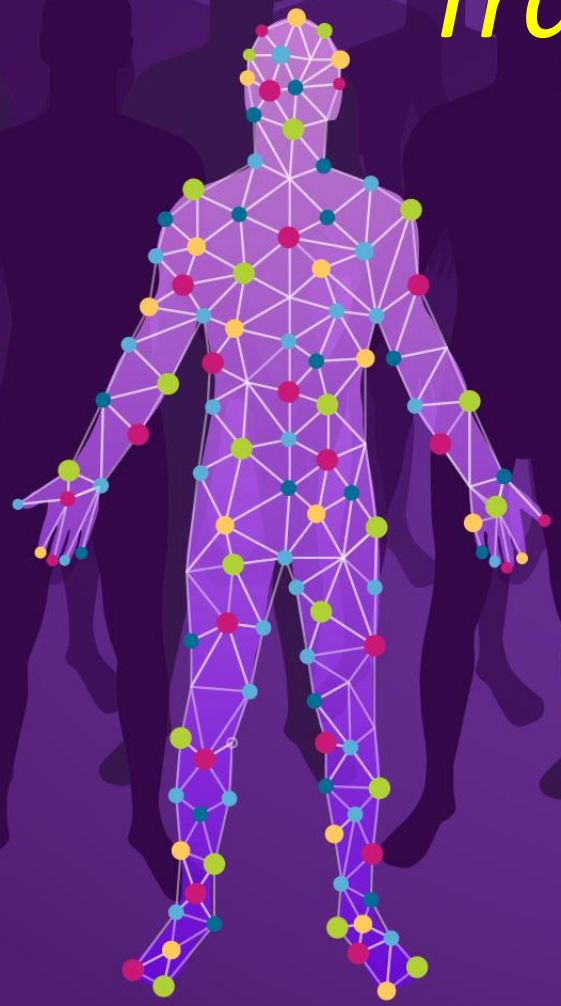
AST | AMERICAN SOCIETY OF TRANSPLANTATION



Transplantation of Patients with Kidney Failure and Diabetes

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Ray D. Owen Professor and Chair

Division of Transplantation

University of Wisconsin

CEOT CUTTING EDGE of **TRANSPLANTATION**

TRANSPLANT SUMMIT 2019

NO SIZE FITS ALL: *Uncovering the Potential of Personalized Transplantation*

FEBRUARY 21–23, 2019 • ARIZONA BILTMORE • PHOENIX, AZ

Disclosures

No relevant personal financial relationships
Medeor: Unpaid advisory board member
eGenesis: Unpaid advisory board member

Learning Objectives

1. Program building for pancreas transplantation

2. Outcomes of pancreas kidney transplantation

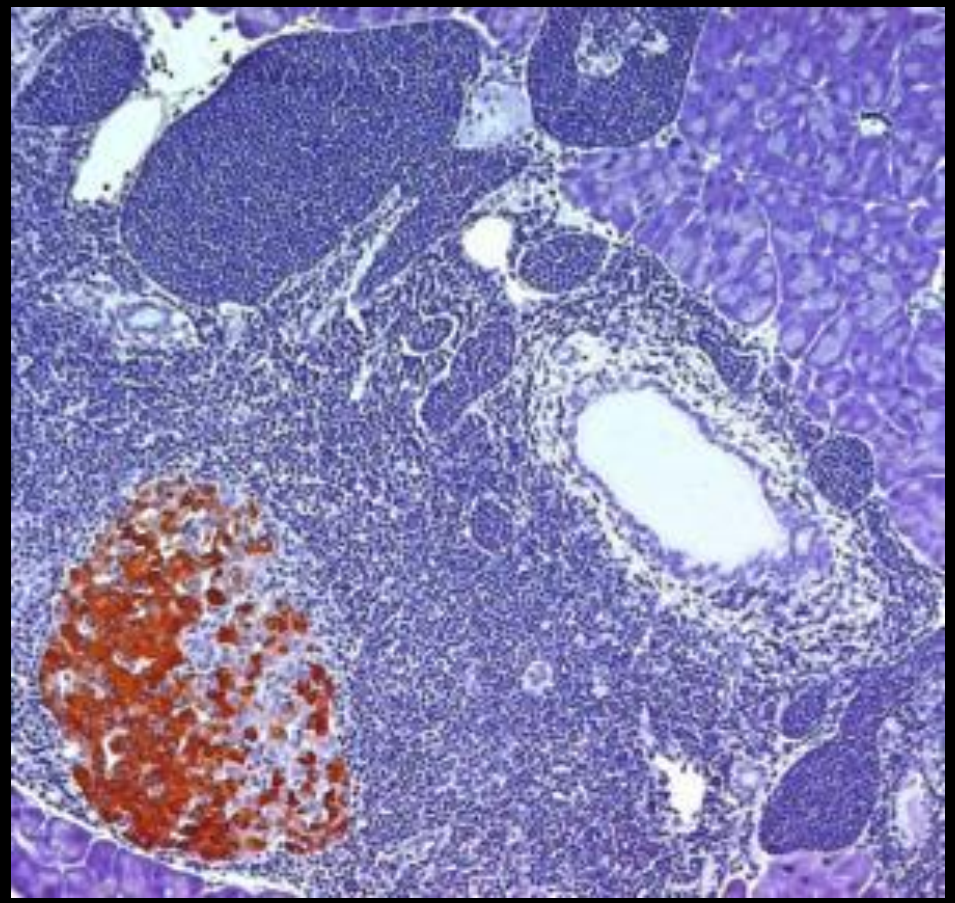
3. Donor and recipient selection strategies for pancreas transpantation

The Enemy

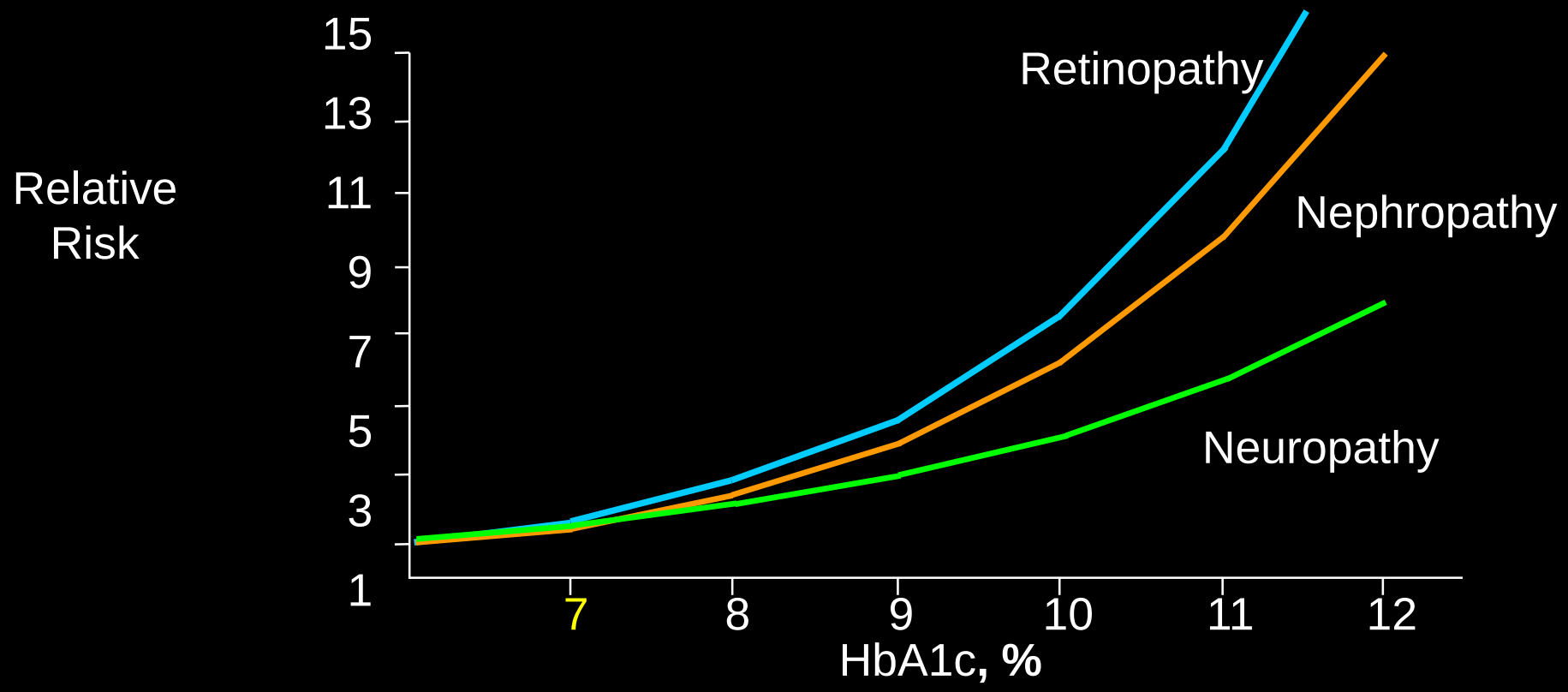
- Type I diabetes results from the autoimmune destruction of insulin producing beta cells in the pancreas

- Long-term therapy with insulin,

  while life saving, may result in:
  - kidney disease
  - blindness
  - cardiovascular disease
  - peripheral neuropathy

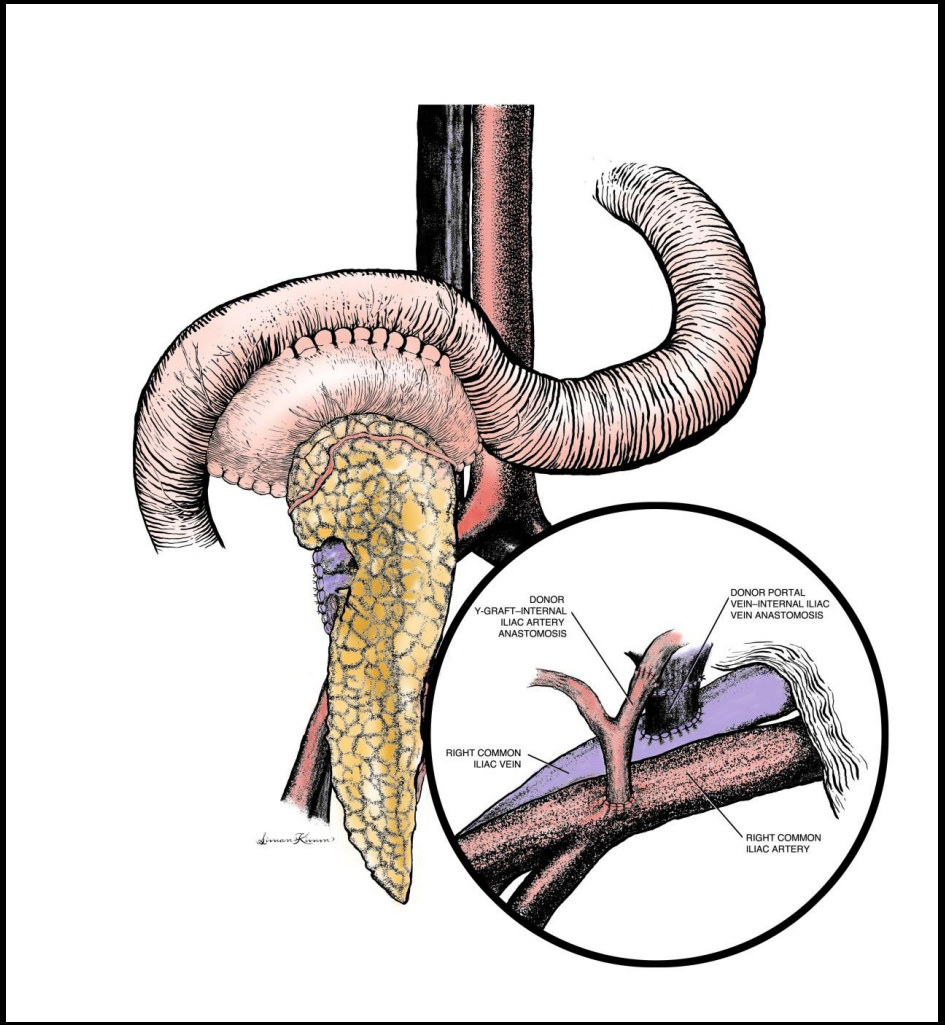


Relationship of HbA_{1c} to Risk of Microvascular Complications

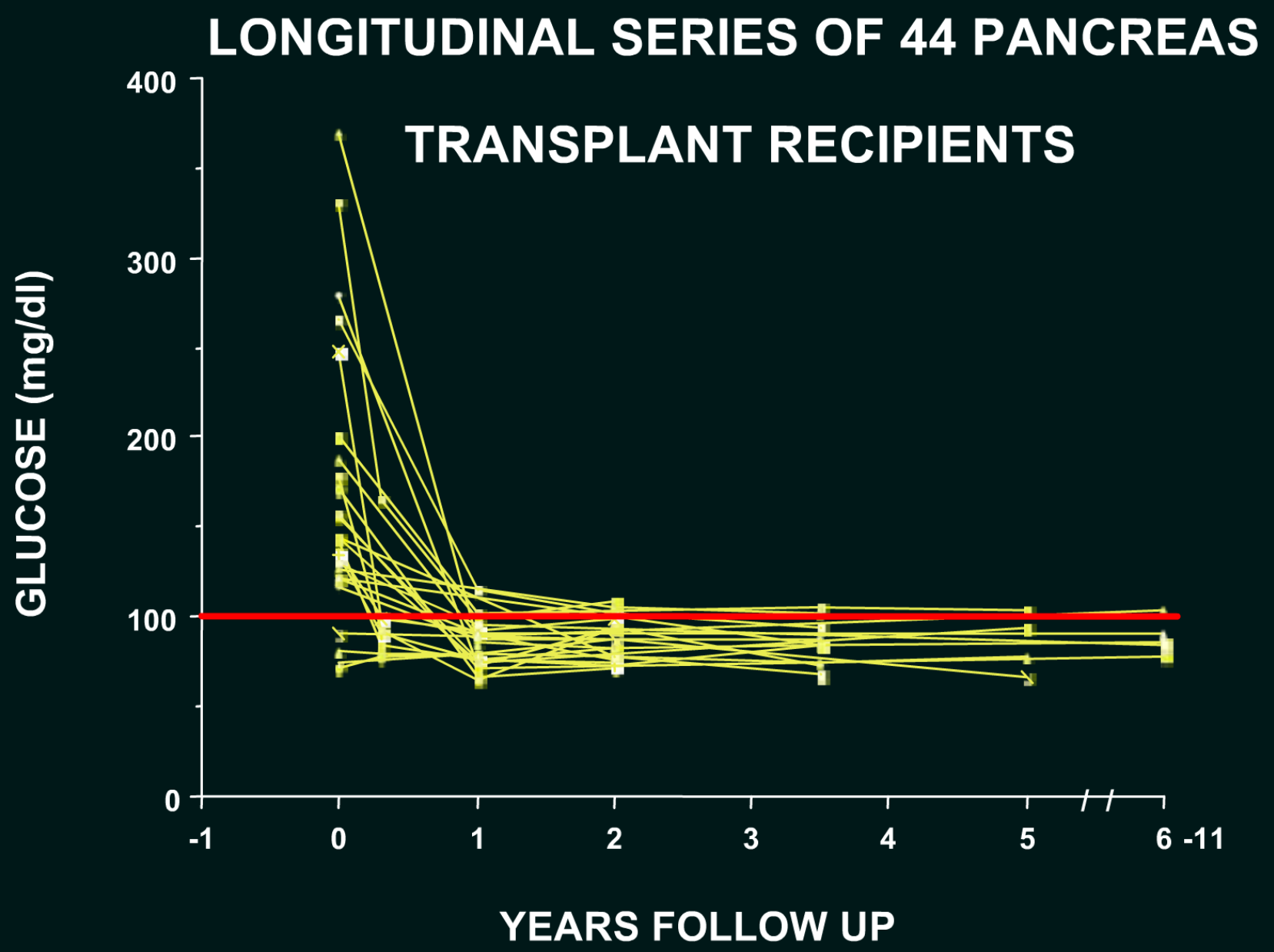


DCCT Research Group. *N Engl J Med.* 1993;329:977-986.

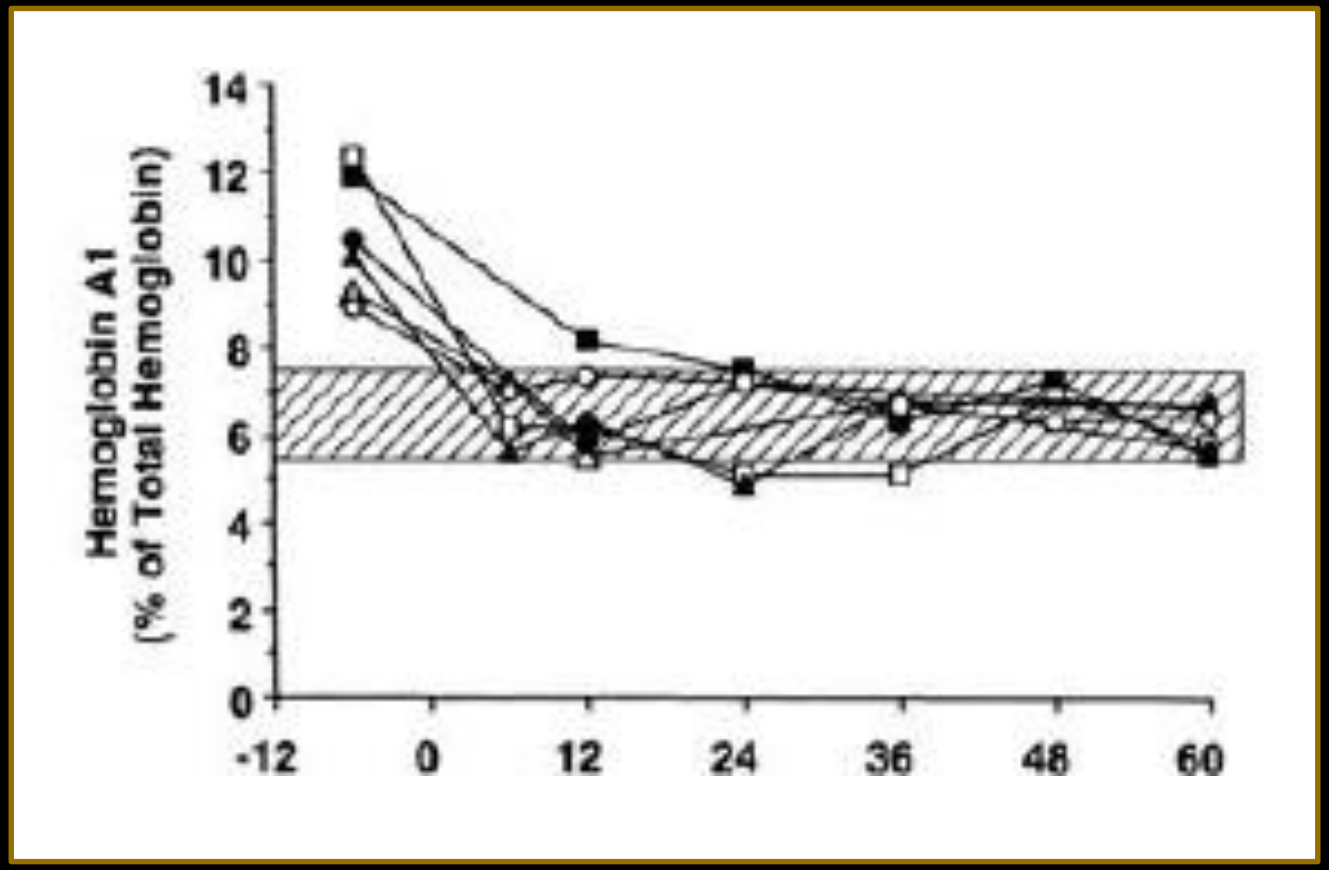
The Hero
The Pancreas Transplant



FASTING PLASMA GLUCOSE

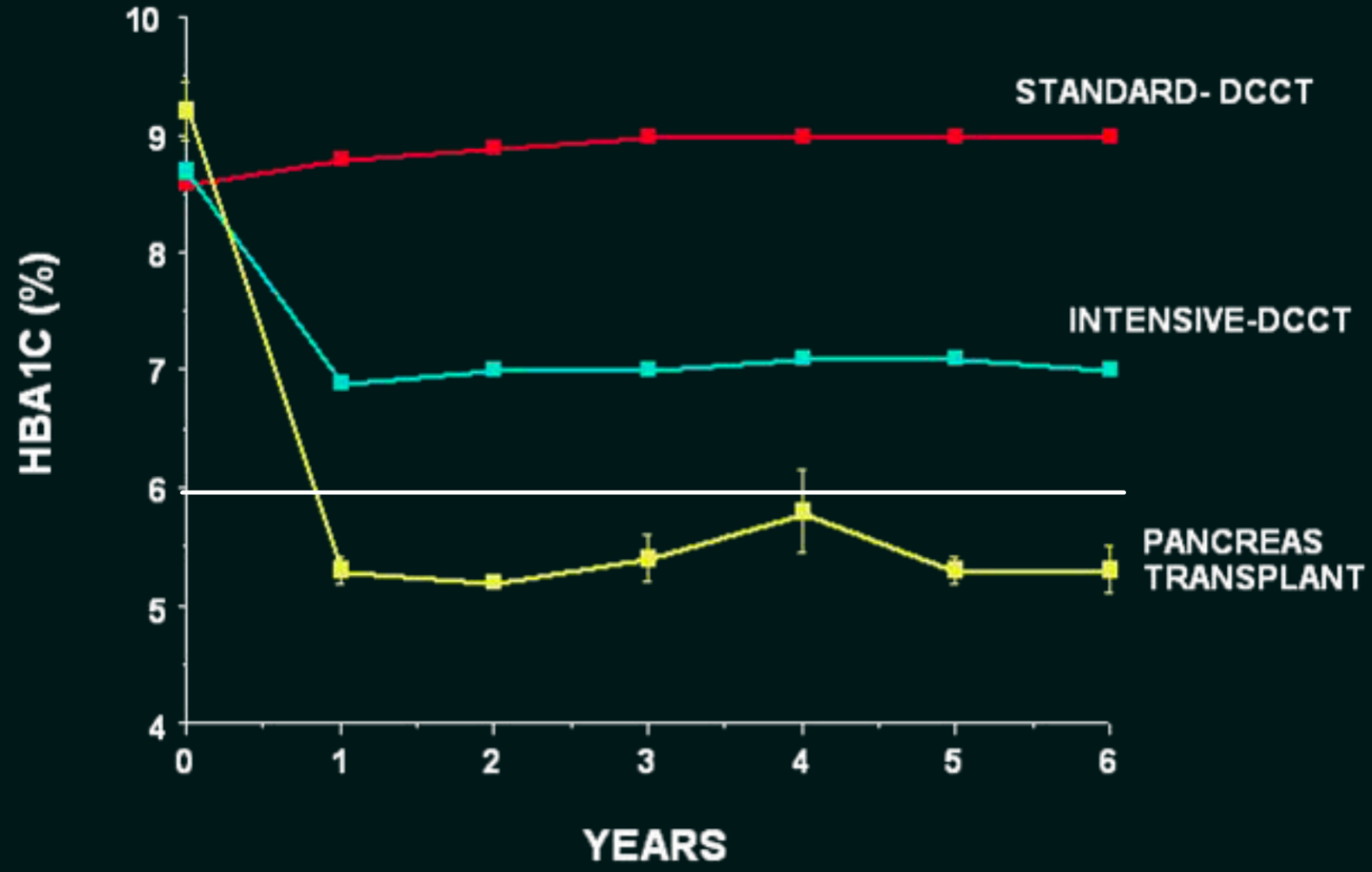


HgbA1C and pancreas transplants
Long-term results



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

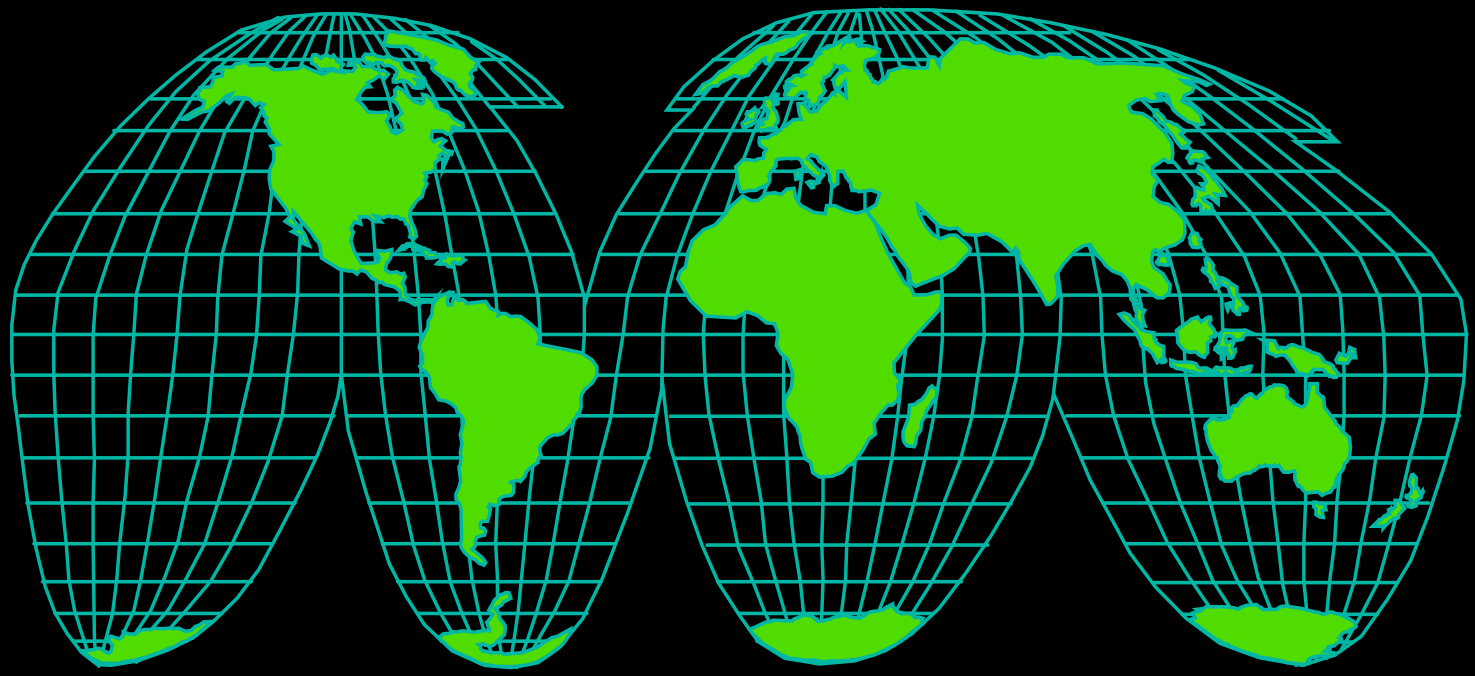


Indications for Pancreas Tx

Diabetes Mellitus (T1 or T2) with:

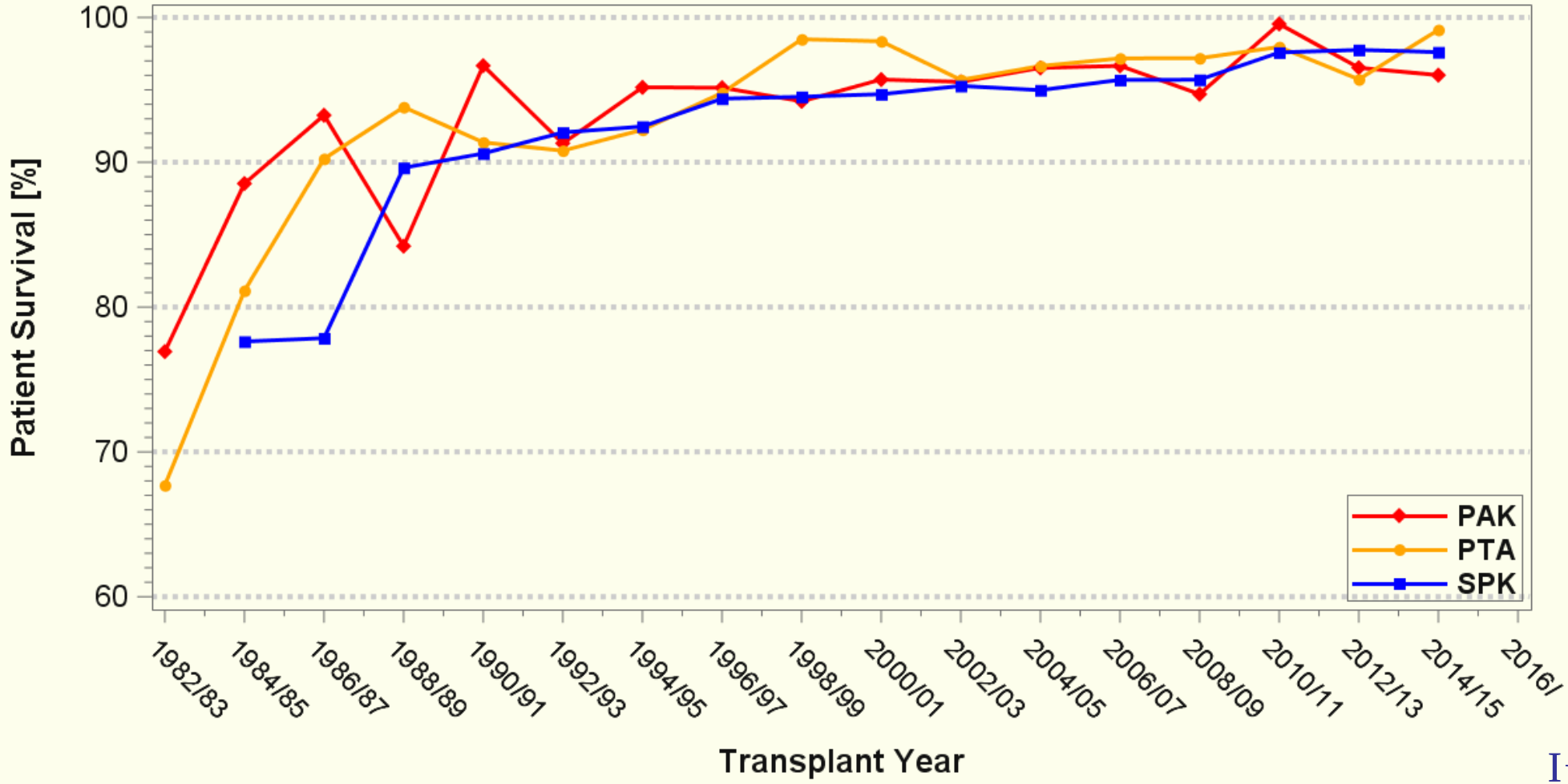
- Renal failure requiring simultaneous kidney transplant (SPK). 75-80%
- Functioning kidney transplant already on immunosuppression (PAK). 5-10%
- Brittle diabetes with hypoglycemic unawareness (PTA). 10-15%

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



1-Year Unadjusted Patient Survival

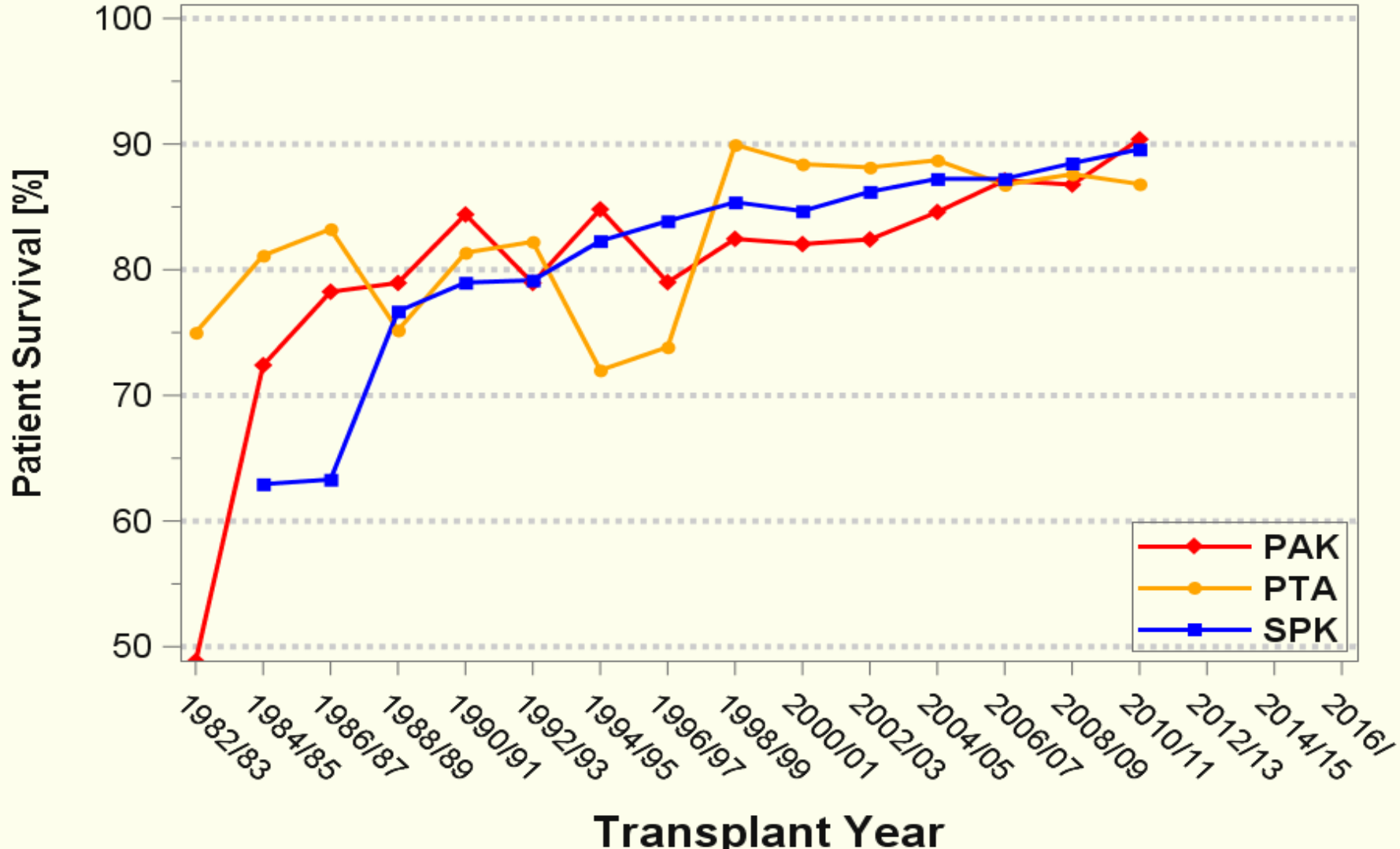
USA Primary DD Pancreas Transplants, 1/1/1982 – 12/31/2016



IPTR/UNOS

5-Year Unadjusted Patient Survival

USA Primary DD Pancreas Transplants, 1 /1/1982 – 12/31/2016



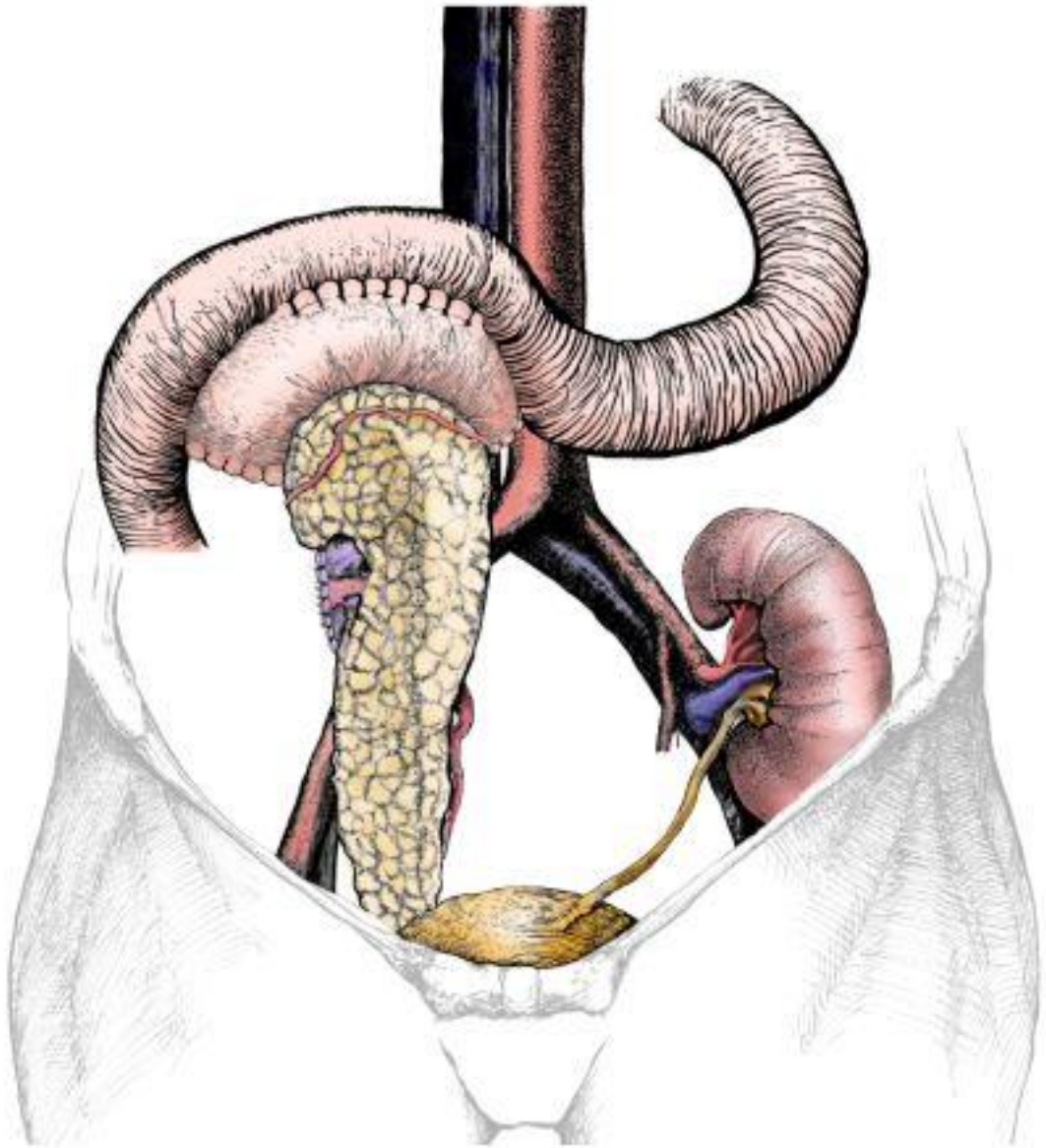
IPTR/UNOS

Comparative Patient Survivals

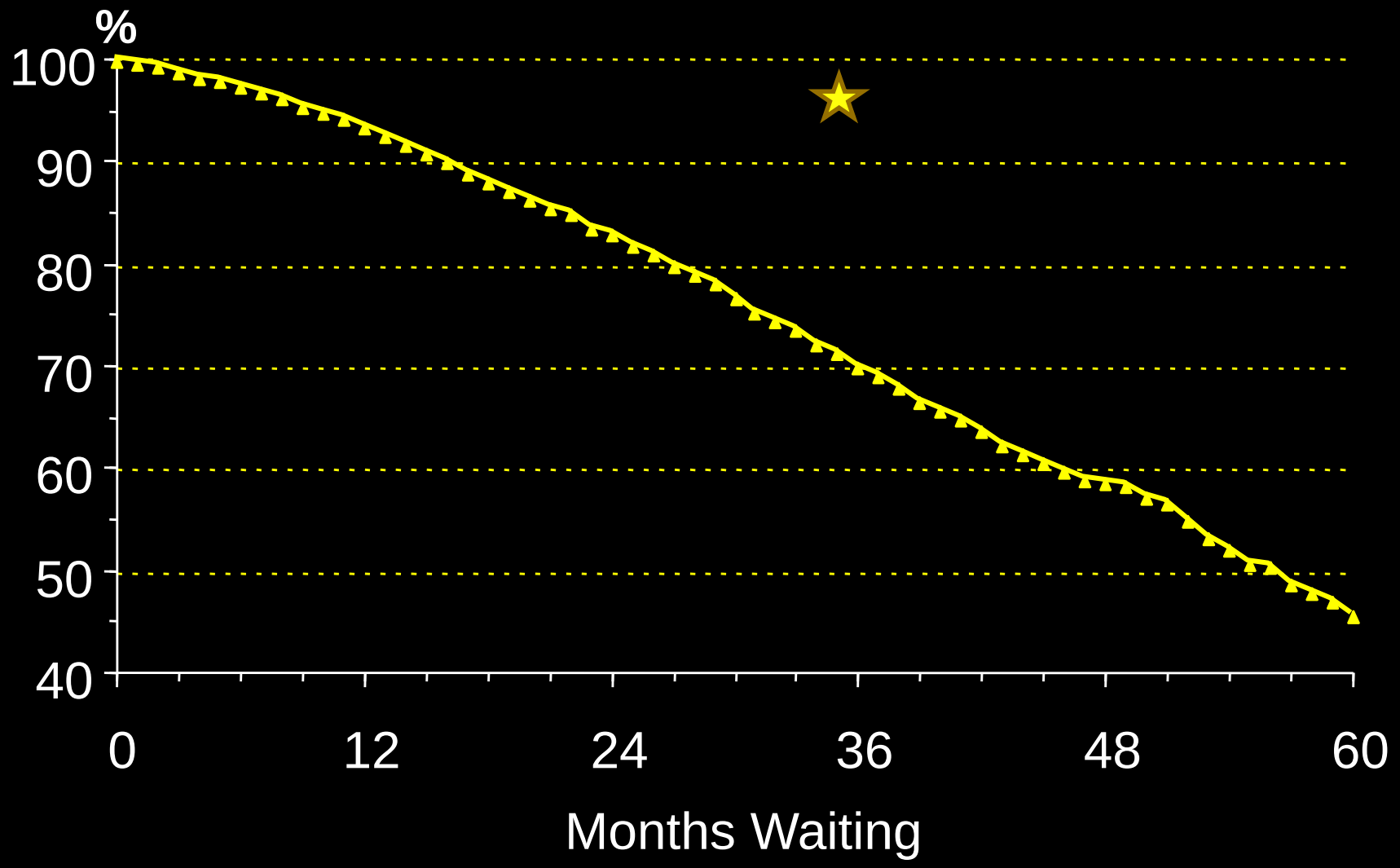
Organ	1-year	3-year
LD Kidney	98.9%	96.5%
SPK	97.7%	95.6%
DD Kidney	96.6%	92.3%

Pancreas transplants do not threaten lives!

PANCREAS TRANSPLANT WITH ENTERIC DRAINAGE IN SITU

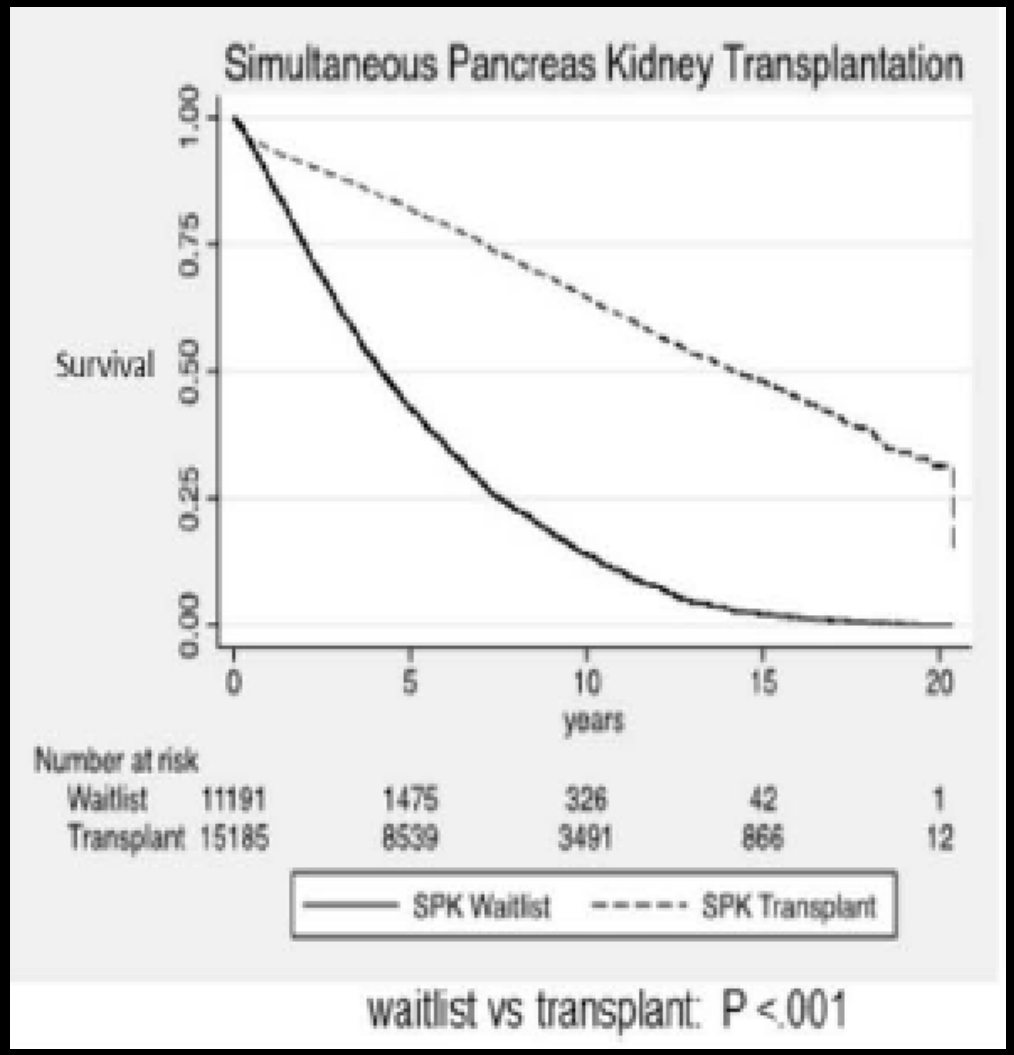


Diabetic Uremic Patient Survival while Waiting



Survival Benefit of Solid-Organ Transplant in the US

A Rana, A Gruessner, VG Agopian, Z Khalpey, IB Riaz, BKaplan, KJ Halazun, RW Busuttil, RG Gruessner
JAMA Surg. 2015;150(3):252-259



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

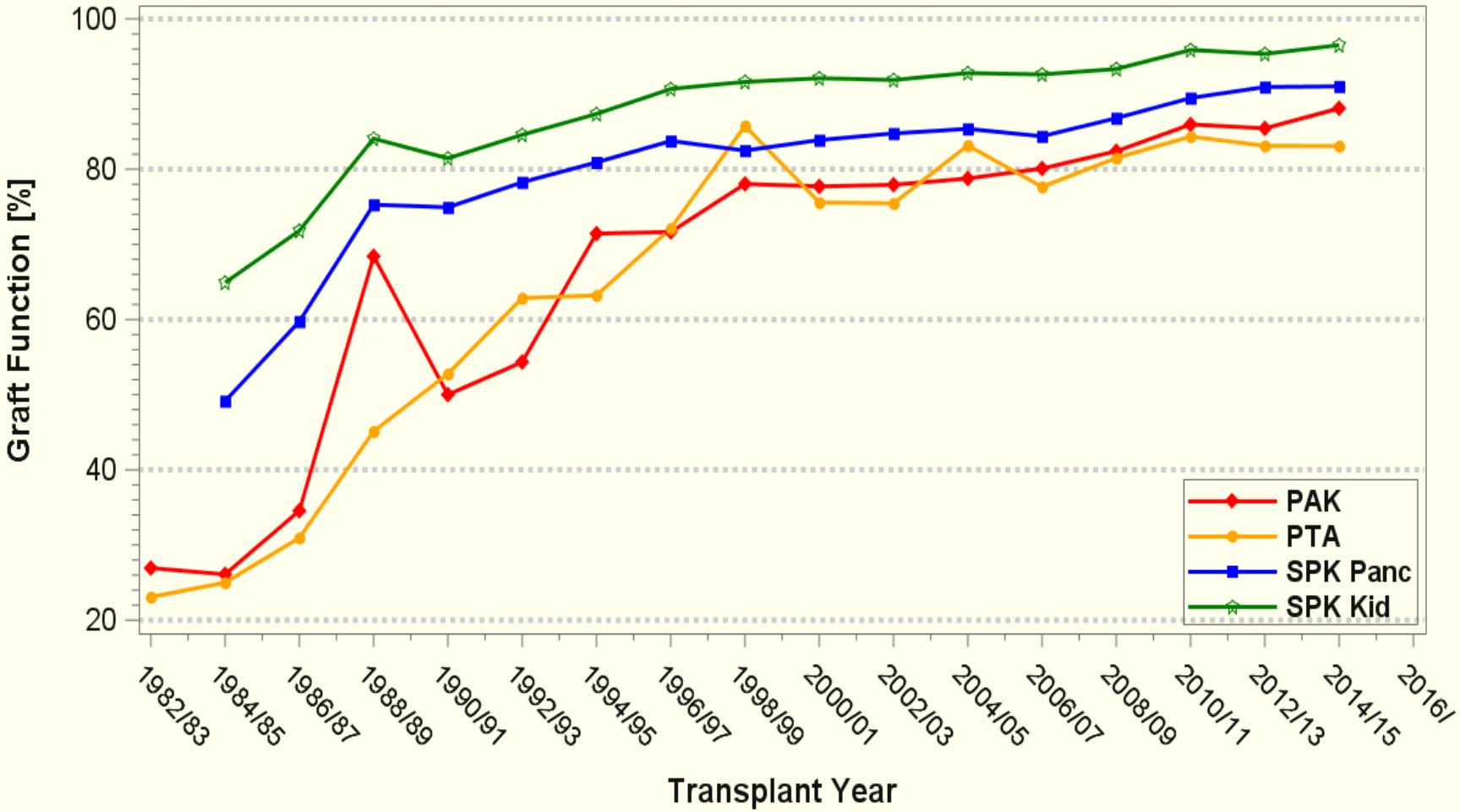
UNOS database: 1987 - 2012

Table 1. Survival Benefit of Solid-Organ Transplant

			Observed No.	Observed No. of Life-years	
Pancreas-kidney					
Waiting list	14 195	33 979	...	...	4.2
Transplant	16 995	119 620	79 198	4.6	14.5
Pancreas					
Waiting list	8568	26 733	...	...	8
Transplant	6177	34 193	14 903	2.4	13.3

1-Year Pancreas/Kidney Graft Function

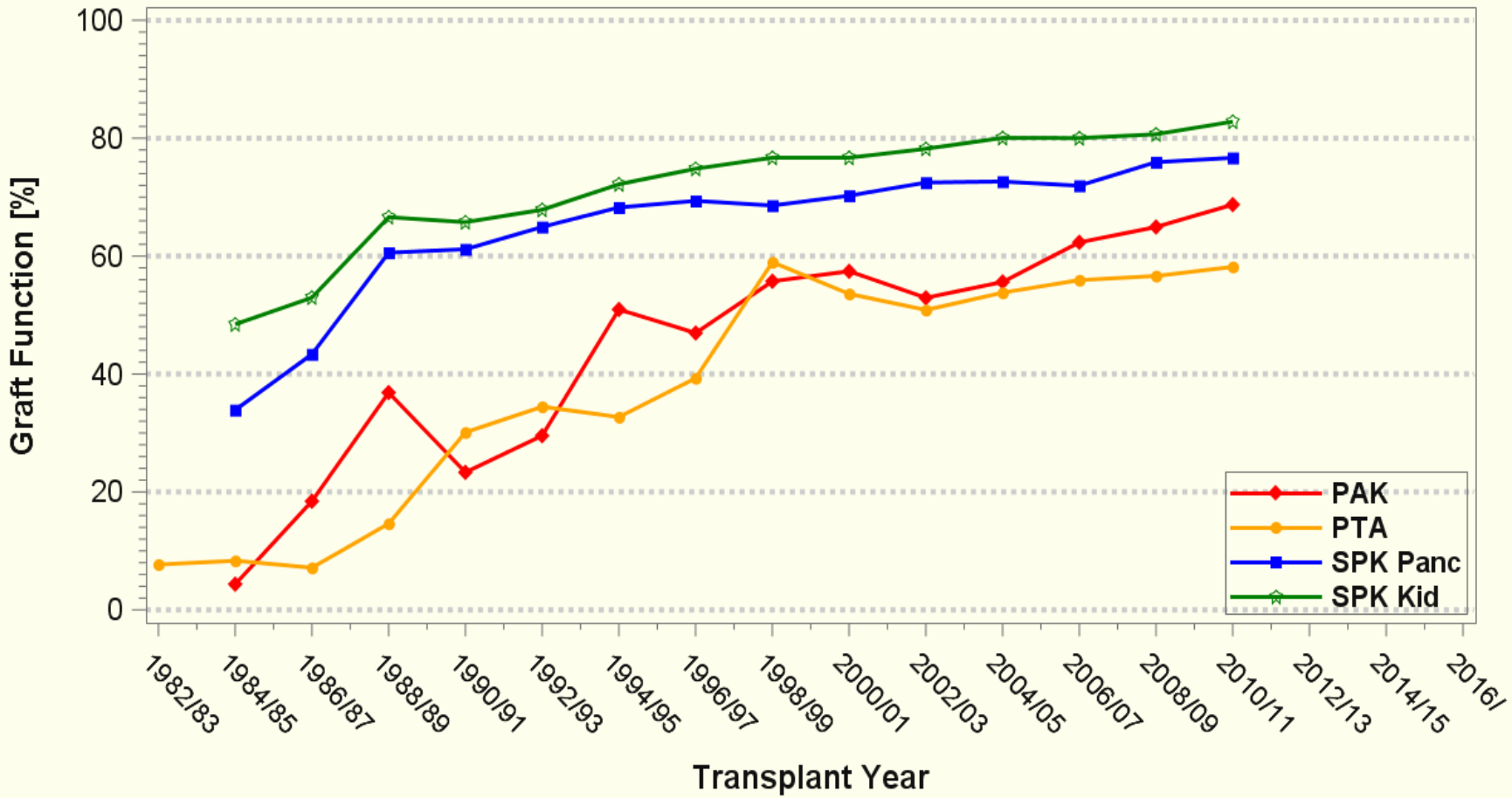
USA Primary DD Pancreas Transplants, 1 /1/1982 – 12/31/2016



IPTR/UNOS

5-Year Pancreas/Kidney Graft Function

USA Primary DD Pancreas Transplants, 1 /1/1982 – 12/31/2016



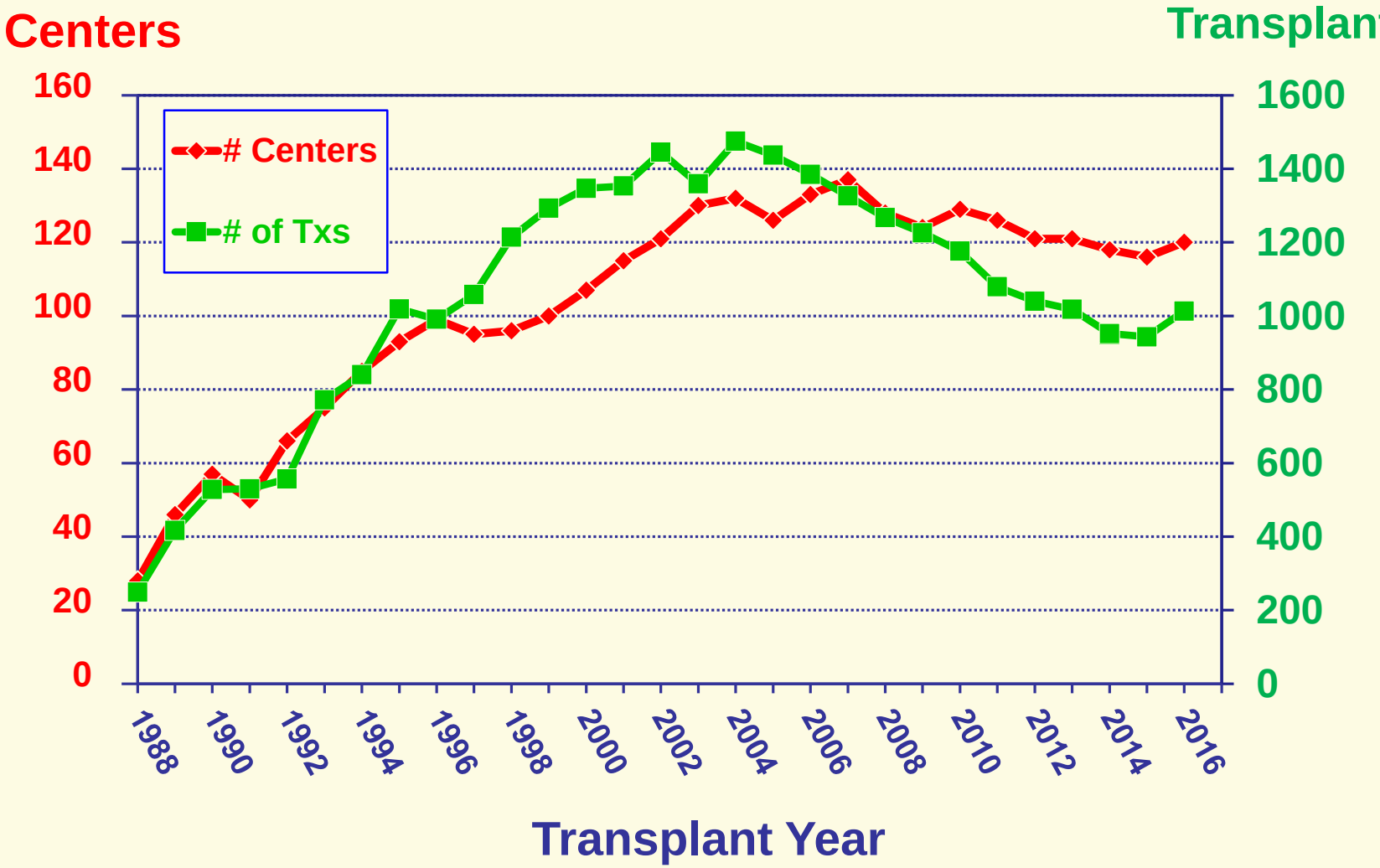
IPTR/UNOS

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

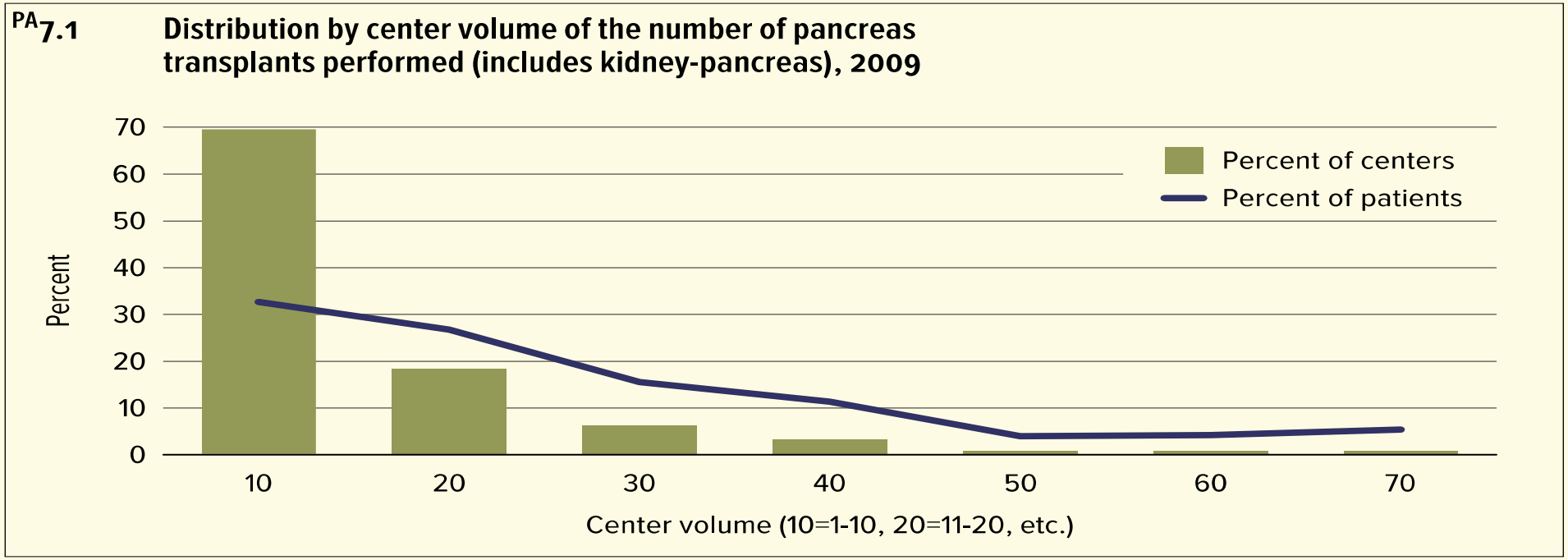
Number of Tx Centers and Number of Txs

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

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

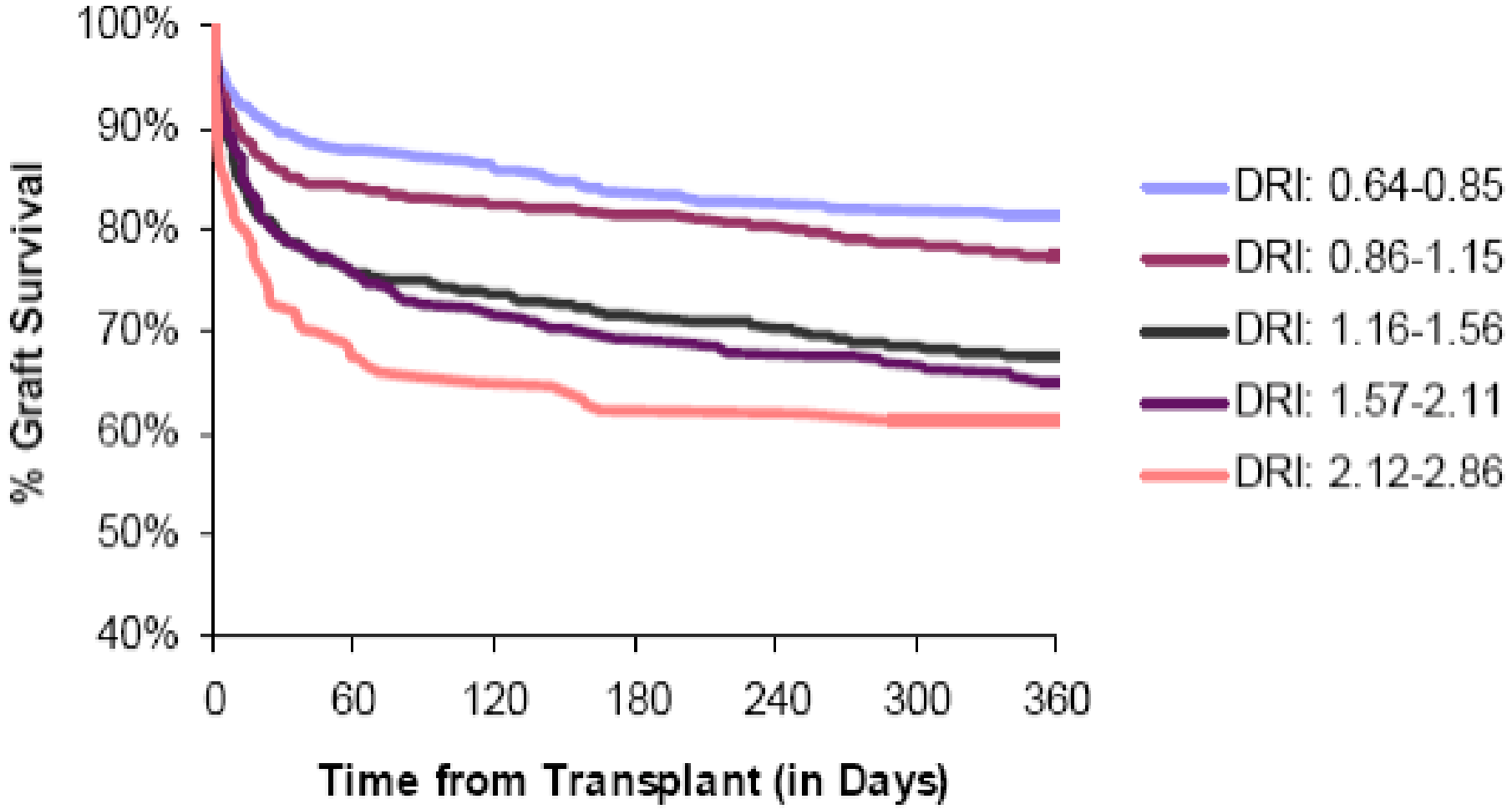
Pancreas Donor Risk Index

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.

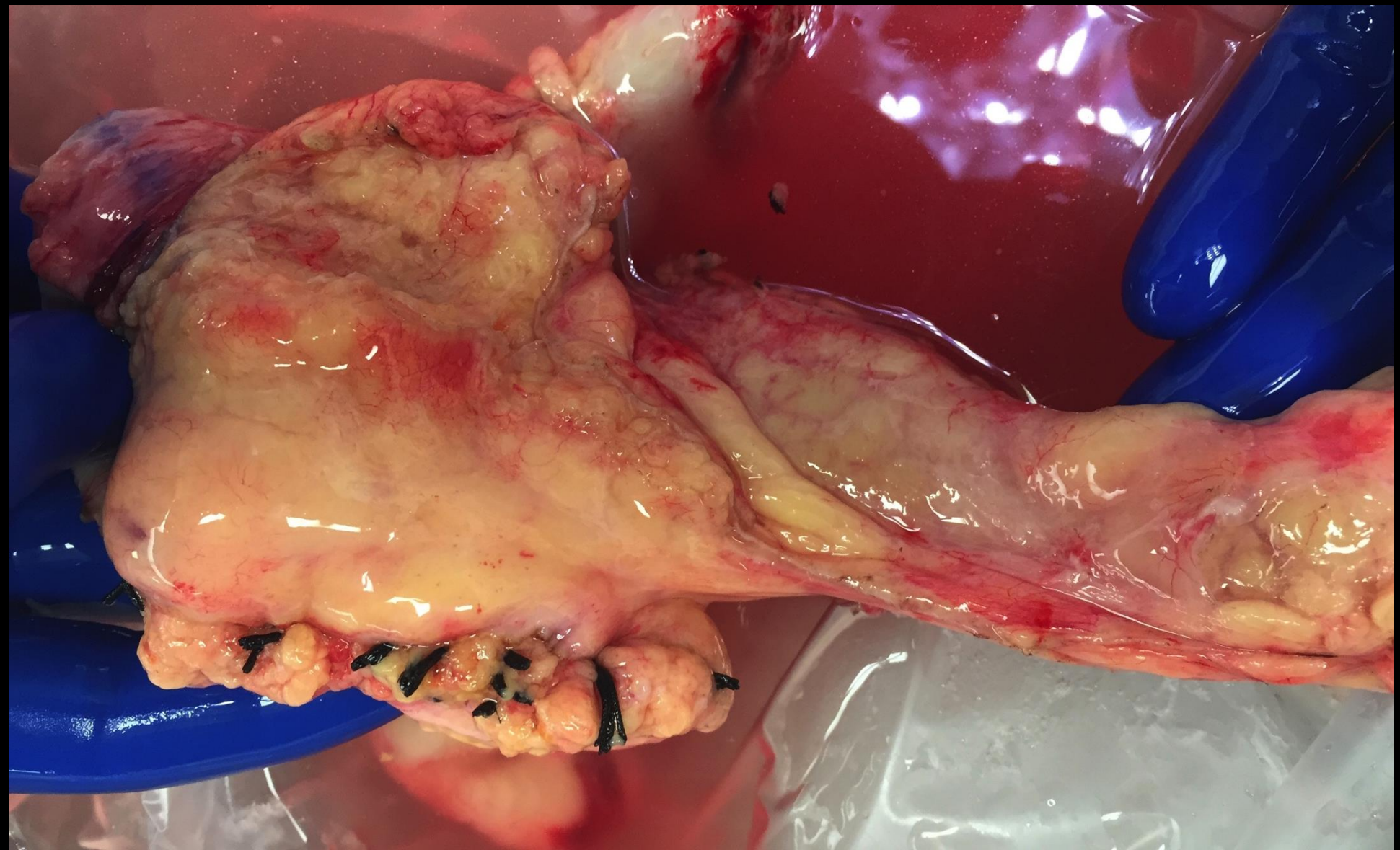
For imports, request anatomic waivers and visualize

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

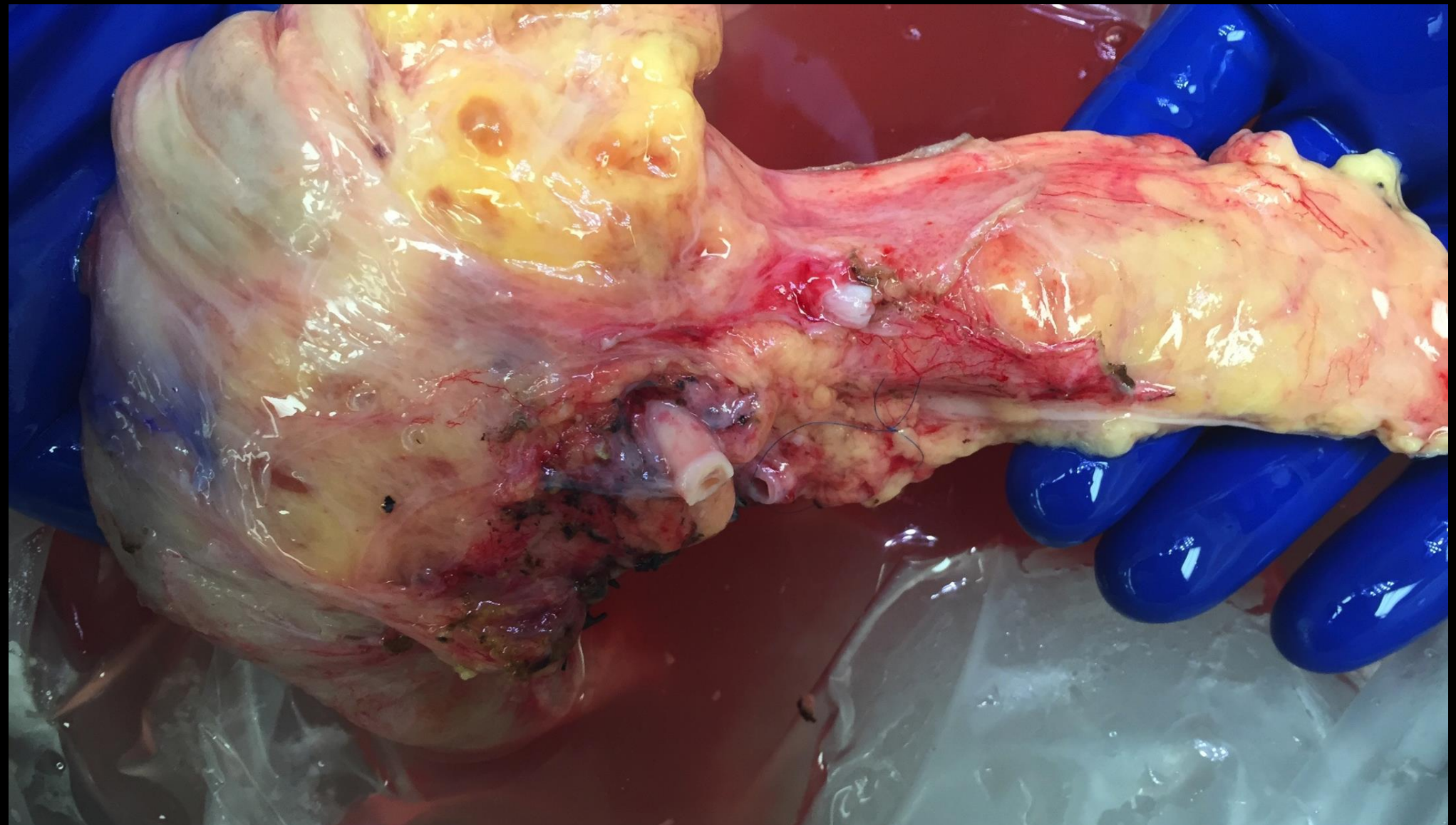
Grade A Pancreas Graft

Grade B Pancreas Graft

Grade C Pancreas Graft



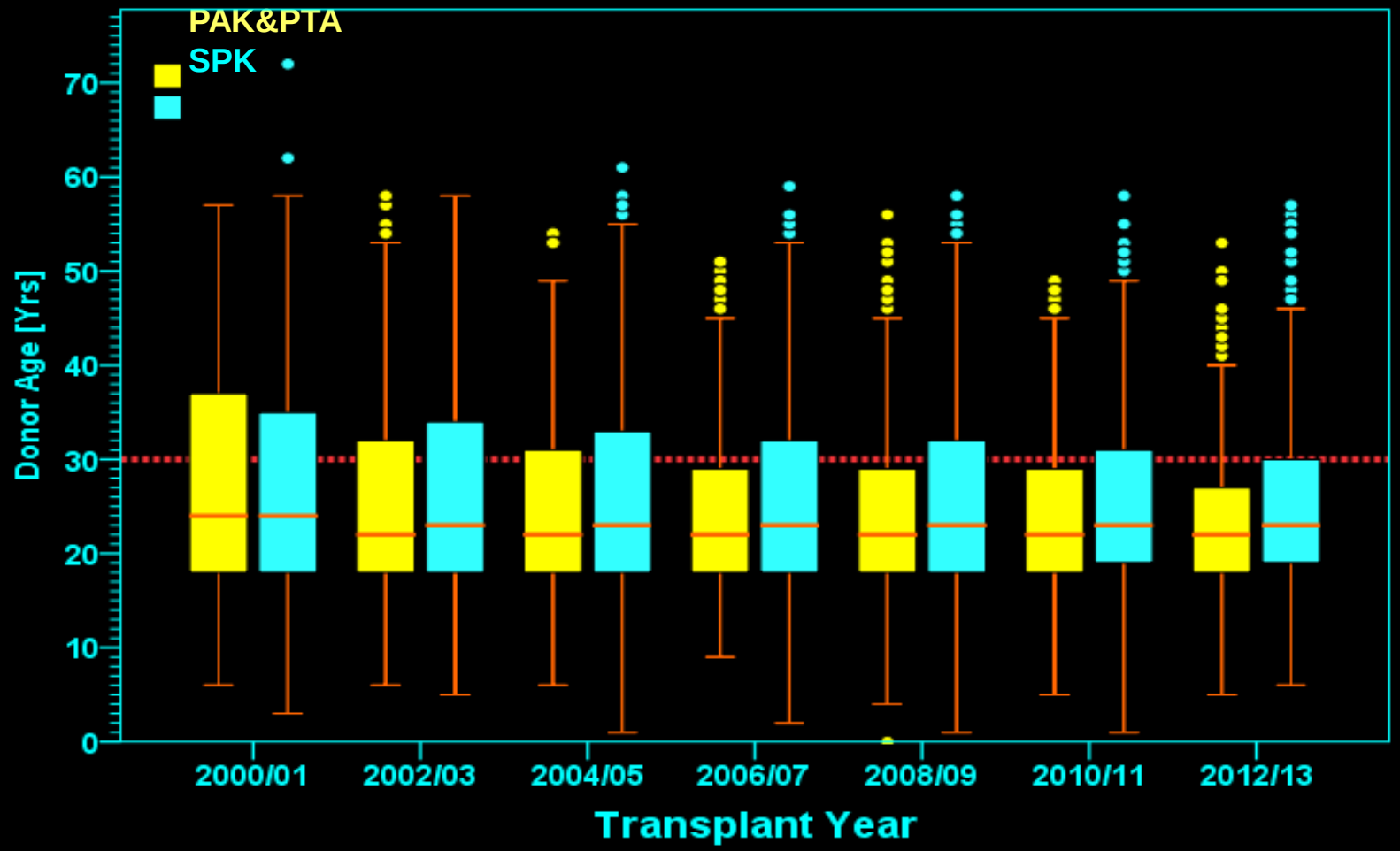
Grade C Pancreas Graft



Grade A- Pediatric Pancreas Graft

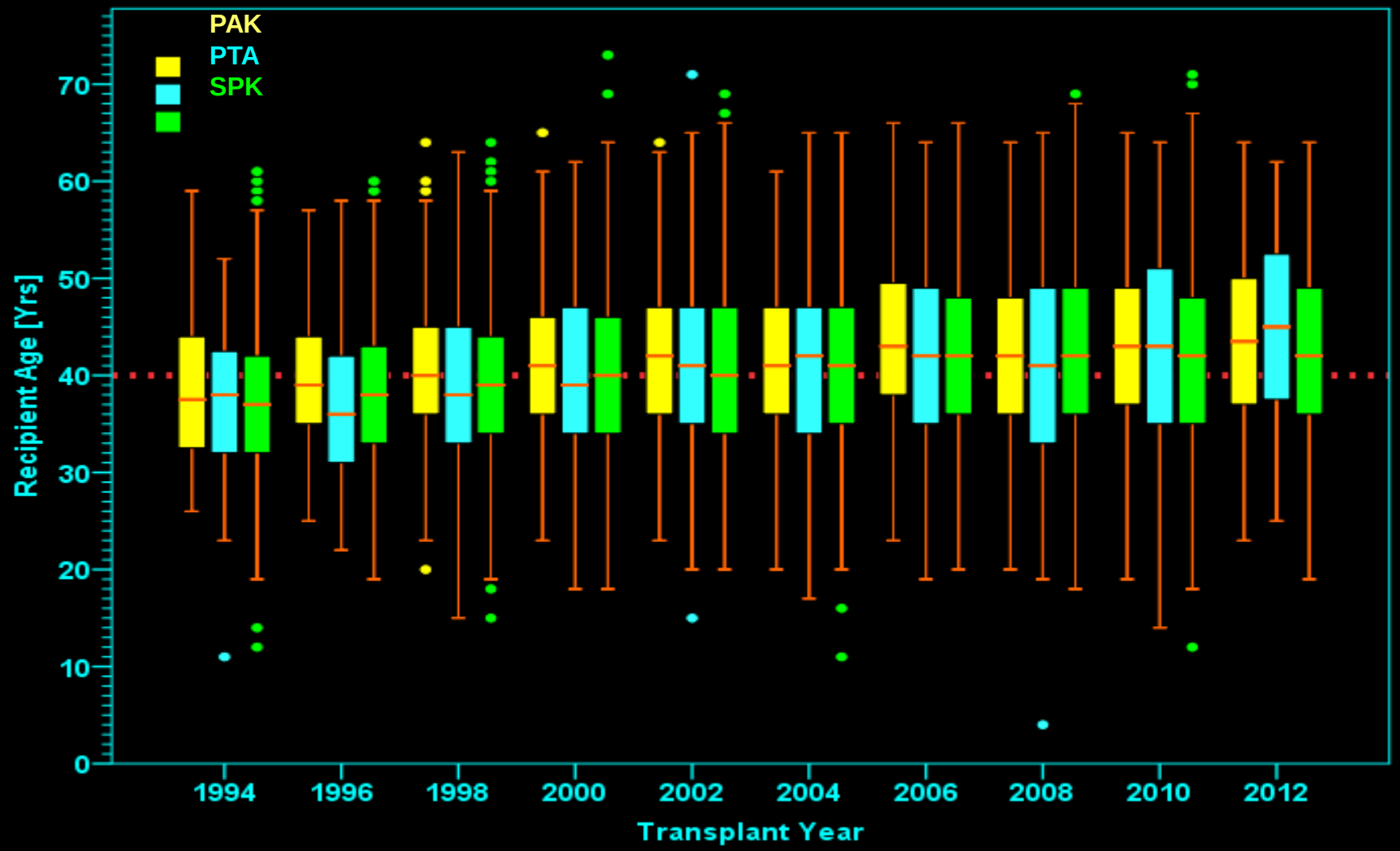
Deceased Donor Age

USA Primary Pancreas Transplants 1/1/2000 – 12/31/2012



Recipient Age

USA Primary Pancreas Transplants 1/1/1994 – 12/31/2012



Typical Demographics for Pancreas Tx

Donors:

- DBD local donors
- <50 years of age
- BMI <30

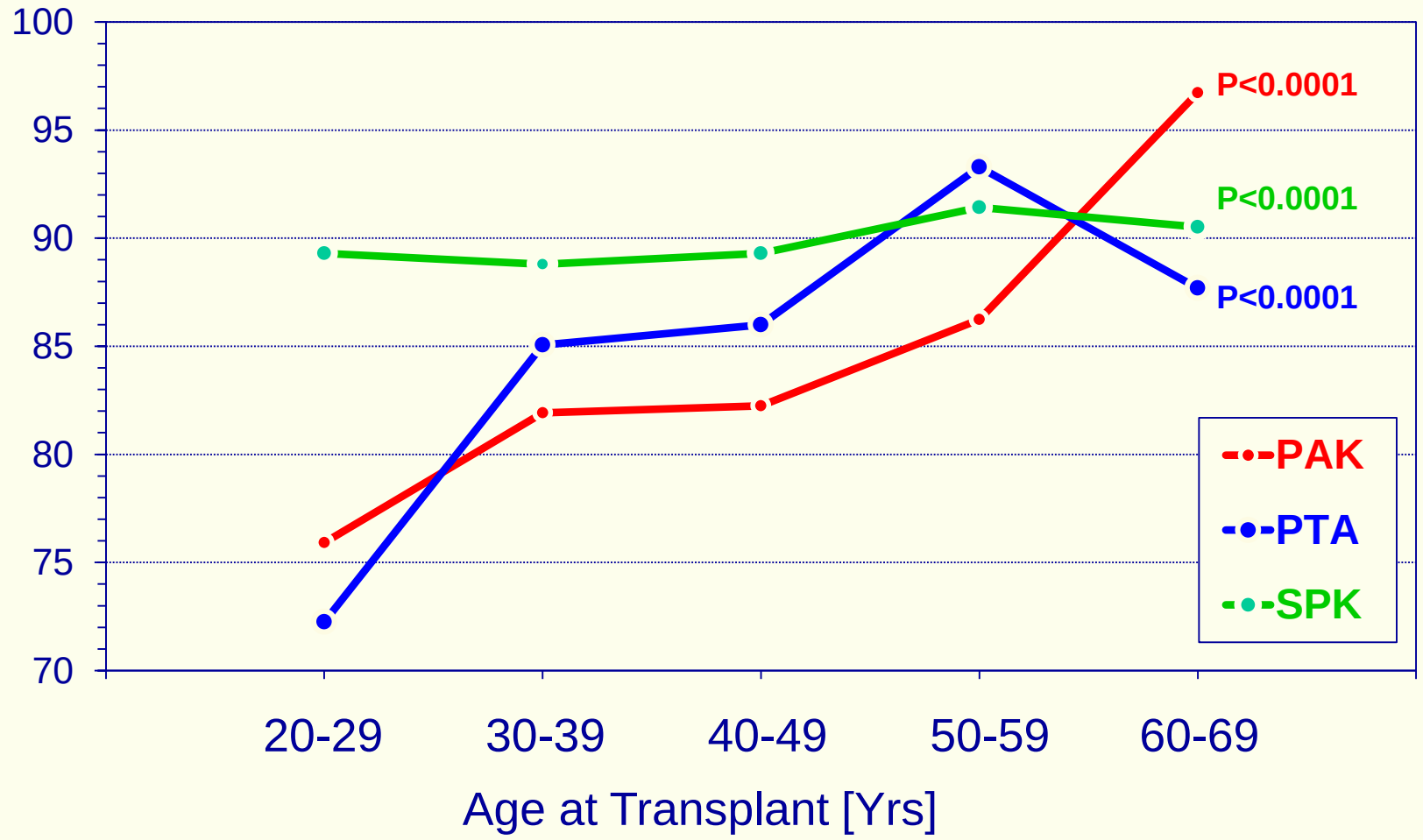
Recipients:

- 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

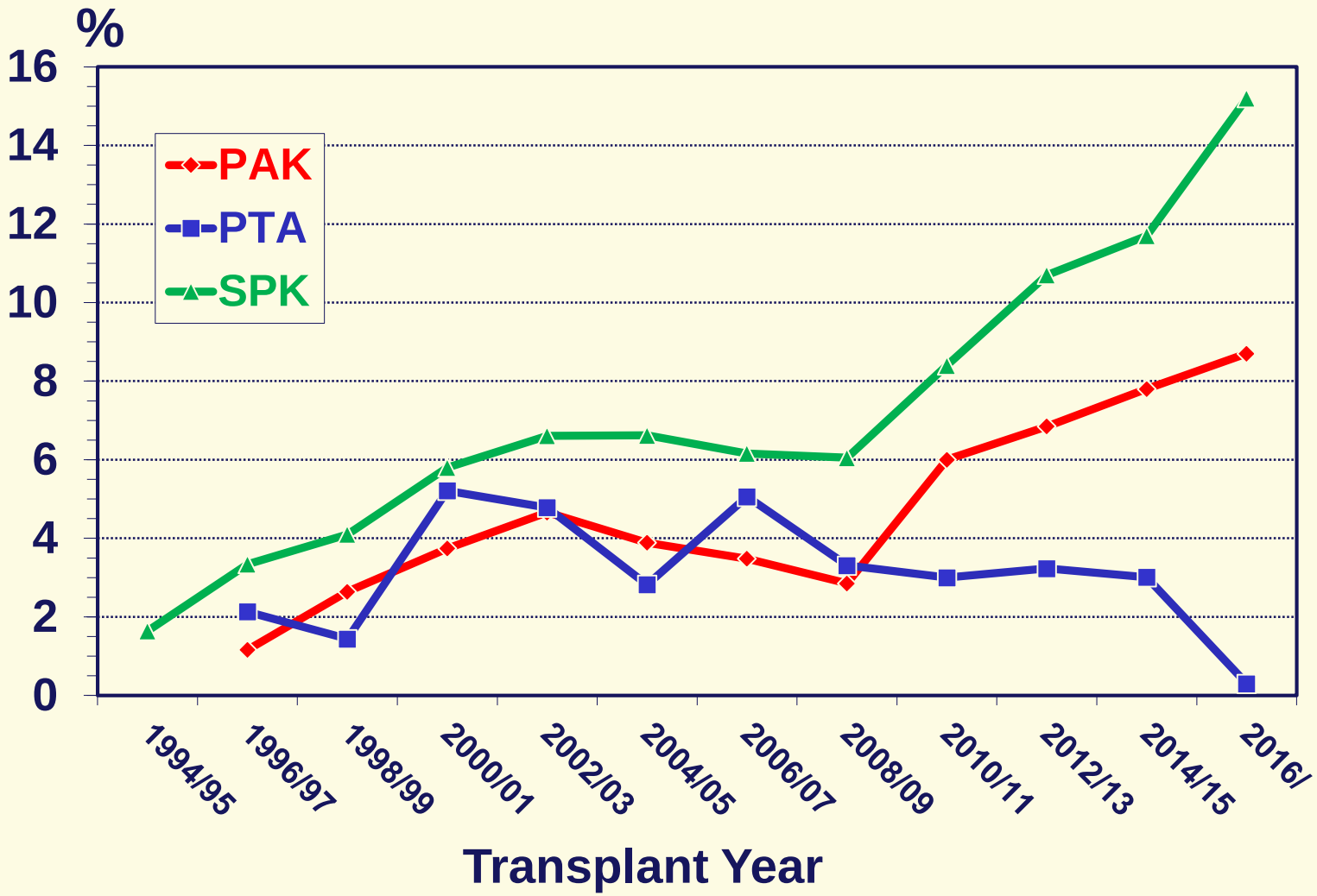
USA Primary Pancreas Transplants in Type 1 DM 1/1/2010 – 12/31/2016



IPTR/UNOS

Patients with Type 2 Diabetes

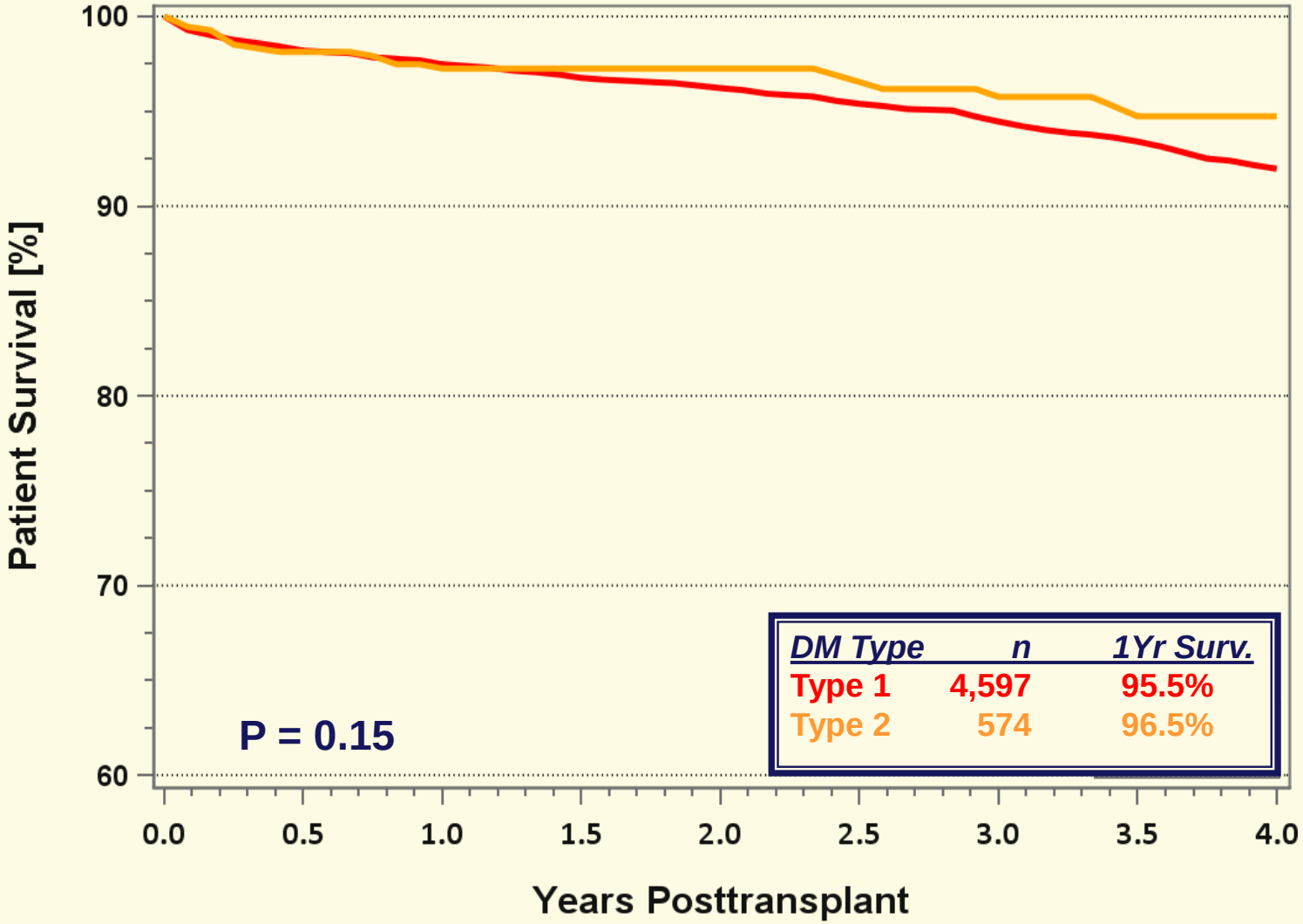
USA Primary DD Pancreas Transplants 1/1/1994 – 12/31/2016



IPTR/UNOS

SPK Patient Survival by Diabetes Type

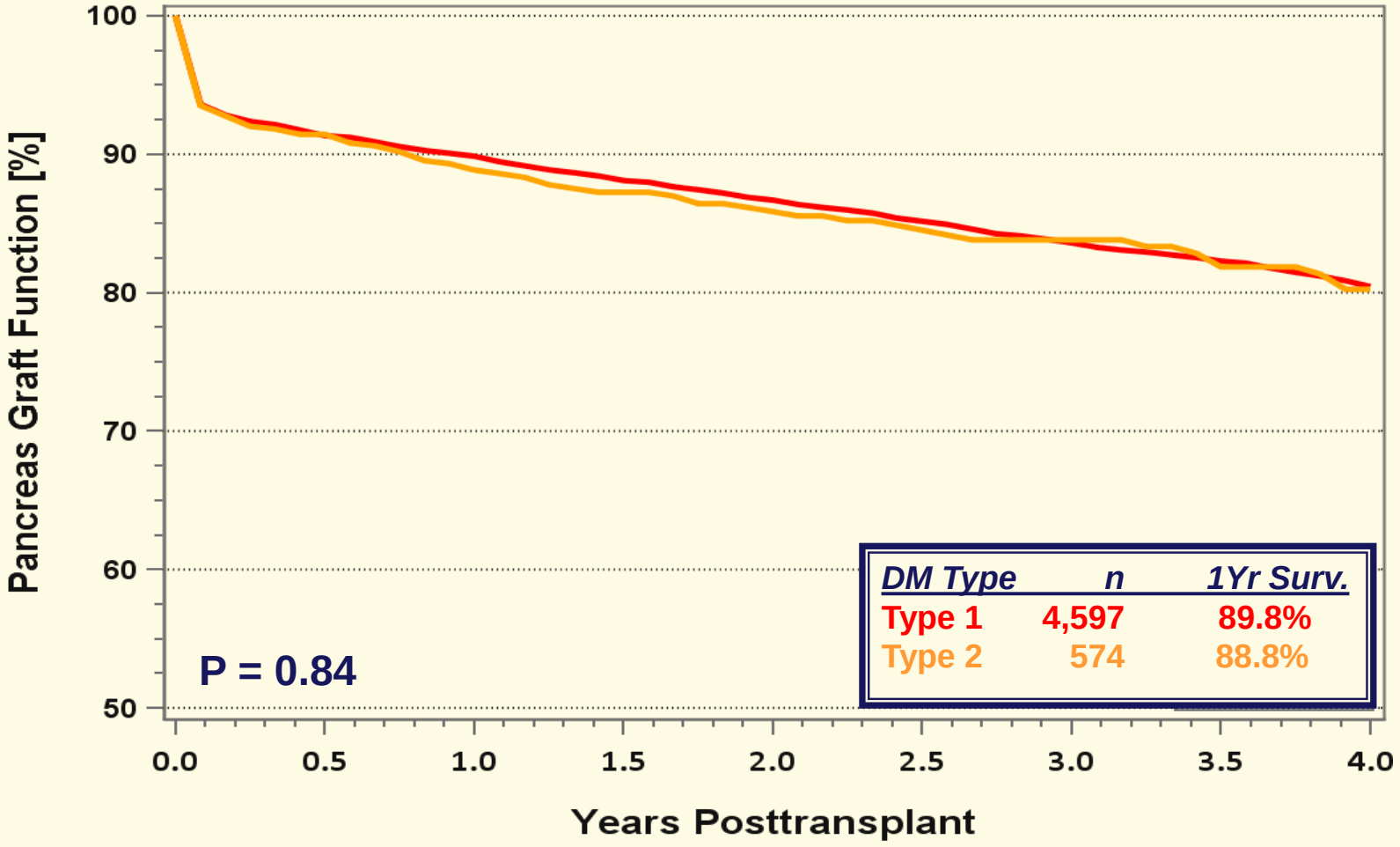
USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016



IPTR/UNOS

SPK Pancreas Graft Function by Diabetes Type

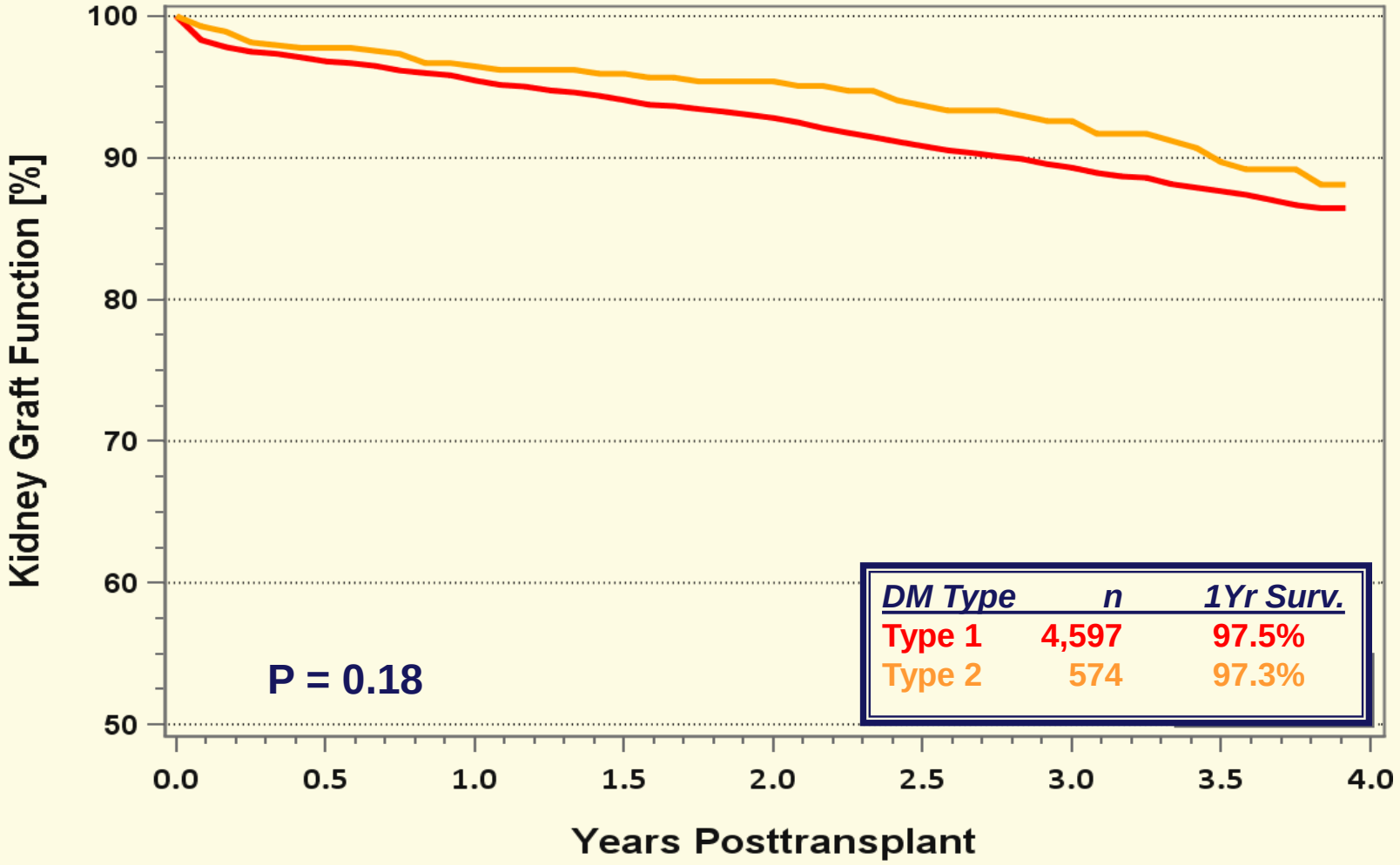
USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016



IPTR/UNOS

SPK Kidney Graft Function by Diabetes Type

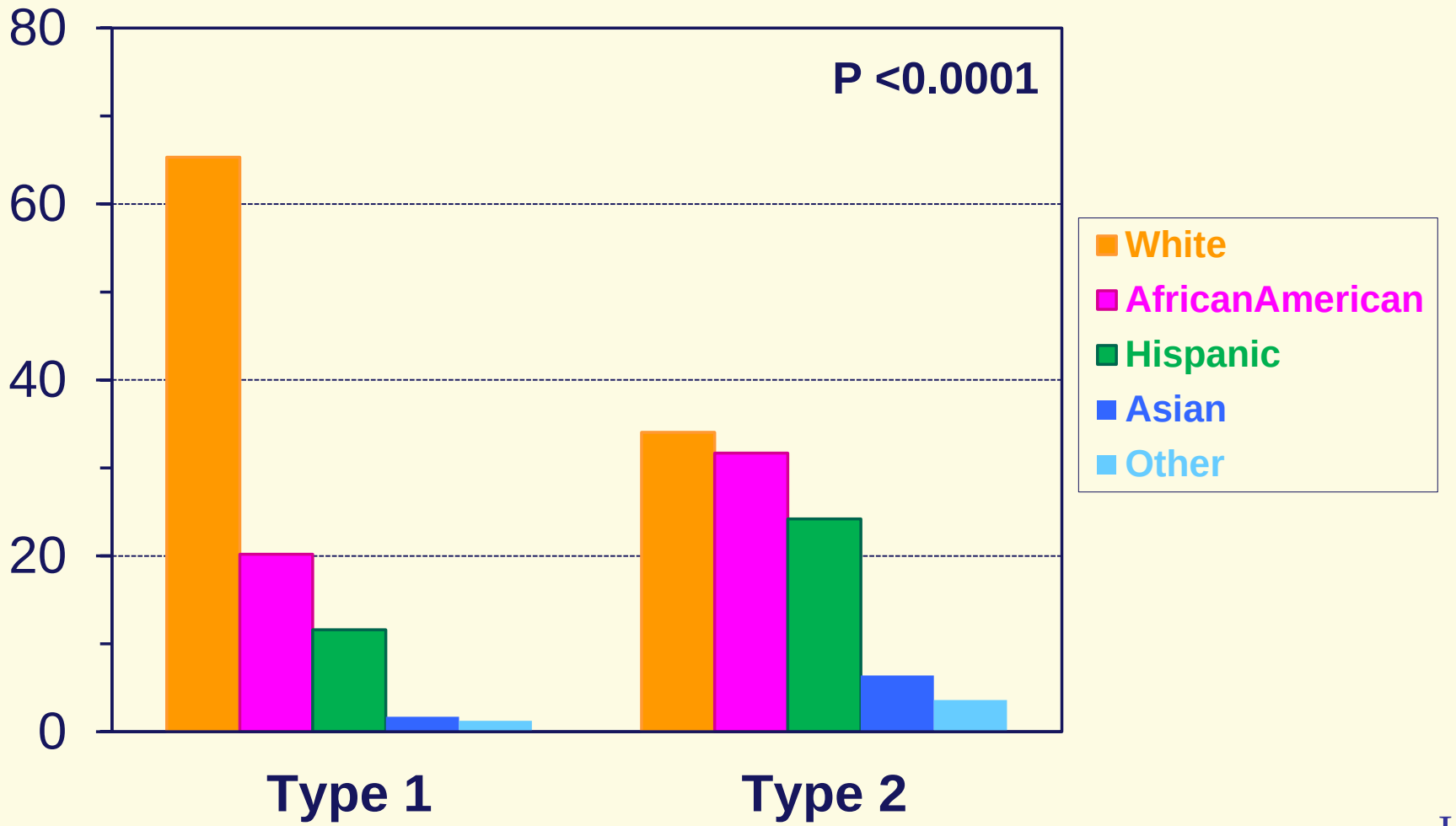
USA Primary DD SPK Transplants 1/1/2010 – 12/31/2016



IPTR/UNOS

Diabetes Type and Race

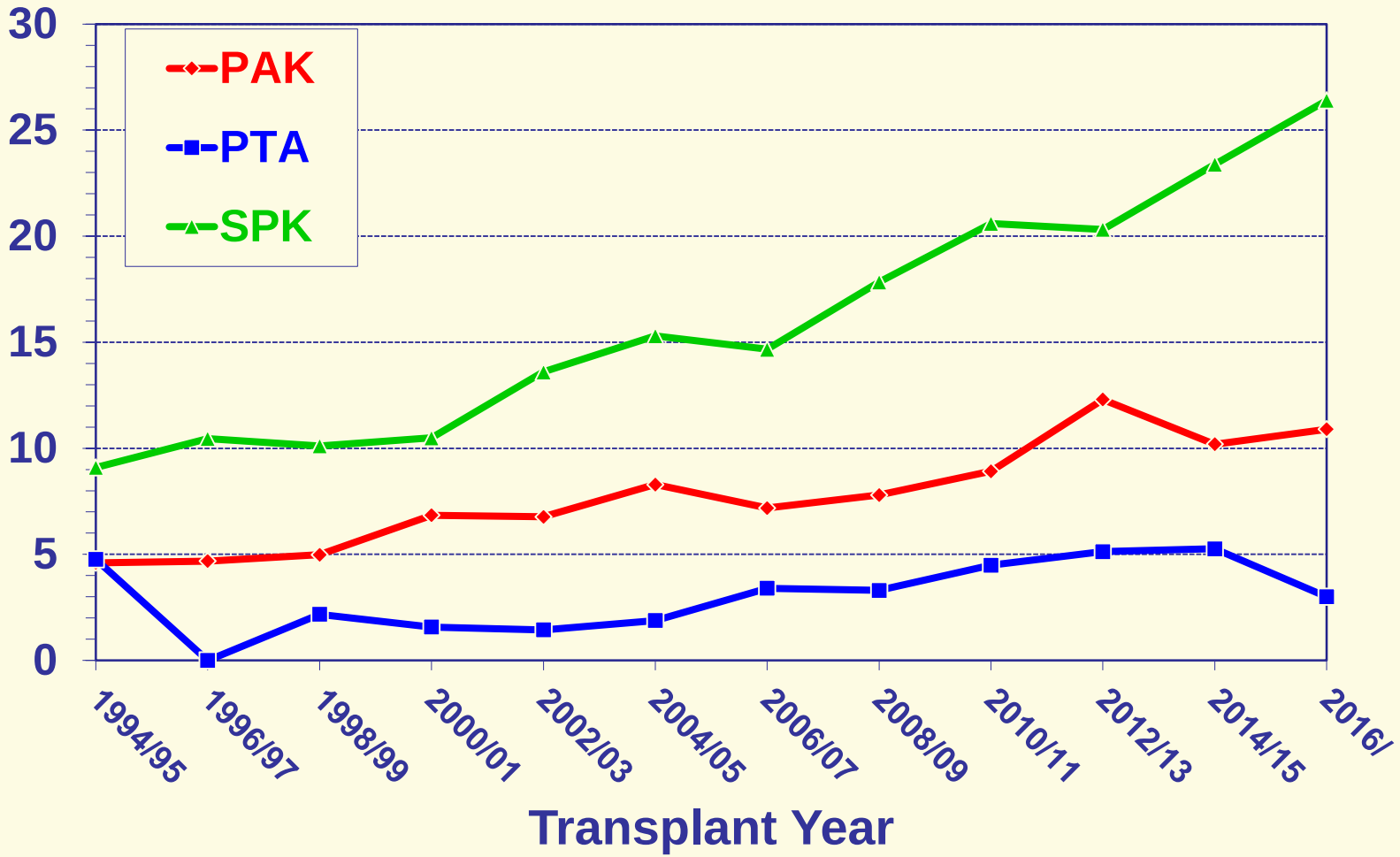
USA Primary DD Pancreas Transplants 1/1/2010 – 12/31/2016



IPTR/UNOS

African American Recipients

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



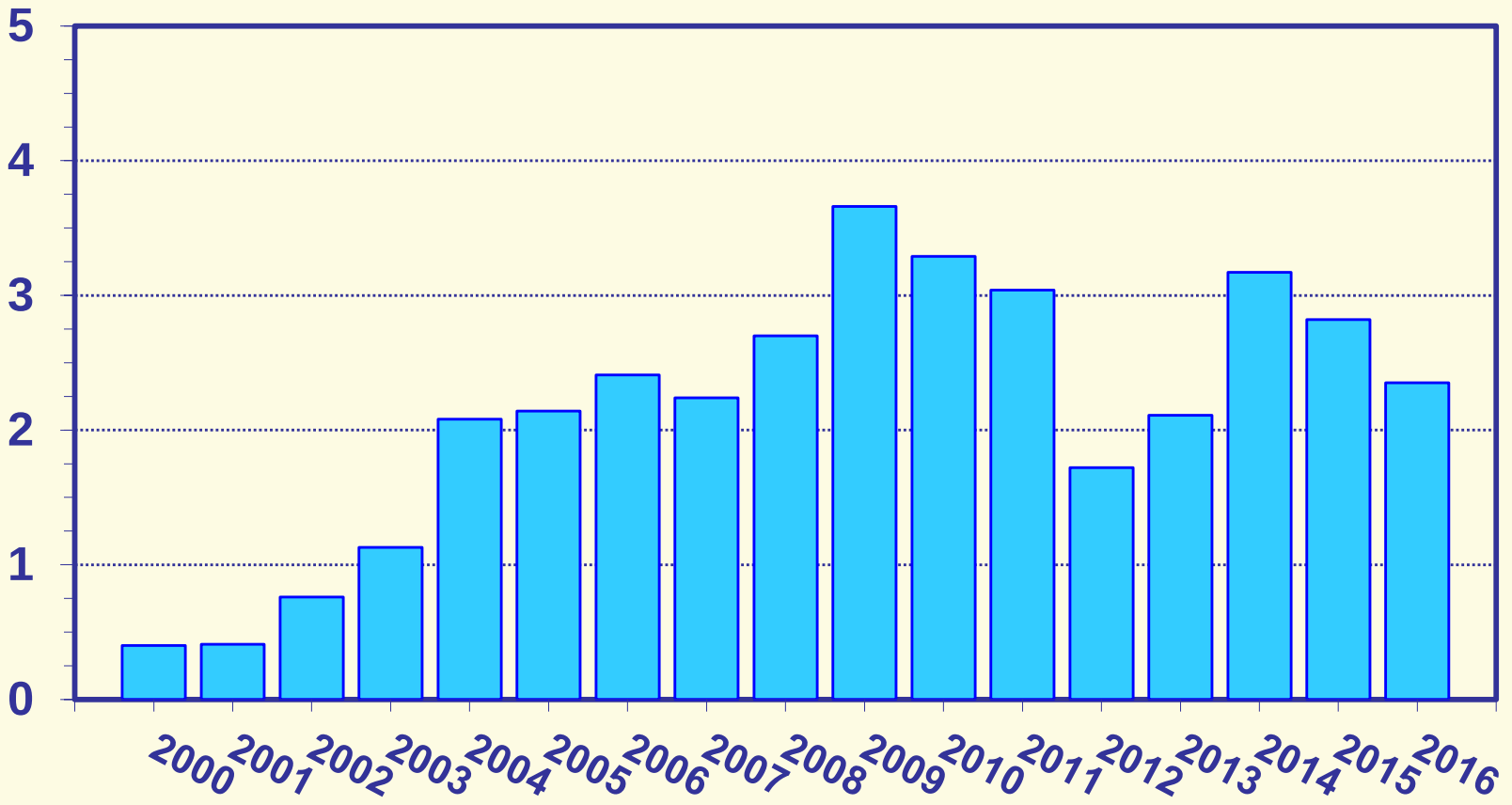
IPTR/UNOS

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

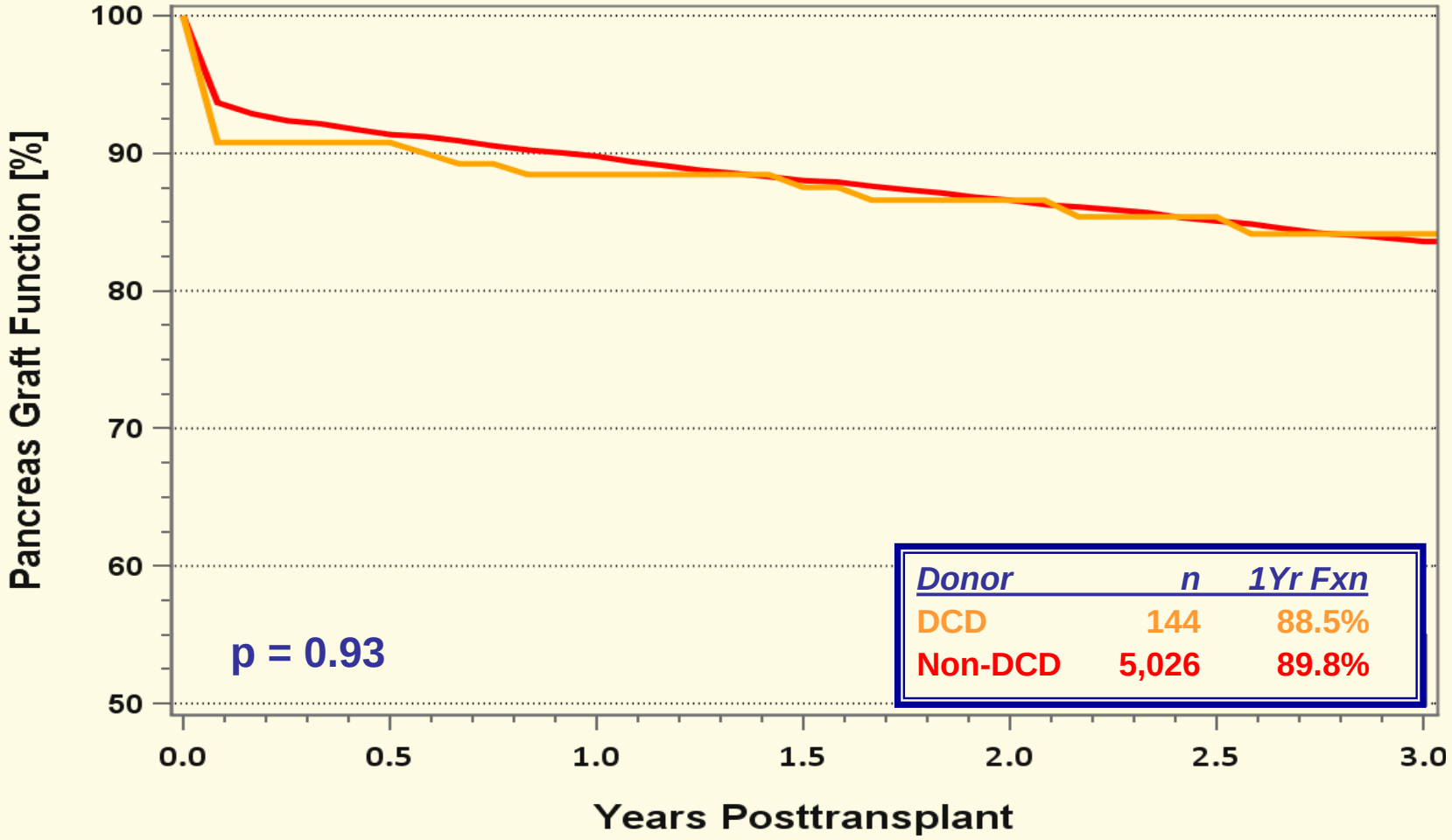
USA DD Pancreas Transplants 1/1/2000 – 12/31/2016



IPTR/UNOS

SPK Pancreas Graft Fxn by Donor Type

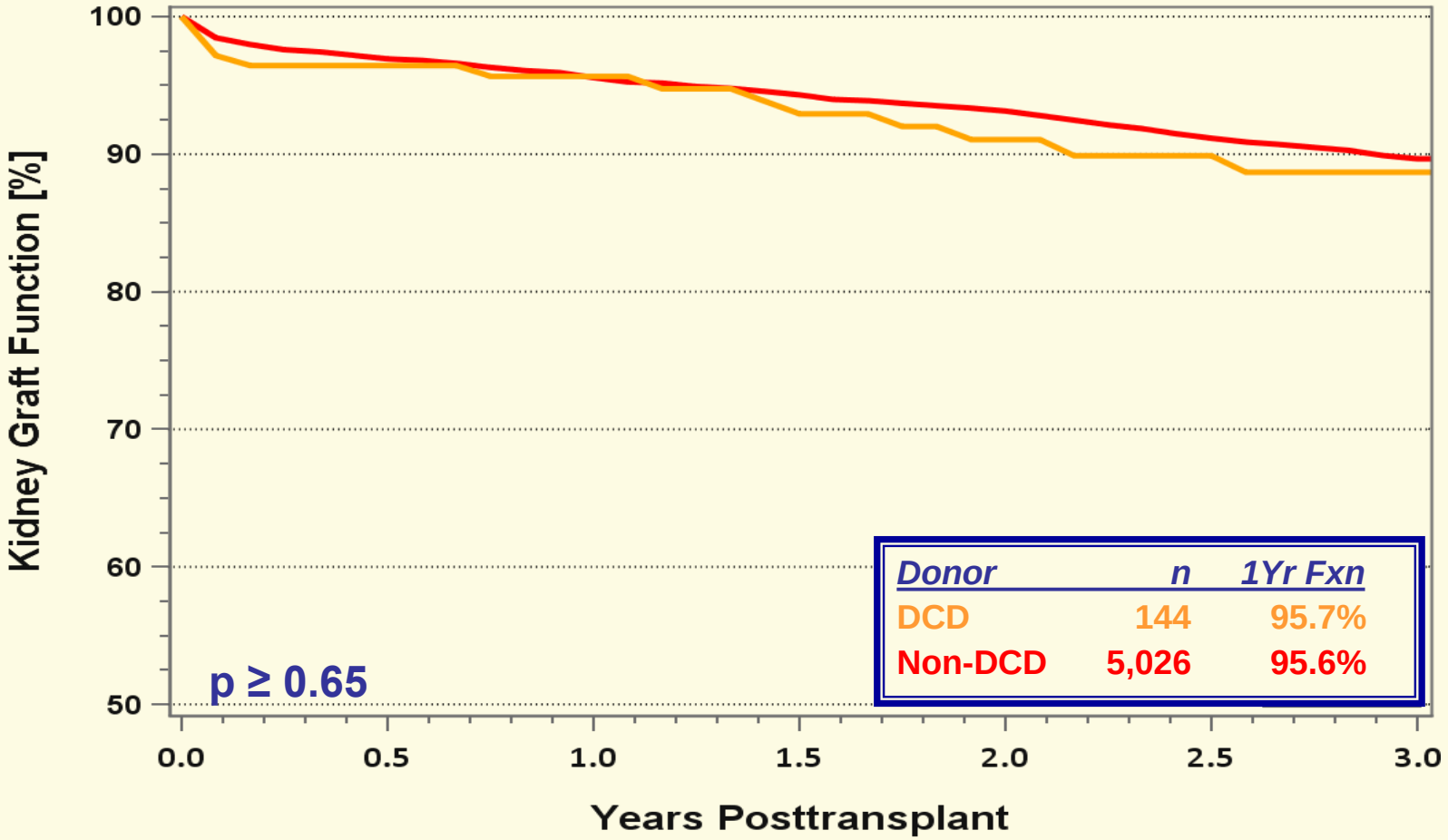
USA DD Primary Pancreas Transplants 1/1/2010 – 12/31/2016



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?

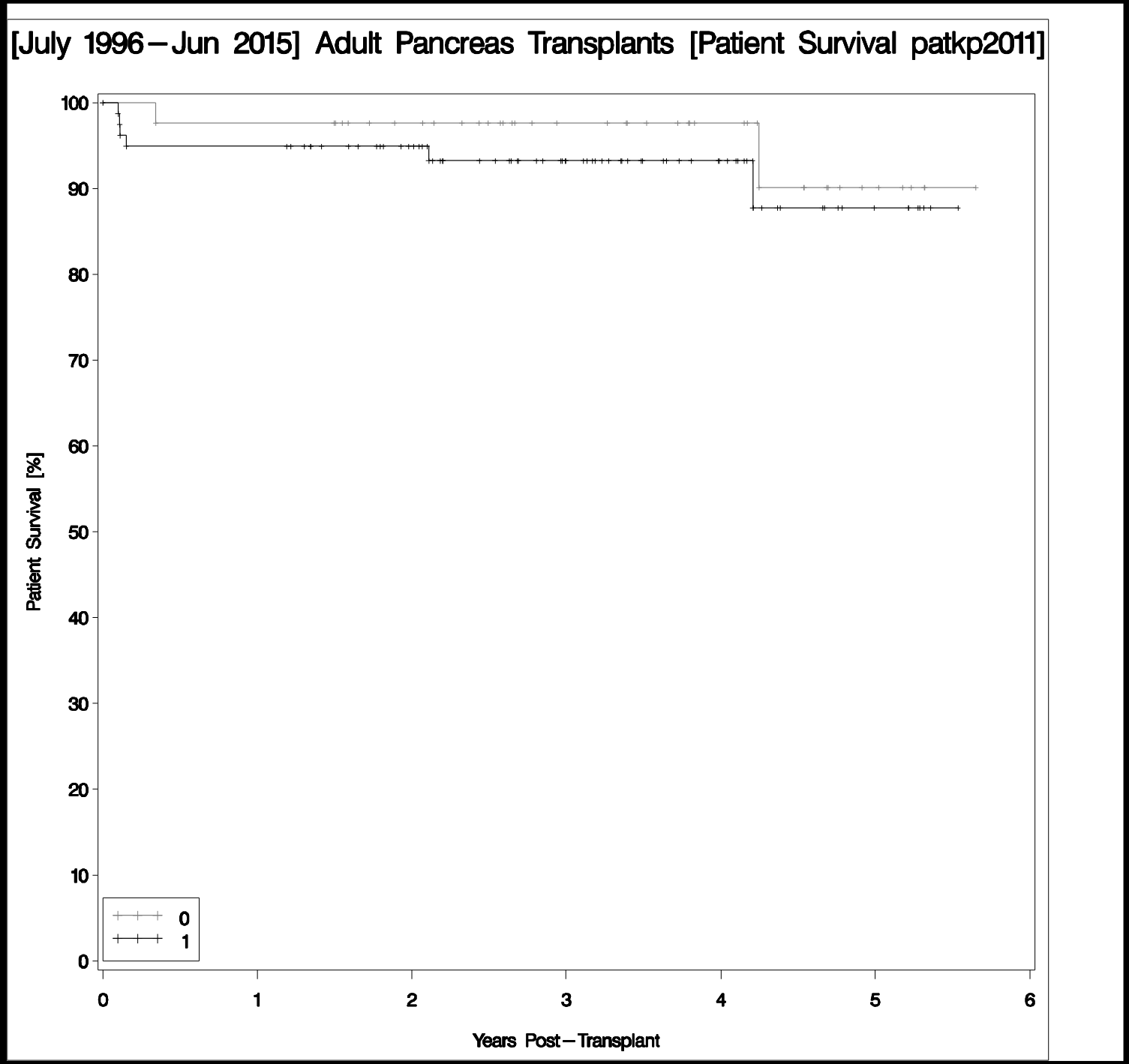
Pancreas Tx Complexity

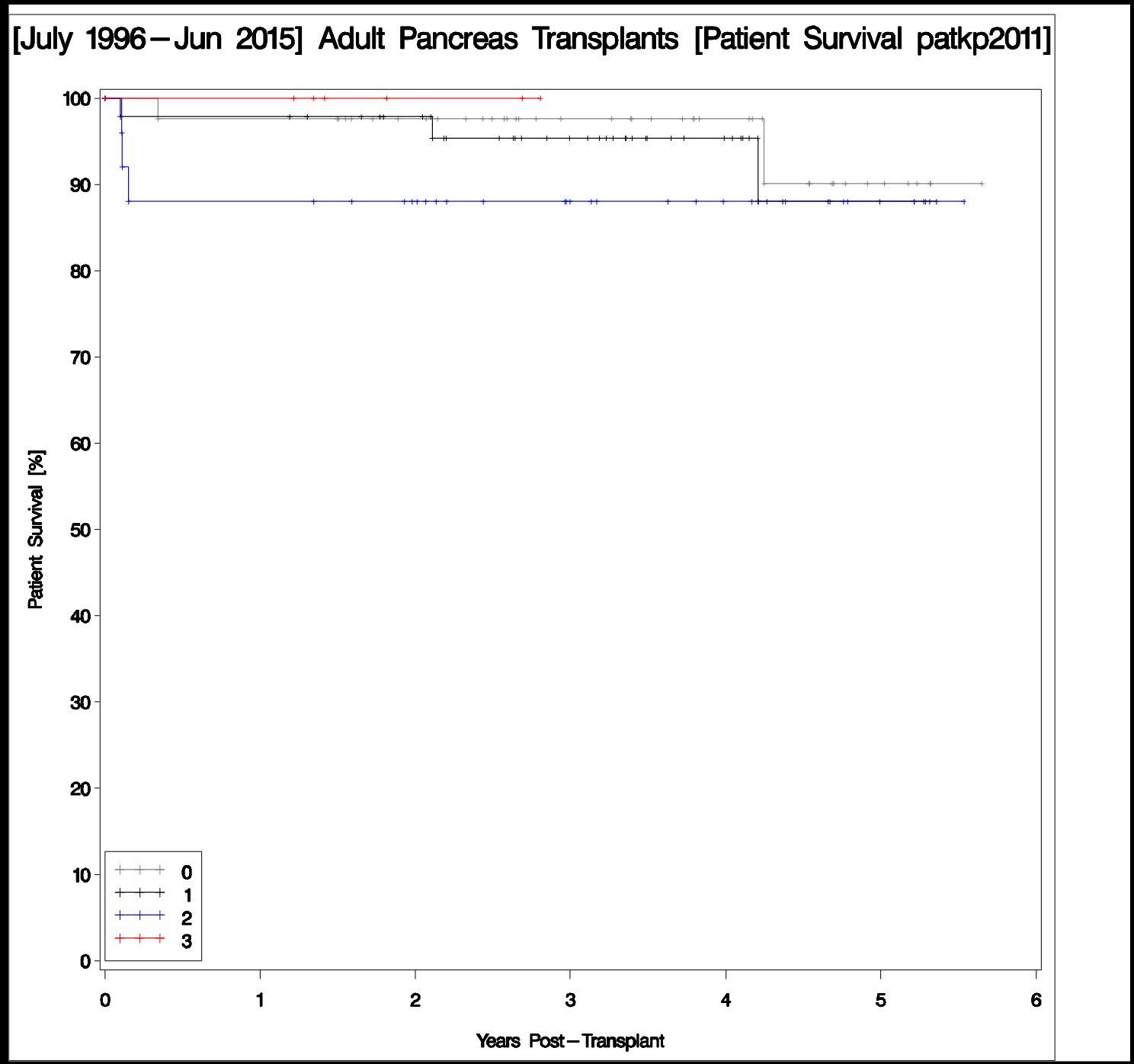
For each of 1060 pancreas txs conducted 1996-2015, we reviewed these specific D/R characteristics and tabulated for each recipient a point for each D/R characteristic that fell outside the norm.

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]
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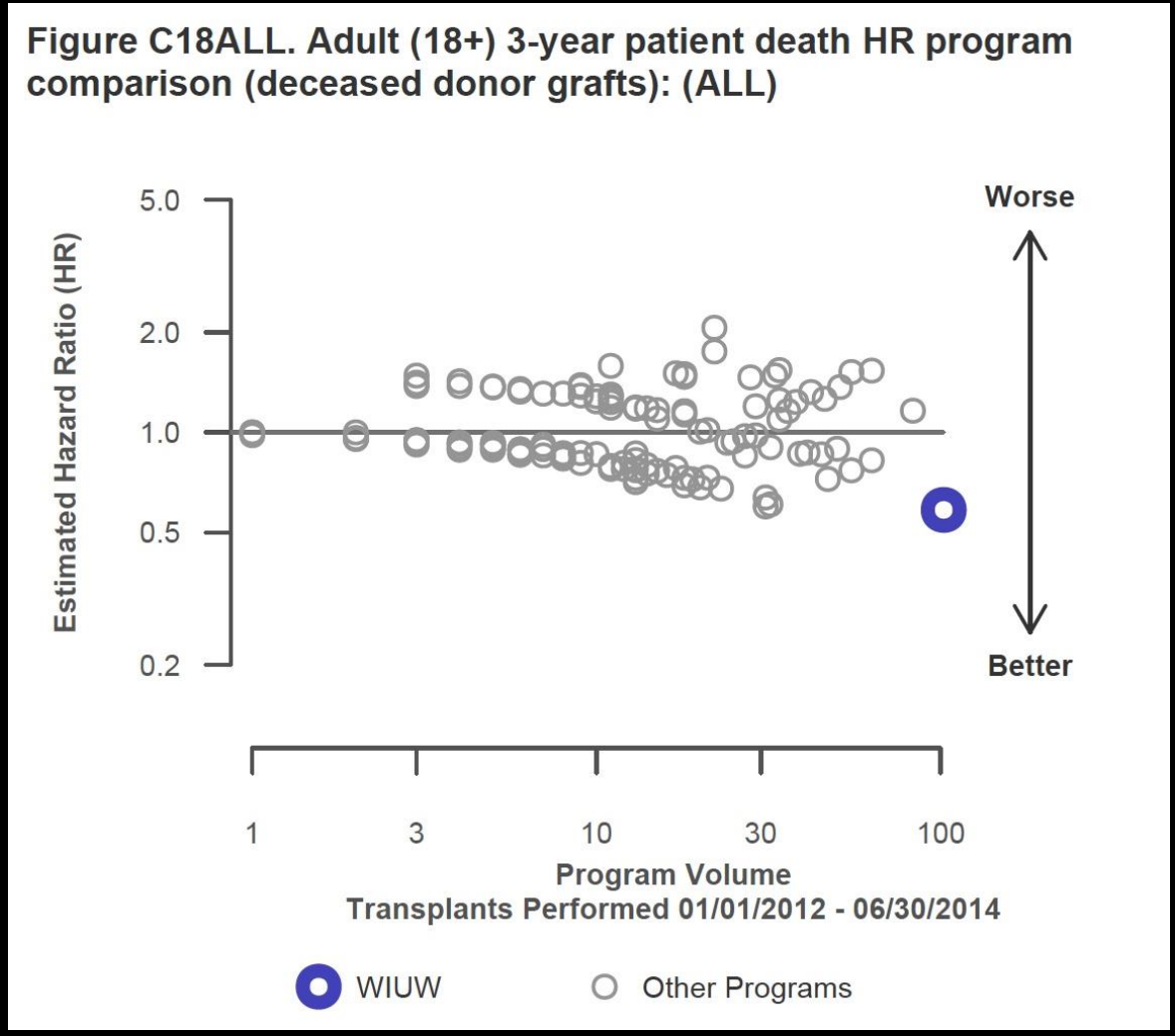
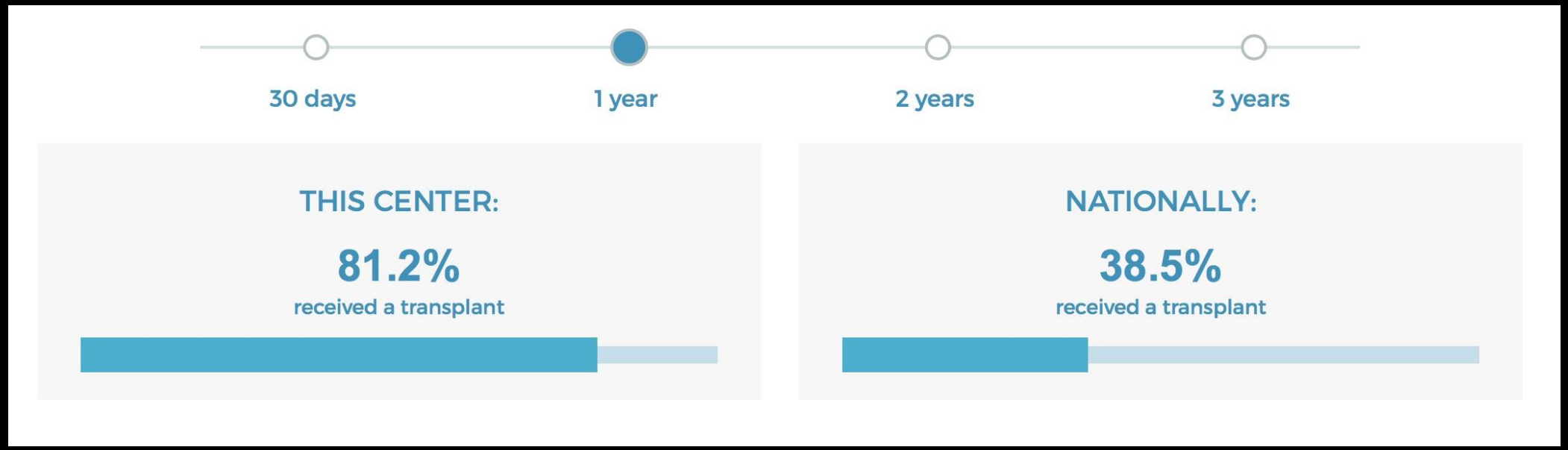
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
Years Post–Transplant
0
1
2
3

12/31/2017 SRTR
3-Year Patient Survival



SPK Waiting Times
% Txed within a year



SPK Transplant Rates
WL Mortality Rates

Transplant Rates

BETWEEN JULY 2016 AND JUNE 2017

271.3 OUT OF **100**
people per year receive a transplant at this hospital

48.8 OUT OF **100**
people per year receive a transplant nationally

Waiting List Mortality Rates

BETWEEN JULY 2016 AND JUNE 2017

0.0 OUT OF **100**
people per year die waiting for a transplant at this hospital

6.2 OUT OF **100**
people per year die waiting for a transplant nationally

Conclusion

- Expanding the donor and/or recipient criteria for for a pancreas transplant can be done without compromise of patient survival rates.
- It results in more patients being able to receive a pancreas tx.
- The practice decreases death on the WL.

Bucking the Trend
Programmatic Approaches

- Expand donor organ acceptance criteria, import organs, and use waivers to increase the number of txs;
- Remember: Pt survival is the PSR metric;
- Focus on eliminating death on the WL.

Bucking the Trend
Systematic Approaches

- UNOS/SRTR should NOT spend efforts developing 0/E metrics of pancreas graft survival rates
  - the field is already one of the safest

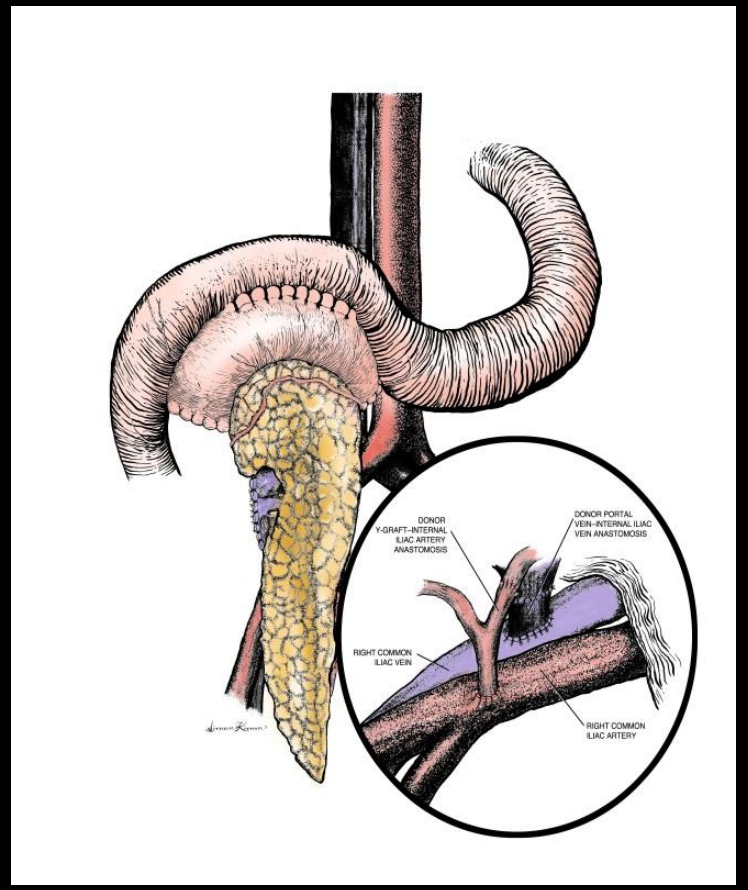
  Pancreas Tx is already too conservative
  - fewer Txs will be performed
  - such a move will result in more deaths on WL
- Promote a culture of internal assessment of safety and quality performance so programs are inspired to improve over time.

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

Comparison is the thief of joy.

Theodore Roosevelt

The Noble Pancreas Transplant



A better life . . .

UW Pancreas Transplant Team

- Jon Odorico, Surgical Director
- Dixon B. Kaufman
- Robert Redfield
- David Al-Adra
- Didier Mandelbrot, Medical Director
- Nancy Radke, RN
- Mary Shanahan, RN
- Christa Finch, RN