# Where Have All the Pancreata Gone? A Crisis in Modern Day Transplantation

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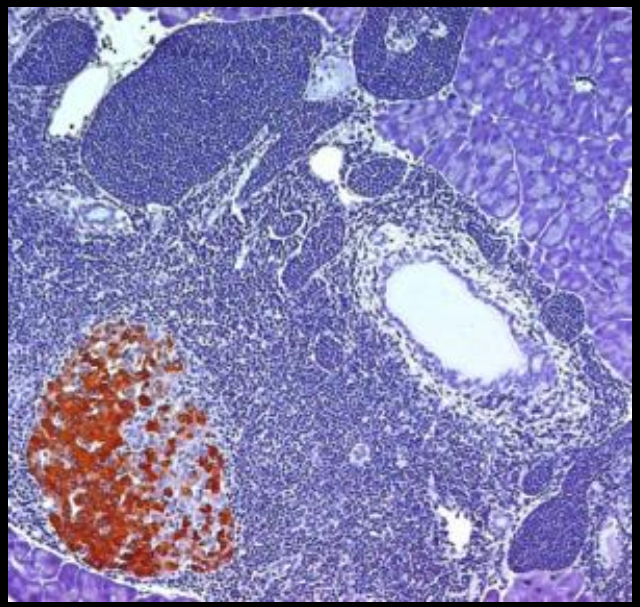
OptumHealth Education's 28th Annual National Conference
Minneapolis, Minnesota
October 15, 2019

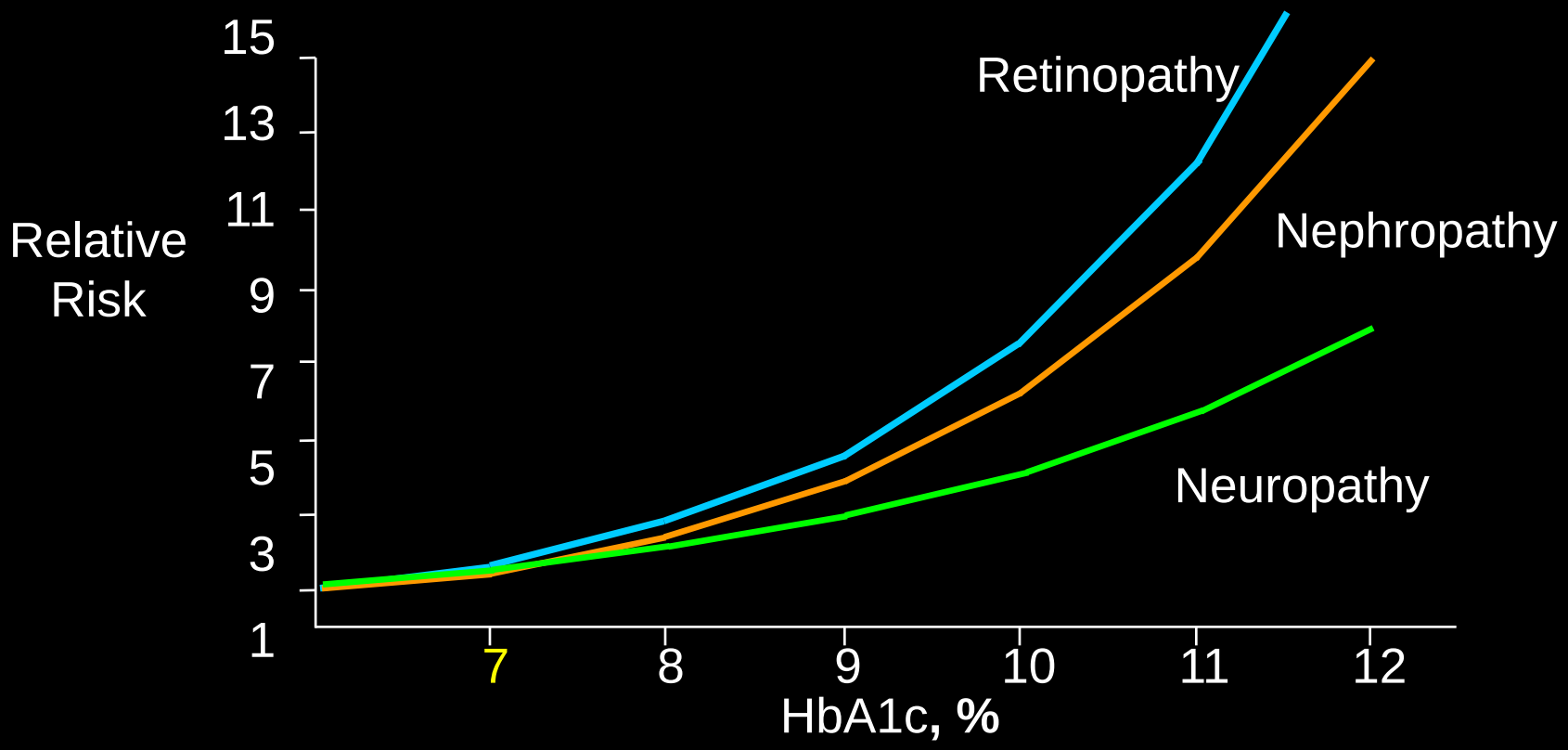
# The Enemy

- Type I diabetes results from the autoimmune destruction of insulin producing beta cells in the pancreas

- Long-term therapy with insulin, while life saving, may result in:
  - kidney disease
  - blindness
  - cardiovascular disease
  - peripheral neuropathy

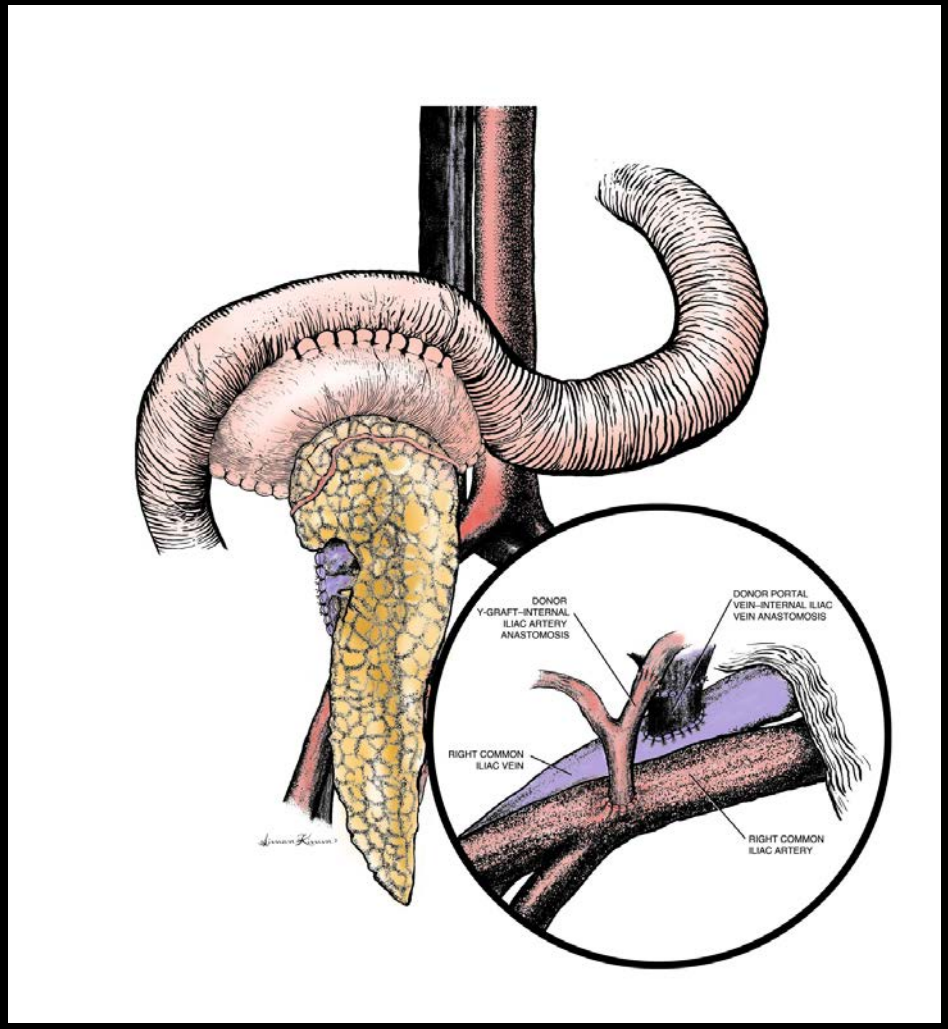


# Relationship of $HbA_{1c}$ to Risk of Microvascular Complications

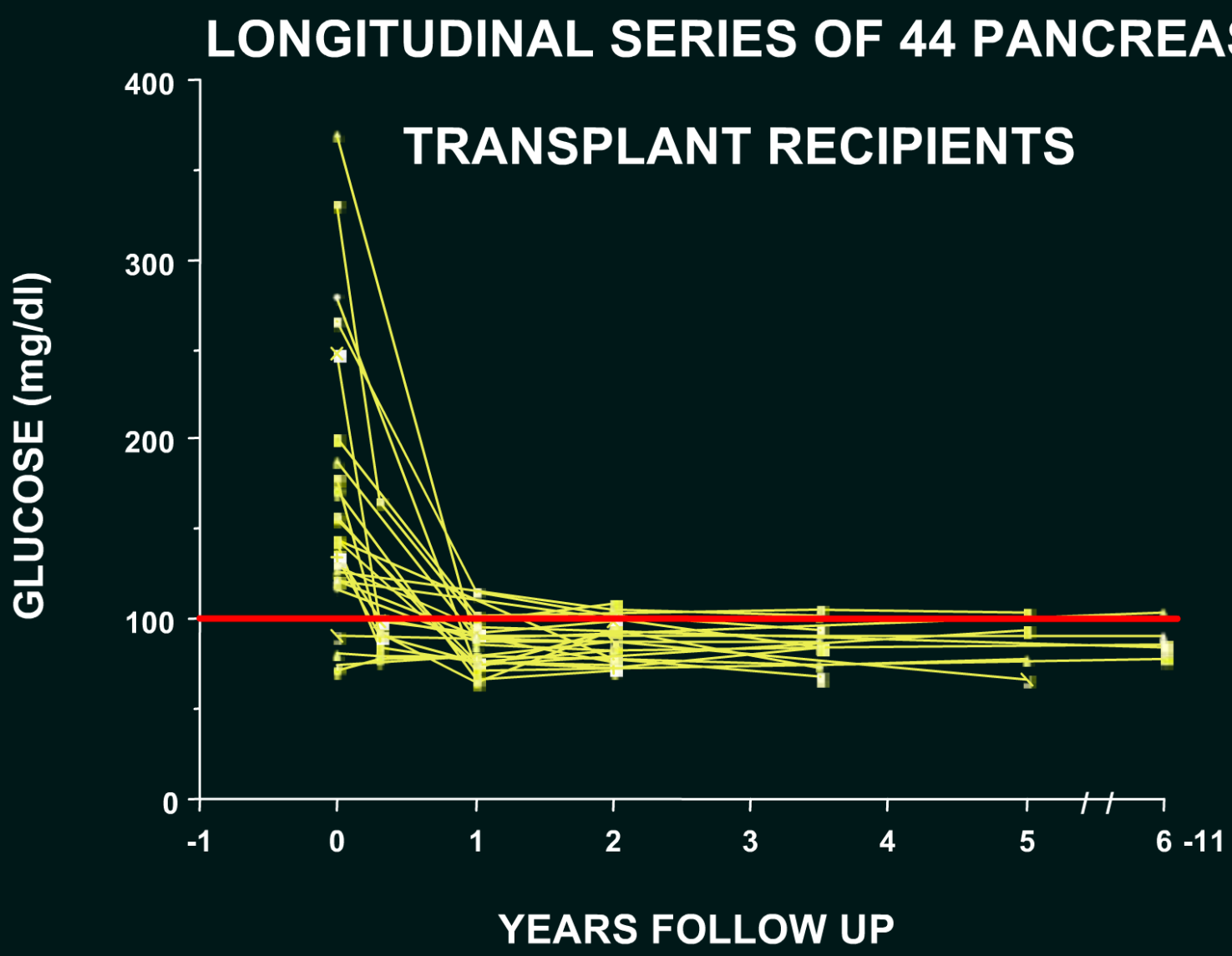



DCCT Research Group. *N Engl J Med.* 1993;329:977-986.

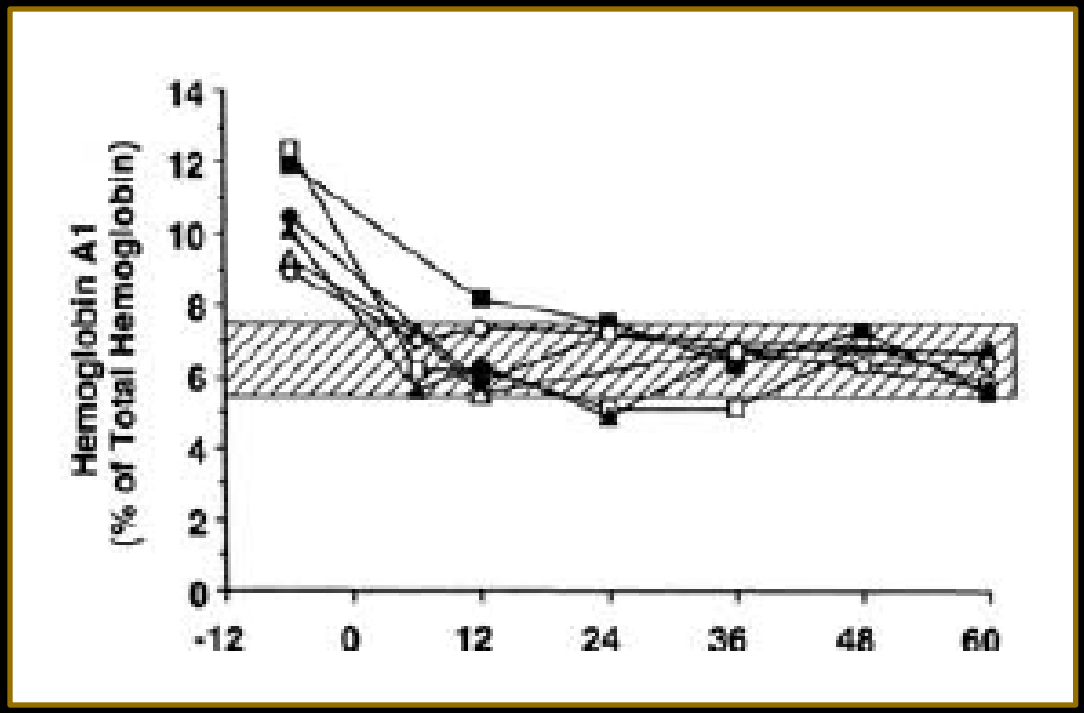
# The Hero
# The Pancreas Transplant



# FASTING PLASMA GLUCOSE

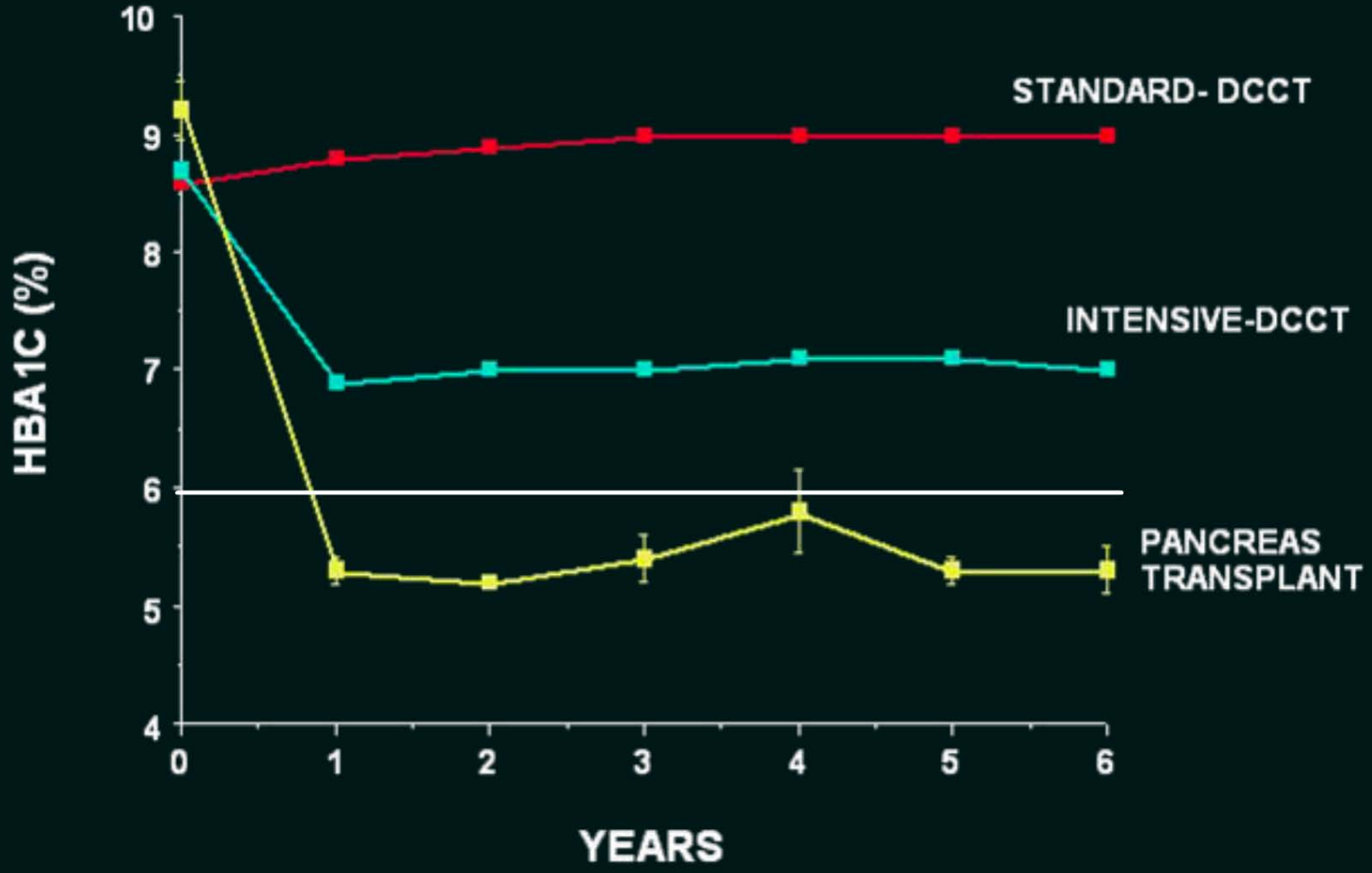


# HgbA1C and pancreas transplants Long-term results




Morel P, Sutherland DER. Long term Glucose Control in Patients with Pancreas Transplants. Ann Int Med 115:994, 1991.

# PANCREAS TRANSPLANTATION vs DCCT HEMOGLOBIN A1C



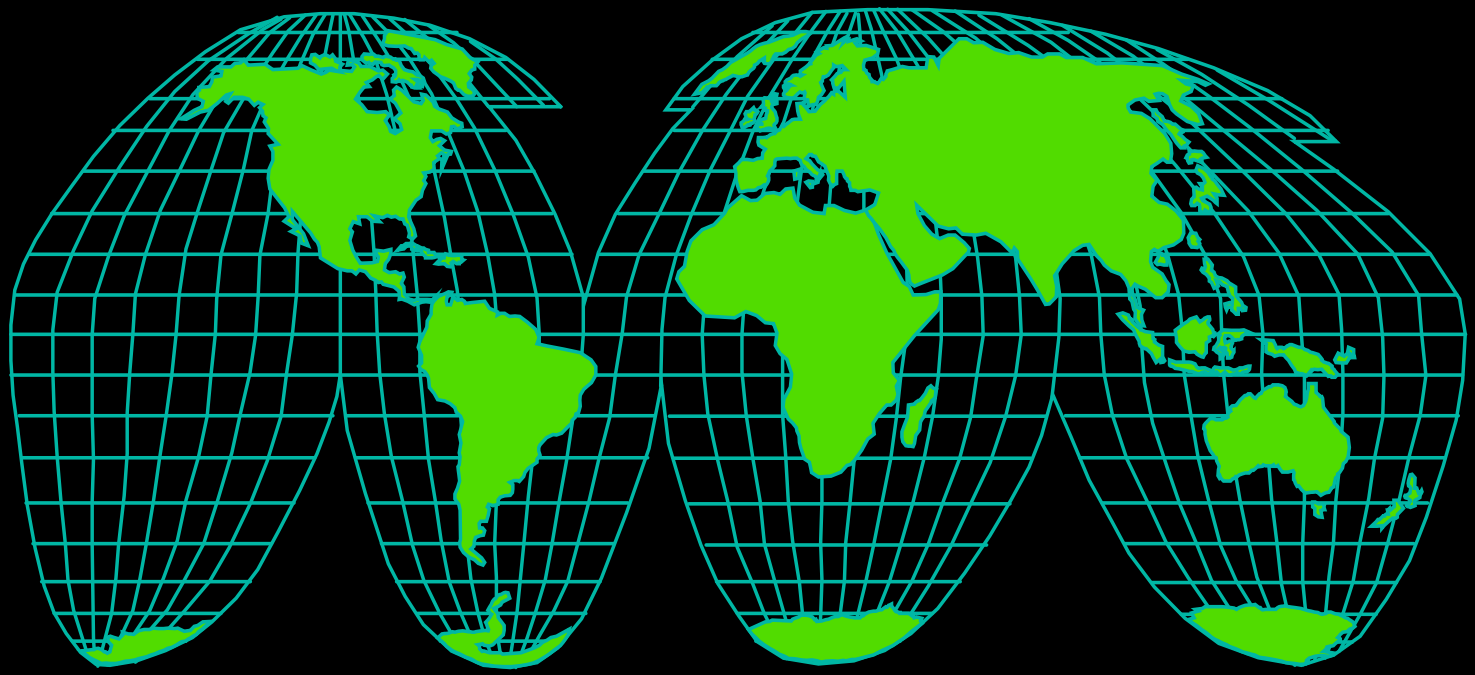
# Goals of Therapy

| | HgbA1c | Hypo | Insulin |
|---|---|---|---|
| Insulin | ↓ | ↑ | + |
| Islet Tx | Nl | ∅ | ↓ |
| Pancreas Tx | Nl | ∅ | ∅ |

# Indications for Pancreas Tx

- Diabetes Mellitus (T1 or T2) with:
  - Renal failure requiring simultaneous kidney transplant (SPK). 75-80%
  - Functioning kidney transplant already on immunosuppression (PAK). 5-10%
  - Brittle diabetes with hypoglycemic unawareness (PTA). 10-15%

International Pancreas Transplant Registry (IPTR)
Scientific Registry of Transplant Recipients (SRTR)
Wisconsin Allograft Recipient Database (WisARD)

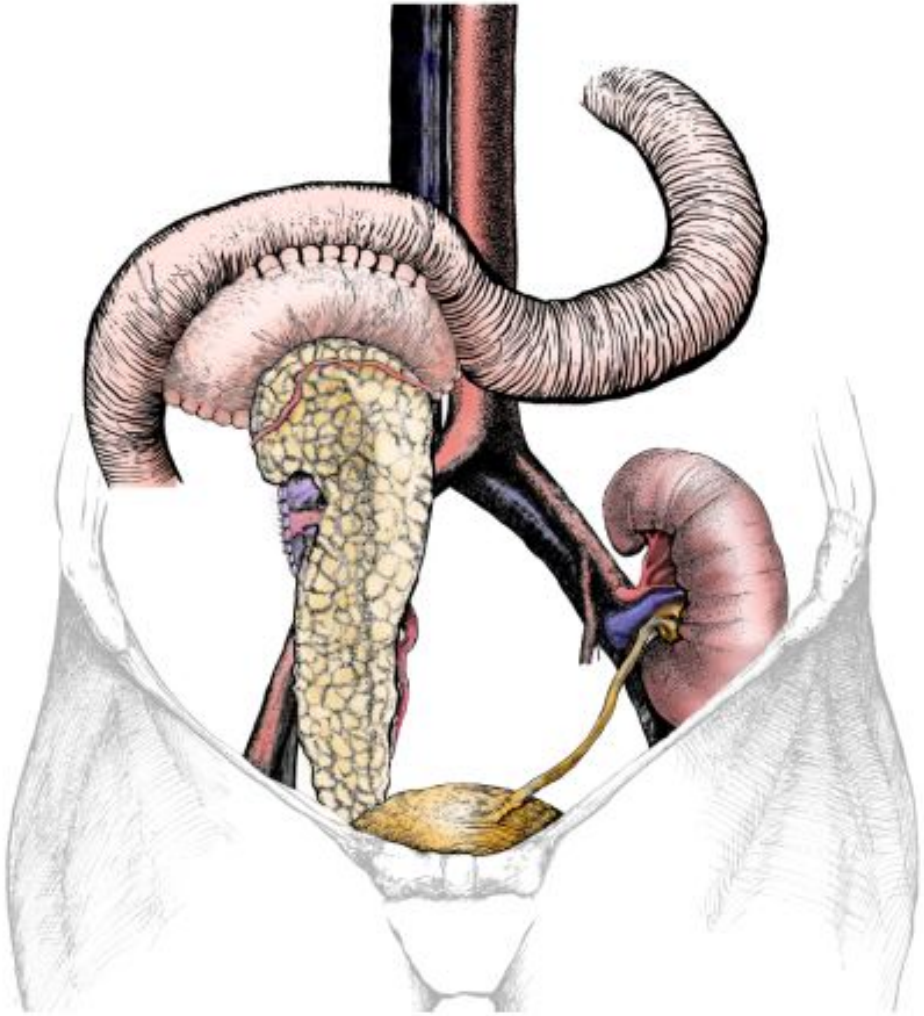


# Comparative Patient Survivals

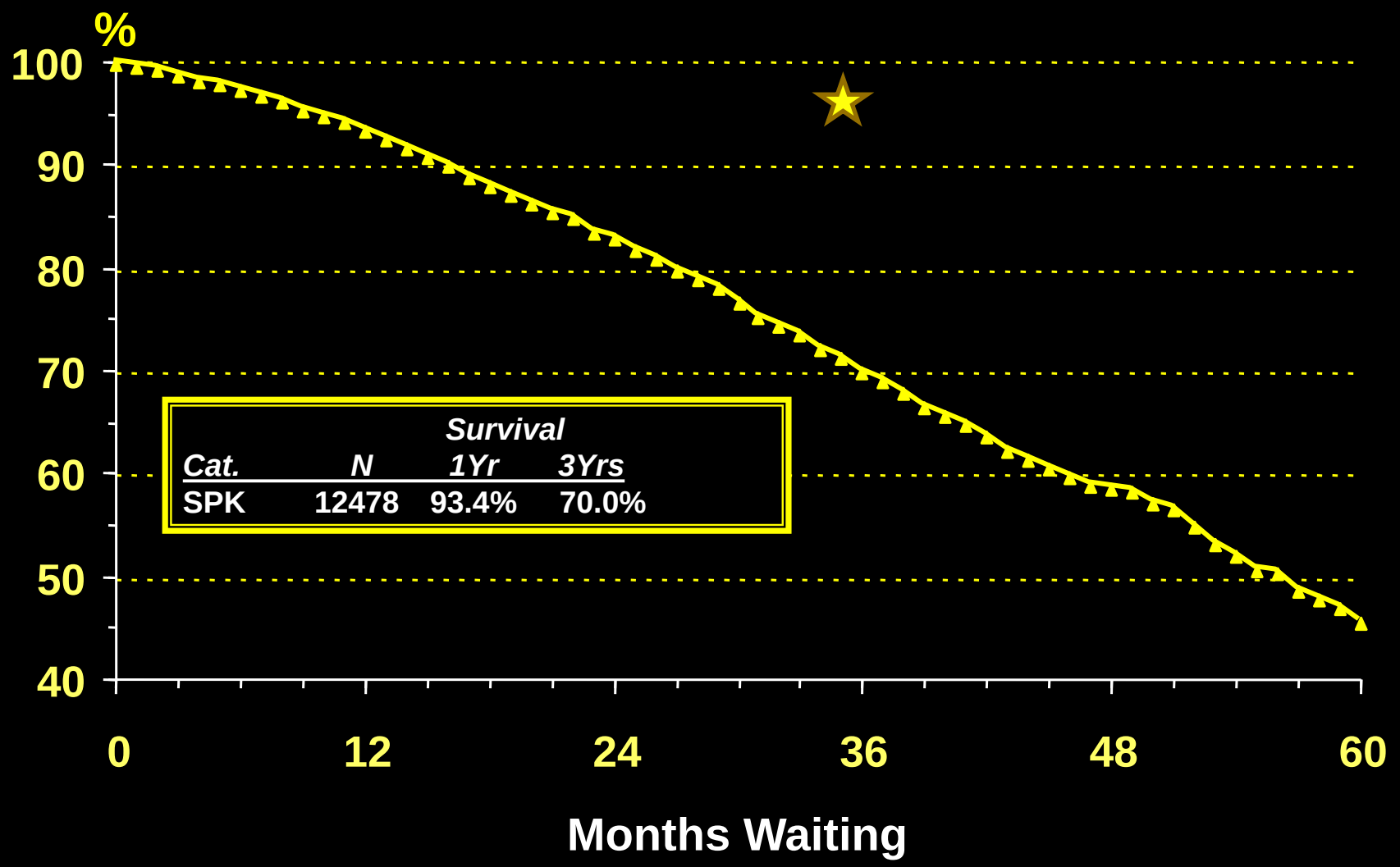
| Organ | 1-year | 3-year |
|---|---|---|
| LD Kidney | 98.9% | 96.5% |
| All Pancreas | 97.8% | 95.2% |
| SPK | 97.7% | 95.6% |
| DD Kidney | 96.6% | 92.3% |

Pancreas transplants
do not threaten lives!

PANCREAS TRANSPLANT WITH ENTERIC DRAINAGE IN SITU



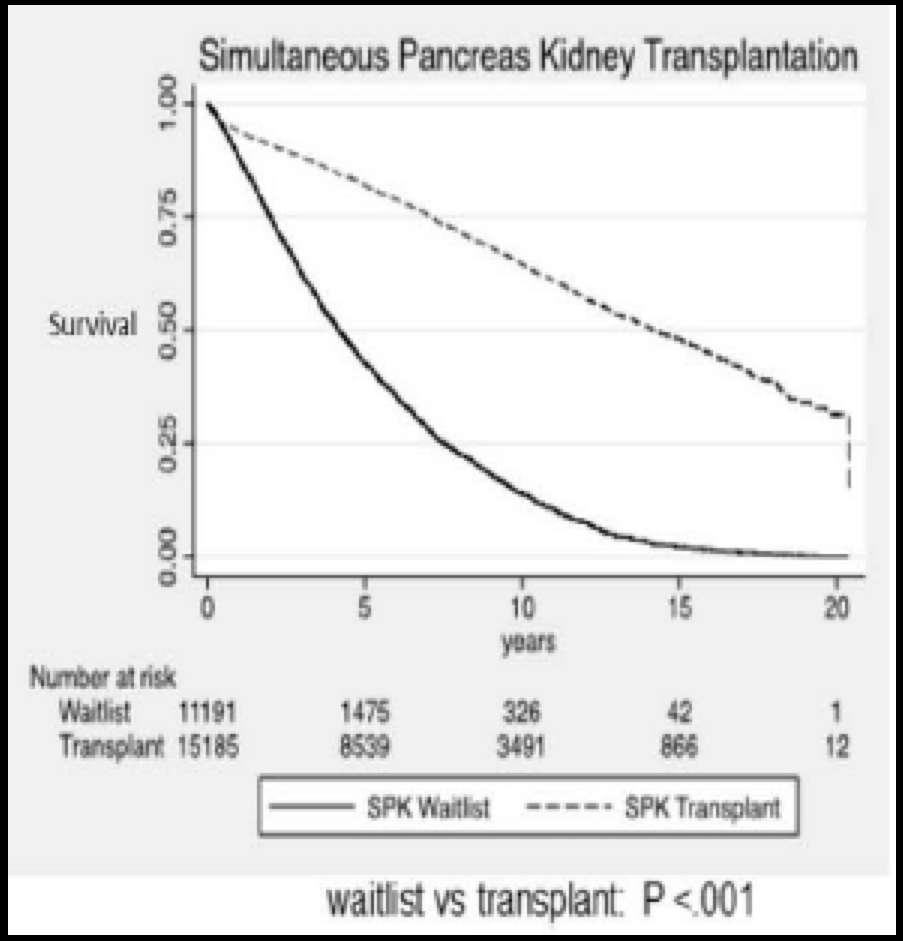
# Diabetic Uremic Patient
# Patient Survival while Waiting



# Survival Benefit of Solid-Organ Transplant in the United States

*A Rana, A Gruessner, VG Agopian, Z Khalpey, IB Riaz, BKaplan, KJ Halazun, RW Busuttil, RWG Gruessner*

*JAMA Surg.* 2015;150(3):252-259

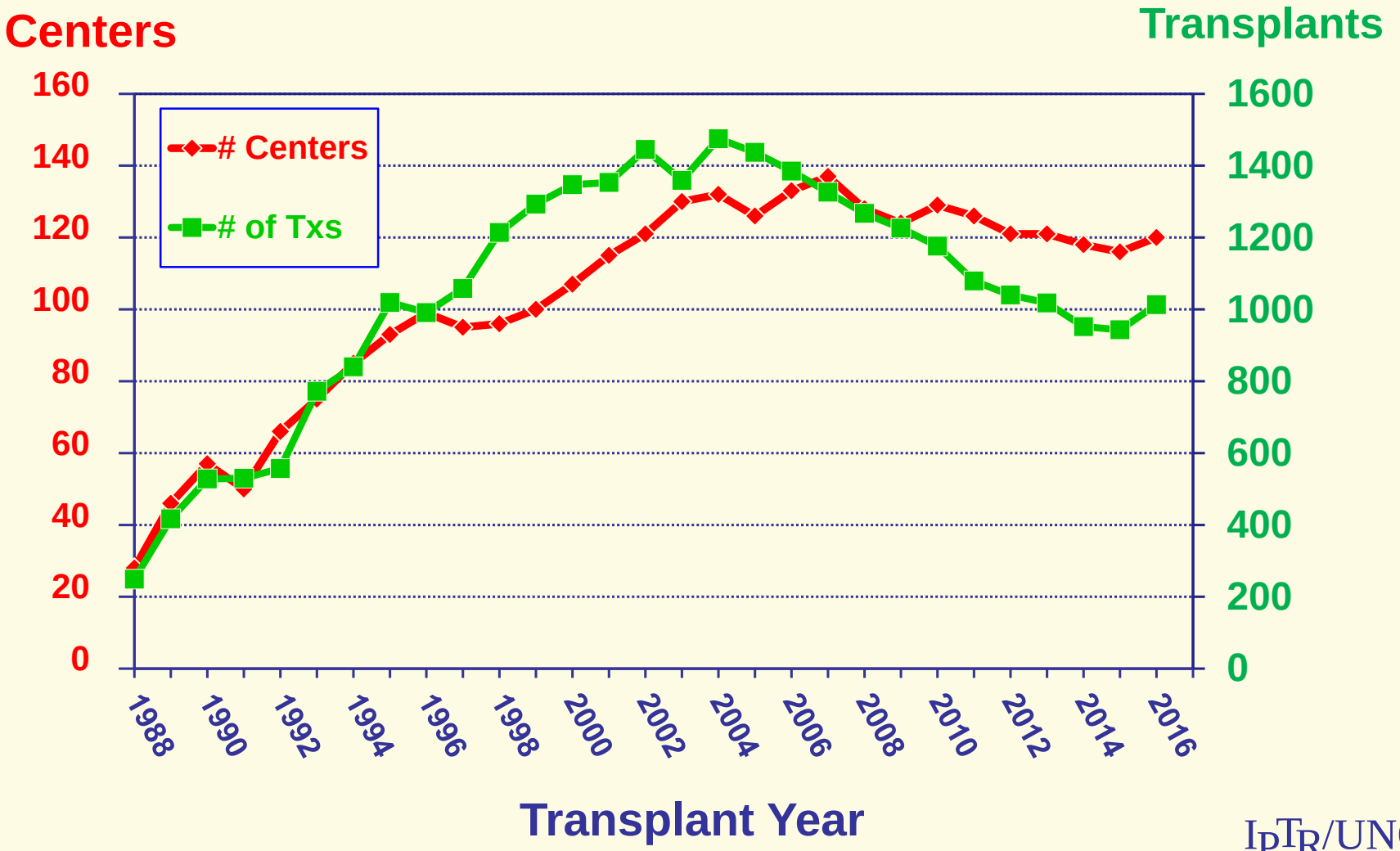


# Successful Pancreas Transplant

- Single organ tx
- Euglycemia without the need for exogenous insulin
- Prevents hypoglycemia
- Normalizes HgbA1c
- Improves patient quality of life
- Reverses peripheral neuropathy
- Prevents recurrent diabetic nephropathy (kidney damage) in transplanted kidneys
- May prolong life

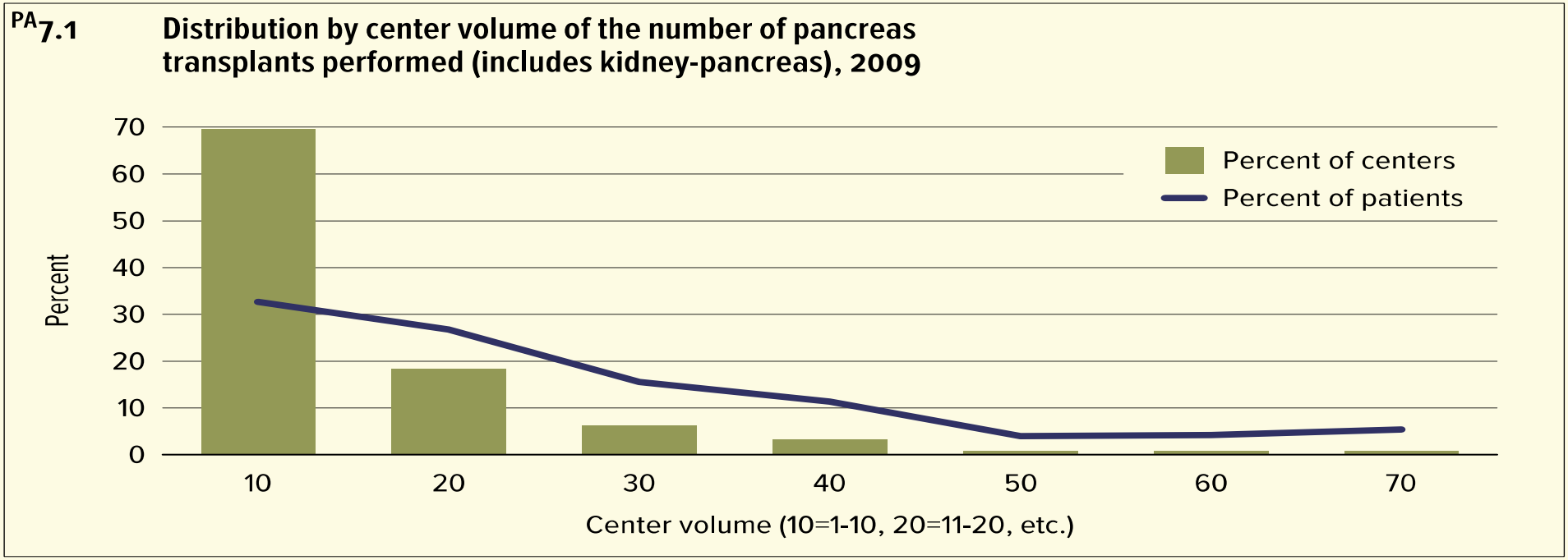
# Number of Tx Centers and Number of Txs

US Pancreas Transplants 1/1/1988 – 12/31/2016




IPTR/UNOS

# Vast Majority of Programs Perform ≤10 Pancreas Transplants Annually




*UNOS SRTR Report Am J Transplant 2011*

# Declining Numbers of Pancreas Txs
## Multifactorial reasons

- Better DM care and delayed progression to nephropathy → ? change in disease patterns
- Competing biological therapies and technologies
- Changing Donor Population

  - aging, more obese and diabetic US population
- Increasing risk aversion due to regulatory scrutiny

# How does one know the pancreas will be good for Tx?

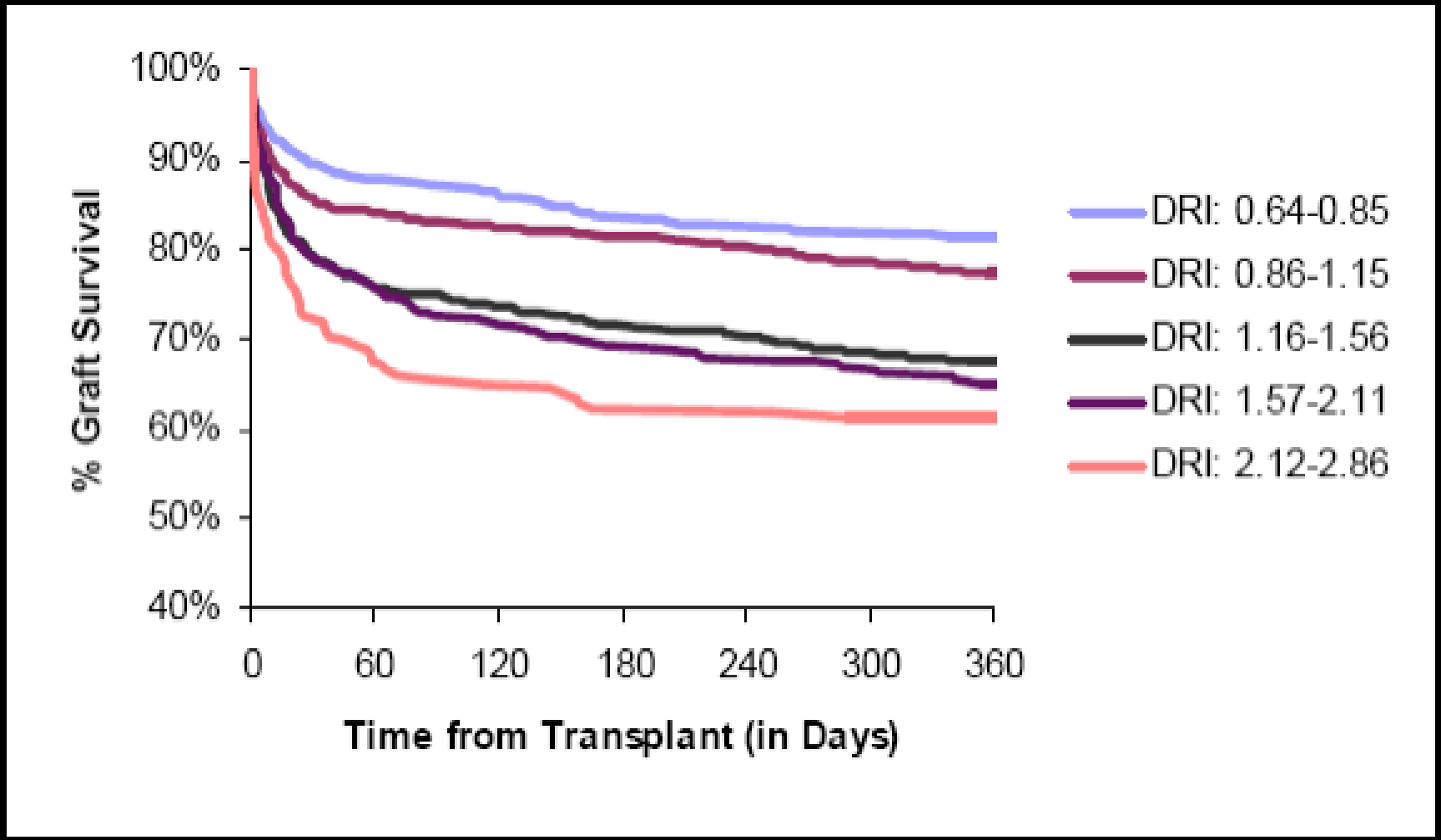
## Pancreas Donor Risk Index

Pancreas Donor Risk Factors and Parameters

- Donor age: 0-20: -0.0083*age+0.166. 20+: 0.0262*age – 0.732.
- Donor female: -0.138. Male: 0.
- Donor African American: +0.240. Non-Black:0.
- Donor Asian: +0.157. Non-Asian: 0.
- Donor Serum Creatinine>2.5: +0.195. SCr ≤ 2.5:0.
- DCD: +0.332. Non-DCD: 0.
- Donor height (cm): -0.0061*Donor Height +1.051.
- Donor BMI: ≤25: -0.00099*BMI+0.0237. >25:+ 0.0323*BMI-0.807.
- Donor cause of death = CVA: +0.210. Other cause: 0.
- Donor cause of death = CVA and PAK recipient: -0.281. Other cause: 0.
- Pancreas Preservation Time (hrs): 0.0147*(Time) – 0.176.

Sum up the above for each donor, and take $e^{SUM}$ to get the PDRI.

# P-DRI: Pancreas Graft Survival (SPK)



# How does one REALLY know if the pancreas will be good for Tx?

Make final decision by direct visual inspection.

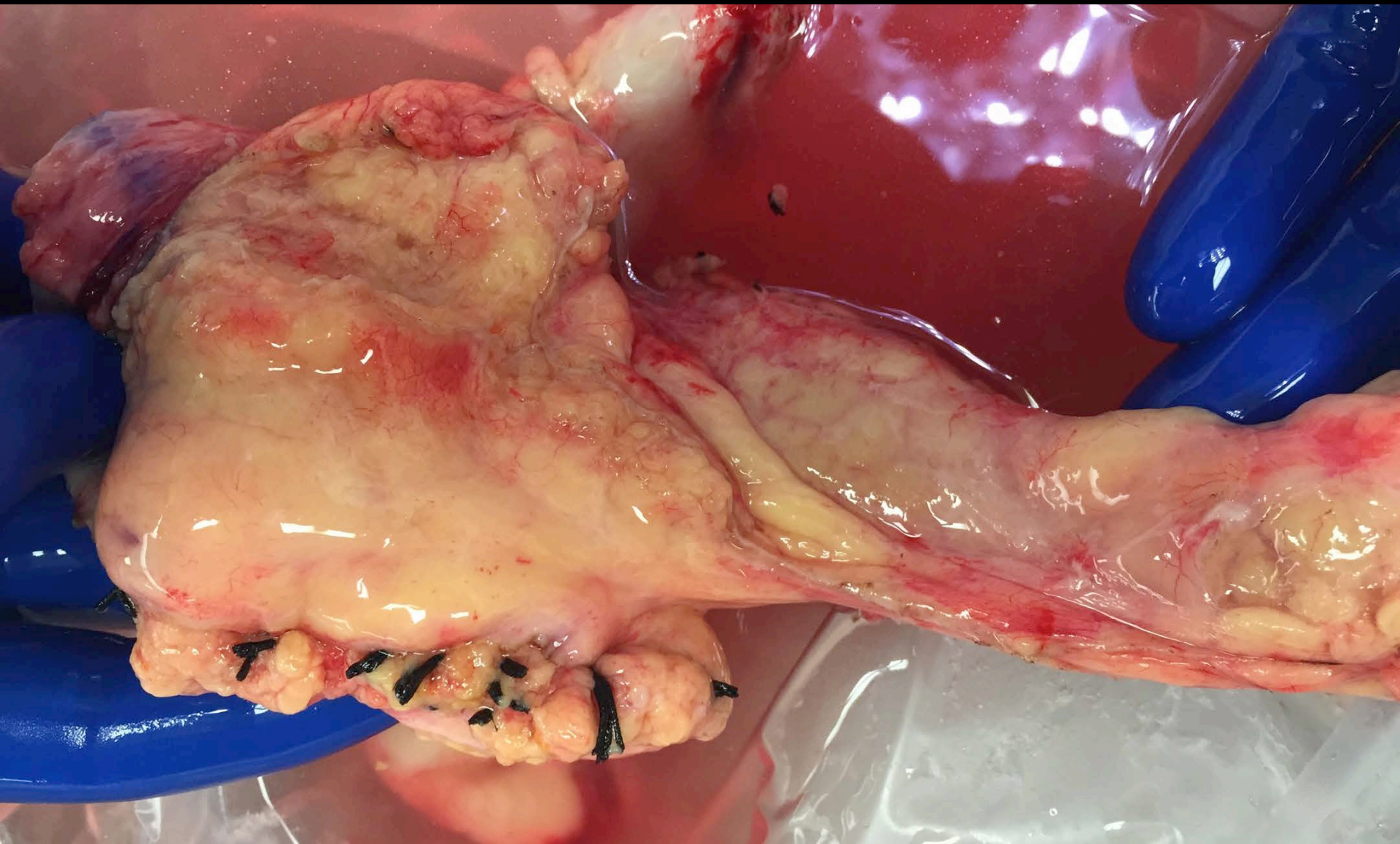
For imports, request anatomic waivers and visualize

Use “A” and “B:” grade pancreata for Tx

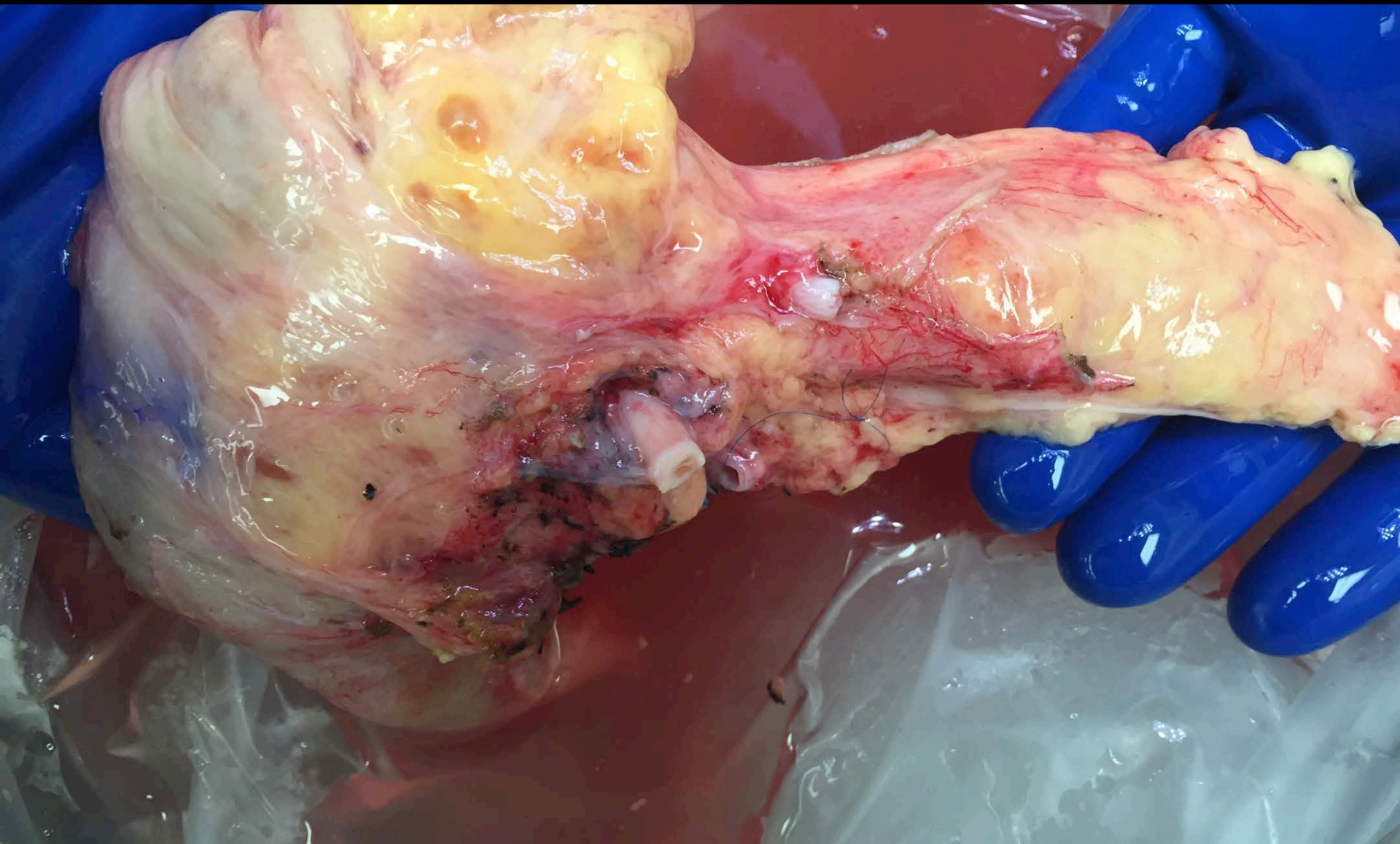
# Grade A Pancreas Graft

# Grade B Pancreas Graft

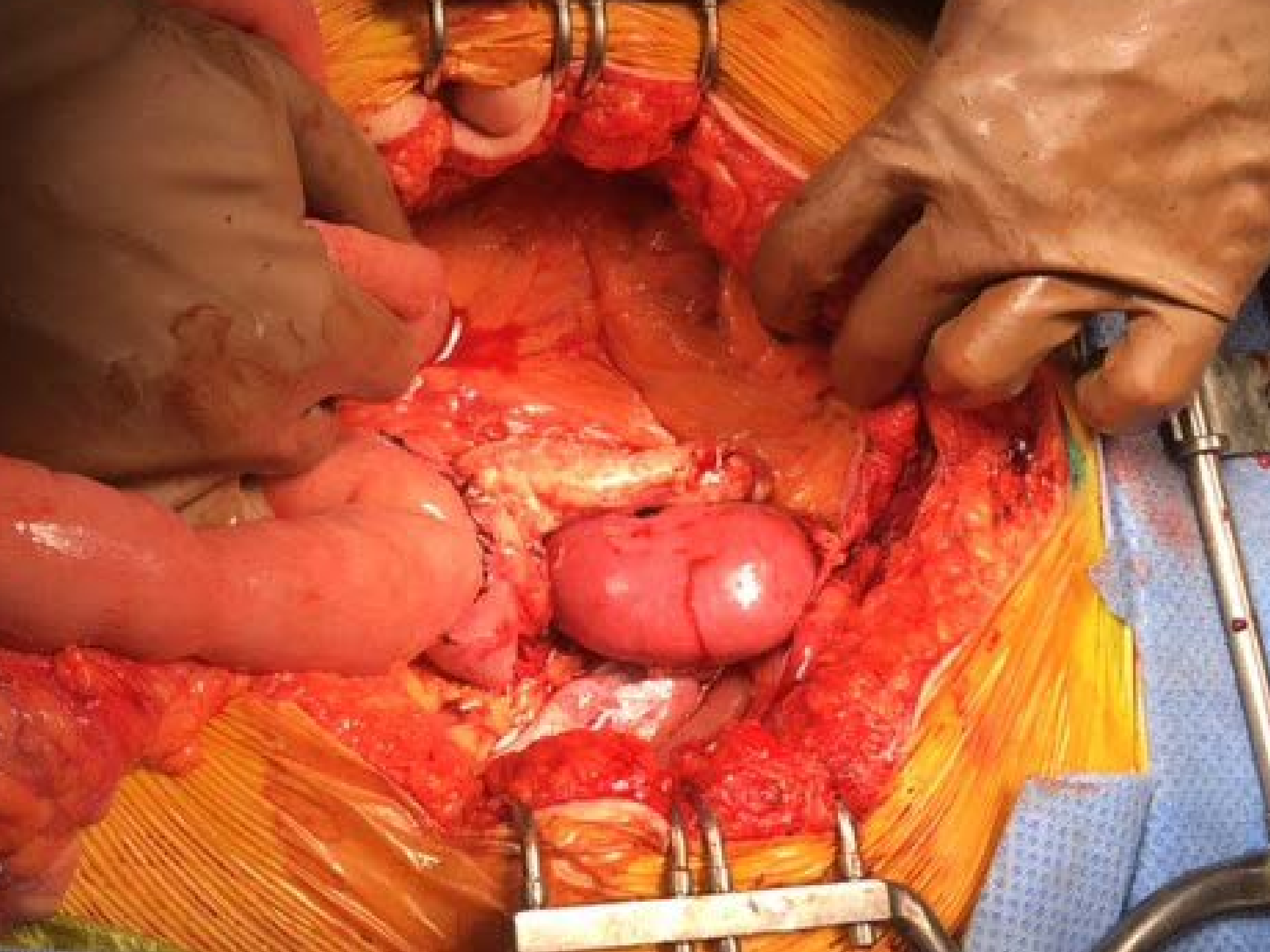
# Grade C Pancreas Graft



# Grade C Pancreas Graft



# Grade A- Pediatric Pancreas Graft



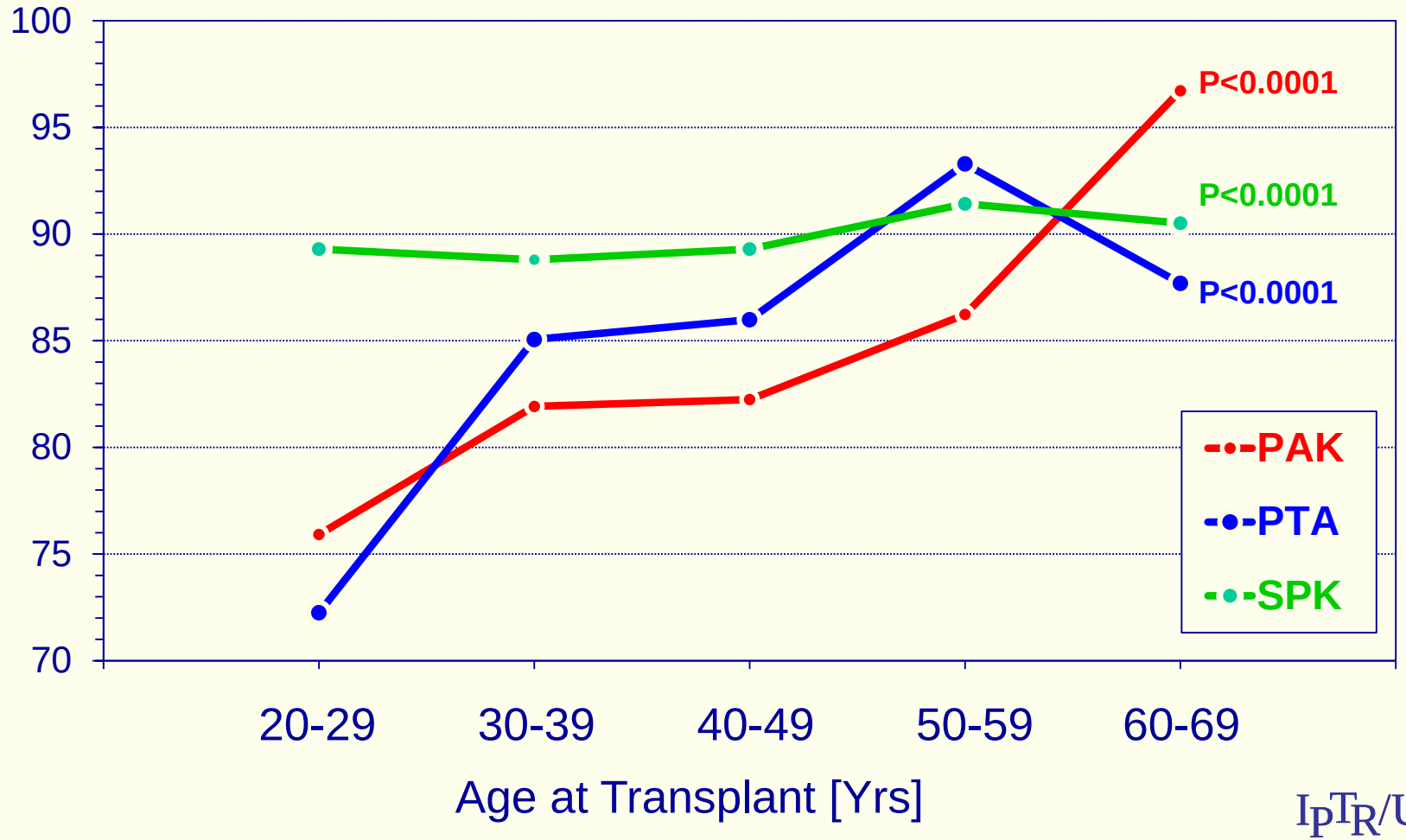
# Typical Demographics for Pancreas Tx

- Donors:
  - DBD local donors
  - <50 years of age
  - BMI <30
- Recipients:
  - Primary Tx
  - Non-highly sensitized
  - Type 1 diabetic recipients
  - <55 years of age
  - BMI <30

Are pancreas txs more complex when D/R characteristics fall outside the norm?

# 1 Yr Pancreas Graft Function by Recip. Age

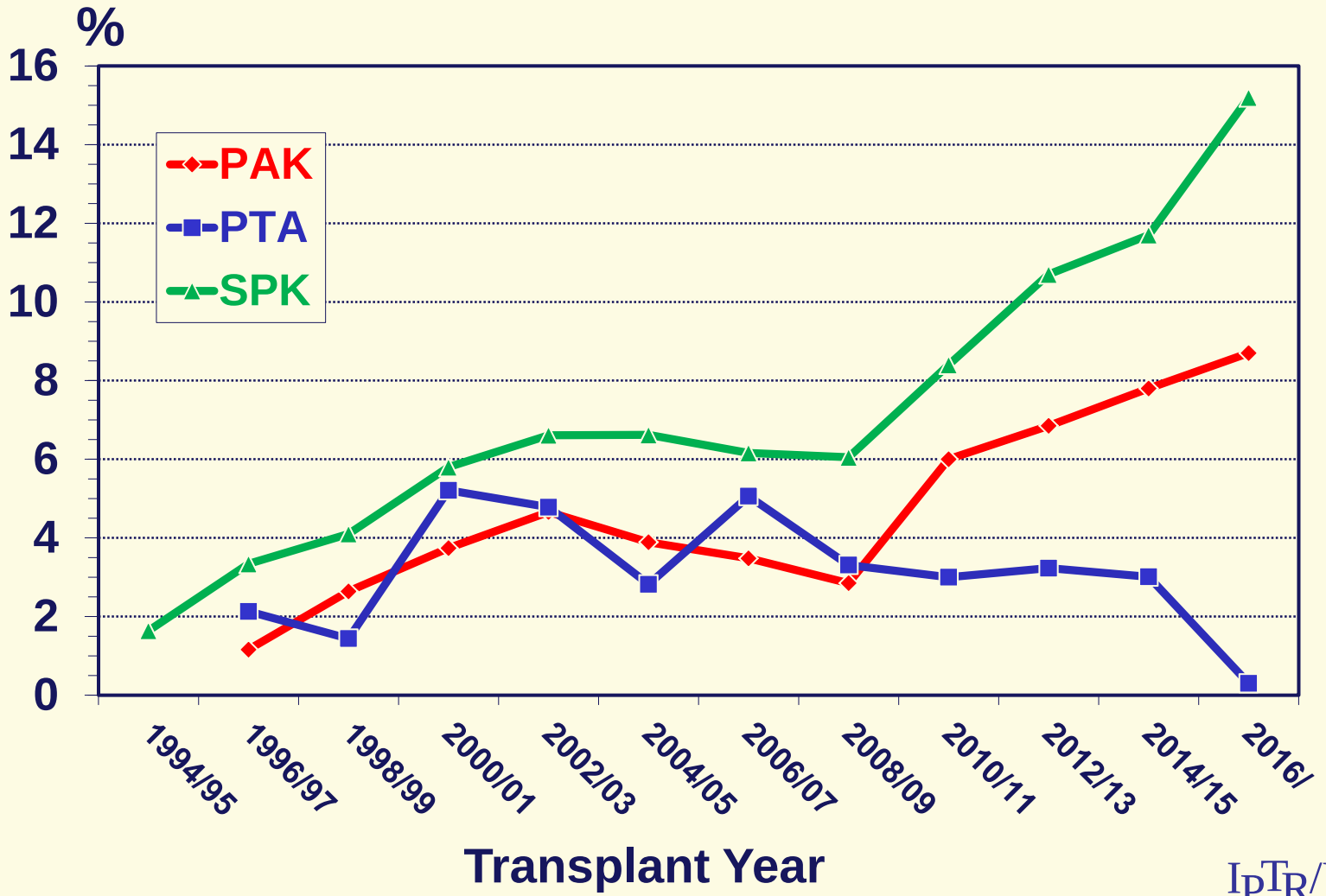
USA Primary Pancreas Transplants in Type 1 DM 1/1/2010 – 12/31/2016




IPTR/UNOS

# Patients with Type 2 Diabetes

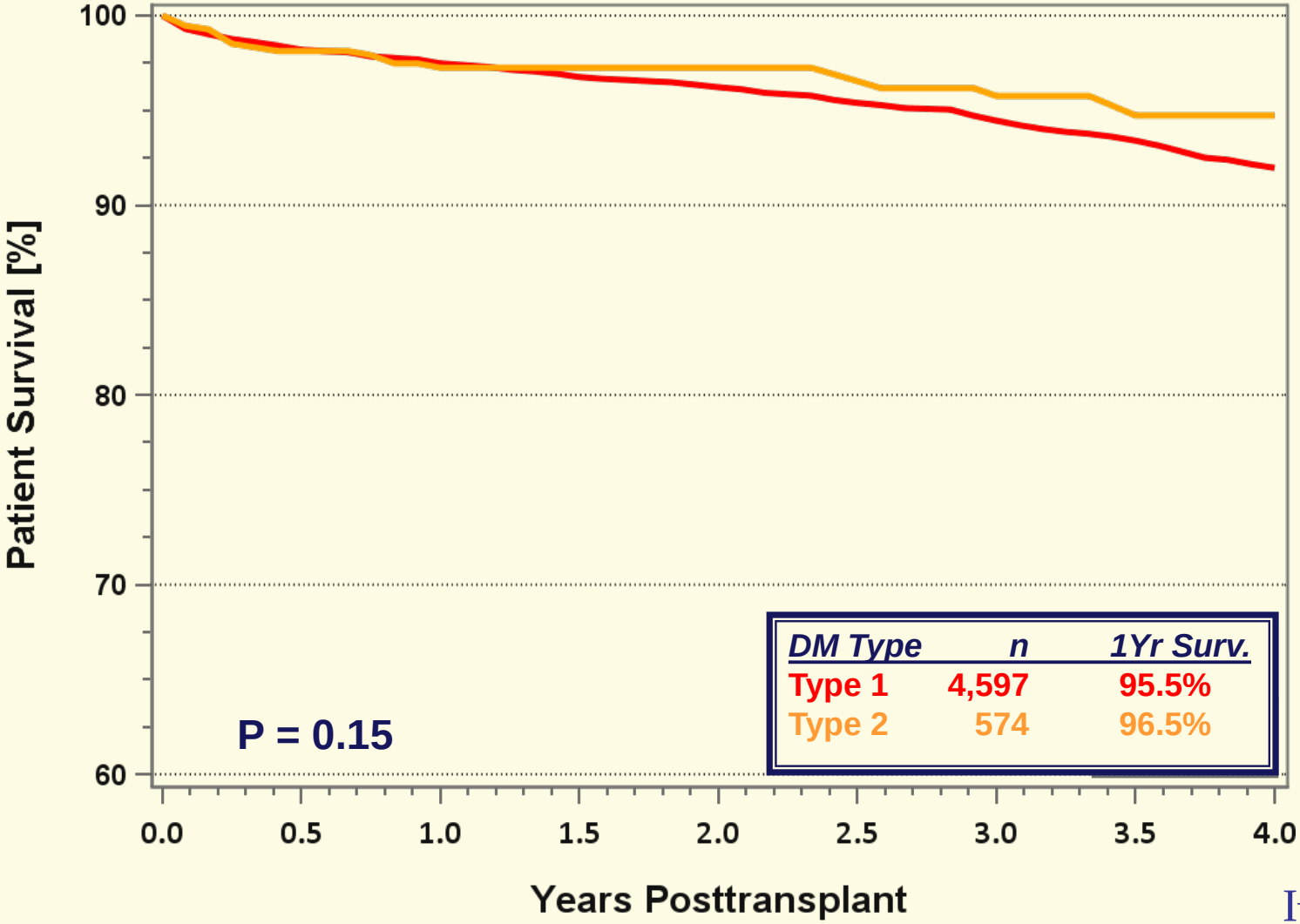
USA Primary DD Pancreas Transplants 1/1/1994 – 12/31/2016




IPTR/UNOS

# SPK Patient Survival by Diabetes Type

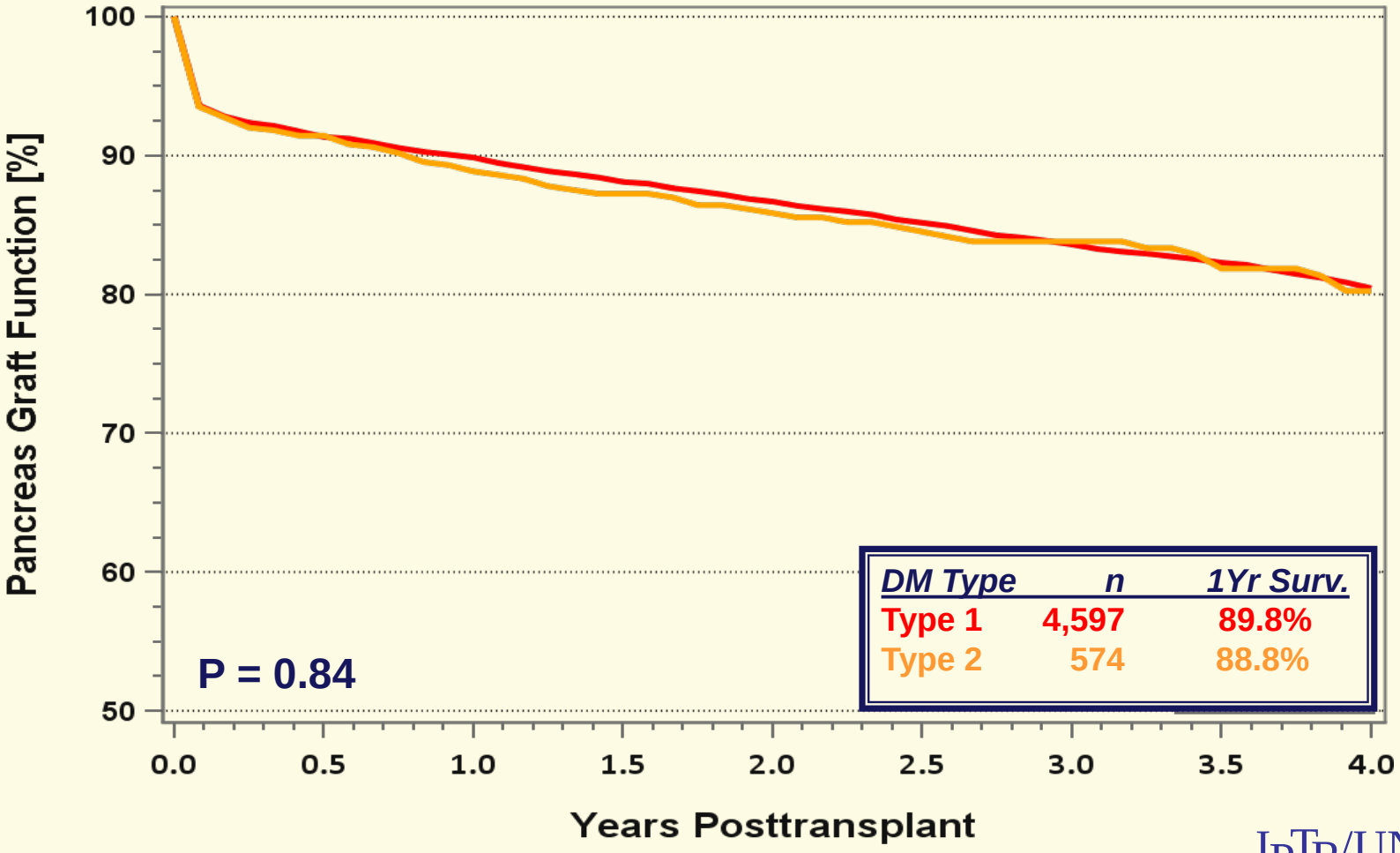
USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016




IPTR/UNOS

# SPK Pancreas Graft Function by Diabetes Type

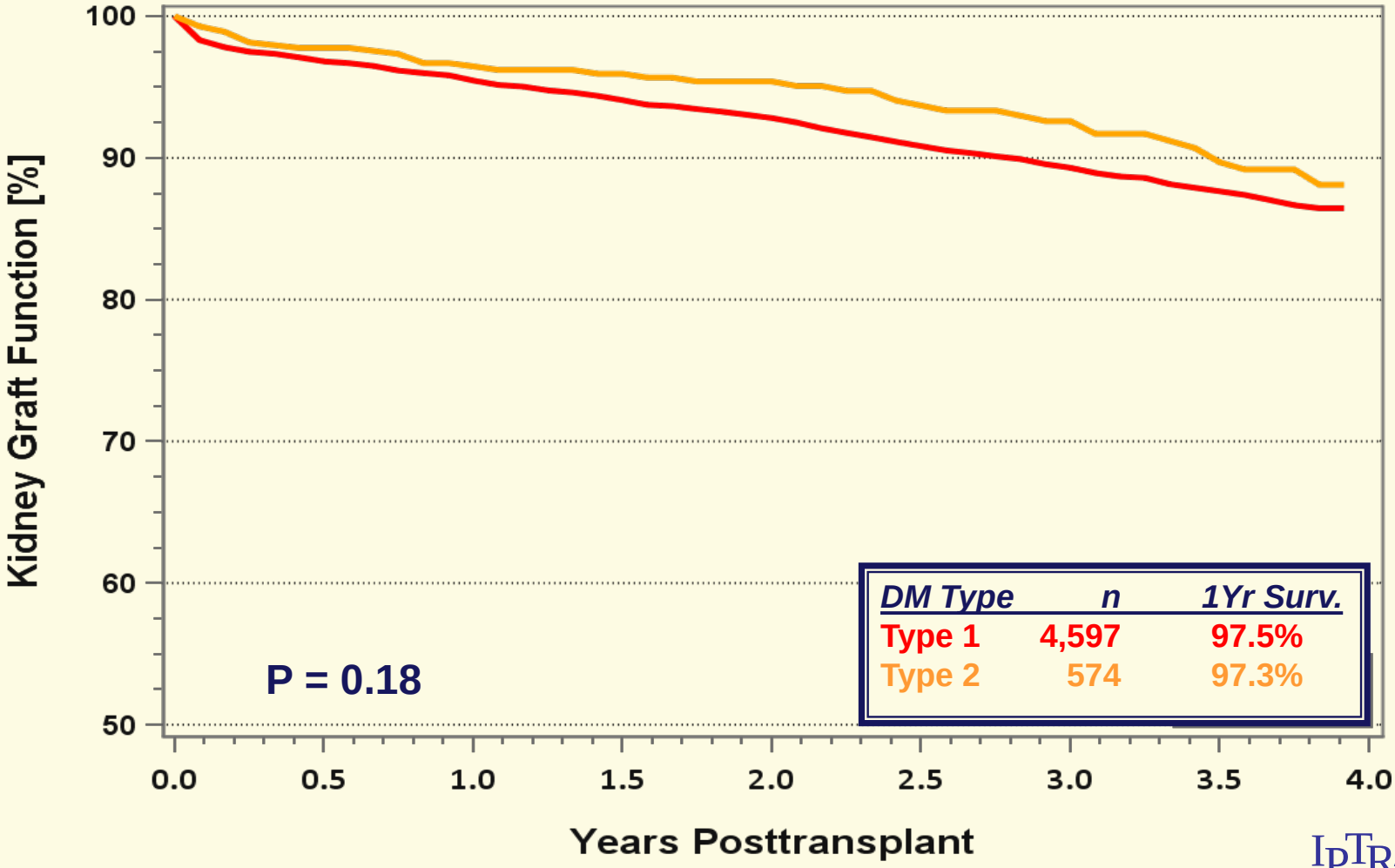
USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016




IPTR/UNOS

# SPK Kidney Graft Function by Diabetes Type

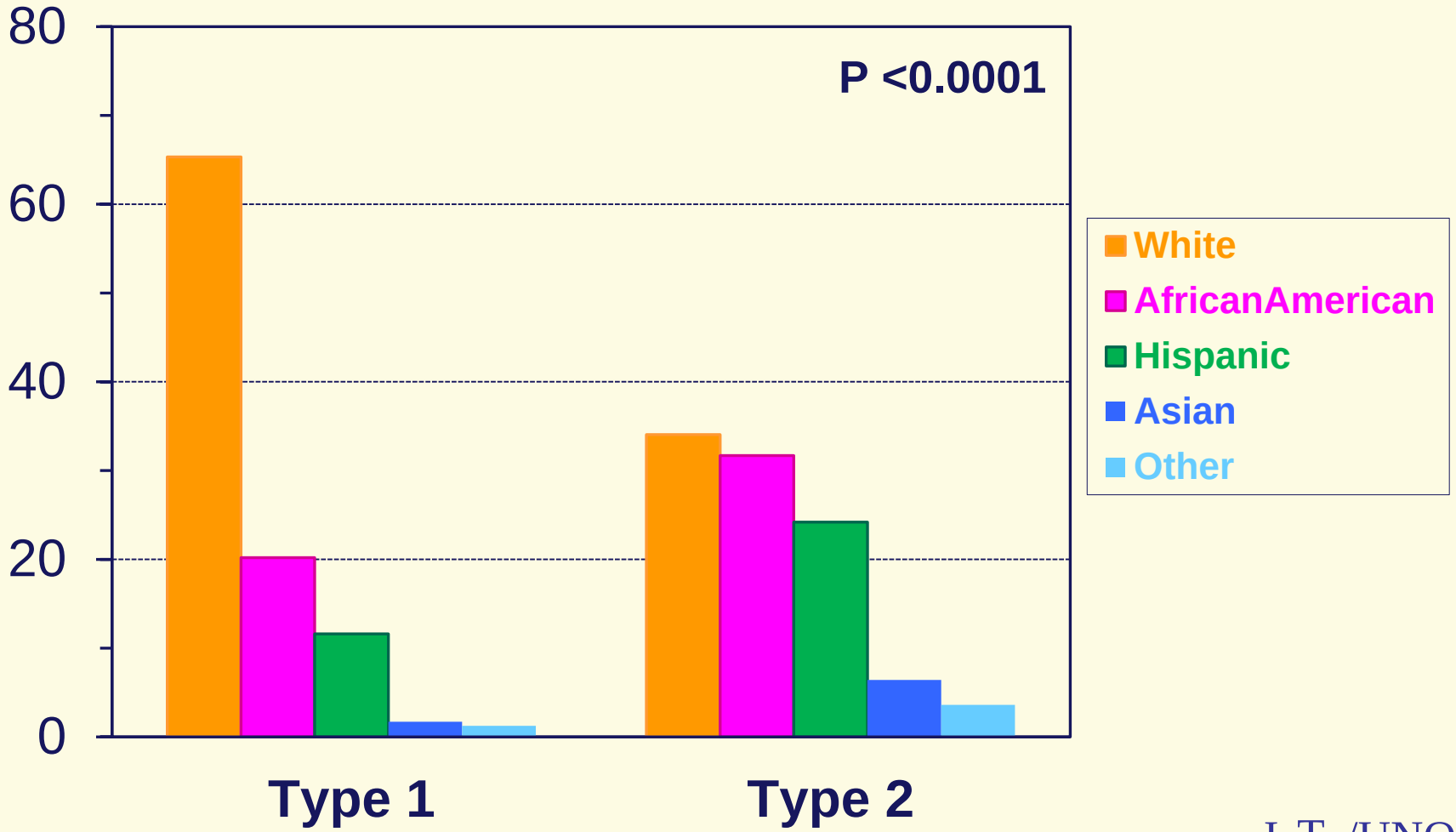
USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016




IPTR/UNOS

# Diabetes Type and Race

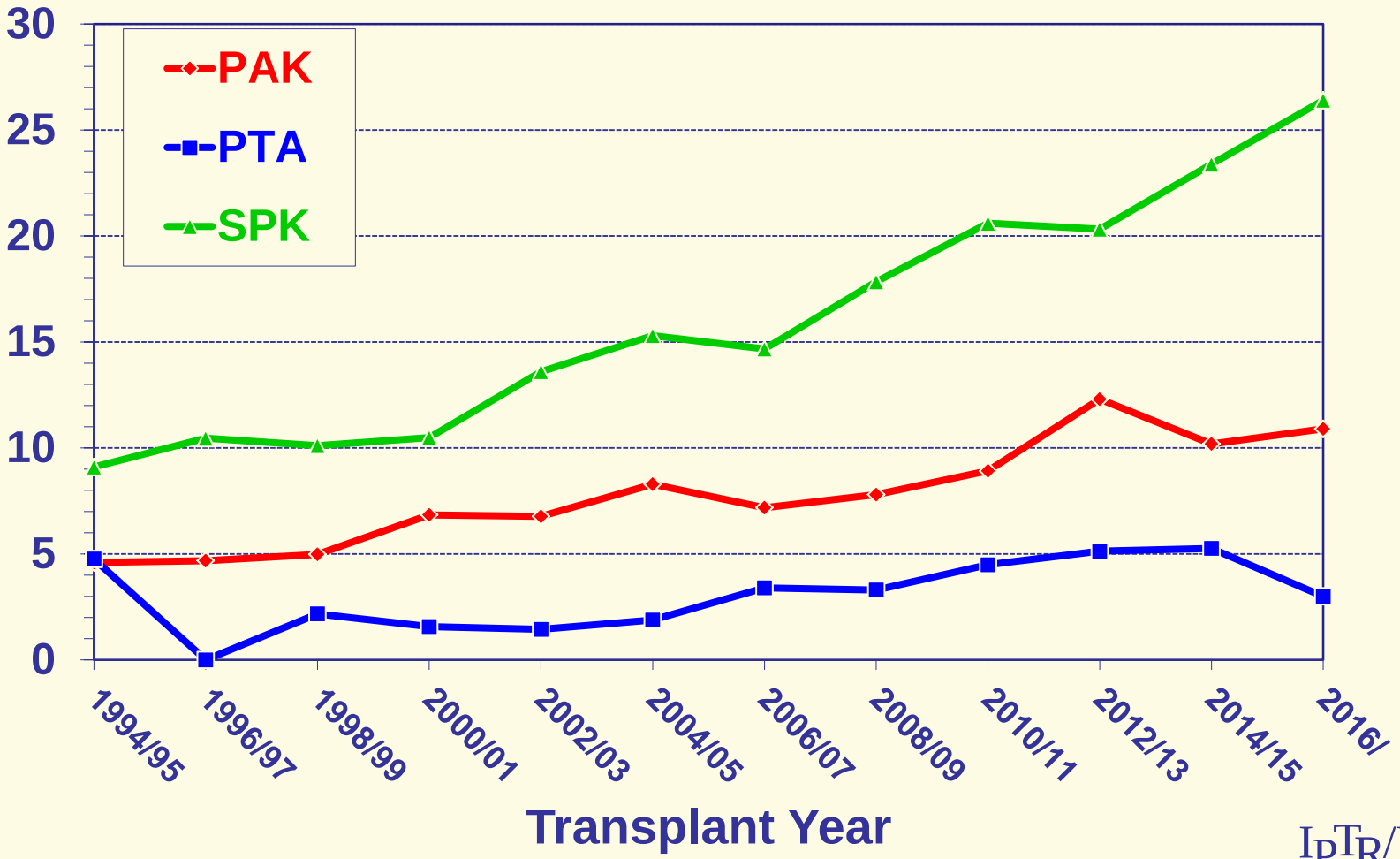
USA Primary DD Pancreas Transplants 1/1/2010 – 12/31/2016




IPTR/UNOS

# African American Recipients

USA Primary DD Pancreas Transplants 1/1/1994 – 12/31/2016



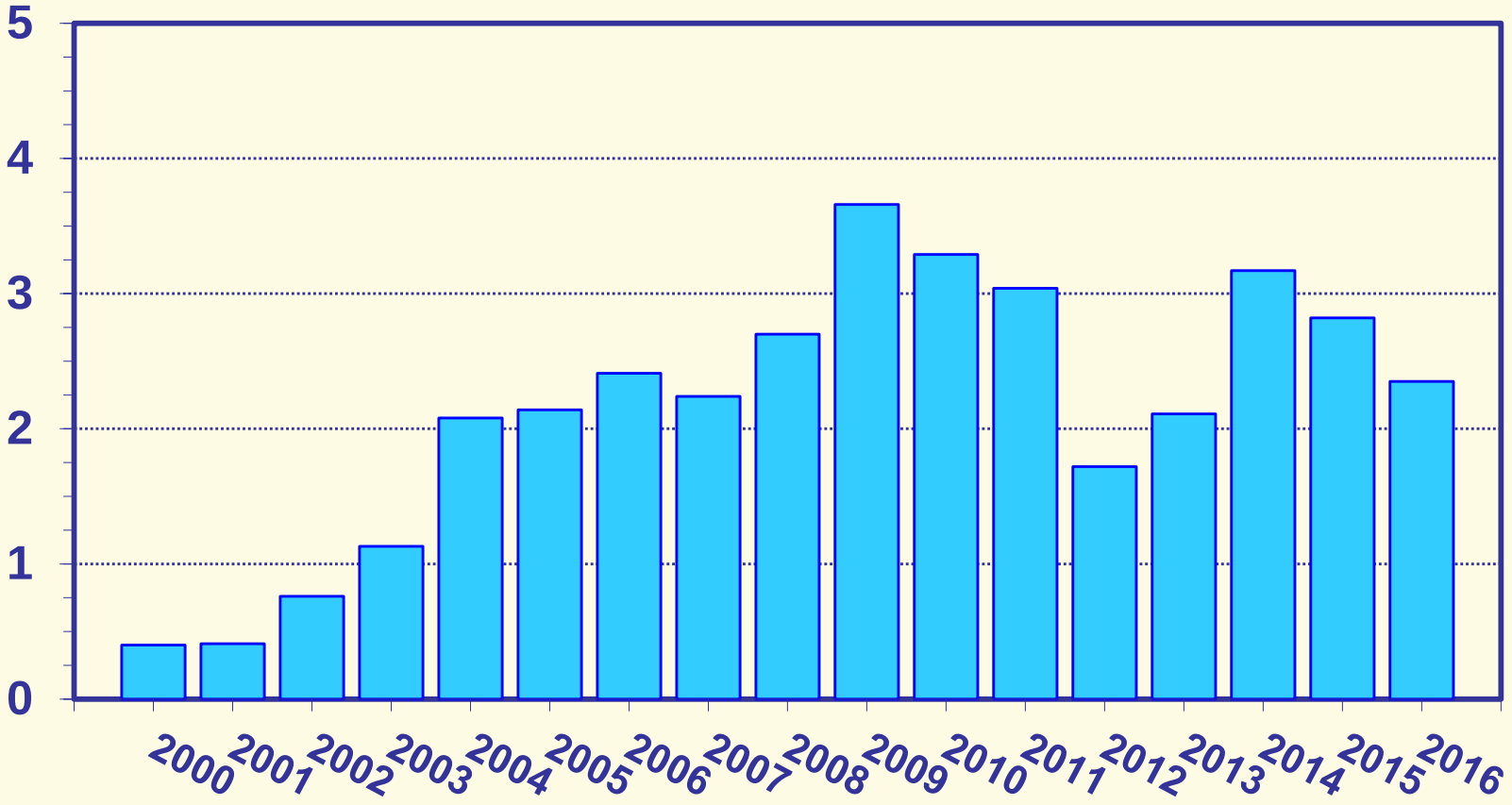

IPTR/UNOS

# The Type 2 Pancreas Transplant Recipient at UW

- Age <55 years
- BMI ≤ 33
- Administering insulin
- Uremic (SPK tx candidate)
- Difficulty with diabetes
  - HgbA1c >7.0

# Rate of DCD-Donors

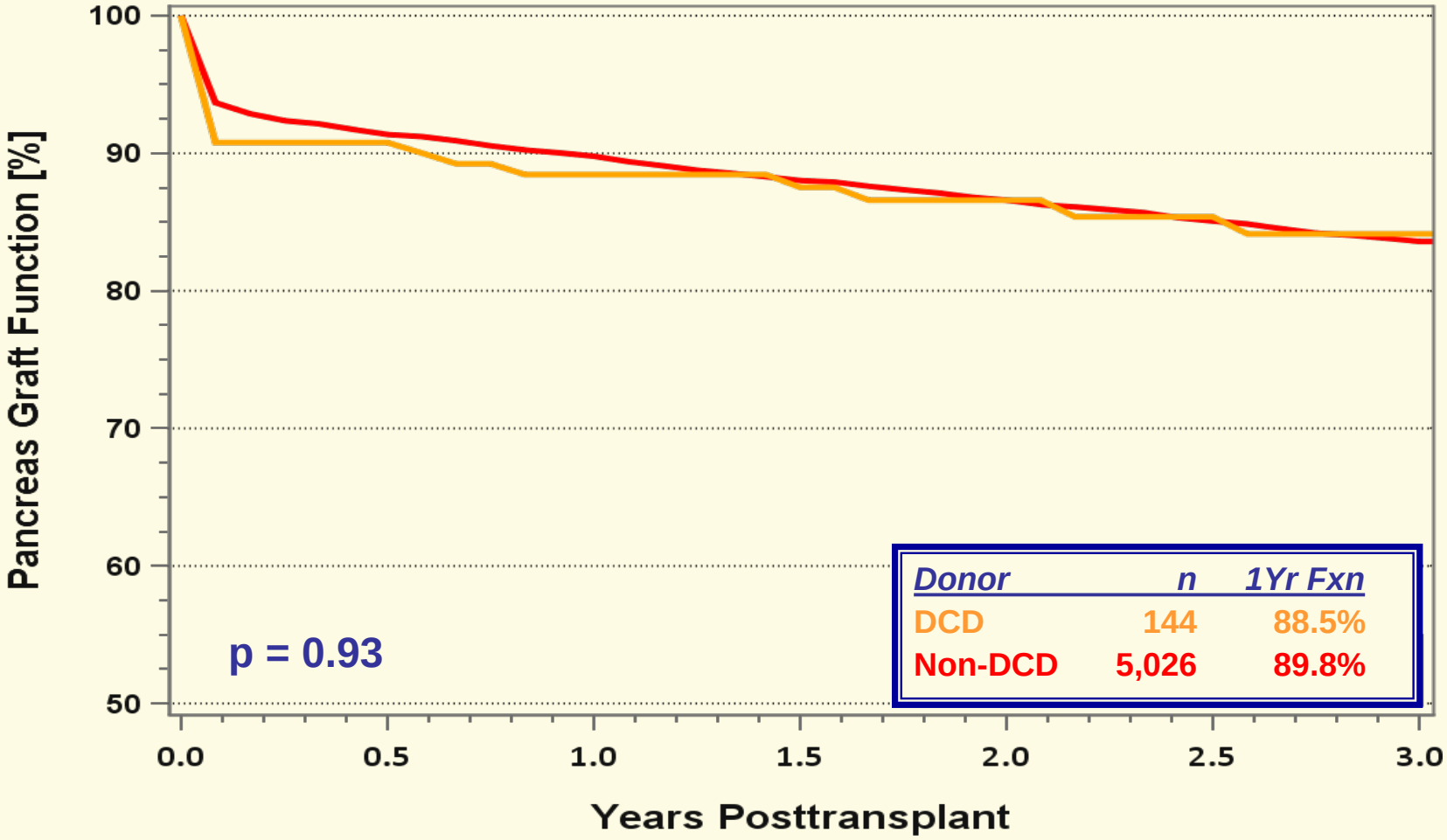
USA DD Pancreas Transplants 1/1/2000 – 12/31/2016




IPTR/UNOS

# SPK Pancreas Graft Fxn by Donor Type

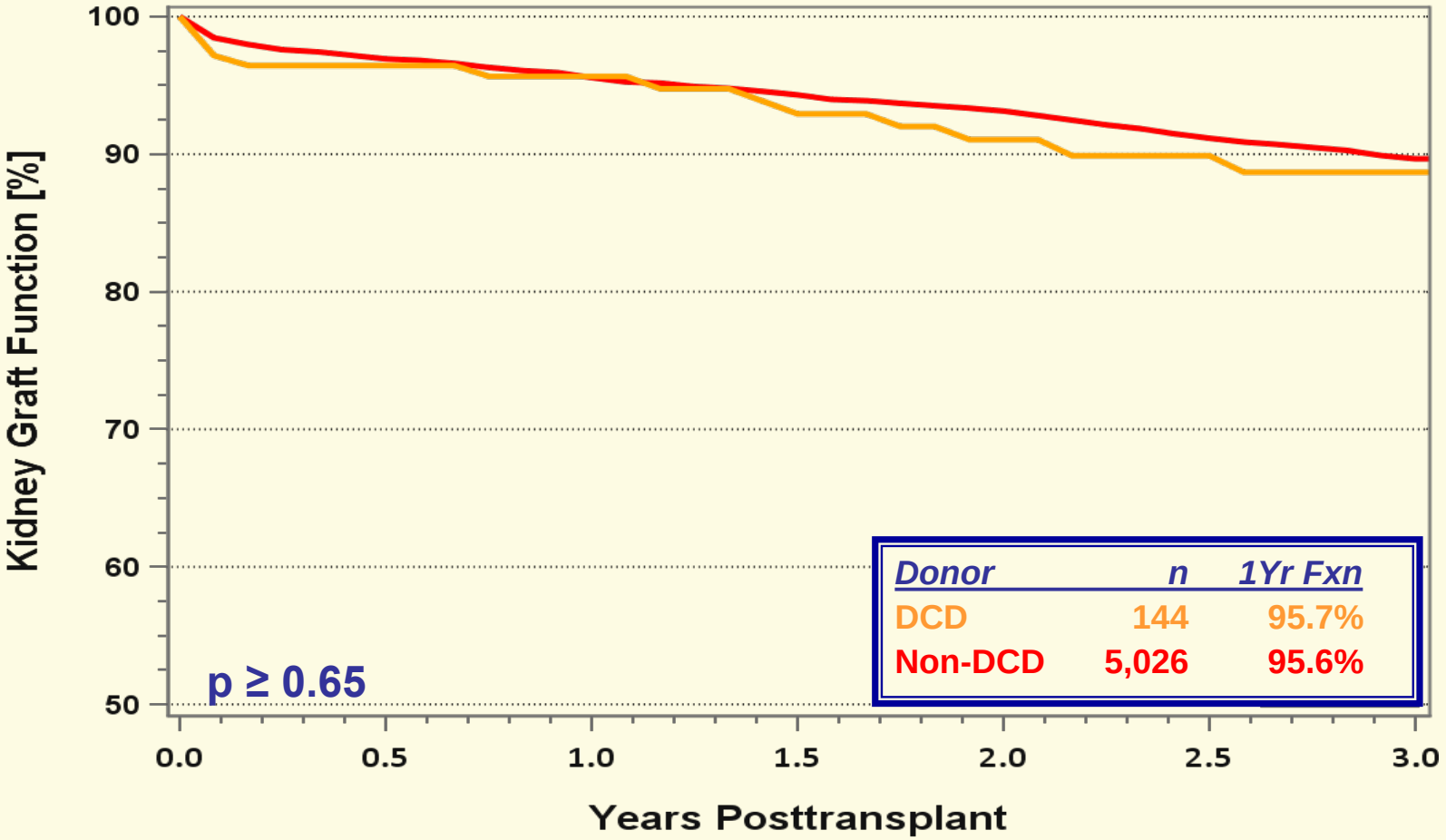
USA DD Primary Pancreas Transplants 1/1/2010 – 12/31/2016




IPTR/UNOS

# SPK Kidney Graft Fxn by Donor Type

USA DD Primary Pancreas Transplants 1/1/2010 – 12/31/2016




IPTR/UNOS

# Evolution of Pancreas Transplant Complexity Over 20 Years At the University of Wisconsin

# Typical Demographics for Pancreas Tx

- Donors:
  - DBD local donors
  - <50 years of age
  - BMI <30
- Recipients:
  - Primary Tx
  - Non-highly sensitized
  - Type 1 diabetic recipients
  - <55 years of age
  - BMI <30

Are pancreas txs more complex when D/R characteristics fall outside the norm?

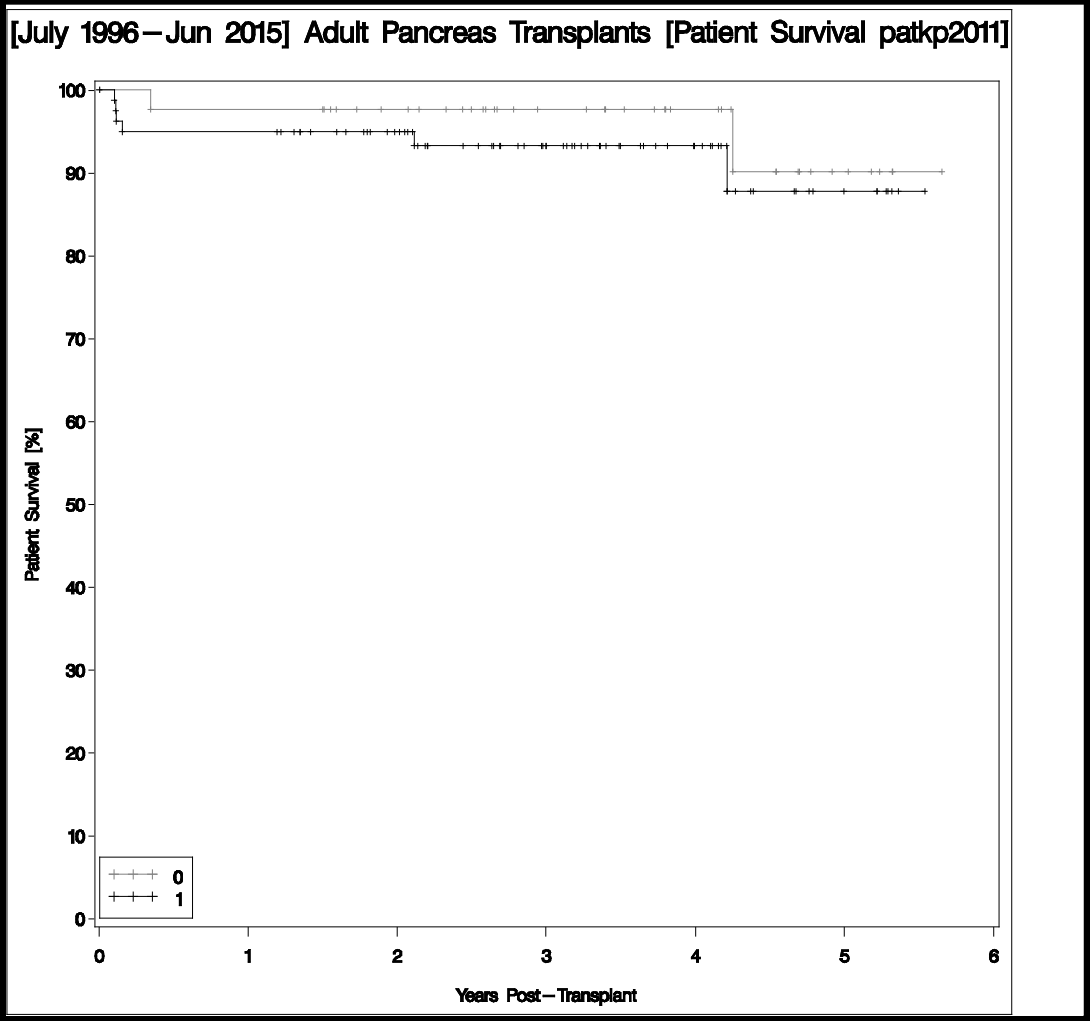
# Pancreas Tx Complexity

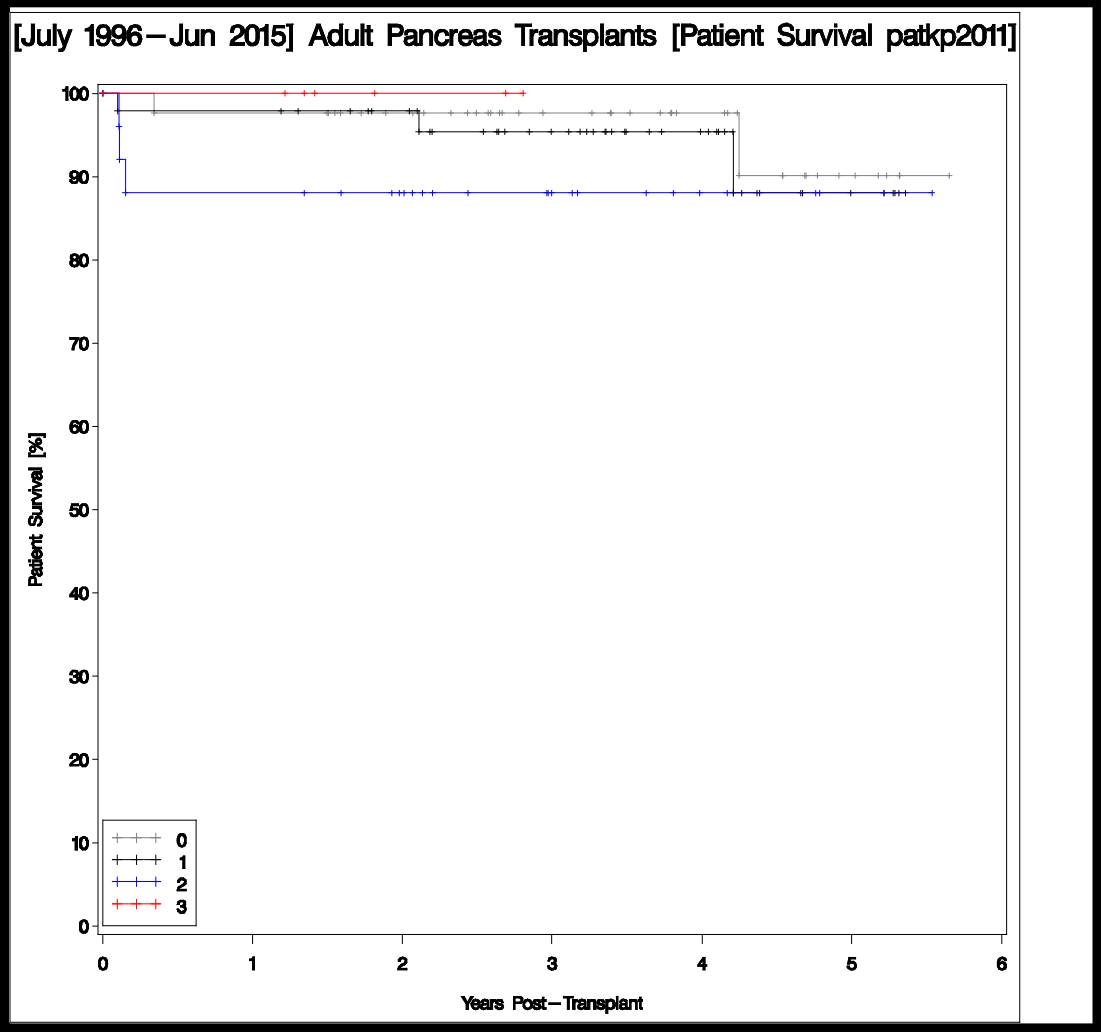
For each of 1060 pancreas txs conducted 1996-2015, we reviewed these specific D/R characteristics and tabulated for each recipient a point for each D/R characteristic that fell outside the norm.

# Pancreas Transplant Complexity According to Era: 1996 - 2015

| ERA | N | % 0 Pts | % ≥1 Pt | % ≥2 Pts |
|---|---|---|---|---|
| 1: 1996-2000 | 305 | 53% | 47% | 14% |
| 2: 2001-2005 | 333 | 48% | 52% | 26% |
| 3: 2006-2010 | 225 | 41% | 59% | 22% |
| 4: 2011-2015 | 197 | 25% | 75% | 37% |

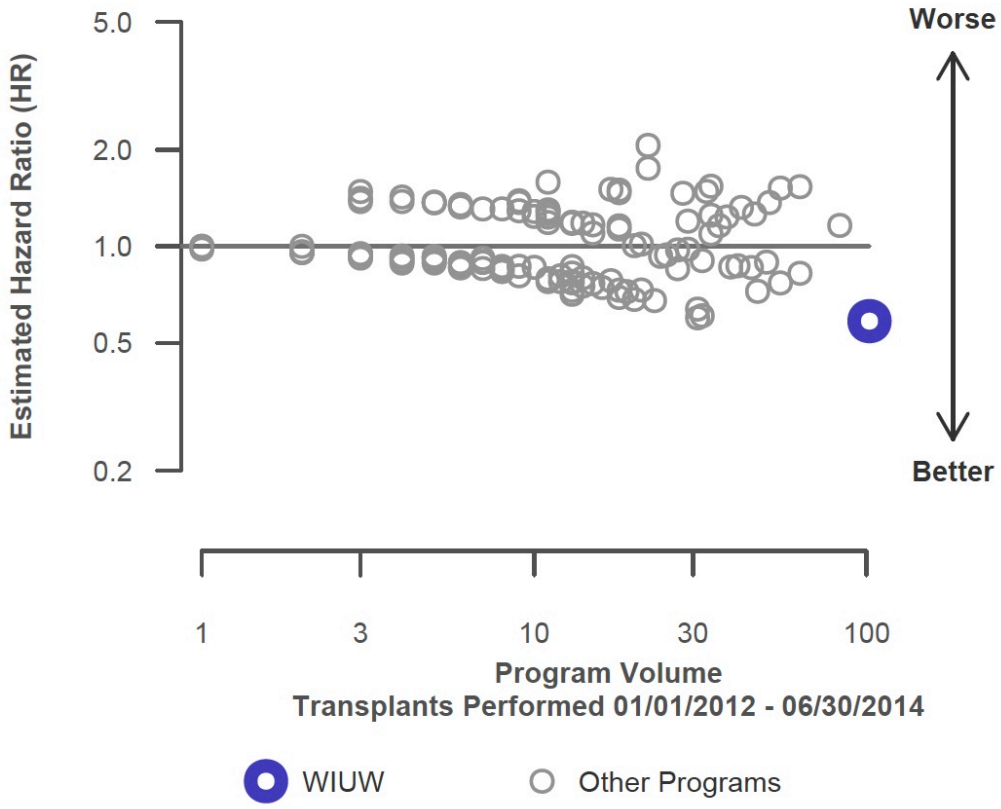
What's the difference between a conservative practice of pancreas transplantation for only 0 pt cases (n=49) vs more complex cases with ≥1 pt (n=148)? Is safety compromised?


[July 1996–Jun 2015] Adult Pancreas Transplants [Patient Survival patkp2011]
Patient Survival [%]
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
Years Post–Transplant
0
1


[July 1996–Jun 2015] Adult Pancreas Transplants [Patient Survival patkp2011]
Patient Survival [%]
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
Years Post–Transplant
0
1
2
3

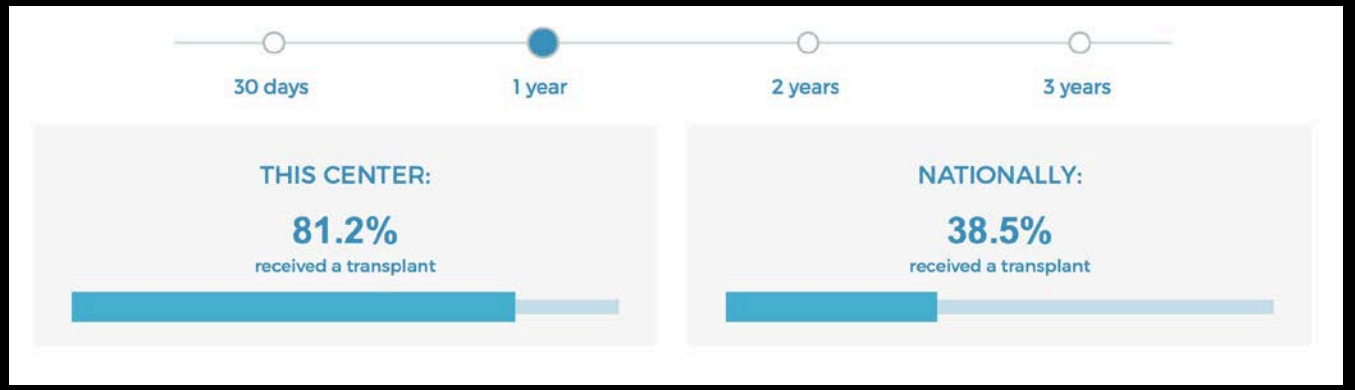
# 12/31/2017 SRTR 3-Year Patient Survival

**Figure C18ALL. Adult (18+) 3-year patient death HR program comparison (deceased donor grafts): (ALL)**

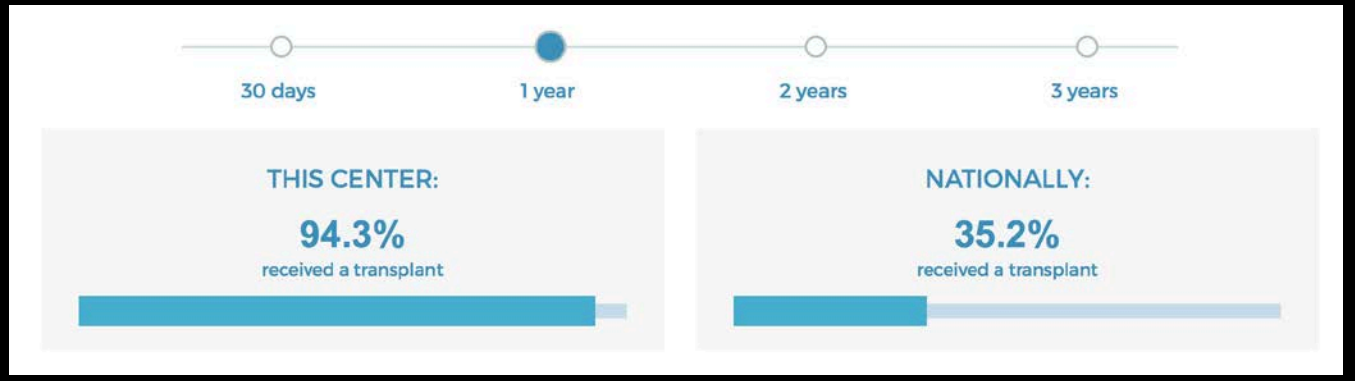


# Waiting Times
# % Txed within a year

SPK



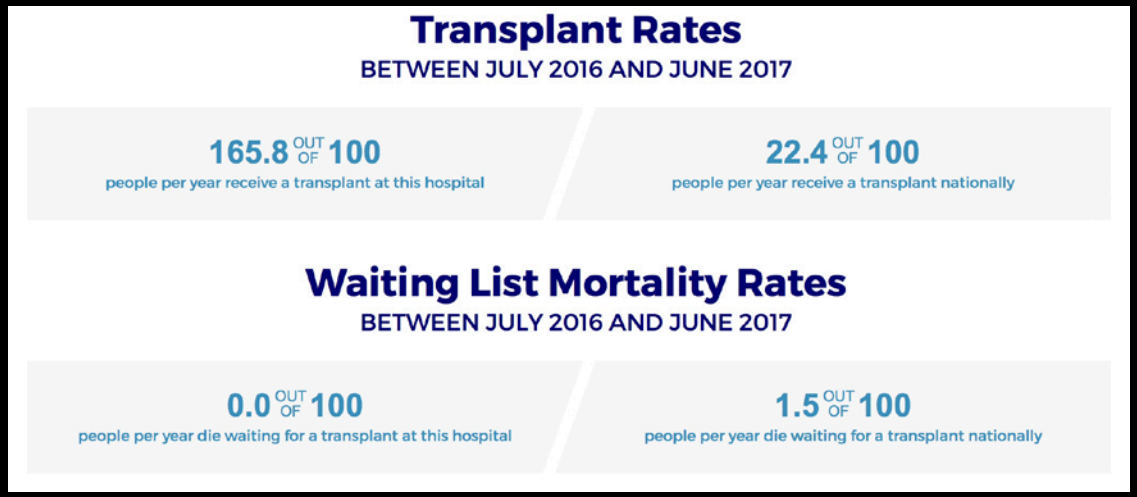

PA



# Transplant Rates
# WL Mortality Rates

SPK


PA



# Program Dashboard
# Pre Tx: SPK

| | Pre-Transplant Phase: SPK | | | | | | |
|---|---|---|---|---|---|---|---|
| ■ | Referrals: SPK (Quarterly) | 30 | n/a | n/a | 22 | 16 | Jul-Sep2019 |
| | Time from Referral to Evaluation: SPK | 61.0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| ■ | New Evaluations: SPK | 20 | n/a | n/a | 16 | 10 | Jul-Sep2019 |
| | Time from Evaluation to Waitlist: SPK* | 46.0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| ▼ | Patients Added to Waitlist: SPK | 9 | n/a | n/a | 10 | 7 | Jul-Sep2019 |
| | Waitlist Volume (Active): SPK | 12 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Waitlist Volume (Inactive): SPK | 8 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | % of Inactive Patients on Waitlist: SPK | 40% | 8 | 20 | n/a | n/a | Jul-Sep2019 |
| ▼ | Mortality on Waiting List (CYTD): SPK* | 1 | n/a | n/a | 0 | 1 | Jul-Sep2019 |
| ■ | SRTR: Waitlist Mortality Rate: SPK | 0.00 | n/a | n/a | 5.20 | n/a | Jul-19 |

# Program Dashboard
# Peri-Tx: SPK

| | Peri-Transplant Phase: SPK | | | | | | |
|---|---|---|---|---|---|---|---|
| | Time from Waitlist to Transplant Date: SPK | 56.0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| ■ | Transplant Volume: SPK (Quarterly) | 11 | n/a | n/a | 10 | 6 | Jul-Sep2019 |
| ▼ | Transplant Volume: SPK (CYTD) | 30 | n/a | n/a | 39 | 24 | Jul-Sep2019 |
| ■ | Transplant Actual vs Expected Rate: SPK* | 1.4 | 11.0 | 8.0 | 1.0 | 0.8 | Jul-Sep2019 |
| | Average LOS- Per UWHC Definition: SPK* | 10.6 | n/a | n/a | n/a | n/a | Jan-Mar2019 |
| | Transplant to Discharge LOS in Days: SPK | 8 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Cold Ischemic Time: SPK* | 13.5 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| ■ | ABO Verification Compliance: SPK* | 100.0% | n/a | n/a | 100.0% | 90.0% | Jul-Sep2019 |

UW Health

# Program Dashboard
# Post Tx: SPK

| | Post-Transplant Phase: SPK | | | | | | |
|---|---|---|---|---|---|---|---|
| ■ | 24 Hour Waitlist Removal - Transplanted Patients -SPK | 100 | n/a | n/a | 100 | 99 | Jul-Sep2019 |
| | 30 Day All-Cause Readmission Rate: SPK (Pancreas/Kidney)* | 40.0% | 4.0 | 10.0 | n/a | n/a | Jan-Mar2019 |
| | Patient Deaths (CYTD): SPK | 0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| ● | SRTR: Kidney Graft Survival Rate - 1 Year: SPK* | 95.8% | n/a | n/a | 96.0% | 95.9% | Jul-19 |
| ■ | SRTR: Kidney Graft Survival Rate - 3 Year: SPK | 98.5% | n/a | n/a | 91.8% | n/a | Jul-19 |
| ■ | SRTR: Patient Survival Rate - 1 Year: SPK* | 97.7% | n/a | n/a | 97.2% | n/a | Jul-19 |
| ■ | SRTR: Patient Survival Rate - 3 Year: SPK | 98.4% | n/a | n/a | 94.6% | n/a | Jul-19 |
| ■ | Catheter-Associated UTI Rate (93650-B46) | 0.0 | 0.0 | 120.0 | 0.0 | 2.4 | Jul '19 |
| | Central Line Associated Bloodstream Infection (93650-B46) | 4.0 | 1.0 | 250.0 | n/a | n/a | Jul '19 |
| ■ | C. difficile (93650-B46) | 0.00 | 0.00 | 891.00 | 0.00 | n/a | Jul '19 |

UW Health

# Program Dashboard
# Pre-Tx: Pancreas

| | Pre-Transplant Phase: Pancreas | | | | | | |
|---|---|---|---|---|---|---|---|
| | Referrals: Pancreas (Quarterly) | 18 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Time from Referral to Evaluation: Pancreas* | 37.0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | New Evaluations: Pancreas | 7 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Time from Evaluation to Waitlist: Pancreas* | 33.0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Patients Added to Waitlist: Pancreas | 8 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Waitlist Volume (Active): Pancreas | 9 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Waitlist Volume (Inactive): Pancreas | 8 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | % of Inactive Patients on Waitlist: Pancreas | 47% | 8 | 17 | n/a | n/a | Jul-Sep2019 |
| | Mortality on Waiting List (CYTD): Pancreas* | 0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | SRTR: Waitlist Mortality Rate: Pancreas | 0.00 | n/a | n/a | 1.90 | 4.90 | Jul-19 |

# Program Dashboard
# Peri-Tx: Pancreas

| | Peri-Transplant Phase: Pancreas | | | | | | |
|---|---|---|---|---|---|---|---|
| | Time from Waitlist to Transplant Date: Pancreas | 108.0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| 🔴 | Transplant Volume: Pancreas (Quarterly) | 3 | n/a | n/a | 5 | 4 | Jul-Sep2019 |
| 🔴 | Transplant Volume: Pancreas (CYTD) | 10 | n/a | n/a | 21 | 16 | Jul-Sep2019 |
| 🔴 | Transplant Actual vs Expected: Pancreas* | 0.8 | 3.0 | 5.0 | 1.0 | 0.8 | Jul-Sep2019 |
| | Average LOS- Per UWHC Definition: Pancreas* | 6.3 | n/a | n/a | n/a | n/a | Jan-Mar2019 |
| 🟩 | Transplant to Discharge LOS in Days: Pancreas | 8 | n/a | n/a | 8 | 12 | Jul-Sep2019 |
| | Cold Ischemic Time: Pancreas* | 15.2 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| 🟩 | ABO Verification Compliance: Pancreas* | 100% | 4 | 4 | 100% | 90% | Jul-Sep2019 |

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# Program Dashboard
# Post Tx Pancreas

| | Post-Transplant Phase: Pancreas | | | | | | |
|---|---|---|---|---|---|---|---|
| ■ | 24 Hour Waitlist Removal - Transplanted Patients - Pancreas | 100 | n/a | n/a | 100 | 99 | Jul-Sep2019 |
| | 30 Day All-Cause Readmission Rate: Pancreas* | 33.3% | 1.0 | 3.0 | n/a | n/a | Jan-Mar2019 |
| | Patient Deaths (Quarterly): Pancreas | 0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | Patient Deaths (CYTD): Pancreas | 0 | n/a | n/a | n/a | n/a | Jul-Sep2019 |
| | SRTR: Graft Survival Rate - 1 Year: Pancreas* | n/a | n/a | n/a | n/a | n/a | Jul-19 |
| | SRTR: Graft Survival Rate - 3 Year: Pancreas | n/a | n/a | n/a | n/a | n/a | Jul-19 |
| ● | SRTR: Patient Survival Rate - 1 Year: Pancreas: PTA* | 96.7% | n/a | n/a | 98.4% | n/a | Jul-19 |
| ● | SRTR: Patient Survival Rate - 1 Year: Pancreas: PAK* | 66.7% | n/a | n/a | 92.9% | n/a | Jul-19 |
| ■ | SRTR: Patient Survival Rate - 3 Year: Pancreas: PTA | 100.0% | n/a | n/a | 97.0% | n/a | Jul-19 |
| ■ | SRTR: Patient Survival Rate - 3 Year: Pancreas: PAK | 100.0% | n/a | n/a | 99.0% | 91.7% | Jul-19 |
| ■ | Catheter-Associated UTI Rate (93650-B46) | 0.0 | 0.0 | 120.0 | 0.0 | 2.4 | Jul '19 |
| | Central Line Associated Bloodstream Infection (93650-B46) | 4.0 | 1.0 | 250.0 | n/a | n/a | Jul '19 |
| ■ | C. difficile (93650-B46) | 0.00 | 0.00 | 891.00 | 0.00 | n/a | Jul '19 |

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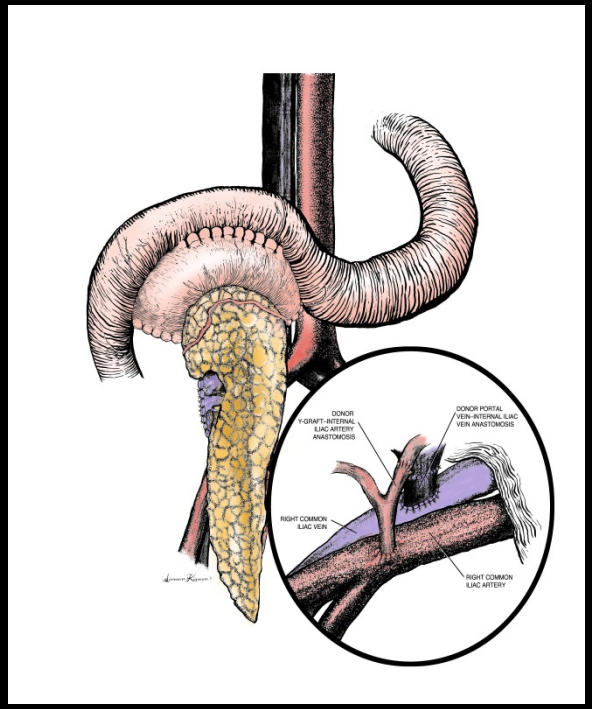
# Conclusion

- There is no pancreas shortage.
- Expanding the donor and/or recipient criteria for for a pancreas transplant can be done without compromise of patient survival rates.
- Monitoring outcomes: QAPI and dashboards
- It results in more patients being able to receive a pancreas tx.

THERE IS NOTHING
NOBLE
IN BEING SUPERIOR TO
YOUR FELLOW MEN. TRUE
NOBILITY
LIES IN BEING
SUPERIOR
TO YOUR FORMER SELF

# The Noble Pancreas Transplant




A better life . . .

# UW Pancreas Transplant Team

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