



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Evaluation of the Living Donor Candidate

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Disclosures

None related to the talk



Outline

ESRD current state

Why Kidney Transplantation?

Why Living Donor Kidney Transplant?

Donor evaluation

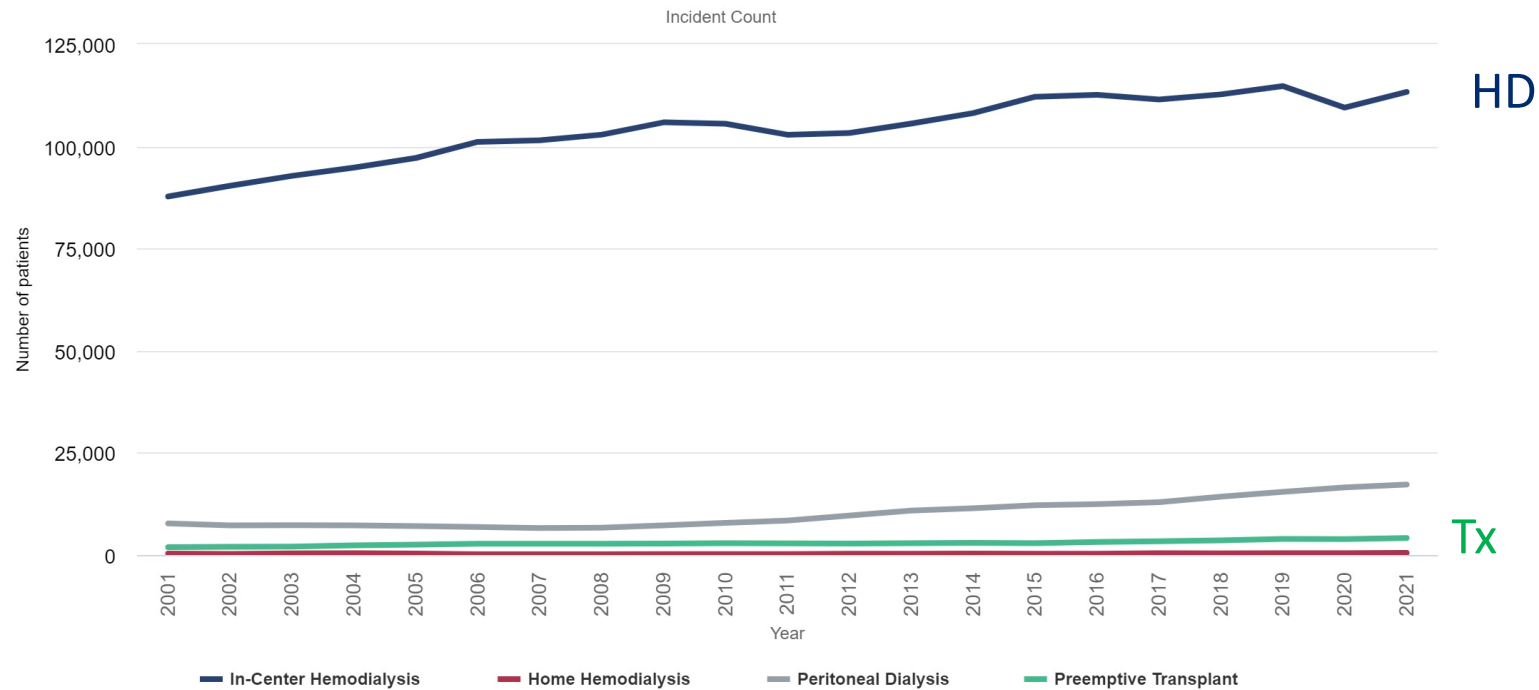
Risk of kidney donation

Questions



ESRD & Modalities

Figure 1.2 Incident ESRD by modality, 2001-2021



Data Source: 2023 United States Renal Data System Annual Data Report

>800,000 patient in the US have ESRD

83.9% start treatment with HD, 12.7 % PD, and 3.1% preemptive kidney transplant

Overall mortality: 162.6/1000 Patients-years

\$50.8 billion, accounting for 7.2% of overall Medicare paid claims



Case 1

32 year old woman presents for advice regarding CKD

- Biopsy proven IgA nephropathy 10 years ago, treated with ACEi in the past
- Creatinine 3.5 (eGFR 16), Hgb 10
- She is fatigued
- She is married and would like to have children
- She is an attorney
- Father deceased MI; mother with dyslipidemia
- BP 148/90. BMI 25. PE unremarkable
- Urinalysis 2+ heme, 5-10 RBCs



Which method to treat her renal failure should you recommend?

- a. Pre-emptive, live donor kidney transplant
- b. AVF placement, hemodialysis, followed by live donor transplant
- c. PD cath placement, PD followed by live donor transplant
- d. AVF placement, hemodialysis, followed by deceased donor kidney transplant



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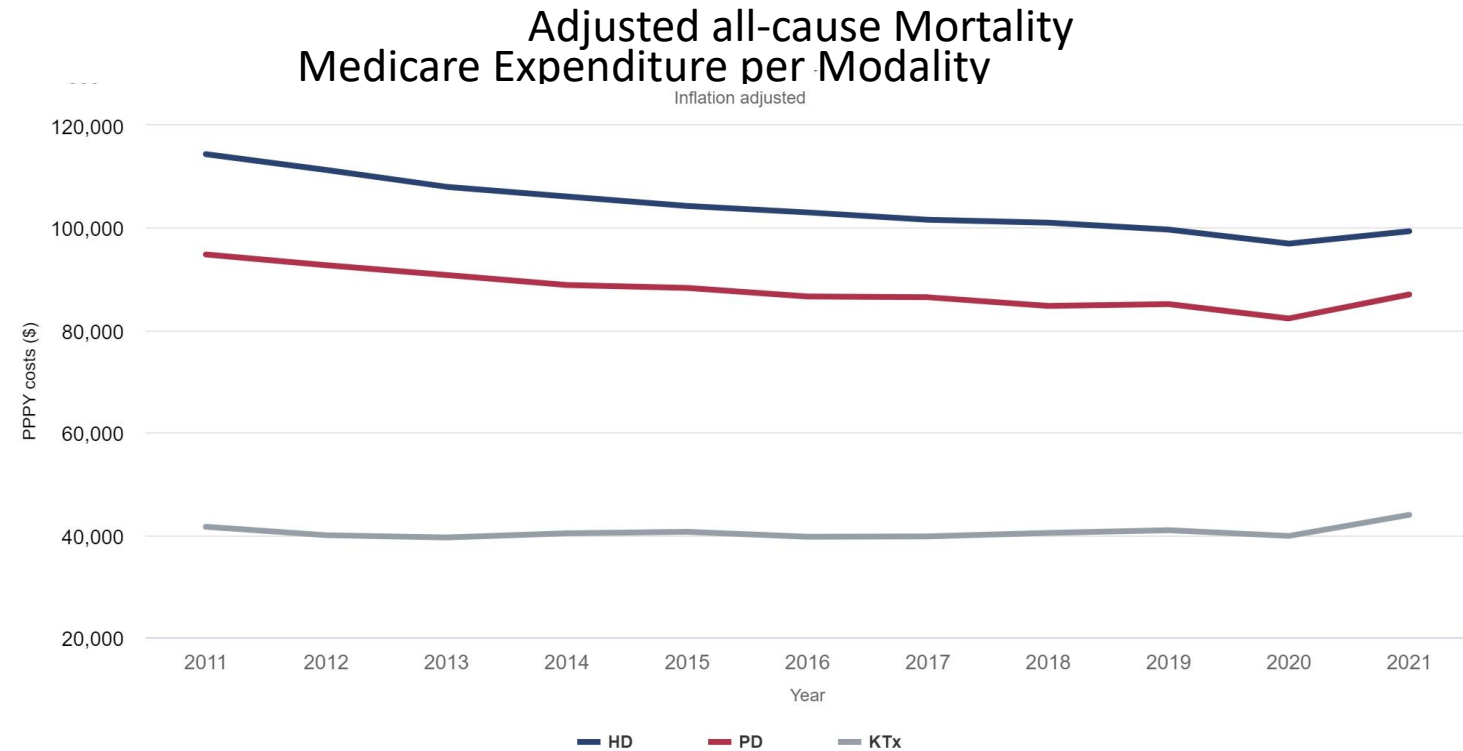


Why Kidney Transplantation?

Survival advantage

Quality of Life Advantage

Cost effectiveness



Data Source: 2023 United States Renal Data System Annual Data Report

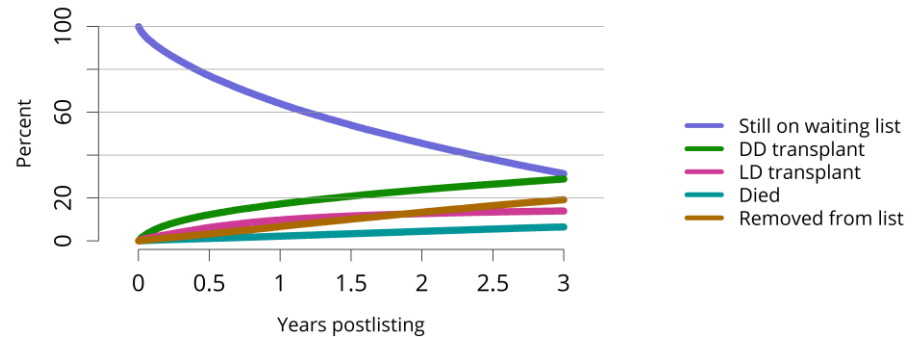


Kidney Transplant Wait List is a “First Come First Serve” model



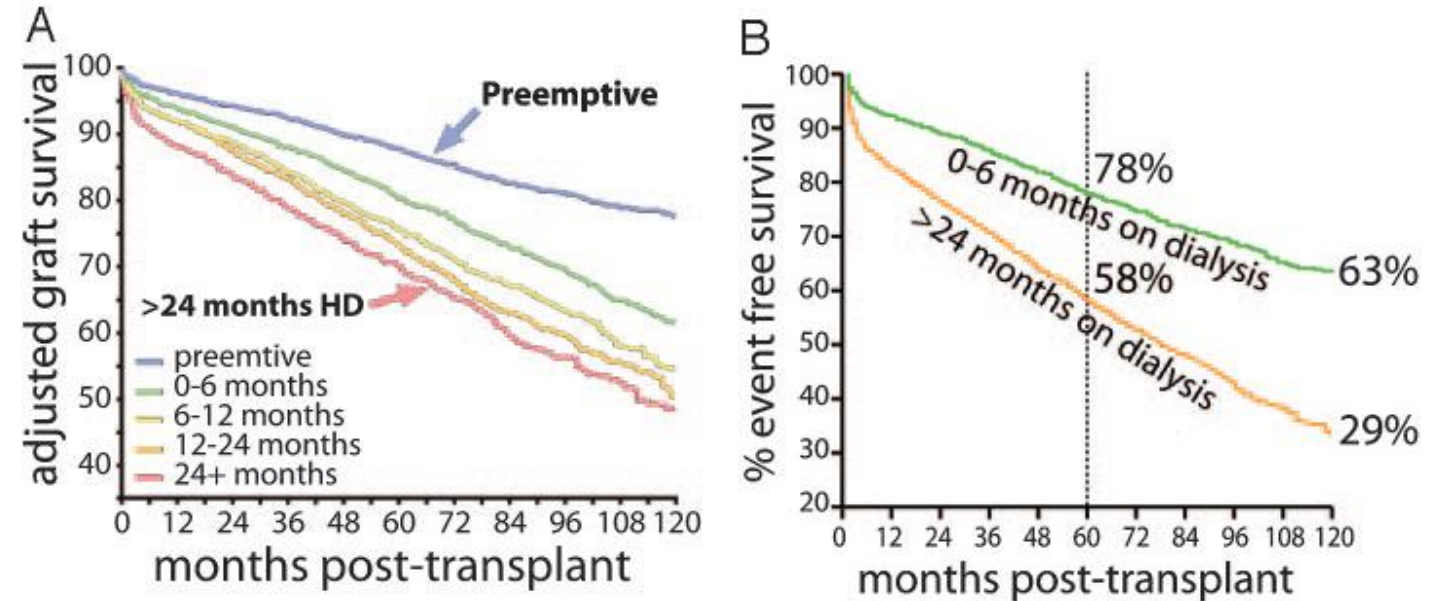
Implications of waiting on the list

Figure KI 22: Three-year outcomes for adults waiting for kidney transplant, new listings in 2017-2019



OPTN/SRTR 2022 Annual Data Report

Event Free Graft Survival at 10 years

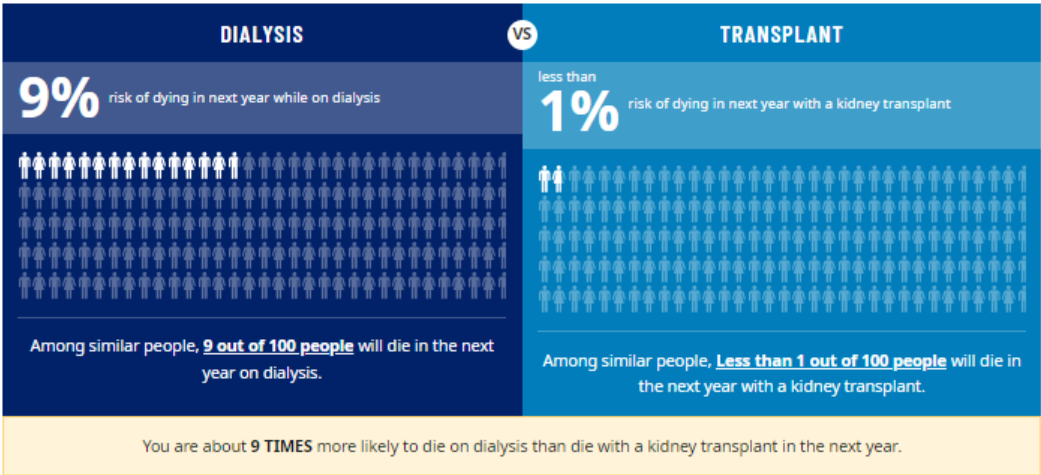


“The median time to transplant for candidates has not been calculable for more than a decade, because 50% of candidates on the waiting list have not undergone transplant since 2008.”

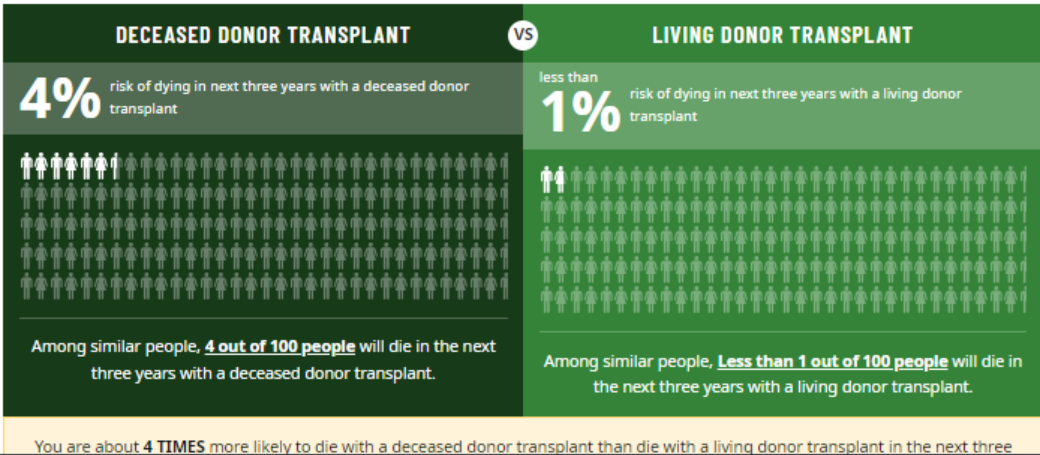
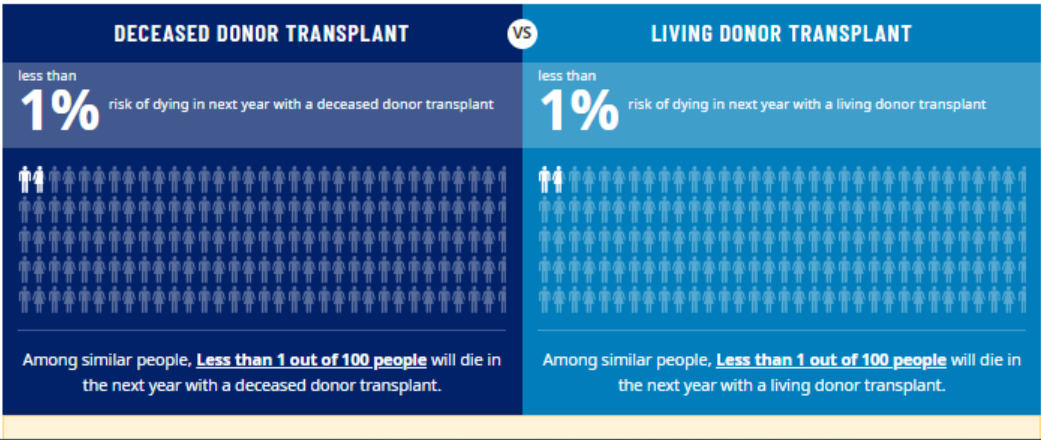
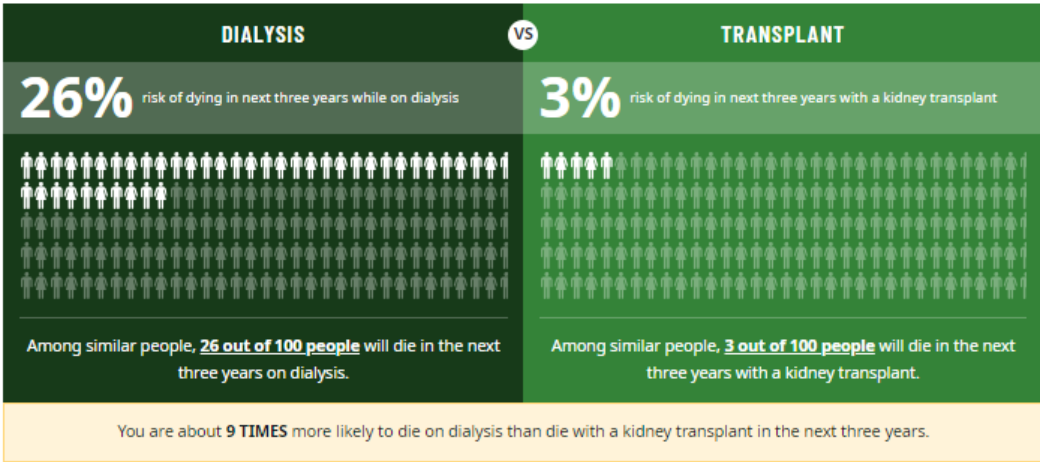


Real Life Example

1-Year Mortality Risk



3-Year Mortality Risk

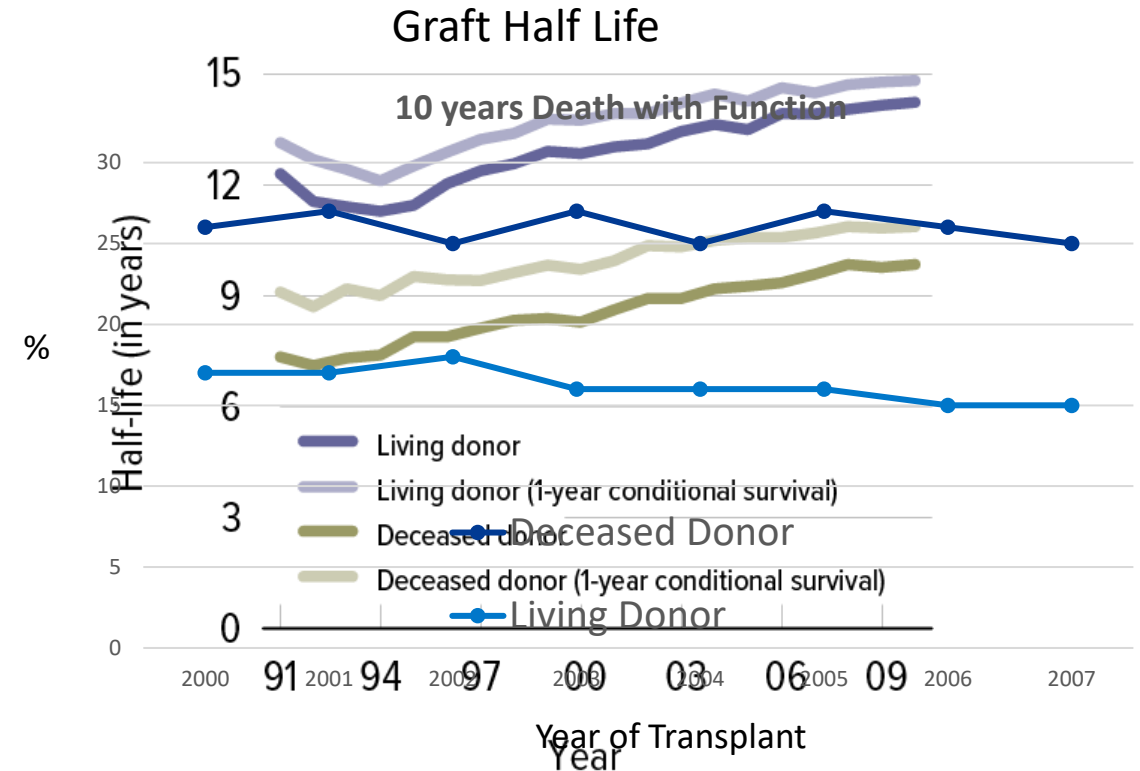


37 years old white non Hispanic man on home HD for 8 months for ESRD from diabetes comes in for evaluation.
Blood type O.



The Living Donor Kidney Tx Advantage

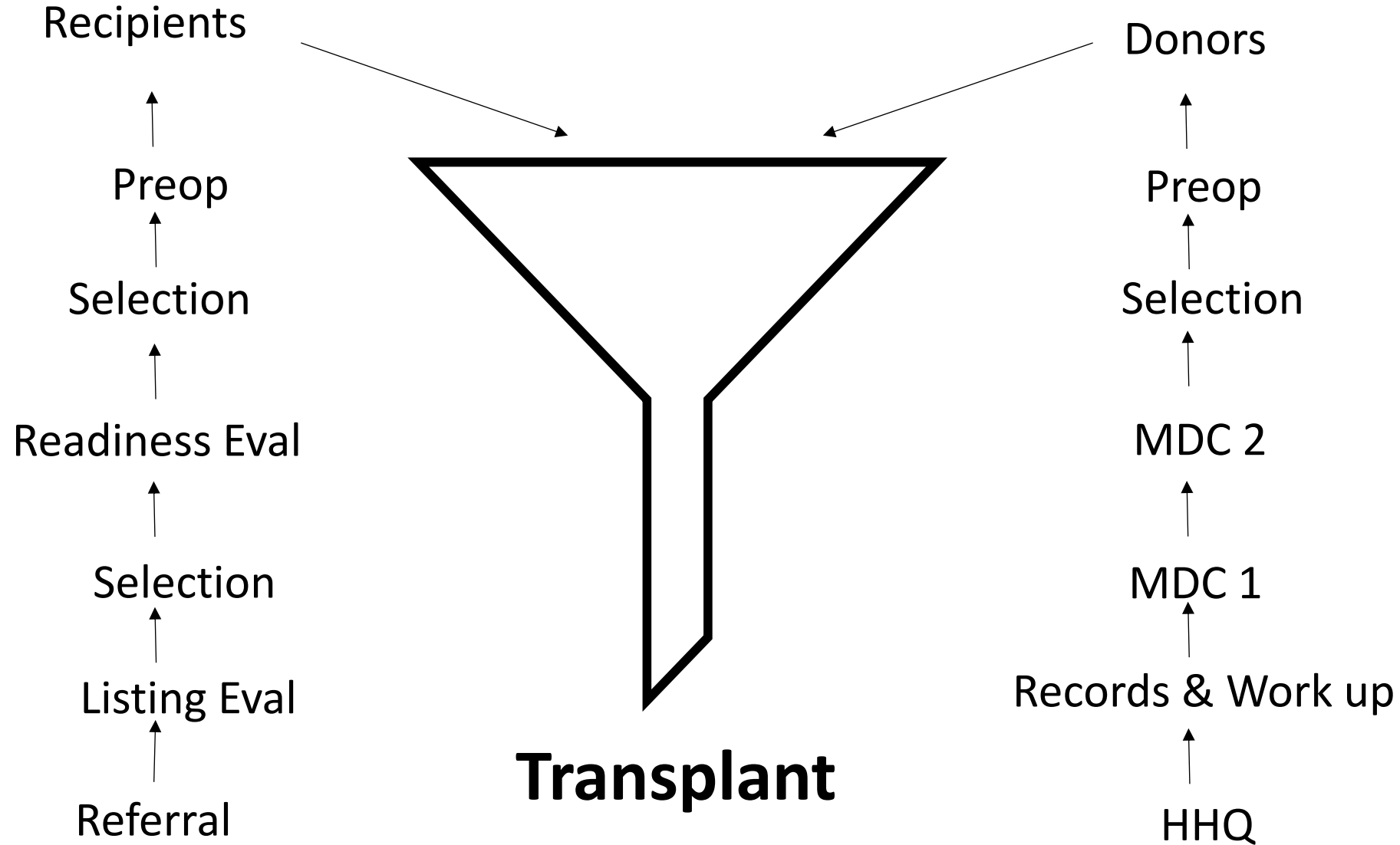
- No to little wait time
- Preemptive
- Immediate function
- Longer graft half-life
- Superior outcomes
- Elective surgery scheduled when recipient's healthy is optimal
- Allows for paired exchange for:
 - ABO-I, HLA-I, Age-I, Location-I



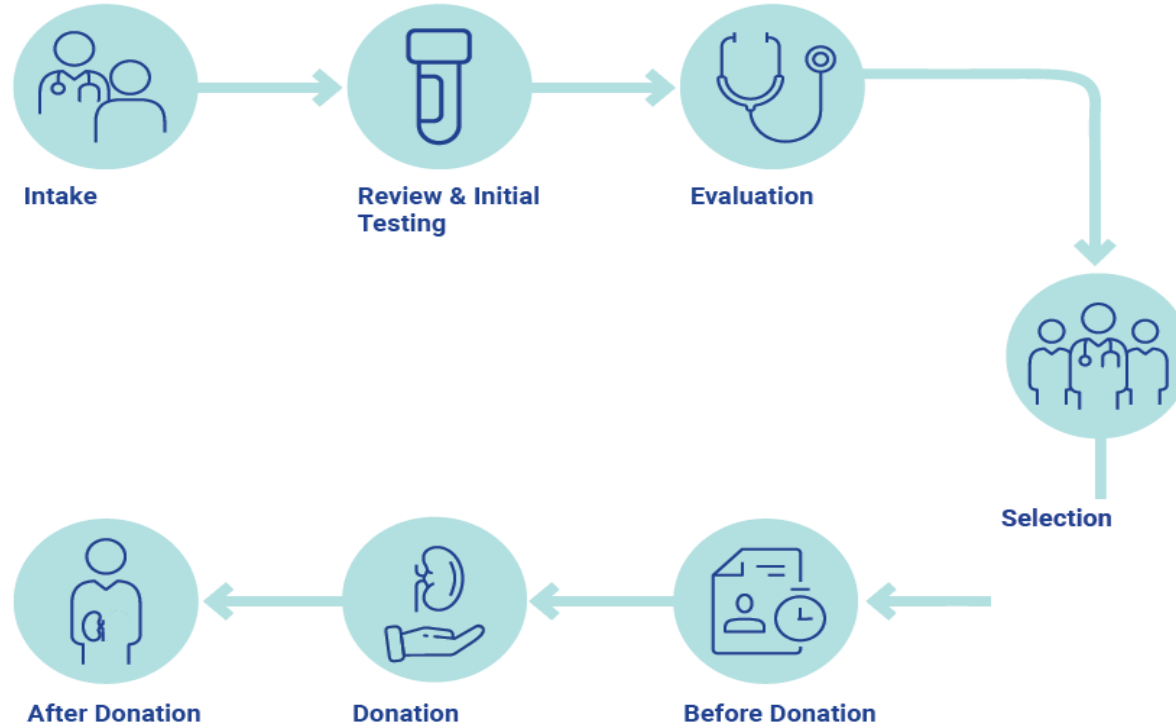
Living Donor Kidney Transplant is the only Solution for
the long wait time for an organ (at least for now)



The Living Donor Transplant Funnel



Kidney Living Donor Program Roadmap



Donor Evaluation: Records and Work up

Chemistries , fasting glucose, lipids, LFTs, CBC, Coags, B-HCG.
HgA1c or OGTT if risk factors.

ABO (2 separate occasions) & Tissue Typing

HBV, HIV, HCV, RPR; TB spot if risk factors present; EBV; CMV;

Others as needed

Urinalysis and urine protein screen

Age appropriate cancer screening (reviewed/documented)

ECG, Chest-Xray

Assessment of GFR: 24 hour urine CrCl or measured GFR

As needed: stress test; metabolic stone screen



Exclusions

Age less than 18 years (higher for non directed donors)

Mentally incapable of making informed decision

Uncontrollable hypertension, or history of hypertension with evidence of end organ damage

~~Diabetes mellitus~~ (only type 1 is now a rule out, controlled DM could be considered)

Active or incompletely treated cancer

Evidence of acute symptomatic infection (until resolved)

High suspicion of donor coercion

High suspicion of illegal financial exchange between donor and recipient

Diagnosable psychiatric conditions requiring treatment before donation, including evidence of suicidality



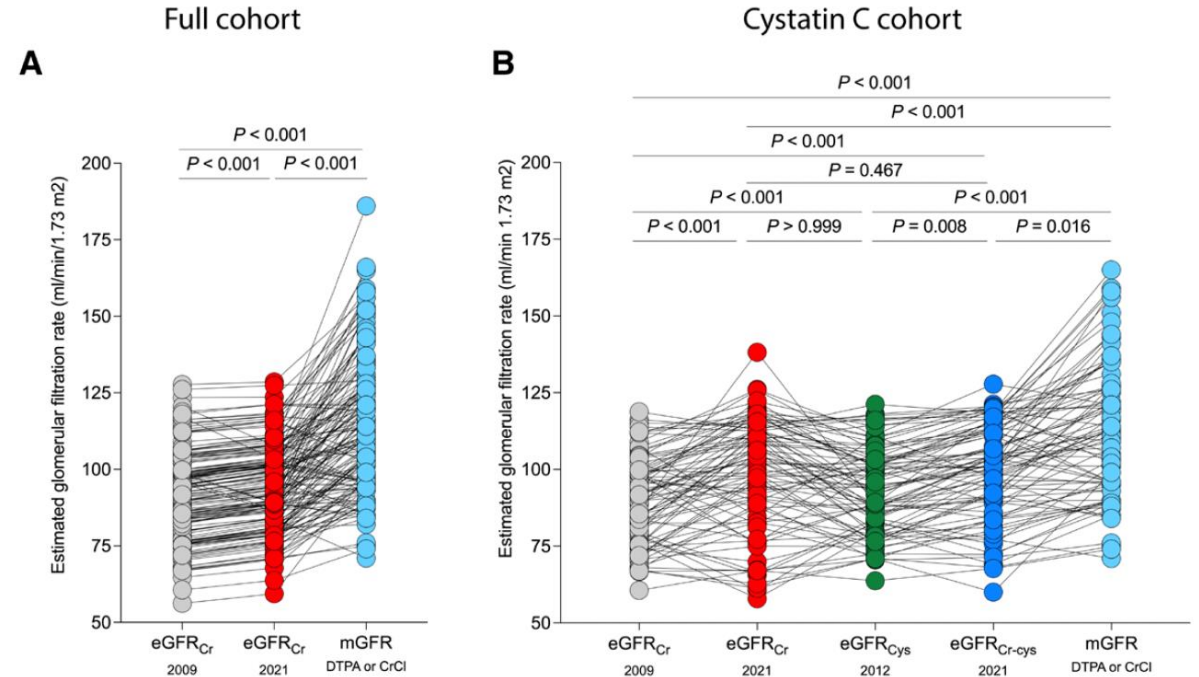
Donor GFR

Donors need adequate kidney function for themselves and recipients

- >80 ml/min/1.73 m² if >35 years old
- >90 ml/min/1.73 m² if <35 years old

Measured GFR reserved for ambiguous cases, very young or very old donors (failure for adequate collections...)

eGFR underestimates significantly GFR in healthy candidates. Should not be used for screening out donors (even the 2021 Formulas)



Multidisciplinary Clinics

Education session and consultation with trained donor coordinator

Social work evaluation

- Attempt to exclude coercion, mental illness, substance abuse. Discuss psychosocial / financial risks

Nephrology evaluation

- Consent for evaluation is signed
- Public health “Increased Risk” Disclosure signed
- H&P focusing on BP on 2 occasions; hematuria, proteinuria, diabetes risks; family history (CV/DM); NSAID use; kidney stones; malignancy

CT scan (with IV contrast)

Visit with living donor advocate

- Independent of recipient evaluation

Visit with psychiatrist, financial coordinator, dietician (as needed)

Visit with surgeon



How about risks on the donor?



Case 2

45 year-old man presents for advice about donating a kidney to his 50 year old brother and specifically his post-donation risks of ESRD and the benefits to his brother who has CKD 5 due to DM1

Potential donor:

- No medical problems
- Takes no medications
- Father with HTN; Mother is healthy
- BP 118/78. PE is normal.
- 24 hour creatinine clearance is 136 ml/min/1.73
- No protein in his urine



Which of the following are true?

- a. He should avoid live donation which is unsafe; a DDKT is adequate for a diabetic
- b. He should definitely donate, there are no risks to live donation
- c. Live kidney donation comes with a small risk of perioperative mortality and a small increased risk of ESRD post-donation, risks most donor candidates gladly accept
- d. Most live kidney donors regret their decision to donate



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HEALTH NEWS

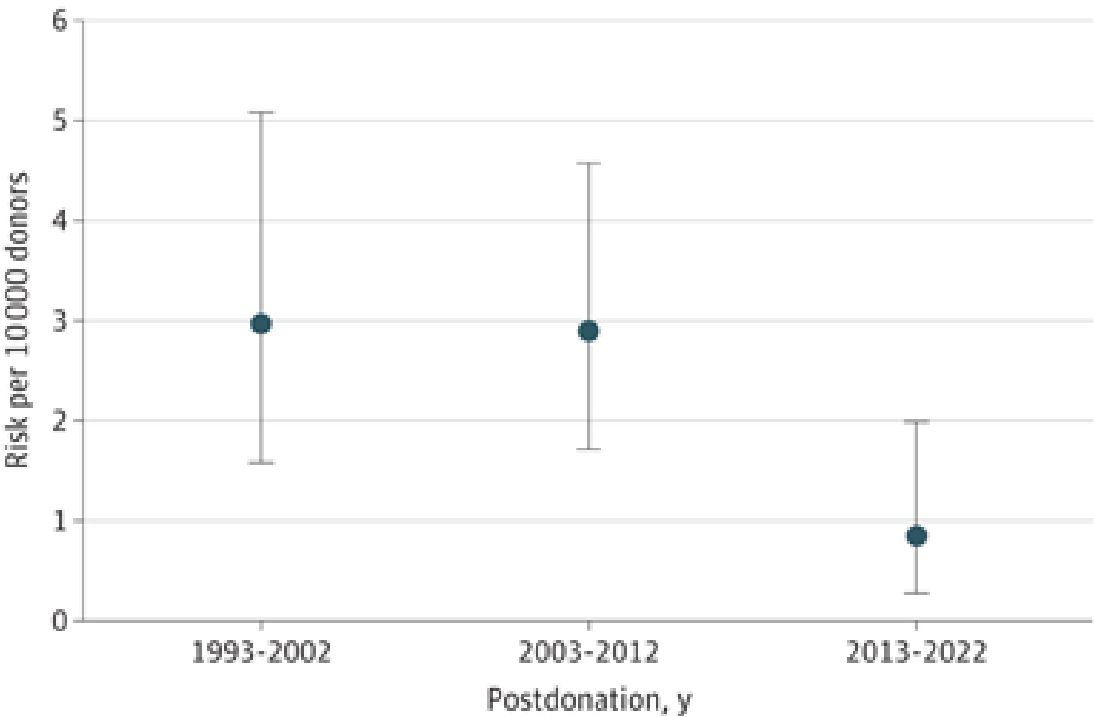
Donating a kidney is safer than ever, reassuring research finds

The overall risks for a kidney donor have always been low, but advances in surgery and medical care, along with more careful donor selection, have improved the odds even more.

Peri-o- and 1-Year Mortality

Perioperative mortality 1/10,000

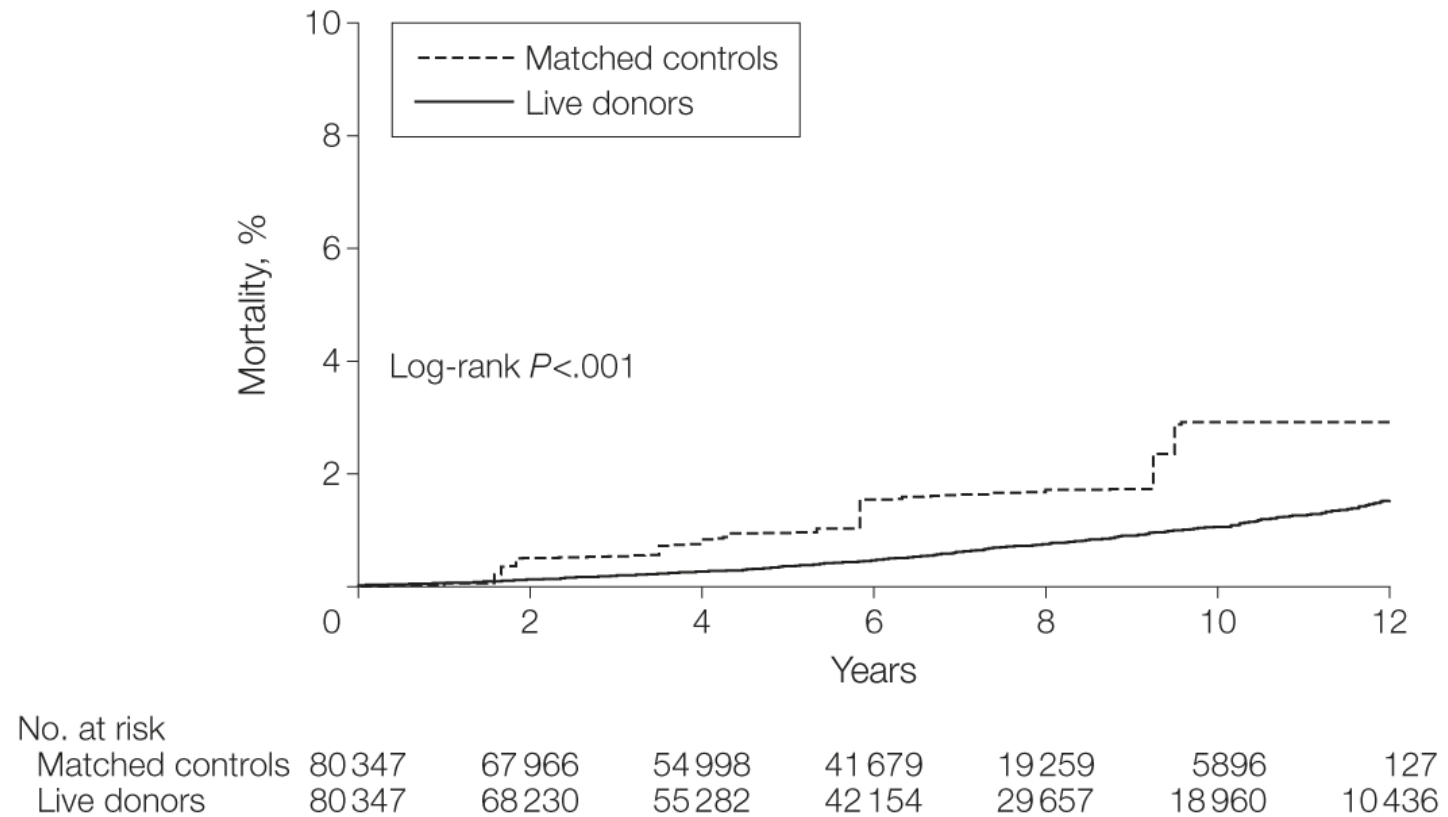
90-d Mortality risk by era



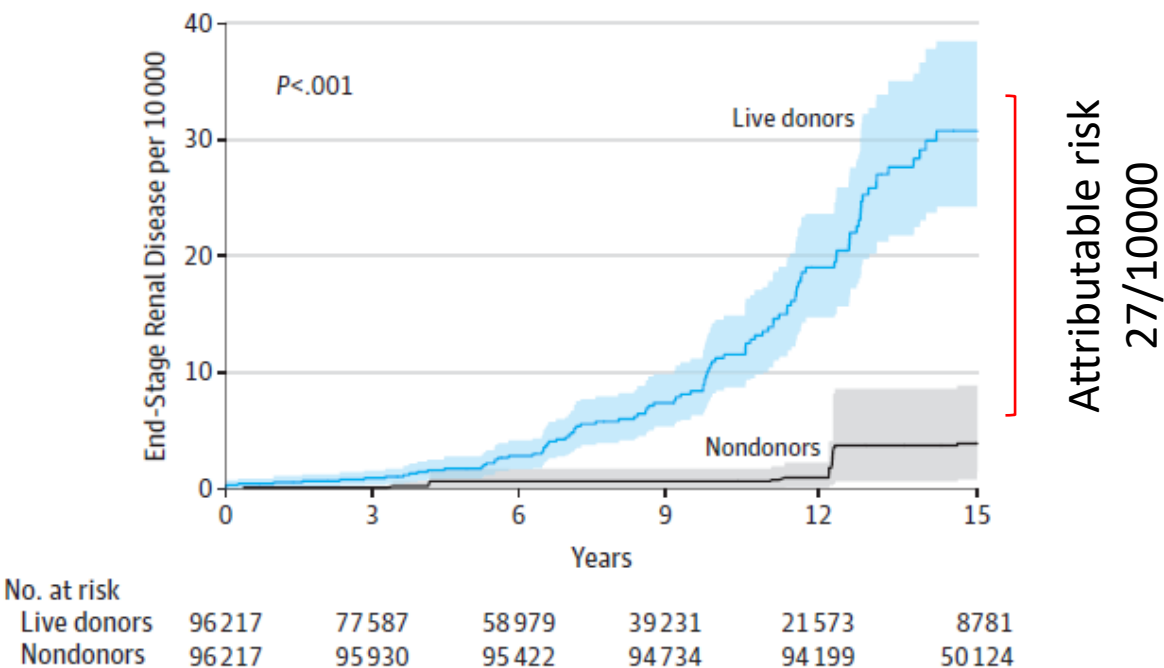
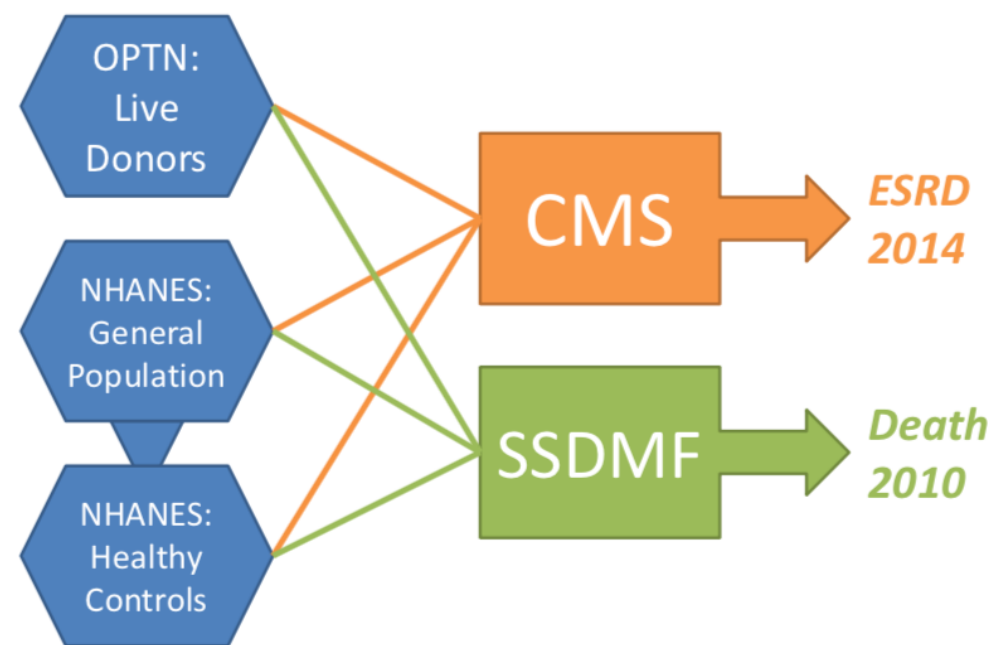
	Timing of death	Primary attributable cause(s) of death ^a
Kidney donors	Within 24 h	Bleeding (surgical)
		Bleeding (surgical)
		Bleeding (surgical) + Other medical
	24 h to 1 wk	Bleeding (surgical)
		Other medical: Unknown
	1 wk to 1 mo	Other surgical: pulmonary embolus
	3 mo to 1 y	Other medical: Auto accident
		Other medical: Psychological
		Other medical: Suicide
		Other surgical + Other medical: Overdose on psych meds 6 months postdonation
	>1 y	Cardiac (medical)
		Other medical: Accident
		Other medical: Trauma
		Other medical: Alcohol overdose
		Other medical: Suicide
		Other surgical: Bowel injury and perforation
		Cardiac (medical) + Other medical: unknown



Long-term Survival



15 Years ESRD Risk in Live Donors



ESRD. 30.8/10,000 vs 3.8/10,000



Risk of Pregnancy in Live Kidney Donors

- 60% of living donors are women
- Physiologic adaptation of the kidneys during pregnancy
- Is donation associated with higher pregnancy risks?

Outcome	Pregnancies in Donors (N = 131)	Pregnancies in Nondonors (N = 788)	Odds Ratio (95% CI)	P Value*
<i>no. of events (%)</i>				
Primary outcome: gestational hypertension or preeclampsia	15 (11)	38 (5)	2.4 (1.2–5.0)	0.01
Secondary outcomes				
Gestational hypertension†	7 (5)	17 (2)	2.5 (0.9–6.5)	0.06
Preeclampsia	8 (6)	21 (3)	2.4 (1.0–5.6)	0.05
Cesarean section	41 (31)	224 (28)	1.2 (0.7–2.1)	0.44
Postpartum hemorrhage	≤5 (≤4)‡	24 (3)	0.9 (0.3–2.9)	0.91
Preterm birth with gestation of <37 wk	10 (8)	52 (7)	1.2 (0.5–2.5)	0.70
Low birth weight of <2500 g	8 (6)	31 (4)	1.7 (0.7–4.0)	0.21

Retrospective: Ontario Canada; 1992-2010:

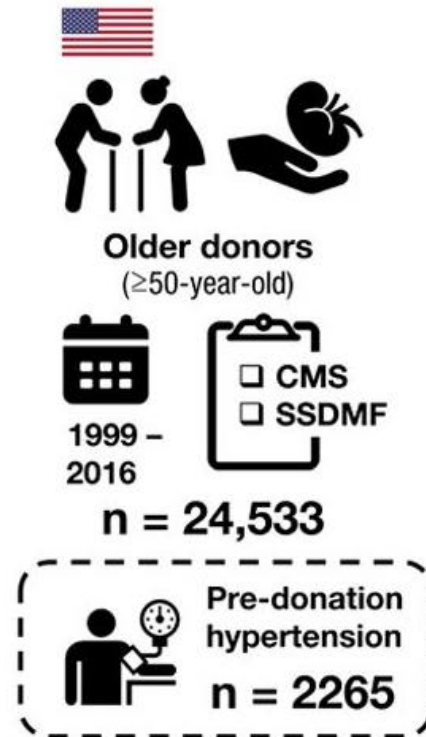
Women donors (n=85); Matched healthy non-donors (n= 510)

16 studies were identified, with a total of 1399 post-donation pregnancies. The absolute risk of pre-eclampsia increased from ~1%–3% pre-donation (lower than the general population) to ~4%–10% post-donation (comparable to the general population).



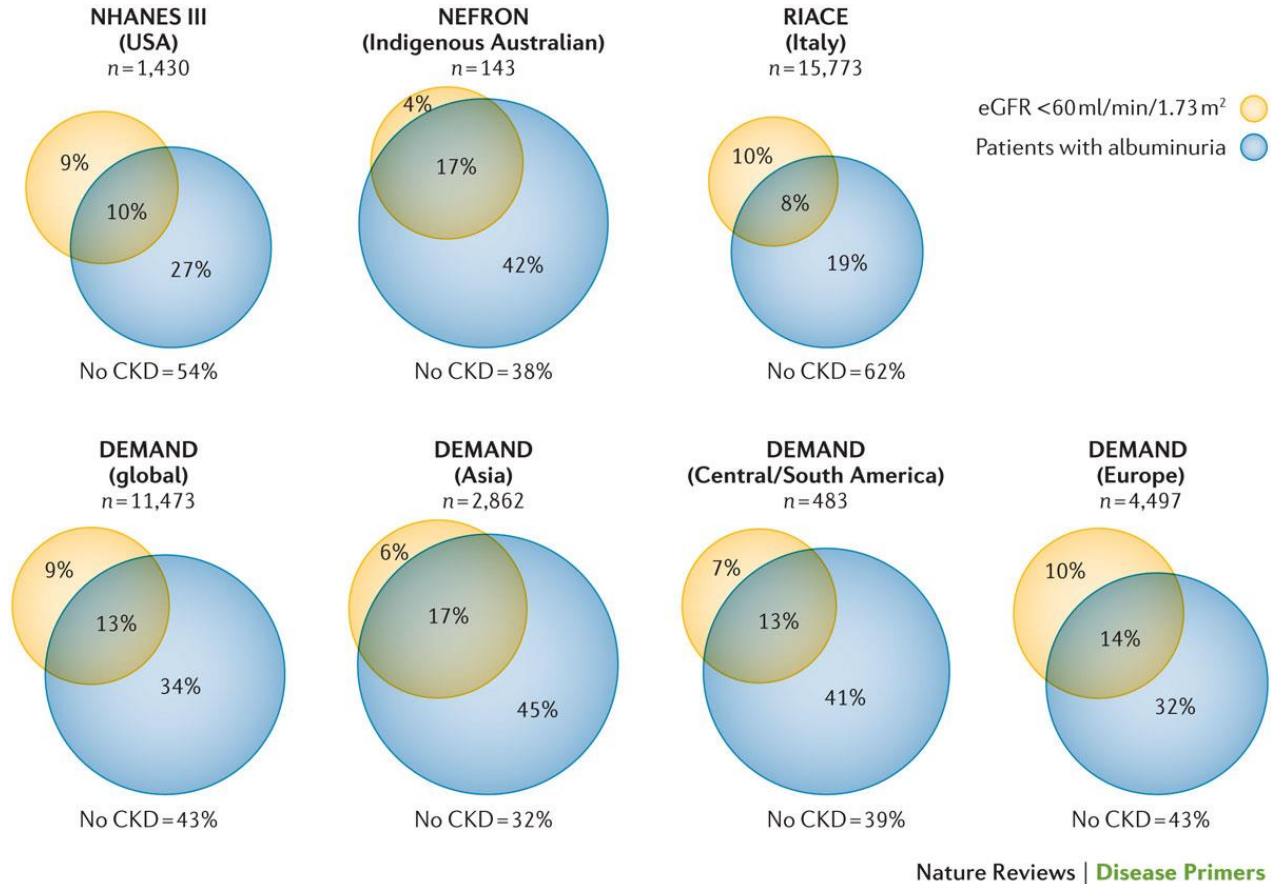
Donors with hypertension

- Generally acceptable if > 50 years old with a controlled BP and without end-organ damage evidence (LVH, albuminuria)...
- Recent data suggest increased risk of ESRD (absolute risk is still low) but mortality is similar
- Partnership with patient's PCP is critical for long term follow up with



15-years risk 0.8% in Donors with hypertension vs. 0.2% in Donors without hypertension

The Donor Candidate with Diabetes



Risk factors for Kidney disease:

Non-modifiable

- Young age at onset, increasing age, prolonged duration, genetics, ethnicity, FH of diabetes

Modifiable

- Poor Glycemic Control, HTN, DL, Obesity, Smoking, Hyperuricemia

The prevalence of CKD in different populations with type 2 diabetes



The Donor Candidate with Diabetes

We Continue to exclude type 1 diabetic patients and exclude those with type 2 only if they have any of the below criteria:

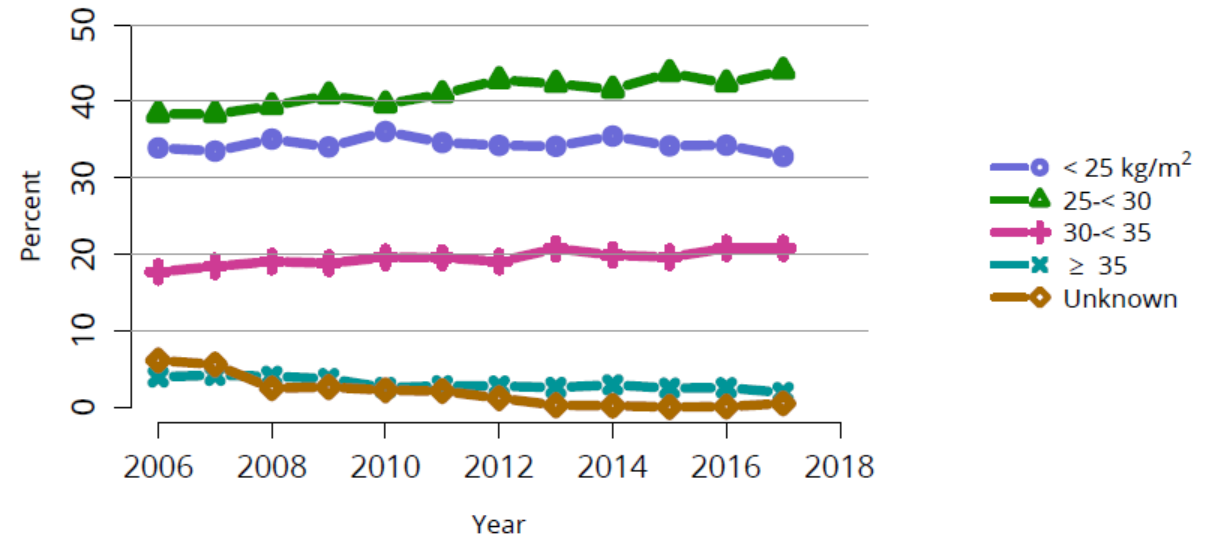
- <50 years old
- BMI >30
- Albuminuria, neuropathy, or retinopathy
- Associated metabolic syndrome: LDL > 100, gout, HTN, or steatosis of the liver
- HbA1C >7
- Family history of diabetic kidney disease

Donors who have diabetes and end up donating a kidney will need a HbA1C added to the 6 months, 1 year, and 2 years labs



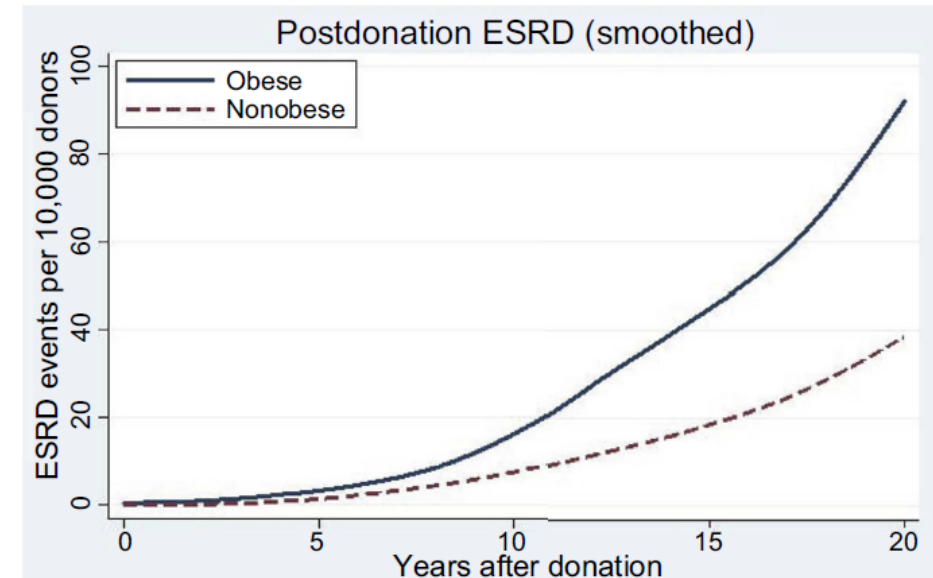
High BMI

- > 25% of LD are now considered obese vs 8% in the 1980s
- Most center criteria are a decline if BMI > 35
- Work on a target of BMI of 32 at the time of donation
- One of the instances where donor get medical benefit as they could be very motivated to donate and manage to lose significant amount of weight



The donor with High BMI-What are the risks?

- Close to 120K donors with max follow up of 20 years linked to CMS data base
- Risk goes up as of BMI of 27
- Absolute risk continue to be low but candidates need to be informed
- Authors emphasized on pre donation weight loss programs

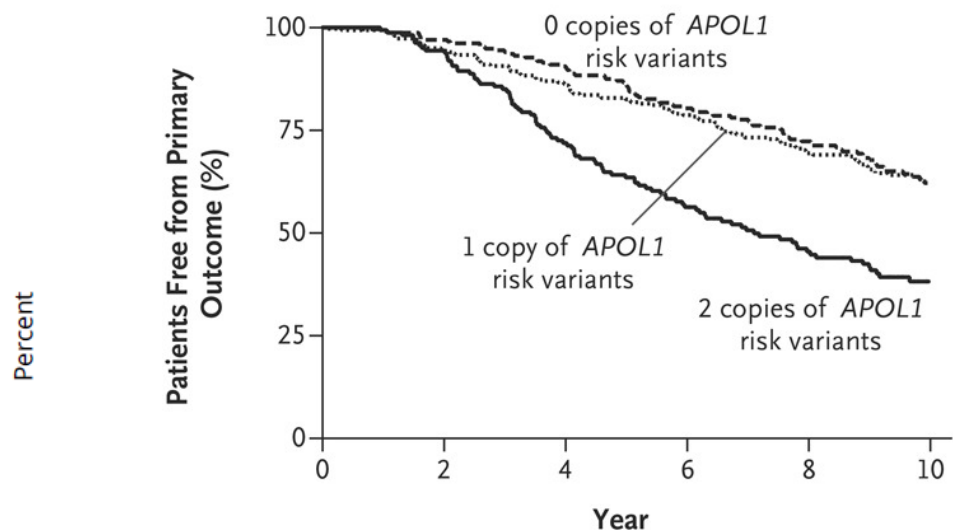


Obesity status	5 yrs	10 yrs	15 yrs	20 yrs
Obese (BMI ≥ 30 kg/m ²)	3.2	15.2	42.5	93.9
Nonobese (BMI < 30 kg/m ²)	1.0	7.4	17.5	39.7

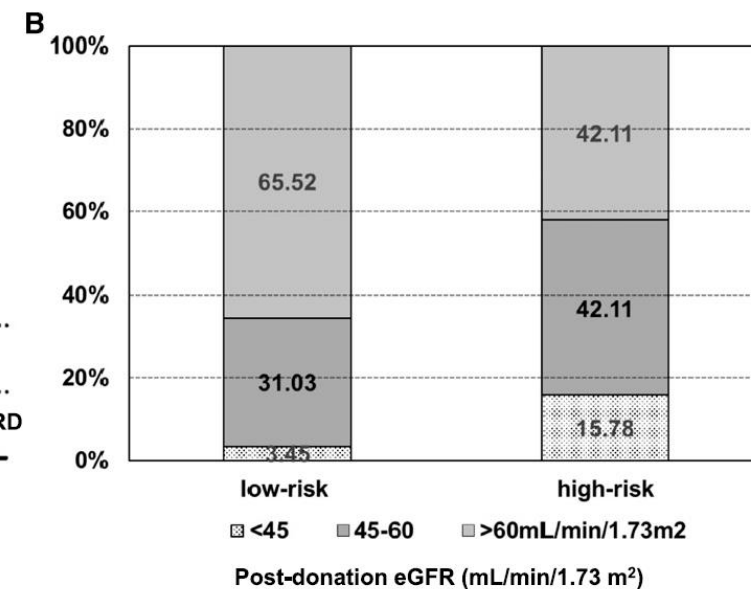
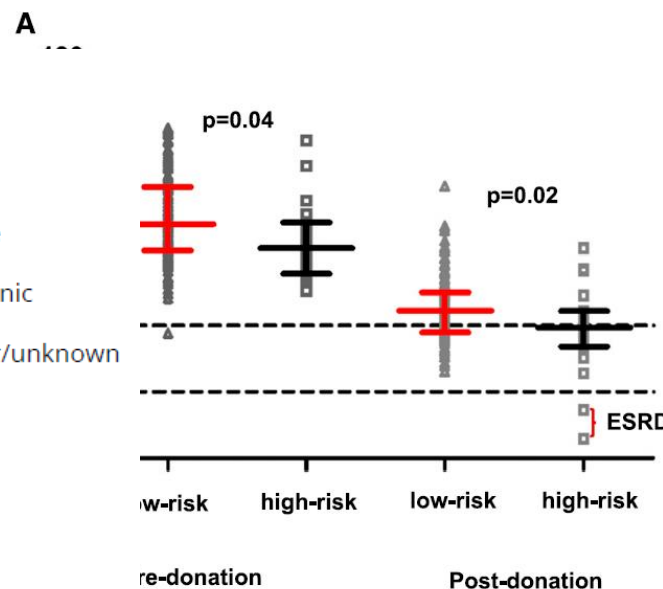
Multiple imputation Analysis



The APOL-1 question: To test or not to test?



No. at Risk						
0 <i>APOL1</i> variants	234	225	208	177	146	80
1 <i>APOL1</i> variants	299	283	254	223	179	111
2 <i>APOL1</i> variants	160	151	114	85	61	30



- Suspect a genetically inherent increased risk of ESRD in donors of African Descendance who are homozygote for APOL1 risk allele
- The association is far from universal!
- Routine pre-screening practice is center dependent without clear guidelines



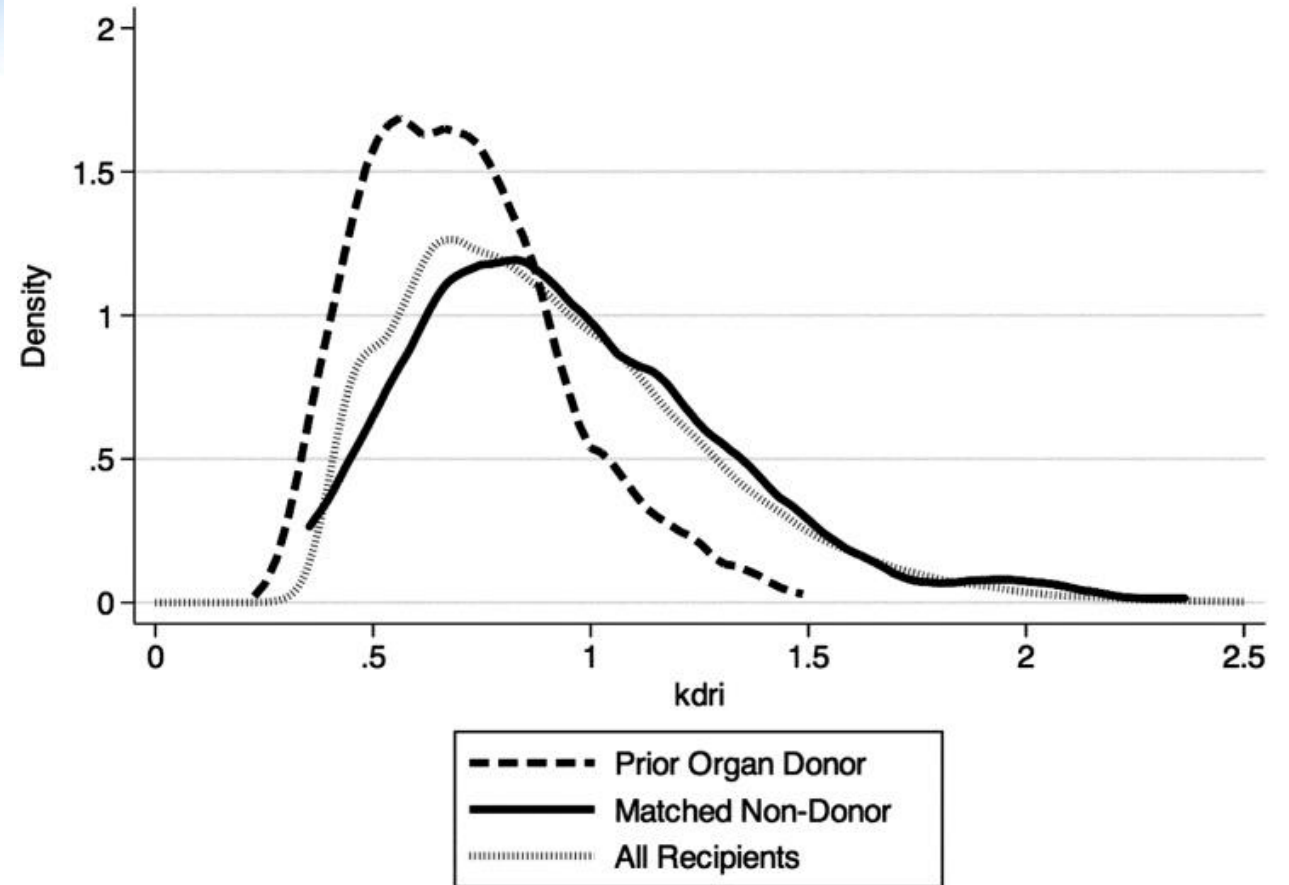
The APOL-1 question: To test or not to test?

- Young candidates, related to the recipients, who have high risk alleles are discouraged from donation
- Older candidates without hypertension or proteinuria, unrelated to the recipients, are explained the risks. APOL1 testing is done if the candidates wish to do so
- Shared decision making with the donor candidate
- APOLLO study (NCT03615235) enroll 5000 subjects looking at living donors and recipient (DDKT or LDKT) outcomes-



What's the plan B?

Sequence A KDPI ≤20%	Sequence B KDPI >20% but ≤35%	Sequence C KDPI ≥35% but ≤85%	Sequence D KDPI >85%
Highly Sensitized 0-ABDRmm (top 20% EPTS) Prior living donor	Highly Sensitized 0-ABDRmm Prior living donor Local pediatrics	Highly Sensitized 0-ABDRmm Prior living donor Local	Highly Sensitized 0-ABDRmm Local + Regional National



Section 301 of the National Organ Transplant Act (NOTA)
*“ * * * [i]t shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce.”*

Financial Burden

Travel Cost
Time off for work up cost
Out of work/loss of wages
Difficulty getting life insurance

Available Help

- Some states offer tax credits
- Donors get 30 days paid time off
- National Living Donor Assistance Center (funded by HRSA...)
- H.R.1270 - Living Donor Protection Act of 2023 (introduced bill, for the 6th time)



Other not so straightforward scenarios

- History of kidney stone
- History of cured breast cancer
- History of mental illness
- History of substance abuse
- Lack of support
- Prediabetes or strong family history of diabetes
- Liver steatosis
- Latent TB or previous HCV
- Mild atherosclerosis
- Multiple vessels
- Asymmetric kidney size/volume on imaging
- International living donors



Most Challenging Situation: No Candidates at all

- Multifaceted barriers
- A lot of myths and misconceptions (risk, cost, perfect match,....)
- Partnership with transplant centers, community, scientific body, and media need to happen to increase awareness
- Monthly Webinar example @ MGH (MD + Coordinator + SW + Peers)



The screenshot shows the website of the Massachusetts General Hospital Transplant Center. The header includes the hospital's name and logo, along with navigation links for 'The Mass General Difference', 'Conditions & Treatments', 'Patients & Visitors', and 'Research & Innovation'. A search bar is located in the top right corner. Below the header, a dark blue navigation bar contains links for 'Transplant Center', 'About Us', 'Transplant Programs', 'Center for Transplantation Sciences', 'Research & Clinical Trials', 'Education & Career Opportunities', and 'Patient Resources'. The main content area features a large heading for the 'Event Series: How to Find a Living Kidney Donor'. Below this, the 'About the Series' section describes the center's commitment to providing quality care and support, and introduces a new virtual education series called 'How to Find a Living Kidney Donor'. A list of topics to be covered in the series is provided, including common myths, leveraging social media, and finding additional resources. A link to a 'Guide to Finding a Living Donor (PDF)' is also present. The 'Schedule' section is partially visible. On the right side, there are social media icons for Facebook, Twitter, LinkedIn, and YouTube. Below these, a 'Learn More' section contains buttons for 'Register for an upcoming event' and 'Email us'. Further down, a 'Living Kidney Donor Program' section describes the act of donating a kidney and provides a link to 'Become a living donor'. At the bottom, an 'FAQs About Kidney Living Donation' section mentions that the team answers common questions about becoming a living kidney donor.

Ethical Considerations



AUTONOMY

Making
informed
decision



BENEFICENCE

QOL
Benefits
for donors



NONMALEFICENCE

Short and
long-term
risks



JUSTICE

Equal and
equitable
access



In summary,

- Living donor kidney transplantation is the superior modality to treat ESRD
- Living donation is relatively safe, risk or perioperative mortality is very low but not zero, donors are at a slight increased risk of developing ESRD
- Consent and careful selection are needed
- Controlled HTN or Diabetes isolated without complications are OK
- Resources are being made available to living donors to overcome financial burden



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Thank You

