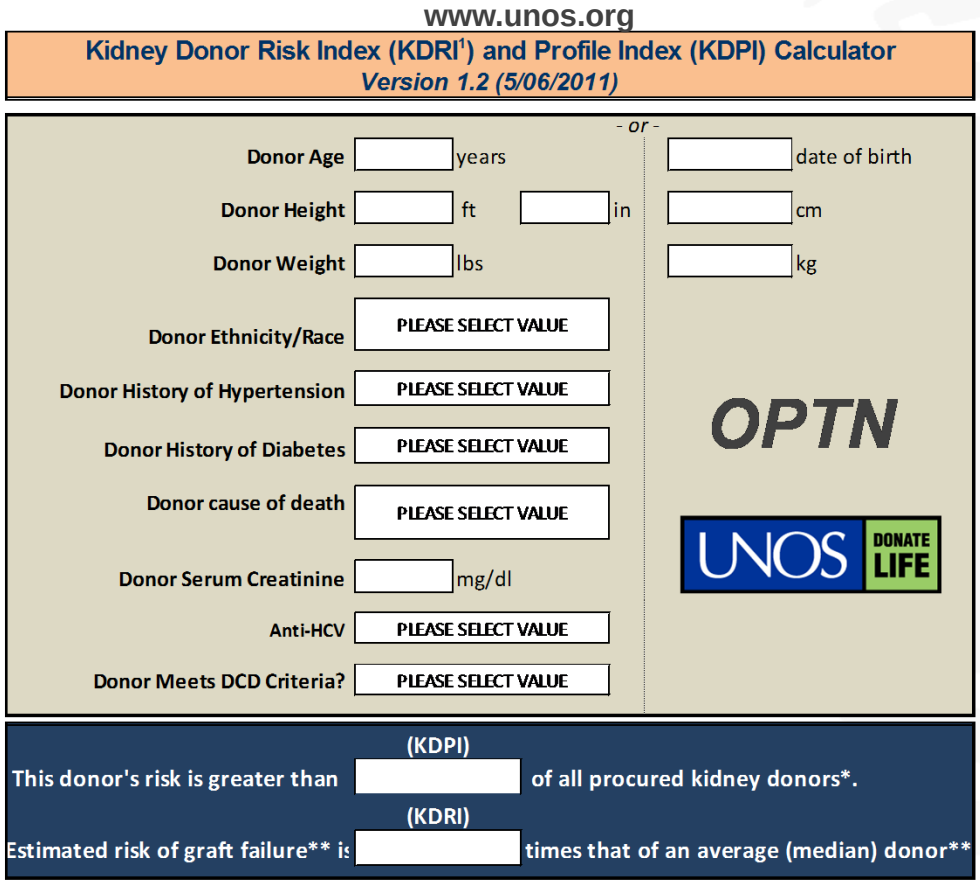
NOT in the Current System:
Expanded Criteria Donor (ECD)
Standard Criteria Donor (SCD)

Overview of the New Kidney Allocation Policy

Wait-Listed Candidates			
KDPI≤0.20	**KDPI 0.21–0.34**	**KDPI 0.35–0.85**	**KDPI>0.85**
Local CPRA 100%	Local CPRA 100%	Local CPRA 100%	Local CPRA 100%
Regional CPRA 100%	Regional CPRA 100%	Regional CPRA 100%	Regional CPRA 100%
National CPRA 100%	National CPRA 100%	National CPRA 100%	National CPRA 100%
Local CPRA 99%	Local CPRA 99%	Local CPRA 99%	Local CPRA 99%
Regional CPRA 99%	Regional CPRA 99%	Regional CPRA 99%	Regional CPRA 99%
Local CPRA 98%	Local CPRA 98%	Local CPRA 98%	Local CPRA 98%
0 HLA mm top 20	0 HLA mm	0 HLA mm	0 HLA mm
Prior living donors	Prior living donors	Prior living donors	Local, regional adult
Local pediatric	Local pediatric	Local	National adult
Local top 20	Local adult	Regional	
0 HLA mm bottom 80	Regional pediatric	National	
Local bottom 80	Regional adult		
Regional pediatric	National pediatric		
Regional top 20	National adult		
Regional bottom 80			
National pediatric			
National top 20			
National bottom 80			

Israni, et al. JASN 2014. 25:1842-1848

The KDPI and KDRI
A Measure of Donor Quality Based on 10 Donor Characteristics



www.unos.org

Kidney Donor Risk Index (KDRI[1]) and Profile Index (KDPI) Calculator
Version 1.2 (5/06/2011)

- or -

Donor Age	years		date of birth
Donor Height	ft	in	cm
Donor Weight	lbs		kg
Donor Ethnicity/Race	PLEASE SELECT VALUE		
Donor History of Hypertension	PLEASE SELECT VALUE		
Donor History of Diabetes	PLEASE SELECT VALUE		
Donor cause of death	PLEASE SELECT VALUE		
Donor Serum Creatinine	mg/dl		
Anti-HCV	PLEASE SELECT VALUE		
Donor Meets DCD Criteria?	PLEASE SELECT VALUE		

OPTN

UNOS DONATE LIFE

(KDPI)
This donor's risk is greater than _____ of all procured kidney donors*.

(KDRI)
Estimated risk of graft failure** is _____ times that of an average (median) donor**

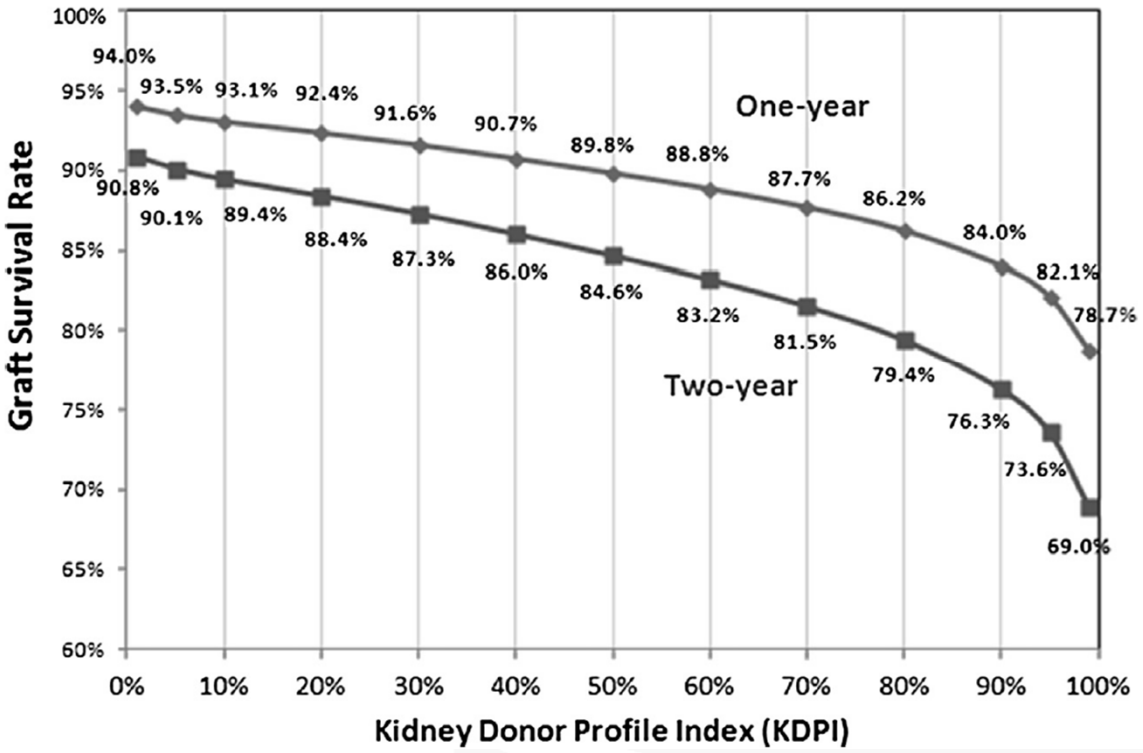
The KDPI

- Continuous variable 0-100 %
- Lower number is better score, longer projected survival
- Factors not included
  - Biopsy results
  - High risk behavior, substance abuse
  - Cold ischemia time
  - Donor management issues

The KDRI

- Relative risk of graft failure (Hazard Ratio)
- Values above 1 higher risk vs. Defined Median Donor

Projected Kidney Allograft Survival vs. KDPI



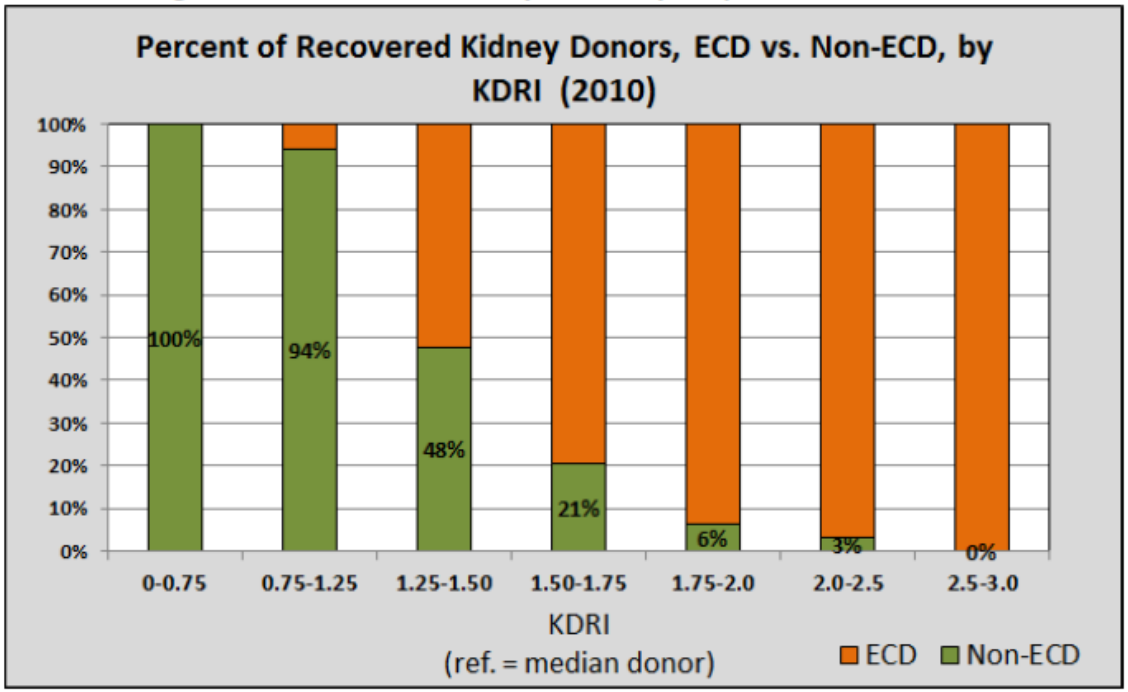
Friedewald et al. Surg Clin N Am 2013. 93:1395-1406

Acceptable KDPI Range is Defined for Each Recipient Candidate by the Transplant Center

Acceptance of KDPI >85% Kidneys Requires Patient Informed Consent (Prior ECD Consents Accepted)

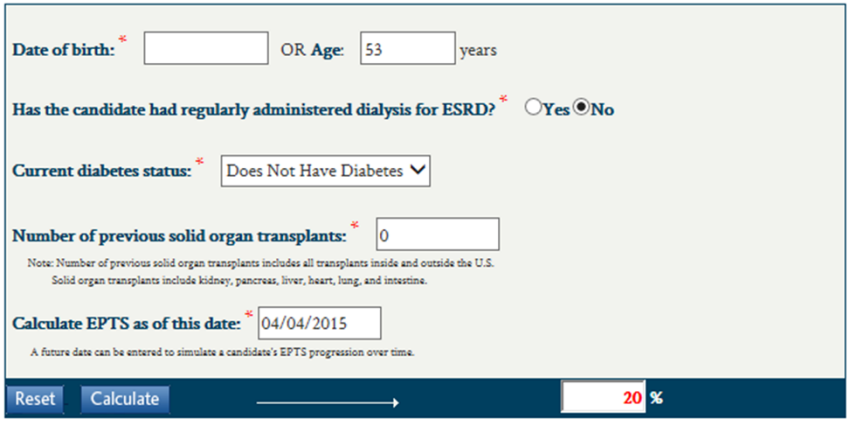
KDRI vs. ECD Designation

Figure 1: Distribution of Kidney Donors by ECD/non-ECD and KDRI



Estimated Post-Transplant Survival (EPTS)
A Relative Measure of Expected Recipient Life Span

Attention: The EPTS % may change on a daily basis due to age and time on dialysis.

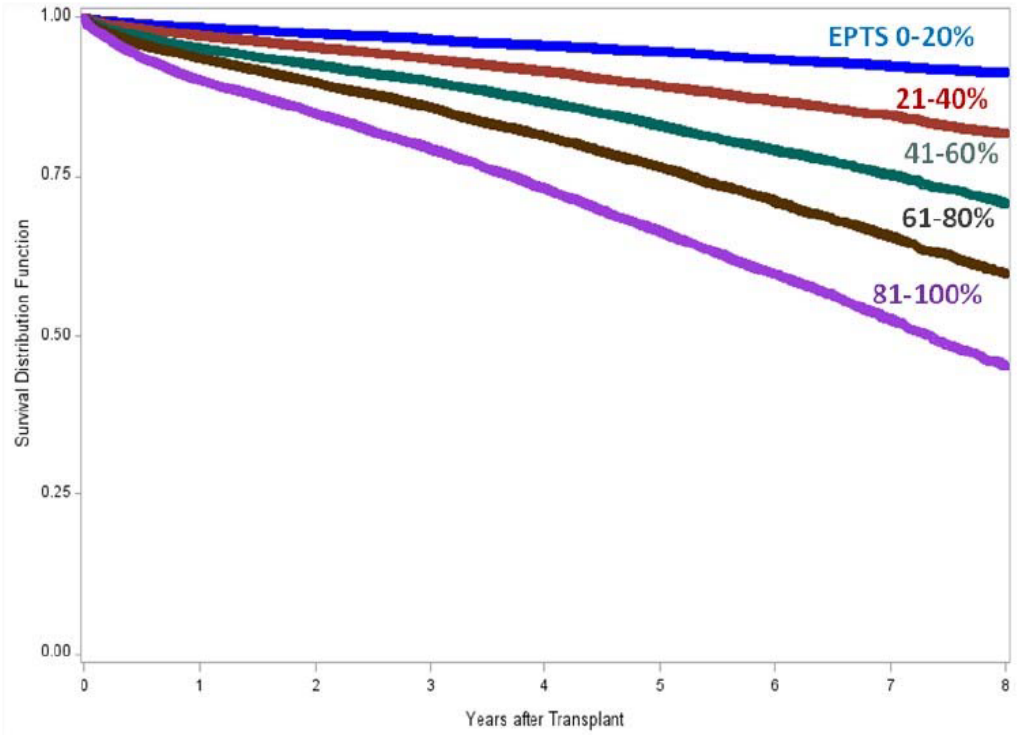


Based on a reference population as of 09/30/2013, this candidate's EPTS of 20% is in the national Top 20%, making them eligible for increased priority for kidneys from donors with KDPI in the Top 20%.

The EPTS Score

- Continuous Variable (0-100%)
- 1% score = anticipated life span longer than 99% of recipient candidates
- Pediatric patients (<18 yo) excluded from calculation
- Factors not included innumerable
- **Top 20 vs. Bottom 80 crucially important to patients**
  - Still binary with regard to allocation
  - e.g. 21% vs. 91% not important in allocation algorithm

Figure 1: Kaplan-Meier Patient Survival Curves by EPTS Score
Deceased Donor, Adult, Solitary Kidney Transplants from 2003-2010
Based on OPTN data as of Feb 7, 2014

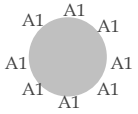


Bead Technology Has Improved Sensitivity and Specificity of HLA Antigen Testing

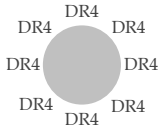
Class I Flow Bead

Class II Flow Bead

Class I Single Antigen Flow Bead



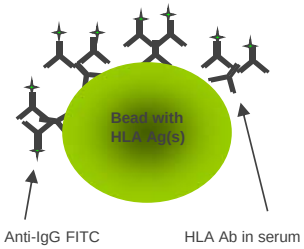
Class II Single Antigen Flow Bead

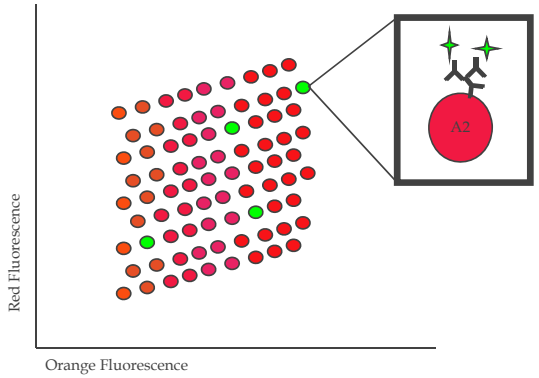


- Highly sensitive
- Limited false reactions due to non-HLA Ab
- Available as a qualitative screen or panel
- to determine PRA and specificity
- Can have interference from high dose IVIg

Courtesy of John Schmitz,PhD

Pre-Transplant Antibody Testing





Screen/ID

- Detect sensitization
- Identify target antigens
- cPRA – points (Unacceptable Ag)

Final Crossmatch

Assess risk

Transplant ?

Courtesy of John Schmitz, PhD

Unacceptable Antigen Designation and Impact on CPRA

CPRA CALCULATOR

UNACCEPTABLE ANTIGENS

Check the antigens that are unacceptable.

Check all A unacceptable antigens:

☐1 ☐2 ☐3 ☐9 ☐10 ☐11 ☐19 ☐23 ☐24 ☐25
☐26 ☐28 ☐29 ☐30 ☐31 ☐32 ☐33 ☐34 ☐36 ☐43
☐66 ☐68 ☐69 ☐74 ☐80 ☐203 ☐210 ☐2403 ☐6601 ☐6602

Check all B unacceptable antigens:

☐5 ☐7 ☐8 ☐12 ☐13 ☐14 ☐15 ☐16 ☐17 ☐18
☐21 ☐22 ☐27 ☐35 ☐37 ☐38 ☐39 ☐40 ☐41 ☐42
☐44 ☐45 ☐46 ☐47 ☐48 ☐49 ☐50 ☐51 ☐52 ☐53
☐54 ☐55 ☐56 ☐57 ☐58 ☐59 ☐60 ☐61 ☐62 ☐63
☐64 ☐65 ☐67 ☐70 ☐71 ☐72 ☐73 ☐75 ☐76 ☐77
☐78 ☐81 ☐82 ☐703 ☐804 ☐1304 ☐2708 ☐3901 ☐3902 ☐3905
☐4005 ☐5102 ☐5103 ☐7801 ☐8201

Check BW unacceptable antigen:

○4 ○6 ○N/A

Check all C unacceptable antigens:

☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10
☐12 ☐13 ☐14 ☐15 ☐16 ☐17 ☐18

Check all DR unacceptable antigens:

☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10
☐11 ☐12 ☐13 ☐14 ☐15 ☐16 ☐17 ☐18 ☐103 ☐1403
☐1404

Check DR51/52/53 unacceptable antigens:

☐51 ☐52 ☐53

Check all DQ unacceptable antigens:

☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9

Reset Calculate

CPRA CALCULATOR

UNACCEPTABLE ANTIGENS

A: 2

B:

BW:

C:

DR:

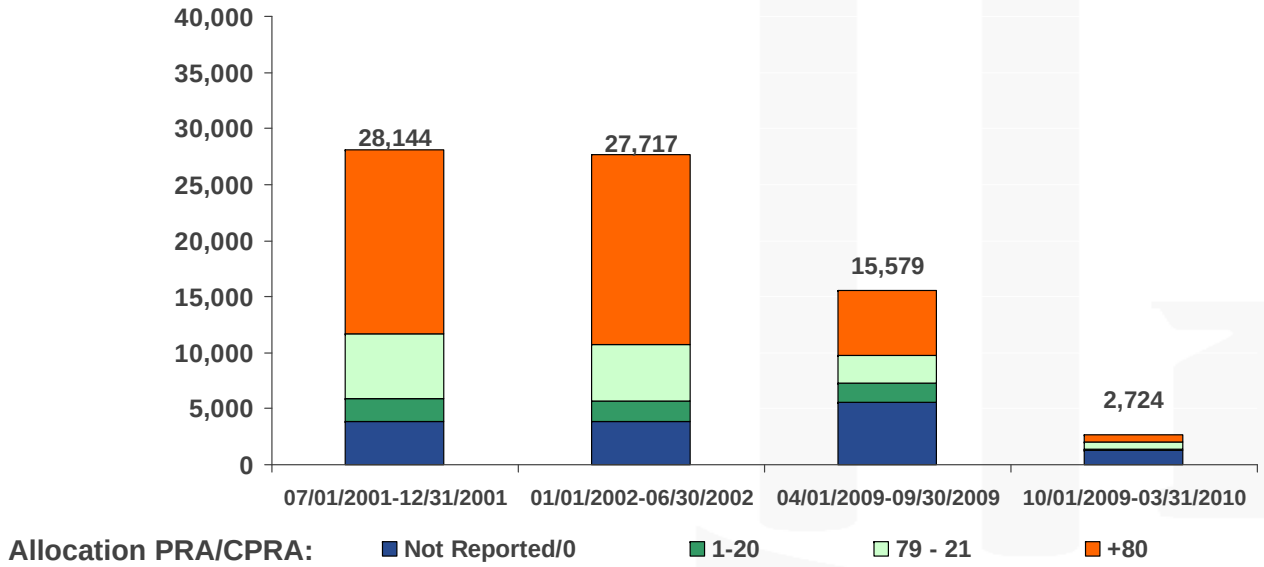
DRW:

DQ:

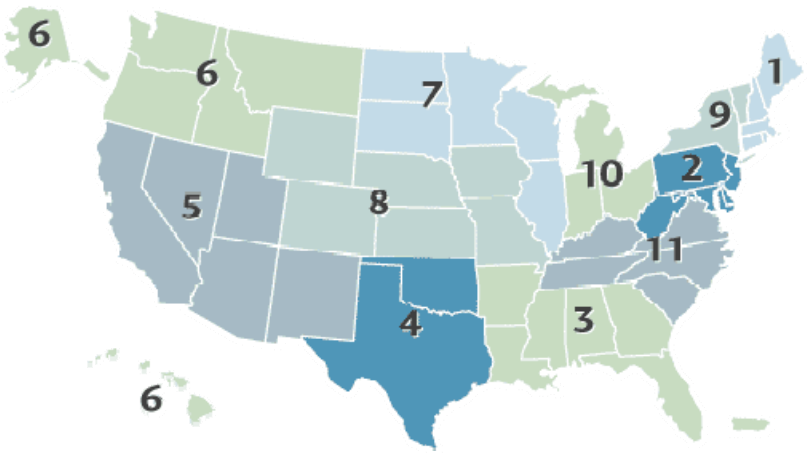
BACK → **CPRA VALUE** 48

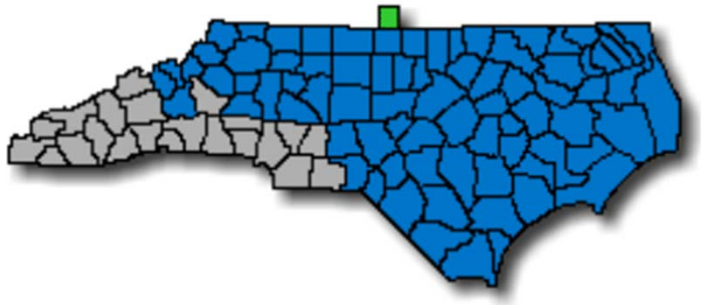
Number of Positive Crossmatches Reported as a Reason for Organ Refusal

Deceased Donor Kidney Match Runs Only



OPO and Regional Sharing





Overview of the New Kidney Allocation Policy

Wait-Listed Candidates			
KDPI≤0.20	**KDPI 0.21–0.34**	**KDPI 0.35–0.85**	**KDPI>0.85**
Local CPRA 100%	Local CPRA 100%	Local CPRA 100%	Local CPRA 100%
Regional CPRA 100%	Regional CPRA 100%	Regional CPRA 100%	Regional CPRA 100%
National CPRA 100%	National CPRA 100%	National CPRA 100%	National CPRA 100%
Local CPRA 99%	Local CPRA 99%	Local CPRA 99%	Local CPRA 99%
Regional CPRA 99%	Regional CPRA 99%	Regional CPRA 99%	Regional CPRA 99%
Local CPRA 98%	Local CPRA 98%	Local CPRA 98%	Local CPRA 98%
0 HLA mm top 20	0 HLA mm	0 HLA mm	0 HLA mm
Prior living donors	Prior living donors	Prior living donors	Local, regional adult
Local pediatric	Local pediatric	Local	National adult
Local top 20	Local adult	Regional	
0 HLA mm bottom 80	Regional pediatric	National	
Local bottom 80	Regional adult		
Regional pediatric	National pediatric		
Regional top 20	National adult		
Regional bottom 80			
National pediatric			
National top 20			
National bottom 80			

Israni, et al. JASN 2014. 25:1842-1848

Time Waiting Remains Very Important
(Though Somewhat Less Than With the Previous KAS)

Factor	Points Awarded
For qualified time spent waiting	1 per year (as 1/365 per day)
Degree of sensitization (CPRA)	0–202
Prior living organ donor	4
Pediatric candidate if donor KDPI<0.35	1
Pediatric candidate (age 0–10 yr at time of match) when offered a zero antigen mismatch	4
Pediatric candidate (age 11–17 yr at time of match) when offered a zero antigen mismatch	3
Share a single HLA-DR mismatch with donor	1
Share a zero HLA-DR mismatch with donor	2

Israni, et al. JASN 2014. 25:1842-1848

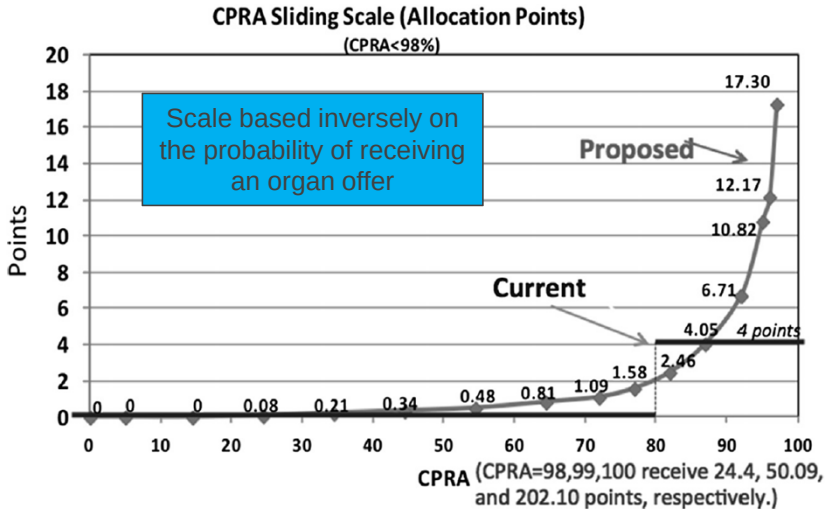
Wait Time Accrual Starting Point

- Adults - **Earlier** of the following:
  - WL registration date and GFR or calculated Cr Cl <20 ml/min
  - Date after WL registration when GFR or Cr Cl first reaches < 20 ml/min
  - Date of initiation of maintenance dialysis
- Children (<18) – **Earlier** of the following:
  - WL registration date (no clinical criteria)
  - Date of initiation of dialysis

High CPRA Candidates Receive Huge Points

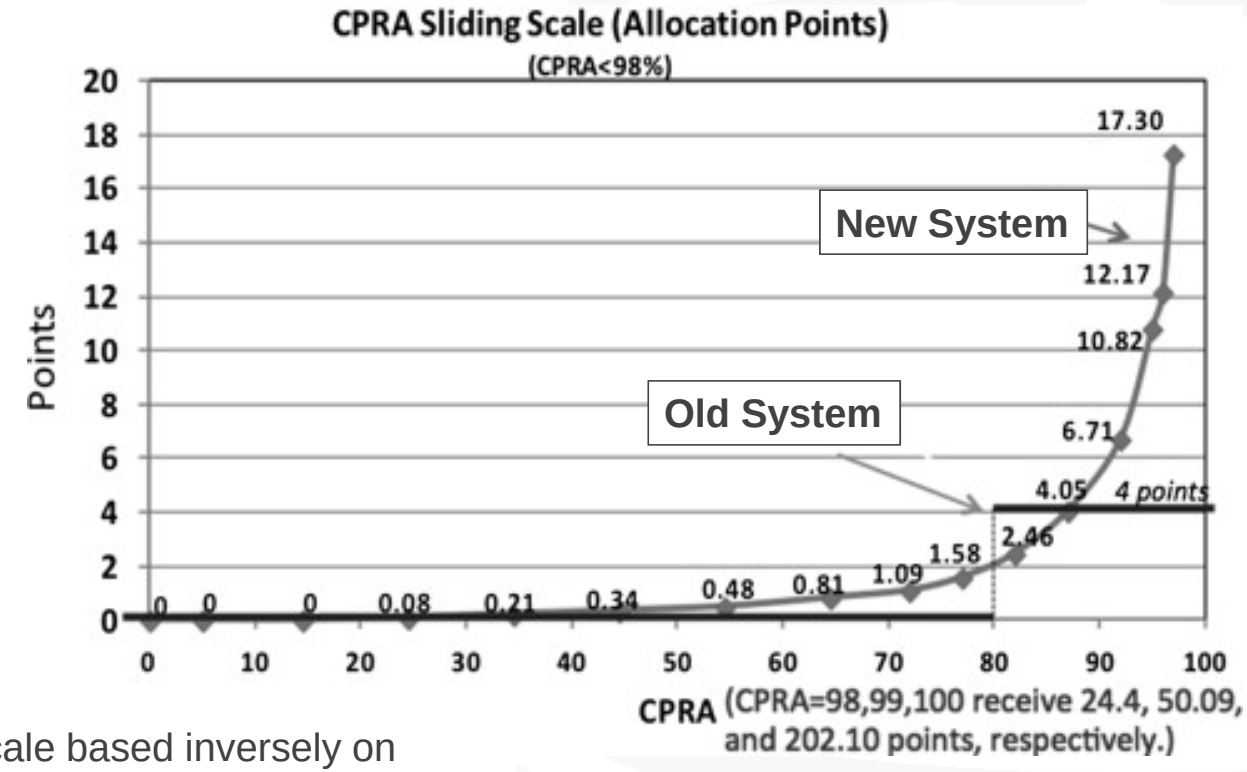
Factor	Points Awarded
For qualified time spent waiting	1 per year (as 1/365 per day)
Degree of sensitization (CPRA)	0–202
Prior living organ donor	4
Pediatric candidate if donor KDPI<0.35	1
Pediatric candidate (age 0–10 yr at time of match) when offered a zero antigen mismatch	4
Pediatric candidate (age 11–17 yr at time of match) when offered a zero antigen mismatch	3
Share a single HLA-DR mismatch with donor	1
Share a zero HLA-DR mismatch with donor	2

Israni, et al. JASN 2014. 25:1842-1848



Friedewald et al. Surg Clin N Am 2013. 93:1395-1406

CPRA Sliding Scale (Allocation Points)



Scale based inversely on the probability of receiving an organ offer

Friedewald et al. Surg Clin N Am 2013. 93:1395-1406

Organ Allocation and Blood Type

- A2 blood type less immunogenic
- B blood type waiting times are the longest
- Allocation as follows:
  - B to B, unless zero Ag MM
  - O to O, unless zero Ag MM
  - A1 to A
  - A1B to AB
  - A2 and A2B to B
    - Requires patient consent
    - Center must designate acceptable titer of antibody to A2
    - Must update every 90 days
    - Plasmapheresis must be available as needed after transplant

Exceptions Due to Medical Urgency

- Must be medically necessary
  - » Dialysis not possible
  - » No living donor option
- Requires agreement of all centers within OPO
- Single center OPO may be best option for this patient

Impact of the New KAS on Specific Patient Groups

Positively Impacted

- Highly sensitized
- EPTS <20%
  - Younger adults
  - Non-diabetics
- Patients with pre-listing dialysis time
  - Especially for those on dialysis many years
- B blood type
  - If patient consents and center accepts A2
- Adults

Negatively Impacted

- Unsensitized
- EPTS 21-100
  - Older but not old
  - Diabetics
- Patients listed prior to dialysis initiation
  - **Advantage still there vs. late listing**
- Non-B blood type
  - Advantage persists
- Children
  - Still have huge advantage
  - List before 18 if possible

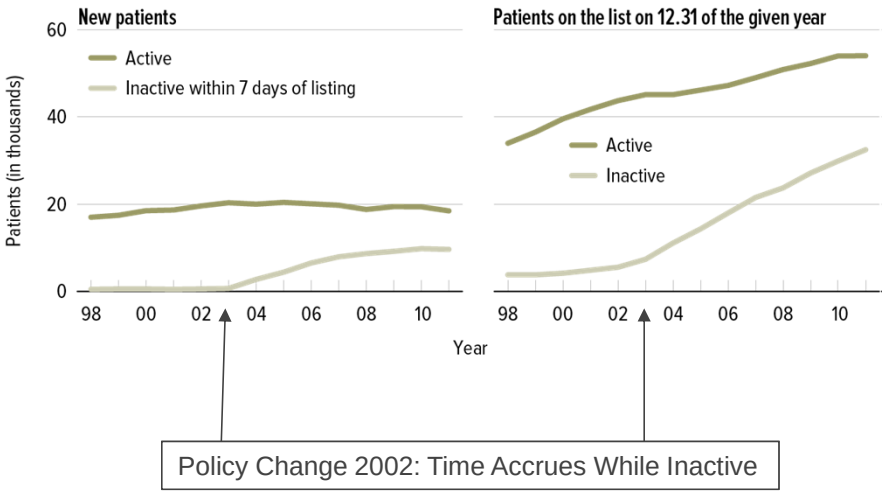
Anticipated National Consequences of the New KAS

- Longevity matching for top 20% of kidneys
  - » Reduced re-transplantation
  - » Improved utility, reduced equity (age, diabetes)
- Lower deceased donor discard rates
  - » No proof yet
  - » >85% KDPI impact unknown
- Anticipated gain in total years of graft function and patient survival for a given number of organs
- More transplants in sensitized patients
  - » Increased regional and national sharing of kidneys
  - » Increase in average cold ischemia time

Anticipated National Consequences of the New KAS

- Reduced penalty for late listing
  - » May increase referral of long-term dialysis patients
- Reduced blood type disparity in time to transplant
  - » Less racial inequity
- Possible impact on living donor transplant rate
  - » EPTS <20% patients may choose to wait for KDPI <20 %
  - » Older patients may be more likely to seek or accept a living donor
- % of Inactive (Status 7) patients likely to decline

A Rule Change in 2002 Led to A High Percentage of Inactive Patients in the Old Kidney Allocation System



- 3 status options established
  - Actively listed
  - Status 7 (inactive but listed) – time still accrues
  - Not listed (delisted or never listed)
- Delisting a listed patient = Loss of all waiting time prior to December 5, 2015
- Transplant centers acting as patient advocates left patients on the list even if:
  - Low (but not zero) likelihood of future transplant
  - Medically indicated observation periods (e.g. cancer diagnosis)
- Patient Impact
  - The Good: Accumulated waiting time
  - The Bad: Testing often continued to maintain listing status
    - Cost
    - Inconvenience
    - Procedural risks

2011 SRTR ADR

Impact of a High Inactive % On Transplant Center Statistics and Behavior

- Inactive patients included in analyses of
  - Waiting time
  - Death on the wait list
  - Transplant rate
- True waiting time, transplant rates obscured
- Center comparison difficult
- Centers experienced negative impact
  - Regulatory concerns
  - Reimbursement and contracts impacted

The New KAS Offers Another Option for Some Patients

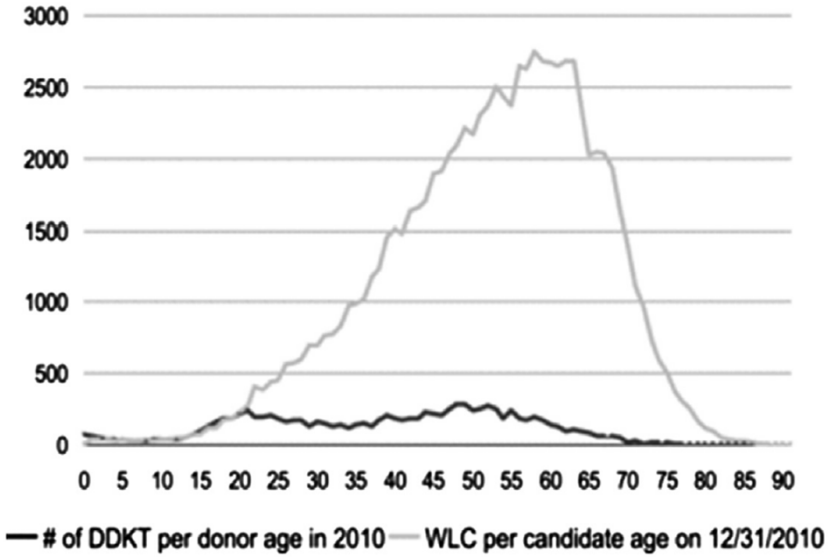
Proposal: The LIFT List

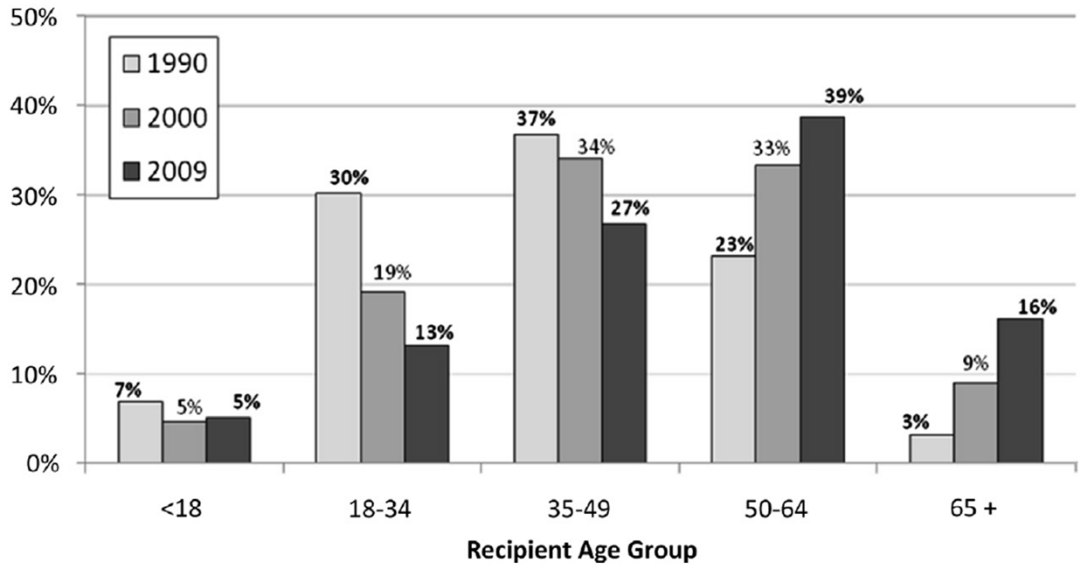
- Current KAS still has 3 status options – Active, Inactive, Not Listed
- The important change as of December 4, 2014
  - » Delisting leads to loss of waiting time only if patients were listed prior to dialysis
- Proposal – A Fourth Listing Option for UNC = List at a Future Time (LIFT)
  - » Applied to patients **without** pre-dialysis waiting time who would previously have been listed as inactive:
    - Includes currently listed and ready to be listed patients who are future potential candidates
  - » Examples
    - Weight loss requirements to get BMI <40
    - Cancer waiting period
    - Active foot ulcers, infection
    - Establishing a post-transplant care plan, social support system
    - Drug abuse counseling
- The Risk
    - Cannot forget these patients
    - How will patients react to being delisted vs. being inactive?

Recommendations for Individual Patients

- Refer at eGFR 20 to 25 ml/min
- List CKD children prior to age 18 if they have a chance of future ESRD
- EPTS calculation for each patient
  - » Counsel those <20% when they will cross the 20% line
  - » Active status important when nearing EPTS 20%
- Counsel B blood type patients about A2, A2B donor option
- Counsel carefully anyone we delist that their waiting time since starting dialysis will not be lost
- High risk (diabetic, obese) and elderly patients (>65) must strongly consider living donor transplants

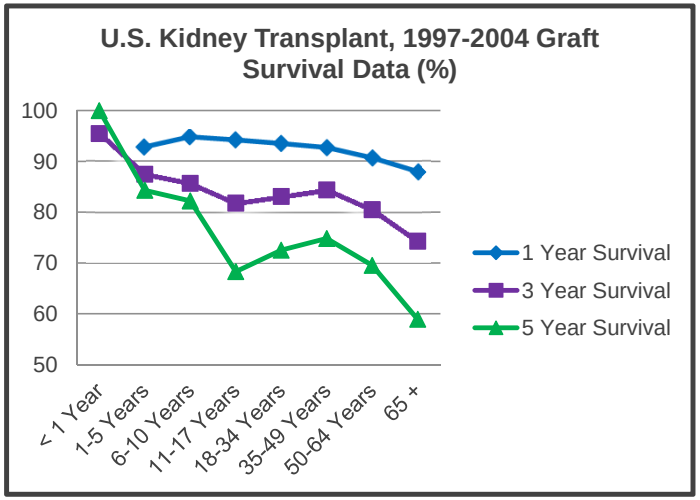
Age Distribution of Recipients

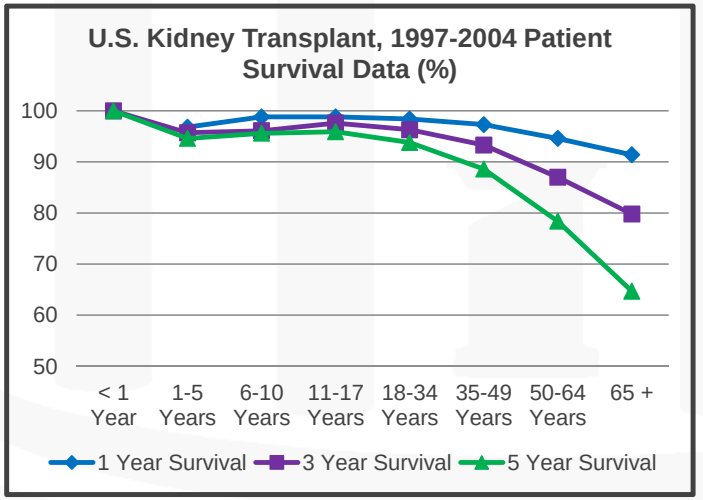




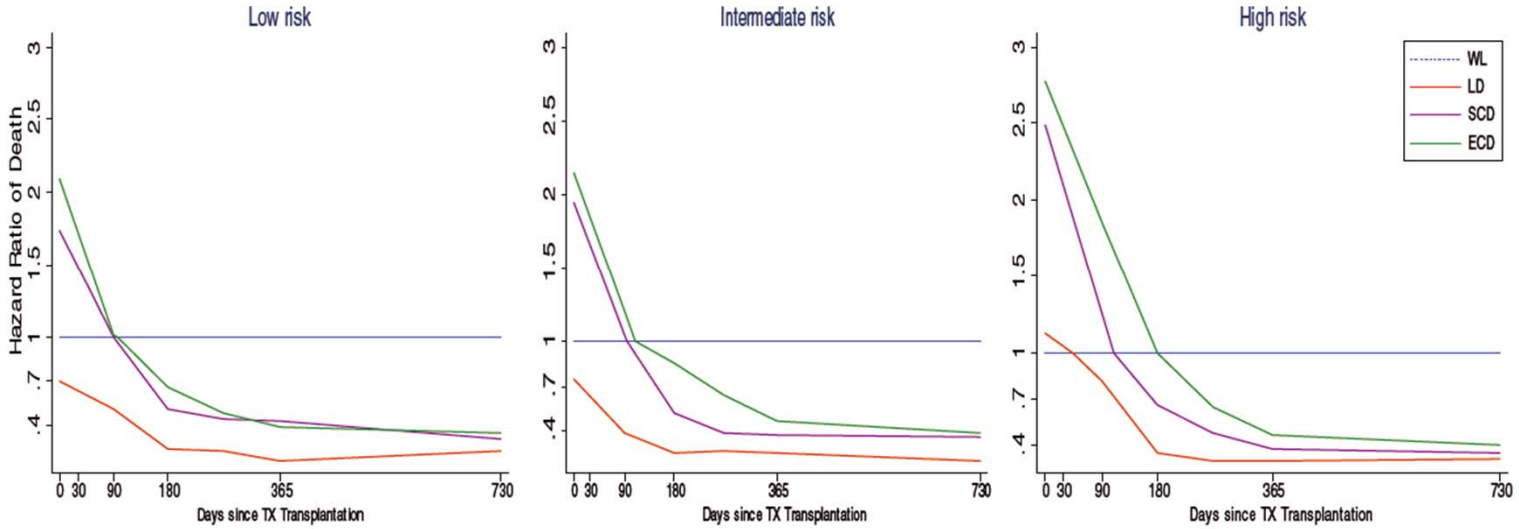
Friedewald et al. Surg Clin N Am 2013. 93:1395-1406

SRTR Data


U.S. Kidney Transplant, 1997-2004 Graft Survival Data (%)
100
90
80
70
60
50
< 1 Year
1-5 Years
6-10 Years
11-17 Years
18-34 Years
35-49 Years
50-64 Years
65 +
1 Year Survival
3 Year Survival
5 Year Survival


U.S. Kidney Transplant, 1997-2004 Patient Survival Data (%)
100
90
80
70
60
50
< 1 Year
1-5 Years
6-10 Years
11-17 Years
18-34 Years
35-49 Years
50-64 Years
65 +
1 Year Survival
3 Year Survival
5 Year Survival

Transplantation, Especially From a Living Donor, Offers Mortality Advantage for Patients >65 Years of Age



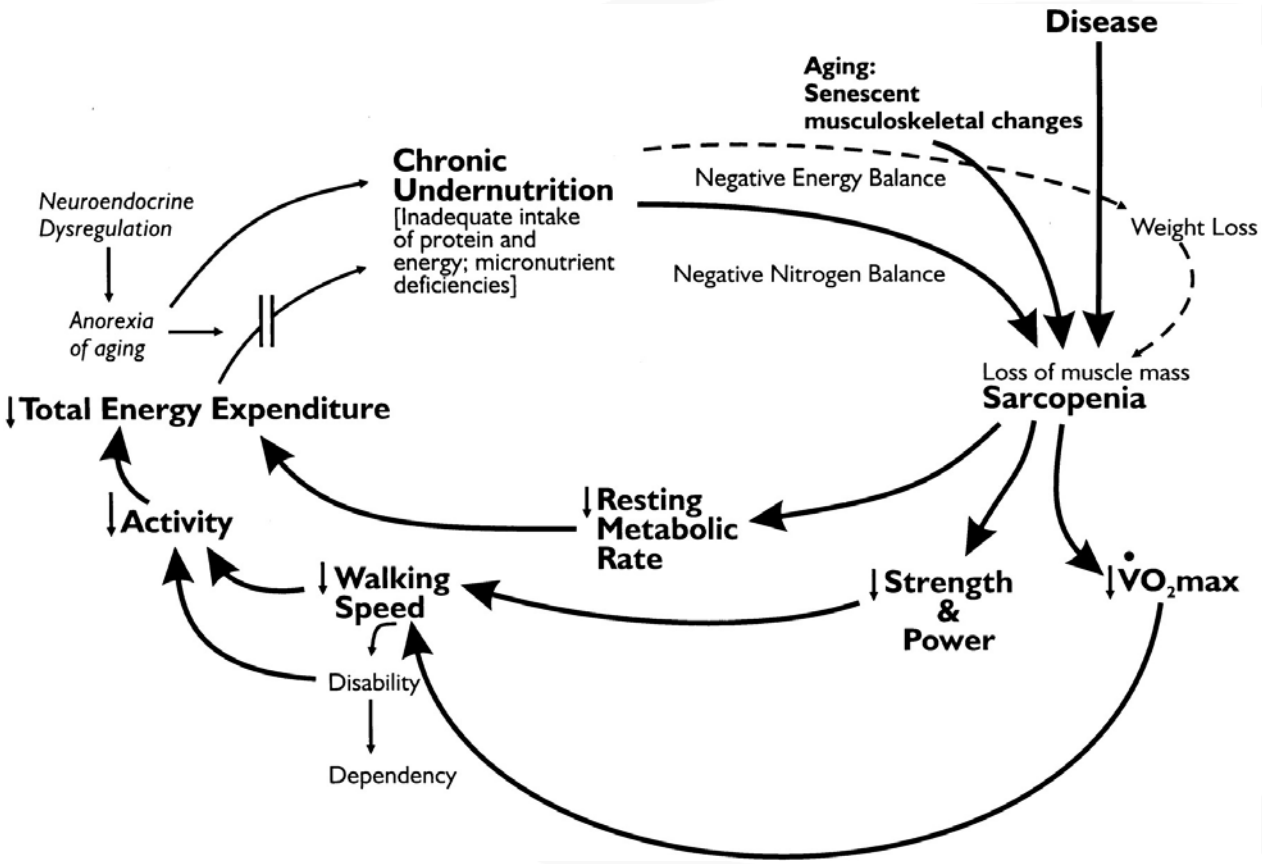
- USRDS 1995-2007
- >65 years of age
- Categorized by CV risk and donor type
- CHF, Ischemic Heart Disease, CVA, PAD used to define CV risk
- DM defined as high risk

Gill, JS. Am J Transpl 13: 427-432, 2013

Is It Possible to Risk Stratify the Older Kidney Recipient Candidate?

Measures of Frailty in the Elderly and the Likelihood of Post-Transplant Success

Cycle of Frailty



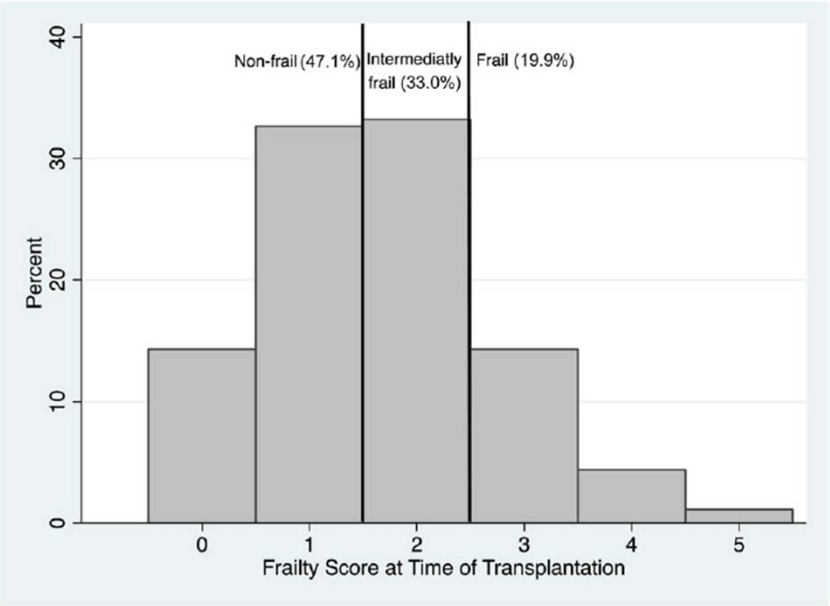
Fried L P et al. J Gerontol A Biol Sci Med Sci 2001;56:M146-M157

Measuring Frailty
The Fried Frailty Scale

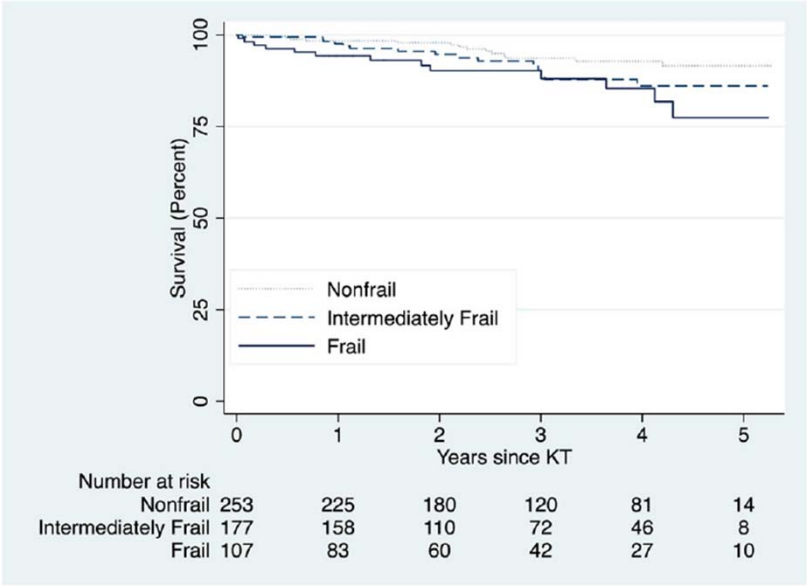
- Shrinking
  - » Unintentional weight loss of > 10 lbs. in last year
  - » At f/u – loss of > 5% previous year's body weight
- Exhaustion
  - » Subjective interview scale
- Strength
  - » Grip Strength
- Low Activity
  - » Kcals per week expended
  - » Men: < 383 Kcals per week frail
  - » Women: < 270 Kcals per week frail
- Low walking speed
  - » 15 feet in 6 or 7 seconds

Frailty Distribution and Outcomes Associations
The Johns Hopkins Experience (2008-2013)

Frailty Distribution at Time of Transplant



Patient Survival by Frailty Status



American Journal of Transplantation 2015; 15: 149–154