

Navigating the wait-list: How to decrease transplant list wait-time

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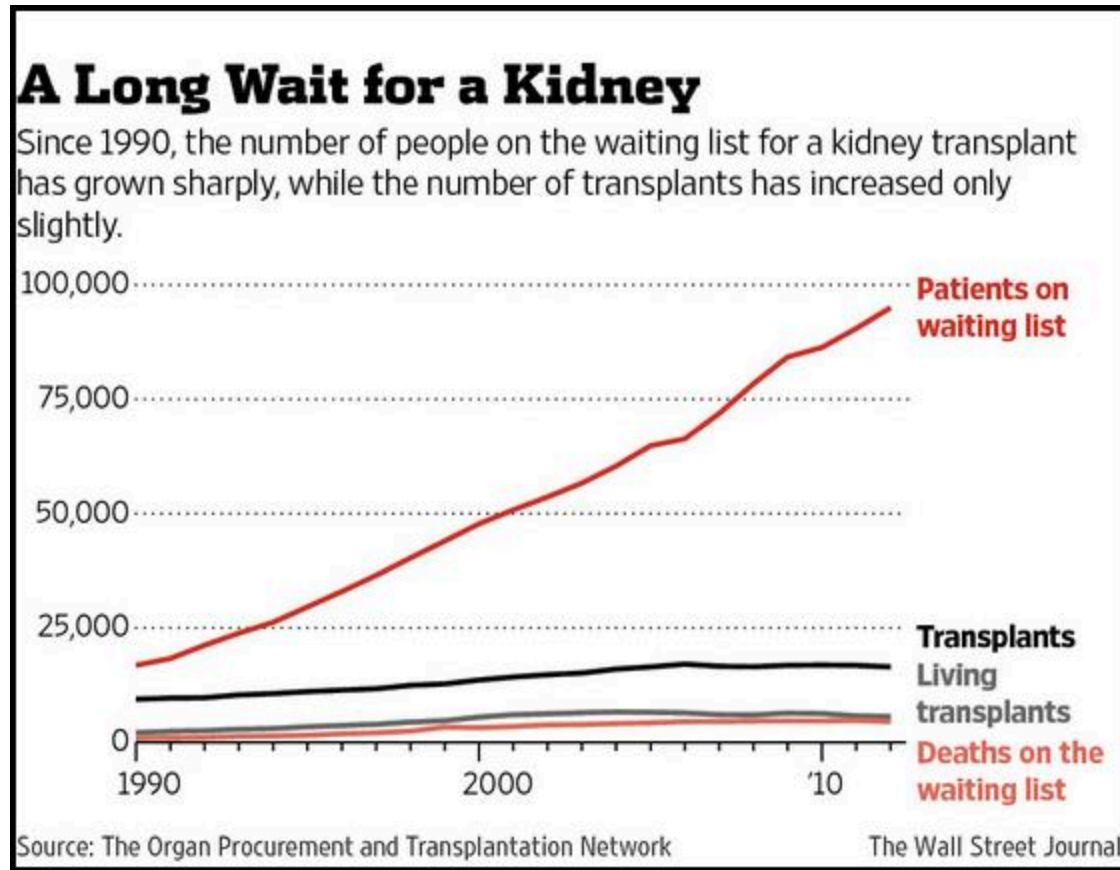
Current waiting time for a deceased donor kidney transplant

Time to transplant for waiting list candidates (months)

	Saint Barnabas	OPO (NJ centers)	Region	USA
5 th percentile	1.4	1.6	1.6	1.3
10 th percentile	3.1	3.7	3.8	3.3
25 th percentile	12.6	14.6	14.0	12.7
50 th percentile	59.1	Not observed	Not observed	61.8

Not observed means that fewer of 50% of patients received a transplant over the follow-up period of 65 months

The waiting time is increasing



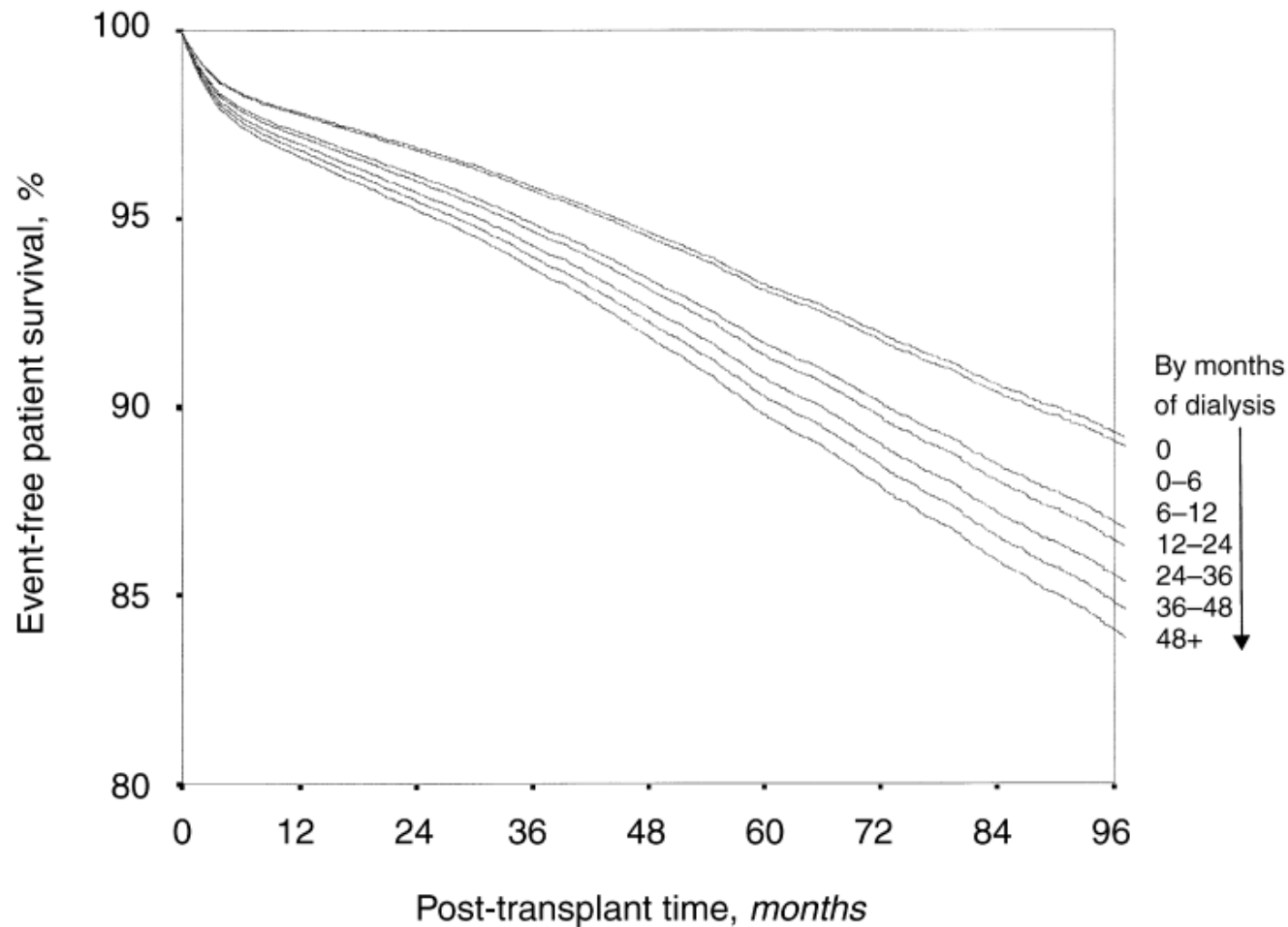
What happens to patients on the wait-list?

- Mortality on the wait-list
 - Approximately 6% of wait-listed patients die each year while waiting for a deceased donor kidney transplant
- Removal from the wait-list
 - Approximately 7% of patients are removed from the wait-list each year
 - Medical condition deteriorates (ex- heart attack, stroke, newly diagnosed cancer)
 - Reach the age limit of 75 (age limit is 70 if they have several co-morbidities, such as heart disease, peripheral vascular disease, diabetes, and/or poor exercise tolerance)

What is the chance of receiving a deceased donor kidney transplant?

- Median wait-time at Saint Barnabas is 5 years
 - 13% of patients will either die or be removed from the list each year
 - $13\%/year \times 5 \text{ years} = 65\%$
 - Almost 2 out of 3 patients will not receive a deceased donor kidney transplant if they have to wait 5 years on the wait-list
 - Higher risk in older patients

Effect of dialysis duration on transplant outcome



How can we reduce the wait-time for a deceased donor kidney transplant?

- Use of PHS-high risk organs
 - Examples: IV drug use, prostitution, incarceration, etc
 - Testing for HIV and viral hepatitis are negative
 - Risk of disease transmission is <1%
 - Donors tend to be young without other co-morbidities
 - Majority of our wait-listed patients are now consented for these type of organs

How can we reduce the wait-time for a deceased donor kidney transplant?

- Transplanting blood group A2 organs into blood group B recipients
 - Blood group has two subtypes: type A1 blood and type A2 blood
 - Type A2 blood does not elicit a strong immune response if anti-A2 titer is low
 - Blood type B is more common in African Americans
 - Old allocation system: only can receive organs from O or B donors
 - New allocation system: can receive organs from O, B, A2, and A2B organs (if anti-A2 titer is low)
 - No extra desensitization needed for A2/A2B to B transplant
 - 10 year graft survival
 - A2/A2B to B: 72%
 - B to B: 69%

How can we reduce the wait-time for a deceased donor kidney transplant?

- Living donation!

Year	Deceased donor transplants	Living donor transplants
2018	29,680	6,849
2017	28,588	6,182
2016	27,630	5,980
2015	24,985	5,989
2014	23,720	5,820
Total	134,603	30,820

244 kidney transplant centers in USA

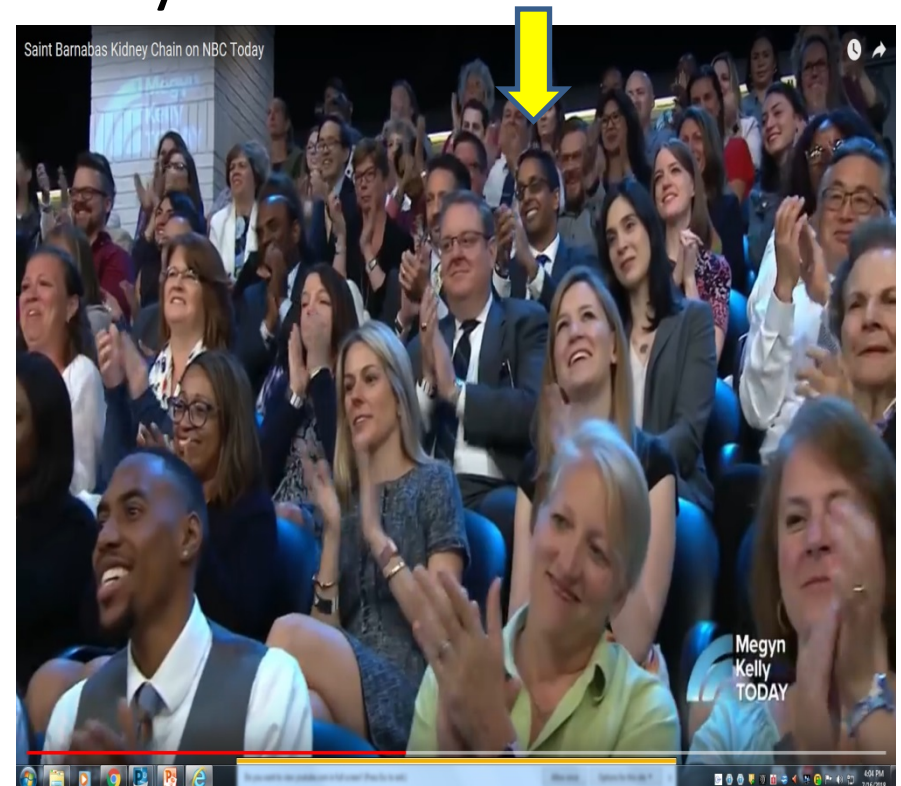
Average # of living donor kidney transplants per year for a center= 25

Average # of living donor kidney transplants per year at SBMC= 150

- Only 18.6% of transplants were from living donors over the past 5 years in the USA
 - 49.4% of our transplants are from living donors

Living donor kidney exchange program

- Saint Barnabas Medical Center recently participated in an internal 23 way exchange (23 donors and 23 recipients)
 - Featured on the Megyn Kelly show on NBC:

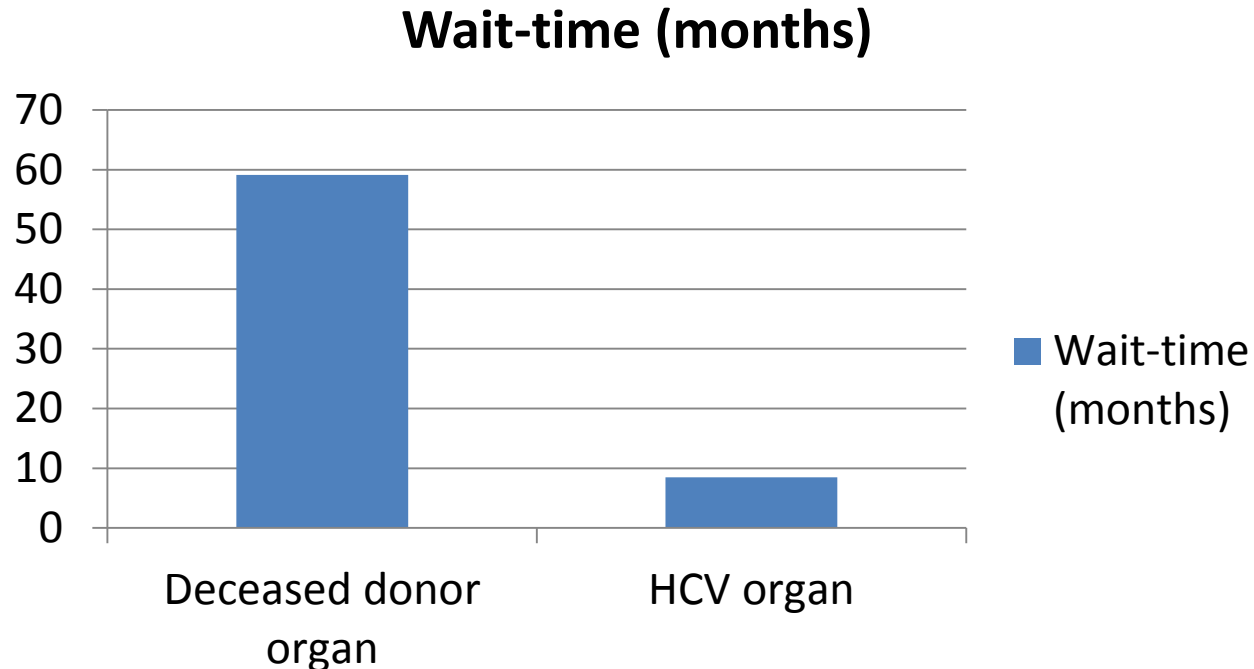


How can we reduce the wait-time for a deceased donor kidney transplant?

- Use of deceased donor organs that have hepatitis C (HCV) for patients who do not have HCV
- Use of deceased donor organs that have HIV for patients who have HIV

HCV donor organ

- Is the median wait-time for a HCV organ shorter than the median wait-time for a deceased donor organ?
 - Our patients (n=12) who received a HCV donor organ from 1/1/2015-12/31/2017 had median wait-time of 8.5 months



Chances of receiving a deceased donor organ

- Approximately 13% of wait-listed patients lose the ability to receive a deceased donor transplant annually
 - Mortality on wait-list= 6% per year
 - Removal from wait-list= 7% per year
- Deceased donor organ wait-time= 5 years
 - 5 years x 13%= 65% chance of not receiving a transplant
- HCV organ wait-time= 0.7 years
 - 0.7 years x 13%= 9% chance of not receiving a transplant

Why are HCV organs available?

- Fewer transplant candidates with (+)HCV viral load due to newer HCV medications
 - Historically, these were the only patients who could accept a HCV organ
- IVDA epidemic = increased HCV donors
 - Over 500 HCV donor kidneys discarded in USA annually

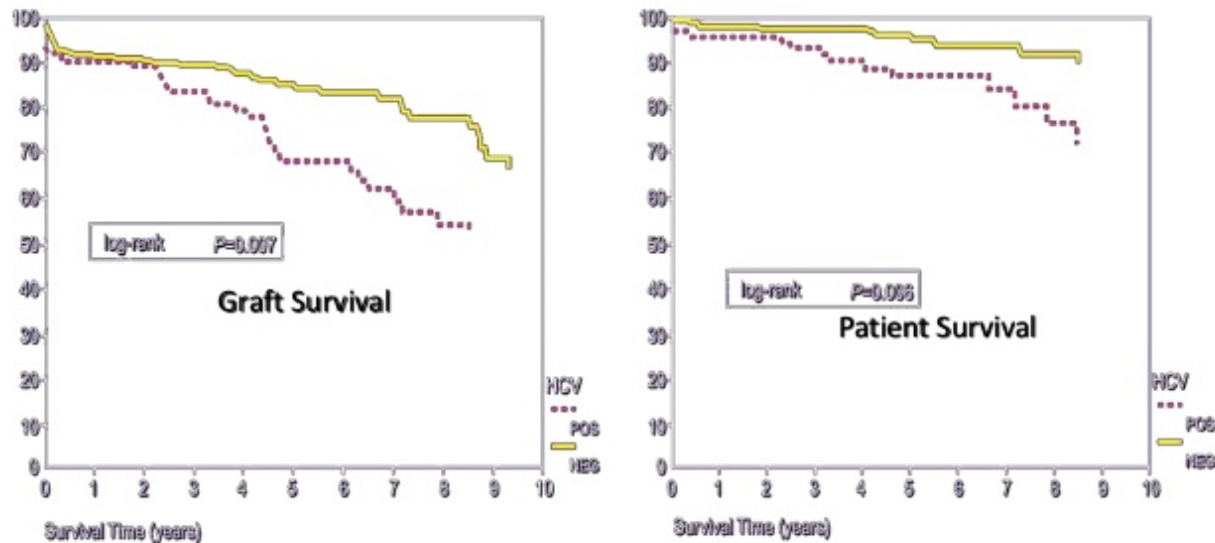
Will I get HCV if I take a HCV organ?

- What is risk of HCV+ donor into HCV negative kidney transplant recipient without treatment?
 - One study demonstrated that 7/13 patients developed HCV viremia
 - 6/7 with severe transaminitis
 - 1/7 with HCV-related liver death
 - Another study demonstrated that 10 out 10 patients developed HCV viremia

N engl j med 376;24. June 15, 2017

Decreased graft and patient survival in kidney transplant patients with HCV

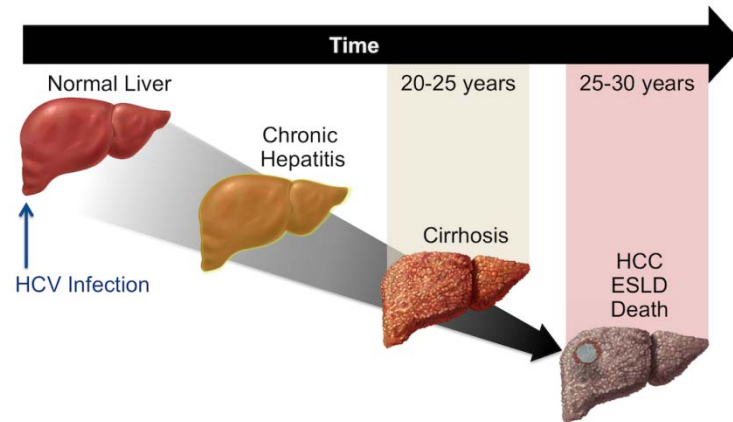
HCV infection is associated with lower graft and recipient survival



Gentil MA et al. Nephrol Dial Transplant. 1999;14:2455-2460.

Other complications of chronic HCV infection

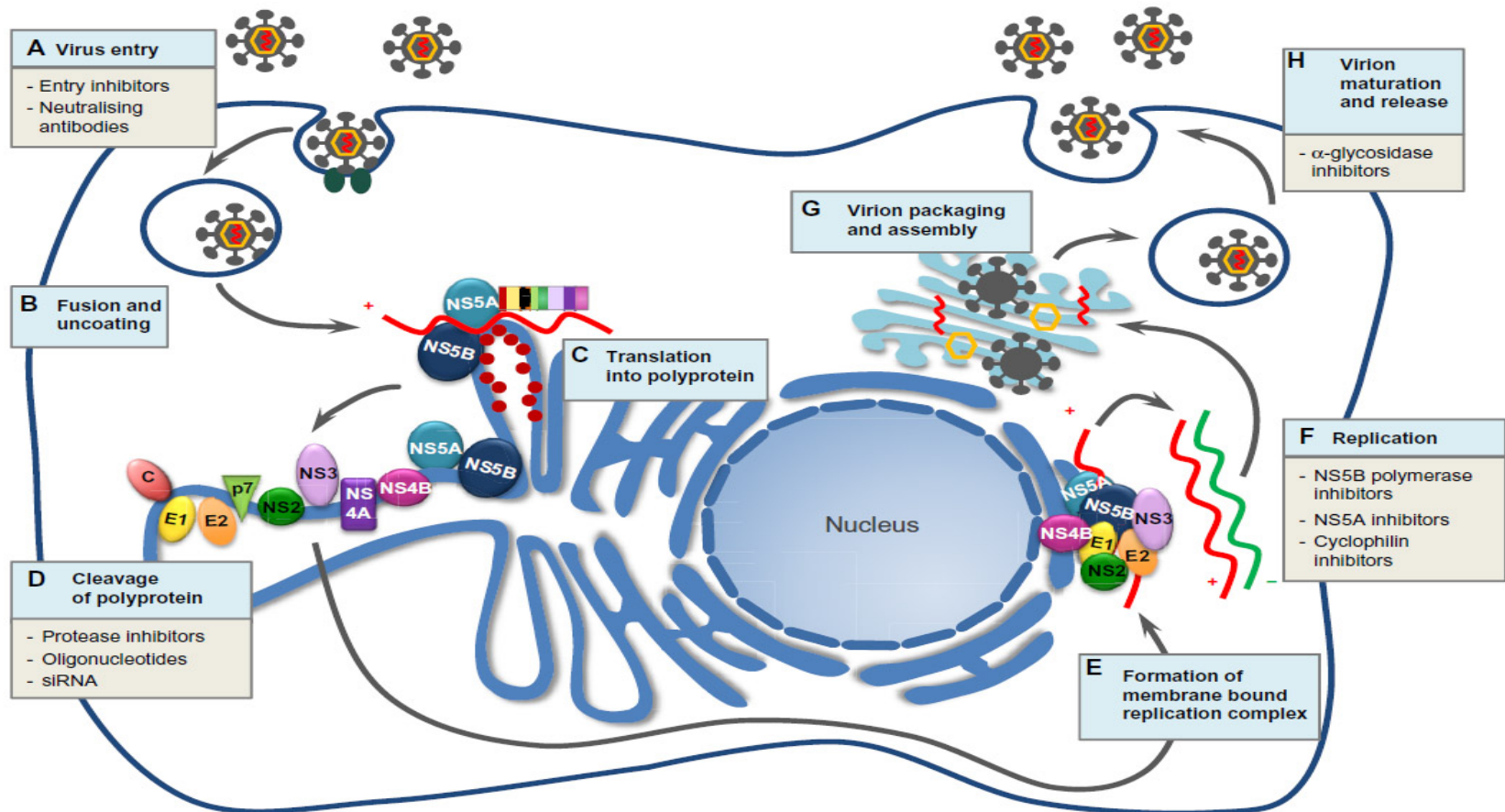
- Cirrhosis
- Fatigue
- Anorexia
- Increased risk of liver cancer
- Increased risk of certain renal diseases
 - Membranoproliferative glomerulonephritis
 - Cryoglobulinemia
 - Diabetes mellitus



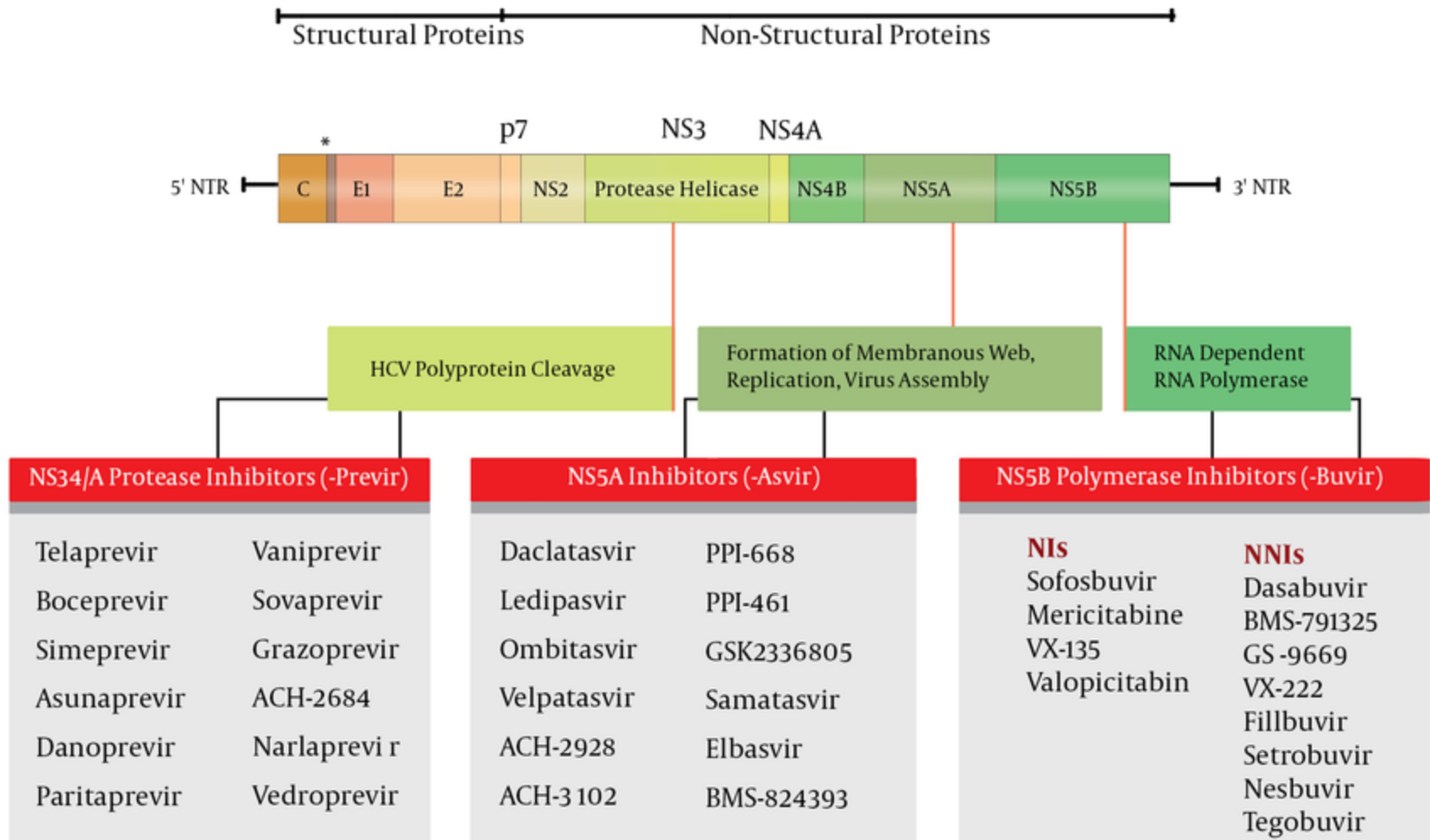
Can we prevent HCV-associated adverse events?

- Treatment of HCV infection prior to 2016
 - Interferon and ribavirin
 - Efficacy less than 50% and lower in patients with chronic kidney disease
 - Significant side effects
 - Anemia and leukopenia
 - Depression
 - Influenza-like symptoms
 - Interferon increases the risk of rejection when used post-transplant

- Treatment of HCV infection since 2016
 - Direct acting antiviral therapy (DAAT)



Direct acting antiviral therapy (DAAT)



Direct acting antiviral therapy (DAAT)

- Reported rates of sustained virologic response (SVR) of >95%-100% with various regimens
- Which newer HCV medications should be used?
 - No dose adjustment needed for renal impairment
 - If used post-transplant, minimal drug-drug interaction with tacrolimus
 - Cost
 - Side effect profile

Trials of DAAT in kidney transplant patients

- 10 HCV negative patients received HCV+ deceased donor kidneys
 - HCV treatment initiated once HCV viremia detected post-transplant
 - Treatment consisted of Zepatier x 12 weeks
 - Results
 - 10/10 patients developed HCV viremia
 - 10/10 patients achieved SVR with treatment
 - 2 cases of transient transaminitis

N engl j med 376;24. June 15, 2017

Trials of DAAT in kidney transplant patients

- 10 HCV negative patients received HCV+ deceased donor kidneys
 - Treatment started pre-transplant with Zepatier
 - 5/10 patients never developed viremia
 - 10/10 patients developed SVR
 - No clinical hepatitis

Trials of DAAT in kidney transplant patients

- Study of 80 HCV+ liver transplant and 20 HCV+ kidney transplant organs into recipients who were HCV negative
 - Treated with Mavyret
 - 1/100 with virologic failure (liver transplant recipient)
 - 1 recipient lost to follow-up
 - 98/99 patients developed SVR

Hepatology. 2018 Oct;68(4):1298-1307

Trials of DAAT in kidney transplant patients

- Use of HCV+ deceased donors in HCV- recipients is feasible
 - Excellent SVR rate with DAAT
 - No increase in side effects vs. placebo in previous studies
 - Ok to use with our standard immunosuppressive medications
 - Issues
 - Ideally, would like to give DAAT prophylactically pre-transplant but not allowed by insurance companies
 - DAAT has only been FDA approved for treatment of HCV viremia, not prophylaxis
 - Cost of therapy
 - Insurance approval
 - Interactions with other medications

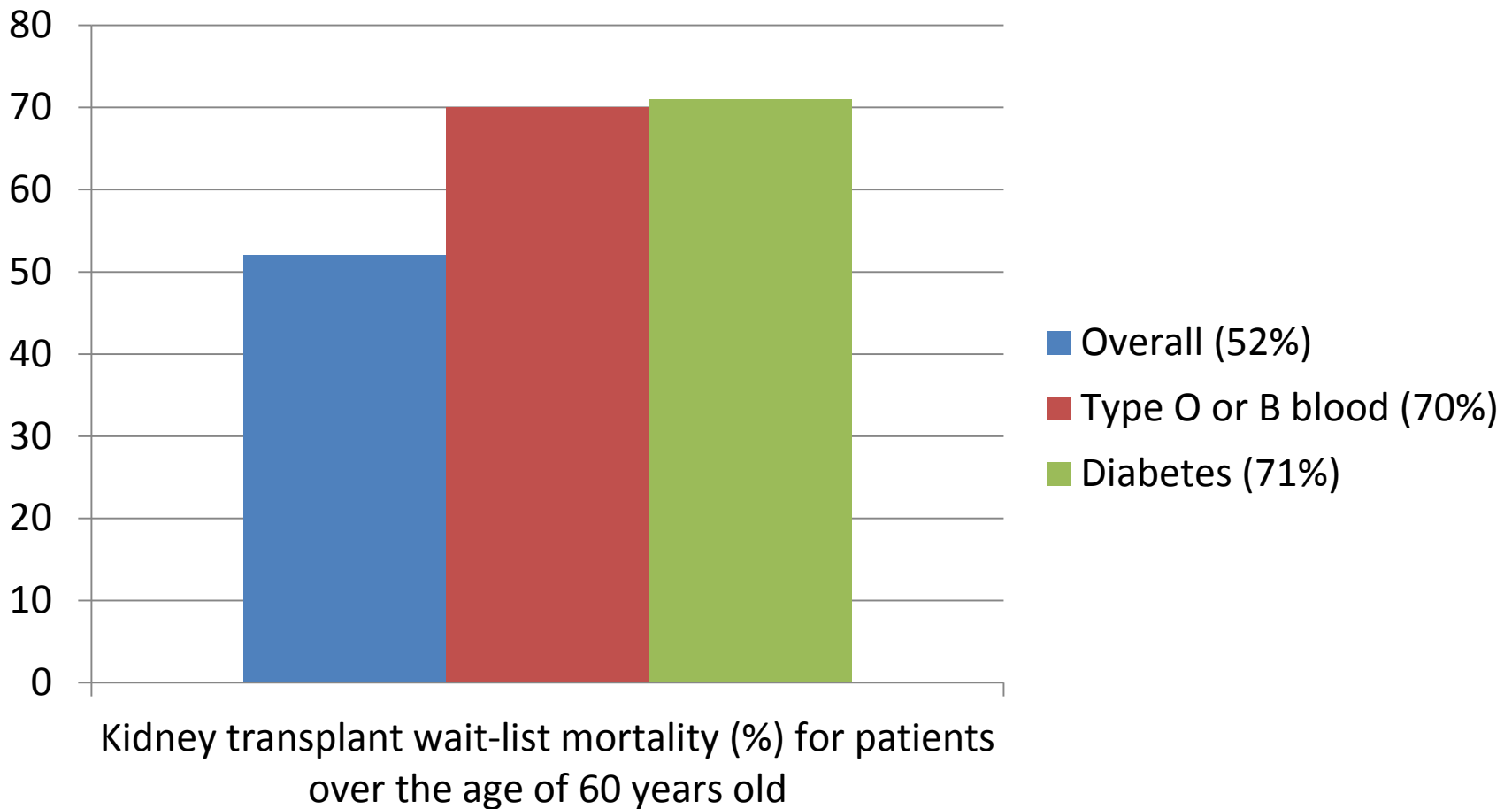
Is there an ideal medication to use?

	Mavyret	Zepatier
Duration of therapy	8 weeks	12 weeks
Cost	~\$26,400	~\$54,600
Efficacy	>95%	>95%
Side effect profile	Similar to placebo	Similar to placebo
Use with cyclosporine	No	No
Use with tacrolimus	Yes	Yes
HCV genotype	All genotypes	1 and 4
Dose adjustment with renal insufficiency	No	No

Are there specific wait-listed patients who would especially benefit from HCV+ organ listing?

- Older patients
 - Average wait-time for a kidney transplant is 5 years
 - Maximum age for a deceased donor kidney transplant is 75 years
 - Age 70 with no wait-list time
 - Age 71 with <1 year wait-list time
 - Age 72 with <2 years wait-list time
 - Age 73 with <3 years wait-list time
 - Age 74 with <4 years wait-list time
 - Maximum age for a deceased donor kidney transplant is 70 years if an individual has multiple co-morbidities (ex- diabetes mellitus, coronary heart disease, etc.)
 - Age 65 with no wait-list time
 - Age 66 with <1 year wait-list time
 - Age 67 with <2 years wait-list time
 - Age 68 with <3 years wait-list time
 - Age 69 with <4 years wait-list time

Are there specific wait-listed patients who would especially benefit from HCV+ organ listing?



ATC Abstract #241 (2008). Schold JD et al.

HCV+ donor into HCV- kidney transplant recipient

- Who should we consent?
 - All listed patients at their first re-evaluation
 - Ok to consent patients sooner if they specifically ask about the protocol
- Exclude:
 - Hepatitis B infection
 - HIV infection
 - Inability to stop one of the contraindicated medications during the first 8 weeks post-transplant
 - History of hepatitis C treatment with interferon or a direct acting antiviral agent
 - Baseline AST and/or ALT >1.5 times higher than the upper limit of normal
 - History of alcohol abuse
 - Complement-dependent cytotoxicity or flow cytometry crossmatch positive

Saint Barnabas experience with HCV+ kidney into HCV- recipient

- 74yo male with ESRD due to type 2 diabetes
 - Listed since 9/2017
 - Type O blood
 - Anticipated transplant date: 9/2023
 - Anticipated age at time of transplant is 78 years old: [not a candidate](#)
 - 11/2/2018: consented for HCV(+) organ
 - 11/10/2018: received a HCV(+) kidney transplant
 - 11/19/2018: HCV PCR (+)
 - Mavyret x 8 weeks started on 11/23/2018
 - Patient achieved sustained virologic response
 - Doing well with a functioning kidney transplant

Saint Barnabas experience with HCV+ kidney into HCV- recipient

- 63yo male with ESRD secondary to HTN
 - Listed since 7/2015
 - Type A blood
 - Anticipated transplant date: 7/2020 (~1.5 years wait-time)
 - Risk of not receiving a transplant= $13\%/year \times 1.5 \text{ years} =$ approximately 20%
 - 12/3/2018: cleared for HCV(+) organ listing
 - 2/15/2019: s/p HCV(+) kidney transplant
 - Started Mavyret and last HCV viral load negative
 - Doing well with a functioning transplant

Saint Barnabas experience with HCV+ kidney into HCV- recipient

- 74yo female with ESRD due to PCKD
 - Listed since 2/2015
 - Type O blood
 - Anticipated age at time of transplant is 76 years old: [not a candidate](#)
 - 2/11/2019: cleared for HCV(+) organ listing
 - 2/19/2019: s/p HCV(+) kidney transplant
 - Last HCV viral load negative
 - Doing well with a functioning transplant

Saint Barnabas experience with HCV+ kidney into HCV- recipient

- 74yo female with ESRD due to chronic glomerulonephritis (DOB: July 1944)
 - Listed since 9/2015
 - Type AB blood
 - Anticipated age at time of transplant is 75 years old: [not a candidate](#)
 - 11/30/2018: cleared for HCV(+) organ listing
 - 3/20/2019: s/p HCV(+) kidney transplant
 - Started Mavyret 4/1/2019
 - Doing well with a functioning transplant

How can we reduce the wait-time for a deceased donor kidney transplant?

- Use of deceased donor organs that are HIV+ for recipients who are HIV+
 - The Hope Act (**HIV Organ Policy Equity Act**)
 - IRB approved research protocol
 - Signed off on by President Obama on November 21, 2013
 - Approximately 200 HIV+ deceased donor kidneys are available annually in the USA

Hope Act: rationale

- Wait-listed patients who are HIV+ have a lower chance of receiving a kidney transplant compared to HIV- wait-listed patients

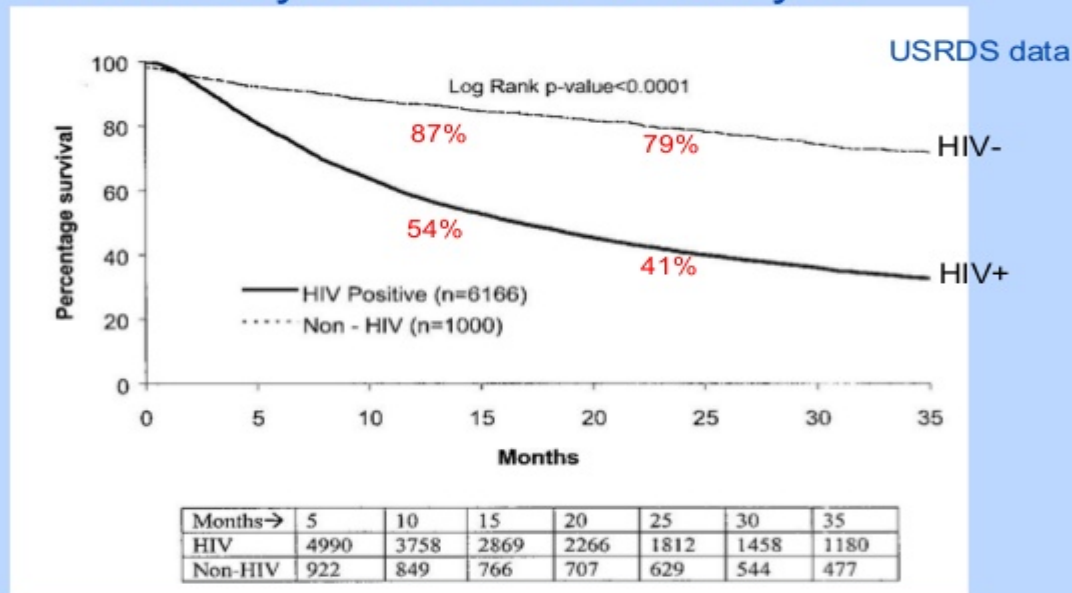
Likelihood of receiving a kidney transplant compared to HIV- patients

	Hazard ratio	95% CI interval	Interpretation
Overall HIV+	0.72	0.64-0.82	28% lower chance of receiving a transplant if HIV+
Deceased donor transplant HIV+	0.87	0.74-1.01	13% lower chance of receiving a deceased donor transplant if HIV+
Living donor transplant HIV-	0.53	0.44-0.64	47% lower chance of receiving a living donor transplant if HIV+

Hope Act: rationale

- Increase in HIV+ wait-listed candidates
- HIV+ patients have much lower survival on dialysis compared to HIV- patients

HIV+ on dialysis vs. HIV- on dialysis

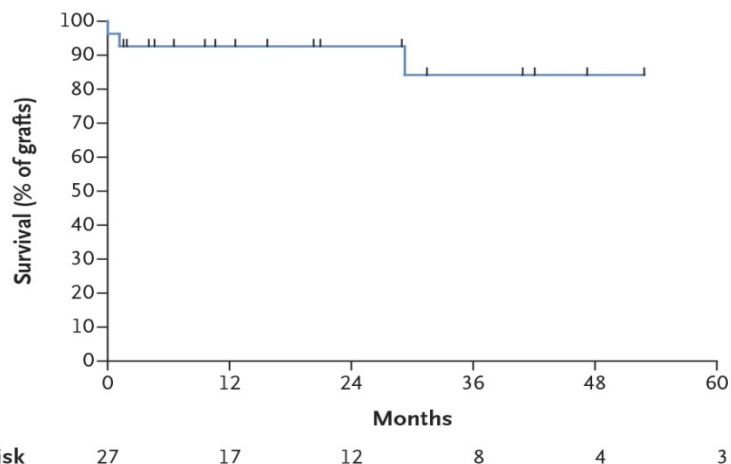


Previous experience with use of HIV+ kidneys: South Africa

- One of the highest incidences of HIV+
- 27 HIV+ patients received a deceased donor kidney transplant from HIV+ donors
 - Median follow-up was 2.4 years
 - Evaluated 1, 3, and 5 year patient and kidney allograft survival

Previous experience with use of HIV+ kidneys: South Africa

A Graft Survival



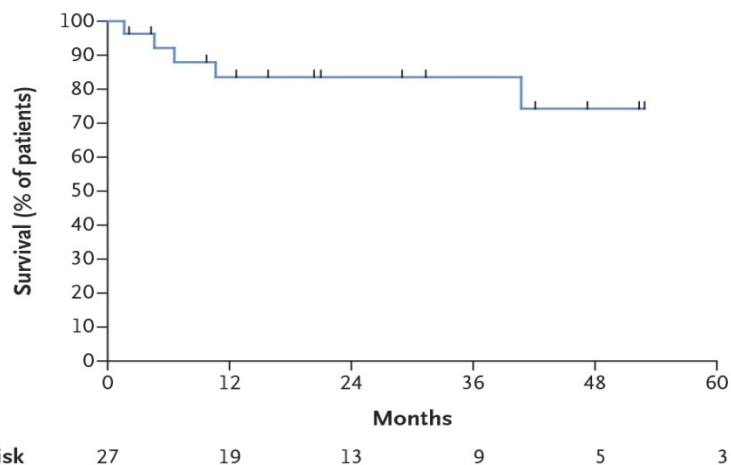
Graft survival:

1 year= 93%

3 year= 84%

5 year= 84%

B Patient Survival



Patient survival:

1 year= 84% (54% in HIV+ dialysis patients)

3 year= 84%

5 year= 74% (82% in HIV- transplant patients)

What is the risk of accepting a HIV+ organ if I already am HIV+?

- Infection with a different HIV strain
 - Might need to alter HIV regimen
 - Potential for side effects
 - Possibility that might not be able to eradicate the new HIV strain
 - Increased risk of malignancy, graft failure, and death
 - Study of 150 HIV+ kidney transplant recipients showed that only 5 (3.3%) did not achieve long-term clearance of HIV viremia (*AIDS. 2016 Jan 28; 30(3): 435–444*)
- Risk of co-infection with hepatitis B and hepatitis C viruses
 - Able to clear both viruses at an extremely high rate

Hope trial

- Prospective observational study
 - Planned enrollment of 360 participants over 3 years
- Primary objective: evaluate the safety of HIV+ deceased donor solid organ transplant for HIV+ recipients
 - Primary outcome is survival

Hope trial

- Transplant programs must provide each HIV+ recipient with an independent advocate
 - Advocate must be independent of the research team and must have knowledge and experience with both HIV infection and organ transplantation
- Important to identify an infectious disease specialist to be involved in the trial
- At the present time, 15 centers across the USA are recruiting patients
 - Saint Barnabas expects to start recruiting patients in the summer of 2019
- Over the past 3 years, 69 transplants from HIV+ donors into HIV+ recipients in the USA

Summary

- Median wait-list time for a deceased donor transplant in the USA is over 5 years
 - The wait-time for a deceased donor organ continues to increase
- Approximately 13% of patients will be removed from the kidney transplant wait-list every year

Summary

- Methods to increase the rate of kidney transplantation
 - Use of PHS high risk organs
 - Extremely low risk of disease transmission
 - Excellent quality organs
 - Transplanting blood group A2 organs into blood group B recipients
 - Living donation
 - Educate patient and family members about importance
 - Educate patient and family members about safety
 - Living donor exchange program

Summary

- Use of HCV+ organs for HCV- recipients
 - Wait-time of less than one year
 - Clearance of HCV viremia in over 98% of patients with a single course of medication
- Use of HIV+ organs for recipients with HIV
 - Excellent chance of keeping HIV viral loads negative post-transplant with highly active antiretroviral therapy (HAART)

Questions?