

# KIDNEY TRANSPLANTATION FOR THE INTERNIST

**Marc Richards MD**

**South Florida Kidney Disease and  
Hypertension Specialists**

**BRRH Grand Rounds 5.8.2018**

# Goal of Lecture:



# OUTLINE

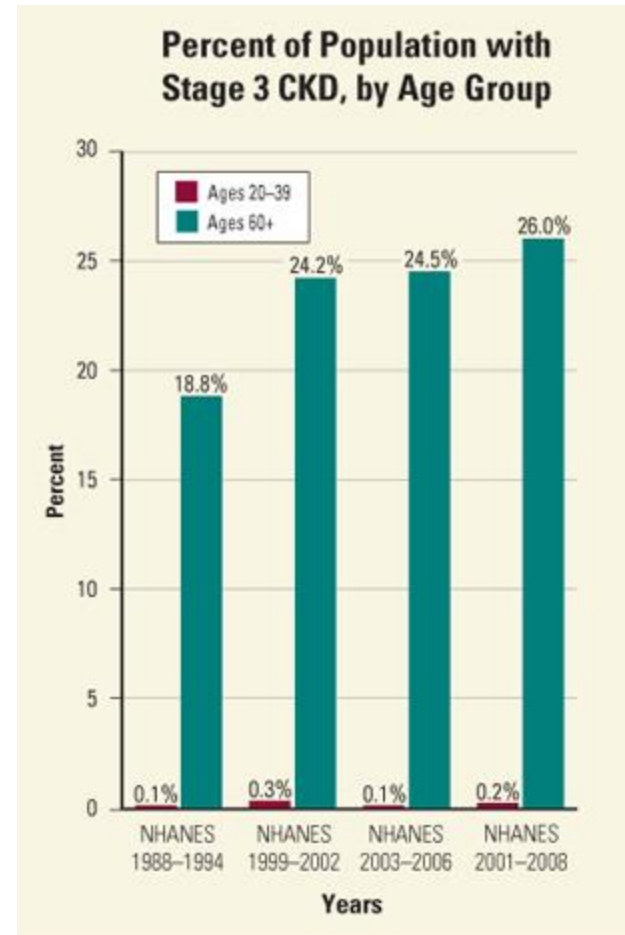
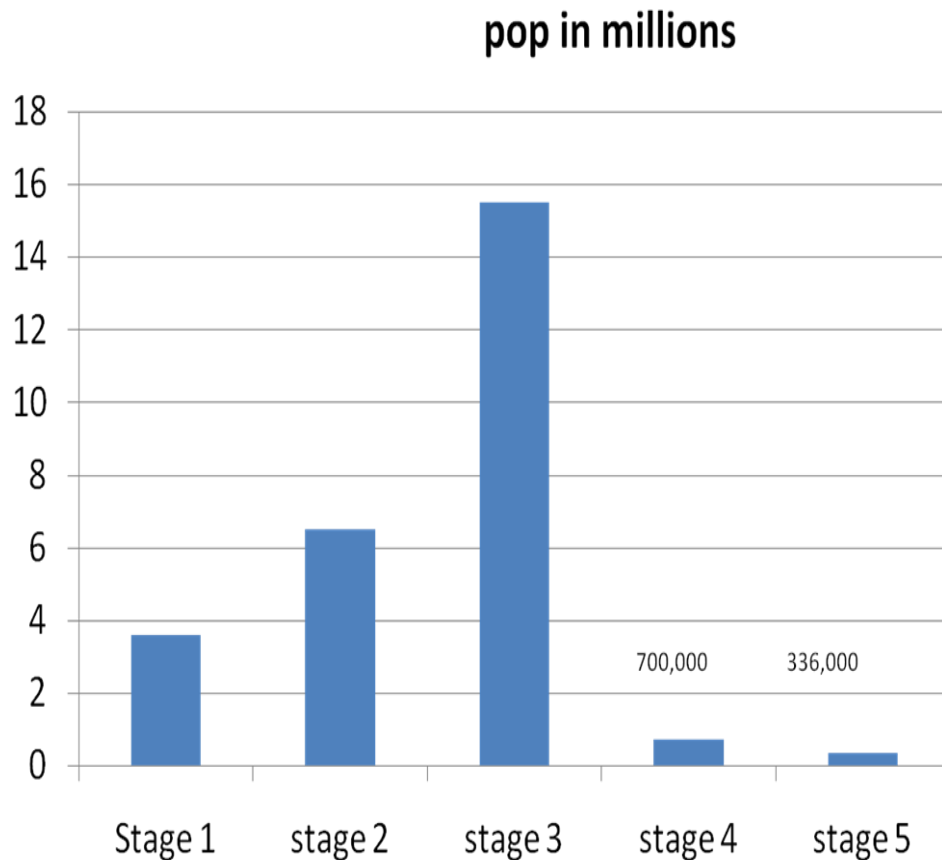


- CKD -> ESRD
- Workup for Transplant
- UNOS Registry
- Immune Suppression
- Infectious Complications
- Noninfectious Complications
- Prognosis

# CKD STAGES

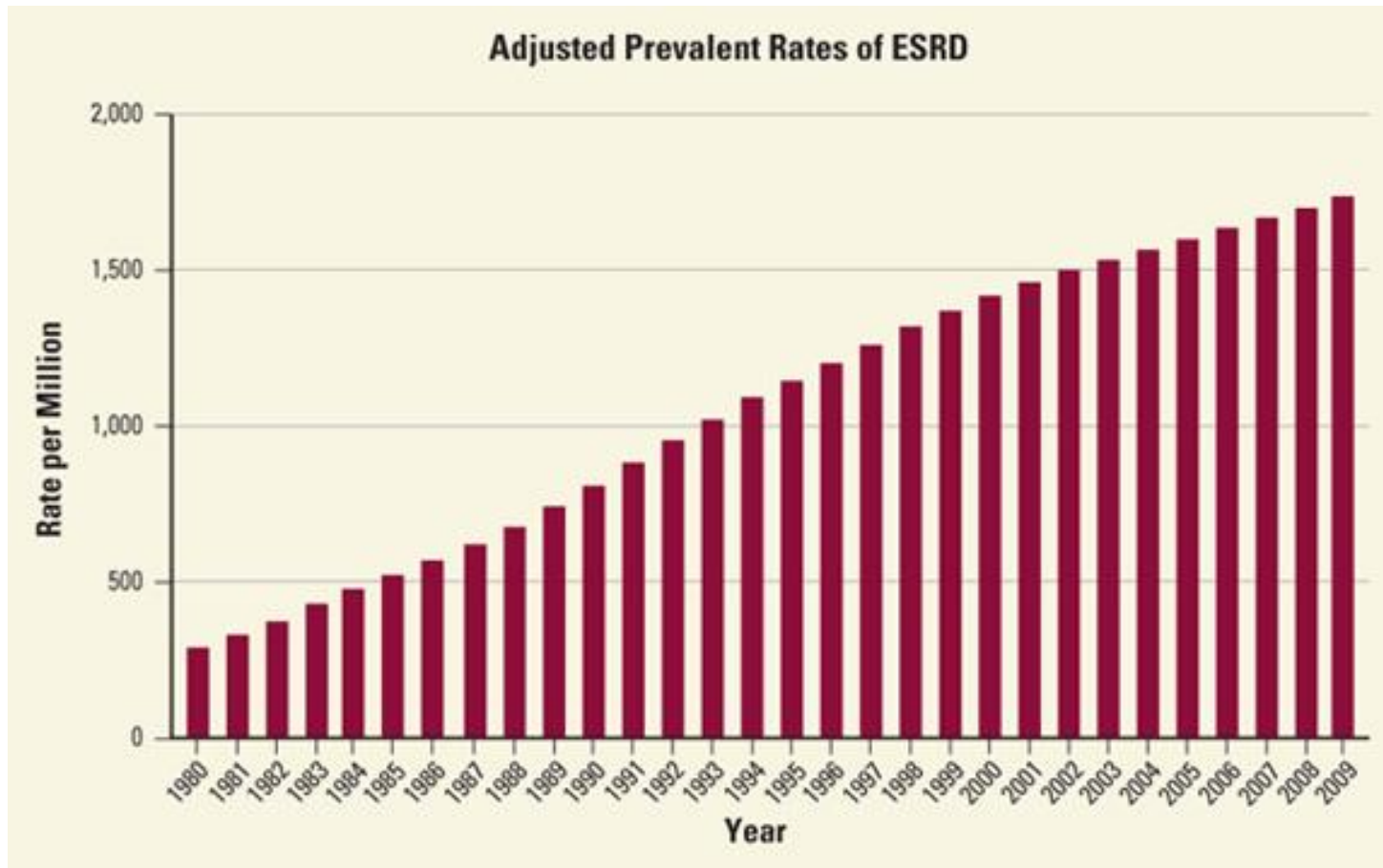
				Persistent Albuminuria Categories, Description and Range		
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g (<3 mg/mmol)	30-300 mg/g (3-30 mg/mmol)	>300 mg/g (>30 mg/mmol)
GFR Categories (mL/min/1.73 m <sup>2</sup> ) Stage, Description, and Range	1	Normal or high	≥90	1 if CKD	1	2
	2	Mildly decreased	60–89	1 if CKD	1	2
	3a	Mildly to moderately decreased	45–59	1	2	3
	3b	Moderately to severely decreased	30–44	2	3	3
	4	Severely decreased	15–29	3	3	4+
	5	Kidney failure	<15	4+	4+	4+

# CKD/ESRD Prevalence



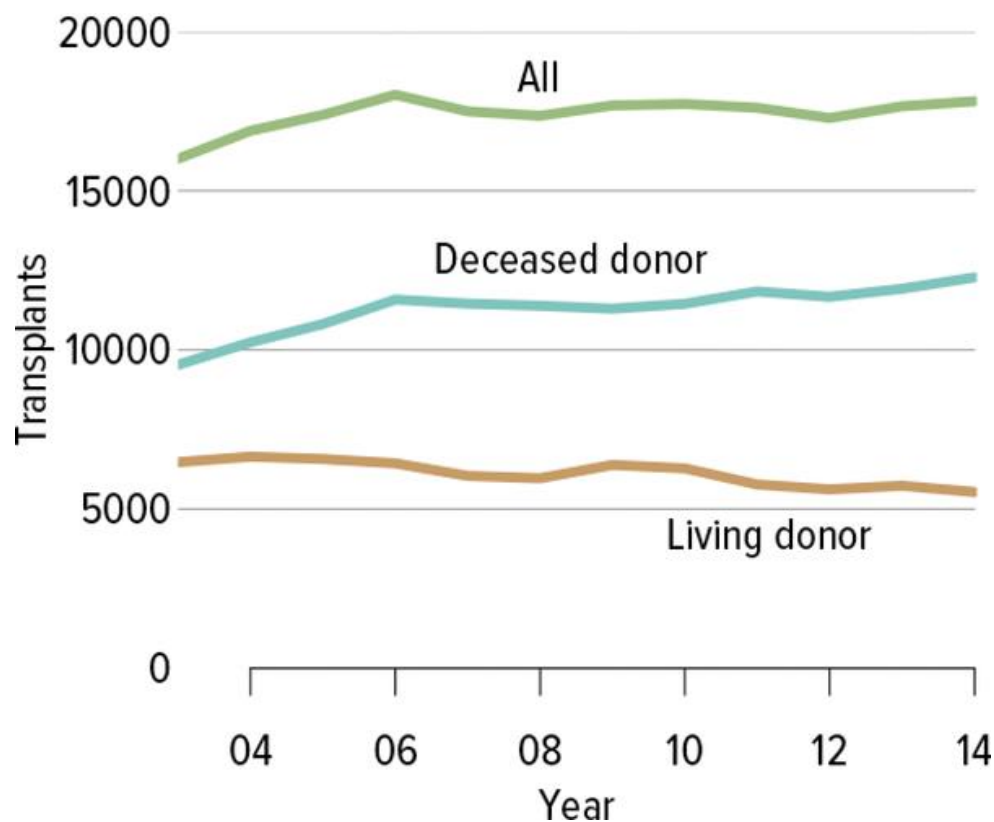
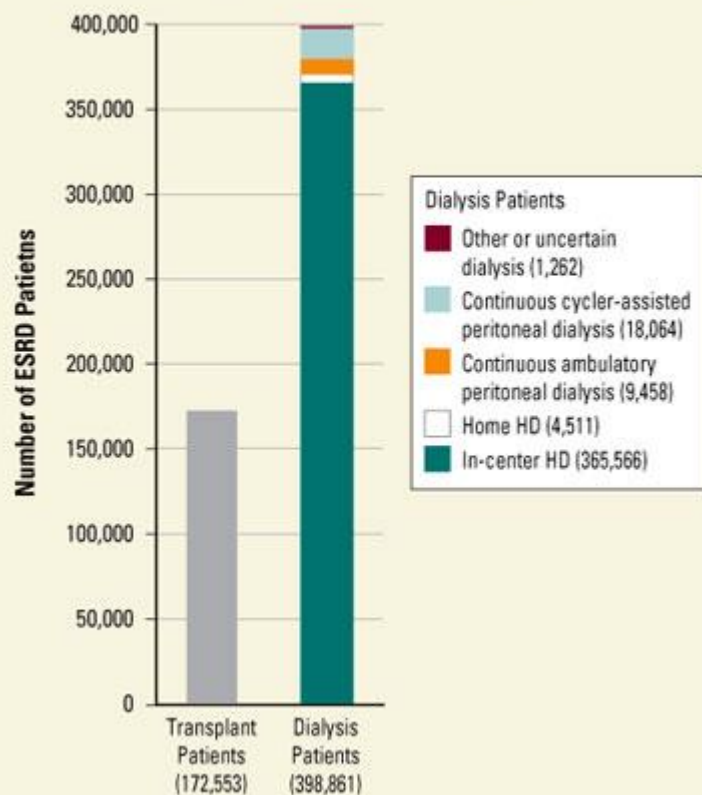
# Prevalence of ESRD is Rising

- Incidence leveling off but prevalence up



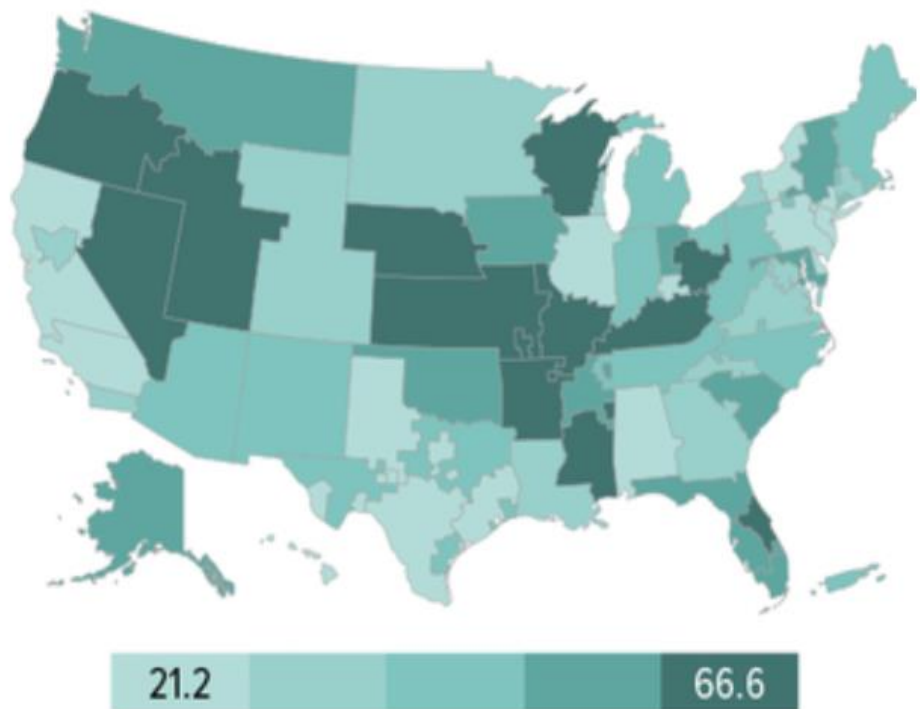
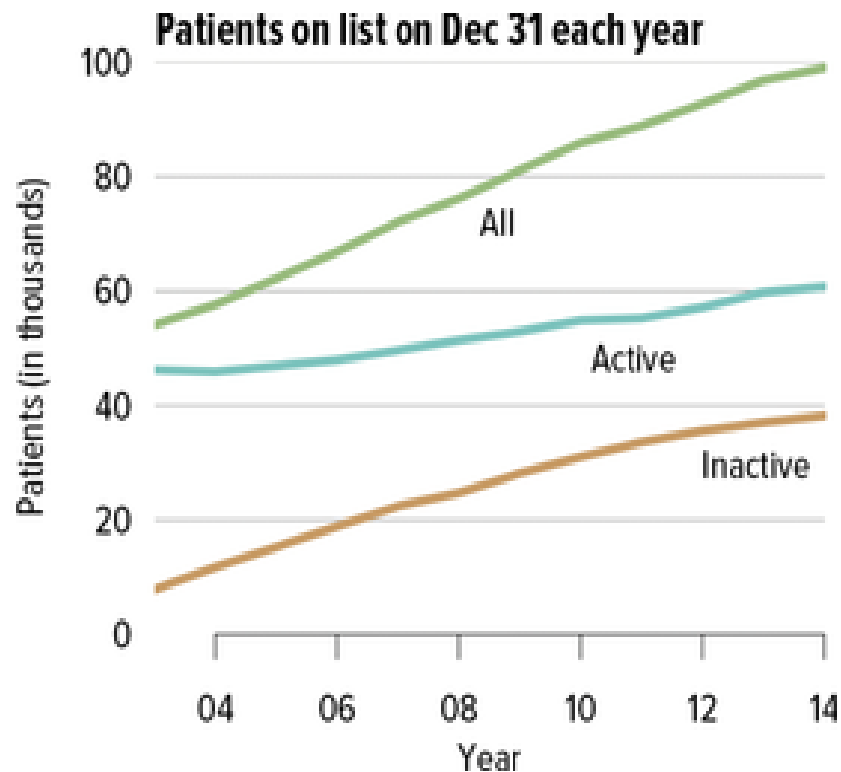
# HD vs TRANSPLANT

**Number of ESRD Patients  
by Treatment Modality**



# Wait List

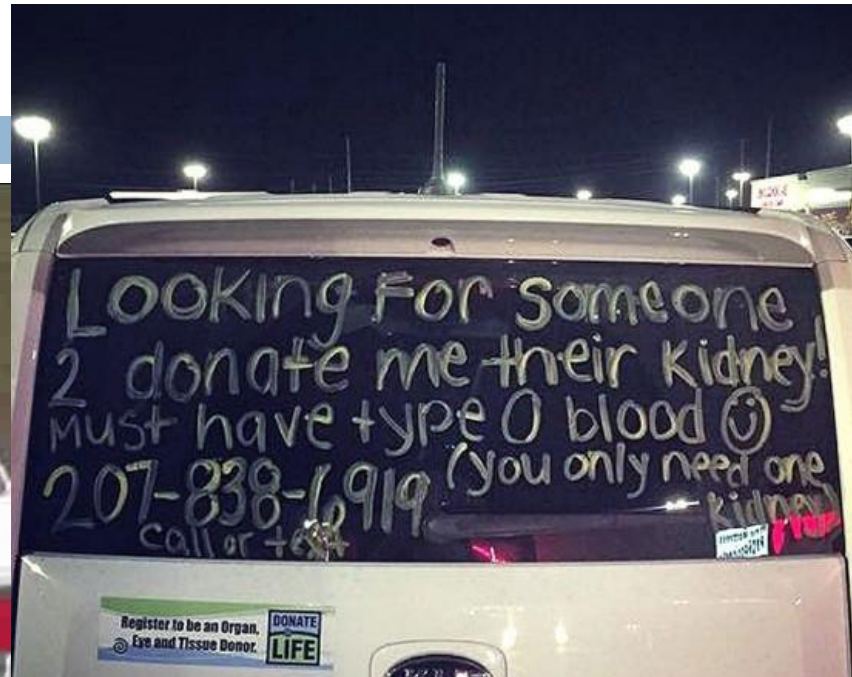
- More eligible patients and plateauing living donor rates → higher WL times



STR



# Advertising???



DENVER POST



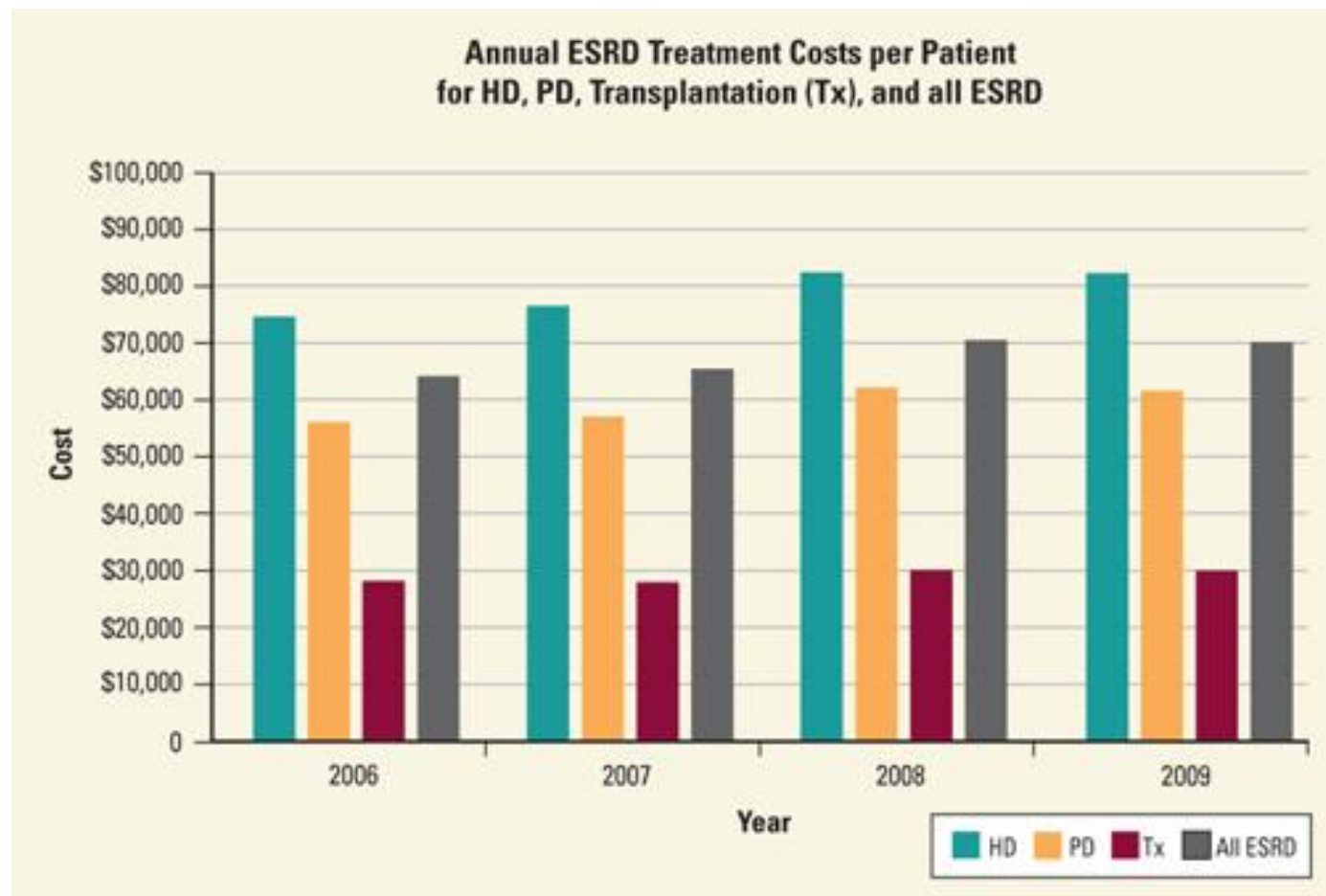
MAN TAKES OUT AD FOR KIDNEY FOR WIFE ON TRUCK

# How to increase # kidney txp?

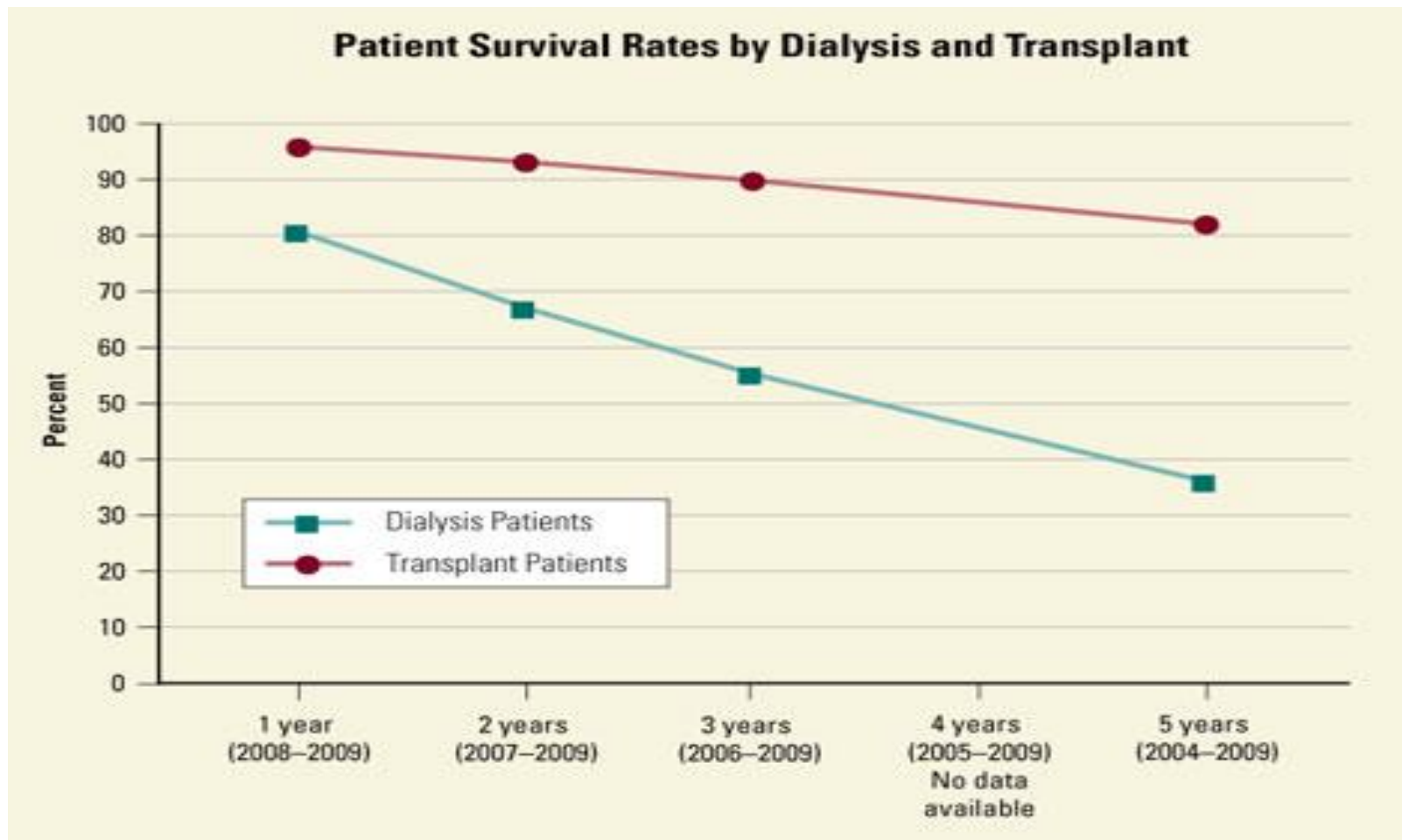
- “Opt-out” vs “opt-in” policy
- Dispelling myths re: living donation
- Swaps/Chains
- Expanded Criteria Donor (ECD) List
  - ▣ > 60
  - ▣ >50 plus 2 of 3: HTN, CVA, Cr > 1.5
- Accepting kidneys from previously “marginal” living donors
- ABOi transplants
- HCV+ Donor

# Transplant Benefits: \$\$\$

- ESRD costs Medicare \$29 billion per year!!!

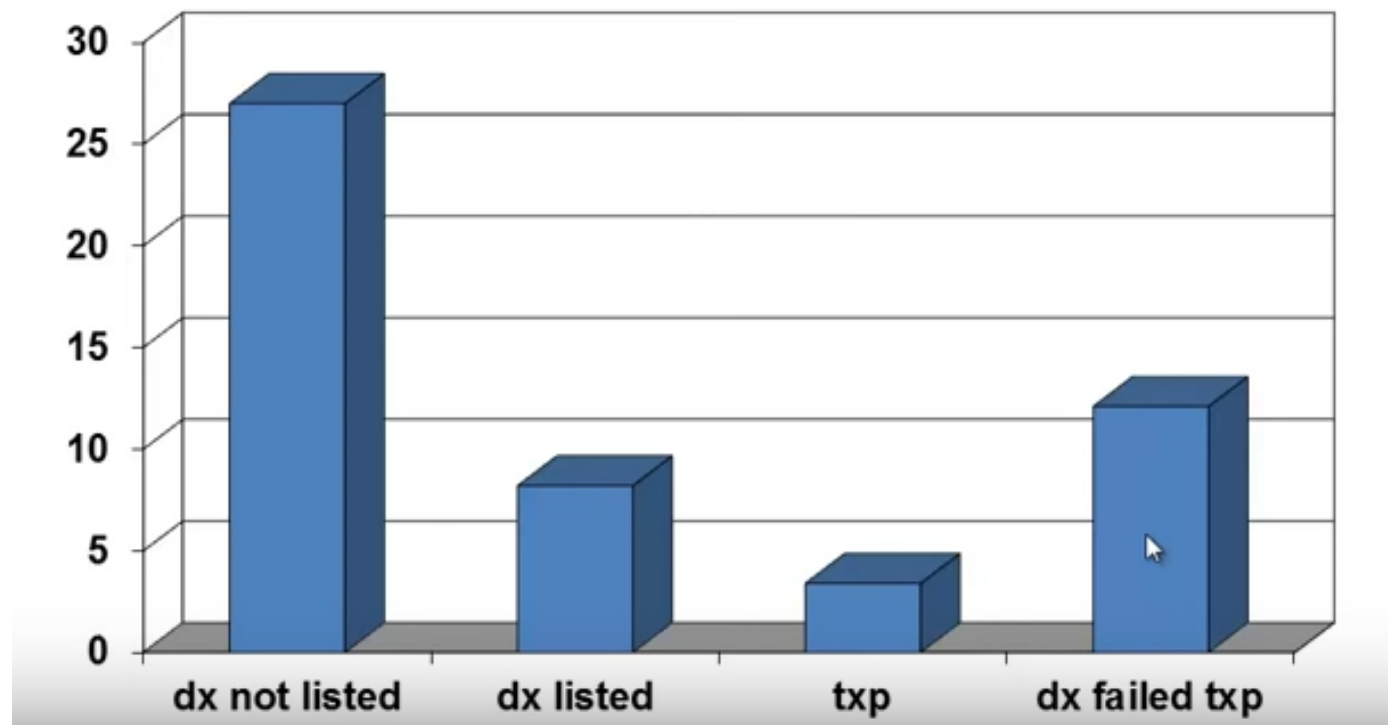


# Transplant Benefits: Mortality

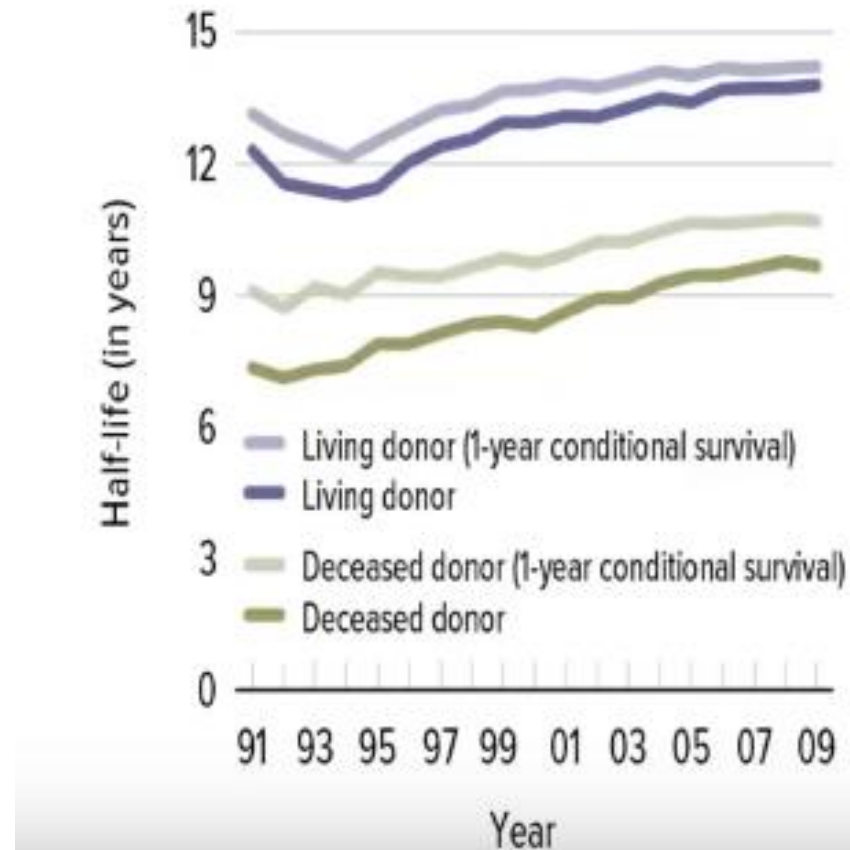
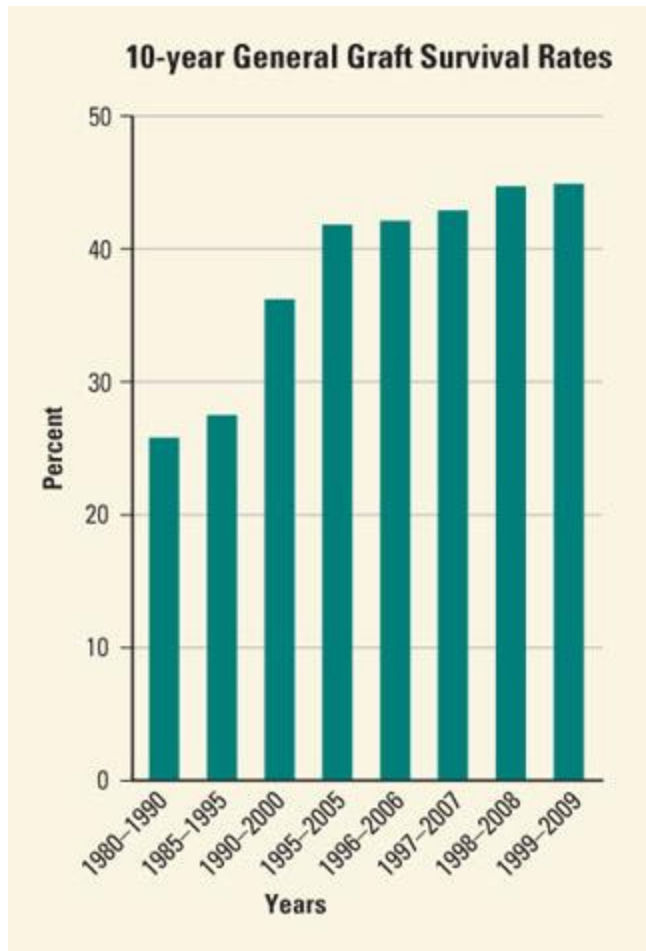


# Transplant Benefits: Mortality

Mortality (% Per Year)  
Dialysis vs. Transplant

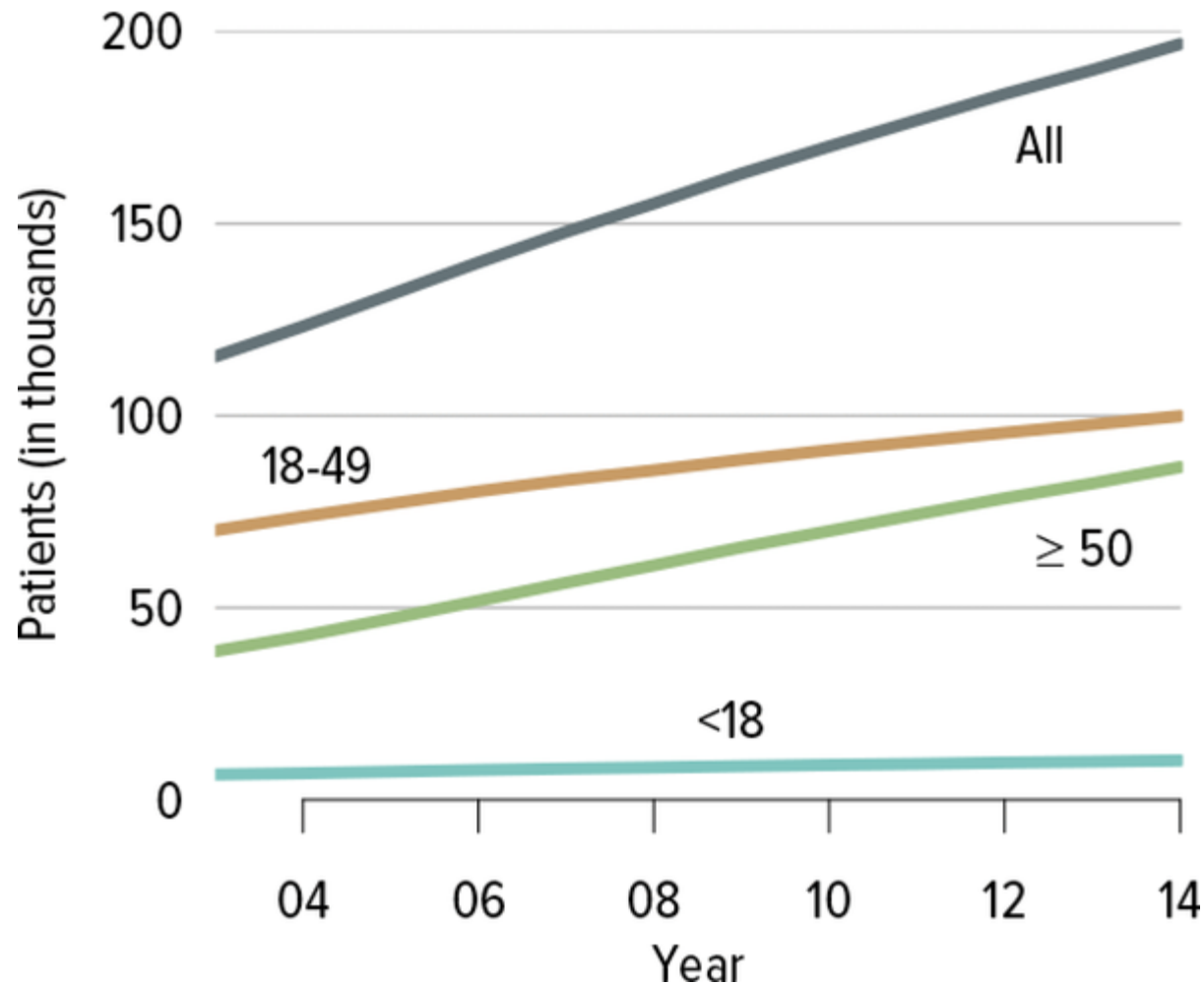


# Less mortality and less rejection



# More living transplant patients

- 200k
- Fastest growing > 50
- We need help caring for these patients!

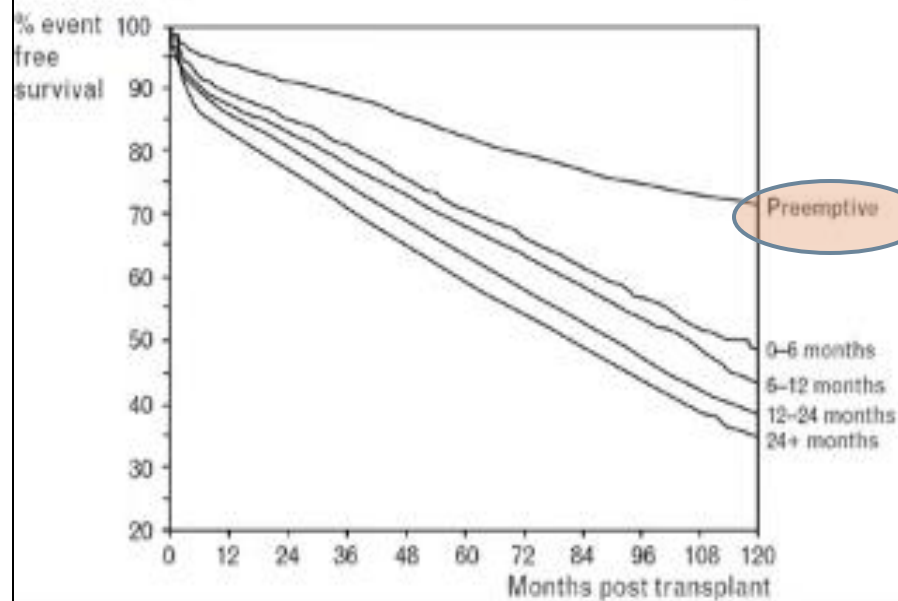




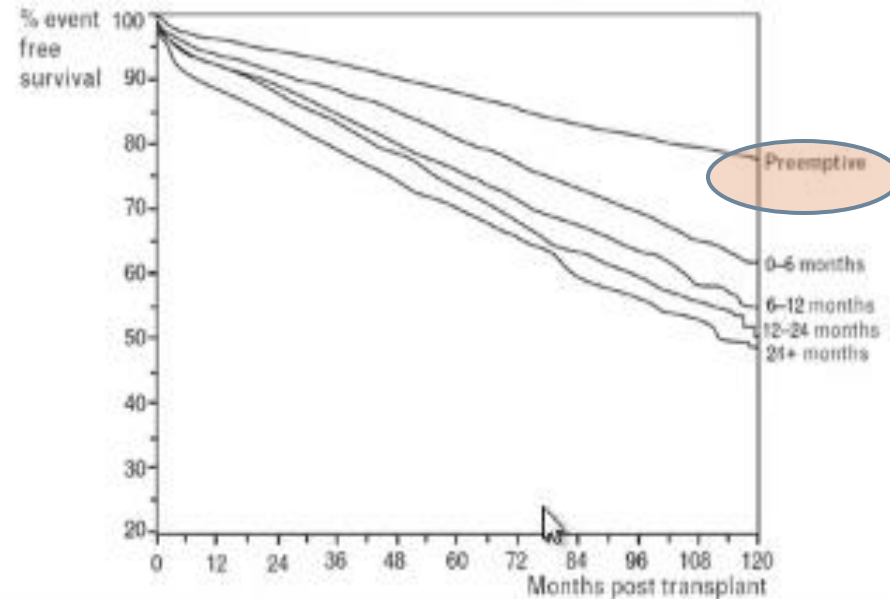
# Kidney Transplant Referral

- Eligible if irreversible progression to  $\text{GFR} < 20\text{mL/min}$

Living Donor Transplants



Deceased Donor Transplants





# Who can be referred?

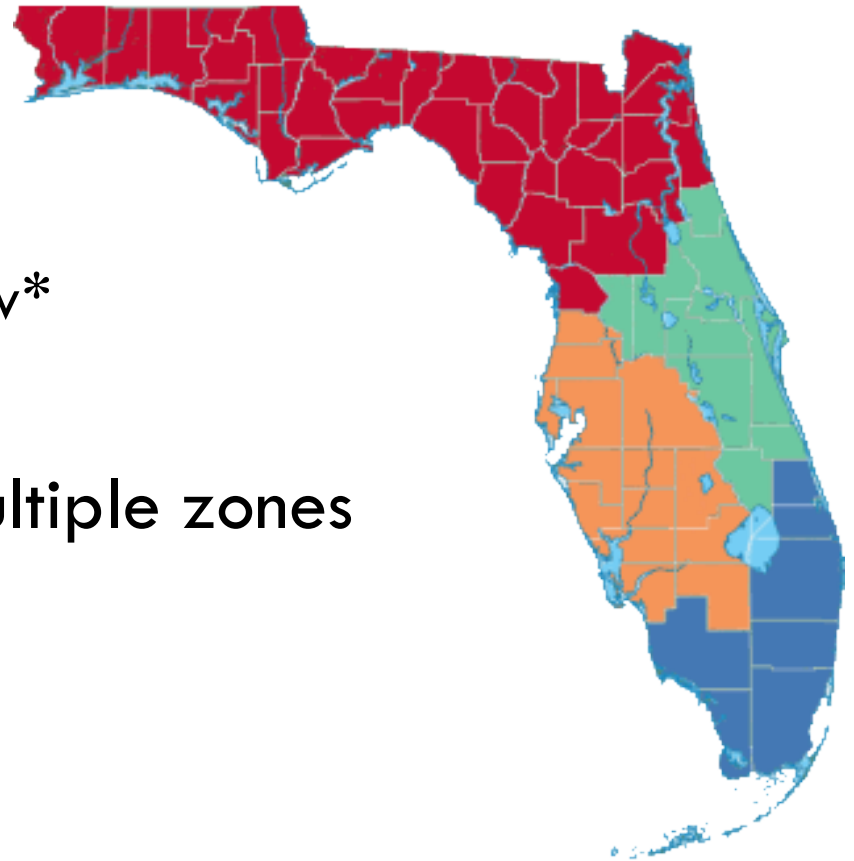
- Just about anybody!
  
- **Absolute** contraindications:
  - ▣ Active malignancy
  - ▣ Active untreated infection
  - ▣ Severe irreversible extrarenal disease
  - ▣ Psychosocial issues
  
- Note what's not on this list:
  - ▣ Age, HIV, HCV, patients eligible for dual organ transplant

# Florida Organ Procurement Offices (OPO)

- Our local zone:

- UM/Jackson
- Cleveland Clinic- FL
- Memorial Hollywood \*new\*

- Pts can be referred to multiple zones



# Recipient Pre-txp Workup

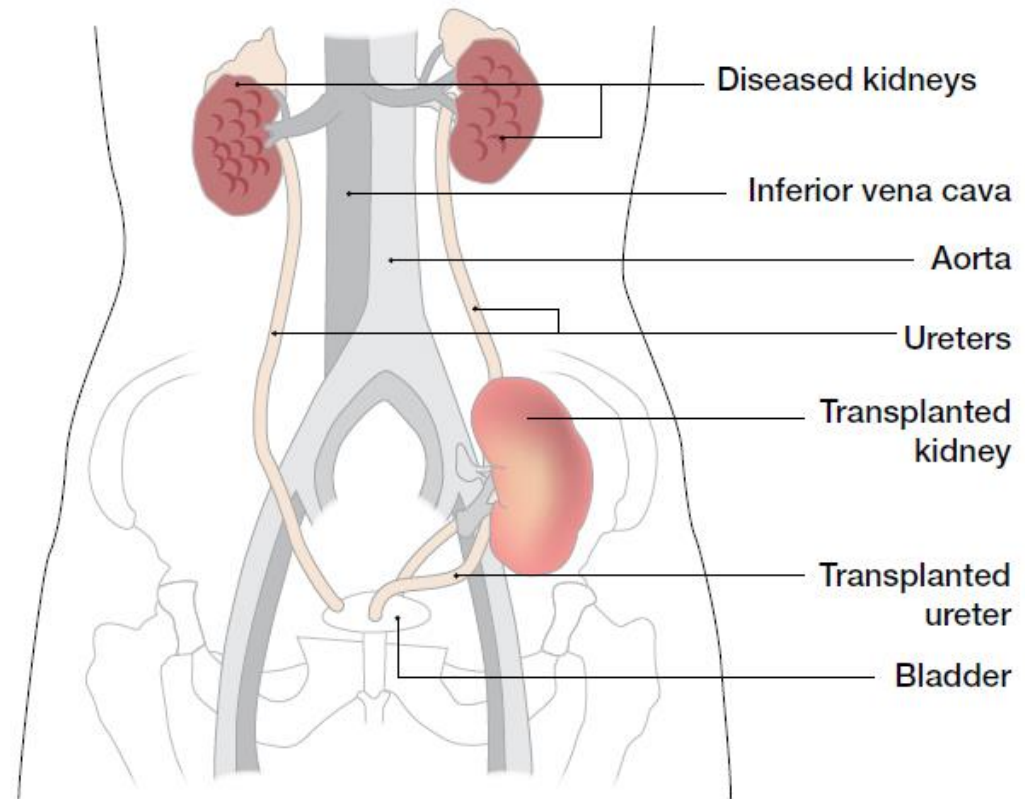
- Basic Labs
- Drug screen
- Infection screen
- Age appropriate cancer screening
- HLA/ABO testing
- Cardiac testing based on RF
- Dental clearance
- Etc

# Living Donation

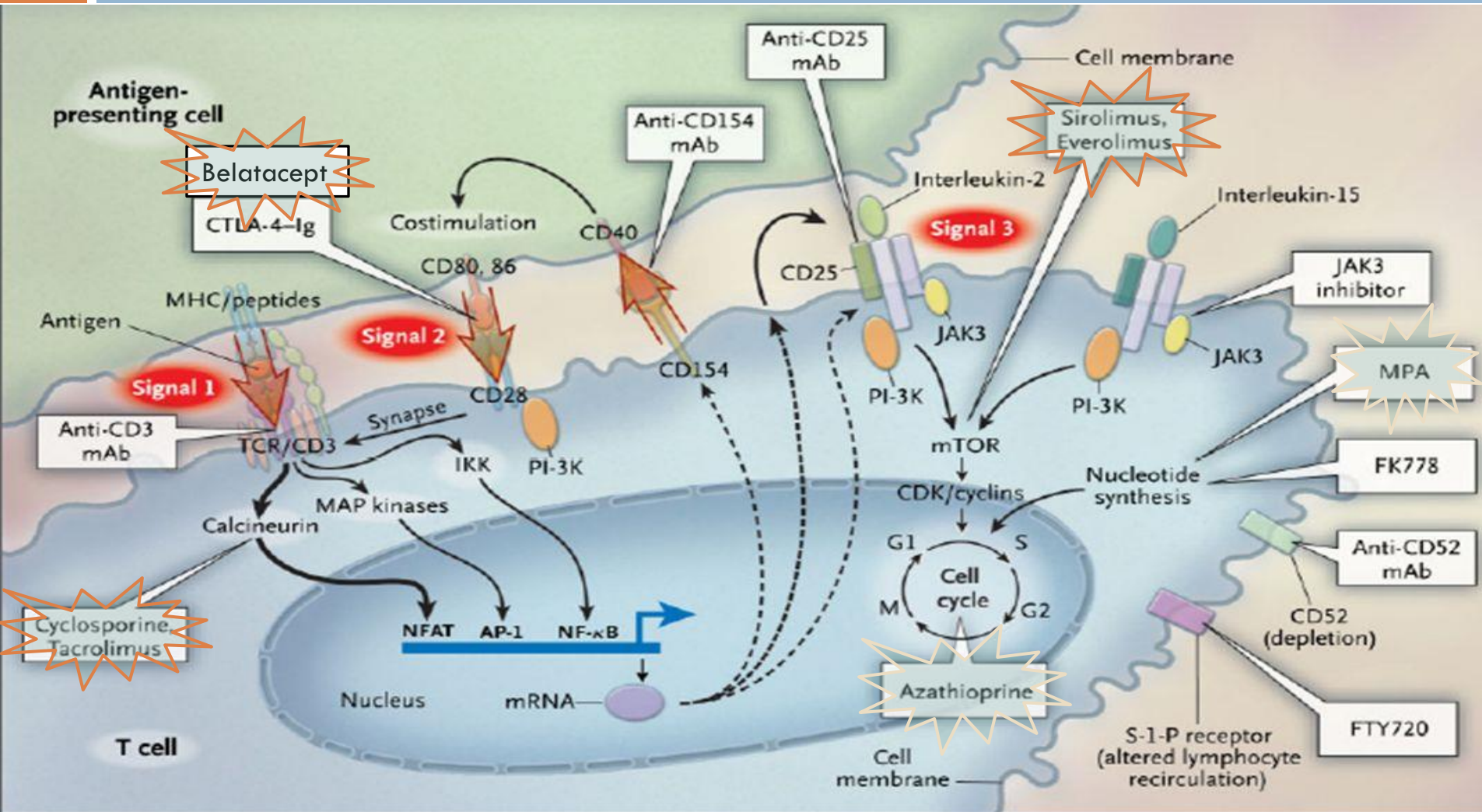
- Medical, Surgical, and Psychosocial evaluation
- Purpose: protect the donor!
  
- Periop 90 day mortality- 1 in 3000 (0.03%)
  
- Long term:
  - ▣ No change in mortality compared to controls
  - ▣ Slightly increased relative risk of HTN, PEC, ESRD
    - (absolute risk low)

# Kidney Transplant Surgery

- Iliac Fossa
- Anastomoses:
  - ▣ Renal A/V
  - ▣ Ureter
- Native kidneys remain!



# Transplant Medications



**Figure 2.** Individual Immunosuppressive Drugs and Sites of Action in the Three-Signal Model.

# Maintenance therapy

- Calcineurin Inhibitors
  - ▣ Tacrolimus > Cyclosporine
  - ▣ Inhibits transcription of IL2 and other cytokines → less T cell activation
- Antiproliferatives
  - ▣ Mycophenolate > Azathioprine
  - ▣ Interferes with DNA/purine synthesis
- Steroids
  - ▣ Prevents cytokine production by T cells and APCs
- Also: *mTOR inhibitors, Belatacept*

# Drug Toxicity

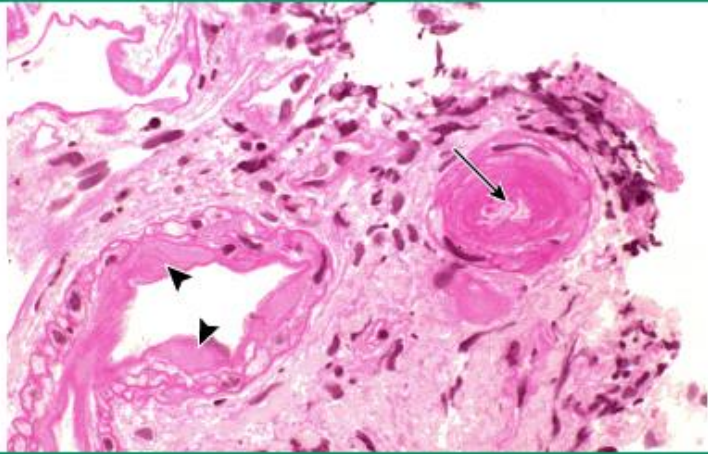
Combination	Hypertension	Diabetes	Hyperlipidemia
Azathioprine	0	0	0
Prednisone	++	++	++
Cyclosporine	+++	+	+++
Tacrolimus ★	++	++++	++
MMF ★	0	0	0
Sirolimus	0	++	++++
Everolimus	0	++	++++
Belatacept	0	0	0



# CNI Nephrotoxicity

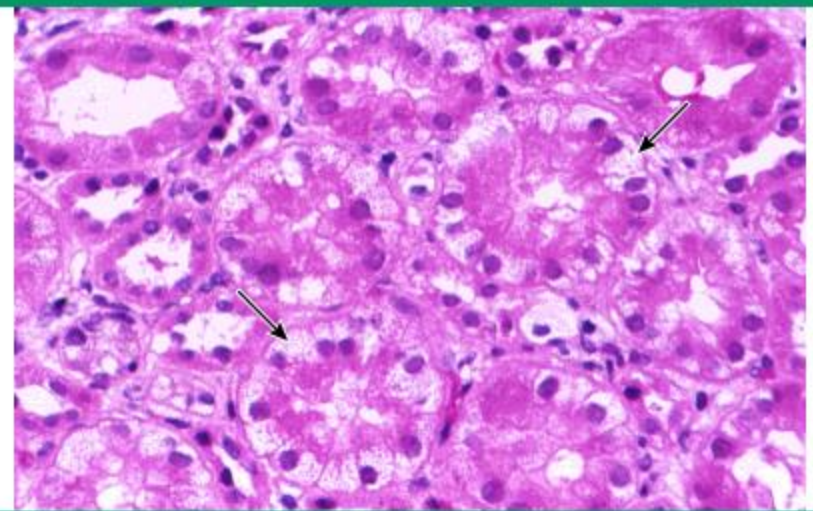
## □ Glomerular afferent/efferent arteriolar vasoconstriction

**Light micrograph showing cyclosporine-induced arteriopathy**



Light micrograph of cyclosporine-induced renal arteriopathy. There is replacement of smooth muscle cells in the media by proteinaceous material (arrowheads), eventually leading to virtual obliteration of the vascular lumen (arrow).

**Light micrograph showing cyclosporine-induced renal tubular injury**



Light micrograph shows vacuolization of the proximal tubular cells (arrows) due to cyclosporine nephrotoxicity.

# CNI Toxicity (cotd)

- Hyperkalemia (hypoaldo)
- Hypomagnesemia (p glycoprotein down with diarrhea)
- Gout
- DM (T>C)
- HTN
- HLD
- TMA
- CsA- hirsutism + gum hyperplasia
- Tacro- alopecia, neuro

# CNI Drug Interactions

## □ Cleared by Cytochrome P450

Increase  
CNI  
levels

- Amiodarone
- ART boosting agents (eg, ritonavir, cobicistat)
- Azole antifungals (eg, fluconazole, posaconazole, voriconazole)
- Grapefruit juice
- HIV protease inhibitors (eg, atazanavir, nelfinavir, saquinavir)
- Macrolide antibiotics (except azithromycin)
- Non-dihydropyridine calcium channel blockers

Decrease  
CNI  
levels

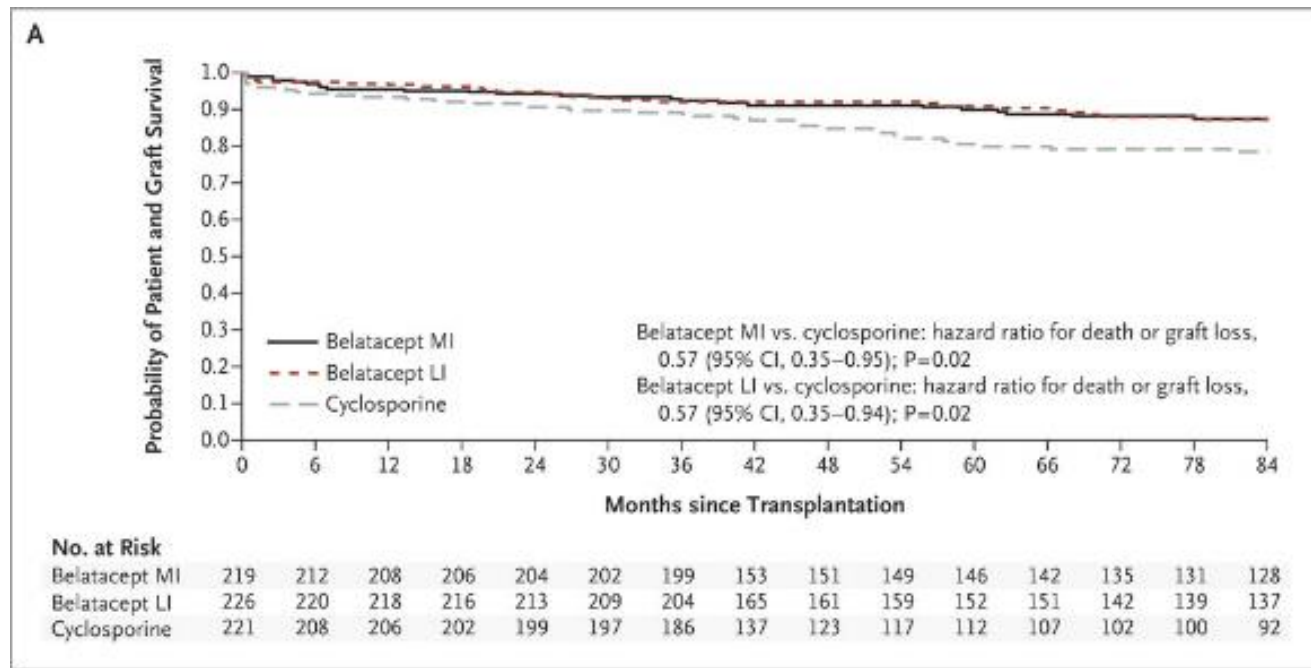
- Antiseizure drugs, enzyme-inducing (eg, carbamazepine, fosphenytoin, oxcarbazepine, phenobarbital, phenytoin, primidone)
- Enzalutamide
- Nafcillin
- Rifamycins (eg, rifabutin, rifampin, rifapentine)
- St. John's wort

# Antiproliferatives

- MMF or AZA
- Careful:
  - ▣ Leukopenia
  - ▣ GI symptoms (MMF)
  - ▣ Drug Interaction of Note: AZA + Allopurinol → severe marrow suppression

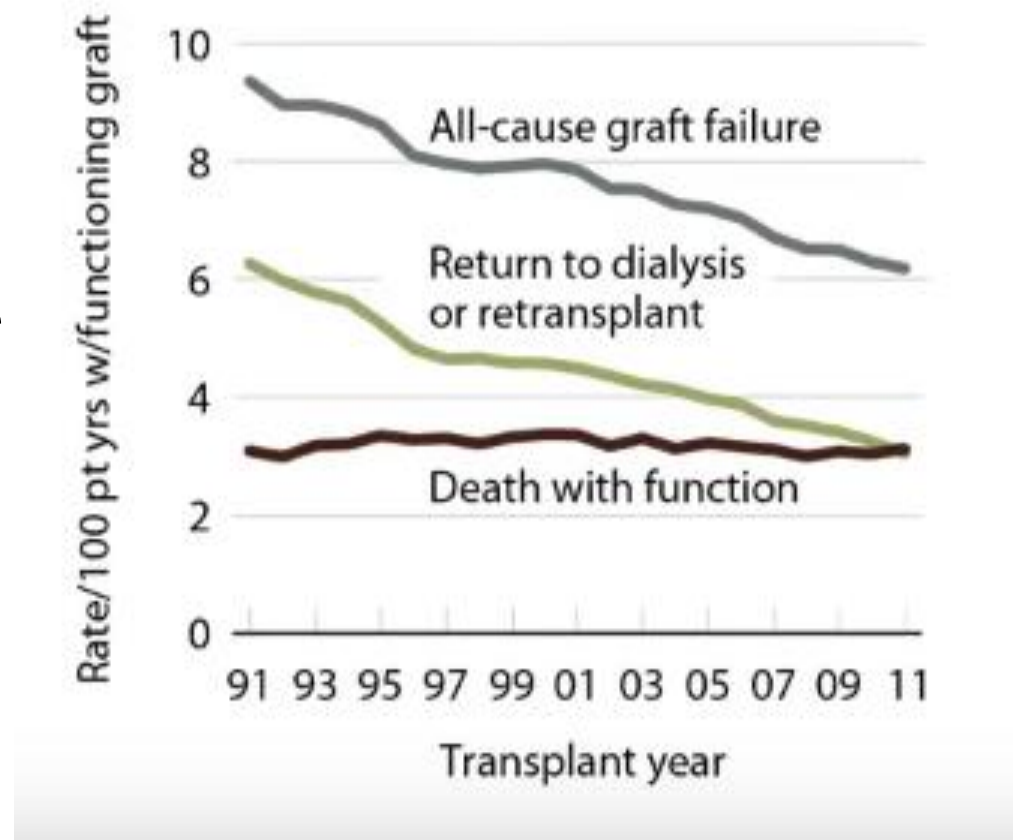
# Belatacept

- Inhibits T cell activation through costimulation blockade
- No known nephrotoxicity or adverse CV effects
- IV Q2-4 weeks
- \$\$\$
- EBV

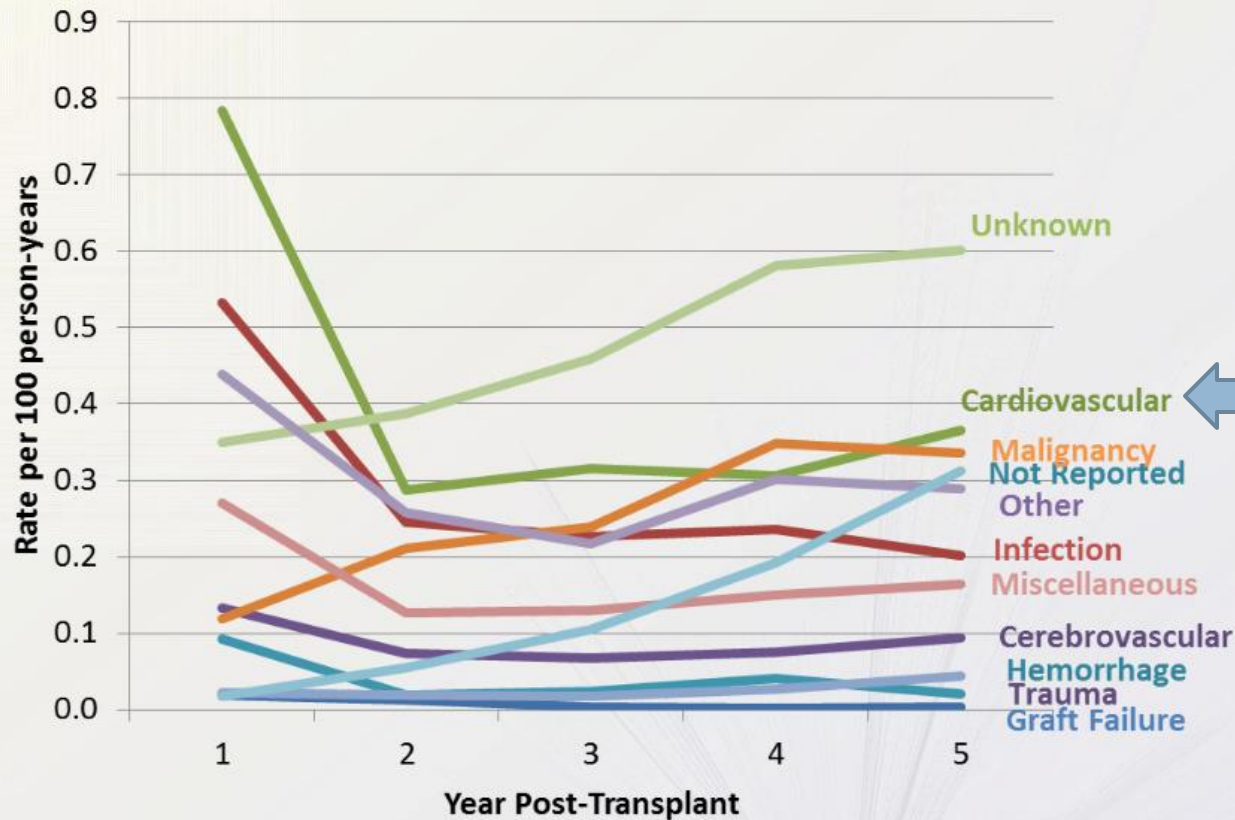


# Pop Quiz

- What is the most common cause of kidney transplant failure?
- Mortality has not improved much in active Transplant pts

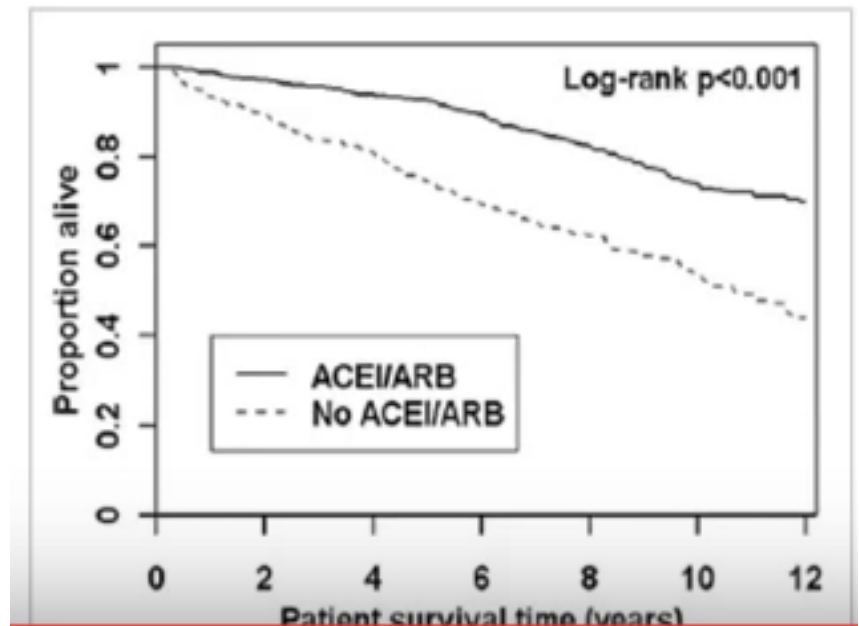


# Causes of death in kidney transplant patients



# HTN

- Target BP 130/80 (no real data)
- CaChB- may reduce CNI induced vasoconstriction
  - ▣ Non-DHP will raise CNI levels
- BB may reduce CV mortality
- ACE/ARB
  - ▣ Retrospective study →
  - ▣ Risks:
    - High K
    - Anemia
    - Transplant RAS/Rejection
    - Confounding rise in Cr



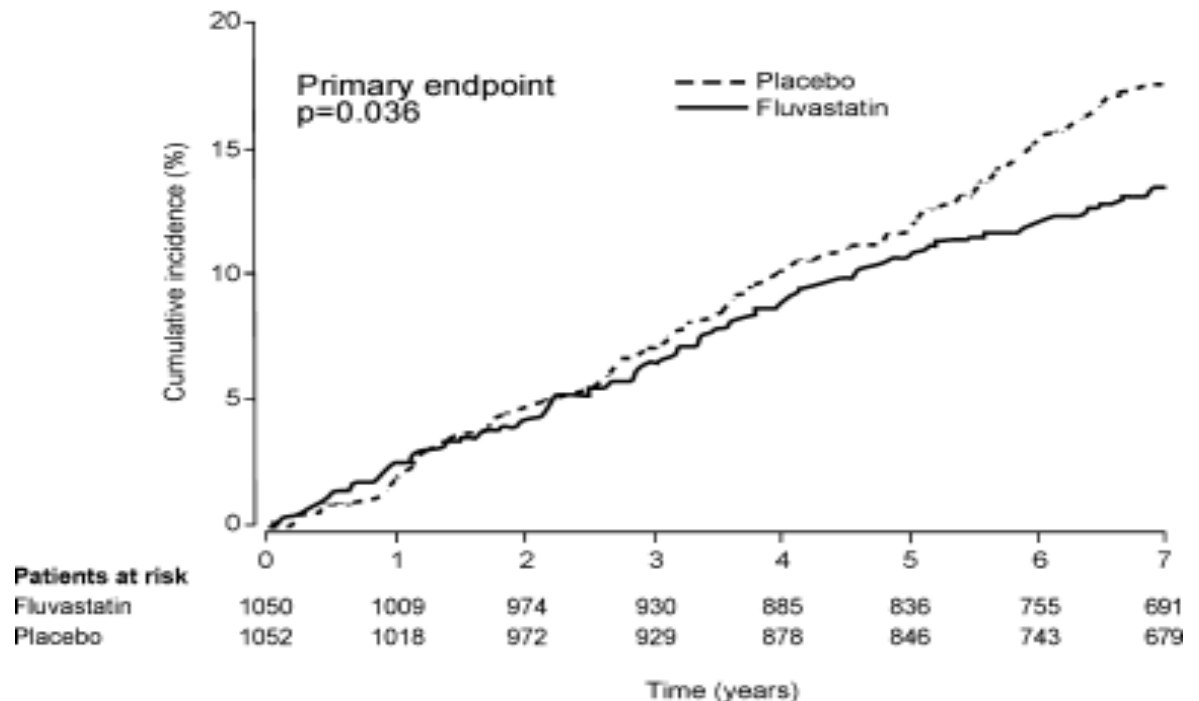


# HLD- STATINS

- ALERT Trial- AJT 2005
  - Fluvastatin 80 v placebo
  - LDL levels lowered
  - RCT

- Fluvastatin
- Atorvastatin
- Pravastatin
- (others can interact with CNIs)

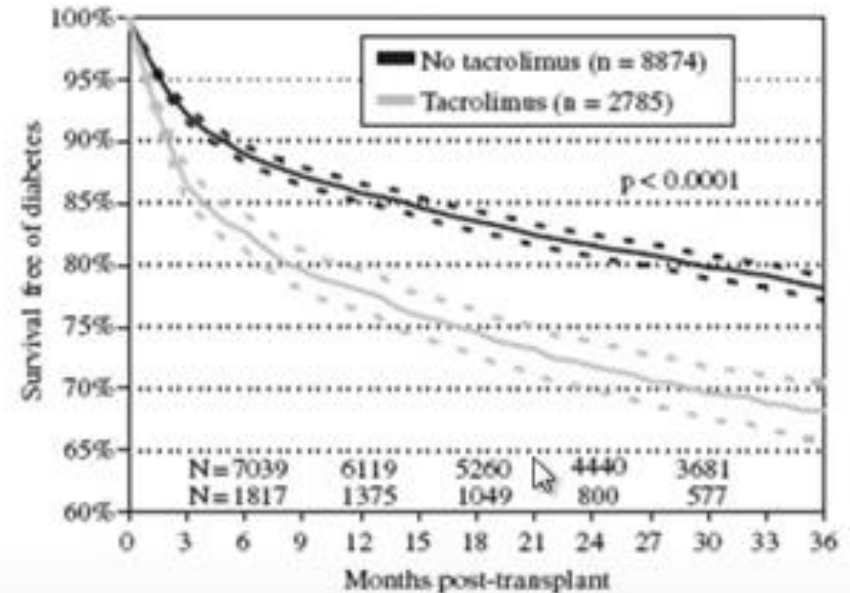
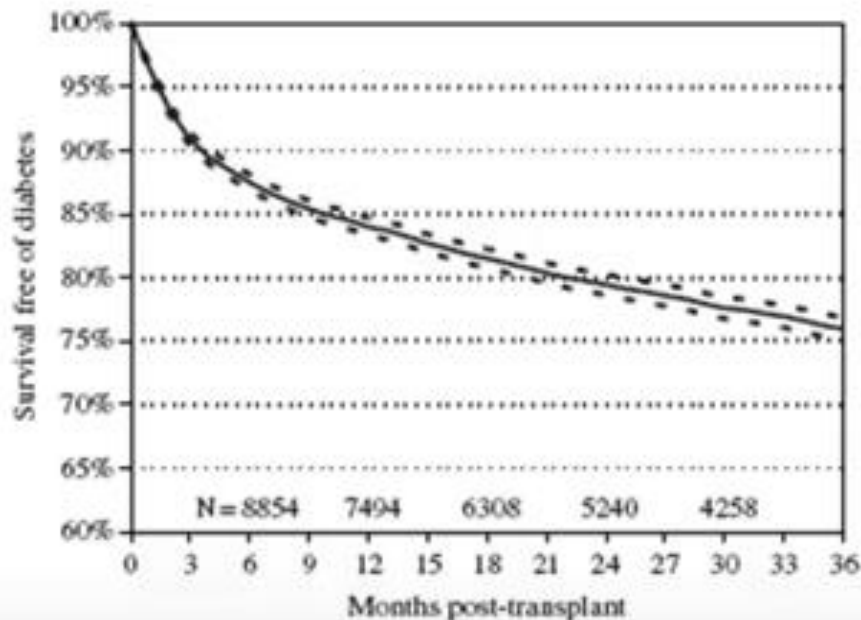
(a)



# Statin adjuncts

- Not well studied and all have risks/SEs
  - ▣ Zetia
    - Can interact with CNI (Vytorin)
    - GI SEs
  - ▣ Fibrates
    - Rhabdo risk
  - ▣ Cholestyramine
    - CNI interactions
  - ▣ Fish Oil
    - No data

- 25% of pts have DM at time of txplt
- 25% of txplt pts develop NODAT within 3 years
- Culprit: tacrolimus (esp. if also on prednisone)



# NODAT

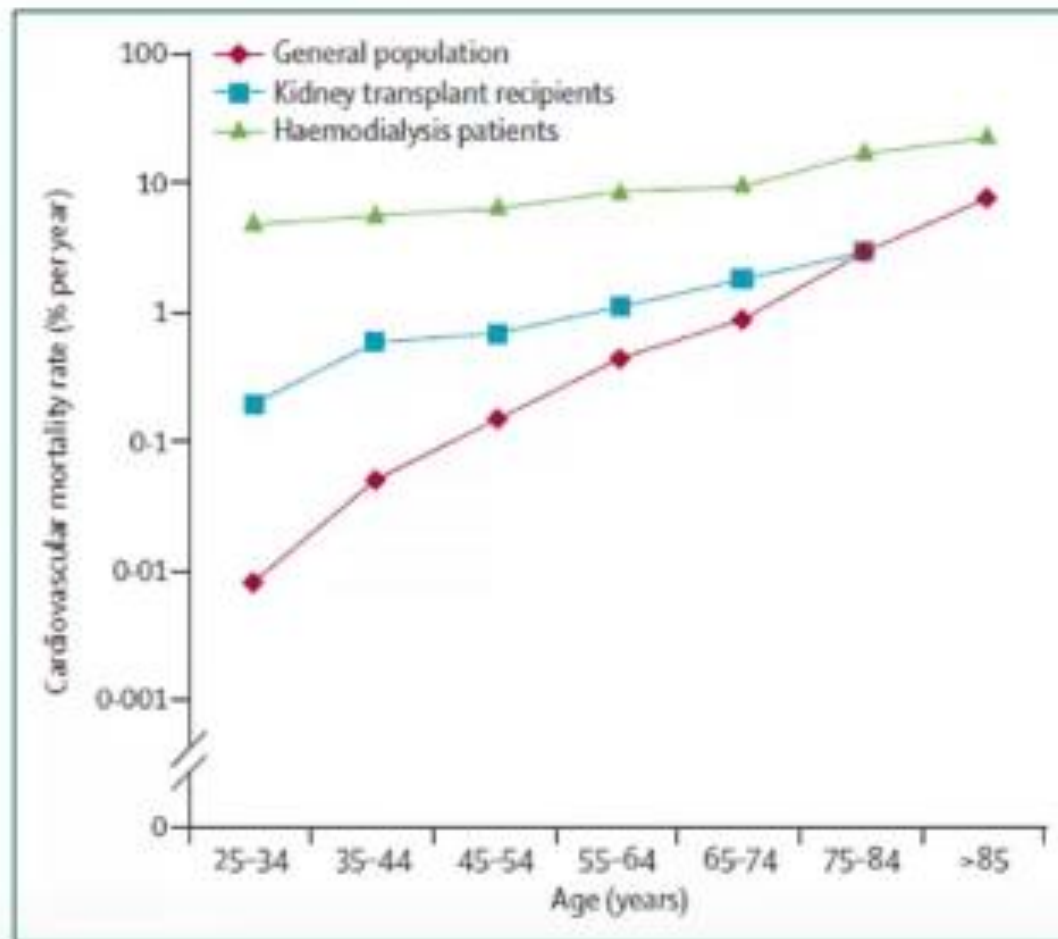
- Worse allograft and patient survival:
- NODAT conferred RR 3.8 for allograft failure (48% vs 70% after 12y)
- RR 1.5-3 for CV mortality

# NODAT

- Tacrolimus
  - ▣ Decreased insulin secretion
  - ▣ Insulin resistance
- Treatment
  - ▣ Lifestyle modifications
  - ▣ Insulin usually needed
  - ▣ \*Metformin should be okay

# CVD after transplant

- Txp lowers CV mortality (4x) vs HD but not general pop.



# CVD different in transplant patients?

- Different RFs?
  - ▣ HPT, phos, time on HD, LVH, wide PP?
  - ▣ Medial vessel wall concentric calcification
    - Vs traditional atherosclerosis/plaque
    - More pulm HTN, LVH, dCHF, wide PP
    - Increased arterial stiffness

# Cancer (USRDS)

- RR >90
  - Non-melanoma skin
- RR 20-90
  - Kaposi's Sarcoma
  - Lymphoma
  - Uterine, Cervical, Vulvovaginal
- RR 5-20
  - Kidney
  - CNS
  - Melanoma
  - Leukemia
  - Larynx/Mouth
  - Endocrine
  - Hepatobiliary
- RR 2-5
  - Breast
  - Prostate
  - Lung
  - Colon
  - Esophagus
  - Pancreas
  - Ovary
  - Testis

3 years post transplant:  
7.5% get skin cancer  
7.5% get other cancers



# Cancer screening recs

- Age appropriate cancer screening
  - ▣ Scope, PAP, testicular self exam, prostate/PSA, mammogram
- Renal US (native kidneys) annually
- Annual derm visits

# Vaccines

- Avoid LIVE ATTENUATED vaccines after transplant:
  - ▣ Zoster, MMR, HPV, Yellow Fever
  
- Post Transplant
  - ▣ Flu every year
  - ▣ PNA every 5 years
  - ▣ TDAP every 10 years
  - ▣ HAV/HBV if not done already on HD

# Posttransplant Infections

- Rate of infection actually **REDUCED** 4x with a transplant compared to HD
- Highest risk early on post transplant with higher doses of immune suppression
  - ▣ Post transplant prophylaxis
- Common things are common!
  - ▣ PNA/URI/UTI

# Viral Infections

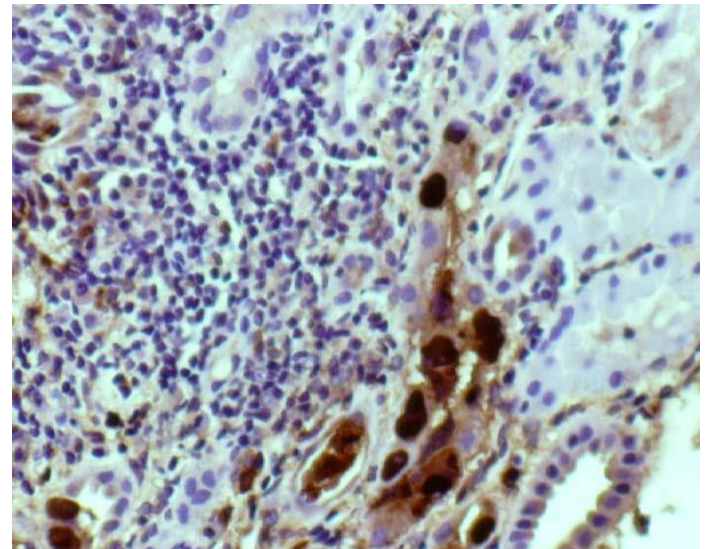
## □ CMV

### ▣ Know “CMV status”

- Did donor have CMV? Did recipient have CMV prior to tx?
- Risk determines course of valcyte ppx post-op

## □ BK

- ▣ Increased immunosuppression
- ▣ +SV40 stain on Bx



# Infection associated malignancy

- EBV → PTLD
- HHV8 → lymphoma & KS
- HPV → SCC oropharynx, gyn
- HBV/HCV → HCC

# Summary



- With better allograft survival rates there are more patients in the community with kidney transplants than ever before
- Always be aware of your patients' immune suppression and understand side effects and potential drug interactions
- Transplant nephrologists and community physicians will need to work together to manage the multitude of issues that can arise in transplant patients

# Thank you!

- ❑ MSD Shadowing Program
- ❑ Interested? Contact me!
- ❑ [marc.richards@gmail.com](mailto:marc.richards@gmail.com)
- ❑ 561-325-1376

