Update on Transplant Nephrology: How Relevant Is It to You?

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Famous People with A Kidney Transplant

George Lopez Sarah Hyland

Alonzo Mourning

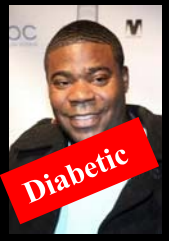
Natalie Cole

Ivan Klasnic

Lucy Davis

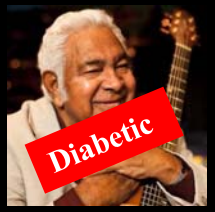
Sean Elliott

Ron Springs – Everson Walls



Tracy Morgan

Gary Coleman



Jimmy Ilttle

Ken Howard

Jennifer Harman

Steve Cojocaru

Neil Simon

A Baltimore Raven gave a Kidney to a Pittsburgh Steeler

"The kidney we got from Ma'ake was probably the largest normal kidney I've ever seen," Dr Bartlett

Chris Kemoeatu

Ma'ake Kemoeatu

"He couldn't play anymore, and I didn't want to be in a position where he couldn't play but I'd keep playing- so I quit football and gave him my kidney "

Selena Gomez

Which of these statements is correct ?

A. **The leading causes of death after kidney transplantation are infection followed by malignancy especially lymphoma**

B. **Due to the side effects of lifelong immunosuppression, transplant patients have the same survival as dialysis patients but have a much better quality of life being free from regular dialysis treatments**

C. **Patients are officially listed for kidney transplantation once they begin dialysis therapy with either hemodialysis or peritoneal dialysis**

D. **The average waiting time for a kidney transplant in the U.S. is approximately 1-2 years**

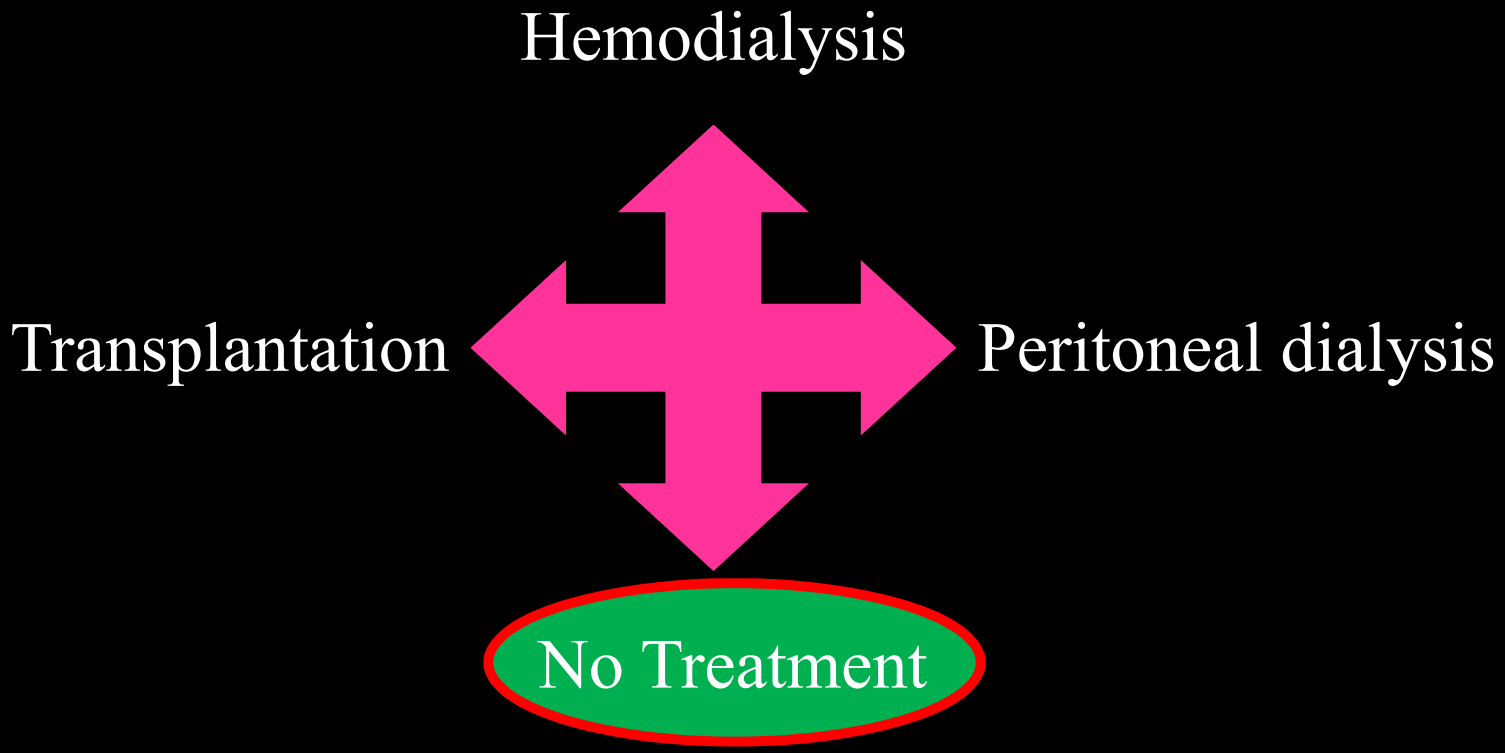
E. **All are correct**

F. **None are correct**

Which of these drugs is nephrotoxic?

A. Mycophenolate Mofetil (Cellcept, Myfortic)
B. Calcineurin inhibitors (Prograf, Cyclosporin,Tacrolimus)
C. Azathioprine (Imuran)
D. Corticosteroids (Prednisone, Medrol)
E. mTOR inhibitors (Rapamycin, Sirolimus, Everolimus)
F. Belatacept
G. All are nephrotoxic
H. I have no idea what most of these drugs are !!
I. None are nephrotoxic

End Stage Renal Disease (ESRD) Options



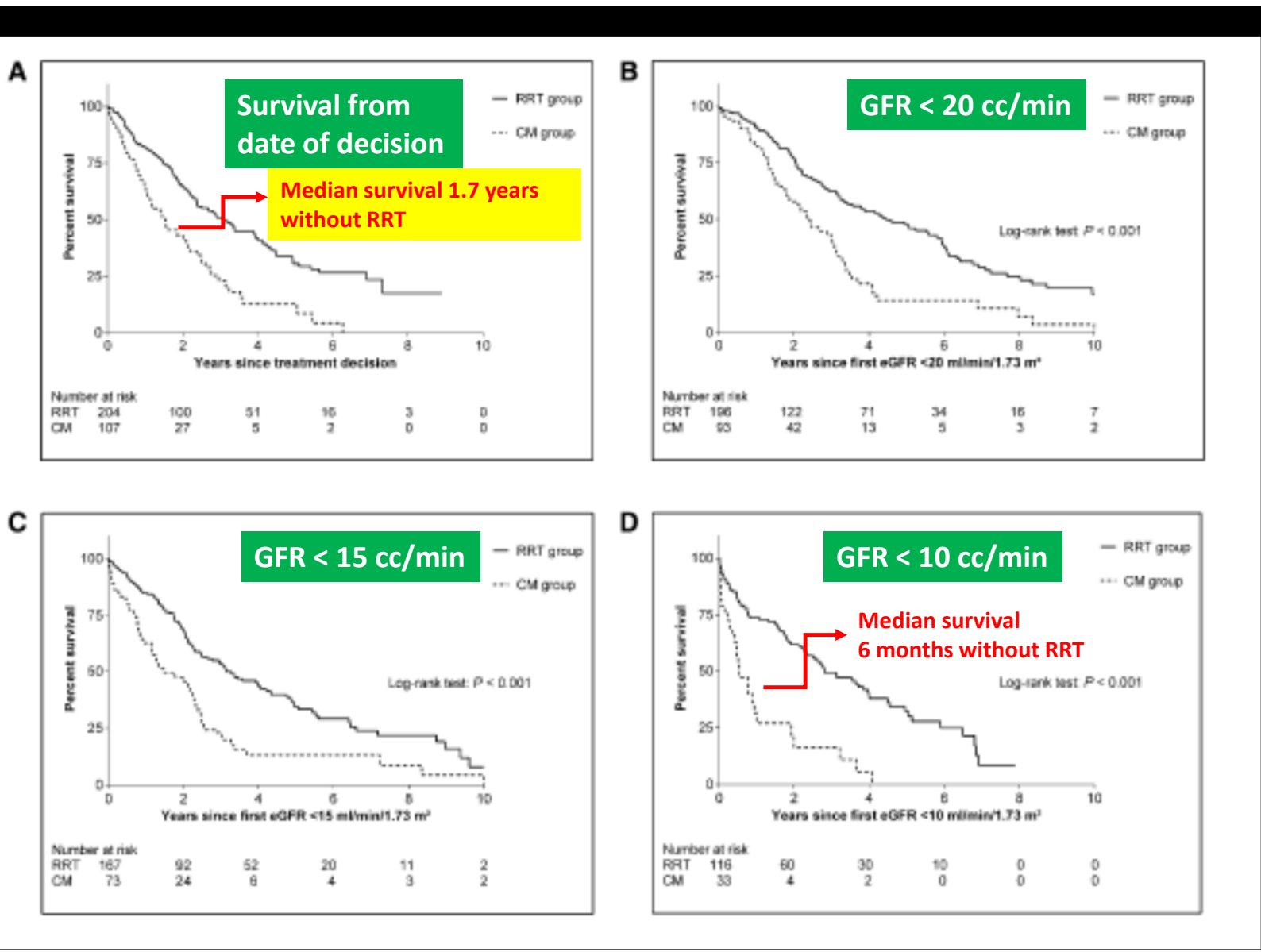
Conservative Care Option for ESRD

- Not every patient will demonstrate an improved quality of life with the initiation of renal replacement therapy
- For ESRD patients > 70 years old –discontinuation of dialysis is responsible for 22% of all deaths
- Extensive co-morbidities may influence the decision to offer renal replacement therapy

Once the GFR < 20 cc/min pts can be listed for TP.
Those pts that decided never to have RRT had a significantly higher mortality at all time periods as the GFR declined compared to the group that chose RRT in spite of standard nephrology care

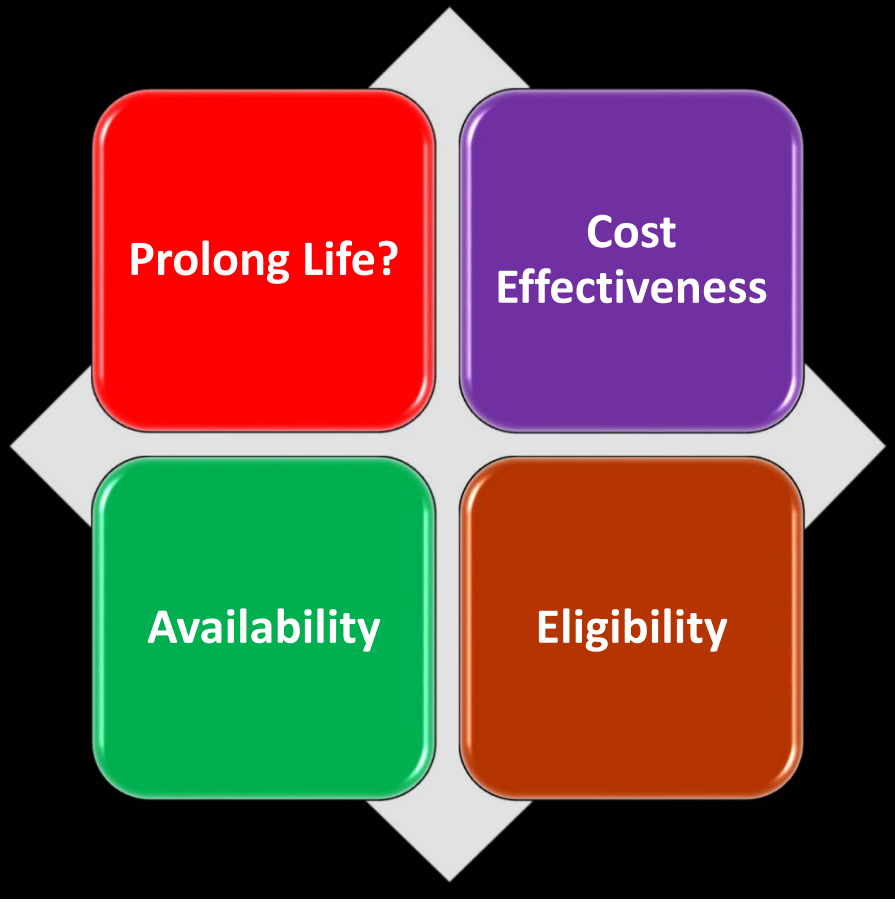
Major demographic differences for the <u>conservative care group</u>
Age > 80
ASVD
ASHD

Initiation of RRT is a shared decision between the nephrologist / patient and family

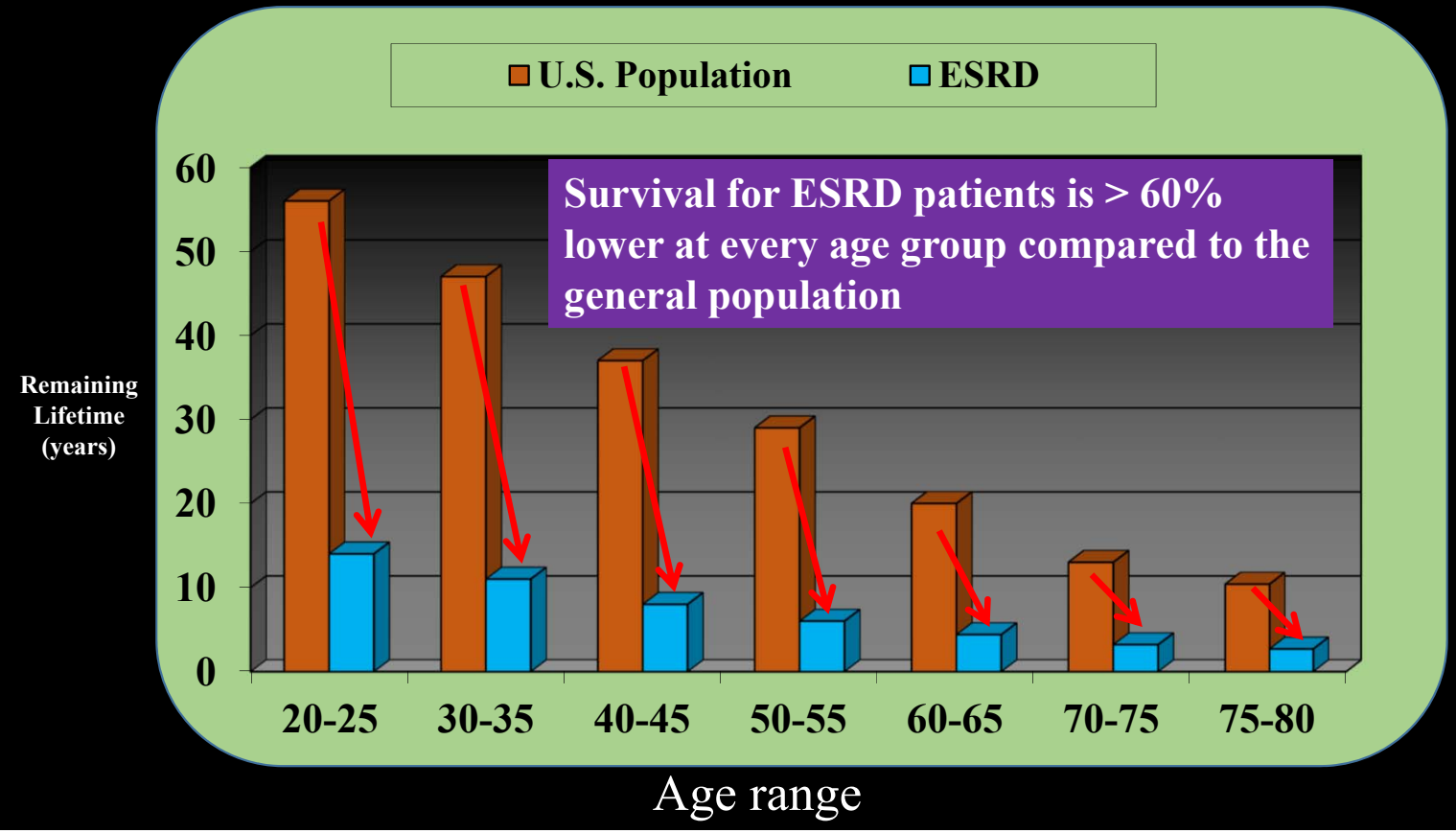


Clin J Am Soc Nephrol 11: 633–640, 2016.

Questions to be Answered About the Option of Kidney Transplantation



Expected Remaining Lifetimes in ESRD Patients, Transplant Patients and U.S. Population



Does Dialysis Actually Replace Kidney Function ?

ESRD

Stage 5 CKD

GFR < 10 cc/min

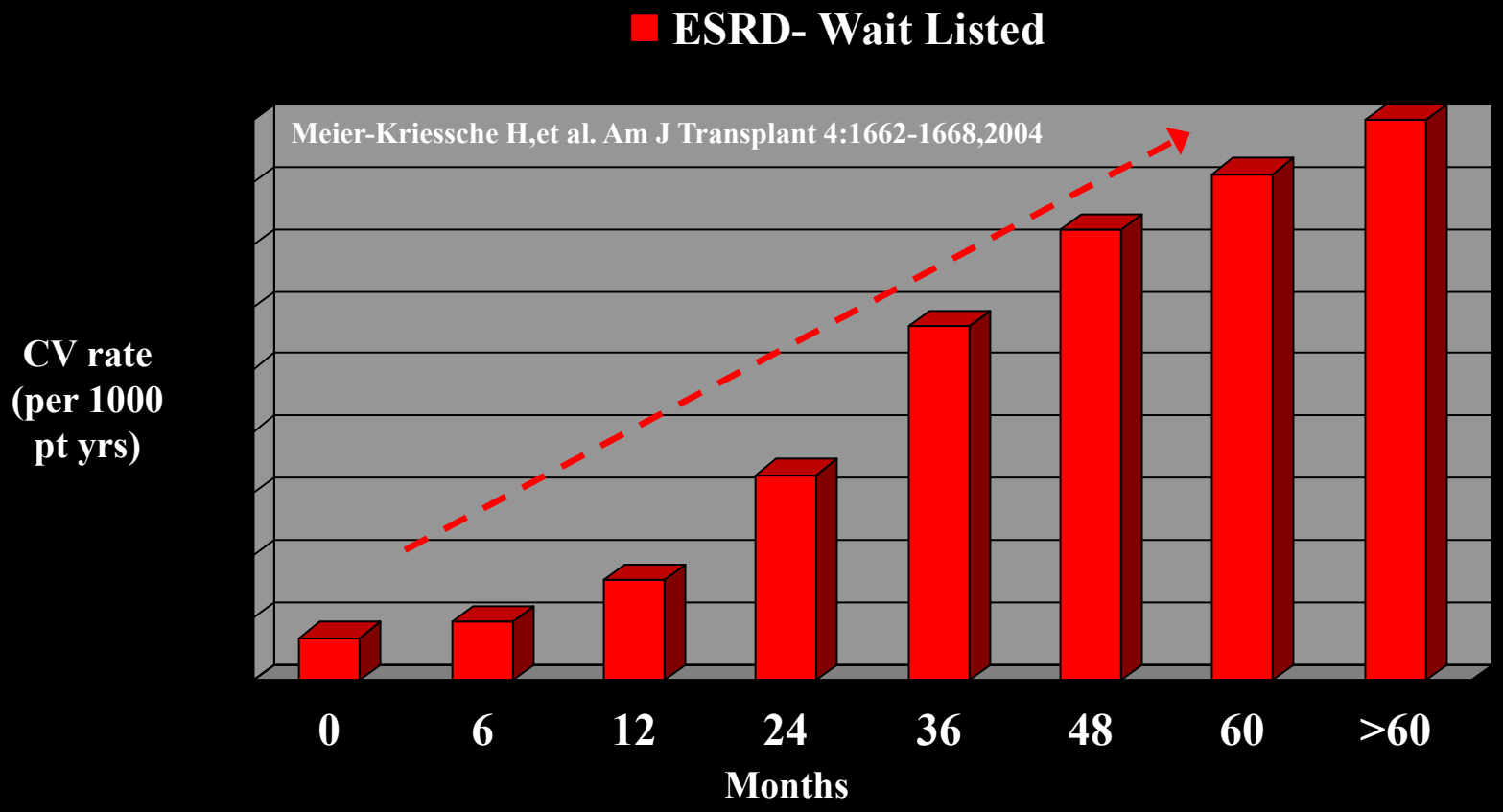
Dialysis

Stage 4 CKD

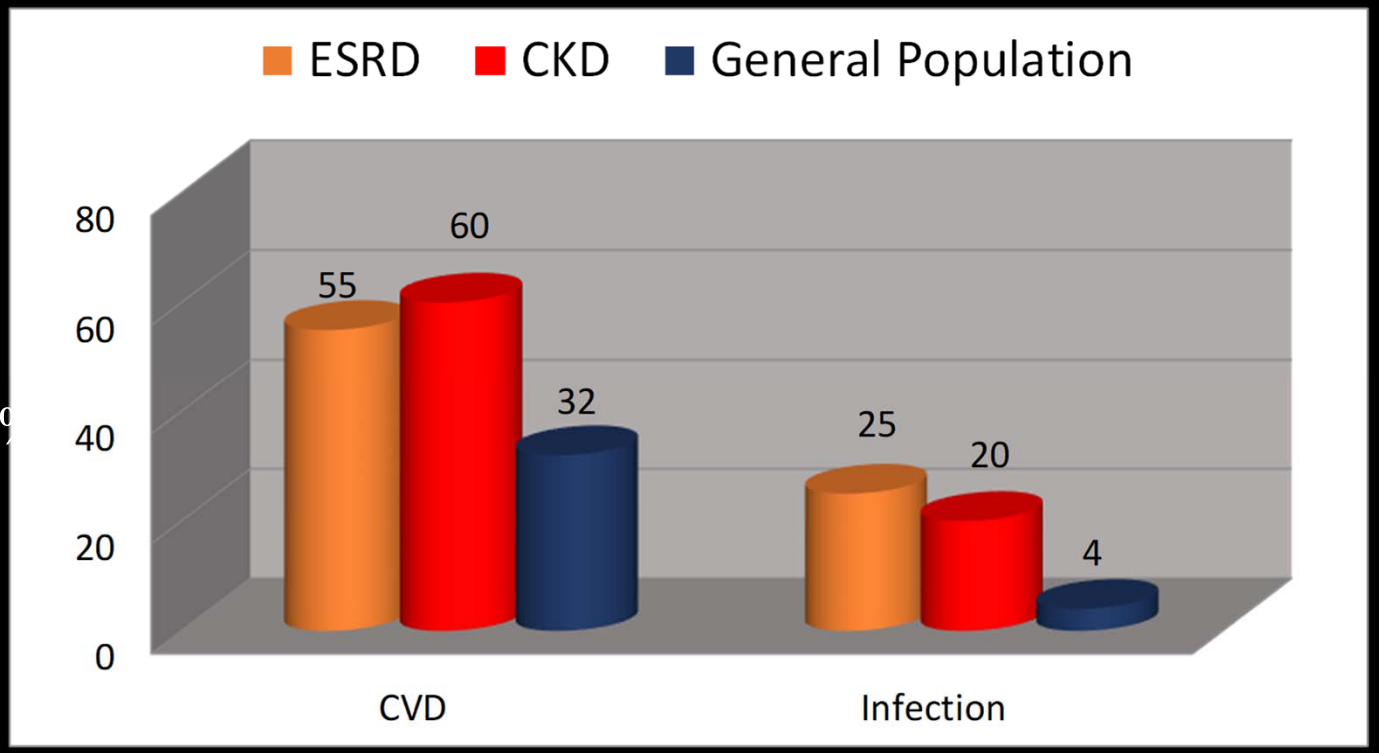
GFR 18-20 cc/min

All Dialysis patients remain with significant CKD and a markedly higher risk of CVD

Cardiovascular Disease and ESRD Patients Waiting for Kidney Transplantation

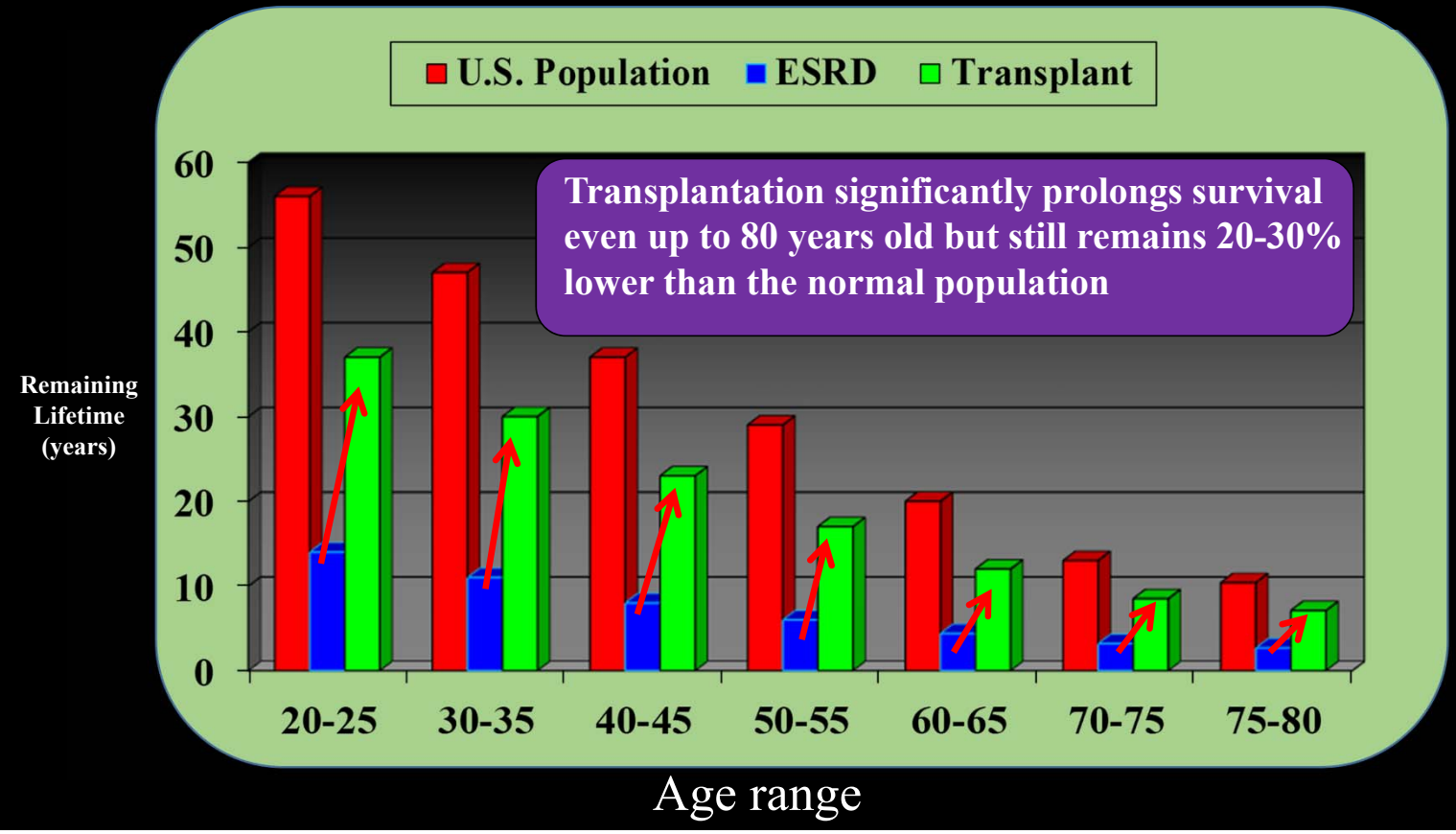


Causes of Death in ESRD and CKD Patients

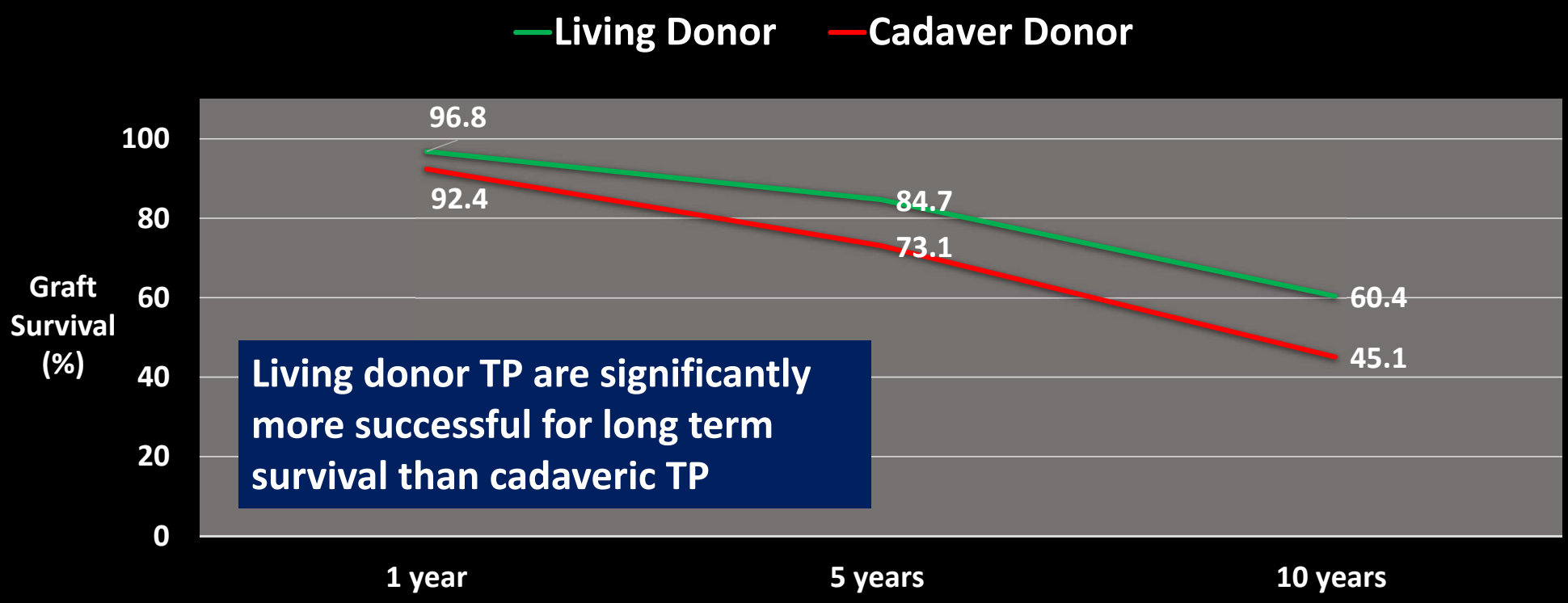


Cardiovascular Disease

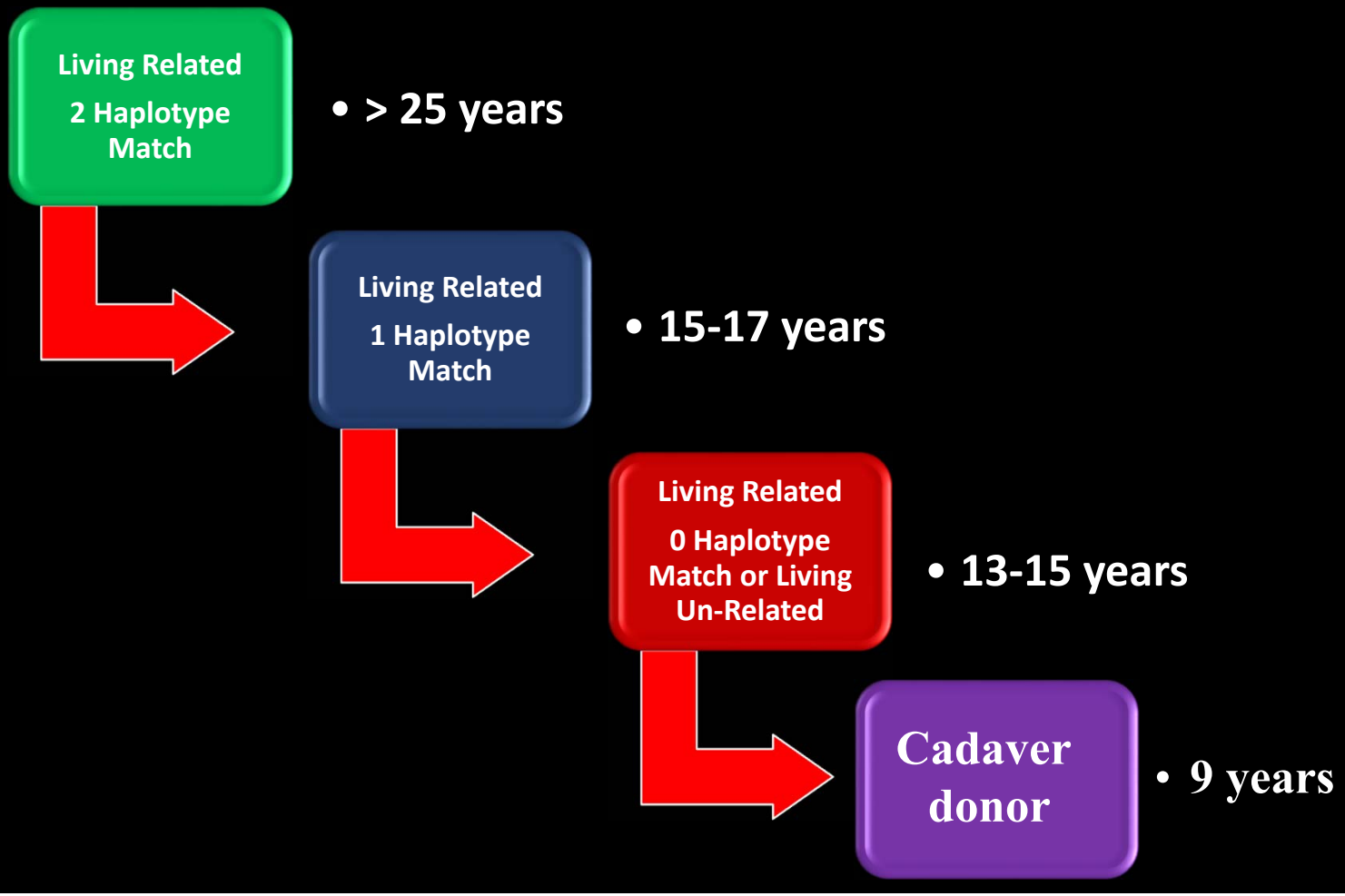
Expected Remaining Lifetimes in ESRD Patients, Transplant Patients and U.S. Population



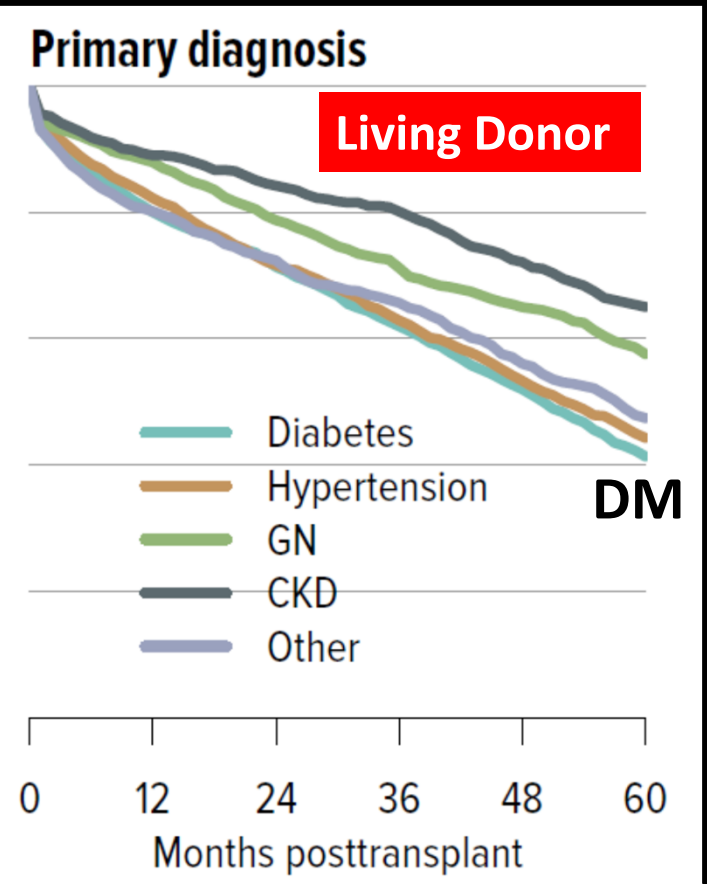
Outcome of Kidney Transplantation

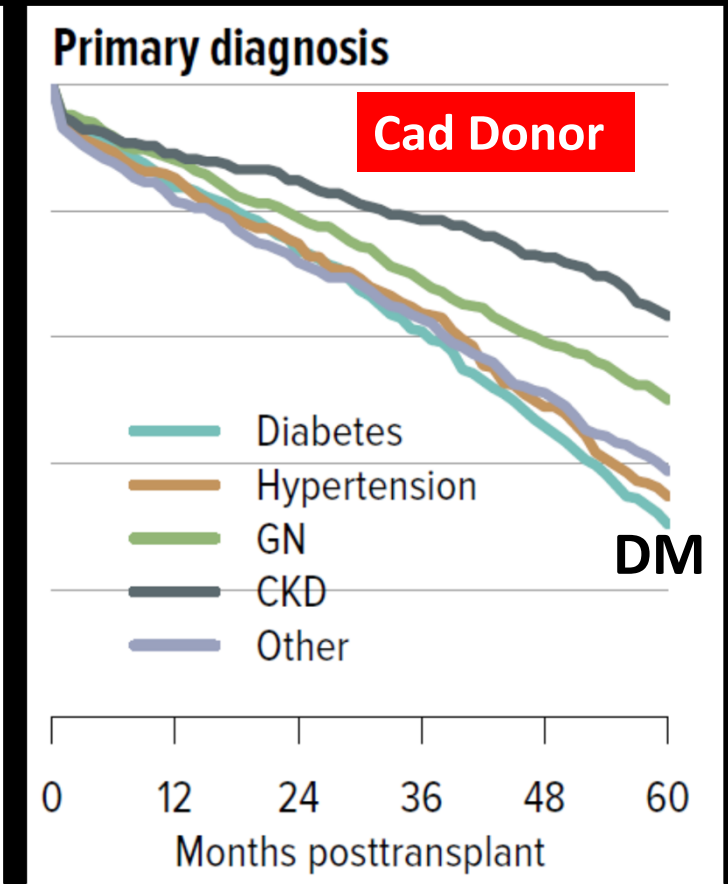


Influence of Donor Source on Renal Allograft Survival



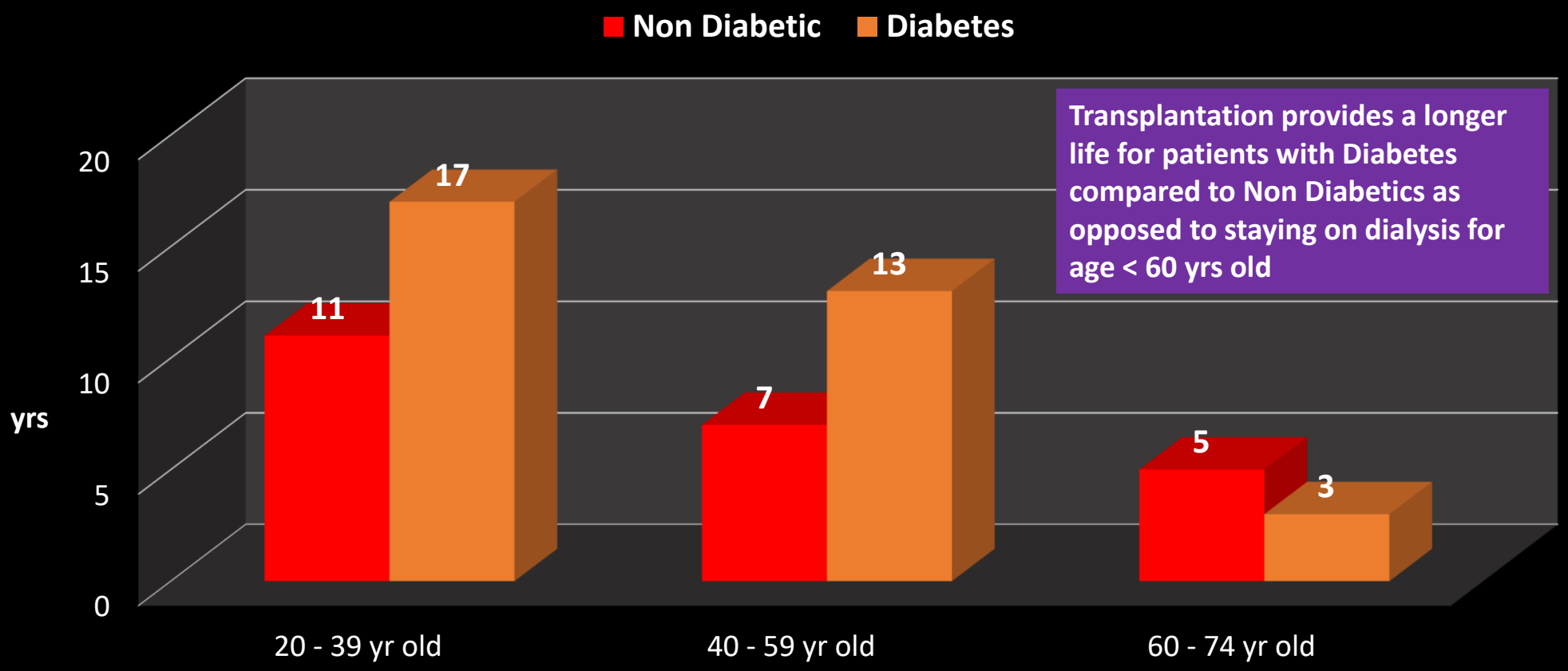
Outcome of Kidney Transplantation based on Etiology of ESRD



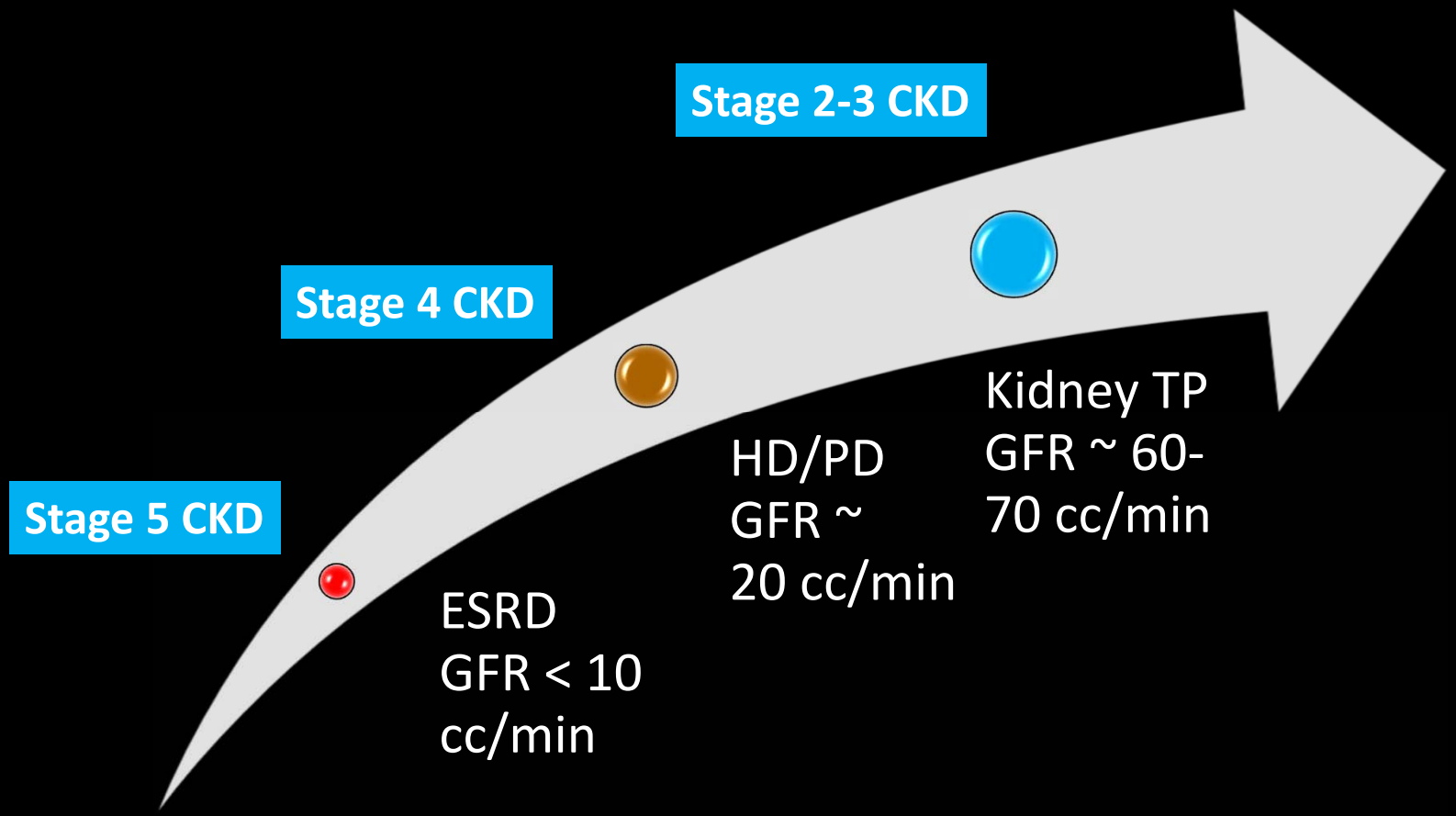


Due to multiple co-morbid conditions , patients with Diabetes experience the lowest graft survival with Living or cadaveric donors but still have a survival advantage over patients remaining on dialysis

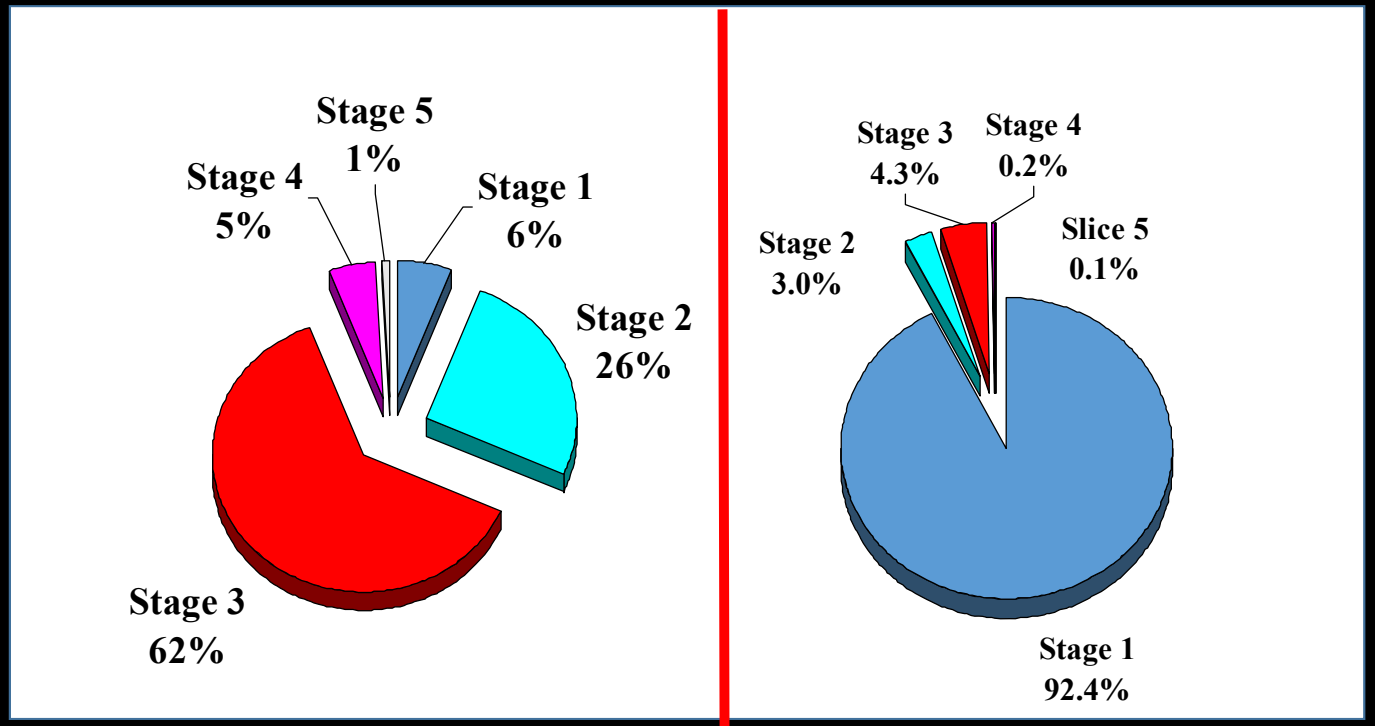
Projected EXTRA Years of Life Provided by Kidney Transplantation Compared to Dialysis



GFR Achieved by Different Renal Replacement Options



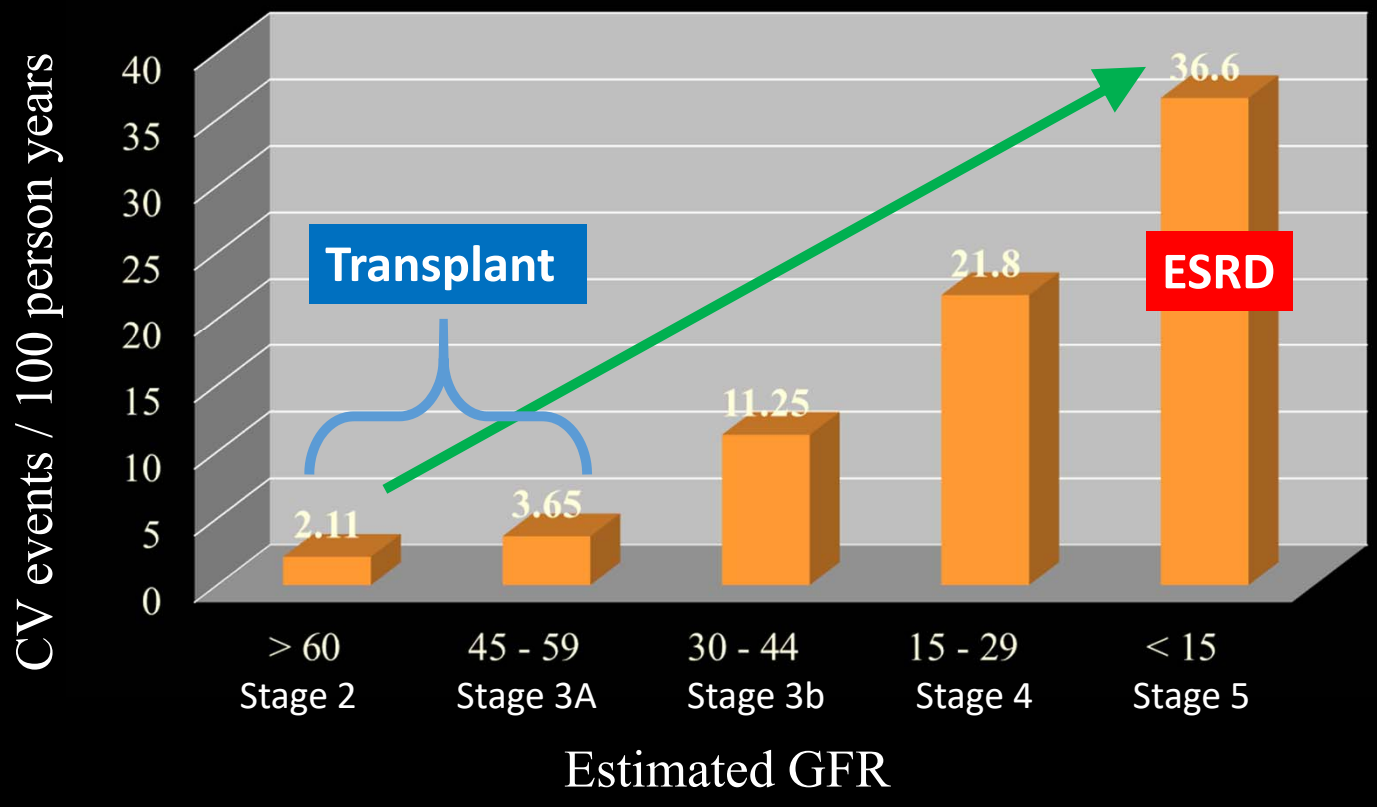
CKD and Renal Transplantation



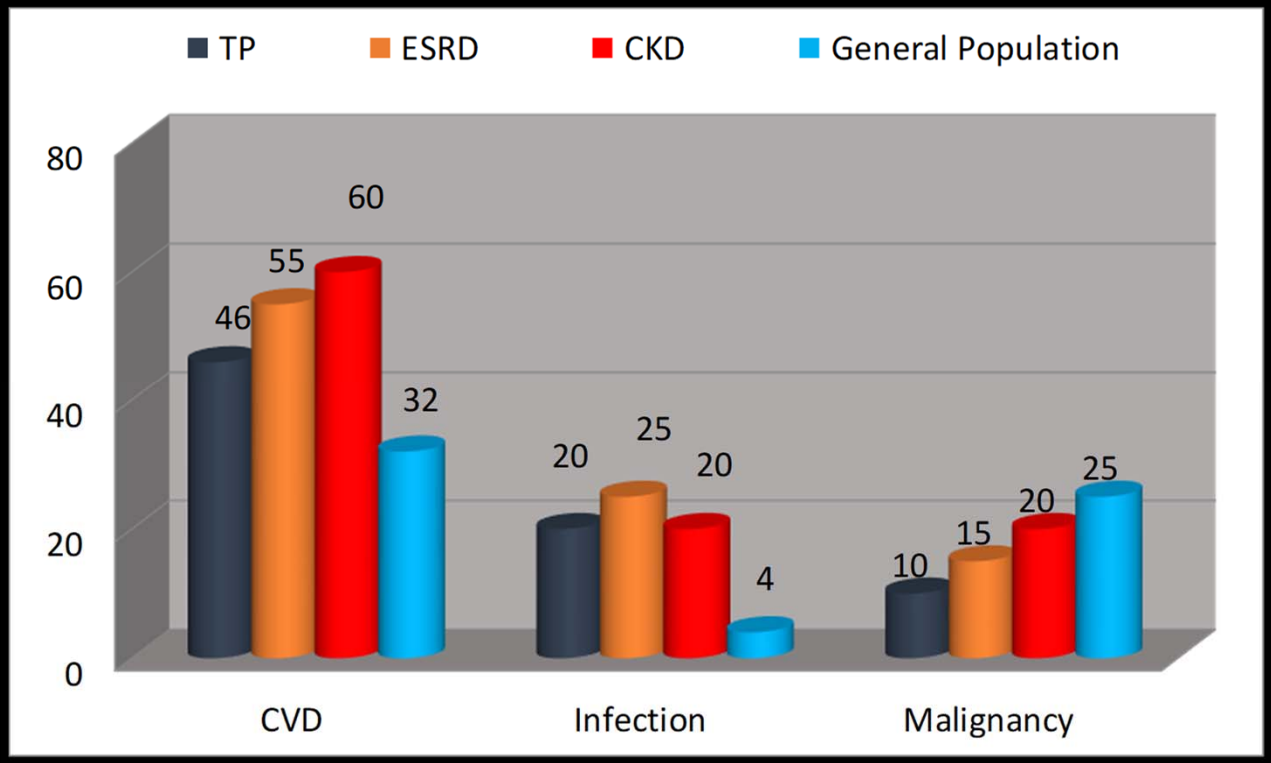
Renal TP

NHANES

Cardiovascular Disease in CKD and ESRD

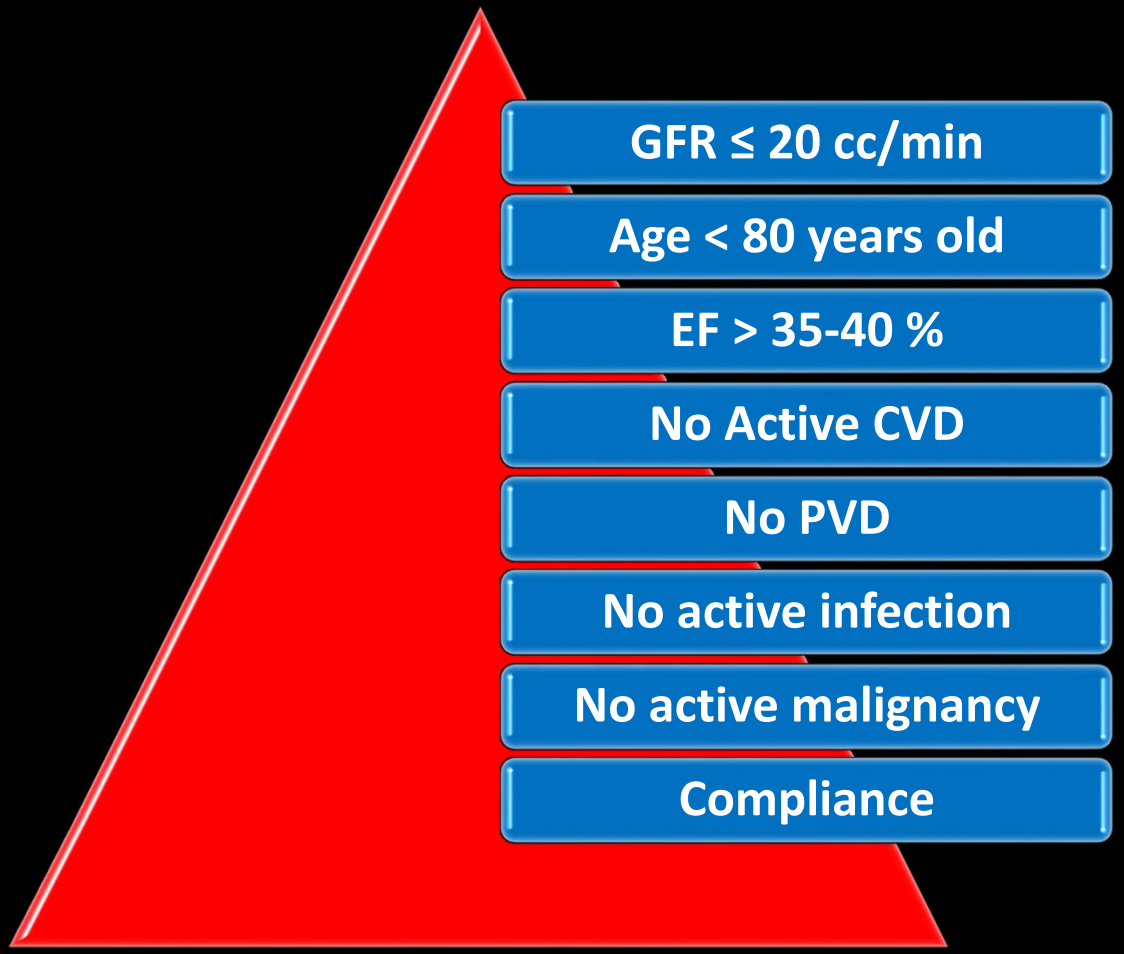


Causes of Death in TP, ESRD and CKD Patients



Cardiovascular Disease

Criteria for Listing for Kidney Transplantation



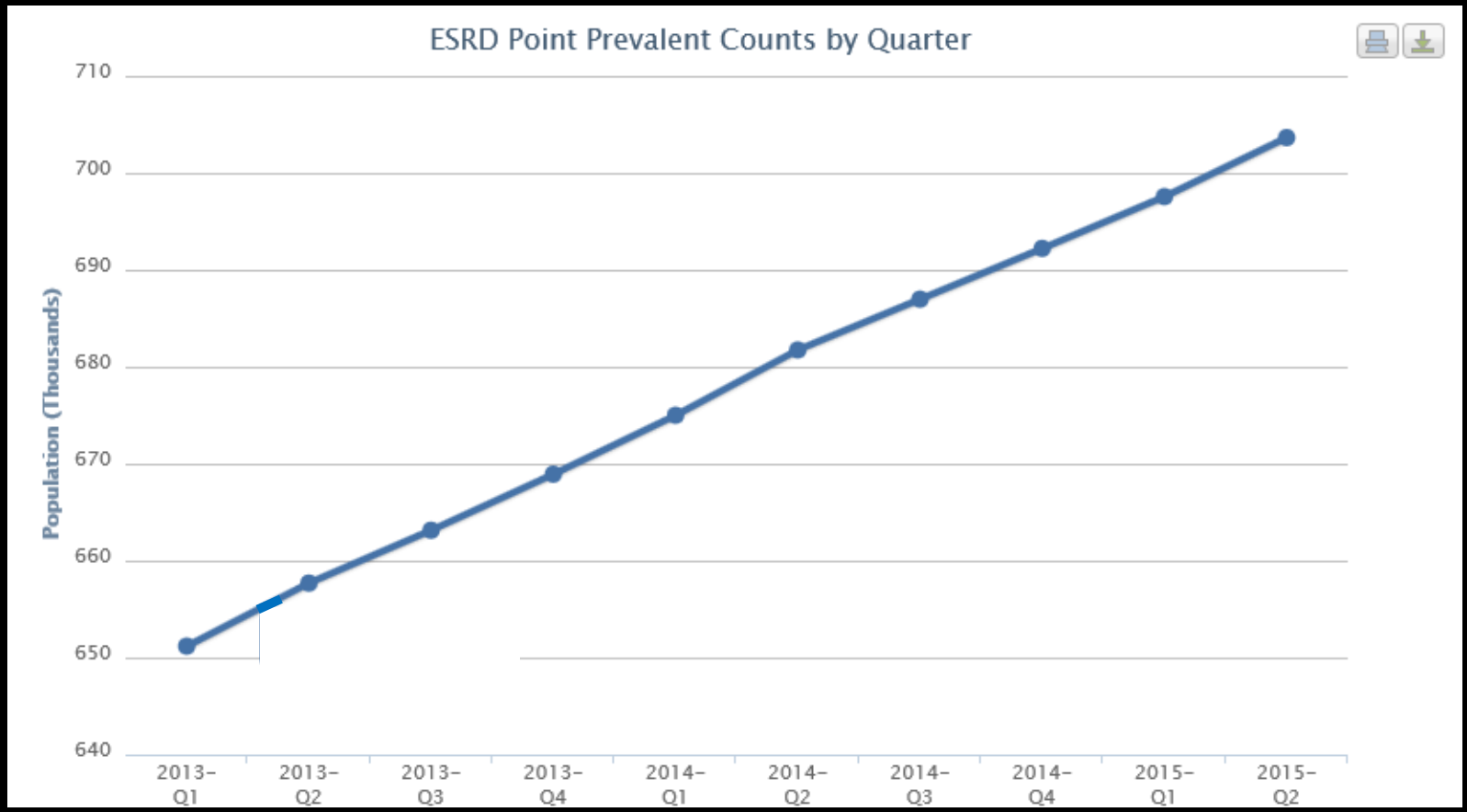
Patient Selection

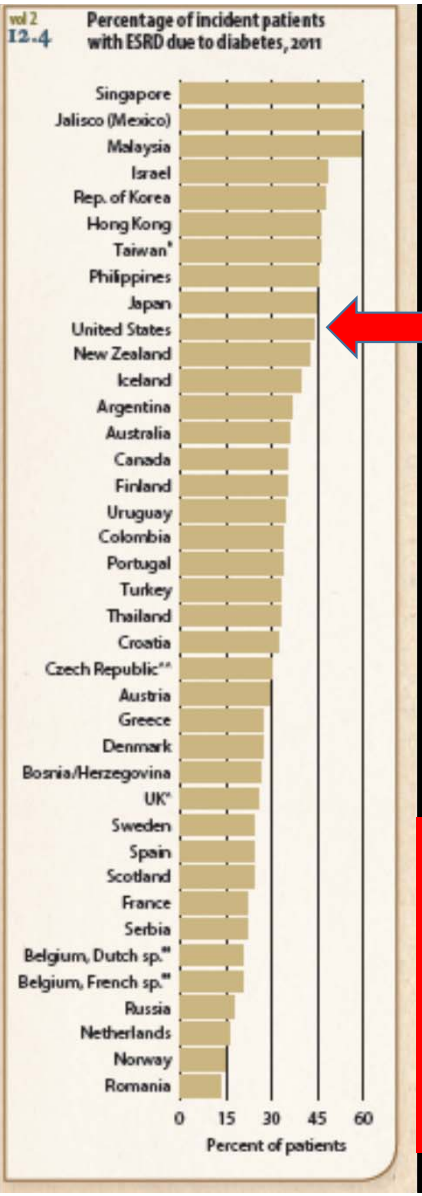
- Unique challenges
  - HIV
    - Patients with HIV are eligible as long as they are on therapy (HAART- Highly Active Anti Retroviral Therapy) and have undetectable HIV viral load by PCR and a CD4 count > 200/ml
    - May receive an HIV + cadaver donor kidney
  - Hepatitis C
    - A serious cause of progressive cirrhosis in dialysis patients and after transplantation
    - Patients need to be monitored closely with liver biopsies and viral load studies
    - HCV positive donors may be used for positive patients
      - Delay HCV treatment until after the transplant

The ESRD Facts

- The increased mortality of patients on dialysis is due to accelerated CVD
- Kidney transplantation offers the only renal replacement therapy that significantly improves quality of life and life expectancy
- Dialysis provides an average GFR of 20 cc/min (Stage 4) while kidney transplantation results in a GFR 60-70 cc/min (Stage 2-3 CKD)
- Risk of CVD is reduced but still present in transplant recipients
- Not every patient is a candidate for RRT (renal replacement therapy)

The Growth of the Dialysis Population Continues to Increase



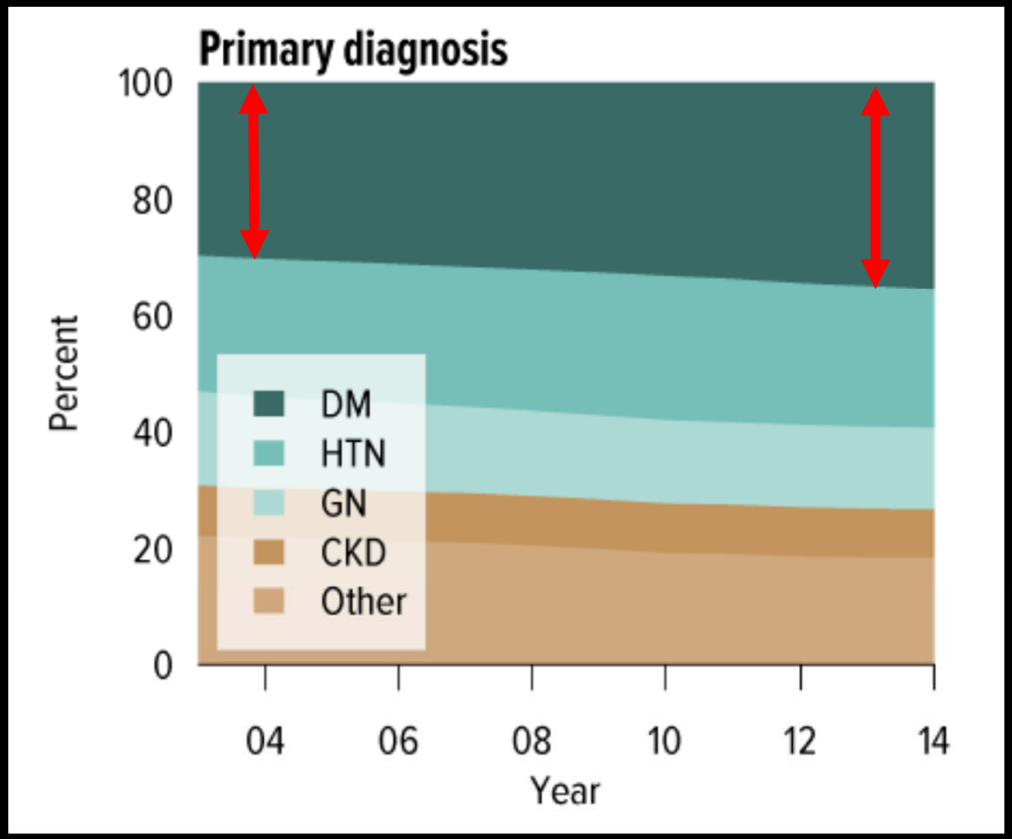


Diabetes as a Cause of ESRD : International Data

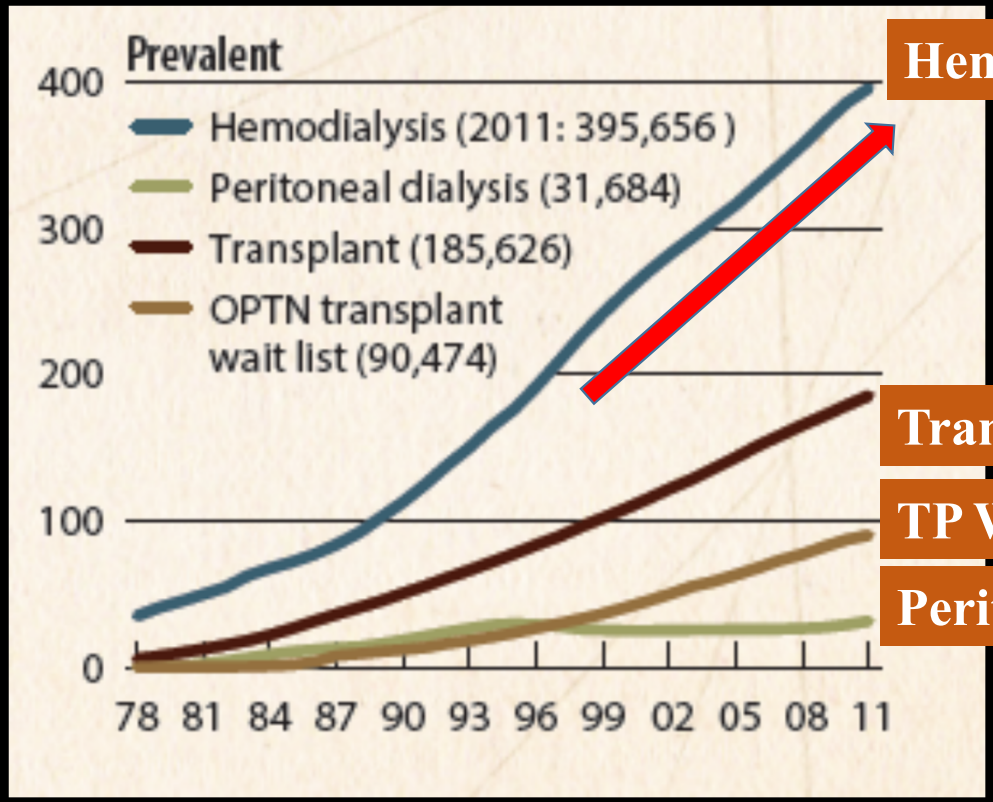
44%

2 million ESRD patients worldwide
Second Fastest Growing Cause
of Worldwide Mortality (HIV/AIDS)

Growing Prevalence of Diabetic Nephropathy on the Transplant Waiting List

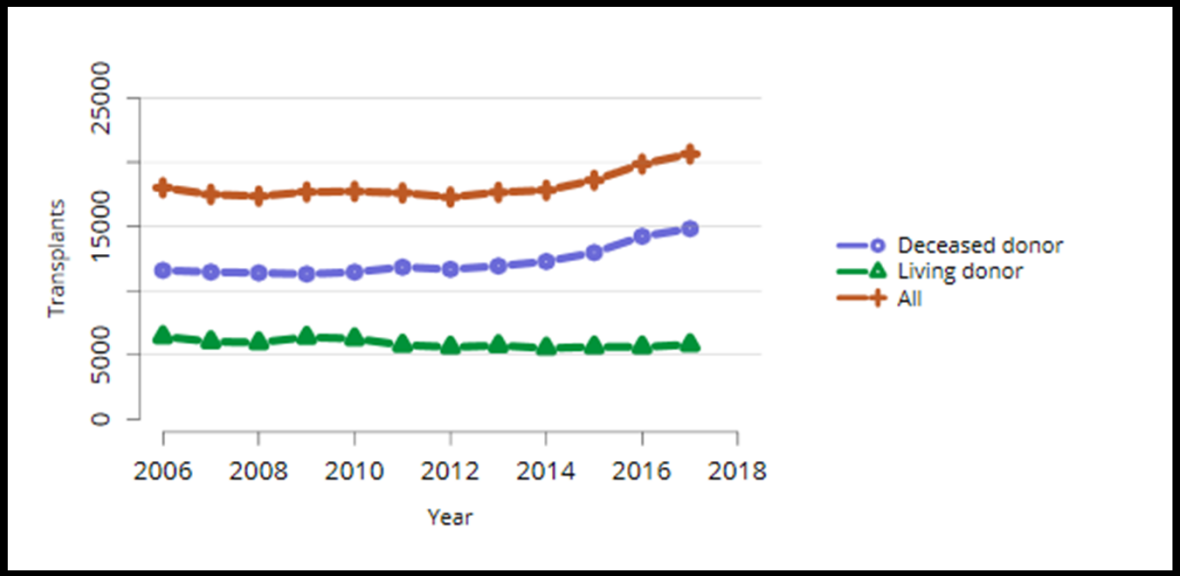


Projected growth of prevalent dialysis and transplant populations



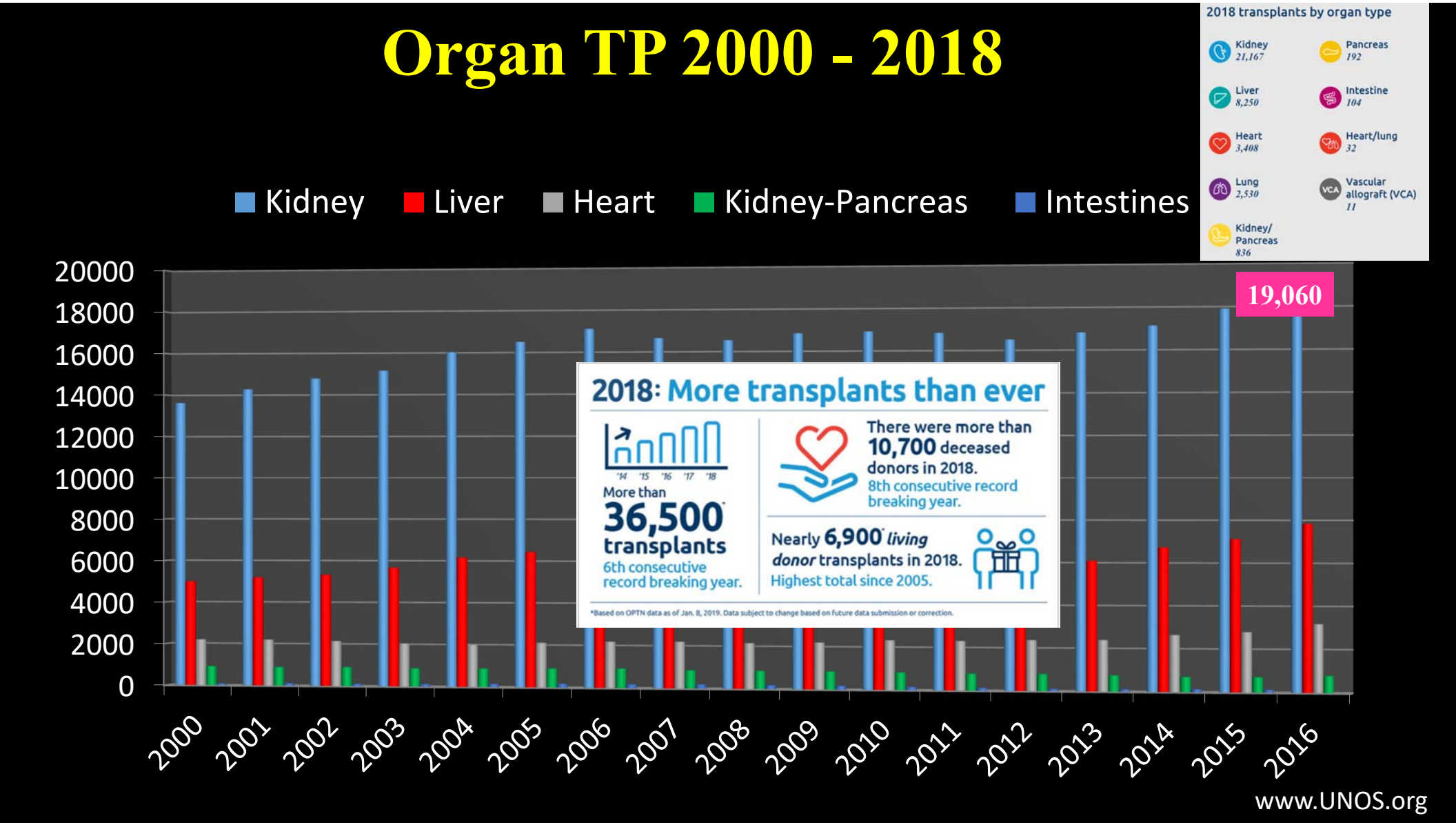
Kidney Transplants Per Year – Minimal Rise

102,809 on the Kidney Waitlist

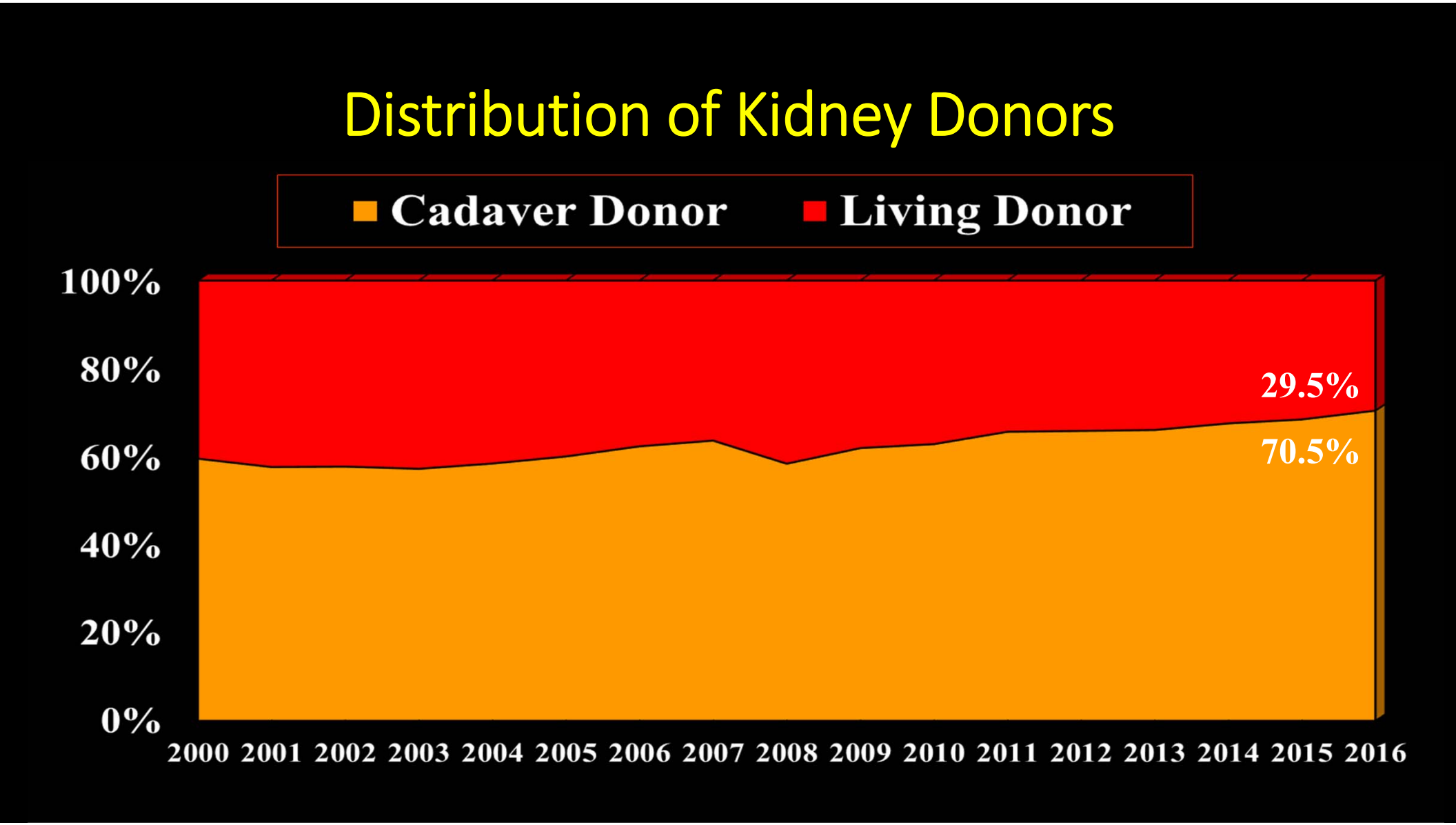


In 2018, 21,167 kidney transplants took place – 14,725 deceased donors and 6,442 living donors

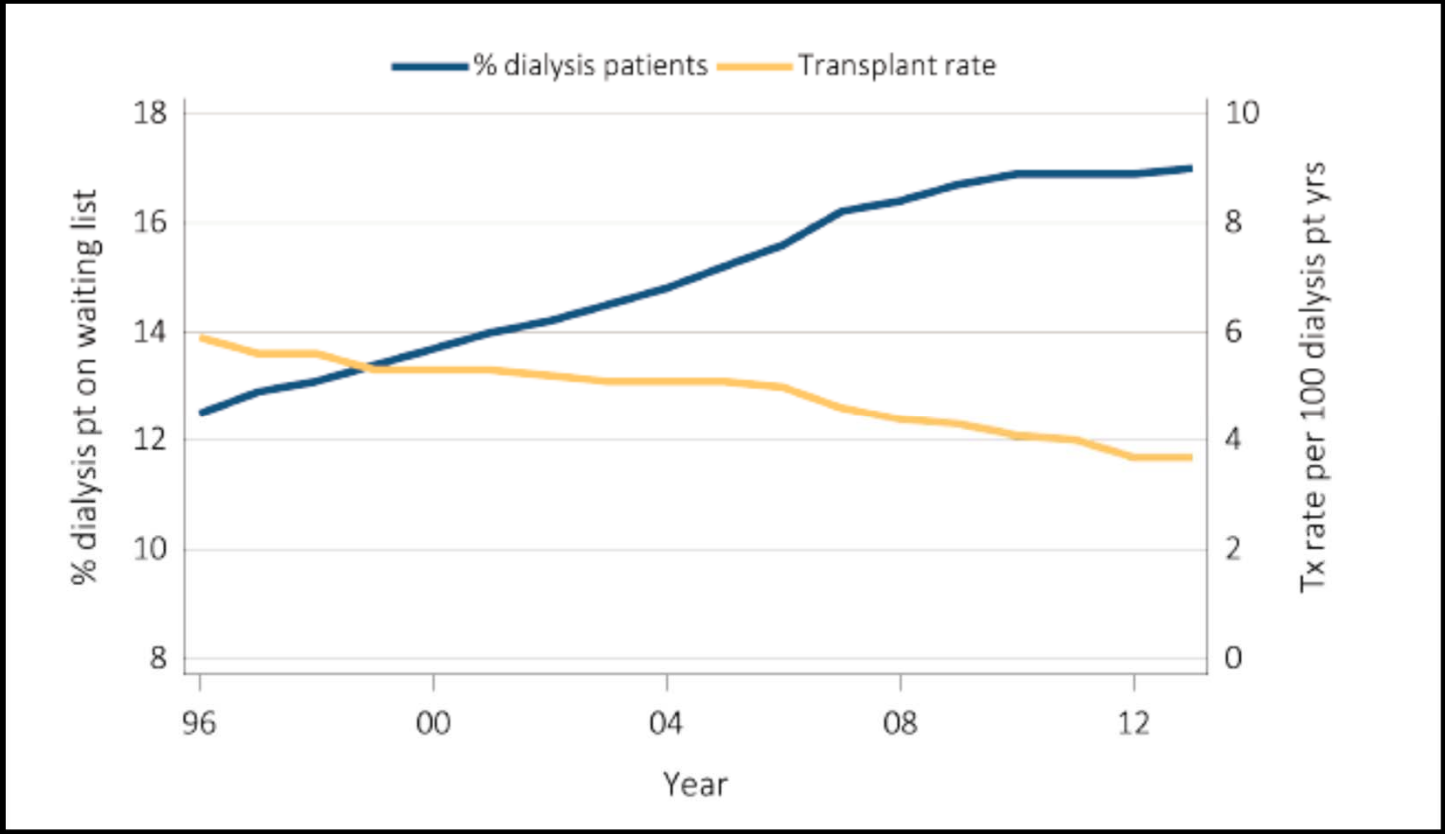
Organ TP 2000 - 2018



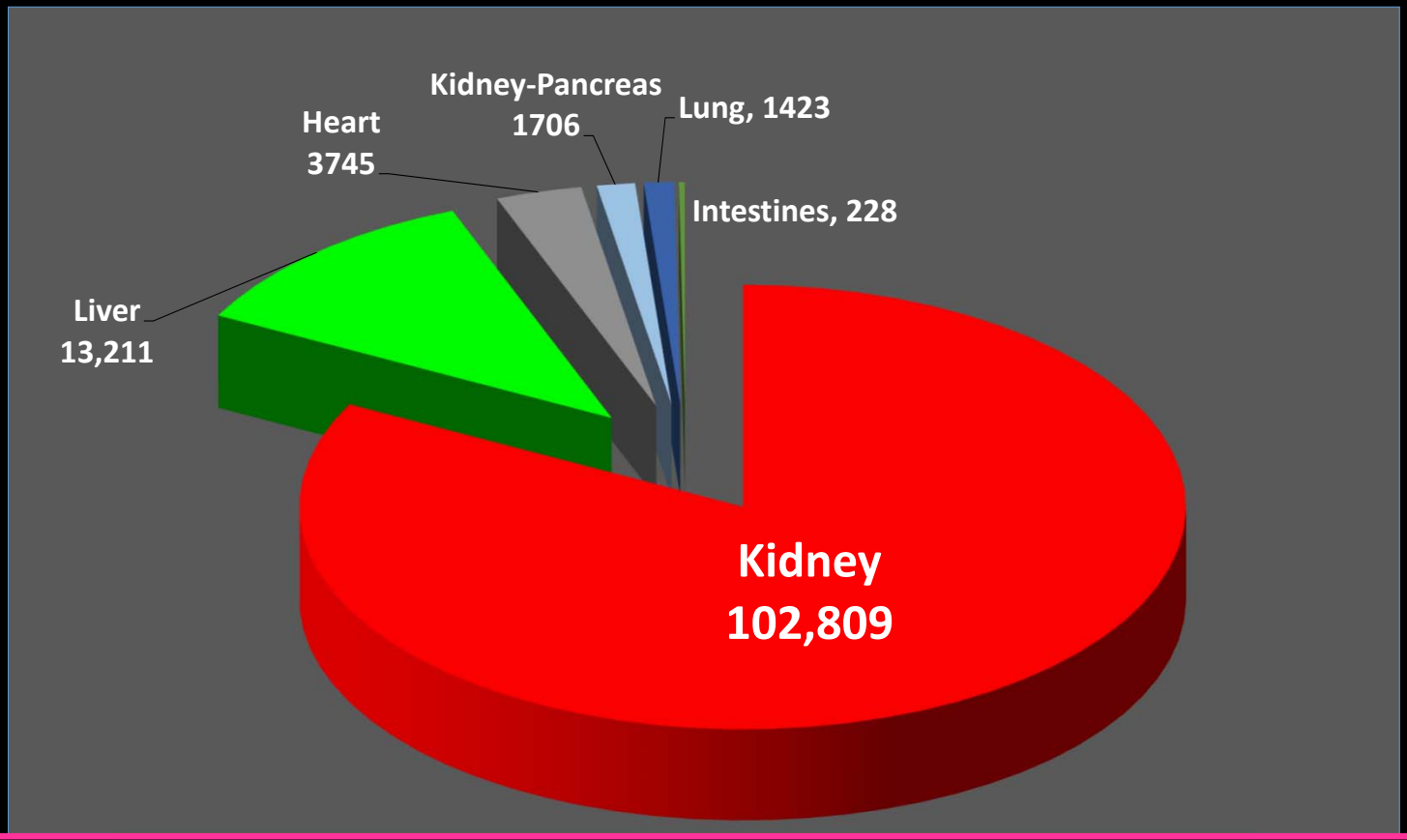
Distribution of Kidney Donors



Growing Disproportion Between Patients on the Waiting List and Those That are Transplanted



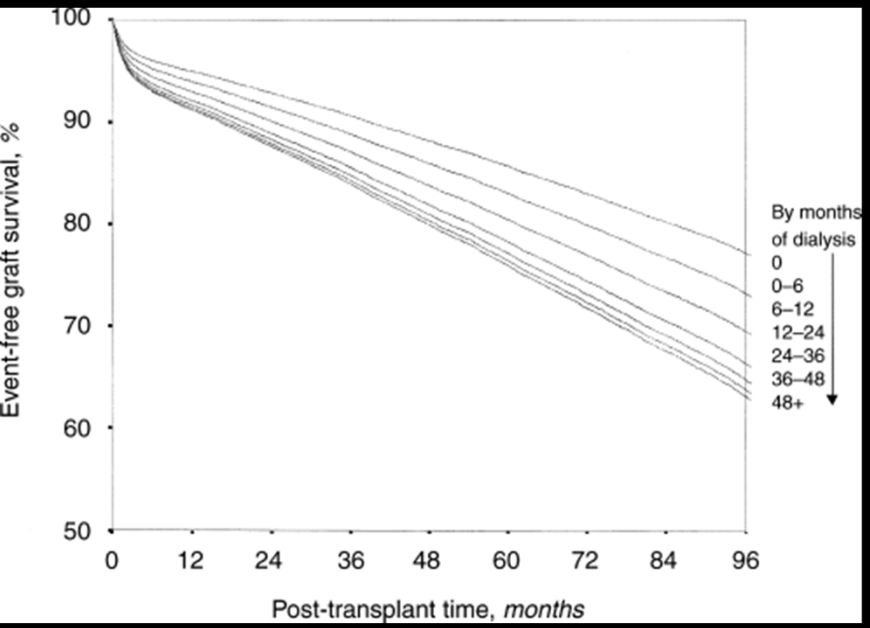
Transplant Waiting List : September 12, 2019



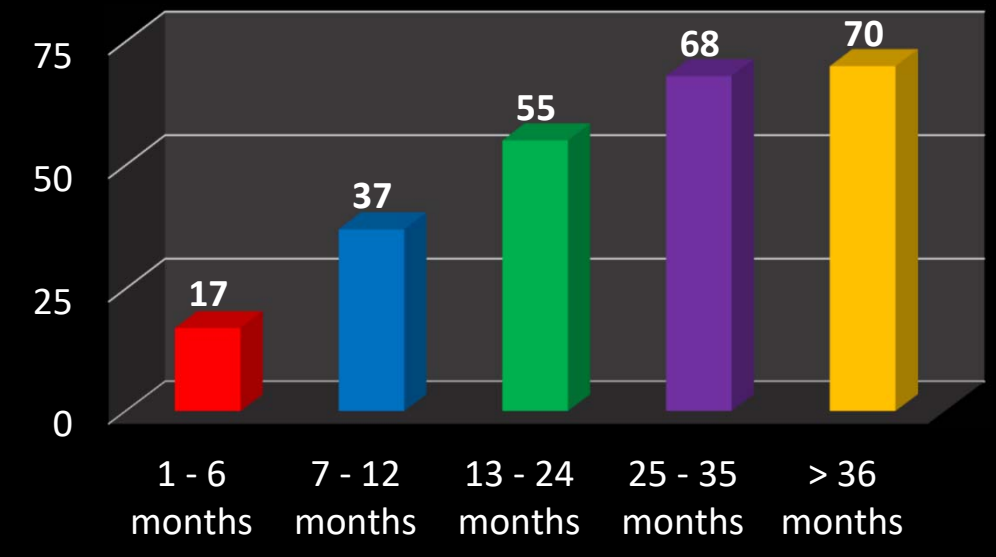
124,030 Candidates for a Solid Organ Transplant

Meier-Kriesche HU. Kidney Int. 2000;58(3):1311

Time on Dialysis Waiting for a Transplant Affects the Outcome of Transplantation

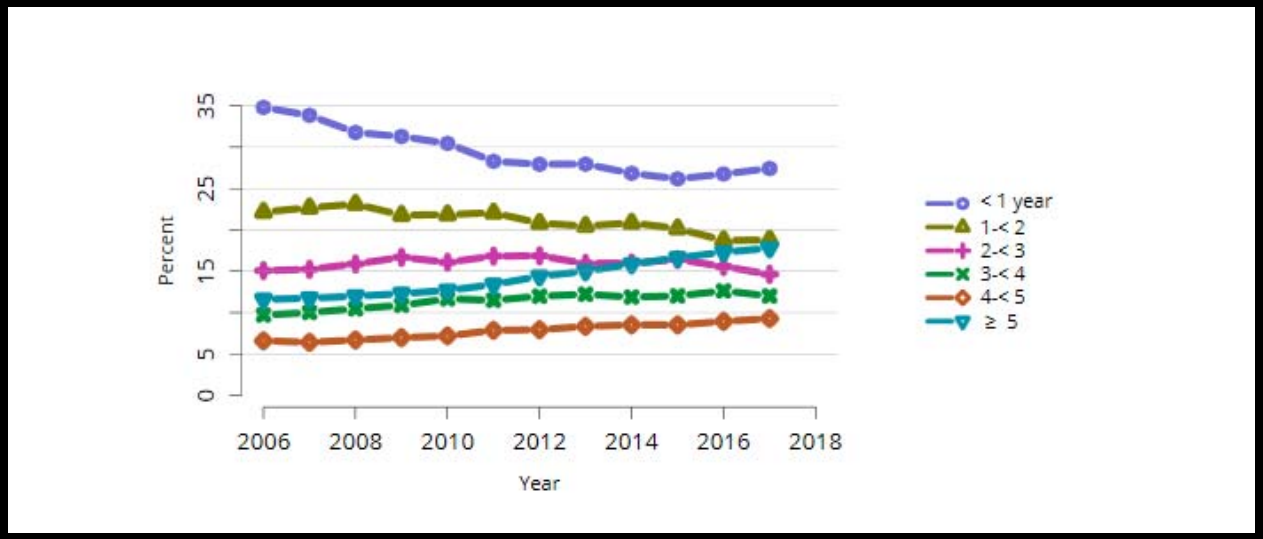


% Higher risk of graft loss



Getting a Transplant before going on dialysis provides the best chance for graft survival
The longer a patient is on dialysis the worse the graft outcome after transplantation

Patients are Waiting Longer and Longer for a Kidney Transplant

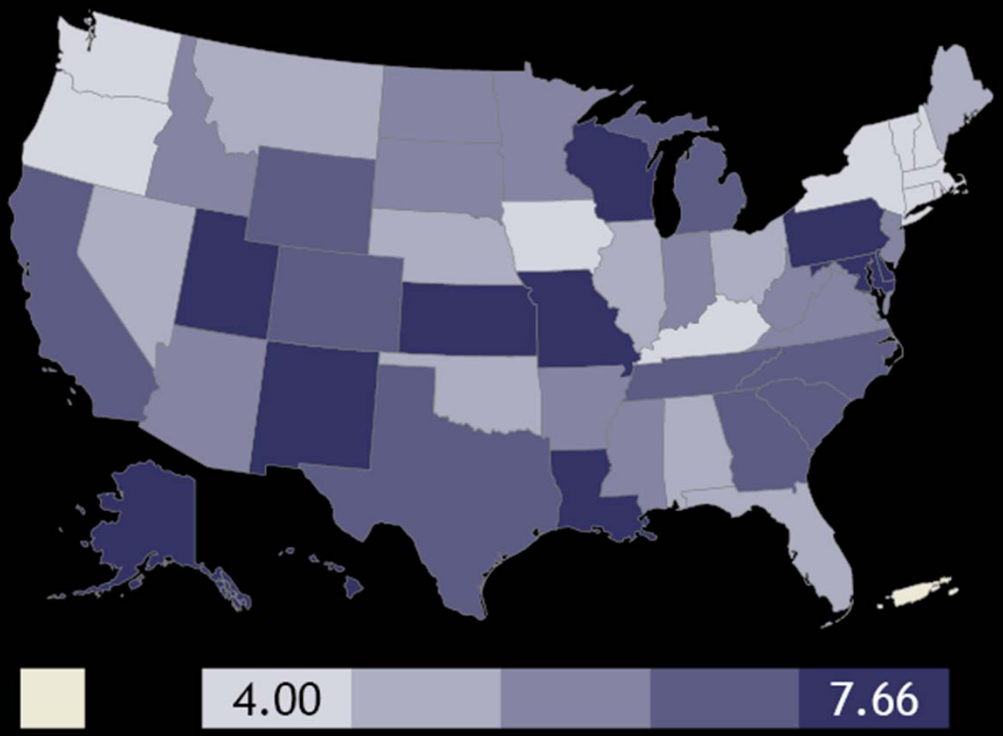


Average waiting time 3-4 years

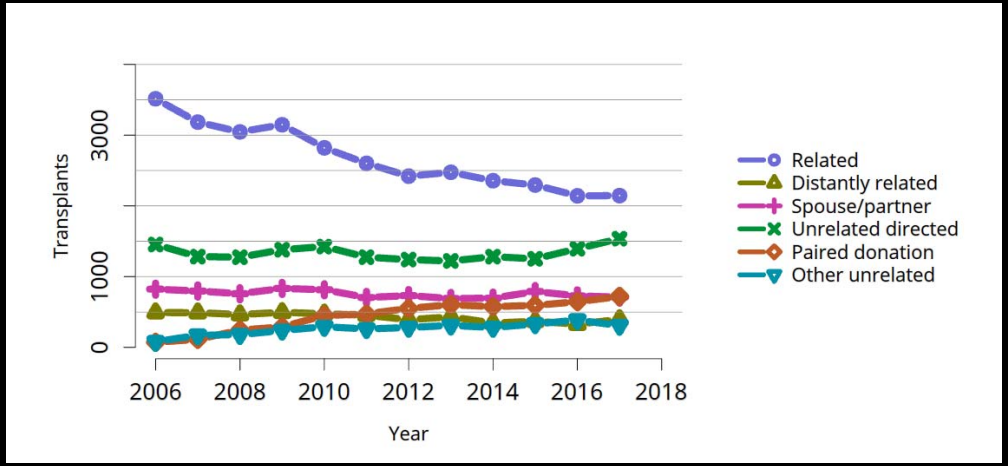
15% of patients are on the list > 5 years

Wide variation in Cadaveric Donation Rates in the U.S.

Cadaveric Kidney Donation rates (per 1000 deaths)



Significant Decrease in Related Living Donor Kidney Transplants



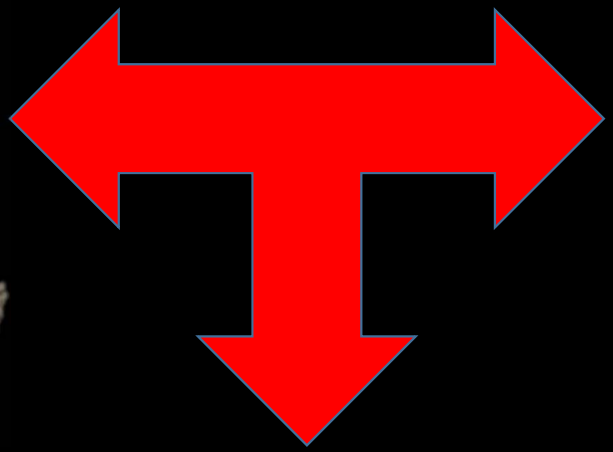
- The epidemic and concordance of obesity, HTN and Diabetes within a given family has led to the disqualification of a significant proportion of potential living donors
- The impact of DM in the U.S. affects not only the patients developing ESRD but also impacts their potential living organ donors

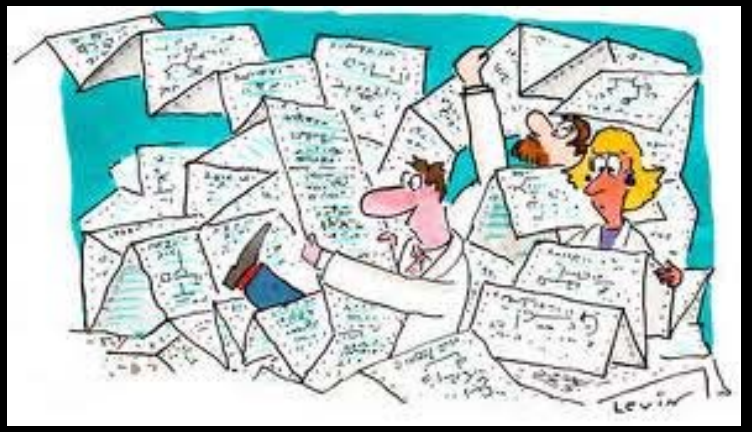
Kidney Donors

- Deceased donors (DDK)
- Living related donors (LRD)
  - HLA identical (ie sibling)
  - One-haplotype match (ie parent, sibling)
  - No HLA match
- Living unrelated donors (LURD)
  - Spouse
  - Friend
  - 'Swapping' programs – Paired exchange
  - Altruistic

Transplanting patients PRE-EMPTIVELY is the goal!

How are Kidneys Allocated to Recipients on the List ?





Who Gets the Next Kidney from the List ?

It used to be this .....

Now it is like this .....

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 Local pediatrics Local top 20% EPTS 0-ABDRmm (all) Local (all) Regional pediatrics Regional (top 20%) Regional (all) National pediatrics National (top 20%) National (all)	Highly Sensitized 0-ABDRmm Prior living donor Local pediatrics Local adults Regional pediatrics Regional adults National pediatrics National adults	Highly Sensitized 0-ABDRmm Prior living donor Local Regional National	Highly Sensitized 0-ABDRmm Local + Regional National

OPTN UNOS DONATE LIFE

EPTS & KDPI in the New System

The best kidneys are mandated to go to the best recipients

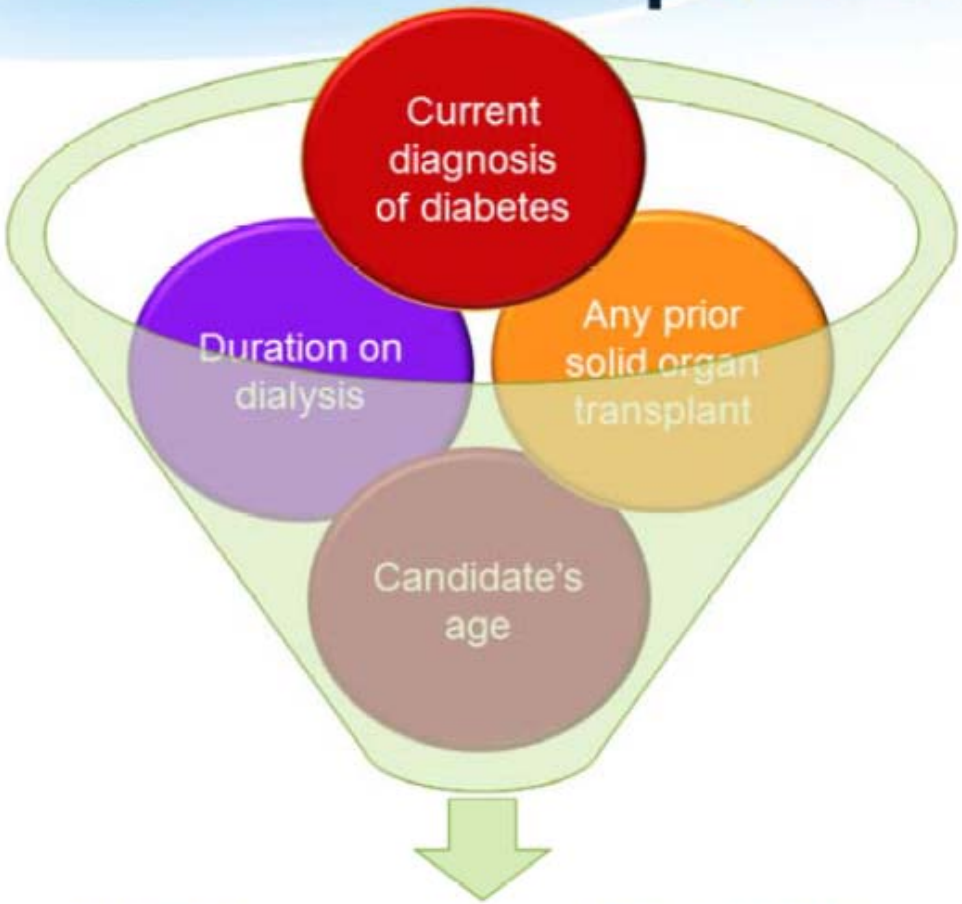
OPTN

UNOS DONATE LIFE
UNITED NETWORK FOR ORGAN SHARING

Allocation of Cadaveric Kidneys : Maximizing the Outcomes

- **December 4 , 2014 marked a turning point in the distribution of cadaveric kidneys with the creation of 2 new indices – EPTS / KPDI**
- **Donor KDPI (Kidney donor Prognostic Index)**
  - Age
  - Height
  - Weight
  - Ethnicity
  - History of Hypertension
  - History of Diabetes
  - Cause of Death
  - Serum Creatinine
  - Hepatitis C Virus (HCV) Status
  - Donation after Circulatory Death (DCD) Status

Estimated Post Transplant Survival



EPTS score range 0%-100%

OPTN

UNOS DONATE LIFE
UNITED NETWORK FOR ORGAN SHARING

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 mismatch	Zero mismatch
Prior living donor	Prior living donor	Prior living	+ Regional
Local pediatrics	Local pediatrics	Local	
Local top 20% EPTS	Local adults	Regional	
Zero mismatch (all)	Regional pediatrics	Nation	
Local (all)	Regional adults		
Regional pediatrics	National pediatrics		
Regional (top 20%)	National adults		
Regional (all)			
National pediatrics			
National (top 20%)			
National (all)			

New categories for highly sensitized candidates

No Priority Given to Pre-emptive Patients – Time Accumulated on the List Based on Dialysis Time

Which of these statements is correct ?

A. **Referral for kidney transplantation should be limited to how sick a patient is on dialysis and only if the potential recipient has a living donor.**

B. **Due to the side effects of lifelong immunosuppression, transplant patients have the same survival as dialysis patients but have a much better quality of life being free from regular dialysis treatments**

C. **Patients are officially listed for kidney transplantation once they begin dialysis therapy with either hemodialysis or peritoneal dialysis**

D. **The average waiting time for a kidney transplant in the U.S. is approximately 1-2 years**

E. **All are correct**

F. **None are correct**

Pre-emptive Transplantation – Key to Successful Patient and Graft Survival

What Needs to Be Done to Improve Transplant Opportunities: Action Is Warranted

HIV patients and Kidney Transplantation….

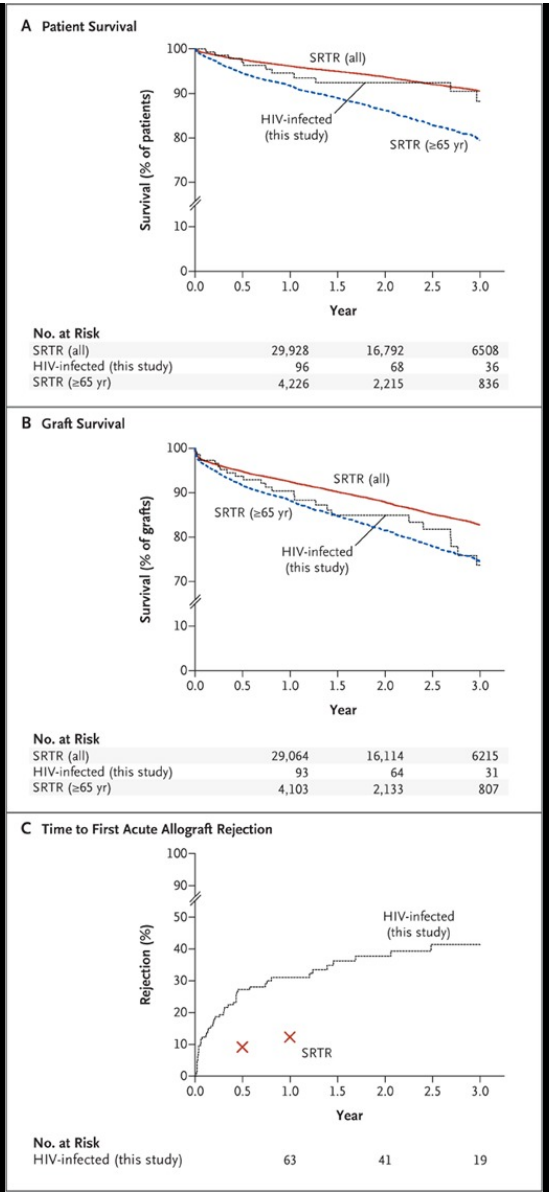
ORIGINAL ARTICLE

Outcomes of Kidney Transplantation in HIV-Infected Recipients

Peter G. Stock, M.D., Ph.D., Burc Barin, M.S., Barbara Murphy, M.D., Douglas Hanto, M.D., Ph.D., Jorge M. Diego, M.D., Jimmy Light, M.D., Charles Davis, M.D., Emily Blumberg, M.D., David Simon, M.D., Ph.D., Aruna Subramanian, M.D., J. Michael Millis, M.D., G. Marshall Lyon, M.D., et al., for the HIV-TR Investigators

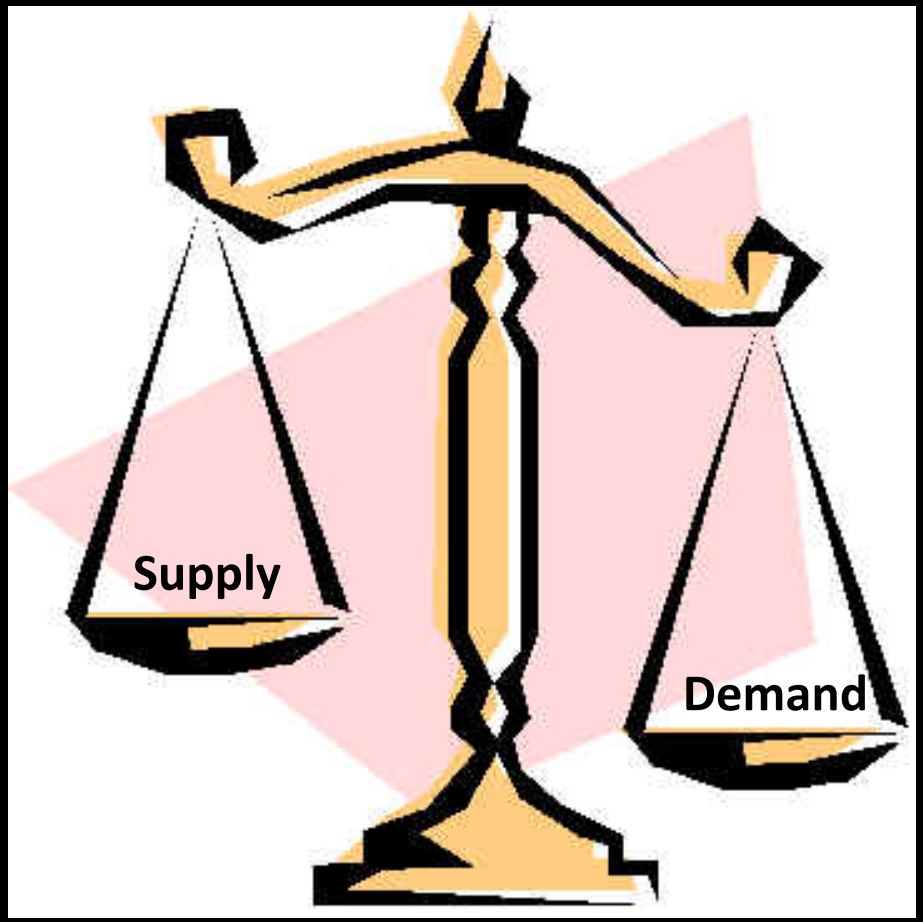
N Engl J Med 2010; 363:2004-2014

HIV- kidneys transplanted into recipients with HIV (under cART)
CD4 > 200
Undetectable viral load



- **Excellent patient and graft survival rate**
- **Higher risk of rejection**
- **Conclusion**
  - **HIV+ patients selected on the basis of having good viral control can successfully receive kidney transplants**

Transplantation in HIV Patients

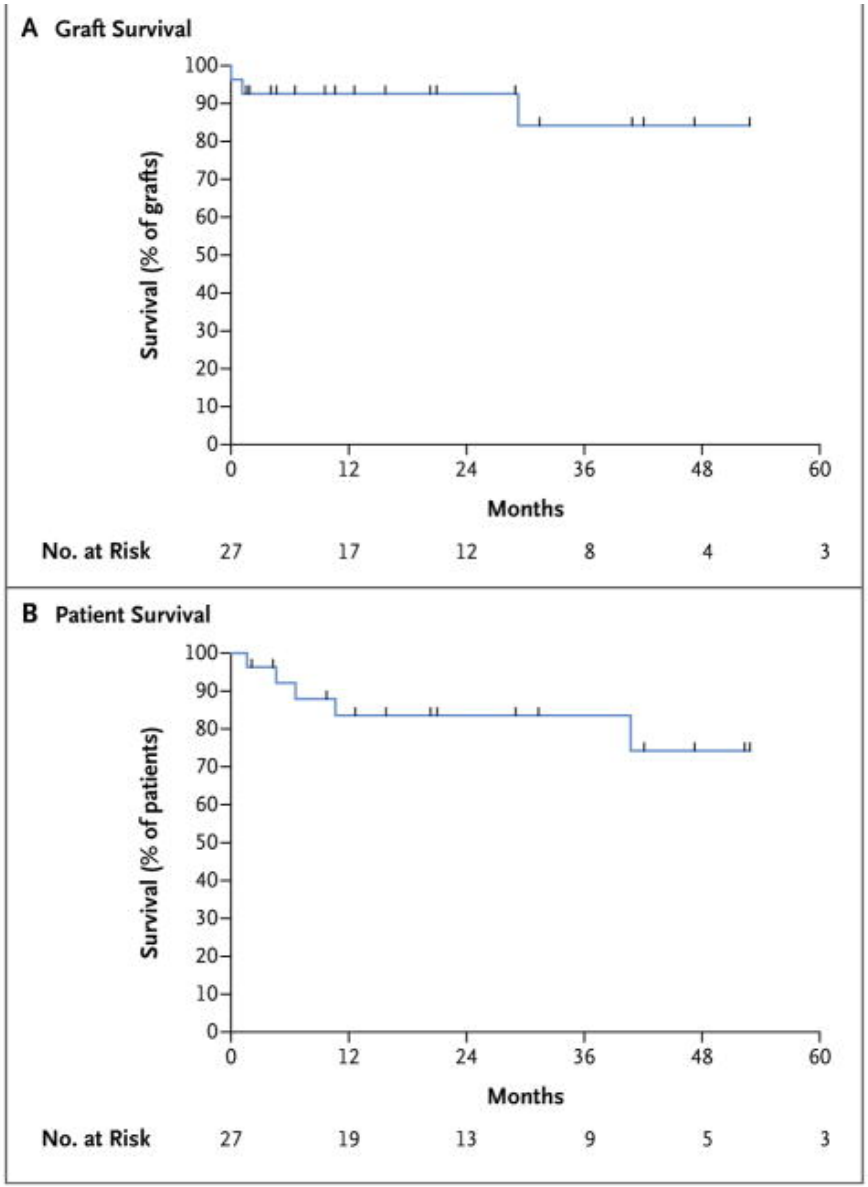


- HIV infected individuals are 28% less likely to receive a transplant overall
- 50% lower chance of getting a living donor kidney

But there is H.O.P.E. for HIV Patients

HIV Organ Policy Equity Act
Signed February 14, 2013

Authorizes clinical research and the revision of rules about organ donation and transportation as a result of the research. Organs from HIV donors would only be going to individuals who are already HIV positive (could lead to 600 additional organ transplants a year)



HIV+ Cadaveric Donors to HIV+ Recipients

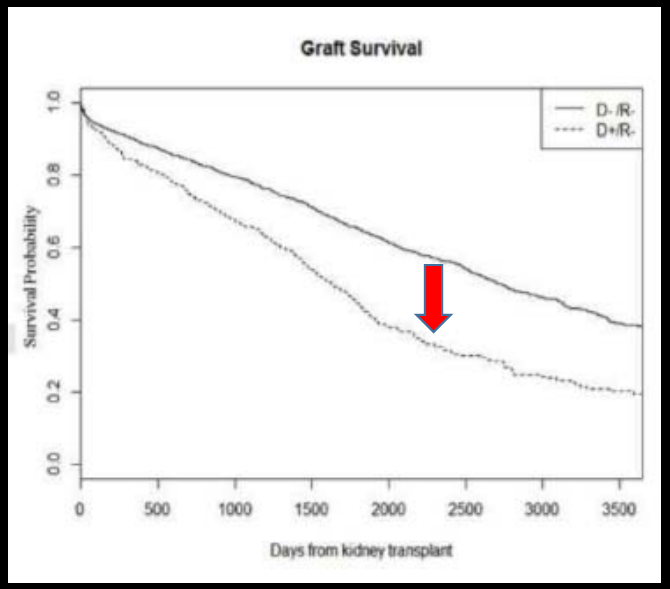
- Similar short and long term survival compared to HIV negative cohort
- No patients experienced an increased HIV viral load
- No transmission of cART resistance was detected
- CD4 counts decreased the first year < 200 but increased afterward
- Risk of rejection was 22%

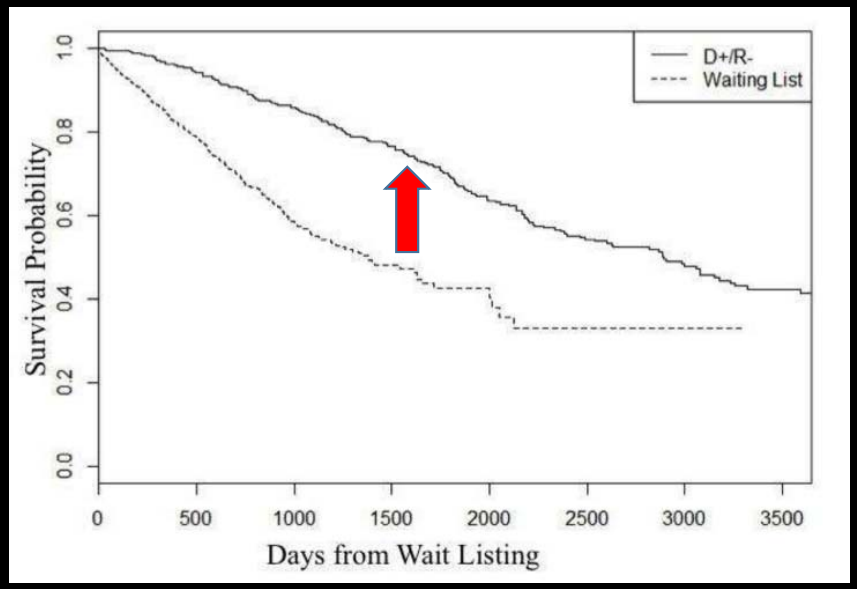
Muller E. N Engl J Med. 2015 May 21; 372(21): 2070–2071.

G Gupta. Clinical transplantation , 2017

HCV+ Donors for HCV- Recipients

- **Recipients will all acquire HCV+ status**
- **Direct Acting Acting Antivirals (DAA) started as soon as possible posttransplant**





- **Although graft survival is inferior to HCV- donors/HCV- recipients , the patient survival is still superior compared to remaining on dialysis therapy**
- **Currently being done under NIH protocols in selected centers**

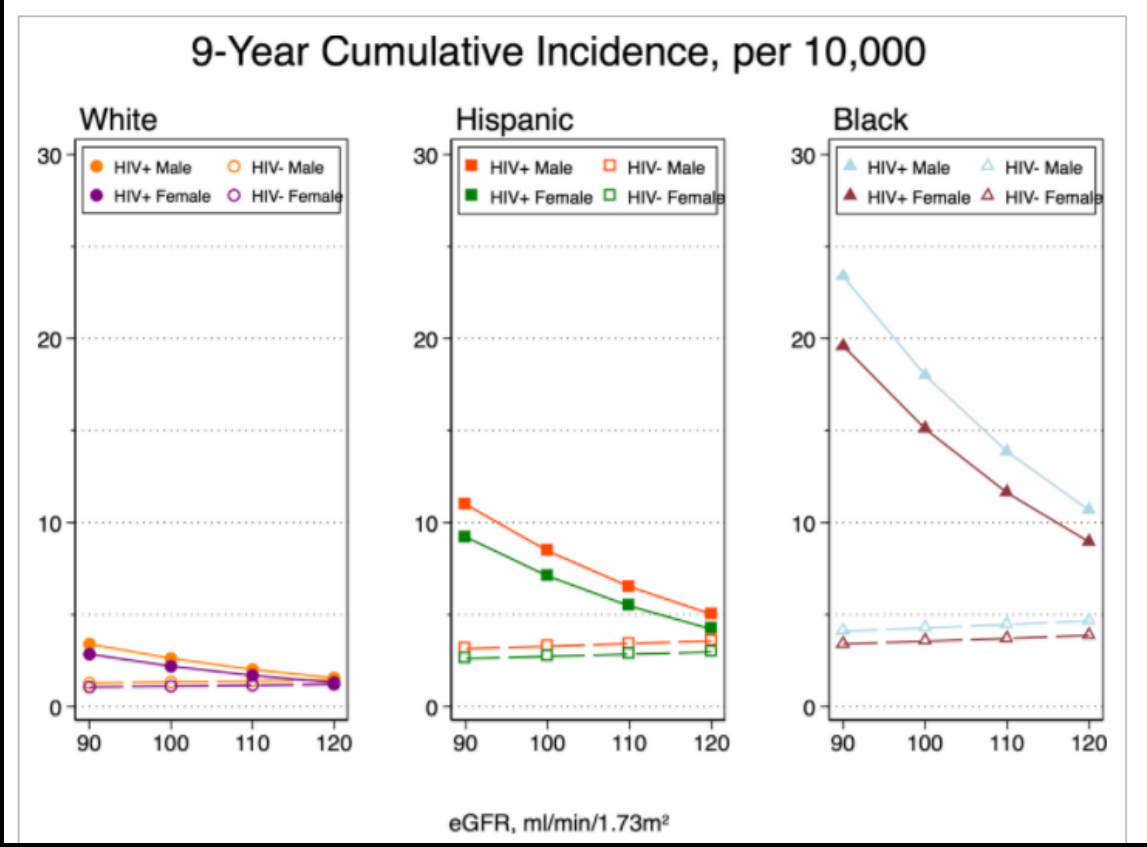
Will transplant centers consider this type of living donor as a possibility?

- Hep C donors – donors are aviremic and now should be considered for possible transplant if no signs of cirrhosis
- HIV Donors – still controversial
- Times are Changing!!!!

HIV+ Living Donors to HIV+ Recipients

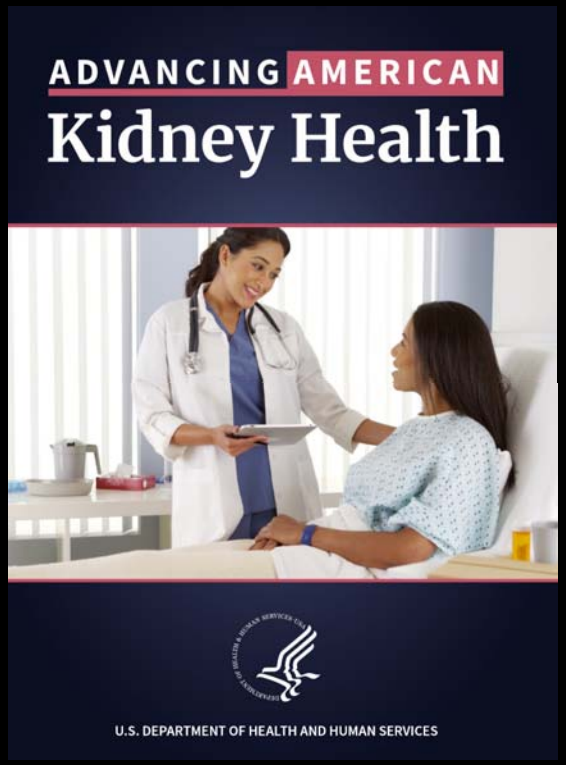
- **Risks**
  - HIV directly infects the kidneys and the donor may experience a higher risk of kidney injury over their lifetime with HIV infection
    - This risk would only be present in black race donors
  - Many cART agents are nephrotoxic : PI , NRTI
  - The effect of hyperfiltration on an HIV infected kidney in the donor is unknown
  - Black race and Hispanic HV+

  - **APOL1 measurement in black race HIV+ donors is essential to estimate the risk of ESRD**



Muzaale A.American journal of transplantation. , 2017, Vol.17(7), p.1823-1832

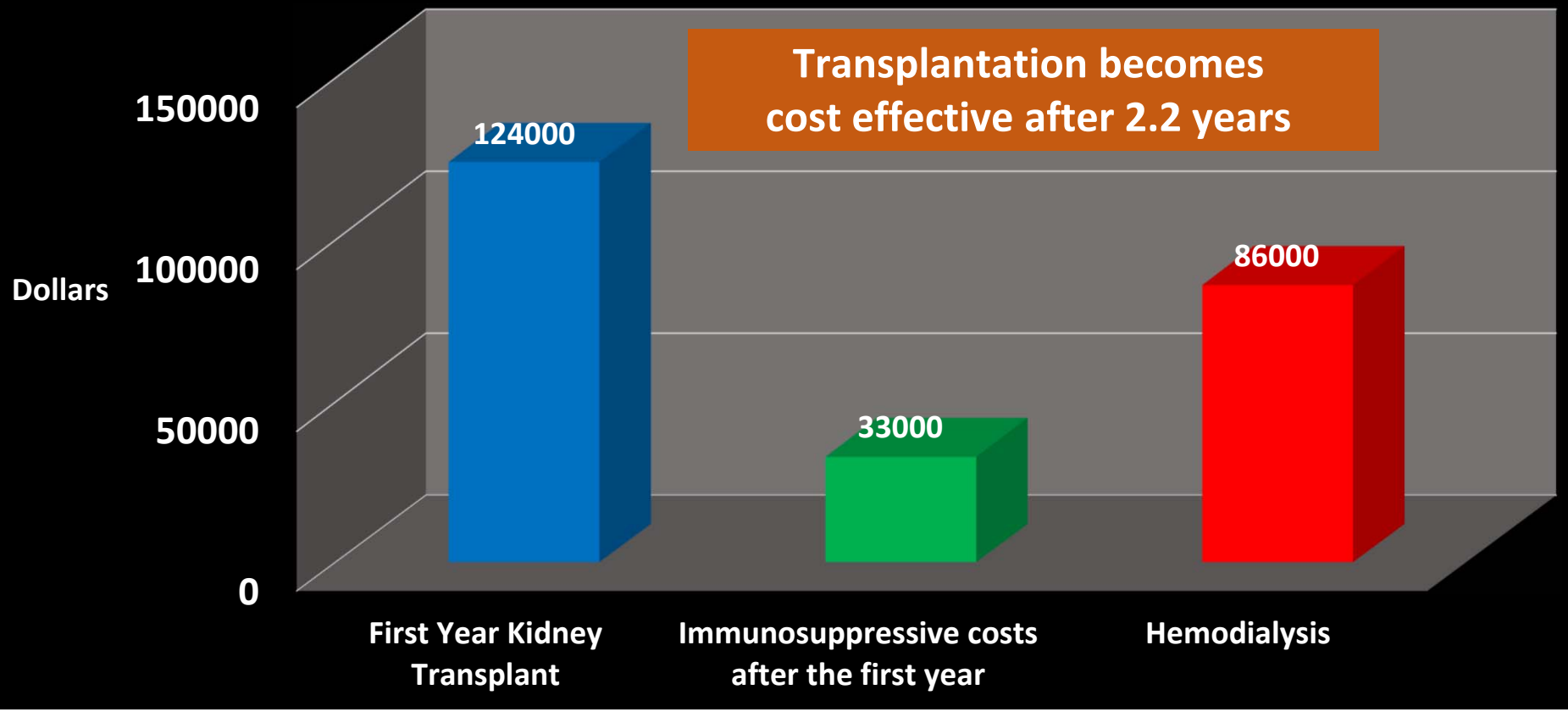
HHS Launches President Trump's 'Advancing American Kidney Health' Initiative 2019



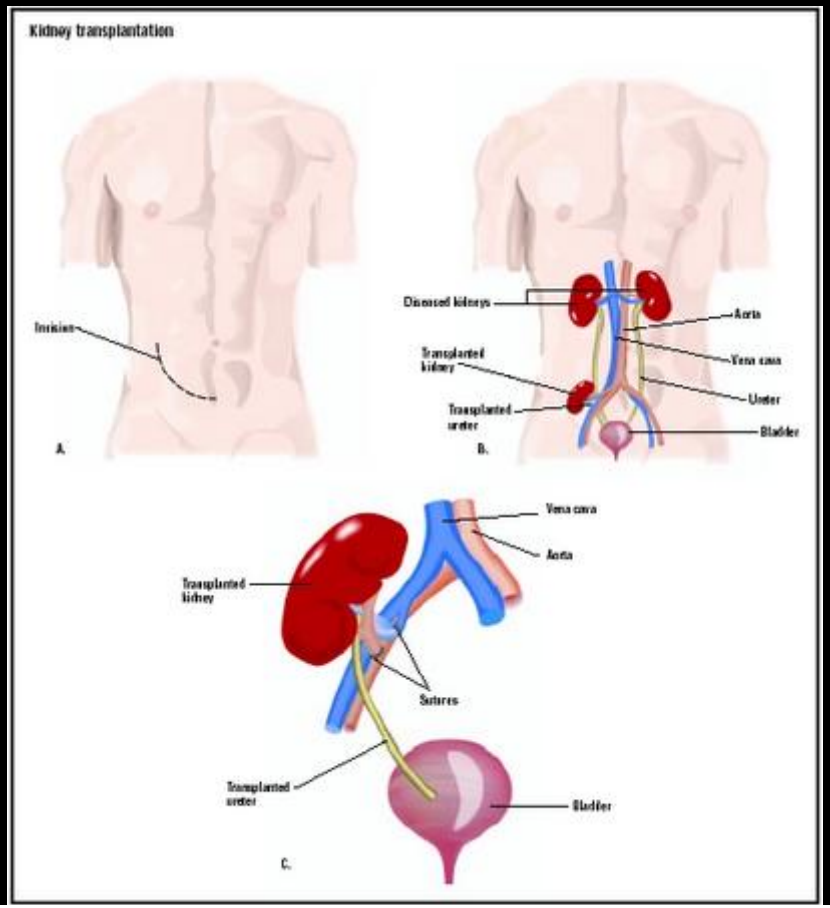
We have set three particular goals for delivering on this vision, with tangible metrics to measure our success:

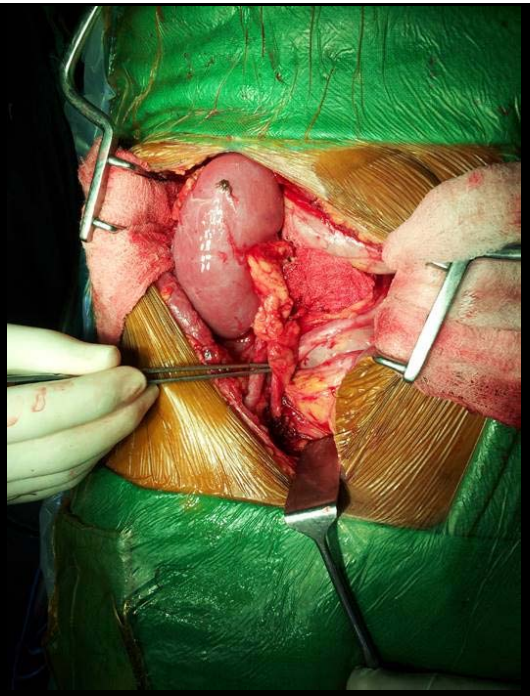
1. We need more efforts to prevent, detect, and slow the progression of kidney disease, in part by addressing upstream risk factors like diabetes and hypertension. We aim to reduce the number of Americans developing end-stage renal disease by 25 percent by 2030.
2. We need to provide patients who have kidney failure with more options for treatment, from both today's technologies and future technologies such as artificial kidneys, and make it easier for patients to receive care at home or in other flexible ways. We aim to have 80 percent of new American ESRD patients in 2025 receiving dialysis in the home or receiving a transplant.
3. We need to deliver more organs for transplants, so we can help more Americans escape the burdens of dialysis altogether. We aim to double the number of kidneys available for transplant by 2030.

Cost Benefit of Kidney Tranpslantation

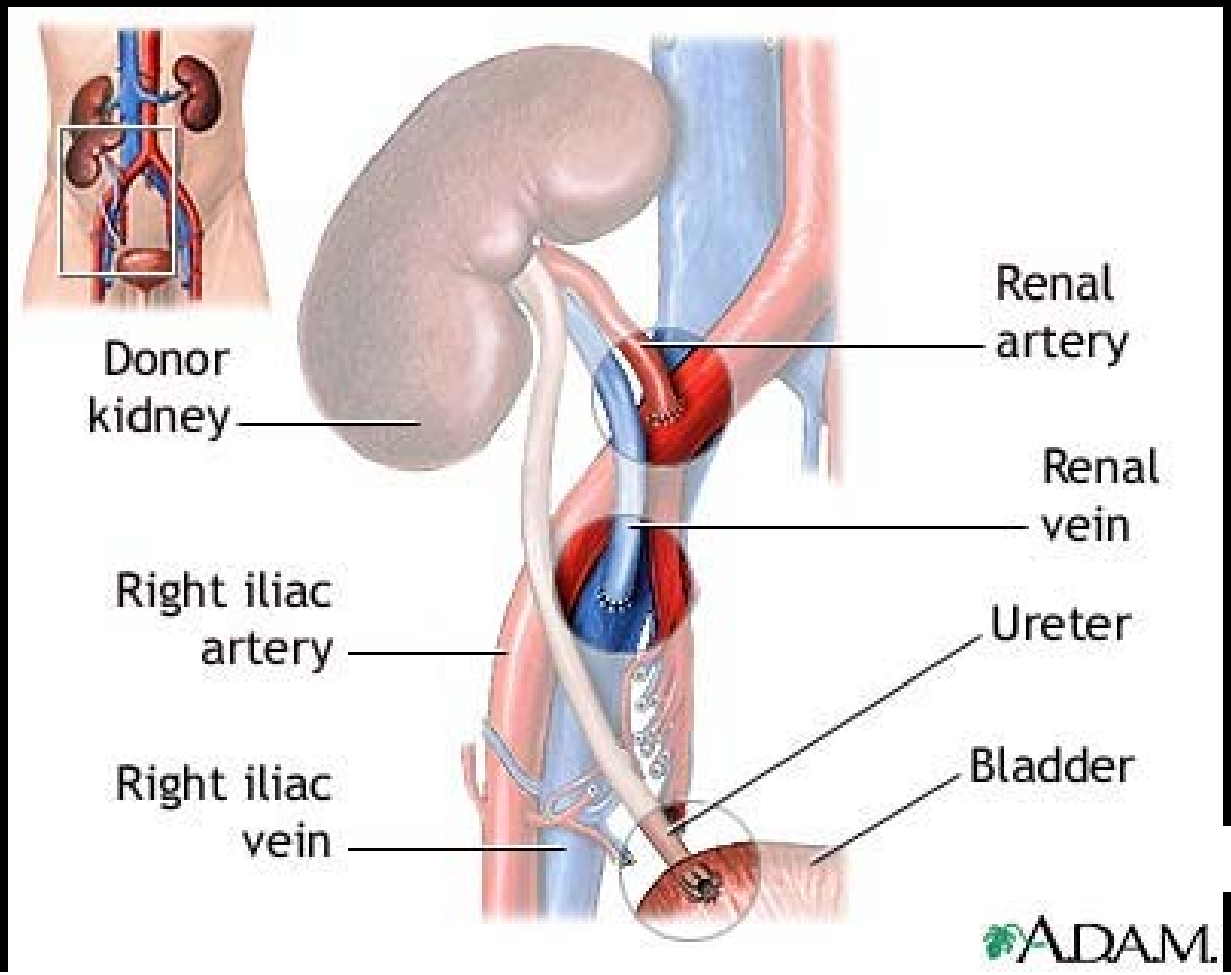


The Kidney TP is Heterotopic (Not in the original position of the native organ) as compared to Liver and Heart TP which are Orthotopic -



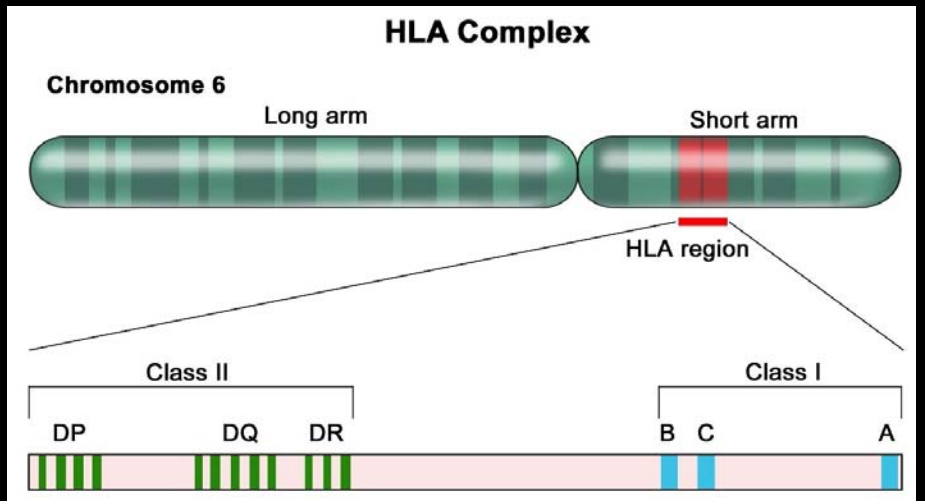


The vascular supply of the kidney comes from the Iliac Artery



Transplant Immunology

- Within each species there is a set of surface cell antigens that allows our immune system to distinguish self from non self
- These antigens are called the Major Histocompatibility Antigens (MHC) or the Histocompatibility Leukocyte Antigens (HLA)
- Coded for by chromosome 6
  - 3 distinct alleles (loci)
    - Physical regions where proteins are coded
  - Each designated by an alphabetical letter : A, B, D
- Co-dominant inheritance

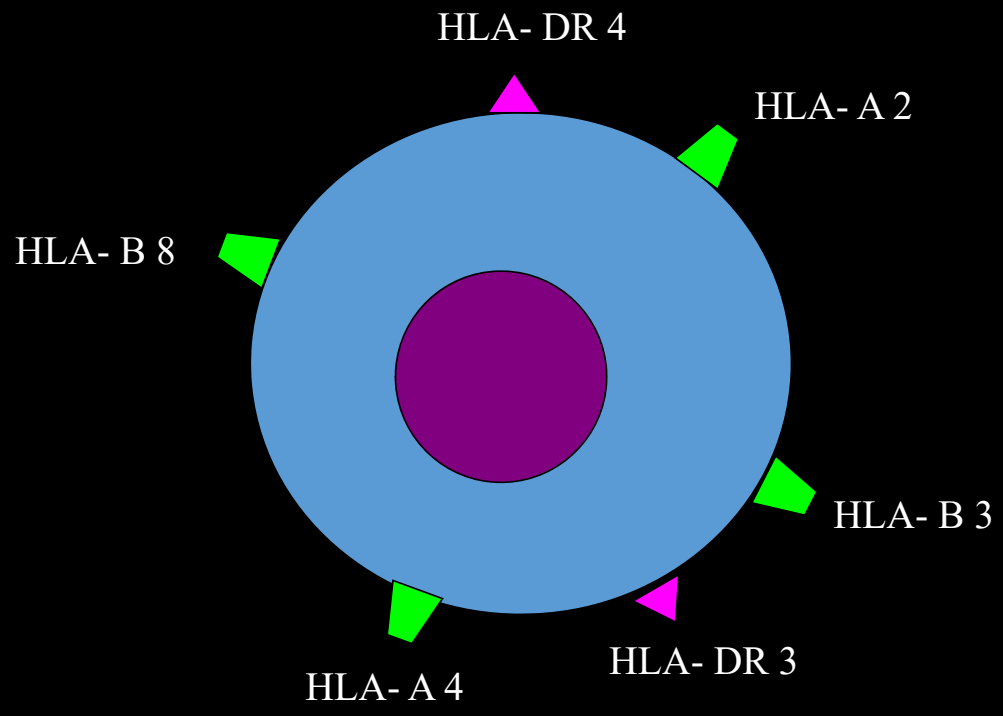


HLA

- Transplantation is based on matching as many of the HLA antigens as possible
- Each person expresses 6 major HLA antigens
  - 2 in the A region
  - 2 in the B region
  - 2 in the D region

  } Over 80 different antigens exist
- Each person's genetic identity is expressed by their 6 major HLA antigens
  - A 2,3 B 7,8 D 3,4
- The D region is the most important because it strongly influences lymphocyte reactivity

Example of HLA Distribution
All Nucleated Cells



The HLA on the surface of the cells can be recognized by the immune system (Lymphocytes) as either self or non self

Transplantation Criteria

- Matching
  - It is possible but very difficult to cross blood groups
    - "O" can be used as a universal donor
  - Allocate kidneys based on the degree of HLA matching
    - Lower risk of rejection with higher levels of matching
  - Example :

Donor	A 2	A 4	B 7	B 8	DR 4	DR 8
Recipient 1	A 2	A 5	B2	B 8	DR 1	DR 3
Recipient 2	A 8	A 9	B7	B16	DR4	DR5

  - Recipient 2 has a 2 antigen match including the most important match of a D region –so they are a better recipient for the donor kidney

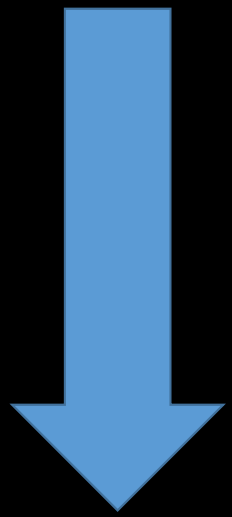
First TP in the U.S. – Brigham, Ma 1954
Identical Twins

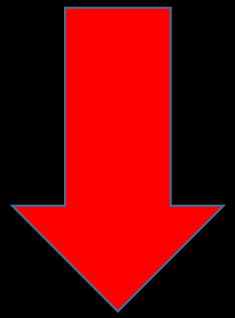
- **"Get out of here and go home" – Note from Richard (Recipient)to Ronald (Donor) Herrick 12/23/54**
- **"I'm here and I'm going to stay and that's it" – response from Ronald to Richard Herrick 12/23/54**

No immunosuppression !!

Richard (recipient) married his post op nurse and they had 2 daughters
The kidney lasted 8 years and failed due to recurrent glomerulonephritis
Ronald (donor) lived a healthy life for 56 more years
"I've had one good kidney all these years and I'm still walking around so I guess it worked out all right."

Transplant Rejection





Acute
T Cell Mediated

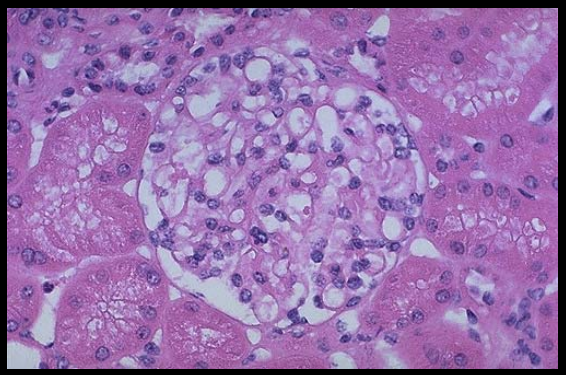
Acute
Humoral Mediated
(B Cell)

Hyperacute
IgG antibody mediated

Only 10-15% of all transplants experience a rejection episode

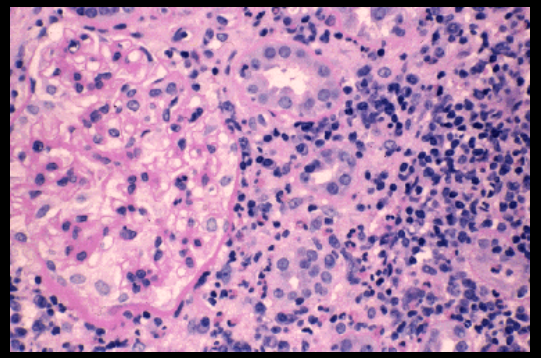
TP Rejection- Cell Mediated

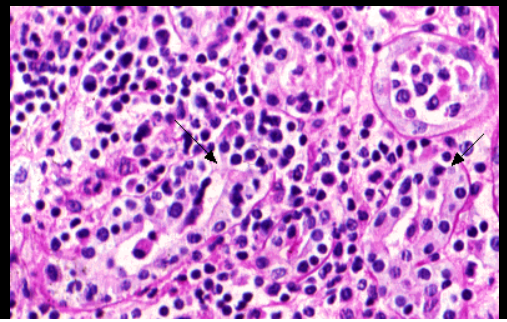
- **Infiltration of the interstitium and tubules by cytotoxic T cells – Tubulitis (The hallmark of Rejection)**



Normal

The patient may have fever with an enlarged, tender kidney



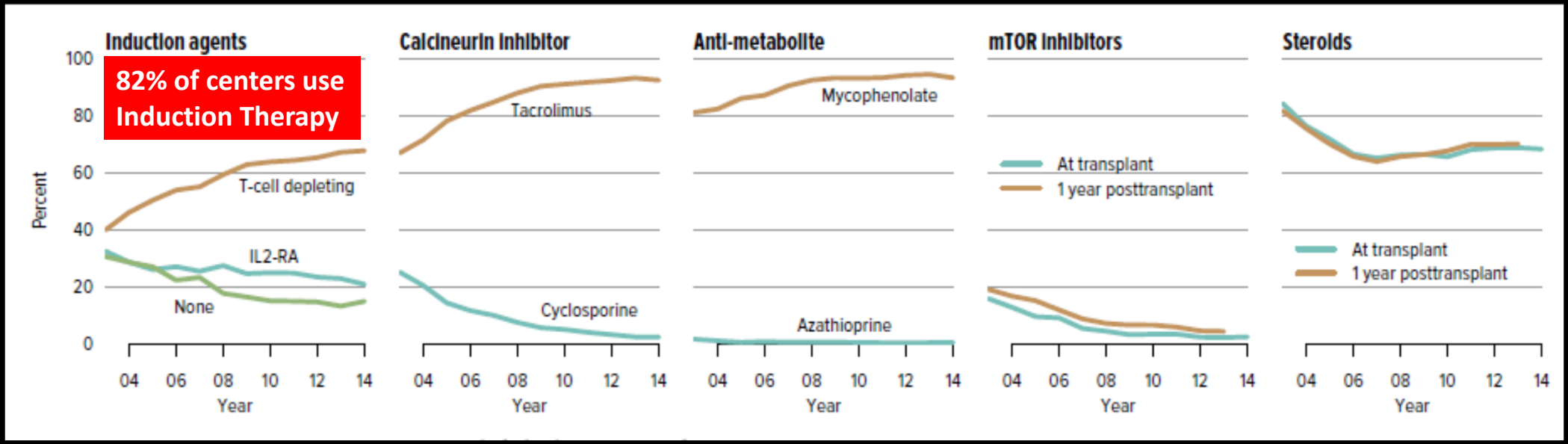


Intense T lymphocyte Invasion of the tubules

Antibody Mediated Acute Rejection

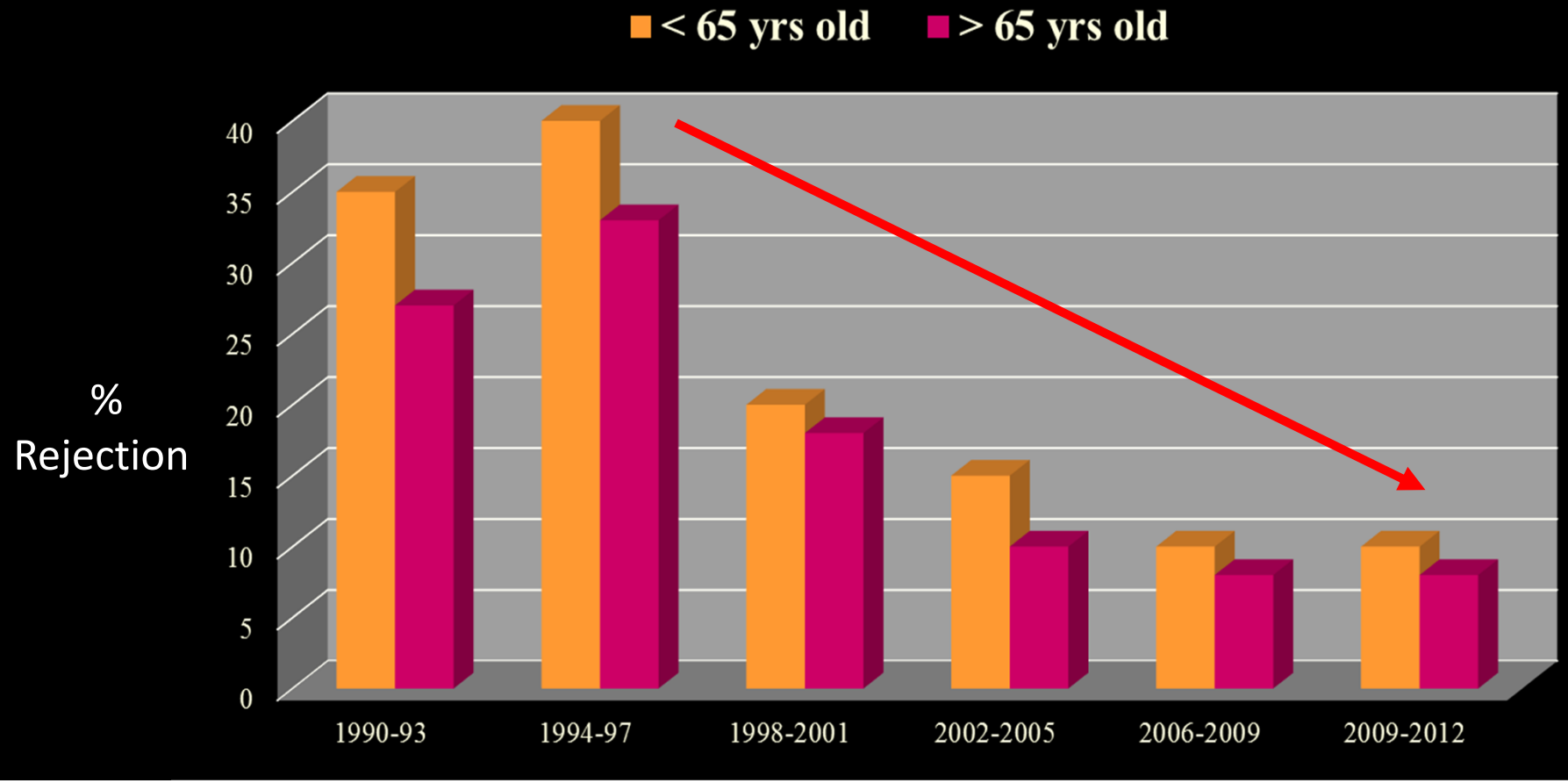
- In addition to acute T cell mediated rejection sometimes patients have a co-existent acute antibody directed attack on the kidney
- This occurs weeks to months after the transplant
- This is a very severe form of rejection often from noncompliance with medication
- Same physioloigc concept as hyperacute rejection but less catastrophic and treatable as the antibodies develop slowly over time

Post Kidney Transplant Immunosuppression 2019

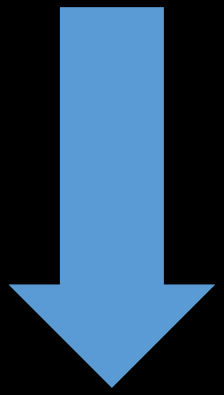


Tacrolimus and Mycophenolate remain the most common agents used with glucocorticoids still being used in 70% of programs

Evolution of Kidney Transplant Rejection Rates over 25 years



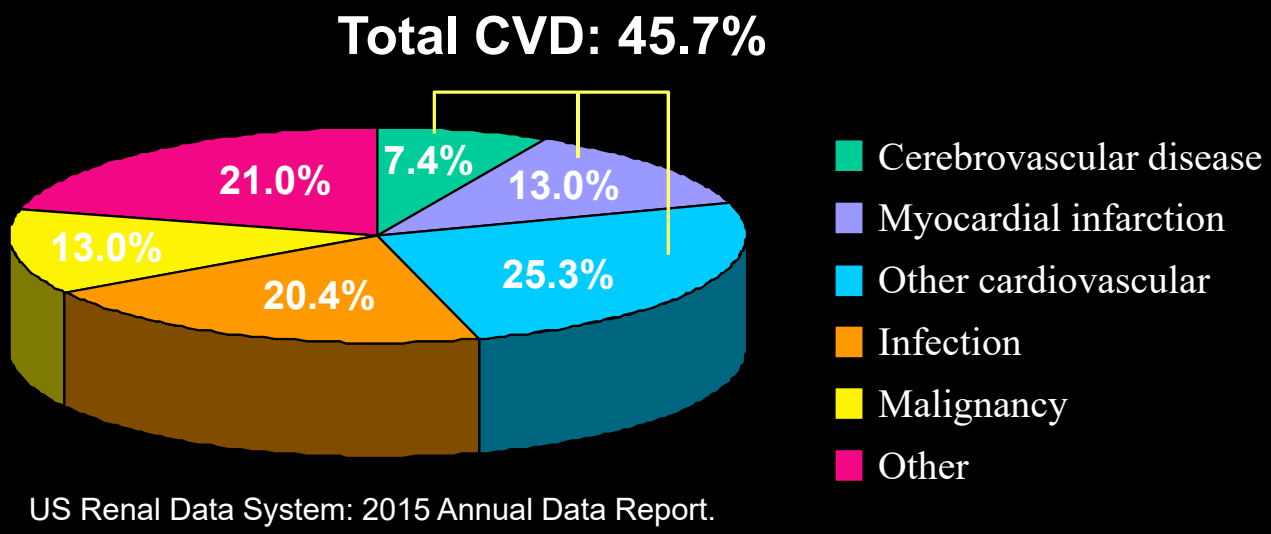
Graft Loss after the First Year Posttransplant



DWFG

Death with a Functioning Graft

Cause of Death in Renal Transplant Recipients With Functioning Transplants



US Renal Data System: 2015 Annual Data Report.

Caveat :
Cardiovascular Disease remains a significantly greater risk for renal transplant recipients compared to infection and malignancy

Immunosuppressive Agents

- **Corticosteroids**
  - Prednisone
- **Calcineurin inhibitors**
  - Cyclosporine (Neoral)
  - Tacrolimus (Prograf)
- **Purine synthesis inhibitors**
  - Azathioprine (Imuran)
  - Mycophenolic acid (Cellcept / Myfortic)
- **mTOR Inhibitors (mTOR = mammalian target of rapamycin)**
  - Sirolimus / Everolimus
    - Trade names : Rapamycin / Zortress

Monotherapy or discontinuation of all therapy is not an option and will lead to rejection

Immunosuppression

- **Calcineurin Inhibitors**
  - The single most important foundation of maintenance immunosuppression
  - Interleukin -2 is the most important cytokine used for T cells to recruit other cells to proliferate
  - The enzyme calcineurin is essential for the production of IL-2
  - Calcineurin inhibitors prevent the production of IL-2 and inhibit the proliferation of T cells
  - They do not affect the bone marrow

Immunosuppression

- Calcineurin Inhibitors
  - Side effects
    - HTN
    - Diabetes
    - Malignancy (Lymphoma)
    - AKI /CKD
      - Nephrotoxic over long periods of use
        - Causes interstitial fibrosis
        - One of the most serious challenges in TP medicine because these drugs are essential to prevent rejection

Immunosuppression

- **Purine Inhibitors**
  - The second most important part of the transplant regimen
    - Mycophenolic acid
    - Azathioprine
  - Used to prevent cell replication
  - Does not prevent the production of IL-2 but the cells can not replicate due to impaired DNA production
    - All replicating cells will be affected
      - Marked bone marrow suppression
  - Also associated with significant gastrointestinal inflammation / ulcers

Immunosuppression

- Corticosteroids
  - Inhibit T cell cytokine production
    - Interleukin -1
    - Responsible for inflammatory response
  - Reduce the number of T cells
  - Side effects
    - HTN
    - Weight gain
    - Diabetes
    - Osteoporosis – inhibits Vitamin D activity

Immunosuppression

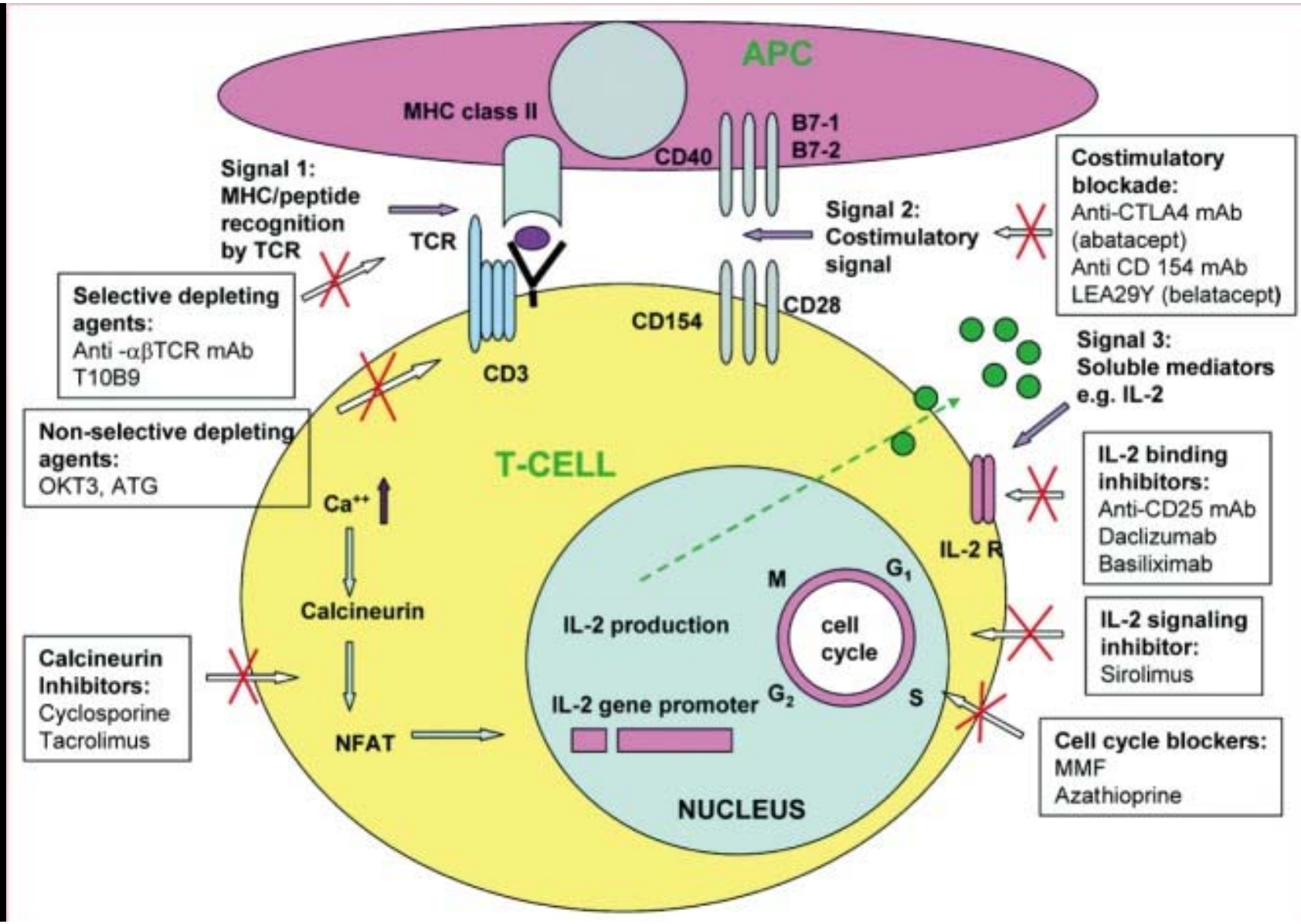
- **mTOR inhibitors**
  - "Mammalian target of rapamycin" = mTOR
  - After Interleukin – 2 binds to its receptor there are intracellular signals that stimulate proliferation
    - mTOR is a key regular of the cell's response to IL-2
    - There is no decrease in T cell number
- **Side Effects**
  - Hyperlipidemia
  - Poor wound healing
  - No direct nephrotoxicity but may cause proteinuria

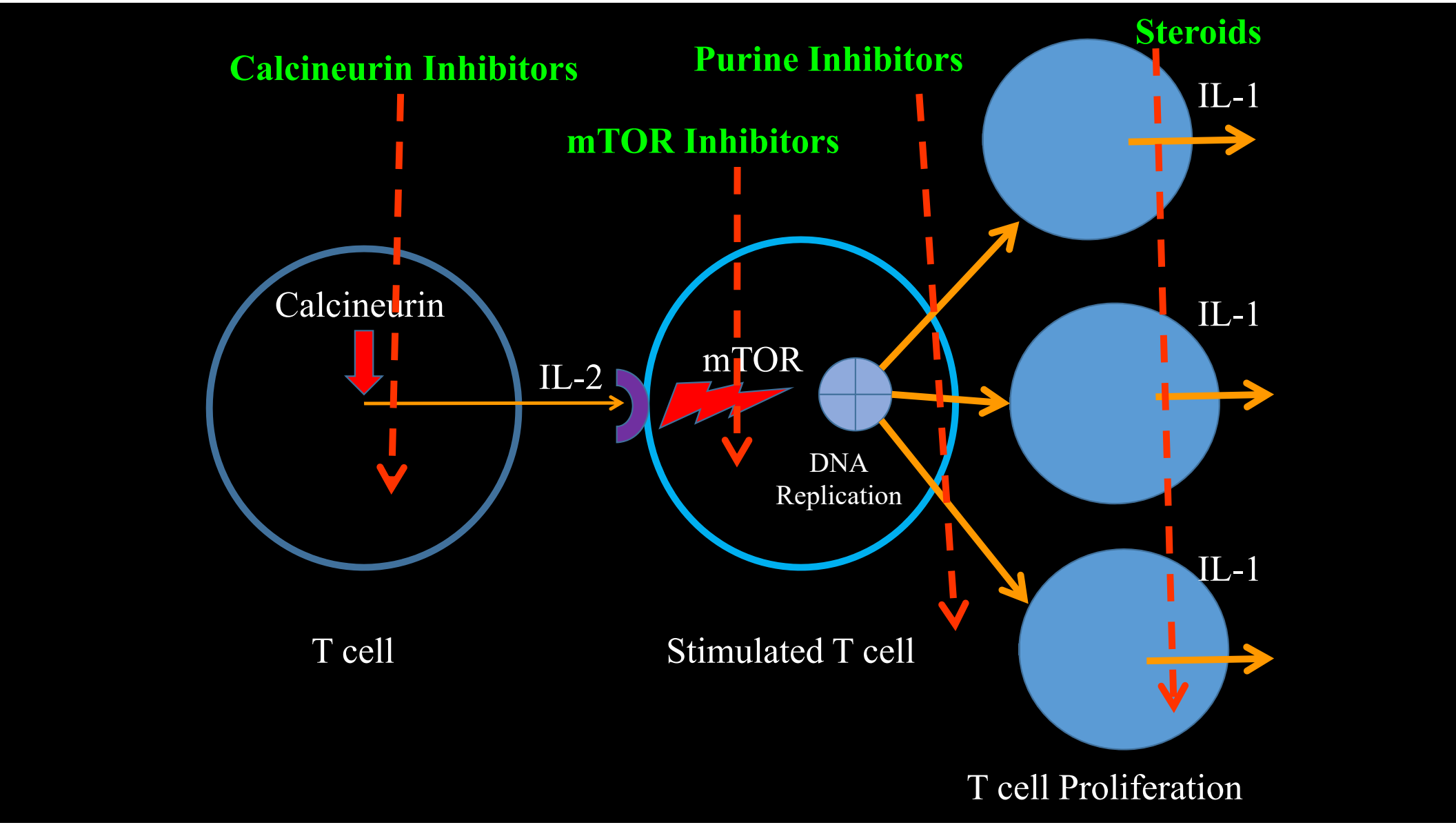
Often used instead of a purine inhibitor if the patient has severe bone marrow suppression

Immunosuppression

- **Belatacept**
  - a selective T-cell (lymphocyte) costimulation blocker. It binds to CD80 and CD86 on antigen-presenting cells, thereby blocking CD28 mediated costimulation of T lymphocytes
- Side effects:
  - Bone marrow suppression
  - Flu like symptoms
  - Nausea and vomiting
  - Malignancy – PTLD in particular if recipient is not EBV +

  - Goal: It is often used in specific cases to avoid nephrotoxicity especially early on if patient has delayed graft function or later on to try to avoid further calcineurin inhibitor damage in hopes of prolonging the life of the allograft.


APC
MHC class II
CD40
B7-1
B7-2
Signal 1:
MHC/peptide
recognition
by TCR
TCR
Signal 2:
Costimulatory
signal
Costimulatory
blockade:
Anti-CTLA4 mAb
(abatacept)
Anti CD 154 mAb
LEA29Y (belatacept)
Selective depleting
agents:
Anti -αβTCR mAb
T10B9
CD154
CD28
CD3
Signal 3:
Soluble mediators
e.g. IL-2
Non-selective depleting
agents:
OKT3, ATG
T-CELL
IL-2 binding
inhibitors:
Anti-CD25 mAb
Daclizumab
Basiliximab
Ca++
IL-2 R
M
G1
Calcineurin
IL-2 production
cell
cycle
IL-2 signaling
inhibitor:
Sirolimus
Calcineurin
Inhibitors:
Cyclosporine
Tacrolimus
IL-2 gene promoter
G2
S
NFAT
Cell cycle blockers:
MMF
Azathioprine
NUCLEUS


Calcineurin Inhibitors
Purine Inhibitors
Steroids
mTOR Inhibitors
IL-1
Calcineurin
IL-2
mTOR
IL-1
DNA
Replication
IL-1
T cell
Stimulated T cell
T cell Proliferation

Transplant Complications

- **Infection**
  - Viral
    - Herpes group family
      - CMV (Cytomegalovirus)
      - EBV (Epstein Barr virus)

    Potentially fatal
    Fever / Pneumonia / Hepatitis / Colitis
  - Fungal
    - Aspergillosis
    - Cryptococcus
    - TB
  - Bacterial

All TP patients receive prophylactic pneumonia vaccination / lifelong antibiotics / anti-viral prophylaxis

Transplant Complications

- Malignancy
  - Skin cancer – most common
    - Squamous cell
      - Contrast to the general population where Basal cell cancer is the most common
  - Lymphoma
    - B cell origin !!!!
      - T cells are eliminated by the immunosuppression allowing B cells to propagate without inhibition
      - Primarily related to EBV
        - Directly infects B cells
  - Solid tumors like Breast/ Lung / Colon and Prostate cancer are slightly increased in risk

Immunosuppression Summary

	HTN	Diabetes	Bone marrow Suppression	Nephrotoxicity	Malignancy	Hyperlipidemia	Weight gain
Steroids	✓	✓				✓	✓
Calcineurin inhibitors	✓	✓		✓	✓	✓	
Purine inhibitors			✓		✓		
mTOR inhibitors						✓	

All increase the risk of Infection !

Different Causes of Graft Failure

- Thrombosis leading to Primary Non-Functioning Kidney
- Hemolytic Uremic Syndrome leading to Necrosis
- Recurrence of Kidney Disease – less than 10% but recurrence with FSGS is more prevalent and graft failure ensues 50% of the time
- Rejection – rarely see accelerated rejection; mostly see ongoing chronic smoldering rejection that doesn't respond to aggressive medical treatment
- Diabetic Nephropathy
- Viruses – Polyoma Virus (BK virus), Cytomegalovirus
- Life-threatening infections that may be donor derived
- PTLD – extremely rare
- Death with a Functioning Graft

- Chronic Allograft Injury – particularly from calcineurin inhibitor nephrotoxicity and/or Transplant Glomerulopathy

Which of these statements is correct ?

A. The l[illegible]g causes of death after kidney transplantation are infection followed by malignancy especially lymphoma

CVD

B. Due to the side effects of lifelong immunosuppression, transplant patie[illegible]survival as dialysis patients but have a better quality of life being free from regular dialysis treatments

Improved survival

C. Patie[illegible]isted for kidney transplantation once they begin dialys[illegible]ither hemodialysis or peritoneal dialysis

GFR < 20 cc/min

D. The a[illegible]ting time for a kidney transplant in the U.S. is approximately 1-2 years

3 -5 years

E. All are correct

F. None are correct

Which of these drugs is nephrotoxic?

A. Mycophenolate Mofetil (Cellcept, Myfortic)
B. Calcineurin inhibitors (Prograf, Cyclosporin,Tacrolimus)
C. Azathioprine (Imuran)
D. Corticosteroids (Prednisone, Medrol)
E. mTOR inhibitors (Rapamycin, Sirolimus, Everolimus)
F. All are nephrotoxic
G. I have no idea what most of these drugs are !!
H. None are nephrotoxic

Kidney Transplantation Conclusions

- Transplantation can provide a significant improvement in patient survival compared to dialysis for all patients especially those with Diabetic patients
- The waiting time for a kidney transplant is unacceptable and is over 3-5 years
- Transplantation is cost effective compared to dialysis
- CVD is the most important cause of death after transplantation and patient death is the most common cause of graft loss
- The most serious consequence of current immunosuppression is the nephrotoxicity from calcineurin inhibitors
- Talk to your patients and family about being organ donors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PUBLIC HEALTH TRUST
IN AFFILIATION WITH
UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE
Thank You