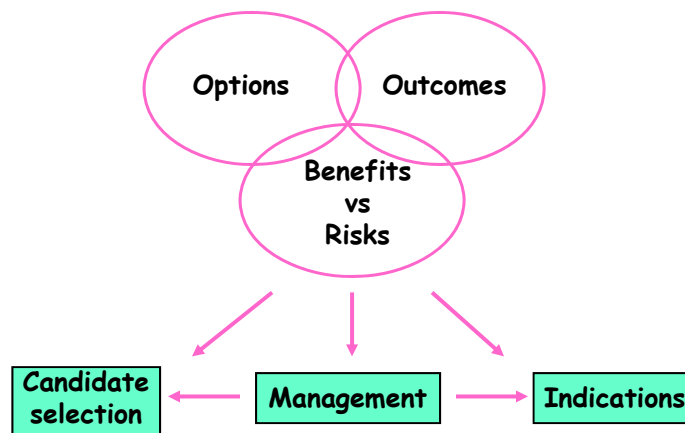


TRANSPLANT OPTIONS FOR THE UREMIC DIABETIC RECIPIENT

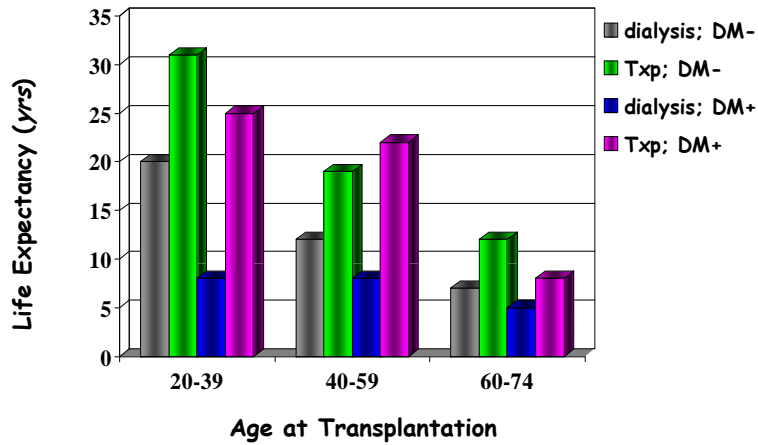
Roy D. Bloom MD
Department of Medicine
University of Pennsylvania



Transplantation for the Uremic Diabetic Recipient

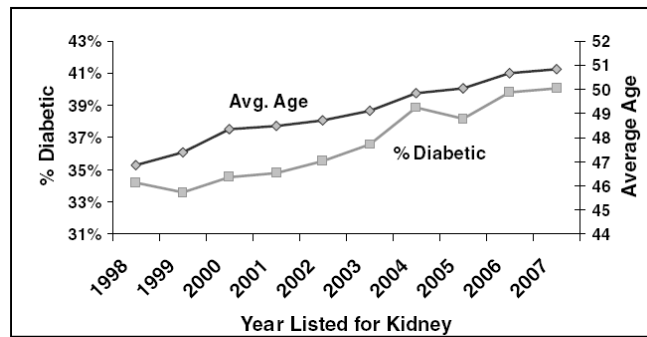


Life Expectancy for Patients with Stage 5 CKD, Dialysis vs Transplantation



Wolfe *et al*, NEJM 1999

Increasing Proportion of Patients with Diabetes on Kidney Waitlist



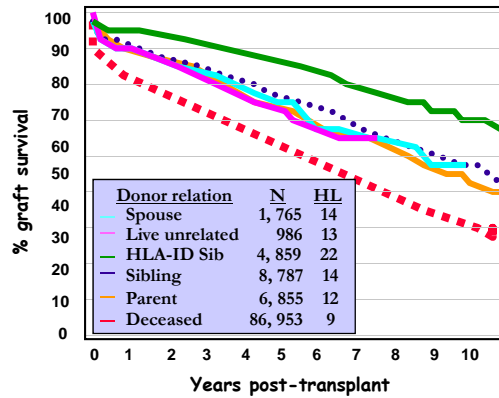
SRTR Annual Report

McCullough *et al*, Am J Trans 2009

Transplant Options for Type I Diabetics with Advanced Kidney Disease

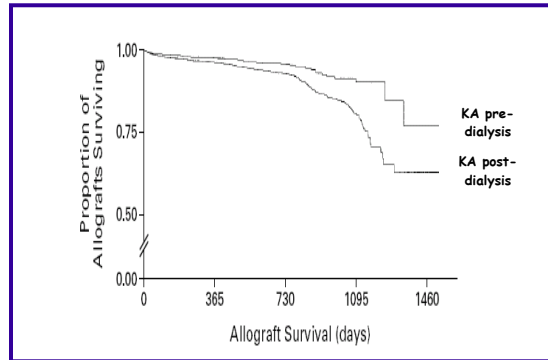
Type of Transplant	Source of Organ	Consideration
Kidney Alone (KA)	living or deceased	<ul style="list-style-type: none"> • minimize dialysis (LD) • insulin dependent
Simultaneous Pancreas-Kidney (SPK)	usually deceased	<ul style="list-style-type: none"> • same donor • high quality donor • longer wait-time
KA with sequential Pancreas-After-Kidney (PAK)	living kidney, deceased pancreas	<ul style="list-style-type: none"> • minimize dialysis • short panc wait time • different donor

Advantages of Living Donor Kidney Transplantation



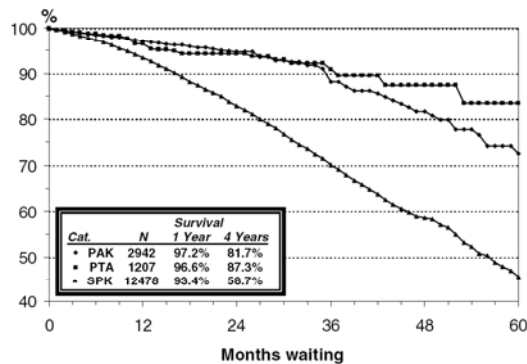
United Network for Organ Sharing, 2000

Kidney Graft Survival Improves with Transplantation Before Dialysis



Mange K *et al*, NEJM 2000

Risk of Death for Patients on the Kidney Waiting List

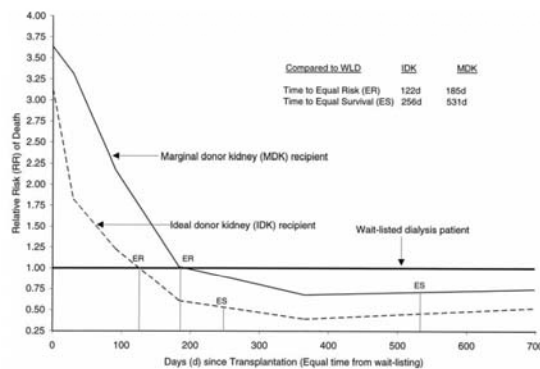


Pts listed 1995-2003 @ UNOS

Gruessner *et al*, Am J Transp 2004

Deceased Donor Options - Benefit of Marginal (ECD*) Kidneys

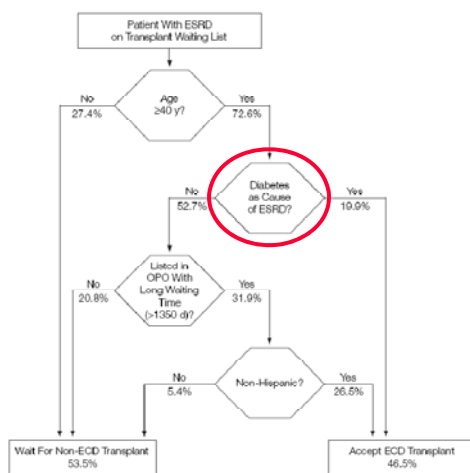
*Expanded Criteria Donor



- Limited life expectancy
- Access failure

Ojo et al. J Am Soc Nephrol. 2001

ECD Kidneys - a Viable Option for Many Diabetics with CKD 5d



Merion et al, JAMA 2005

Rationale for Pancreas Transplantation

- Euglycemia Better (DCCT/EDIC)
 - Stabilize/Reverse Complications
 - Prevent Complications
 - Retinopathy
 - Albuminuria
 - CVD
 - Metabolic Benefits
- Better QOL
- Longer Life Expectancy

Restoring Normoglycemia in Type I Diabetics

- Whole Pancreas Transplantation
- Islet Transplantation
- NO RCTs
 - Registries
 - Series and anecdotes
 - Personal experience
 - Opinions
 - Paucity of contemporary studies

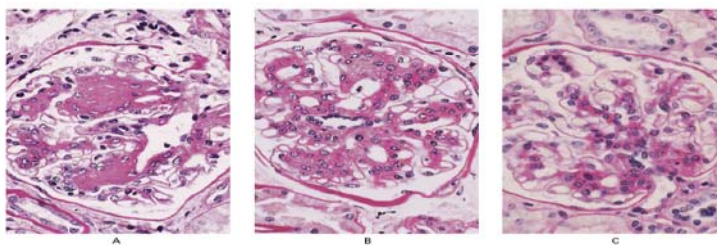
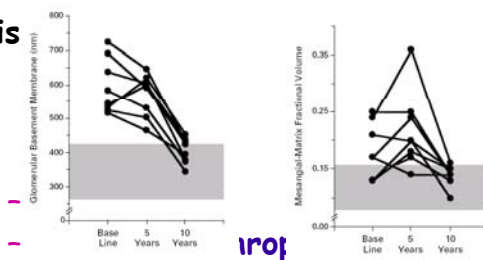
Establishing a Role for Pancreas Transplantation

Four Questions

- Benefit of Pancreas txp vs none?
- Benefit of Pancreas-kidney vs kidney alone?
 - Pt survival
 - Kidney outcomes
- What are risks of pancreas txp?
- Are Benefits > Risk of complications?

Benefits of Pancreas Transplantation: Reversal of Diabetic Nephropathy Lesions

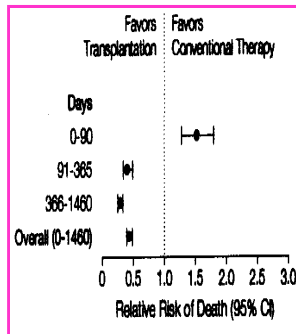
- **Establis**



Fioretto, NEJM 1998

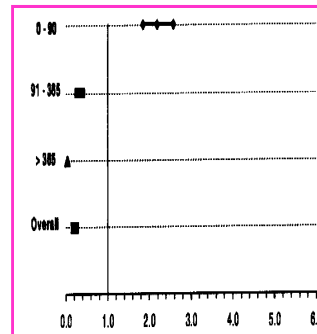
Simultaneous Pancreas-Kidney vs Remaining on Waitlist - Mortality

- n = 11,572
- 1995-2000, listed at UNOS
- control = remain listed
- 4-yr survival rates



Venstrom *et al*, JAMA 2003

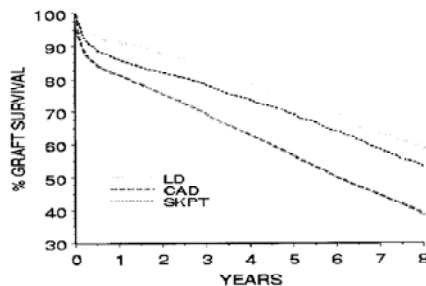
- n = 12,478 pts
- 1995-2003, listed at UNOS
- control = remain listed
- 4-yr survival rates



Gruessner *et al*, Am J Transp 2004

Is the Benefit Related to the Simultaneous Panc-Kidney vs Kidney Alone?

- Txp 1987-1996, n=18,549 Type 1 DM



8-year pt survival:

LD: 72%
 SPK: 72%
 CAD: 55%

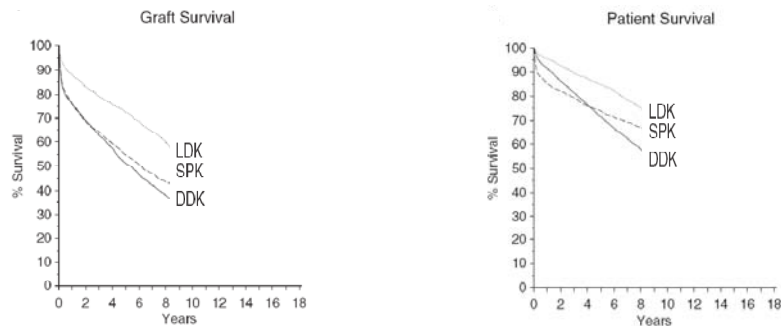
LD advantages

- less I-R injury
- healthy donors
- related donors
- pre-emptive
- minimized dialysis

Reddy *et al*, AJKD 2003

Very Long-Term Transplant Outcomes: Simultaneous Panc-Kidney vs Kidney Alone

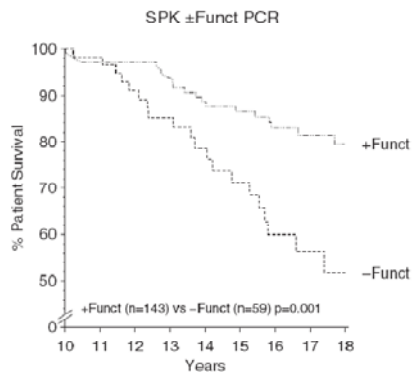
Txpd 1984-1990, 2944 DDKT; 992 LDKT; 850 SPK



- delayed impact of restoration of euglycemia
- LDK pts develop diabetic nephropathy

Morath, JASN 2008

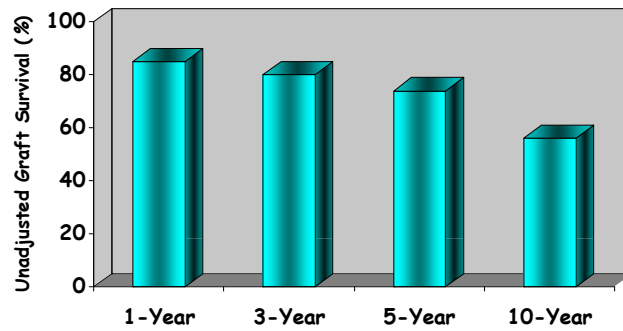
Functioning Pancreas Improves Survival in Long-Term SPK Recipients*



*All with functioning kidneys

Morath, JASN 2008

Long Term Pancreas Graft Survival with SPK Transplantation- USA

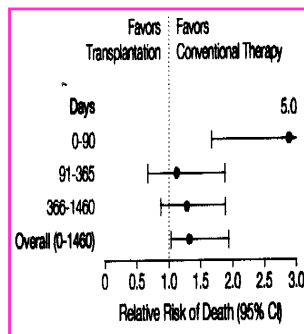


Source: 2007 OPTN/SRTR Annual Report Table 1.13

Leichtman *et al*, Am J Trans 2008

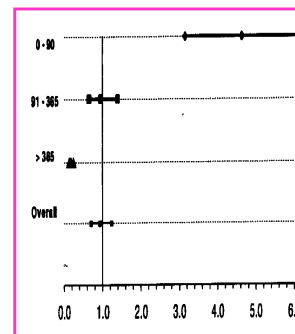
Pancreas After Kidney Transplant vs Kidney Alone

- n = 11,572
- 1995-2000, listed at UNOS
- control = remain listed, on insulin
- 4-yr survival rates



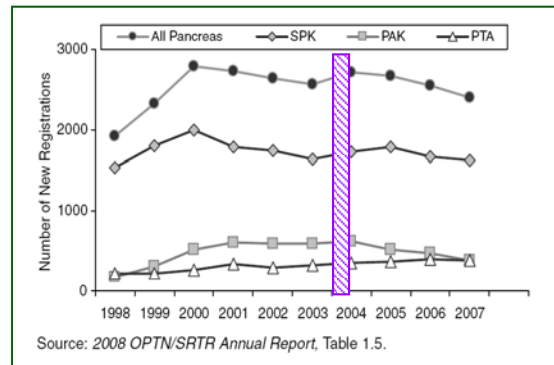
Venstrom *et al*, JAMA 2004

- n = 12,478 pts
- 1995-2003, listed at UNOS
- control = remain listed, on insulin
- 4-yr survival rates



Gruessner *et al*, Am J Transp 2004

Status of Pancreas Transplants in the USA, 1997-2006



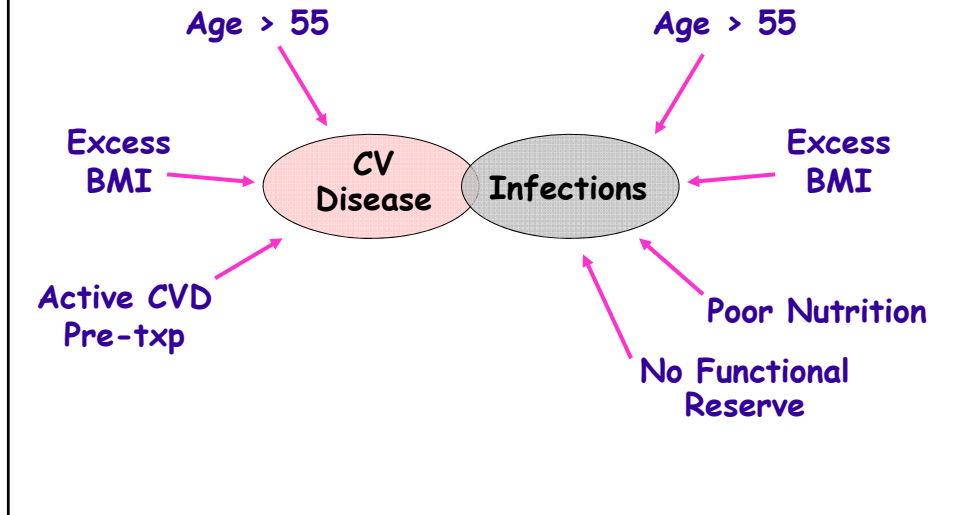
McCullough *et al*, Am J Trans 2009

Patient Survival After Pancreas Transplantation

Reading Between the Lines

- **Simultaneous Kidney-Pancreas**
 - Early Risk
 - Very long-term survival advantage?
 - Kidney
 - Patient
- **Pancreas After Kidney**
 - High early risk
 - Moderate intermediate risk
 - No clear long-term advantage
 - No good data beyond 4 yrs

Reasons for Excess Early Mortality



Metabolic Consequences and Pancreas Allograft Venous Drainage

	Portal	Systemic	Metabolic Syndrome
Fasting insulin	Lower	Higher	Higher

Long-Term Glucose Tolerance After Simultaneous Panc-Kidney

- 45/167 (28%) pts insulin independent 10 yrs after SPK

Table 2 Parameters of pancreas and kidney graft function from 3 months to 10 years after simultaneous pancreas/kidney transplantation.

	3 months (n=38)	1 year (n=38)	3 years (n=38)	5 years (n=38)	10 years (n=38)	P
Fasting blood glucose (mg/dl)	78 ± 2	81 ± 2	82 ± 2	84 ± 2	91 ± 2	<0.01 ^{ab,c,d,e}
HbA _{1c} (%)	4.6 ± 0.1	4.9 ± 0.1	4.9 ± 0.1	5.0 ± 0.1	5.3 ± 0.2	<0.001 ^{fa,b,d,g,h}
120 min glucose (mg/dl)	118 ± 7	122 ± 9	110 ± 9	118 ± 9	150 ± 13	<0.05 ^{d,g,i}
Normal glucose tolerance (%)	67	56	68	66	37	<0.05 ^{b,g,i}
BMI (kg/m ²)	21.1 ± 0.4	21.9 ± 0.5	22.4 ± 0.5	22.8 ± 0.5	23.5 ± 0.7	<0.05 ^{ab,c,d,g}
Fasting insulin (μU/ml)	21 ± 2	23 ± 2	18 ± 1	18 ± 1	16 ± 1	<0.05 ^d
S-creatinine	1.3 ± 0.1	1.3 ± 0.1	1.4 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	Ns

Mean ± S.E.M. ANOVA with repeated measurements.

^a3 months versus 5 years. ^b3 months versus 10 years. ^c1 year versus 5 years. ^d1 year versus 10 years. ^e1 year versus 3 years. ^f3 months versus 1 year. ^g3 years versus 10 years. ^h3 years versus 5 years. ⁱ5 years versus 10 years. ^j3 months versus 3 years.

Adapted from Dieterle *et al*, Eur J Endocrin 2007

Loss of Insulin Independence After Pancreas Transplantation

low c-peptide
(islet failure)

- Rejection
 - Acute
 - Chronic
- Autoimmune DM
- Islet exhaustion
- CNI, Srl

Normal/high c-peptide
(insulin resistance)

- Type II DM
 - Wt gain
 - High BMI
- Steroids

Considerations in Selecting Patients for Pancreas Transplantation

- Newer insulins and techniques
- Cost-benefit relationship
- Surgical risks and complications
- Side effects of immunosuppression

Who is a Pancreas Transplant Candidate?



- Robust
- Well-nourished
- No active CV disease
- Non-obese
- Emotional and mental stability

American Diabetes Association Position

- Pancreas txp acceptable alternative to insulin
 - imminent/established ESRD
 - no surgical C/I
- Pancreas alone
 - frequent, acute metabolic complications
 - incapacitating problems with insulin
 - insulin failure
- Islet
 - Research studies only

