Strategies to Expand Kidney Exchange, and an Update of the US System
2nd part

Dorry Segev, MD, PhD
Professor of Surgery and Epidemiology
Associate Vice Chair, Department of Surgery
Director, Epidemiology Research Group in Organ Transplantation
Johns Hopkins University

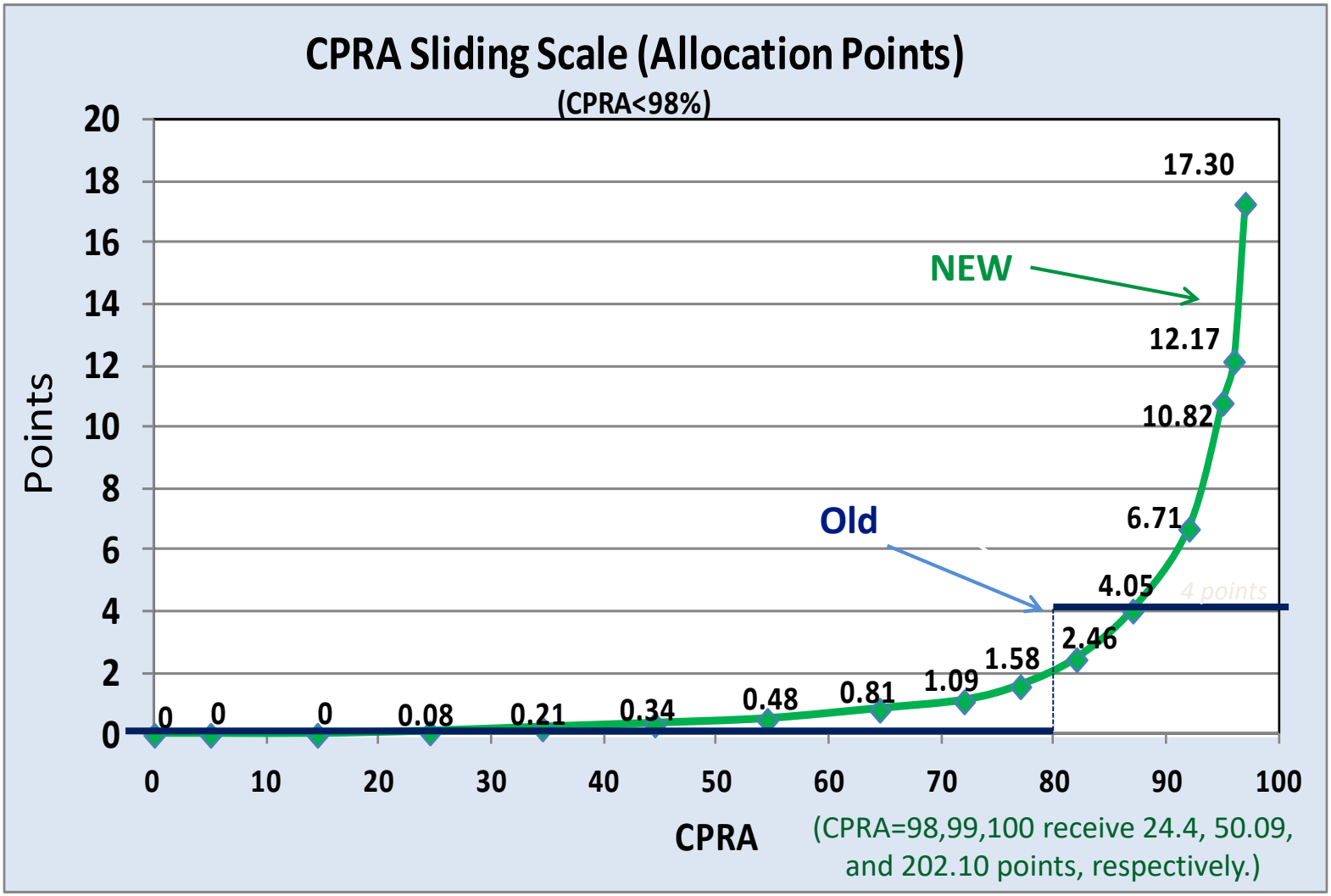
Overview

- Role of Kidney Exchange in the context of new allocation priorities and desensitization
- New calculators

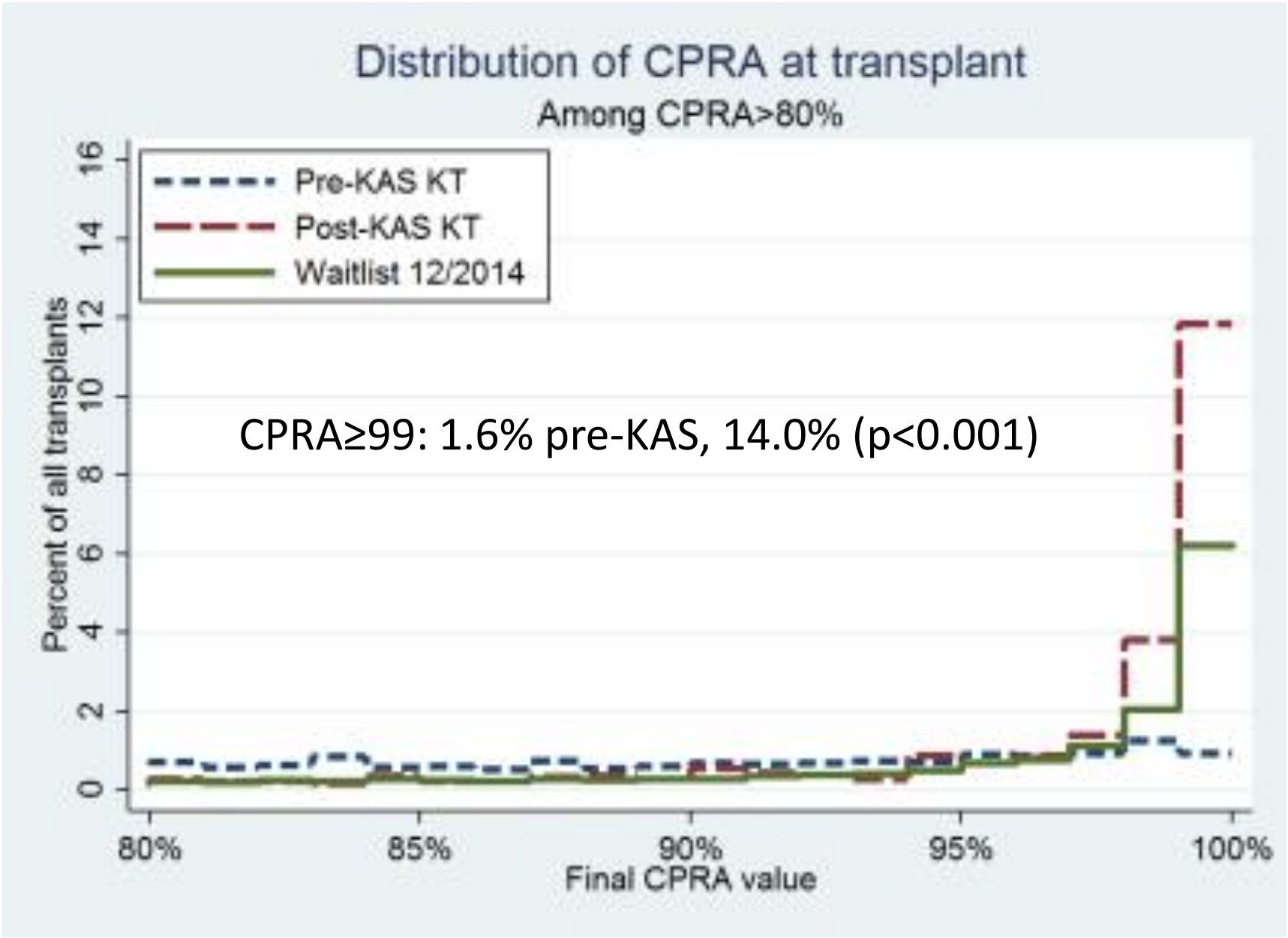
ROLE OF EXCHANGES WITH NEW ALLOCATION, DESENSITIZATION

Sequence A KDPI <=20%	Sequence B KDPI >20% but <35%	Sequence C KDPI >=35% but <=85%	Sequence D KDPI>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
Zero mismatch (top 20% EPTS)	Zero mismatch	Zero misma	Zero mismatch
Prior living donor	Prior living donor	Prior livin	Regional
Local pediatrics	Local pediatrics	Local	
Local top 20% EPTS	Local adults	Regiona	
Zero mismatch (all)	Regional pediatrics	Nation	egories in
Local (all)	Regional adults		D
Regional pediatrics	National pediatrics		to adult
Regional (top 20%)	National adults		
Regional (all)			
National pediatrics			
National (top 20%)			
National (all)			

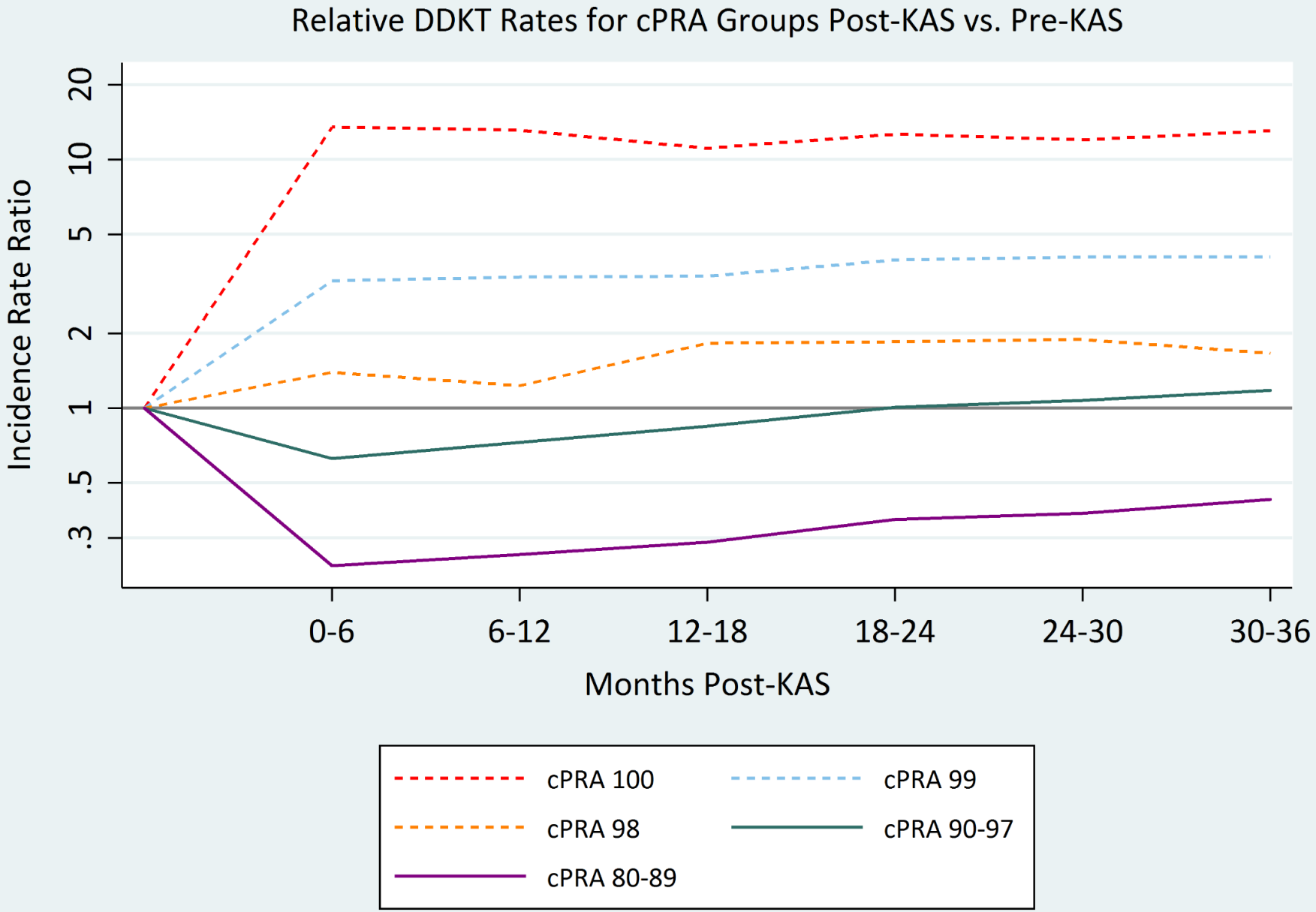
New categories for highly sensitized candidates



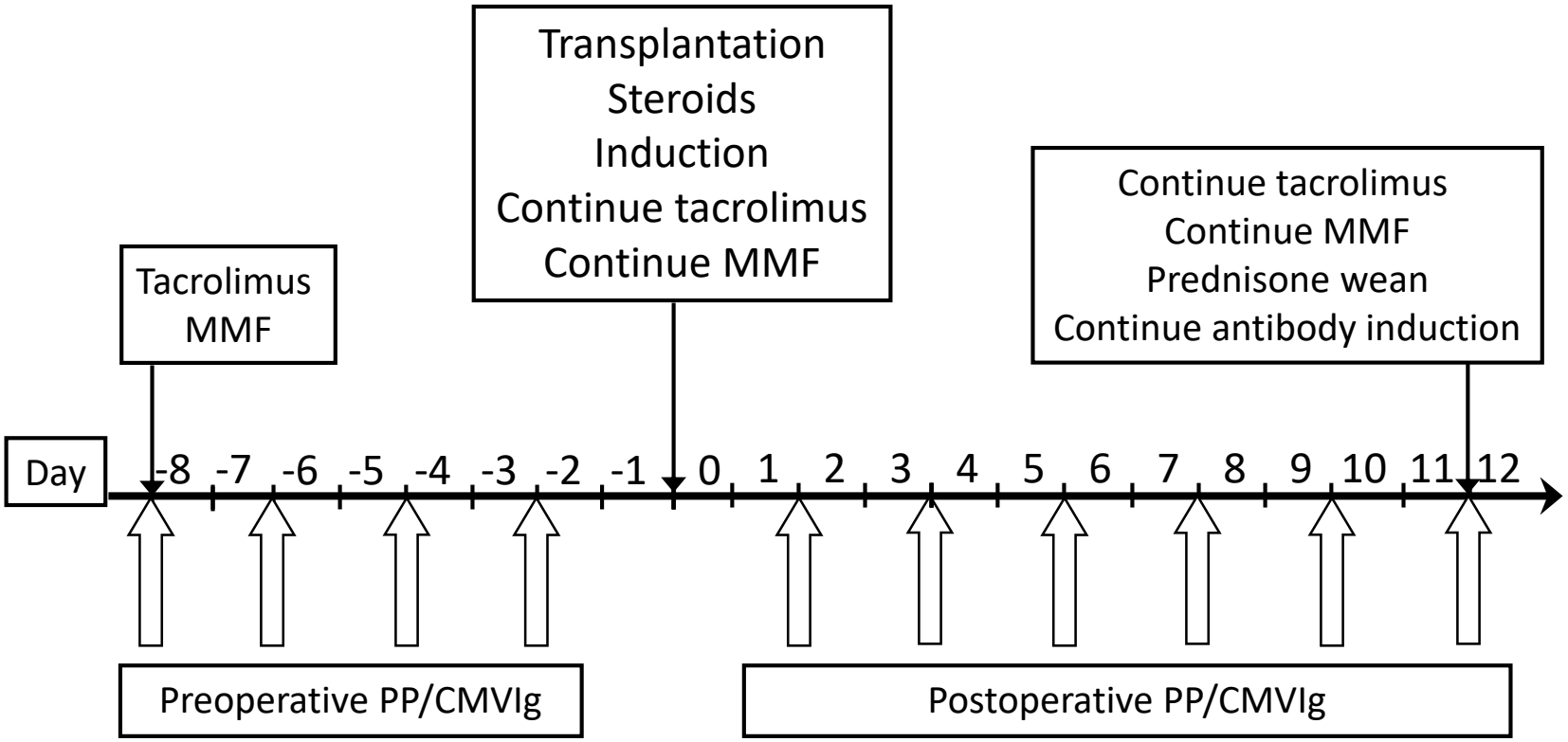
Old policy: 4 points for CPRA>=80%. No points for moderately sensitized.
NEW: sliding scale starting at CPRA>=20%



Massie/Segev, JASN, 2017


Relative DDKT Rates for cPRA Groups Post-KAS vs. Pre-KAS
Incidence Rate Ratio
.3
.5
1
2
5
10
20
0-6
6-12
12-18
18-24
24-30
30-36
Months Post-KAS
cPRA 100
cPRA 99
cPRA 98
cPRA 90-97
cPRA 80-89

Desensitization



Montgomery/Segev NEJM 2011

Desensitization

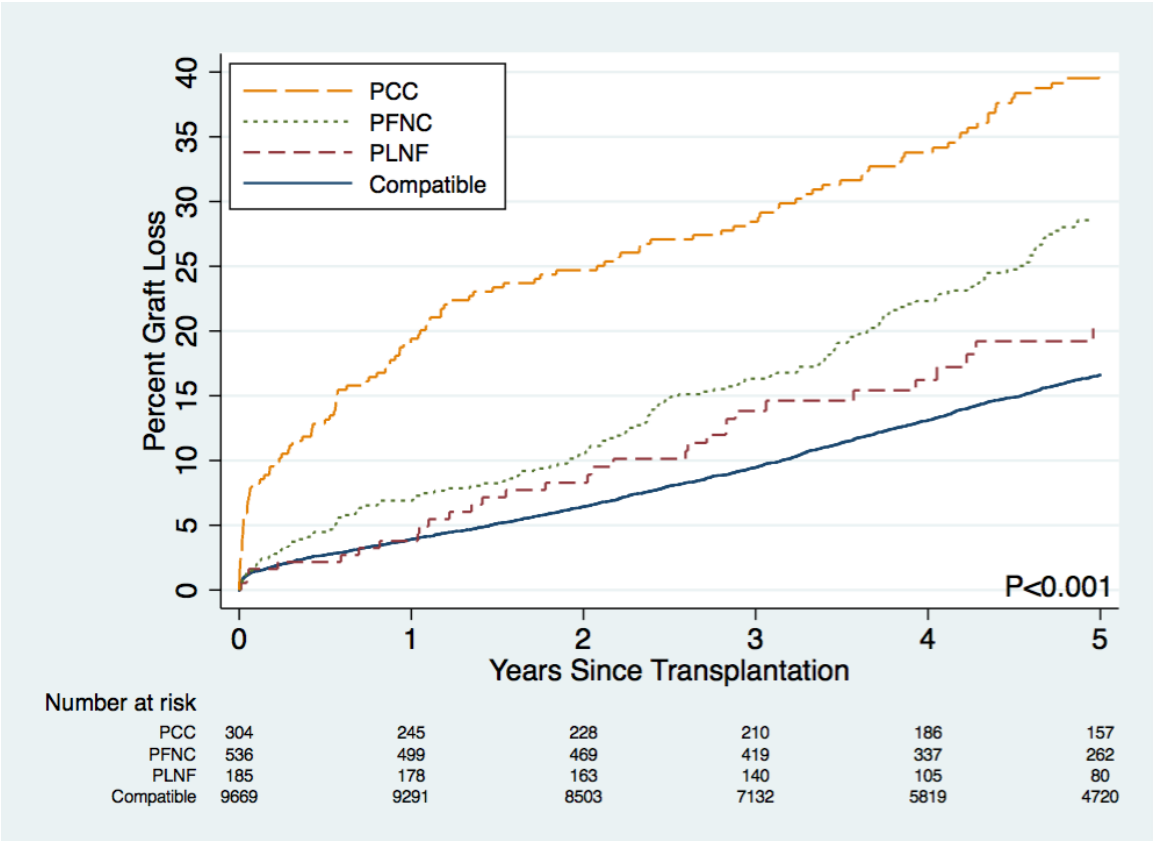
- Treatment risks
  - Plasmapheresis
  - B cell modulators
  - Complement cytotoxicity inhibition
- Early risks
  - Memory response (splenectomy, eculizumab, …)
  - Early AMR
- Late risks
  - Late AMR

versus alternatives…?

Desensitization: HLA Incompatible

- 21-center observational study
- 1025 patients
  - 185 Luminex positive (negative flow xm)
  - 536 Flow positive (negative CDC xm)
  - 304 Cyto CDC positive
- Controls
  - Similar compatible patients at those centers during that time period (n=10,694)

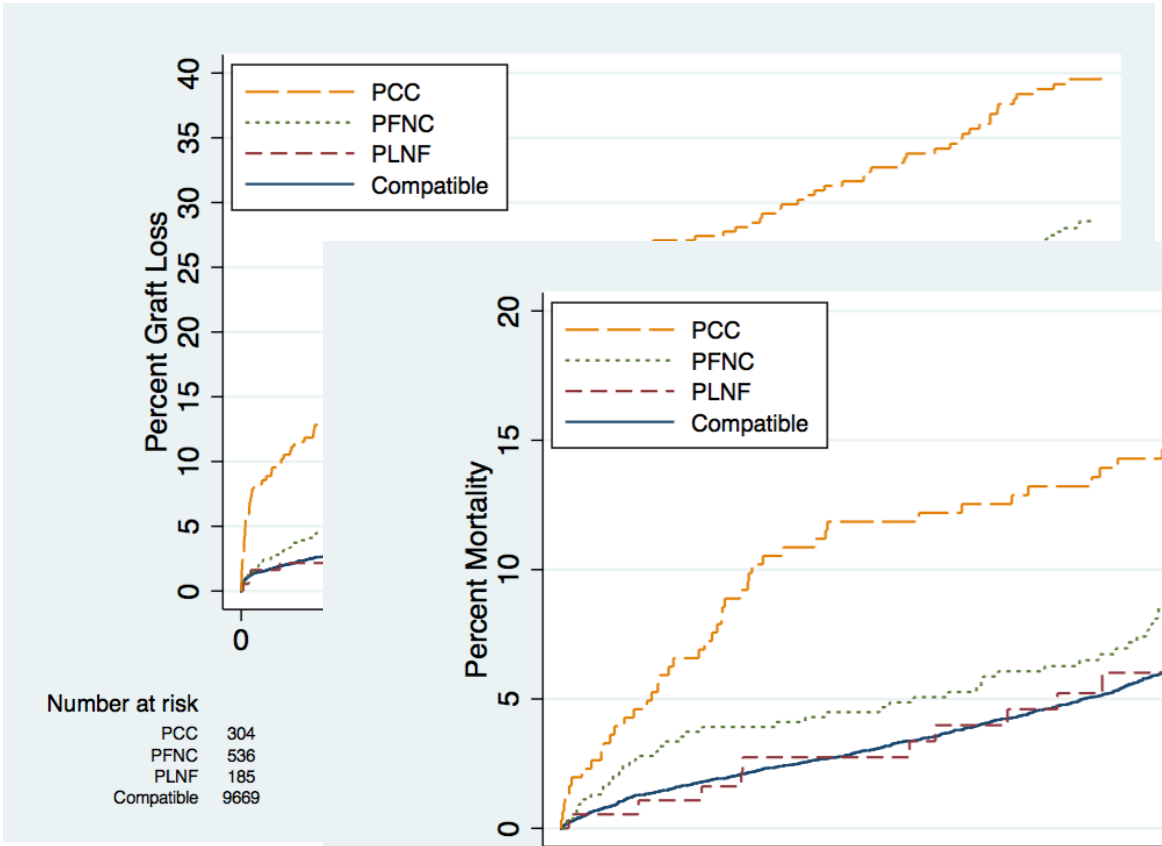
Orandi/Segev, AJT 2014



HLAi: Graft Loss

Orandi/Segev, AJT 2014

HLAi: Mortality



Orandi/Segev, AJT 2014

Antibody Strength	All-Cause Graft Loss		Mortality	
	aHR ≤1 Year	aHR >1 Year	aHR ≤1 Year	aHR >1 Year
Compatible	Reference	Reference	Reference	Reference
Positive Luminex, Negative Flow Crossmatch	0.91 (0.43-1.94) p=0.8	1.20 (0.83-1.75) p=0.3	0.83 (0.26-2.62) p=0.8	0.84 (0.48-1.48) p=0.6
Positive Flow, Negative Cytotoxic Crossmatch	1.64 (1.15-2.33) p=0.007	1.65 (1.36-1.99) p<0.001	2.04 (1.28-3.26) p=0.003	1.32 (1.02-1.70) p=0.037
Positive Cytotoxic Crossmatch	5.01 (3.71-6.77) p<0.001	1.80 (1.42-2.29) p<0.001	4.59 (2.98-7.07) p<0.001	1.51 (1.13-2.03) p<0.001

Desensitization

- Advantages
  - Can transplant immediately
  - Does not require coordination with other patients / surgeons / centers
- Disadvantages
  - Requires work (for both patient and provider)
    - Up-front (the desensitization itself)
    - Later (antibody monitoring, protocol biopsies, etc)
  - Magnitude of long-term risks unknown

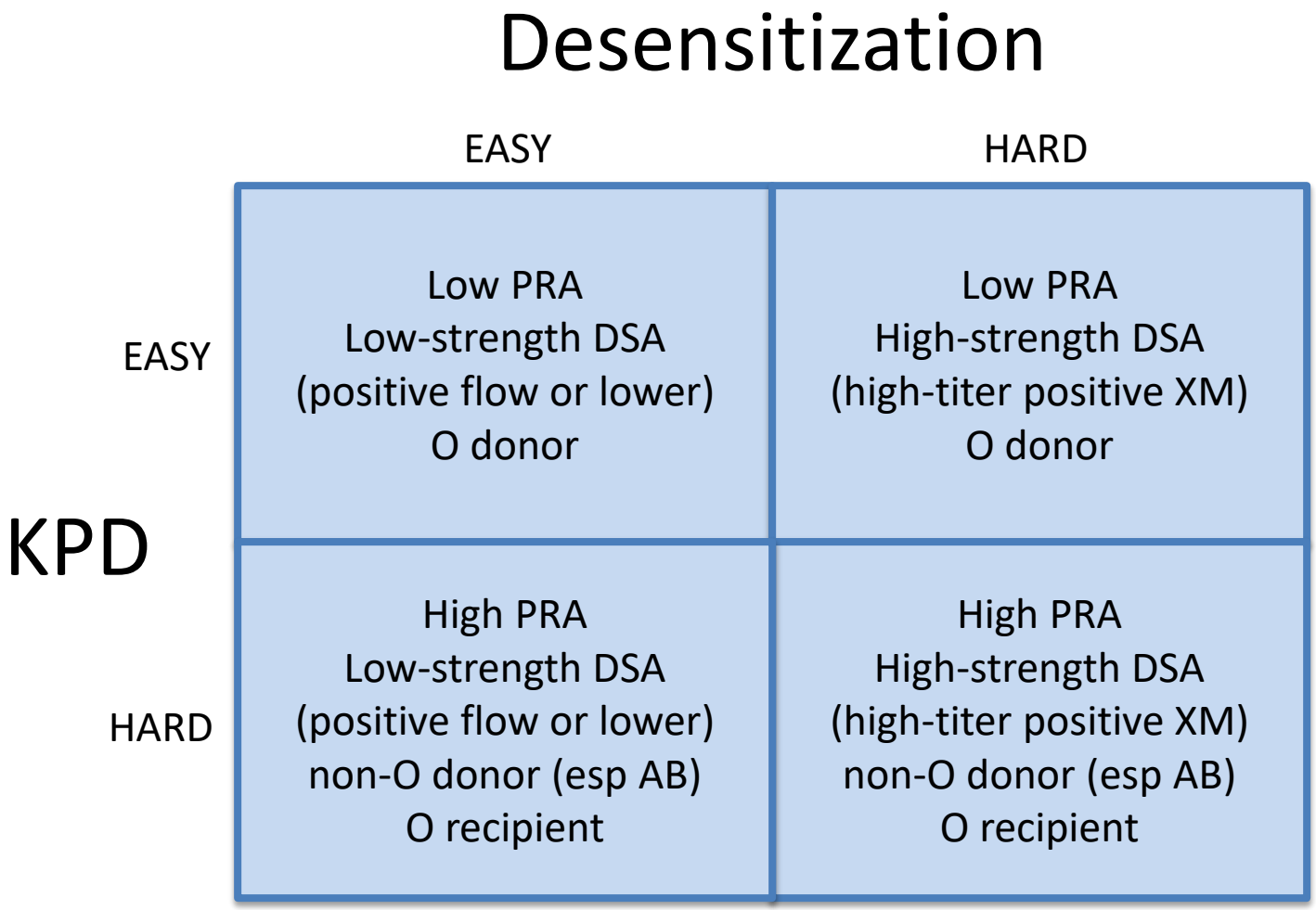
KPD

- Advantages
  - Compatible transplants
    - Can be done at any center that does LDKT
    - Outcomes are just like any other transplants
    - Long-term management just like any other transplant
- Disadvantages
  - Requires a match -- so might have to wait
  - Requires coordination with other centers (sometimes)

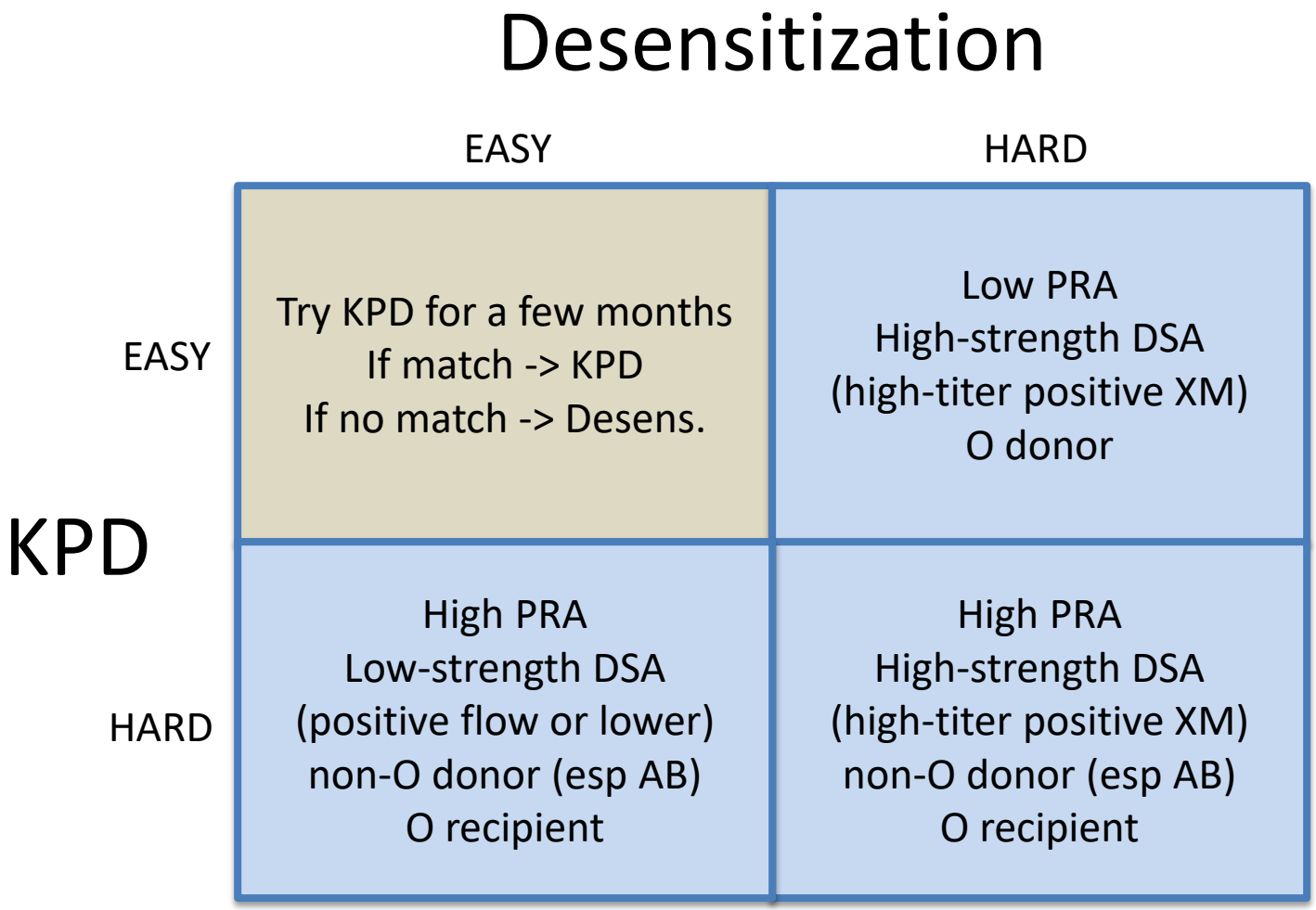
Desensitization vs KPD = PRA vs DSA

- PRA = ability to match
  - Patient might have very high strength DSA to one particular antigen, but low PRA
  - Blood types also affect ability to match (O donors or AB recipients make a pair easier to match)
- DSA = ability to desensitize
  - Patient with many antibodies (broadly sensitized, very high PRA) might have low strength antibody to a particular donor's particular antigens

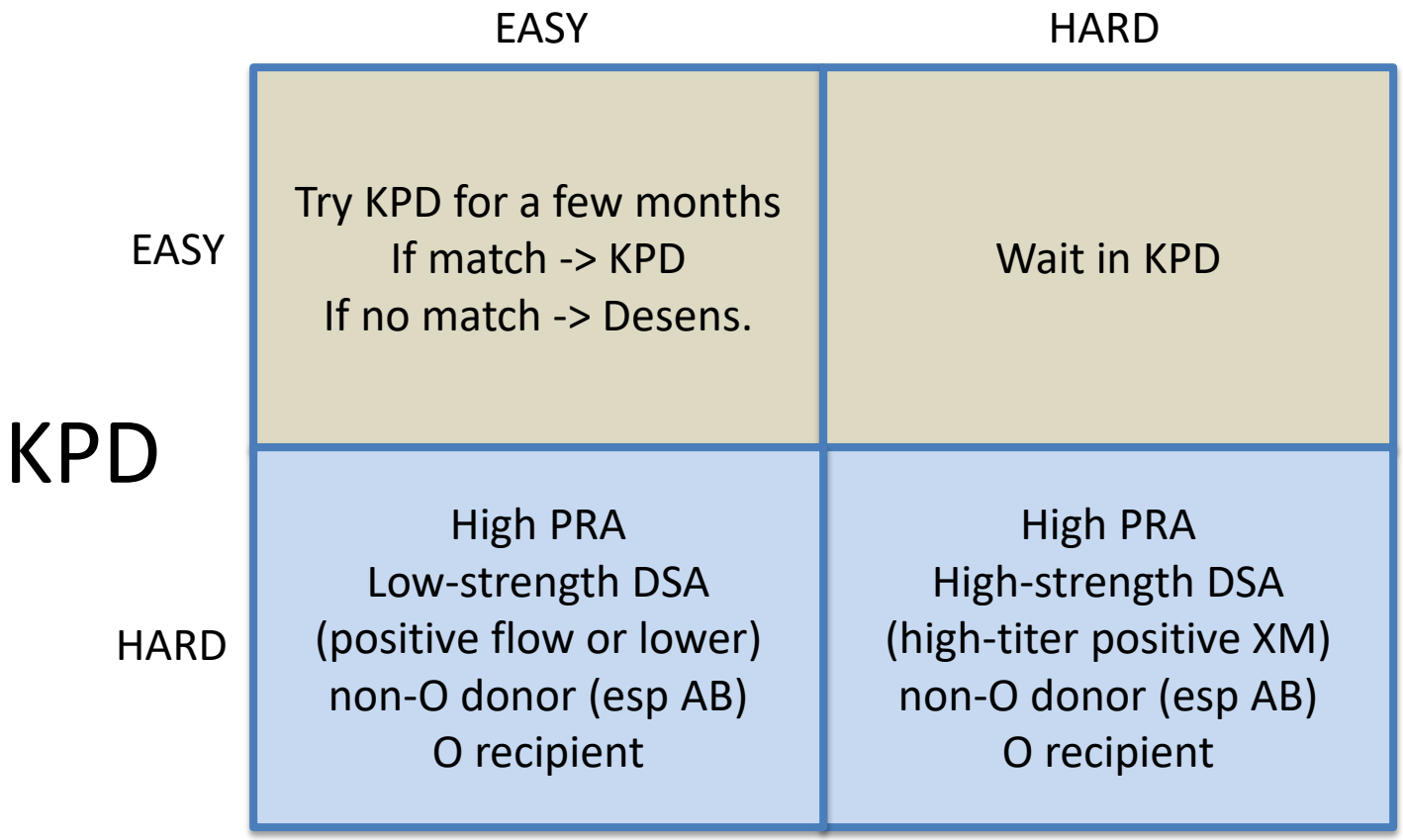
Characterizing the Donor/Recipient Pair



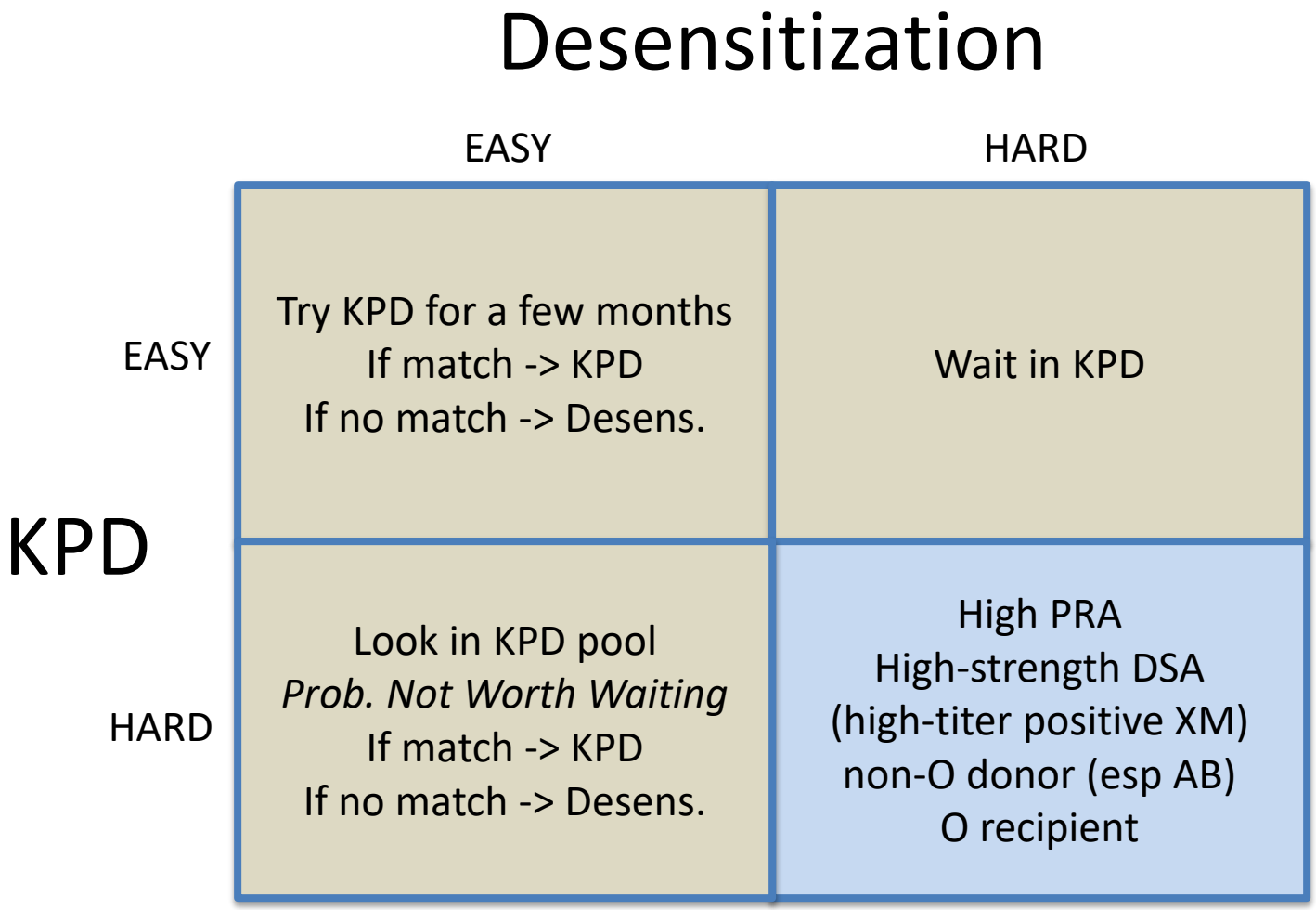
Characterizing the Donor/Recipient Pair



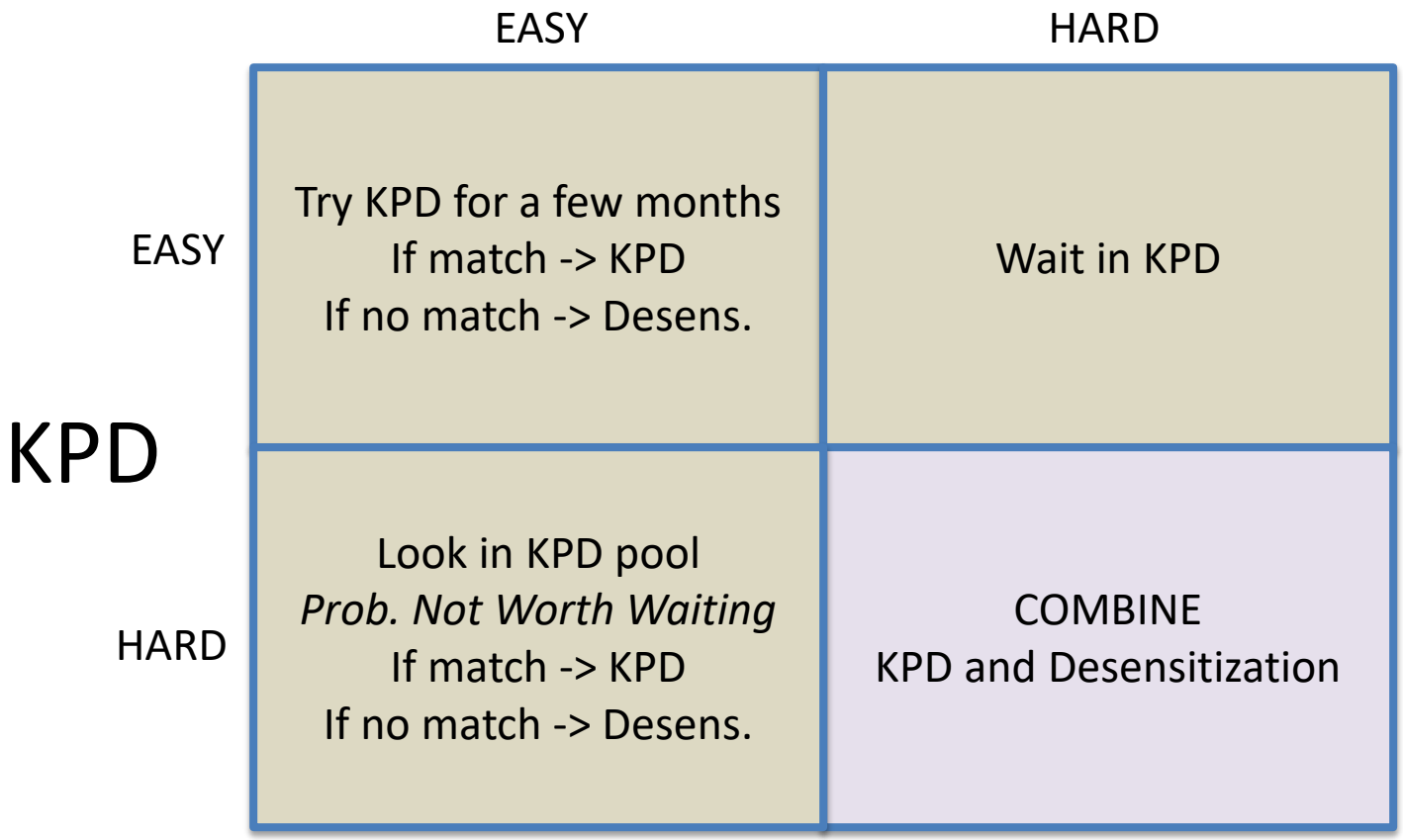
Characterizing the Donor/Recipient Pair



Characterizing the Donor/Recipient Pair

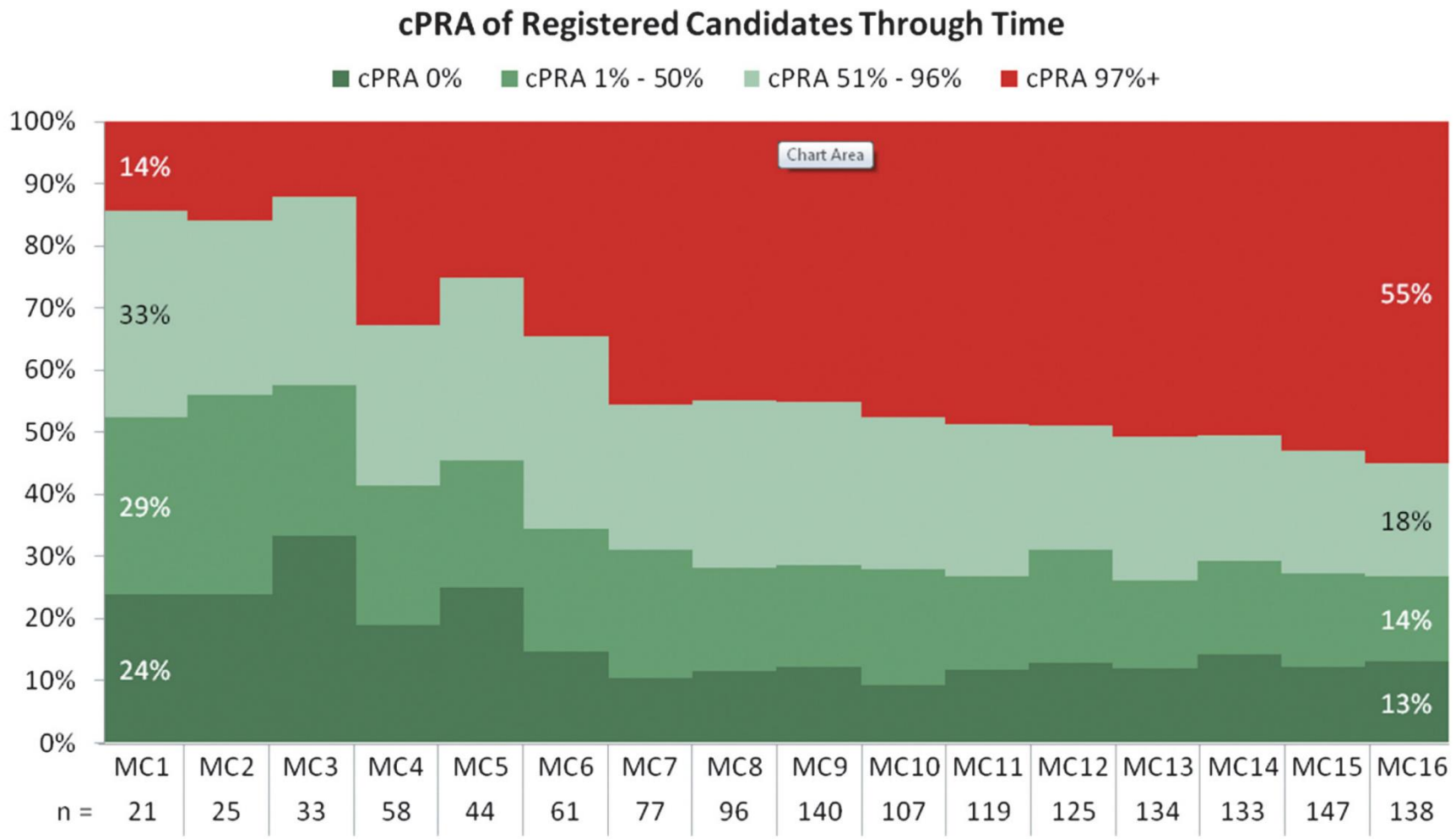


Characterizing the Donor/Recipient Pair



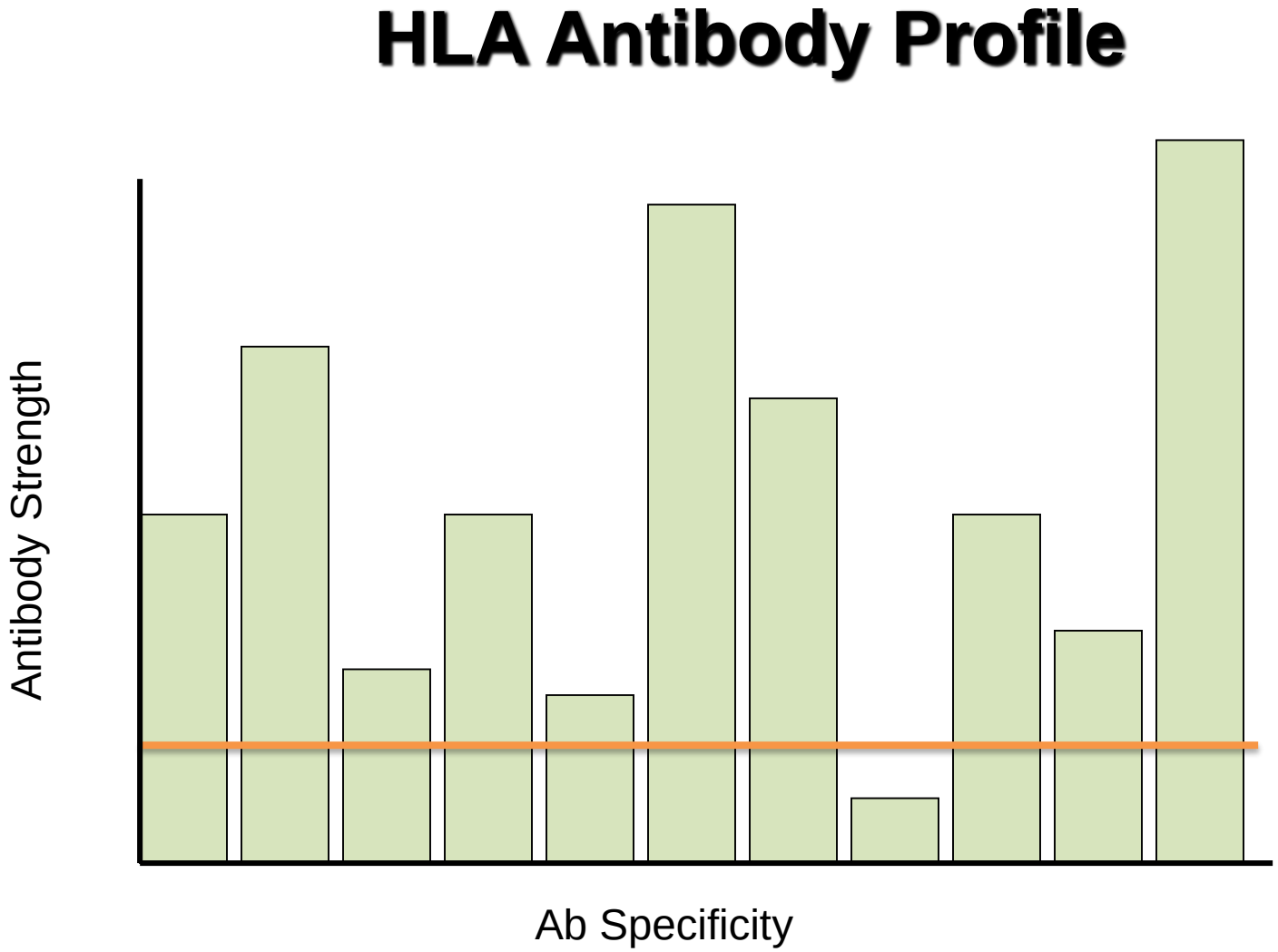
Combining KPD and Desensitization

- From any pool of recipients, many will not match.
- Hard-to-match pairs will accumulate. Most of these are broadly sensitized.
- Results with desensitization with low-titer positive XM are excellent

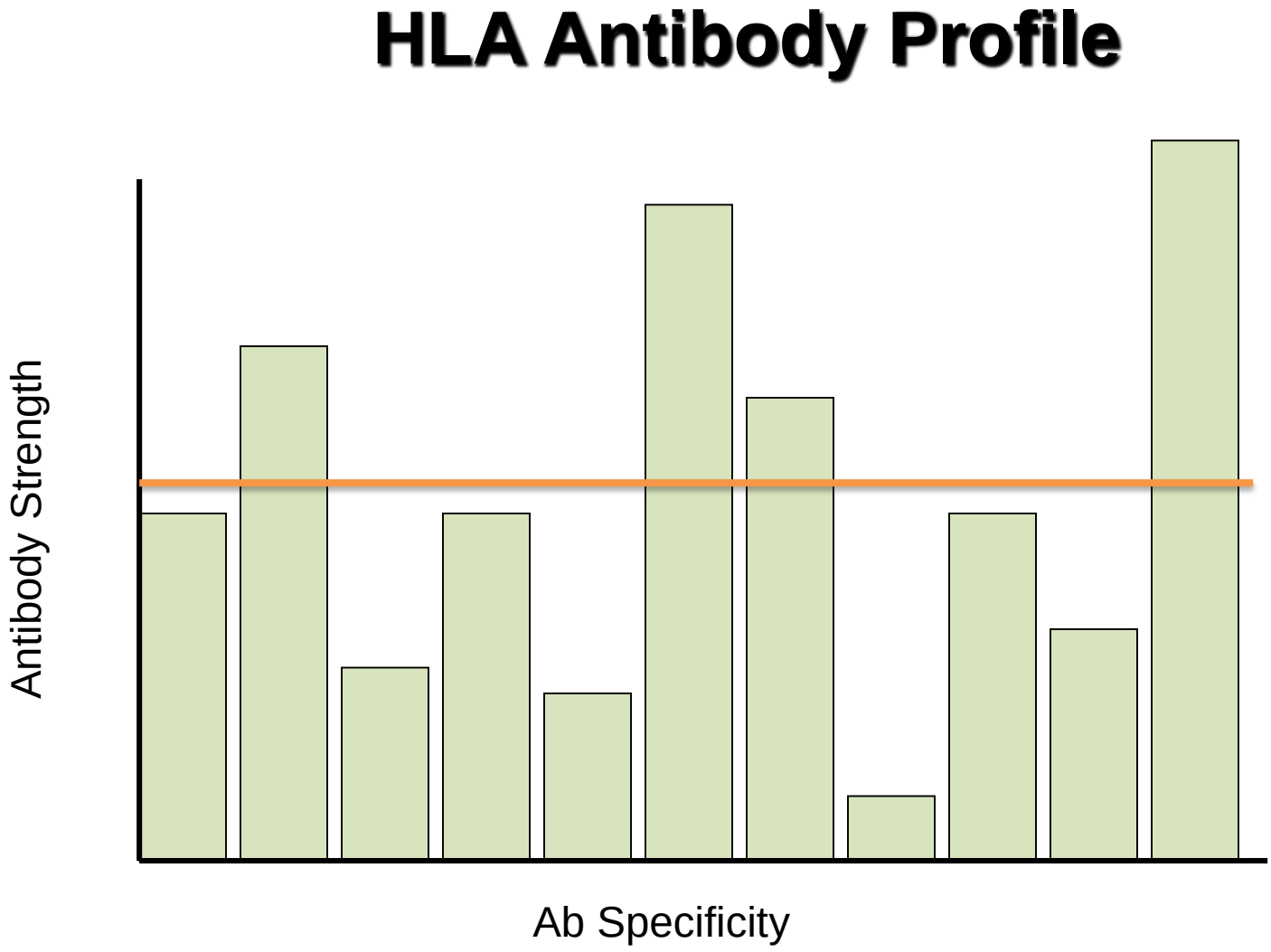


Cole et al, Transplantation 2015

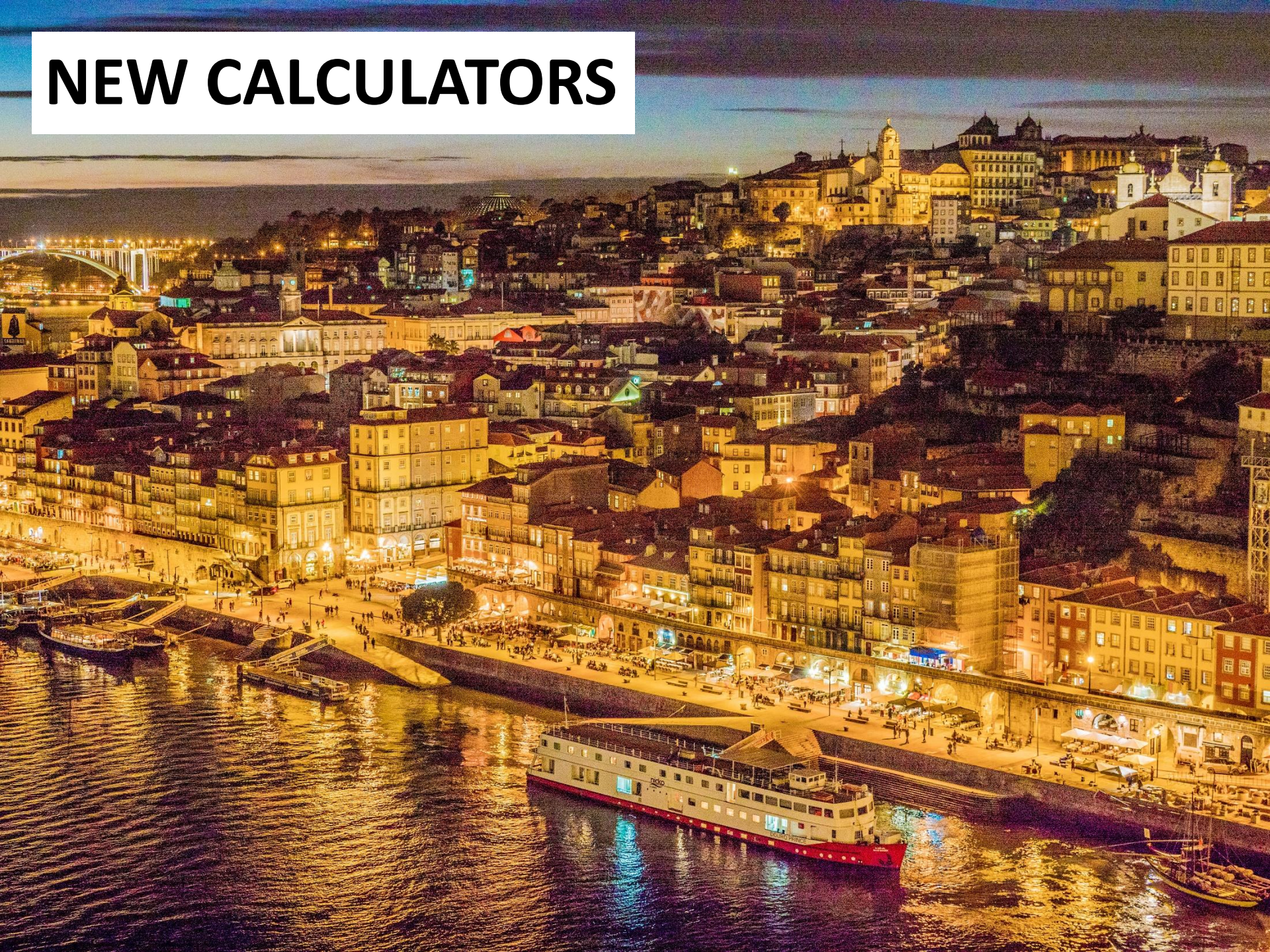
Combining KPD with Desensitization



Combining KPD with Desensitization



NEW CALCULATORS



"The only remaining problem was the ethical decision concerning the removal of a healthy organ from a normal person for the benefit of someone else. For the first time in medical history a normal healthy person was to be subjected to a major surgical operation not for his own benefit.“

Joseph Murray, Nobel Lecture, 12/8/90

Questions We Want to Answer

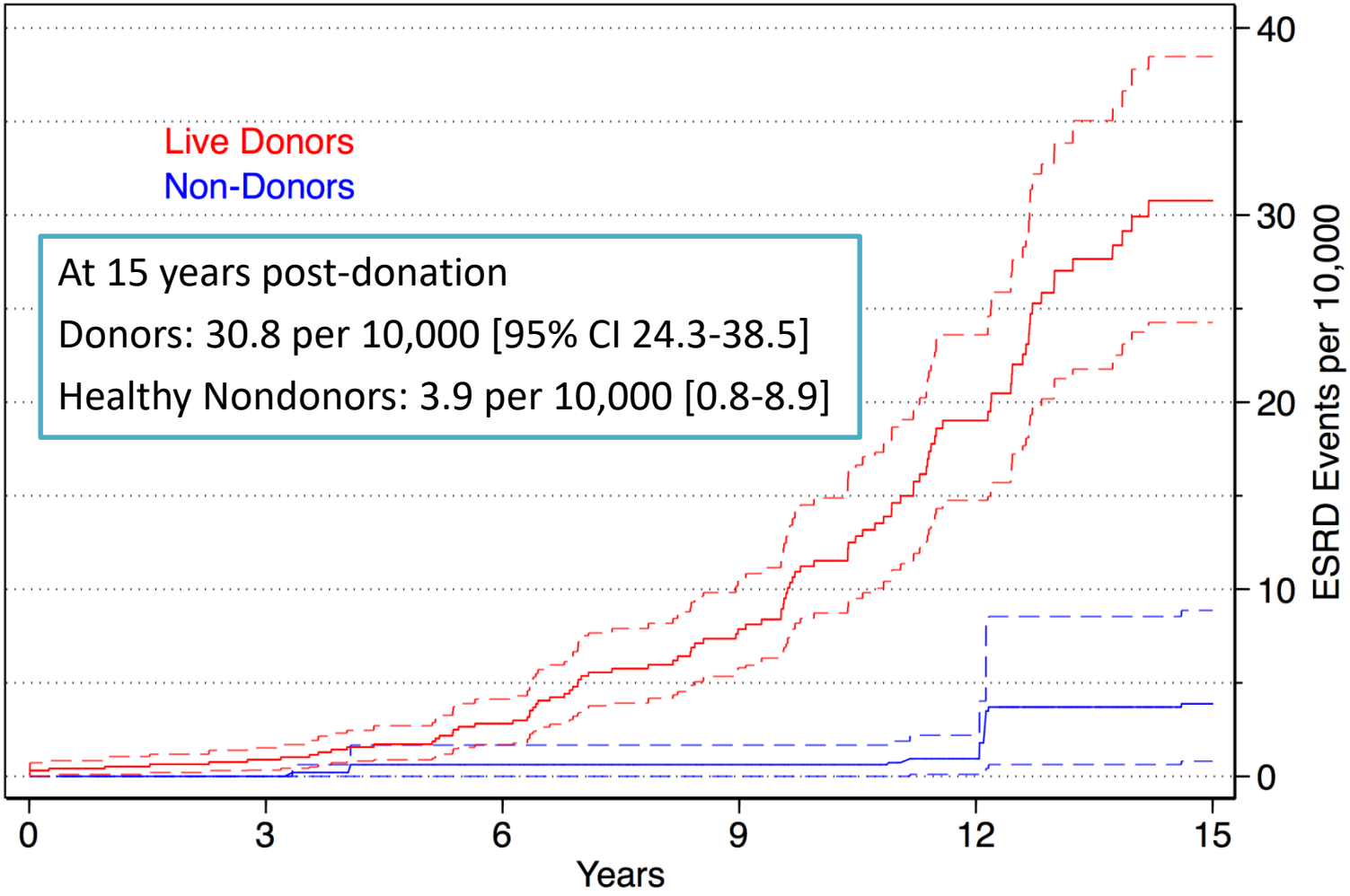
- *Baseline risk*
  (risk individual will have if doesn't donate)
- *Absolute risk*
  (total risk individual faces if donates)
- *Attributable risk*
  (extra risk individual faces if does donate)
- By race, age, sex, BMI, GFR, etc?

OPTN Live Donor Registry

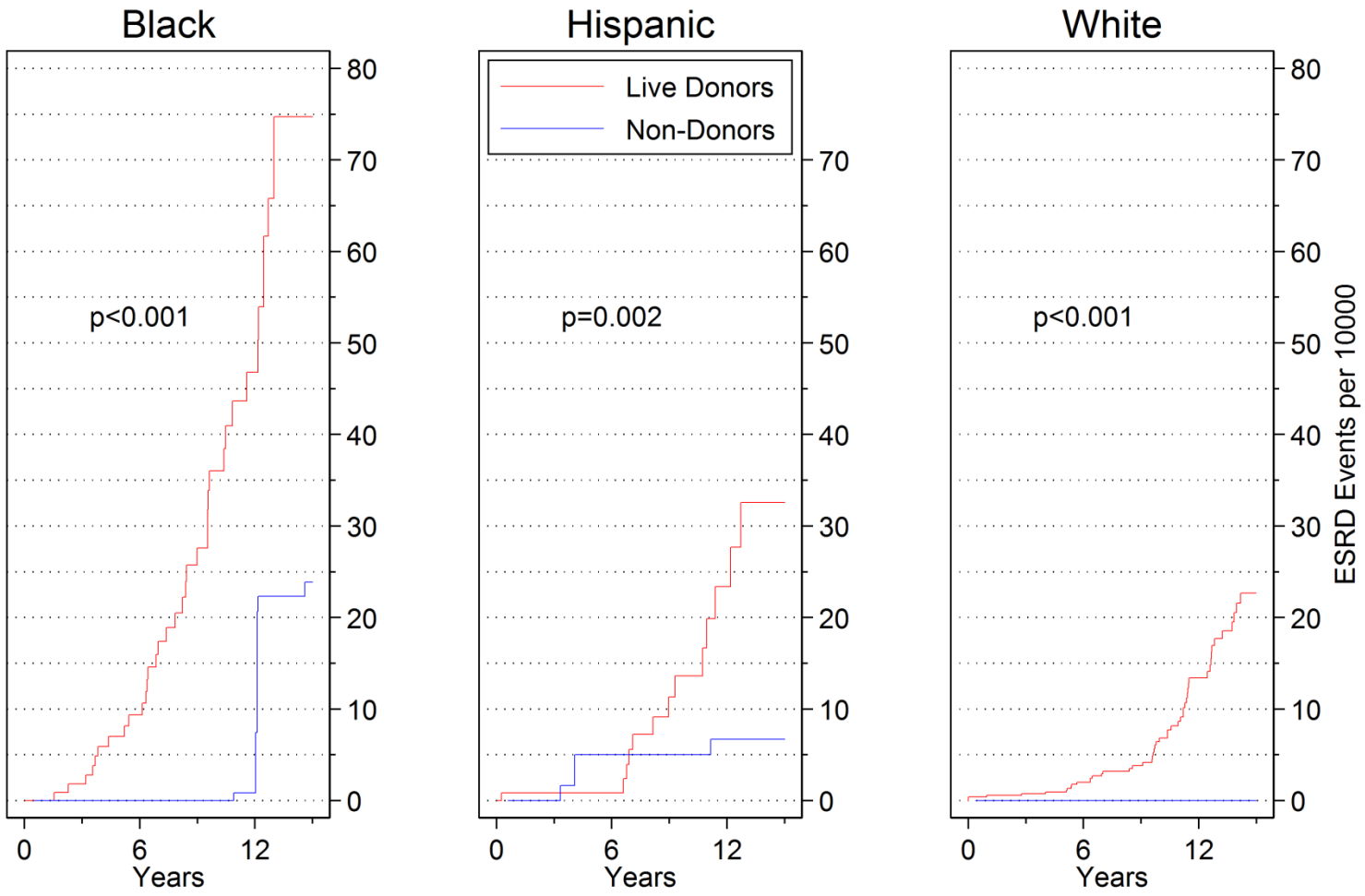
- Every single live donor in the US since 1988
- Currently N>145,000
- Advantages: massive, unbiased
- Disadvantages:
  - Incomplete, limited-term outcome capture
  - But… SSN captured since 1994 – linkage
- Medicare (CMS)
- Social Security (SSDMF)

NHANES-III

- Interviews, physical examination, and laboratory tests of 20,024 adults and 13,000 children administered by medical personnel
- Very detailed initial visits
- Can identify “healthy non-donors”
- Cross-sectional: no follow-up (except linkage)
- Medicare (CMS)
- Social Security (SSDMF)



Muzaale/Segev, JAMA, 2014



Muzaale/Segev, JAMA, 2014

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 4, 2016 VOL. 374 NO. 5

Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate

CKD Prognosis Consortium

KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES KDIGO

Transplantmodels.com

Grams et al, NEJM, 2016

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 4, 2016 VOL. 374 NO. 5

- ACR 4 mg/g
- SBP 120 mmHg
- No diabetes
- No hypertension meds
- Non-smoker
- BMI 26

Age	Base-case eGFR
20	114
30	106
40	98
50	90
60	82
70	74
80	66

Risk Modeling: Donors

Characteristic	Hazard ratio	p
Male sex (at age 40)	$_{1.49}1.91_{2.44}$	<0.001
AA race (at age 40)	$_{2.66}3.05_{4.11}$	<0.001
Age per 10y: non-AA, male	$_{1.35}1.58_{1.85}$	<0.001
Age per 10y: non-AA, female	$_{0.98}1.22_{1.52}$	0.07
Age per 10y: AA	$_{0.63}0.79_{0.98}$	0.03
BMI per 5 units	$_{1.23}1.59_{2.06}$	<0.001
Biologically unrelated	$_{0.43}0.64_{0.96}$	0.03

Transplantmodels.com

Massie/Segev, JASN, 2017

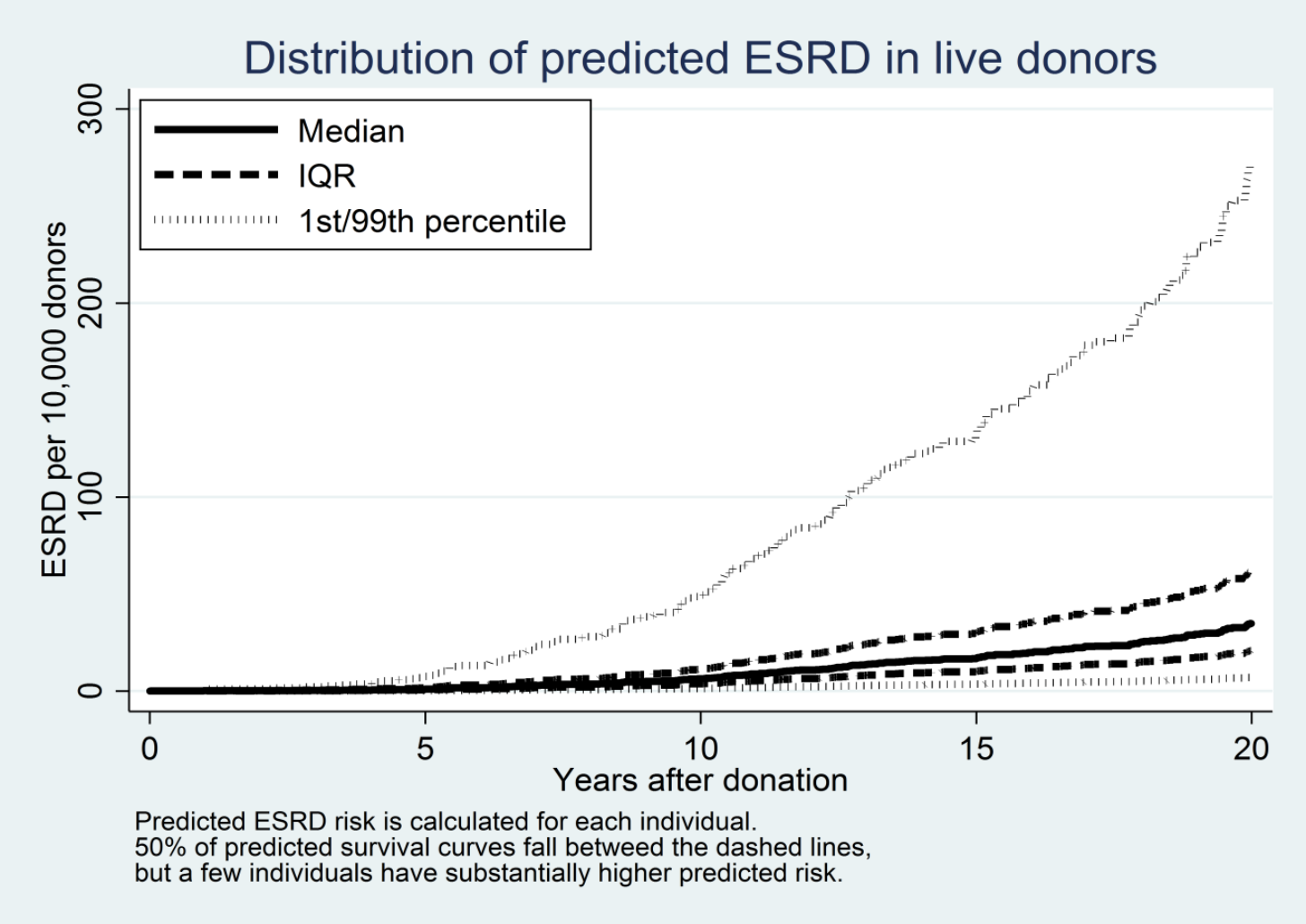
Review

OPEN

Summary of Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors

Krista L. Lentine, MD, PhD,[1] Bertram L. Kasiske, MD,[2] Andrew S. Levey, MD,[3] Patricia L. Adams, MD,[4] Josefina Alberú, MD,[5] Mohamed A. Bakr, MD,[6] Lorenzo Gallon, MD,[7] Catherine A. Garvey, RN,[8] Sandeep Guleria, MBBS, MS, DNB,[9] Philip Kam-Tao Li, MD,[10] Dorry L. Segev, MD, PhD,[11] Sandra J. Taler, MD,[12] Kazunari Tanabe, MD, PhD,[13] Linda Wright, MHSc, MSW,[14] Martin G. Zeier, MD,[15] Michael Cheung, MA,[16] and Amit X. Garg, MD, PhD[17]

Risk Modeling: Donors



Massie/Segev, JASN, 2017

Implications

- We currently allow individuals to donate who have a very wide range of ESRD risk
- We currently decline potential donors who have conditions associated with a very wide range of ESRD risk
- We currently accept donors who have much higher risks than donors who we decline
- A new data-driven risk paradigm is here

Epidemiology Research Group in Organ Transplantation

Dorry Segev, MD PhD, Founder and Director

Core Faculty

Andrew Cameron, MD PhD
Associate Professor of Surgery

Christine Durand, MD
Assistant Professor of Medicine

Jackie Garonzik-Wang, MD PhD
Director of Training and Education
Assistant Professor of Surgery

Sommer Gentry, PhD
Professor of Mathematics (USNA)

Macey Henderson, JD PhD
Director of Policy and External Affairs
Assistant Professor of Surgery & Nursing

Allan Massie, PhD
Director of Data and Analytics
Assistant Professor of Surgery and Epidemiology

Mara McAdams-DeMarco, PhD MS
Assistant Professor of Epidemiology and Surgery

Douglas Mogul, MD MPH
Assistant Professor of Pediatrics

Abimereki Muzaale, MD MPH
Instructor of Surgery

Lauren Nicholas, PhD
Assistant Professor of Health, Policy and Management

Tanjala Purnell, PhD MPH
Director of Community and Stakeholder Engagement
Assistant Professor of Surgery

Residents

Sandra DiBrito, MD, PhD

Christine Haugen, MD

Courtenay Holscher, MD

Kyle Jackson, MD

Lauren Kucirka, MD PhD

Martin Kosztowski, MD

Sharon Weeks, MD

Heather Wasik, MD

Coordinators

Jonathan Konel, MHS

Maria Lourdes Perez, DVM

Madeleine Waldram

Research Analysts

Sunjae Bae, KMD MPH

Mary Grace Bowring, MPH

Qiong (Jenny) Huang, MHS MS

Tanveen Ishaque, ScM

Xun Luo, MD MPH

Alvin Thomas, MSPH

Hao Ying, ScM

Sheng Zhou, MBBS ScM

Med/Grad Students

Jennifer Chen

Karina Covarrubias

Mayara Ivani de Paula, PharmD

Michal Mankowski, MS

Hasina Maredia

Jennifer Motter

Jessica Ruck

Ashton Shaffer

Ashley Xu, RN

Research Assistants

Full Time

Rachel Berkowitz

Jeremy Conte

Annie Eno

Weston Ernst

Ted Frederic

David Helfer

Morgan Johnson

Kathryn Marks

Alexandra Mountford

Christiana Obeng

Sarah Rasmussen

Eileen Rosello

Prakriti Shrestha

Fatima Warsame

Part Time

Shivani Bisen

Nicholas Cepeda

Giovanni Cragnotti

Sofia Cuenca-Aguierre

Maya Flannery

Scott Frankenthaler

Harpreet Gill

Alexander Hsiao

Vincent Huang

Emily Kwan

Kristin Meek

Alexis Mooney

Sanjana Murthy

Salma Tayel

Eileen Yu

Affiliates

Fawaz Al Ammary, MD
Nephrology

Dan Brennan, MD
Nephrology

Errol Bush, MD
Surgery

Josef Coresh, MD PhD
Epidemiology

Morgan Grams, MD PhD
Nephrology

Niraj Desai, MD
Surgery

Elliott Haut, MD PhD
Surgery

Jayme Locke, MD
Surgery (UAB)

Lucy Meoni, ScM
Biostatistics

Babak Orandi, MD PhD MSc
Transplant Surgery, UCSF

Aliaksei Pustavoitau, MD
Anesthesiology

Daniel Scharfstein, ScD
Biostatistics

Kim Steele, MD PhD
Surgery

Ravi Vardhan, PhD
Biostatistics