

Transplant Triumphs
Advancements & Breakthrough in
Solid Organ Transplants

What will we do today?

- 01 Transplants 101
- 02 Which and How many?
- 03 Solid Organ Transplants
- 04 Parting Thoughts
- 05 Future of Solid Organ Transplants



Organ Transplants

- Solid Organ Transplants

- Kidney
- Liver
- Heart
- Lung
- Pancreas
- Intestine
- Combo-Transplants
 - Heart & Lung
 - Pancreas & Kidney
 - Heart & Liver
 - Intestine & Pancreas

- Tissue Transplants

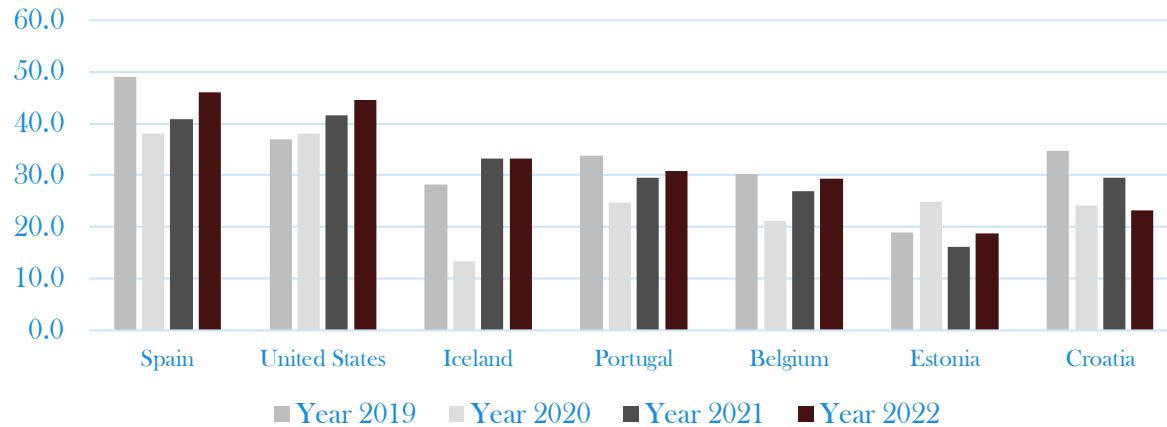
- Bones
- Tendons
- Ligaments
- Skin
- Heart valves
- Blood vessels
- Corneas

Solid Organ Transplants Global & USA

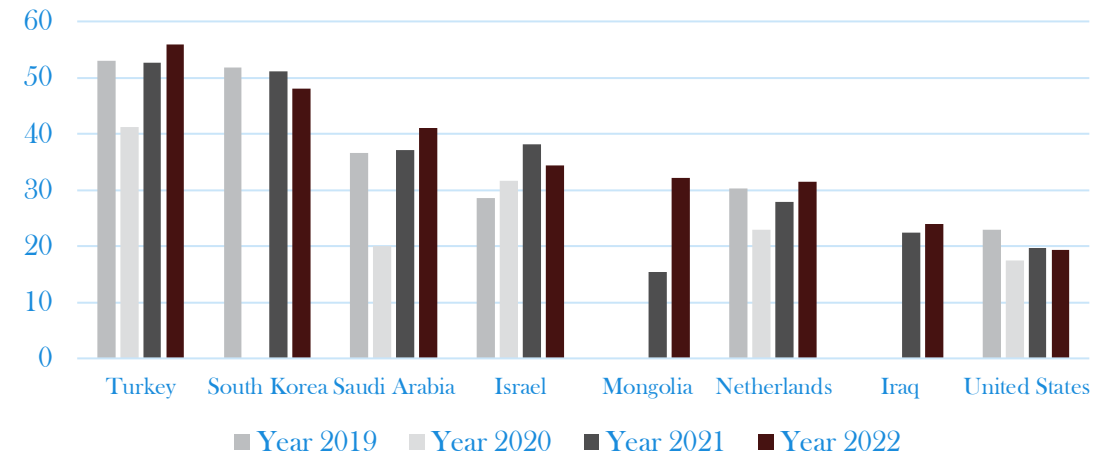


Solid Organ Transplant Trends - International

International Trends in Solid Organ Transplant Rate - Deceased Donor
(Per Million of Population)

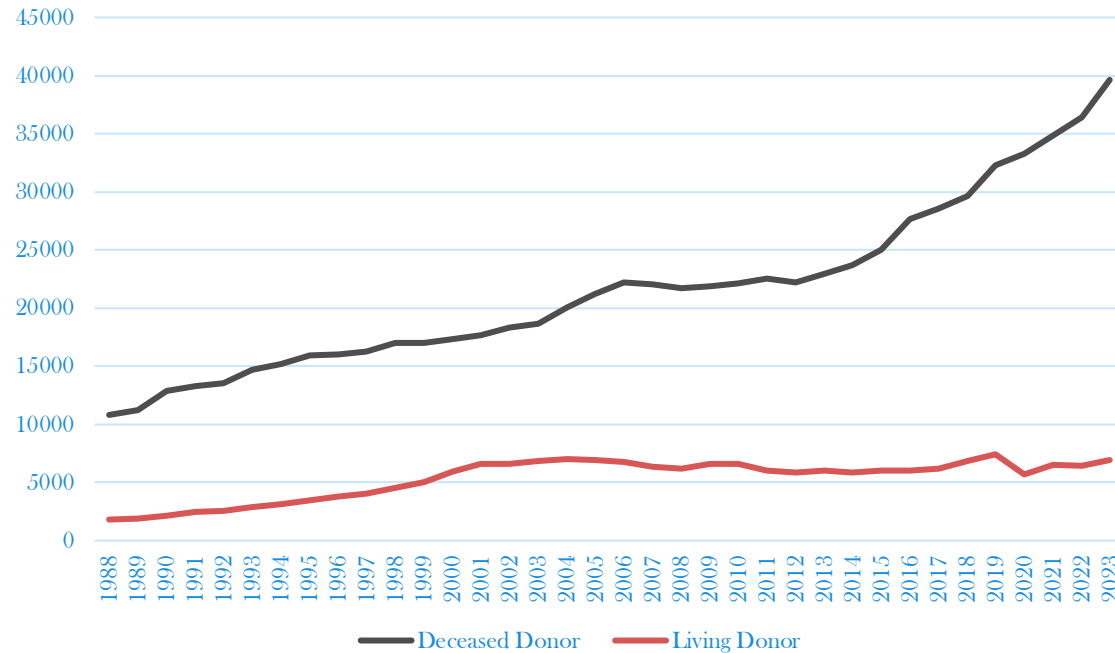


International Trends in Solid Organ Transplant Rate - Living Donor
(Per Million of Population)

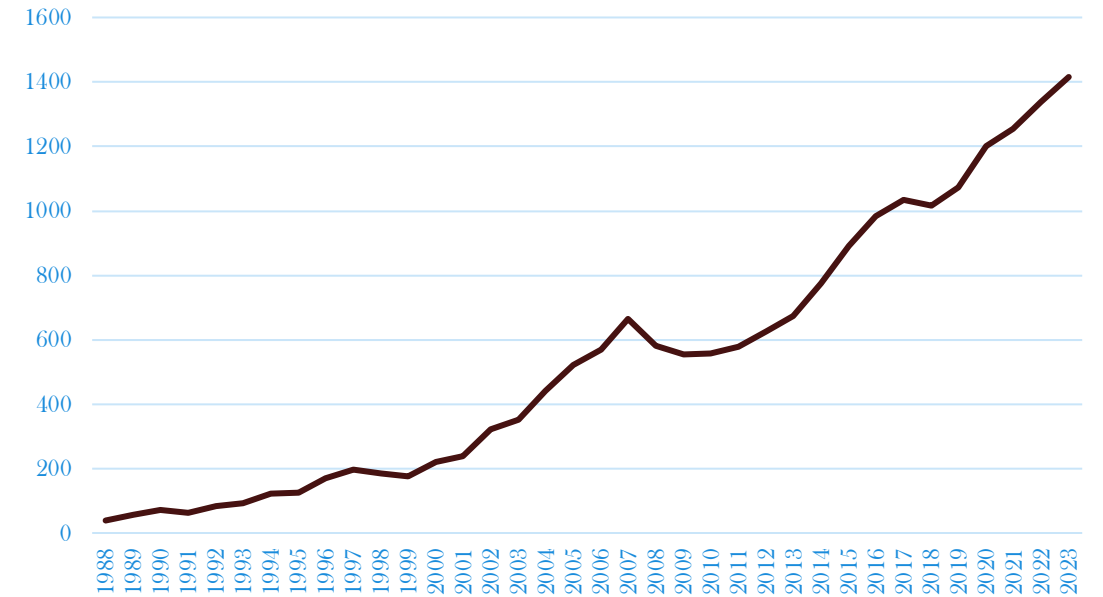


Solid Organ Transplants in USA 1988-2023

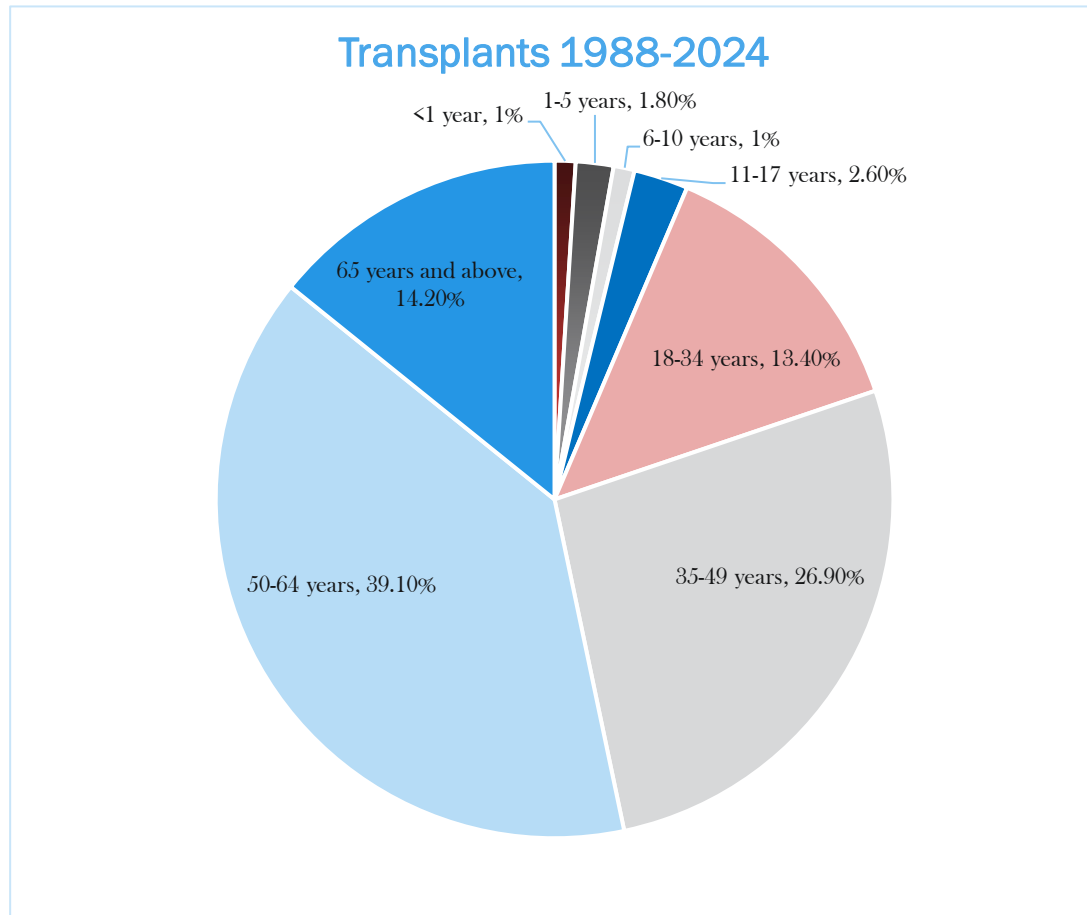
Solid Organ Transplants



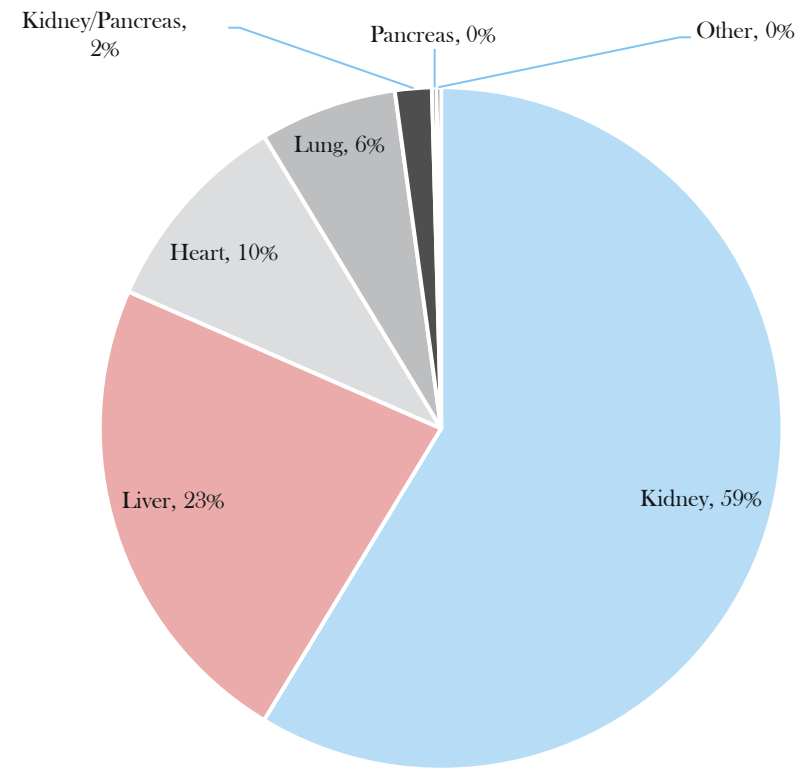
Multiple Organ Transplant



Solid Organ Transplants – Age & Organs



Transplants performed by organs - As of March, 2024



Post-transplant Survival



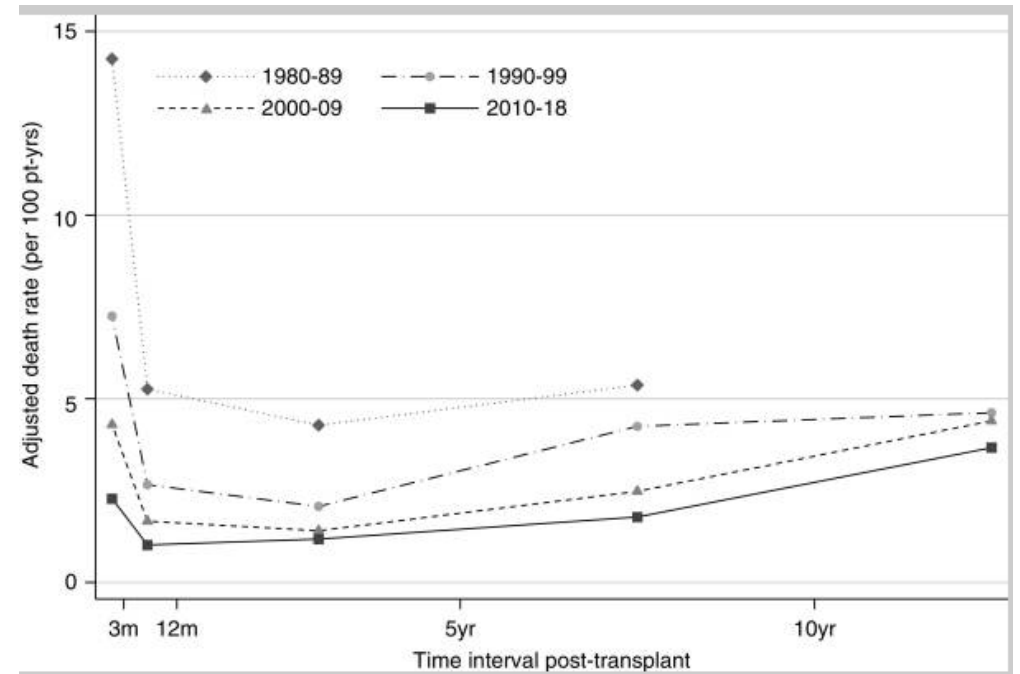
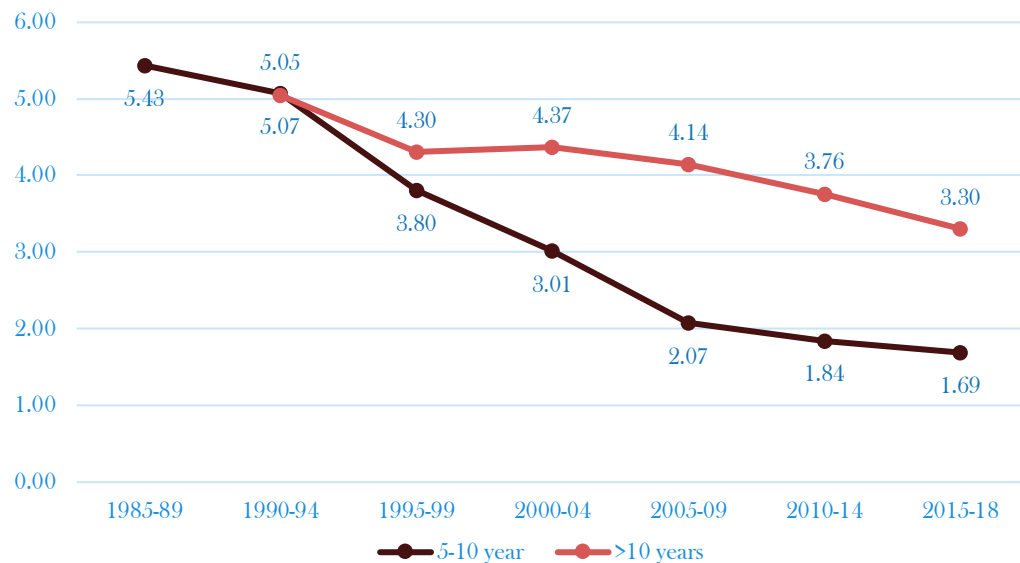
Case Study 1

- Male 67
 - BMI 30.19 and BP 140/82.
 - Medical History: Diabetes, Sleep Apnea, Chronic Pain, and Renal Transplant.
- Solitary (right) kidney transplant in July 2012 for ESRD.
 - Living donor transplant, HLA-matched.
 - On mycophenolate (CellCept) for immunosuppression. Recent follow-up 02/2024 - no graft dysfunction, eGFR 74 in December 2023.
 - Diabetes, HbA1c: 4.7 in Aug and Dec 2023.

What do you think about our case?

Male 67, Diabetic, Renal transplant in July 2012

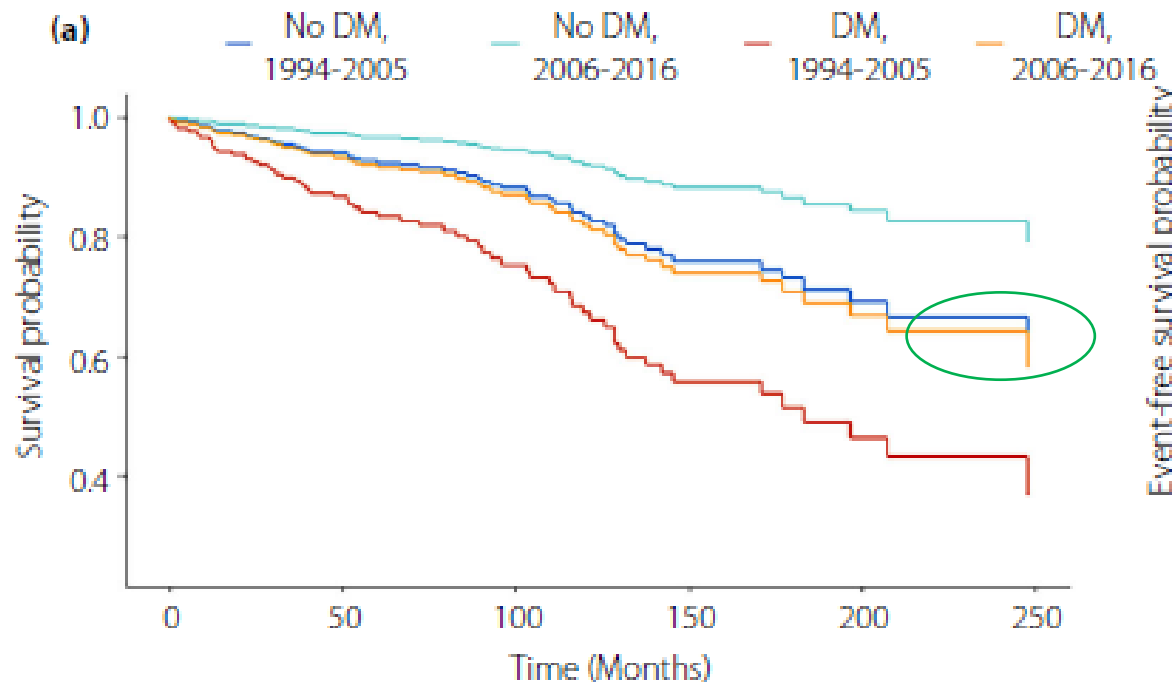
Kidney Transplant - Age adjusted death rates 1985-2018



Ying, Tracey, et al. "Death after kidney transplantation: an analysis by era and time post-transplant." *Journal of the American Society of Nephrology* 31.12 (2020): 2887-2899.

Kidney Transplant

Male 67, Diabetic, Renal transplant in July 2012



Median Survival (In # of years)	Deceased Donor Transplant	Living Donor Transplant	Mortality Ratio
Mean Age - 50 years (US General population)			
Mortality Ratios based on Fasano's Mortality Tables (2020)			
1995-99	8.20	12.10	750
2000-04	8.80	12.90	650
2005-09	9.70	13.90	550
2010-13	10.30	15.70	400
2014-17	11.70	19.20	310

Jeon, Ja Young, et al. "Trends in the effects of pre-transplant diabetes on mortality and cardiovascular events after kidney transplantation." *Journal of Diabetes Investigation* 12.5 (2021): 811-818.
 Poggio, Emilio D., et al. "Long-term kidney transplant graft survival—Making progress when most needed." *American journal of transplantation* 21.8 (2021): 2824-2832.

Underwriting Alerts in Kidney Transplant

Underwriting Alerts	Risk of Death
Deceased Donor transplant vs. Living Donor	1.5- 1.75 X
Diabetes (pre- or post-transplant) vs. Non-Diabetics	1.3-1.5 X
CAD, CHF, angina, MI or other cardiovascular disease vs. None	1.3-1.5 X
With graft dysfunction	>2 X
Failed/inadequate immunosuppression, noncompliance	>2 X



What would be your decision on Case 1

- A. Not within insurable limits
- B. Postpone
- C. Need more information
- D. Insurable with Rating

Male 67

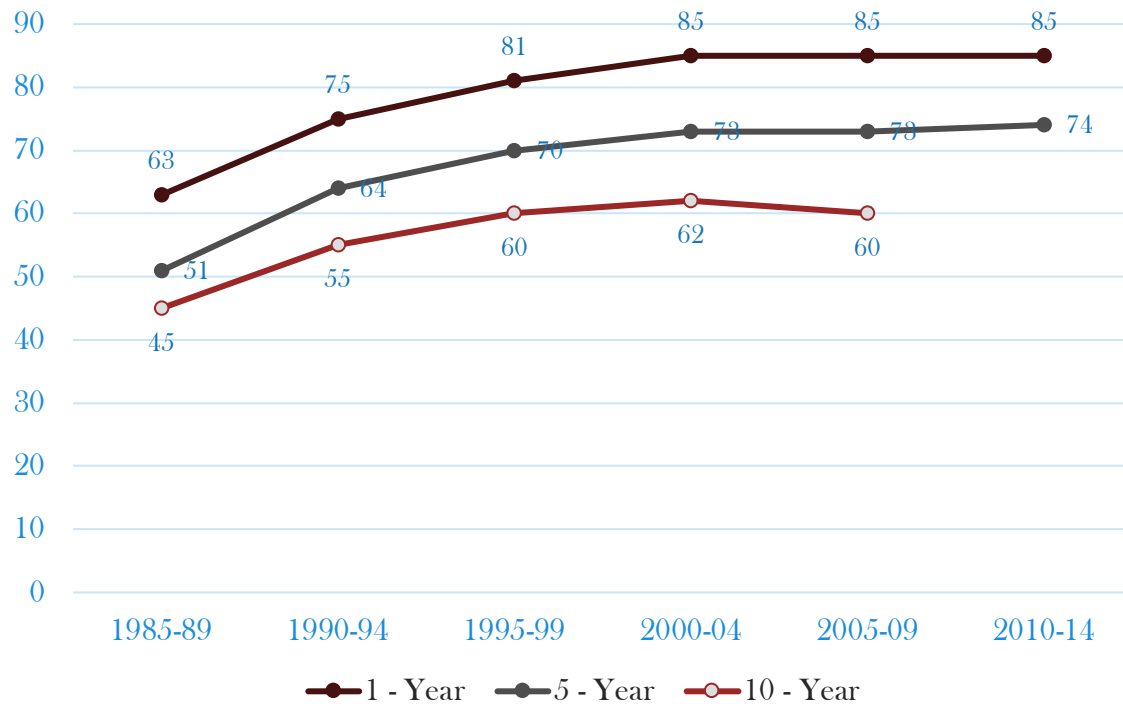
- Solitary Kidney transplant – 12 yrs. since transplant
- Living donor
- Diabetic, HbA1c 4.7
- No graft dysfunction
- No CAD, angina or cardiovascular disease

Case Study 2

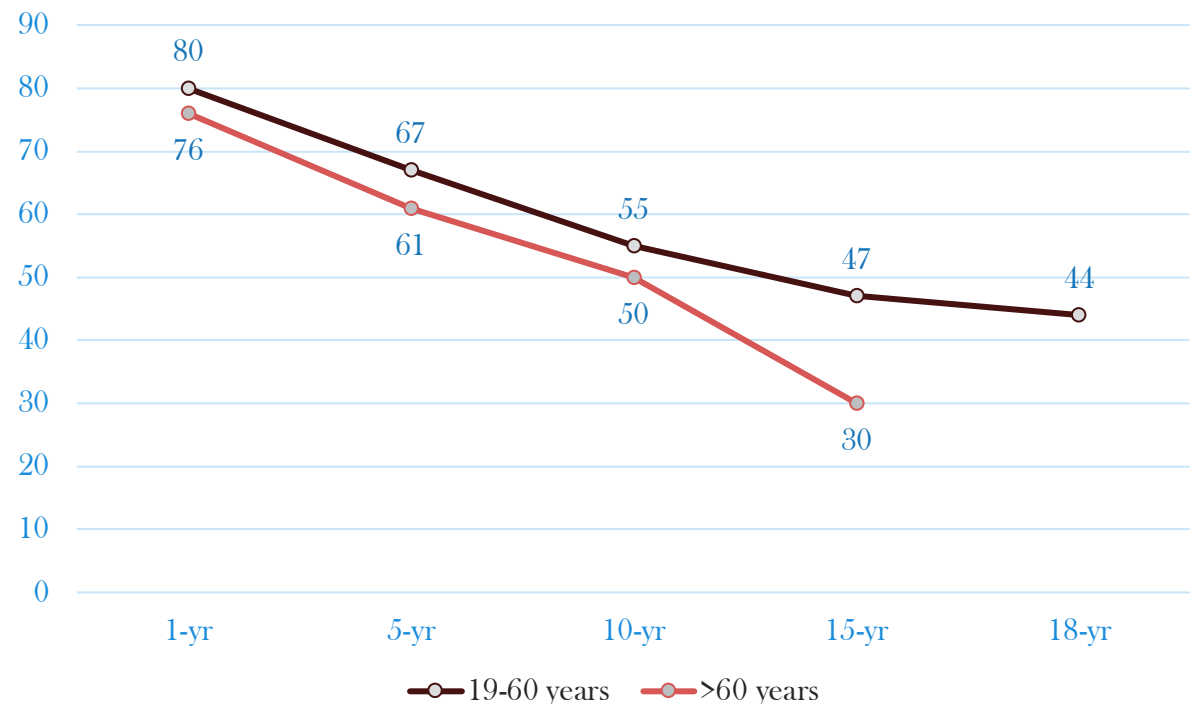
- Male 71
- Medical records July 2019 to Feb 2024: Liver transplant, Pulmonary Embolism + DVT, MGUS
- Deceased donor liver transplant
 - October 2014 for decompensated non-alcoholic liver cirrhosis due to presumed PSC.
 - Full-sized DBD Transplanted liver was CMV positive + NASH. No PSC or malignancy.
 - Regular follow-up, imaging and biopsies. On daily tacrolimus (PROGRAF)
 - Biopsy: 01/2018: Negative for graft rejection
 - 08/2023: MRI abdomen, MRCP, FibroScan® : normal to mildly inflamed liver parenchyma, no cirrhosis, patent transplant, normal resistive indices
 - LFTs: Normal
- PE + DVT: Single episode 2019
- MGUS: 08/2023: IgA/IgM/IgG
- ECHO: 05/2022: No abnormalities, EF 50-55%
- Carotid Ultrasound: 05/2022: No stenosis

Liver Transplant

Survival trends in liver transplant Europe (119,125 patients)

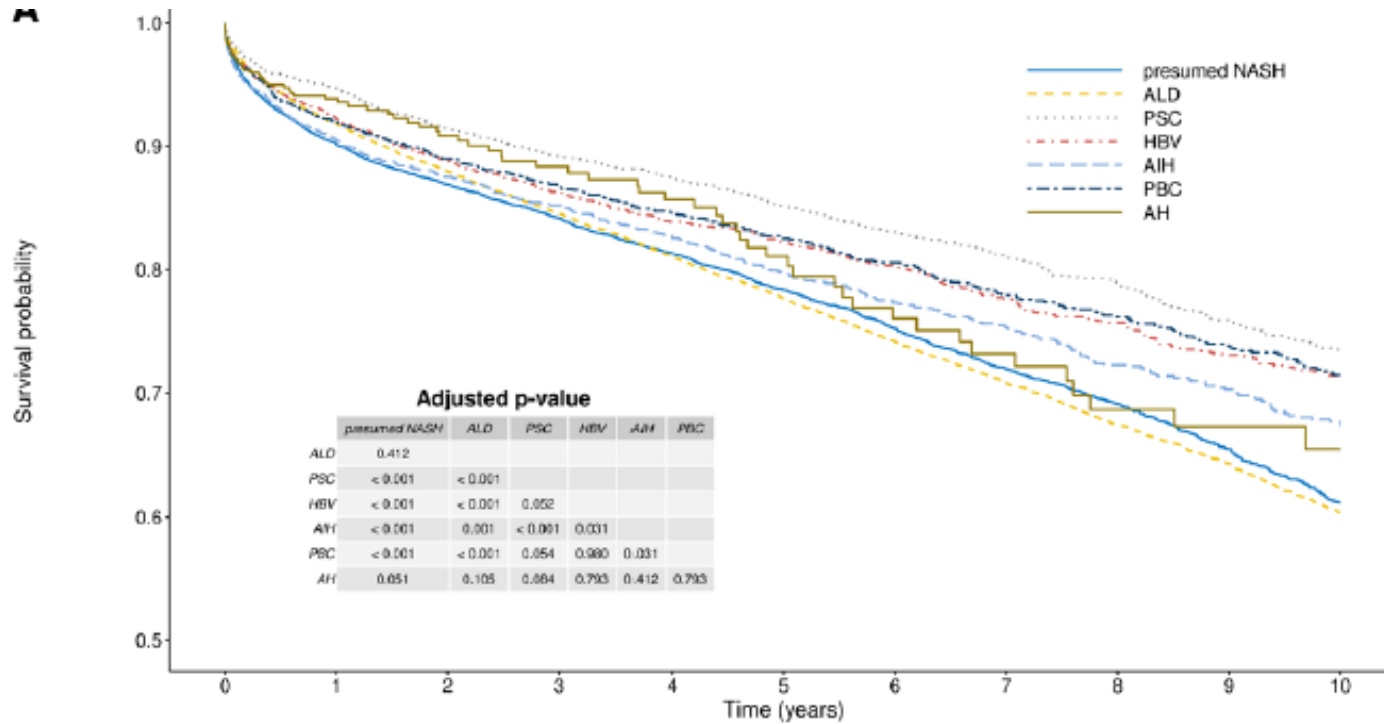


Long-term survival in liver transplant patients



René Adam, Vincent Karam, Valérie Cailliez, John O Grady, Darius Mirza, et al.. 2018 Annual Report of the European Liver Transplant Registry (ELTR) - 50-year evolution of liver transplantation. Transplant International, 2018, 31 (12), pp.1293-1317. 10.1111/tri.13358. hal-02313592

Survival after Liver Transplant



Abbreviations	
NASH	= non-alcoholic steatohepatitis
ALD	= alcoholic liver disease
PSC	= primary sclerosing cholangitis
HBV	= hepatitis B virus
AIH	= autoimmune hepatitis
PBC	= primary biliary cholangitis
AH	= acute alcoholic hepatitis

Jamil, Omar K., et al. "Relatively poor long-term outcomes following liver transplantation for NASH in the United States." *Transplantation* 106.10 (2022): 2006-2018.

Survival in Liver Transplant - NASH

Age at transplant (in years)	LE at transplant (in years)	General Population (GP) LE (in years)	Mortality Ratio	LE 5-year after LT (in years)	LE in 5-year GP (in years)	Mortality Ratio
Males				5-year Survivors		
40	20	39	500	18	34	375
50	16	30	375	14	26	300
60	13	22	275	11	18	200
70	10	15	200	9	11	125
Females						
40	20	43	800	17	38	675
50	16	33	550	14	29	450
60	13	25	400	11	21	300
70	10	17	275	9	13	175

Shavelle, Robert M., et al. "Life expectancy after liver transplantation for NASH." *Progress in Transplantation* 32.2 (2022): 102-111.

Underwriting Alerts in Liver Transplant

Underwriting Alerts	Risk of Death
Graft rejection/dysfunction	Leads to re-transplant or >2 X
1 st Re-transplant	2X
2 nd Re-transplant	3X
Vascular complications	1.25-1.5X
Liver complications	1.25-1.8X
BMI <18	2X
BMI >40	1.5X
Comorbid hepatitis C	>2X
Diabetes	1.15-1.25X
Females	1.15X



What would be your decision on Case 2

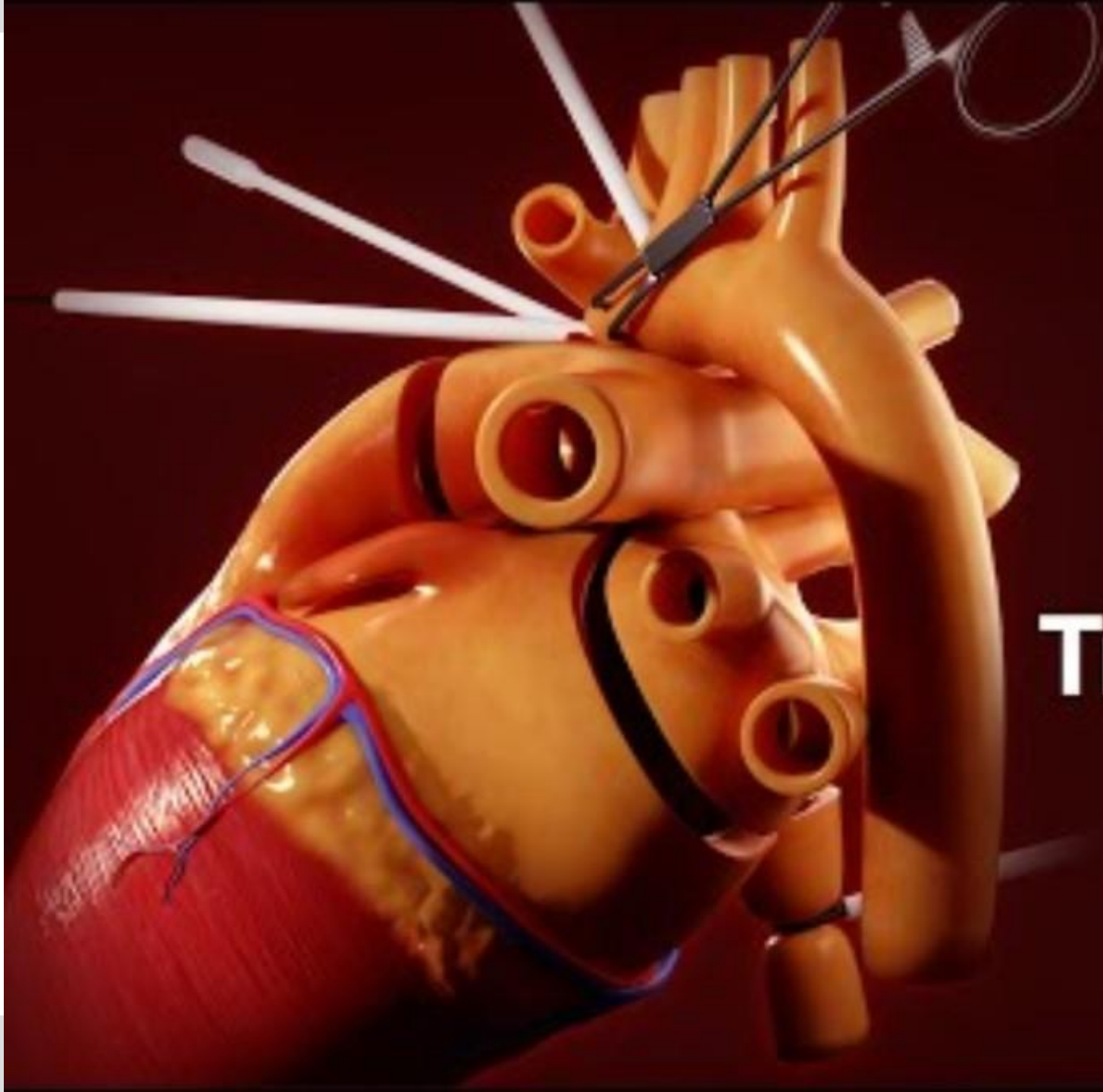
- A. Not within insurable limits
- B. Postpone
- C. Need more information
- D. Insurable with Rating

Male 71

- Full-sized Liver transplant for presumed PSC
– 10 yrs. since transplant
- Sustained virologic response on tacrolimus
- No graft rejection, biopsies negative
- Normal imaging and LFTs

Case Study 3

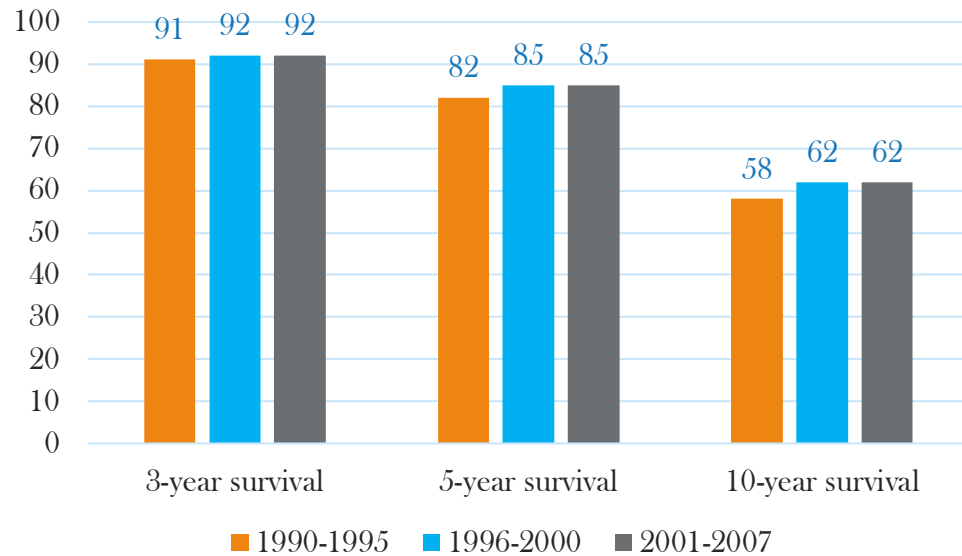
- Male 62
- Medical records 2016 to 2023: Heart transplant, Stroke, Atrial Fibrillation + DVT
- Orthotopic heart transplant
 - Heart transplant in May 2018 for end-stage heart failure due to hypertrophic cardiomyopathy (HCM).
 - Biopsy in June 2018, no acute cellular rejection or antibody mediated rejection.
 - On immunosuppressive medication azathioprine, good compliance
 - CAG in Oct 2018, normal, no obstructive CAD
 - Regular follow up, cardiac work up of 2023: No ischemia, no RWMA, no cardiomyopathy or CHF, normal EF 55-65%, mild LVH
- Stroke: Single episode 2016, no residual. MRI of 06/2023 unremarkable
- DVT: Diagnosed in 2015, extensive disease in LLE. Duplex ultrasound in 2023 - no DVT
- Paroxysmal atrial fibrillation: Prior to heart transplant, continues to be on anticoagulant.



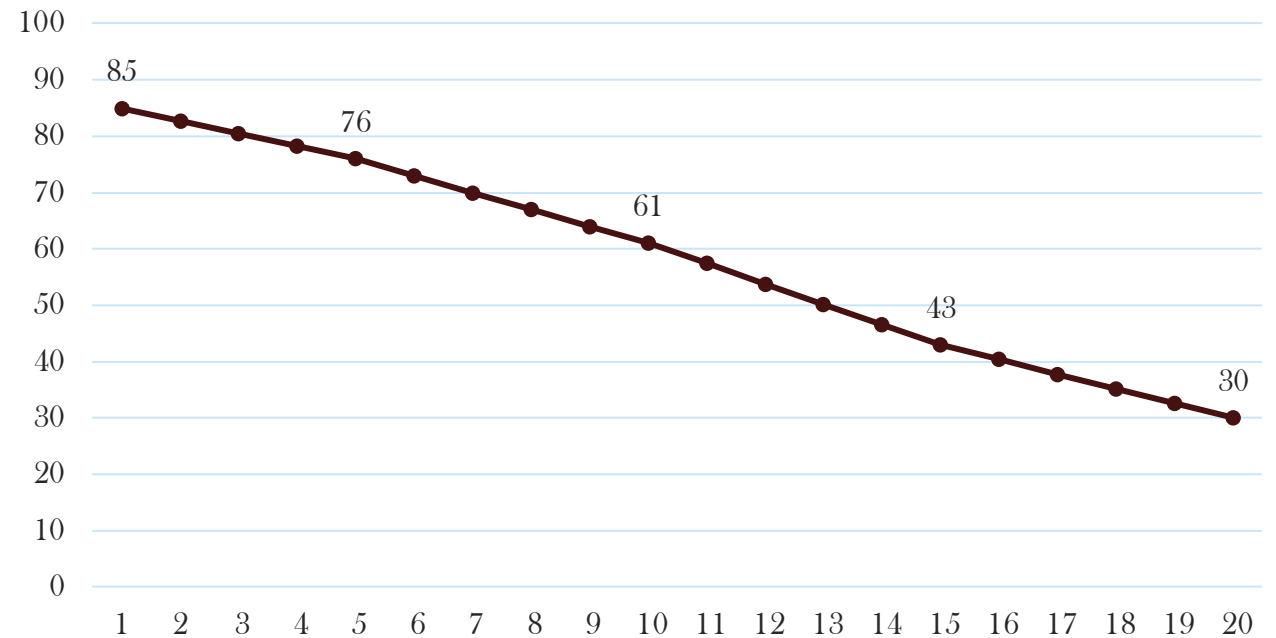
Orthotopic Heart Transplantation

Survival Trends in Heart Transplant

1-year Survivors of Heart Transplant
USA 1990-2017



20-years Survival in Europe 1983-2009

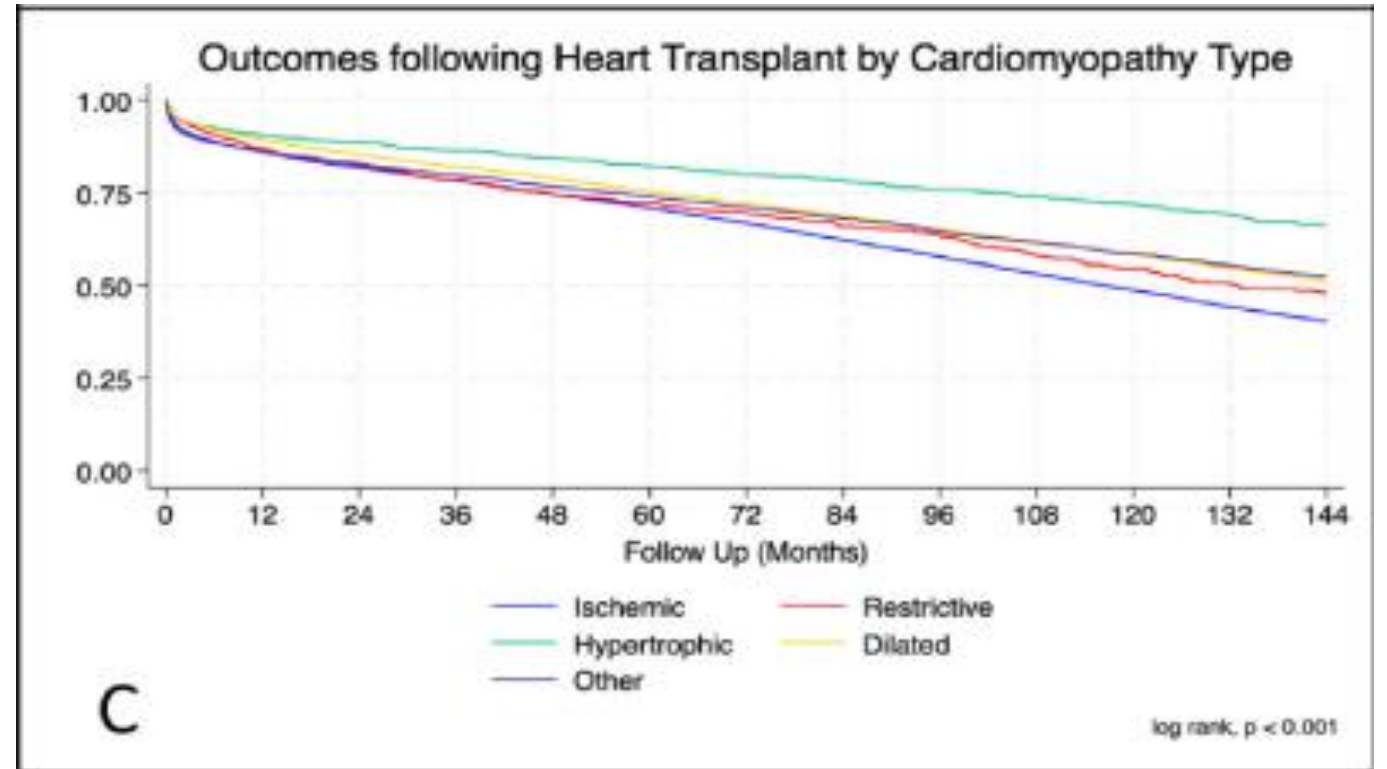


Suarez-Pierre, Alejandro, et al. "Long-term survival after heart transplantation: a population-based nested case-control study." *The Annals of Thoracic Surgery* 111.3 (2021): 889-898.

Dellgren, Göran, et al. "Three decades of heart transplantation in Scandinavia: long-term follow-up." *European journal of heart failure* 15.3 (2013): 308-315.

Heart Transplant

- Indications for transplant
 - Cardiomyopathy
 - Ischemic
 - Restrictive
 - Hypertrophic
 - Dilated
 - Other CM
 - Coronary artery disease
 - Congenital heart disease
 - Valvular disorders
 - Re-transplant

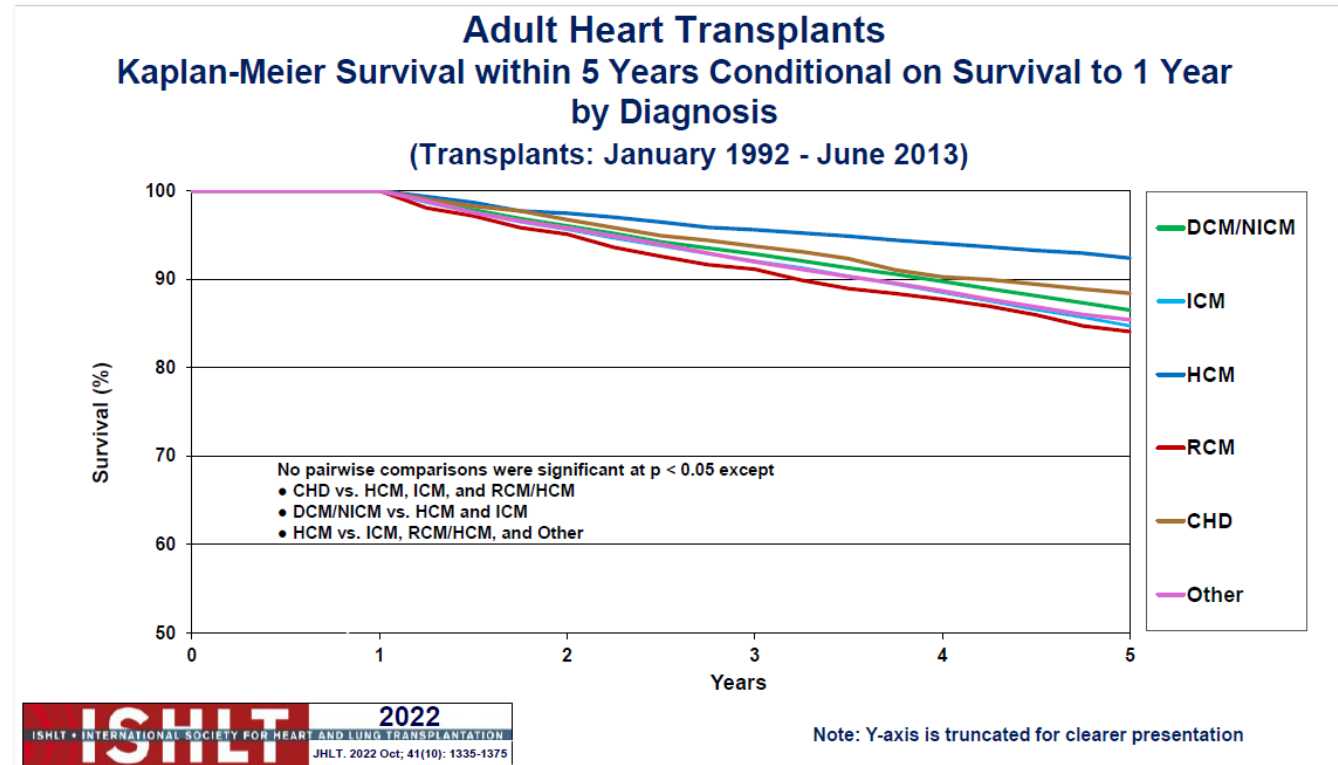


Miklin, Daniel J., and Eugene C. DePasquale. "Heart transplant outcomes in restrictive cardiomyopathy: UNOS registry analysis of the last three decades." *JHLT Open* 3 (2024): 100031.

What do you think about our Case?

Male 62, heart transplant 2018 for HCM, no graft failure, normal cardiac work-up

Variables	Standardized Mortality Ratio (SMR)
Male	2.68
Female	3.63
Transplant Era	
1990-1995	3.09
1996-2000	2.90
2001-2007	2.58
Overall	2.84



Suarez-Pierre, Alejandro, et al. "Long-term survival after heart transplantation: a population-based nested case-control study." *The Annals of Thoracic Surgery* 111.3 (2021): 889-898.

Hsich, Eileen, et al. "The International thoracic organ transplant registry of the international society for heart and lung transplantation: Thirty-ninth adult heart transplantation report—2022; focus on transplant for restrictive heart disease." *The Journal of Heart and Lung Transplantation* 41.10 (2022): 1366-1375.

Underwriting Alerts in Heart Transplant

Underwriting Alerts	Risk of Death
Graft Failure	2X
Infection (non CMV)	>2X
Multiple organ failure	>3X
Re-transplant	1.5-2X
eGFR <50	1.10-2.5X
Donor age >50 years	1.5-2X
BMI <18 and BMI >35	1.5-2X
Current age <55 years	1.5X
Diabetes	1.15-1.5X
Donor CMV +ve	1.2X



What would be your decision on Case 3?

- A. Not within insurable limits
- B. Postpone
- C. Need more information
- D. Insurable with Rating

Male 62

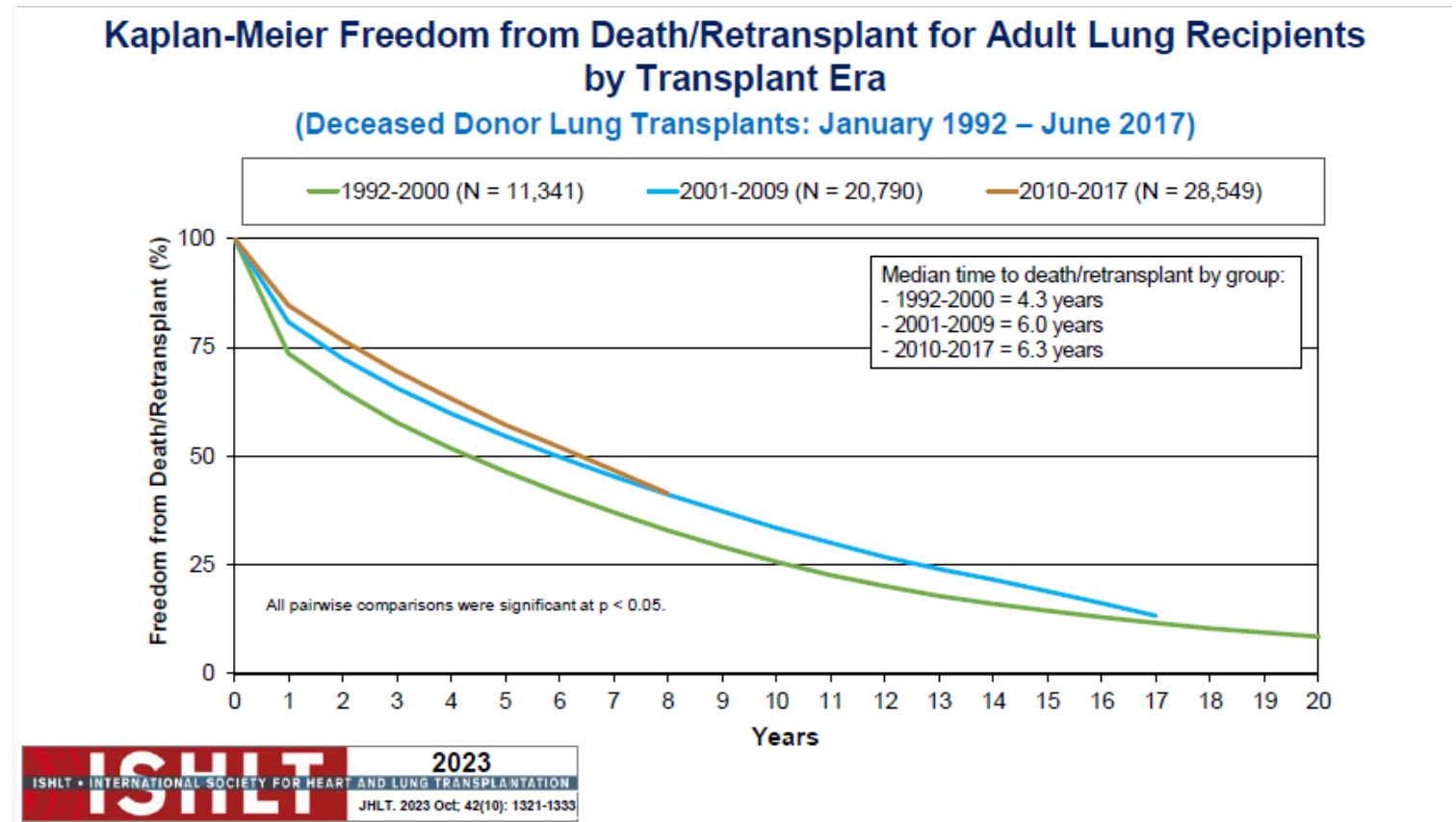
- Heart transplant for HCM - 5 yrs. since transplant
- No graft rejection, biopsies negative
- Normal cardiac work-up
- Paroxysmal atrial fibrillation, stroke, DVT

Case Study 4

- Male 54
- Medical records 2019 to 2023: Double lung transplant, pre-diabetes, chronic kidney disease
- Double lung transplant
 - Double lung transplant in 9/2011 for primary pulmonary hypertension.
 - On immunosuppressive medications, good compliance, no graft failure.
 - PFTs: FVC and FEV1 81% and 79% in 09/2020, 79% and 74% in 03/2021, 77% and 74% in 09/2021, and 81% and 76% in 09/2022.
 - ECHO 11/2023: Normal with PASP 21 mmHg and EF 65%
- Chronic kidney disease: eGFR (N: >60) 47 in 2021, 61 in 03/2022, and 57 in 07/2023.
- Pre-diabetes: Hba1c 5.9 in 09/2021, 6.1 in 09/2022, and 5.5 in 12/2023.

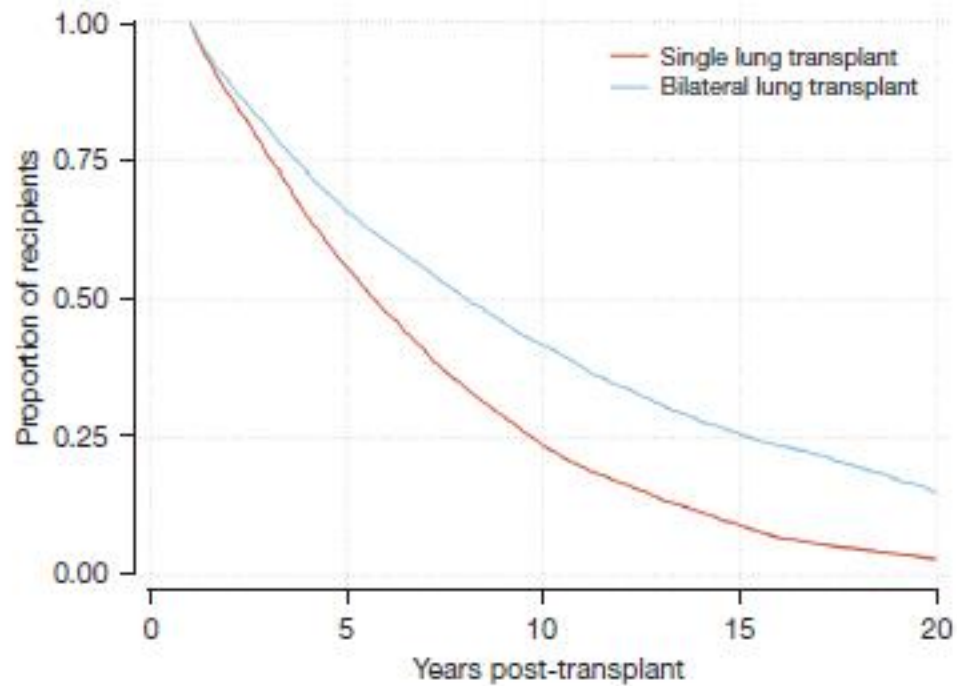
Lung Transplant

- Interstitial lung disease - 40%
 - Idiopathic pulmonary fibrosis
 - Idiopathic interstitial pneumonia
- Chronic obstructive pulmonary disease
- Cystic fibrosis
- Pulmonary arterial hypertension (<5%)
- Alpha-1 antitrypsin deficiency emphysema

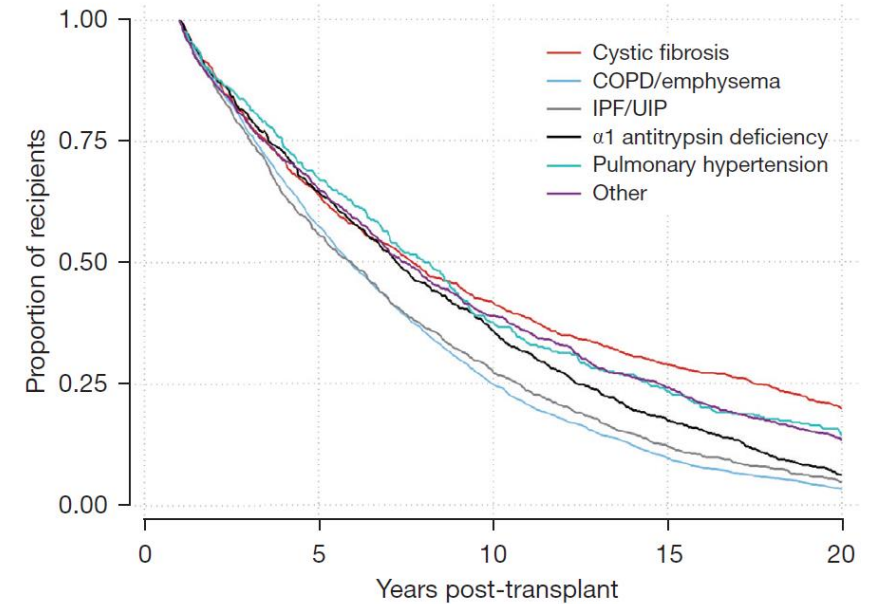


Survival after lung transplant

Long-term survival by transplant type

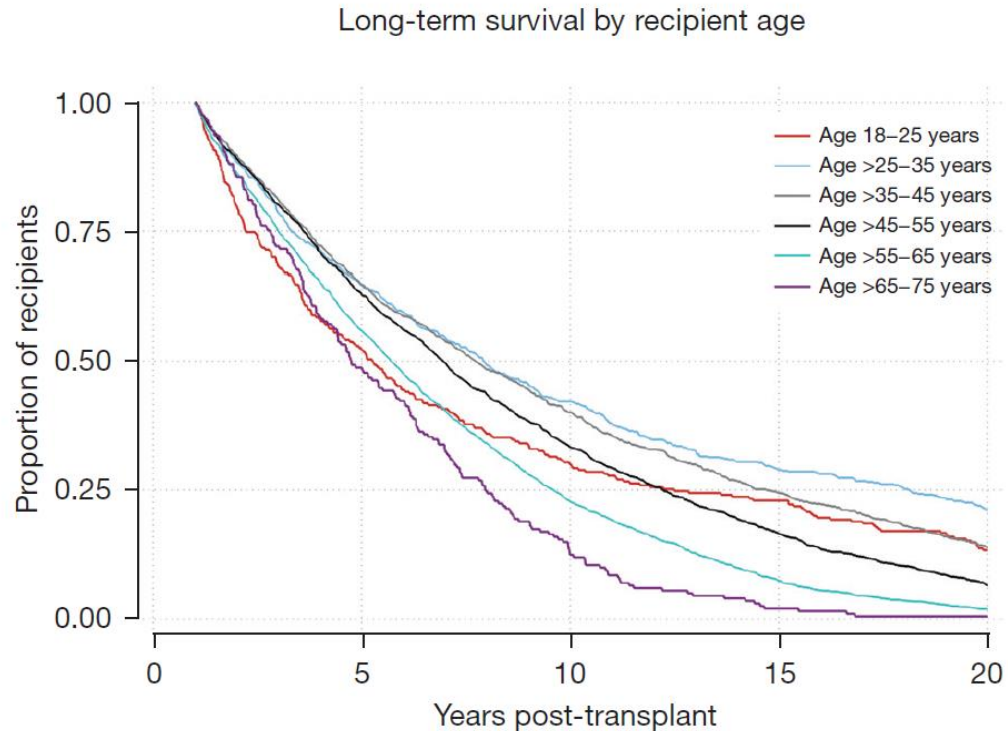


Long-term survival by recipient diagnosis



Miggins, John James, et al. "Twenty-year survival following lung transplantation." *Journal of Thoracic Disease* 15.6 (2023): 2997.

Lung Transplant Survival Rates



Median Age (in yr.)	Survival Rates			Mortality Ratio (General population, US – 20-year survival)
	5-yr.	10-yr.	20-yr.	
21.5	52.05	30.00	13.07	7,075
30	64.87	42.05	21.02	2,975
40	64.87	39.74	13.84	1,000
50	63.07	33.07	6.41	1,275
60	55.64	22.50	1.50	900
70	48.71	12.56	0.25	450

Miggins, John James, et al. "Twenty-year survival following lung transplantation." *Journal of Thoracic Disease* 15.6 (2023): 2997.

Underwriting Alerts in Lung Transplant

Underwriting Alerts	Risk of Death
Primary graft dysfunction	>2X
eGFR <20	2X
Single lung transplant	1.25-1.5X
Cigarette use	1.12-1.25X
Diabetes	1.10-1.25X
Males	1.10-1.2X



Jawitz, Oliver K., et al. "Factors associated with short-versus long-term survival after lung transplant." *The Journal of thoracic and cardiovascular surgery* 163.3 (2022): 853-860.

What would be your decision on Case 4?

- A. Not within insurable limits
- B. Postpone
- C. Need more information
- D. Insurable with Rating

Male 54

- Double lung transplant in 2011 for primary pulmonary hypertension; now 13 years since transplant
- No graft rejection, PFTs show mild obstruction
- Immunosuppressed, good compliance
- Normal echocardiogram with normal PASP
- CKD with eGFR ~ 60s
- Pre-diabetes, Hba1c <6.1

Pancreas Transplant

- Indications for transplant
 - Type 1 Diabetes
 - Early onset Type 2 Diabetes
 - Diabetic complications including renal failure
- Types of transplant
 - Simultaneous Pancreas Kidney Transplant (SPK)
 - Pancreas after kidney transplant (PAK)
 - Pancreas transplants alone (PAT)

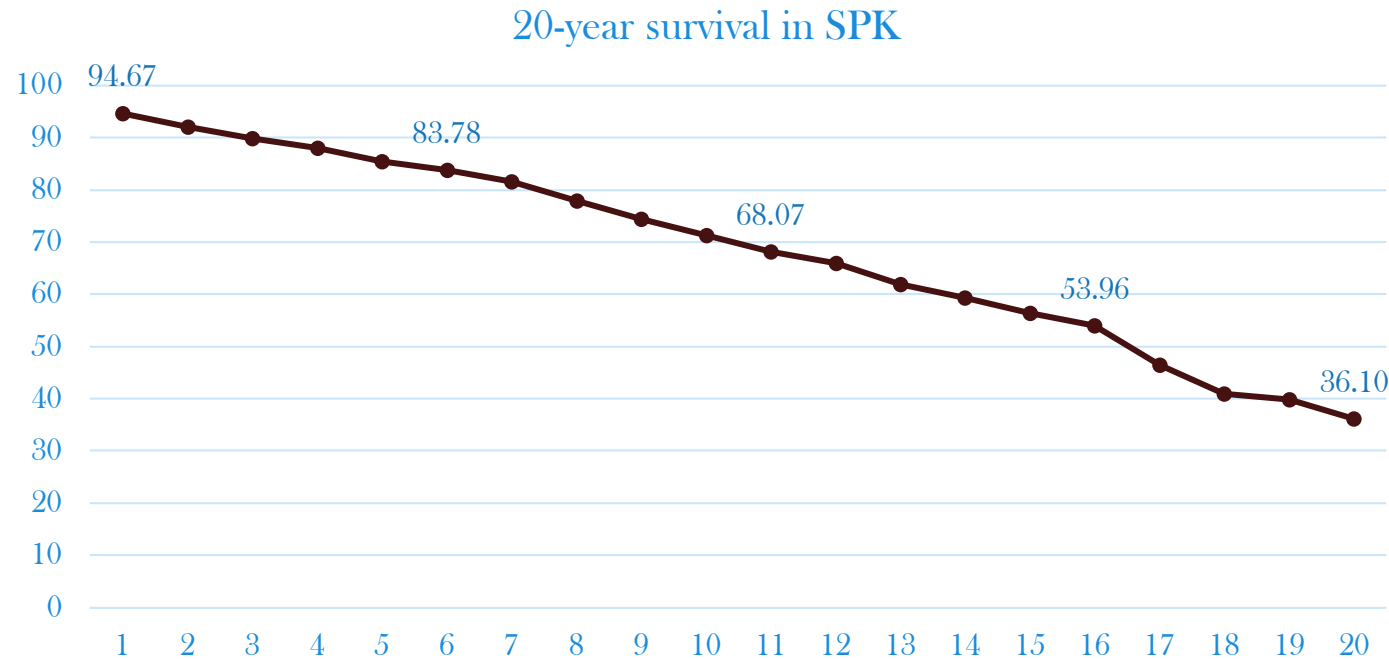
Year of Transplant	SPK	PAK	PAT
	Median Survival Time (In Months)		
1987-1993	109	22	29
1994-1997	130	59	35
1998-2001	137	76	71

Survival Rate	Males		Females	
	SPK	PAT	SPK	PAT
1-year	96.2	82.3	95.2	79.2
5-year	82.2	61.8	79.4	54.7

OPTN US National data for transplants performed between 2008-2015

Gruessner, Angelika C. "2011 update on pancreas transplantation: comprehensive trend analysis of 25,000 cases followed up over the course of twenty-four years at the International Pancreas Transplant Registry (IPTR)." *The review of diabetic studies: RDS* 8.1 (2011): 6.

Simultaneous Kidney Pancreas Transplant



Survival Rate	Corresponding MR
1-year	2,925
5-year	1,650
10-year	1,500
15-year	1,225
20-year	1,275
Mean Age 43 years, SPK during 2000-2015	

Esmeijer, Kevin, et al. "Superior long-term survival for simultaneous pancreas-kidney transplantation as renal replacement therapy: 30-year follow-up of a nationwide cohort." *Diabetes Care* 43.2 (2020): 321-328.

Underwriting Alerts in Pancreas Transplant

Risk of early mortality	Risk of Death
Failed kidney graft	13-25X
Failed pancreatic graft	2.5-4X
With history of kidney re-transplant	1.3-2.25X
Pre-transplant dialysis	1.1-185X
Age >45	1.3-2X



Guessner, Angelika C., and Rainer WG Guessner. "Pancreas transplantation of US and non-US cases from 2005 to 2014 as reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR)." *The review of diabetic studies: RDS* 13.1 (2016): 35.

Summary

- Survival with solid organ transplants continues to improve due to improvements in:
 - Organ donation
 - Surgical methods
 - Evaluation of immunological risks
 - Immunosuppressive medications
 - Regular and consistent monitoring of graft function
- Can be offered insurance?
 - Kidney, heart, and liver transplants
 - Lung, pancreas, intestine and combo transplants
 - Underwriting selection
 - Opportunity to offer short-term products
- Future improvements:
 - Transferring T cells and using immune suppressive dendritic cells



Thank You!



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