Increasing Use of DCD Livers: Are We getting Better?

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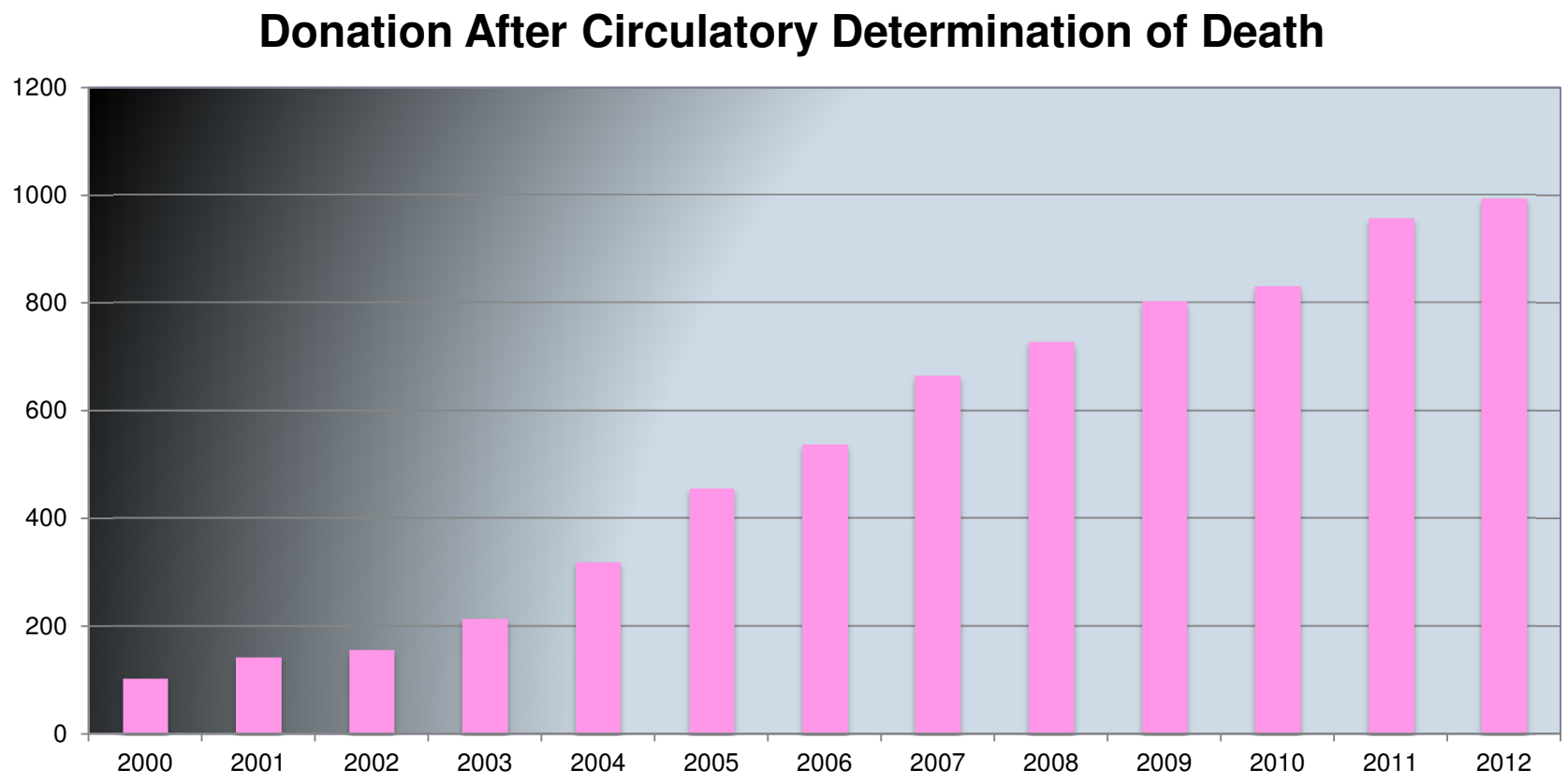
Conflict of Interest Disclosure

- I have no relevant financial relationships to disclose.

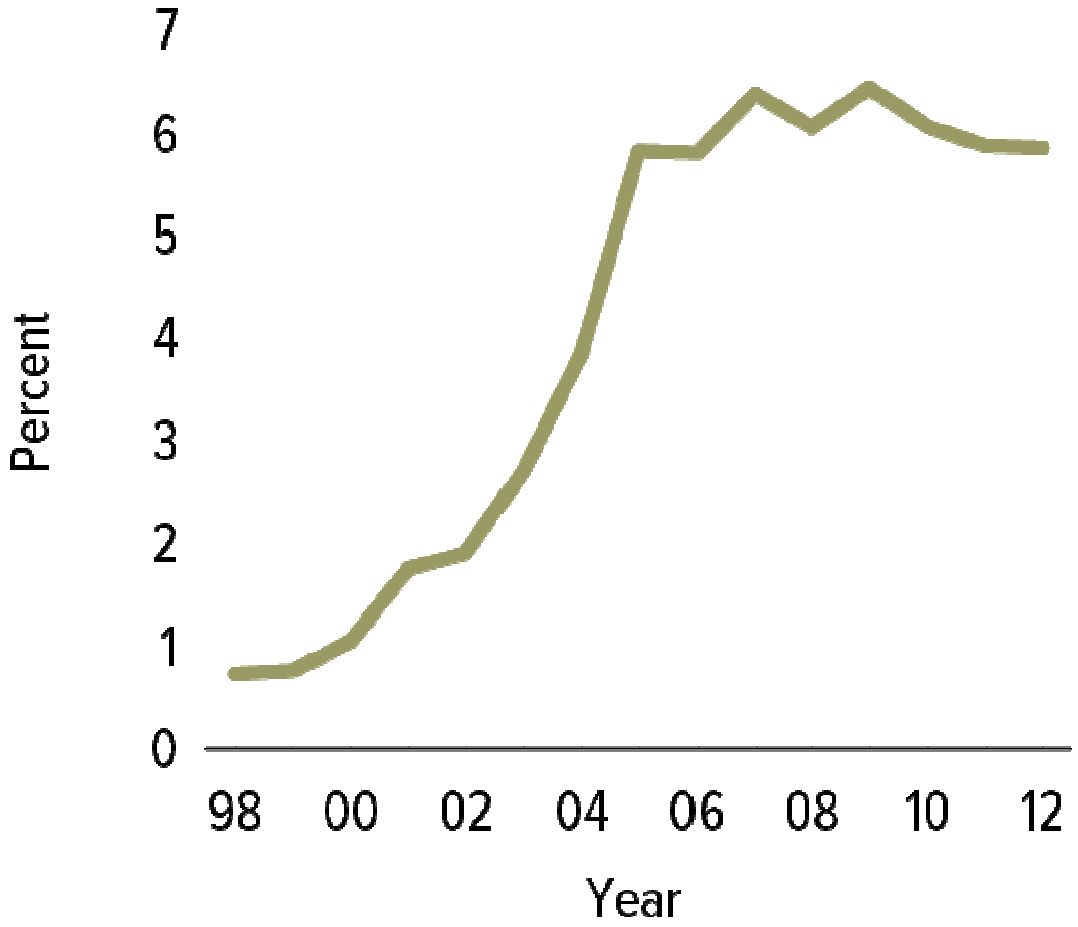
Nationwide Growth in Donation after Circulatory Determination of Death 2000-2012



In 2012, DCD donors provided 1,894 life-saving organ transplants

SRTR

Liver donors who are DCDD



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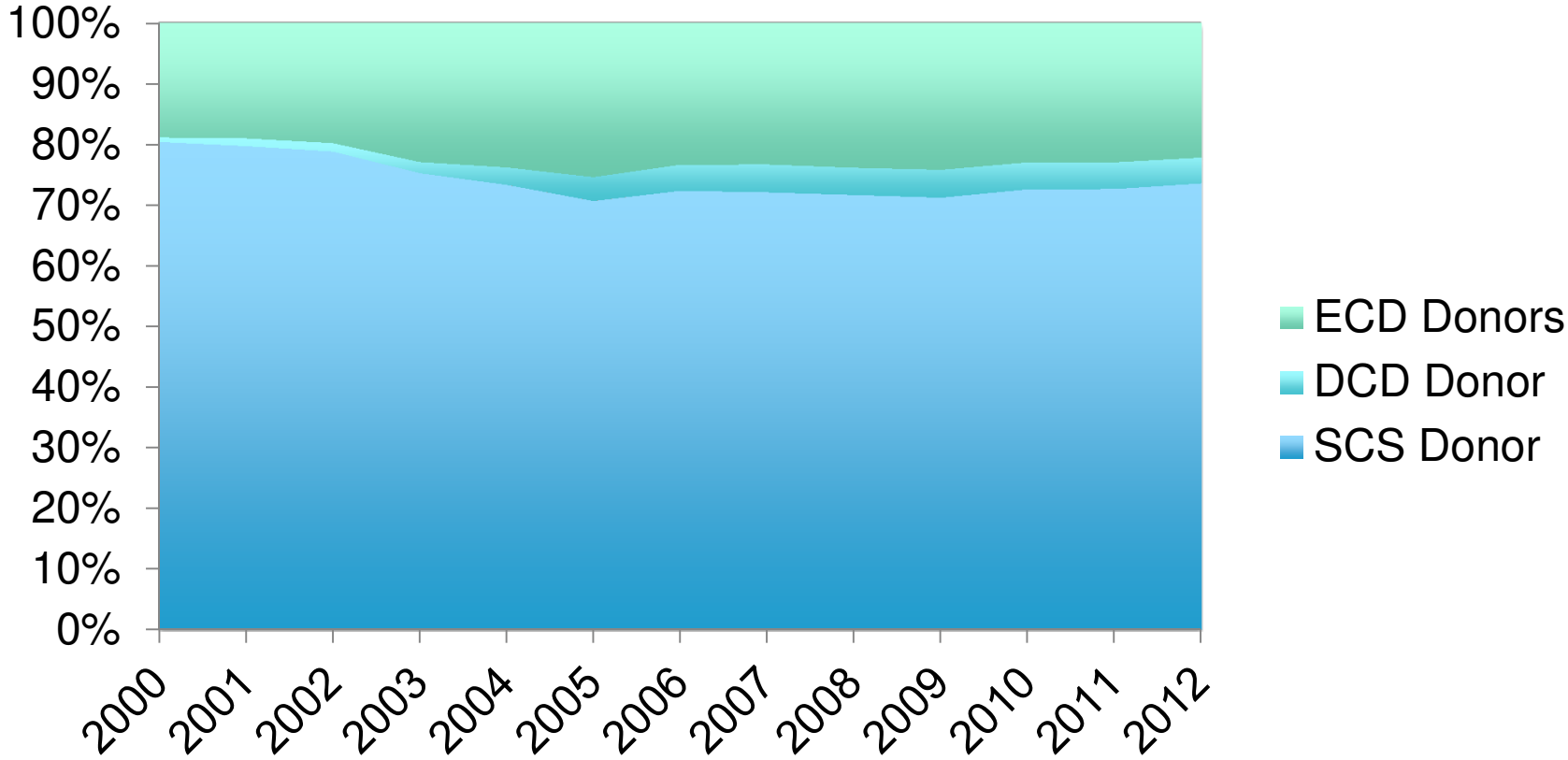
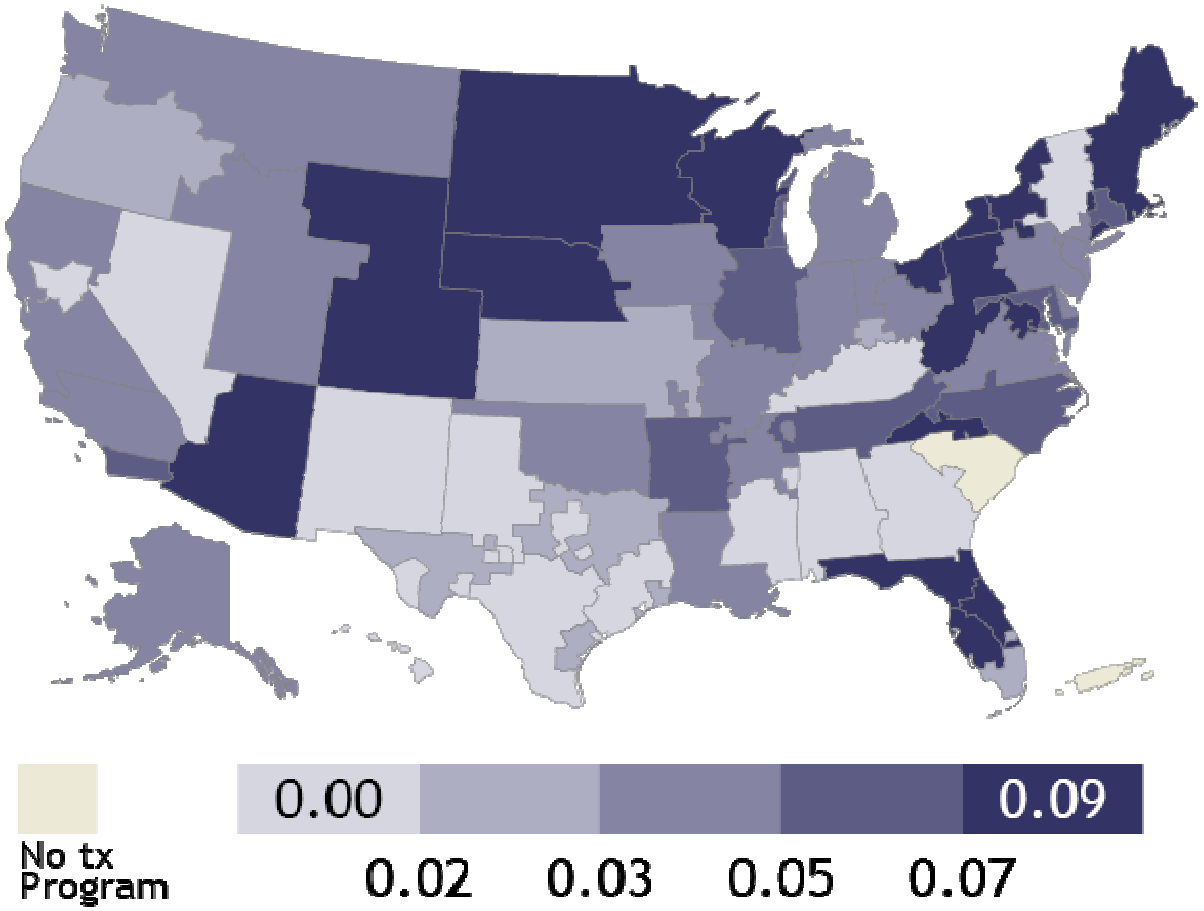
Liver Transplants by Type of Donor: DCDD Represents Only 4.5% of Livers Transplanted Annually



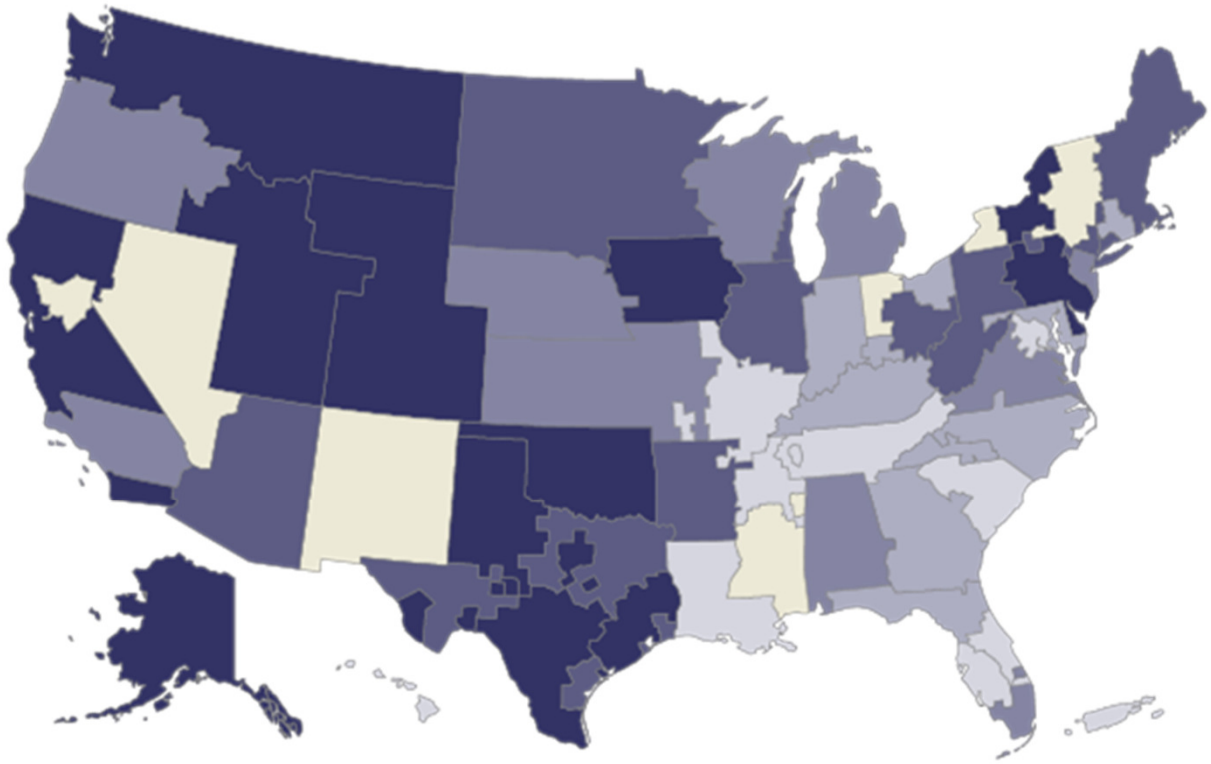
SRTR Annual Report, 2012

Variation in the Use of DCDD Donors Among Deceased Donor Transplant Recipients in 2012 by DSA: Liver



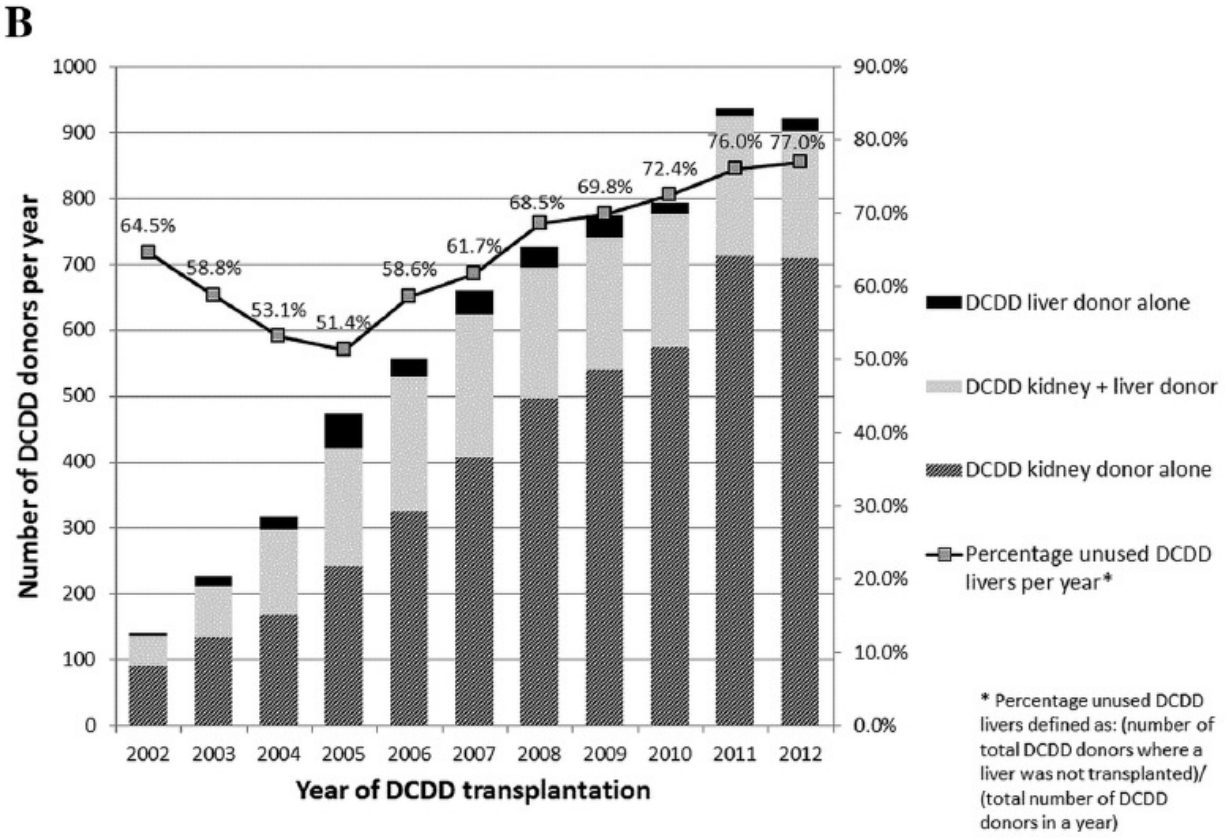
SRTR Annual Report, 2012

Variation in Waiting Time (Months) Among Deceased Donor Transplant Recipients in 2012 by DSA: Liver



SRTR Annual Report, 2012

DCDD Liver Donors Per Year Relative to All DCDD Donors



Goldberg et al. American Journal of Transplantation 2014; 14: 1016–1020

Patient Survival after DCDD Liver Transplantation

Center	Years	n	1 yr (%)	3 yr (%)	5 yr (%)	10 yr (%)	15 yr (%)	20 Yr (%)	p
Univ of Pittsburgh (de Vera et al. AJT, 2009; 9:773)	1993 - 2007	141	79		70	57			ns
Mayo Clinic, FL (Taner et al. Liver Trans 2012; 15:1028)	1998-2010	200	92.6	85.0	80.9				ns
Univ of Wisconsin (Foley et al. Ann Surg, 2011; 253:817)	1993-2008	87	84	72	68	54	**54**		**0.001**
St. James Univ Hospital, England (Pine et al. 2009; Liver Trans; 15:1072)	2002 - 2008	39	82.1	68.2					**< 0.0001**
Northwestern Univ (Skaro et al. 2009; Surgery, 146: 543)	2003 - 2008	32	74	74					ns
King's College, UK (DeOliveira et al. Ann Surg, 2011; 254: 716)	2001-2010	167							ns
Karolinska University, Stockholm, Sweden (Yamamoto et al. AJT, 2010; 10: 602)	**1984- 1988**	24	61.9		42.9	42.9		**38.1**	ns

Graft Survival after DCDD Liver Transplantation

Center	Years	n	1 yr (%)	3 yr (%)	5 yr (%)	10 yr (%)	15 yr (%)	20 yr (%)	p
Univ of Pittsburgh (de Vera et al. AJT, 2009; 9:773)	1993 -2007	141	69		56	44			**< 0.001**
Mayo Clinic, FL (Taner et al. Liver Trans 2012; 15:1028)	1998-2010	200	80.9	72.7	68.9				ns
Univ of Wisconsin (Foley et al. Ann Surg, 2011; 253:817)	1993-2008	87	69	60	56	43	43		**<0.01**
St. James Univ Hospital, England (Pine et al. 2009; Liver Trans; 15:1072)	2002 -2008	39	79.5	63.6					**0.001**
Northwestern Univ (Skaro et al. 2009; Surgery, 146: 543)	2003 - 2008	32	61	53					**0.005**
Karolinska University, Sweden (Yamamoto et al. AJT, 2010; 10: 602)	**1984- 1988**	24	54.2		37.5	37.5		29.2	ns
King's College, UK (DeOliveira et al. Ann Surg, 2011; 254: 716)	2001-2010	167							ns
UCLA (Hong et al. Arch Surg, 2011; 146: 1017-1023).	1994 - 2010	81	78	62	53				

National Database Studies: DCDD Liver Graft Survival

Reference	Years	n	1 yr (%)	3 yr (%)	5 yr (%)	p
Abt et al. Ann of Surg 2004; 239: 87.	1993 - 2001	144	70.2	63.3		**0.04**
Lee et al. Transplantation 2006; 82: 1683	1996 - 2006	874	72.1	61.8	38.8	**< 0.001**
Mateo et al. AJT 2006; 6: 791.	1996 - 2003	367	71	60		**< 0.001**
Merion et al. Ann Surg 2006; 244: 555.	2000 - 2004	472	70	60.5		**< 0.001**

Predictors of Graft Failure

Table 2: Predictors of graft failure following DCD liver transplantation[1]

	Variable	Hazard ratio	95% CI		p-Value
Recipient characteristics					
Age at transplant	<18 years (reference 18–55 years)	0.33	0.11	0.95	0.040
	≥55 years (reference 18–55 years)	1.26	1.05	1.52	0.014
Sex	Female (reference male)	0.73	0.59	0.91	0.004
Race	African American (reference white)	1.38	1.02	1.87	0.038
Diagnosis	Metabolic disorders (reference noncholestatic cirrhosis)	2.13	1.31	3.47	0.003
MELD Score	≥35 (reference 15–25)	1.47	1.00	2.16	0.048
Hospitalization status	ICU or non-ICU hospitalization at transplant (reference ambulatory)	1.39	1.09	1.78	0.008
Medical condition at transplant	On life support (reference no life support)	1.46	1.01	2.13	0.045
Hepatitis C virus serology	Positive (reference no, unknown, missing)	1.23	1.01	1.51	0.041
Donor characteristics					
Donor age	<18 years (reference 18–50 years)	0.71	0.50	1.00	0.0498
	50–60 years (reference 18–50 years)	1.39	1.11	1.75	0.0047
	≥60 years (reference 18–50 years)	1.88	1.29	2.74	0.0011
Donor weight	>100 kg	1.56	1.20	2.04	0.0010
Transplant characteristics					
Donor warm ischemia time[2]	≥35 mins (reference <35 mins)	1.84	1.23	2.74	0.0028
Cold ischemia time	6–10 h (reference <6 h)	1.64	1.29	2.08	<0.0001
	10–13 h (reference <6 h)	2.04	1.50	2.78	<0.0001
	≥13 h (reference <6 h)	3.84	2.57	5.74	<0.0001
	Missing (reference <6 h)[3]	2.42	1.77	3.30	<0.0001

[1]Also adjusted for: donor cause of death, race, sex and height, recipient BMI, diabetes, diagnosis, status 1/1A/1B, on dialysis, previous liver transplant, previous malignancy, previous abdominal surgery, history of portal vein thrombosis at transplant, HBV serology and ABO compatibility.
[2]Warm ischemia time was missing in 8.6% of DCD liver recipients.
[3]Cold ischemia time was missing in 10.3% of DCD liver recipients.

Mathur AK et al. AJT, 2010; 10: 2512.

Biliary Complications with DCDD Liver Transplantation

Center	N	Biliary Complications (%)	Ischemic Cholangiopathy (%)
Univ of Pittsburgh (de Vera et al. AJT, 2009; 9:773)	141	25	
Northwestern Univ (Skaro et al. Surgery, 2009; 146: 543)	32	53	38
Univ of Wisconsin (Foley et al. Ann Surg, 2011;253: 817-825)	87	47	34
St. James Univ Hospital, England (Pine et al. Liver Transpl, 2009;15:1072)	39	33	20.5
Leiden Univ, Netherlands (Dubbeld et al. Br J Surg, 2010; 97: 744-753)	55	28	24
Univ of Washington (Chan et al. Liver Transpl, 2008; 14:604)	52		13.7
UCLA (Hong et al. Arch Surg, 2011; 146: 1017-1023	81	25.5	9.9
Kings College, UK DeOliveira et al. Ann Surg, 2011; 254: 716-723	167	15	5
Mayo, Jacksonville FL Taner et al. Liver Transpl, 2011;18:101-112	200	27	12

Challenges Regarding Liver Transplantation from DCDD Donors

- Inferior graft survival compared to DBD donor livers
- Increased rates of biliary complications (ischemic cholangiopathy: IC)
- Increased postoperative morbidity
  - Cholangitis from IC
  - Frequent biliary procedures
- Increased costs and resource utilization
- Increased rates of re-transplantation for IC
- Insufficient MELD score
  - Prolonged wait-list time for re-transplantation

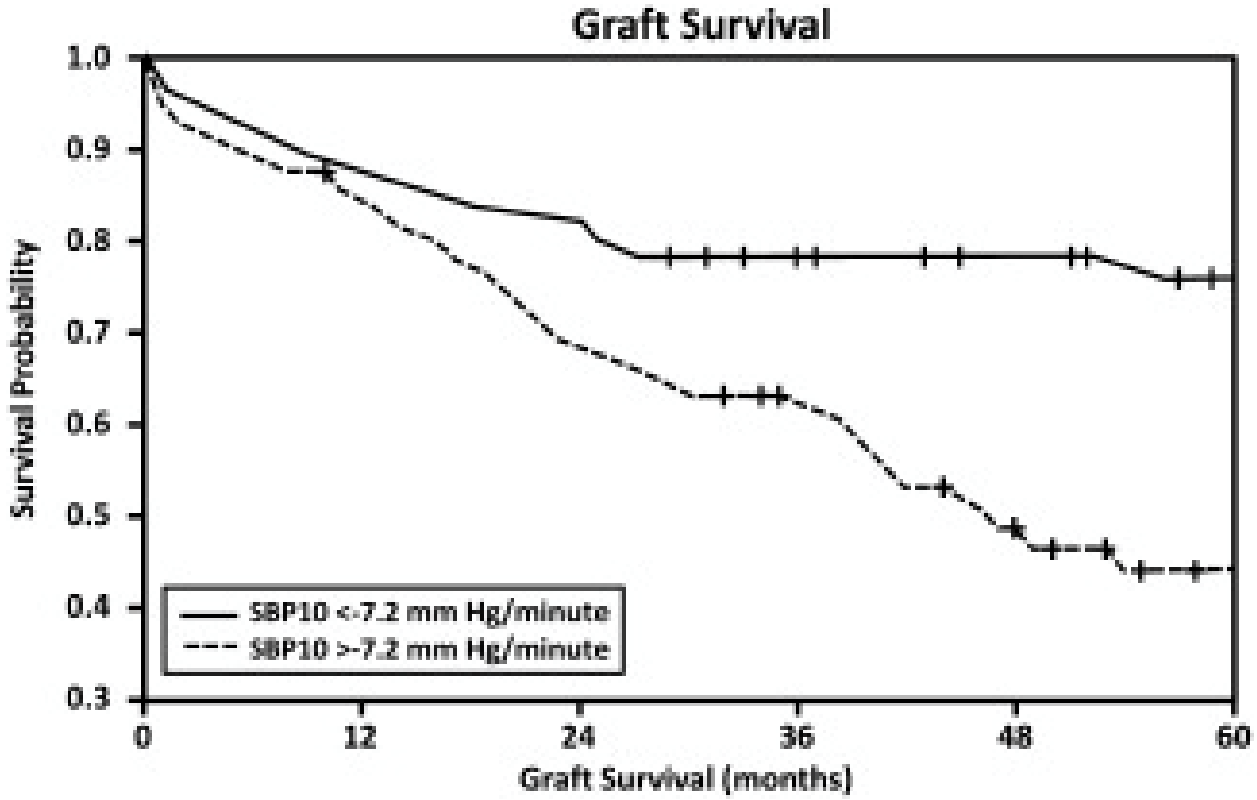
Minimizing Cold Ischemic Time is Essential in Cardiac Death Donor-Associated Liver Transplantation

Endpoint	Patients, *n*	Age, years, mean ± SD	Donor BMI, mean ± SD	Cold time, h, mean ± SD	Extubation to flush, min, mean ± SD	SBP < 50 mmHg to flush, min, mean ± SD	MELD score, mean ± SD
PNF/IC (+)	5	43 ± 4.1	23.4 ± 4.5	7.72 ± 2.6	30.2 ± 9.0	18.8 ± 8.2	22.6 ± 5.7
PNF/IC (–)	17	32.6 ± 13.0	23.3 ± 2.4	5.4 ± 2.9	22.1 ± 5.1	12.4 ± 8.5	17.0 ± 7.4
P-value		0.112	NS	0.021	0.027	0.043	0.12

SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; MELD, Model for End-stage Liver Disease; NS, not significant

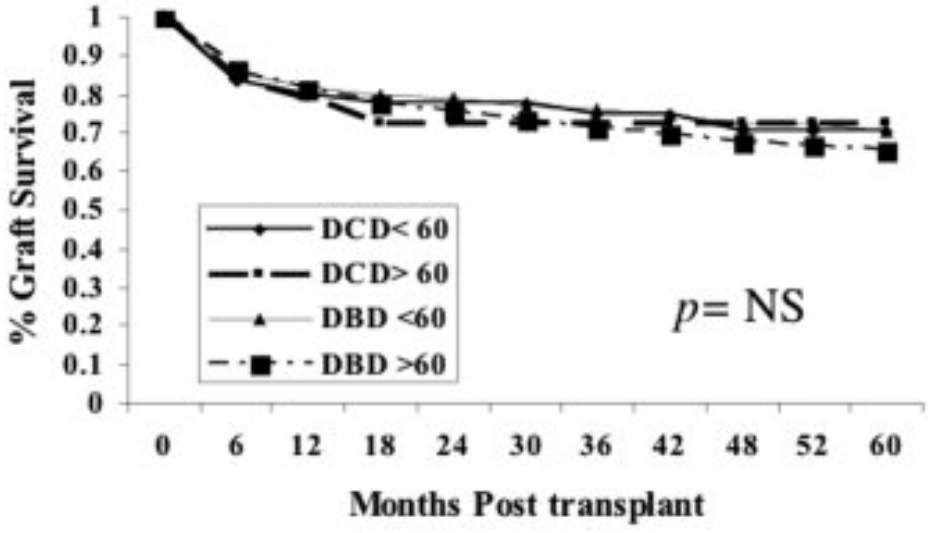
Karp et al. *HPB* 2011;13:411-416

Impact of Donor Hemodynamics of DCDD Graft Survival

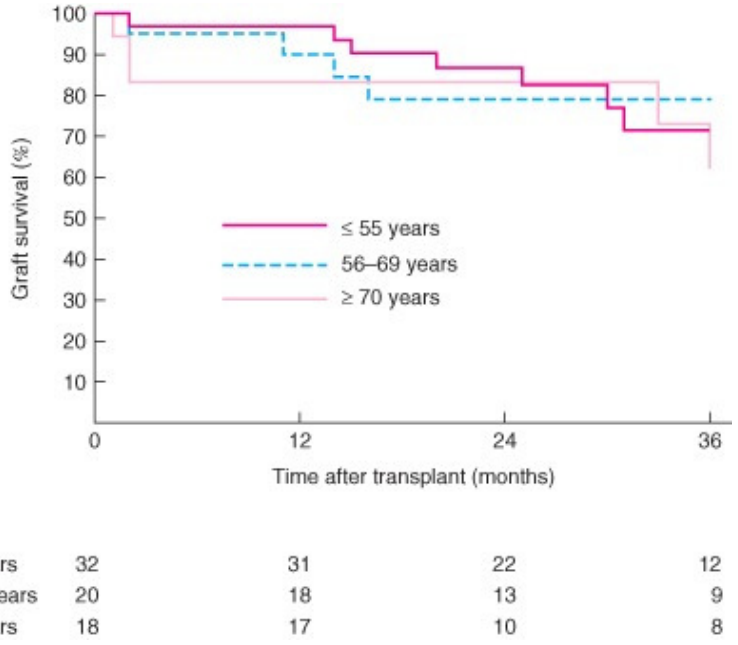


Abt et al. *Liver Transplantation*, 2014

Use of Older DCDD Donors

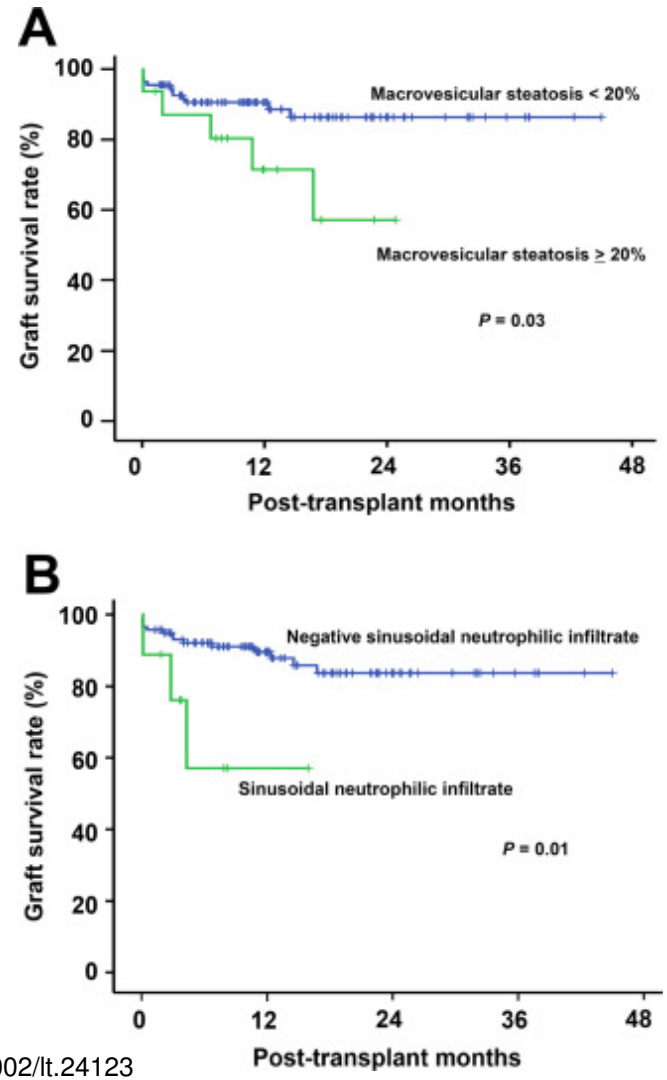


Grewal et al. *Liver Transpl*, 2009



Detry et al. *Br J Surg*, 2014

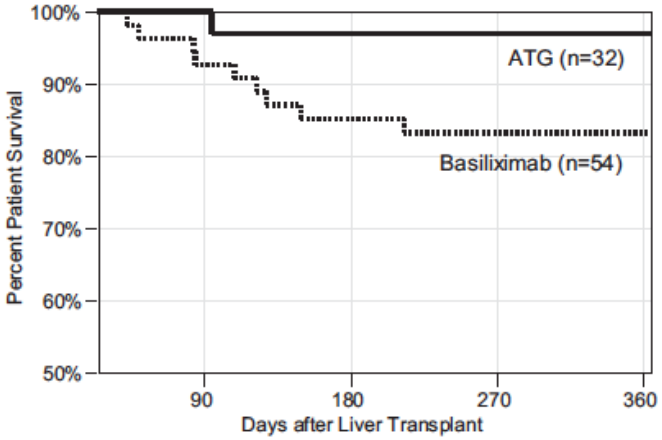
Donation after cardiac death liver transplantation: Graft quality evaluation based on pretransplant liver biopsy



Liver Transplantation
Volume 21, Issue 6, pages 838-846, 9 MAY 2015 DOI: 10.1002/lt.24123
http://onlinelibrary.wiley.com/doi/10.1002/lt.24123/full#lt24123-fig-0002

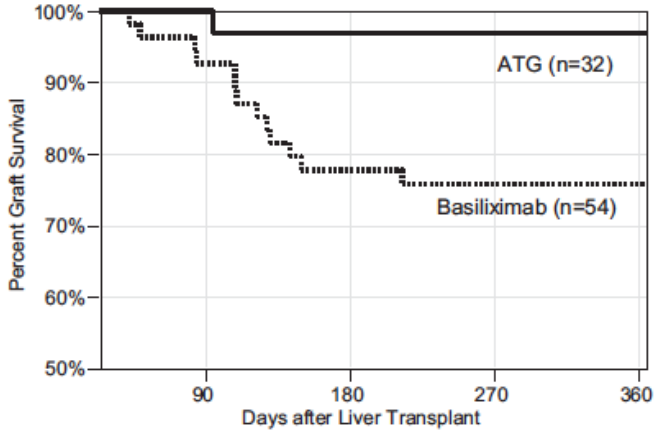
Patient and Graft Survival After DCD Liver Transplantation by Immunosuppression Induction Agent

A Patient Survival



Test	Prob>ChiSq
Log-Rank	0.061

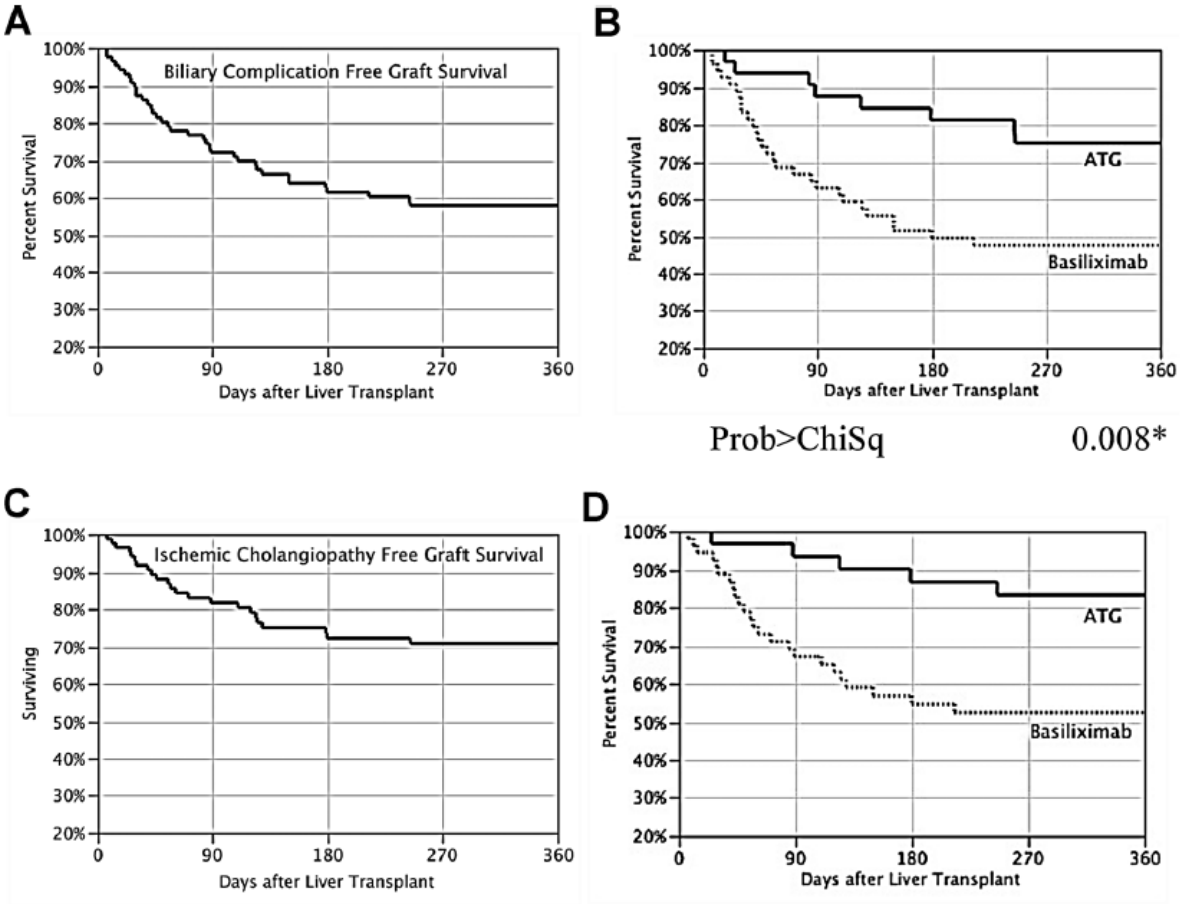
B Graft Survival



Test	Prob>ChiSq
Log-Rank	0.013*

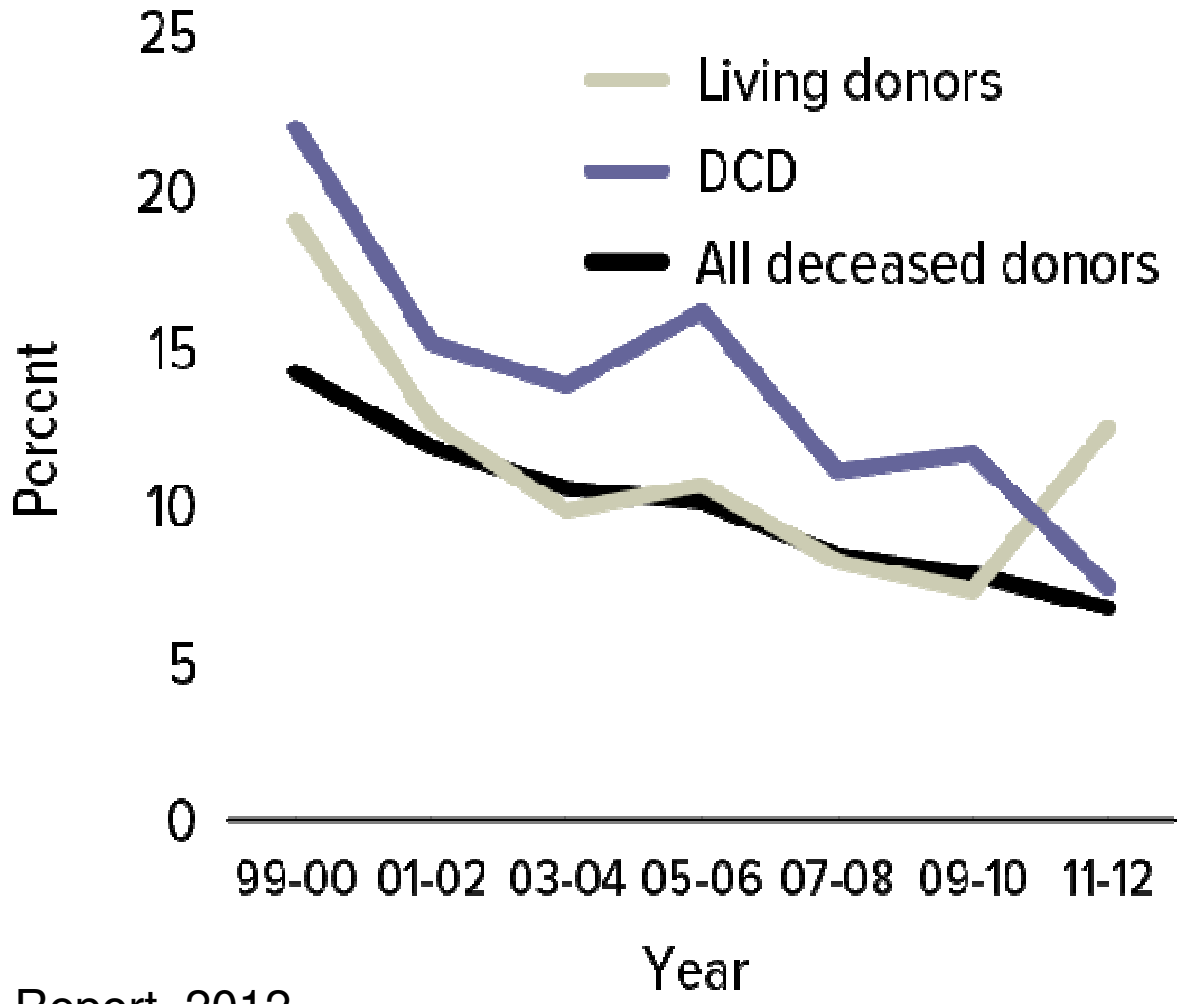
Halldorson et al. *Am J Transplant* 2015;15:251-258

DCD Graft Survival by Immunosuppression Induction Agent



Halldorson et al. *Am J Transplant* 2015;15:251-258

Graft failure within the first 90 days after transplant among adult liver transplant recipients



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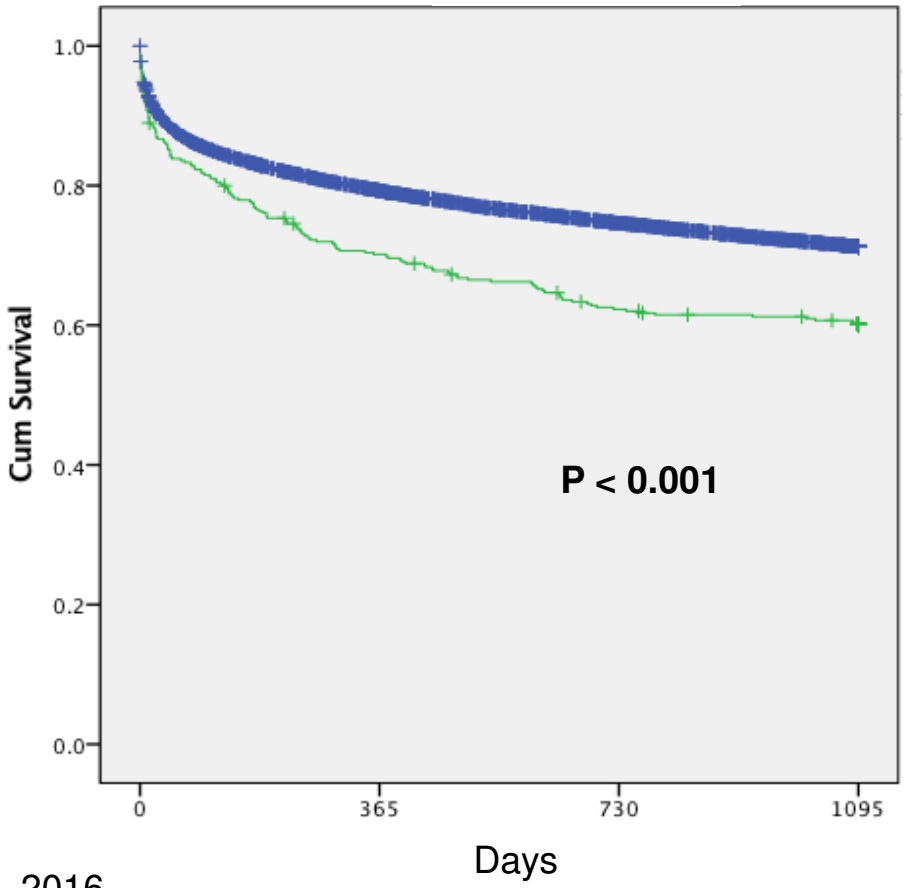
US Liver Transplants (1994-2014)

	DBD 1994-2003	**DCD 1994-2003**	DBD 2004-2008	**DCD 2004-2008**	DBD 2009-2014	**DCD 2009-2014**
n	42,838	**390**	29,298	**1,329**	30,493	**1,475**
Age Donor	35.1 (18.8)	**35.2 (16.8)**	38.8 (19.1)	**35.0 (15.0)**	39.1 (18.4)	**32.6 (13.1)**
Age Recip	45.2 (12.2)	**50.1 (12.5)**	48.5 (16.8)	**53.2 (11.3)**	50.5 (17.0)	**55.4 (10.6)**
BMI Recip	26.5 (6.1)	**27.3 (5.8)**	27.1 (6.1)	**28.0 (5.7)**	27.6 (6.3)	**28.2 (5.6)**
BMI Donor	24.5 (5.5)	**25.0 (5.4)**	26.0 (6.1)	**26.2 (5.7)**	26.8 (6.5)	**26.3 (5.8)**
CIT	8.6 (4.2)	**8.2 (3.2)**	7.4 (3.5)	**7.3 (3.4)**	6.7 (3.2)	**6.2 (3.2)**
MELD	19.8 (10.3)	**19.4 (9.2)**	21.1 (10.5)	**19.6 (9.1)**	22.2 (11.4)	**19.8 (9.9)**

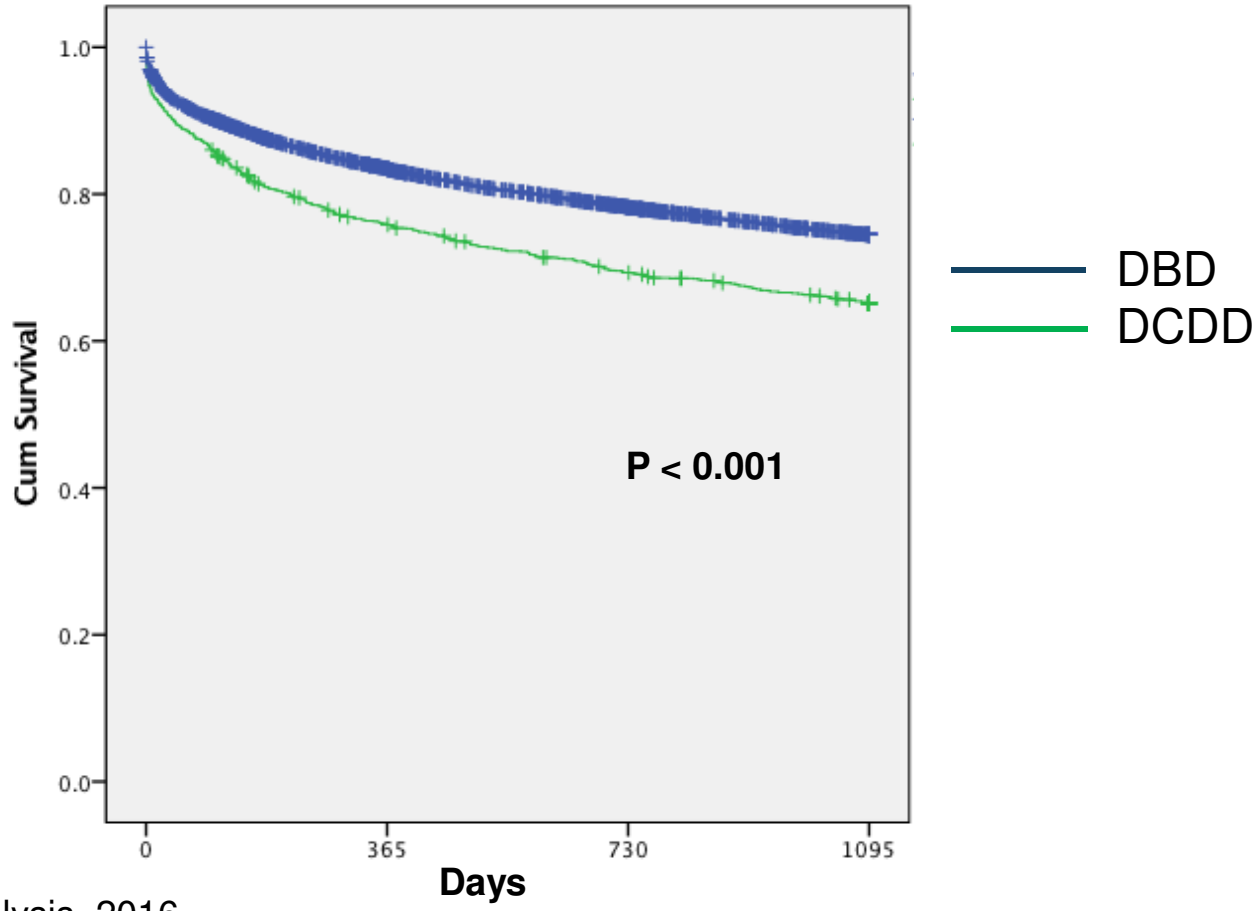
UNOS Database Analysis, 2016

US Liver Transplants 1994-2003
Graft Survival



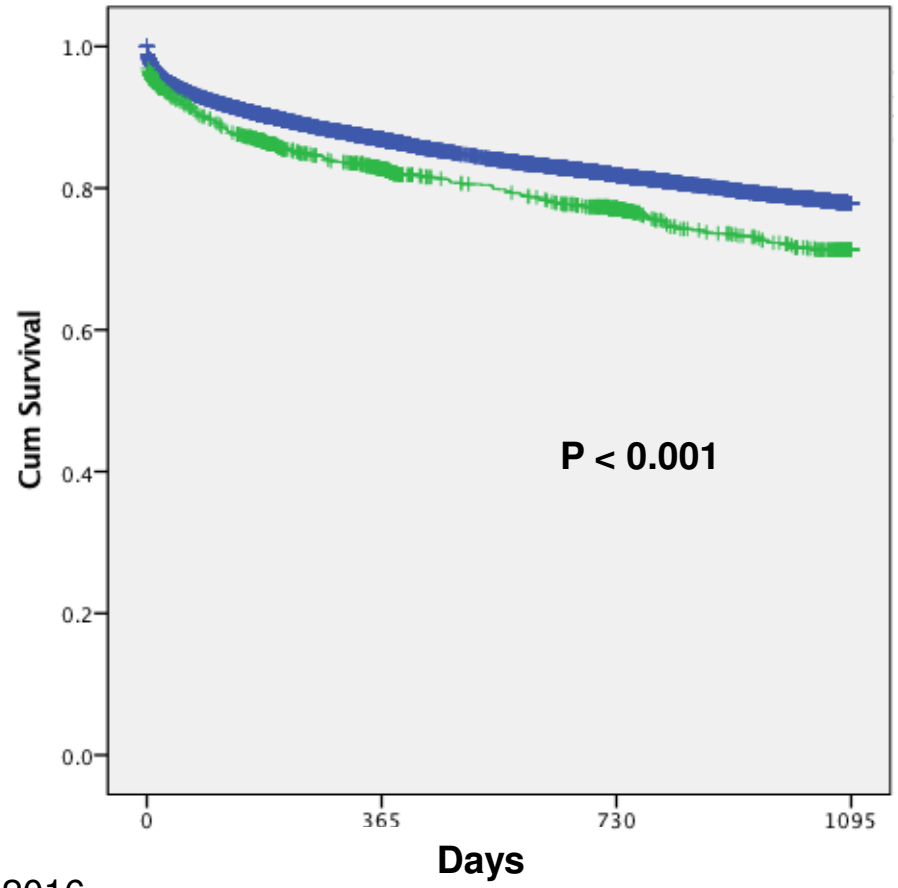
UNOS Database Analysis, 2016

US Liver Transplants 2004-2008
Graft Survival



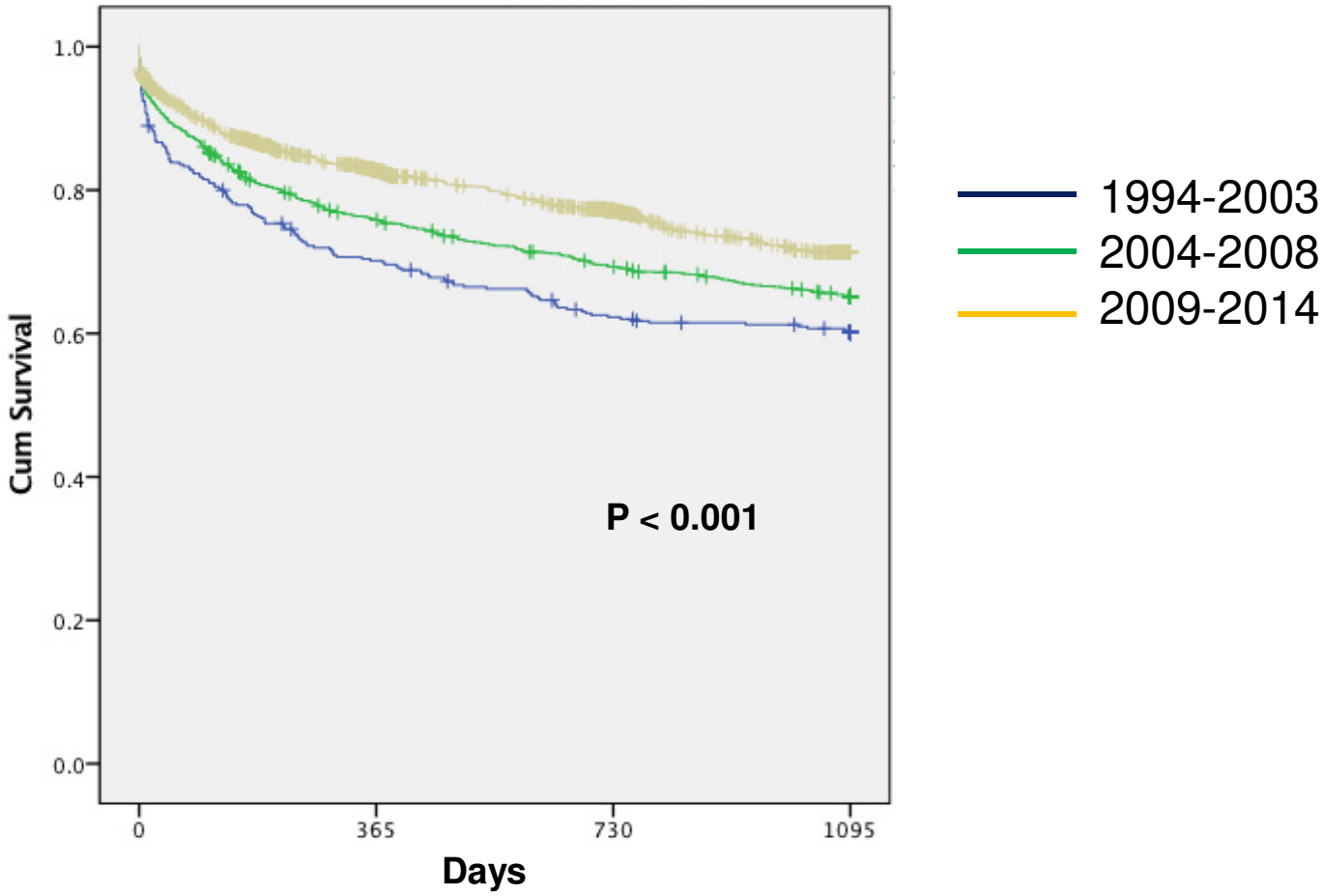
UNOS Database Analysis, 2016

US Liver Transplants 2009-2014
Graft Survival



UNOS Database Analysis, 2016

US DCD Liver Transplants 1994-2014
Graft Survival



Donor Characteristics
2002-2014

	DBD Liver <60 yo	DBD Liver ≥60 yo	DCD Liver <50 yo	p value
Number of	41,181	8,905	2,185	
Mean Age of Donor - years (std)	37.4 (13.7)	67.2 (5.9)	30.1 (11.1)	<0.001
Gender of Donor				
Female (%)	16,198 (39.3)	4,482 (50.3)	686 (31.4)	<0.001
Race of Donor (%)				
White	26,773 (65.1)	6,483 (72.8)	1,826 (83.5)	<0.001
Black	7,321 (17.8)	1,284 (14.4)	177 (8.1)	
Other	7,127 (17.3)	1,138 (12.8)	182 (8.4)	
BMI (sd)	27.2 (6.2)	27.6 (5.9)	26.1 (5.7)	<0.001
Mean CIT- hours (std)	7.00 (3.3)	7.11 (3.3)	6.8 (3.4)	0.543

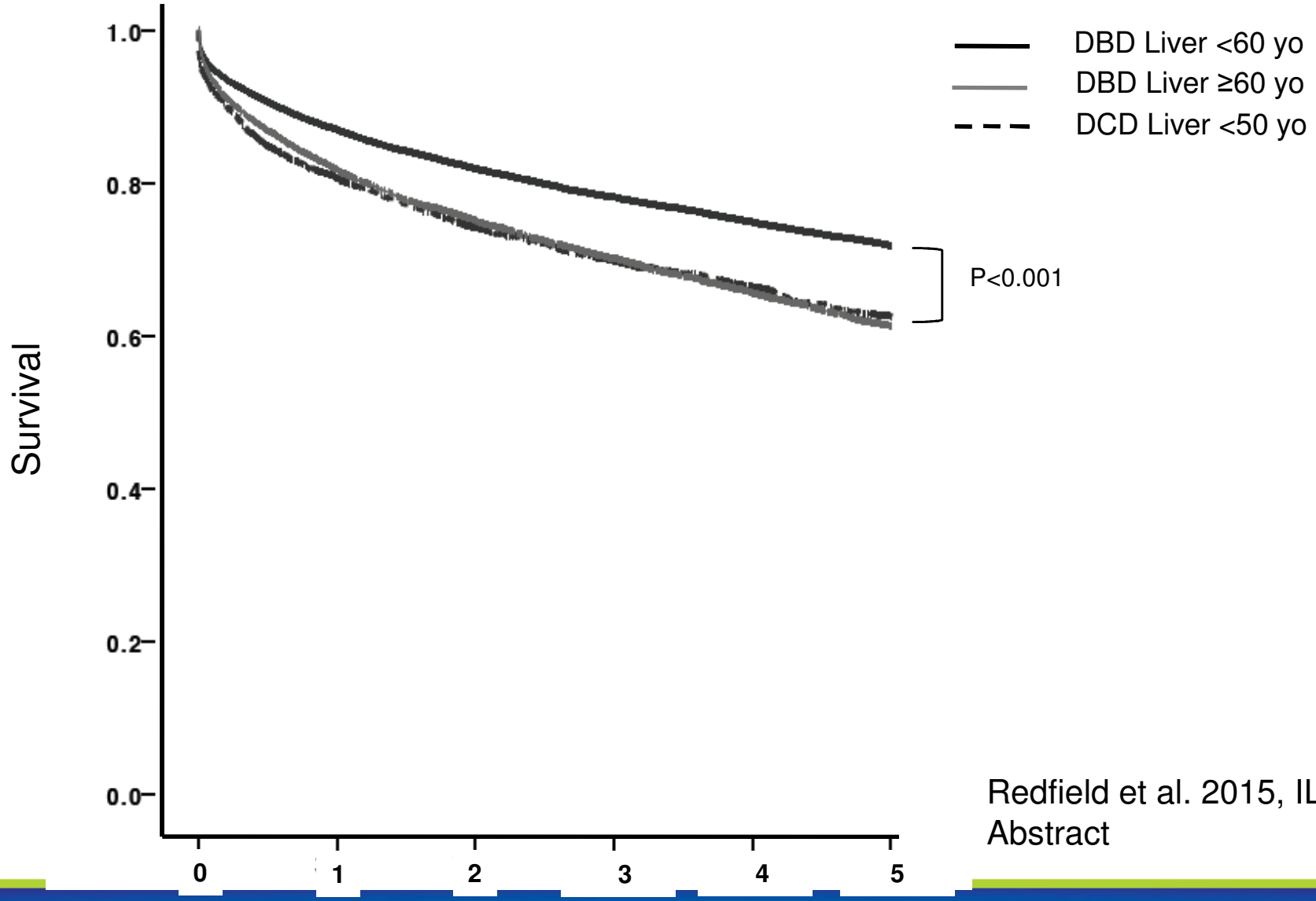
Redfield et al. 2015, ILTS Abstract

Recipient Characteristics
2002-2014

	DBD Liver <60 yo	DBD Liver ≥60 yo	DCD Liver <50 yo	p value
Number of	41,181	8,905	2,185	
Mean Age of Recipient - years (std)	53.9 (10.0)	55.9 (9.4)	54.97 (9.4)	<0.001
Gender of Recipient				
Female (%)	13,089 (31.8)	3,075 (41.6)	669 (30.6)	<0.001
Race of Recipient (%)				
White	29,619 (71.9)	6,517 (73.2)	1,597 (73.1)	<0.001
Black	3,939 (10.0)	677 (7.6)	213 (9.7)	
Other	7,623 (18.1)	1,711 (19.2)	375 (17.2)	
BMI (sd)	28.5 (5.7)	28.4 (5.7)	28.2 (5.4)	0.101
MELD	21.7 (10.4)	19.7 (9.4)	19.4 (9.5)	<0.001
On Vent (%)	2,184 (5.3)	336 (3.8)	81 (3.7)	<0.001

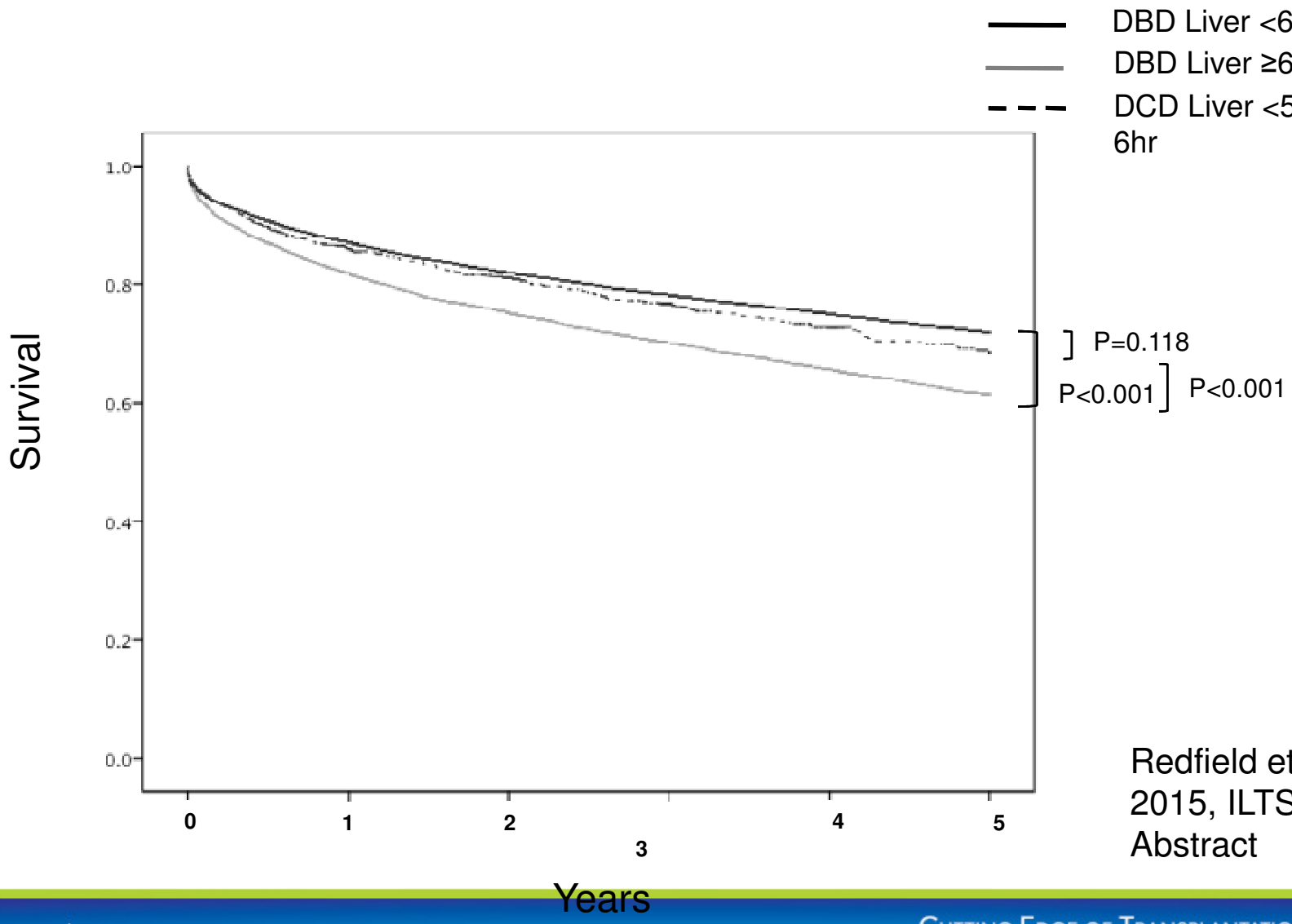
Redfield et al. 2015, ILTS Abstract

5-year Actuarial Graft Survival



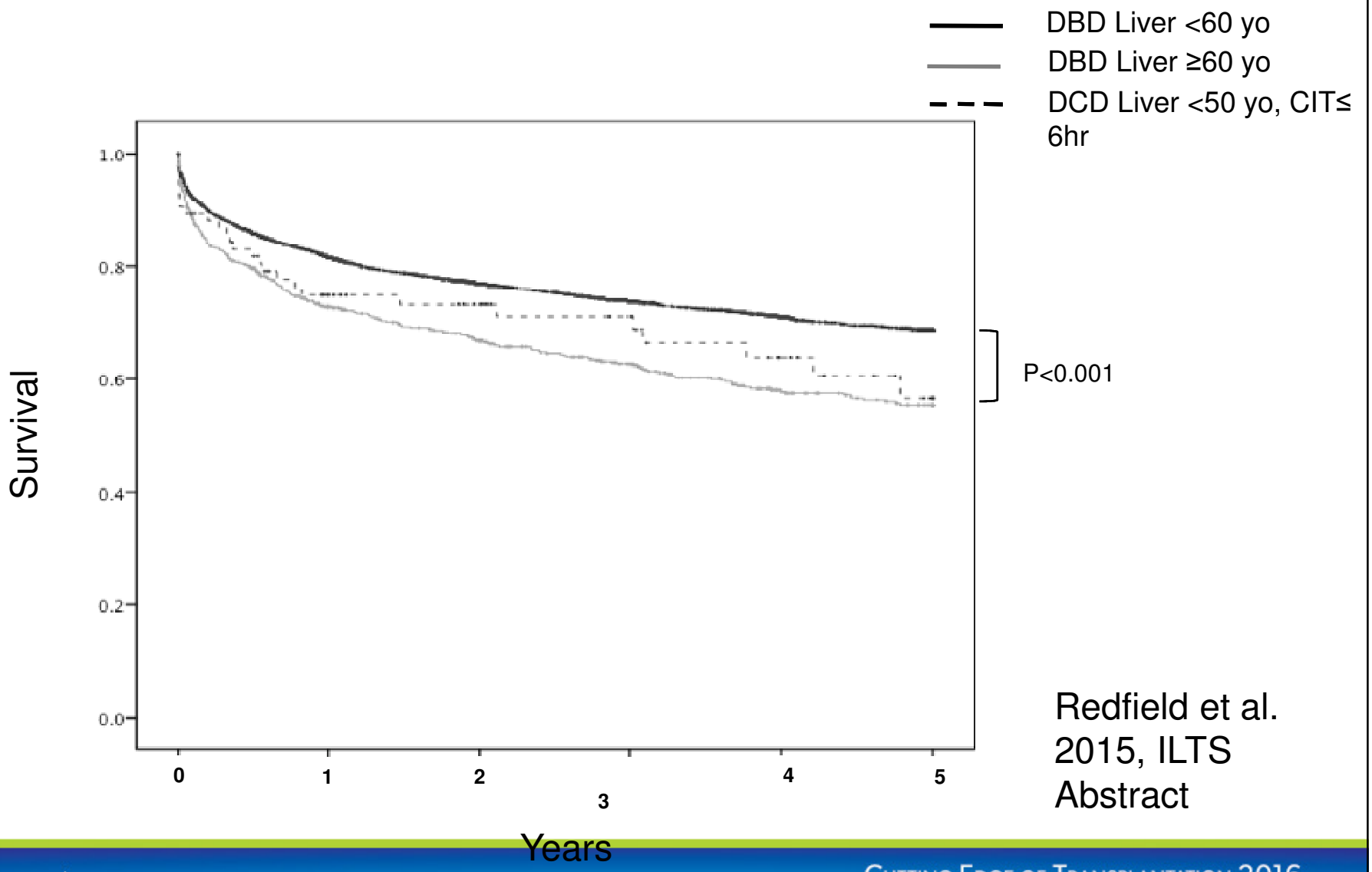
Redfield et al. 2015, ILTS Abstract

5-year Actuarial Graft Survival – DCD ≤ 6 hr CIT



Redfield et al. 2015, ILTS Abstract

5-year Actuarial Graft Survival – MELD≥35



Redfield et al. 2015, ILTS Abstract

Multivariate Analysis

Variable	Multivariate	P Value
Recipient Age	1.012 (1.010 – 1.014)	<0.001
BMI Donor	1.004 (1.001 – 1.007)	0.012
African American Recipient	1.435 (1.355 – 1.520)	<0.001
MELD	1.007 (1.005 – 1.009)	<0.001
ON Vent	1.751 (1.621 – 1.890)	<0.001
CIT	1.022 (1.018 - 1.027)	<0.001
DBD Liver <60 yo	Ref	Ref
DBD Liver ≥60 yo	**1.450** (1.388 – 1.516)	<0.001
DCD Liver <50 yo	1.467 (1.351 – 1.594)	<0.001
DCD Liver <50 yo (CIT≤ 6hr)	**1.203** (1.054 – 1.372)	0.006

Redfield et al. 2015, ILTS Abstract

Liver Discard Rates

	2012	2013	2014
Total DCD donors	1107	1206	1291
DCD recovered	388	427	496
DCD transplanted	263	309	363
Balance* (%)	125 (32)	118 (28)	133 (27)

	2014 Livers					
	Transplanted		Discarded		All livers	
	Total N	%	Total N	%	Total N	%
Donor Age (<50)	315	73.9	111	26.1	426	100
Donor Age (>= 50)	48	68.6	22	31.4	70	100
Total*	363	73.2	133	26.8	496	100

All data for tables 4a and 4b obtained directly from UNOS. *Balance = DCD recovered minus DCD transplanted; **data for 2014.

UW DCD Liver Transplantation 1994-2014

	1994-2003 (n = 38)	2004-2008 (n = 37)	2009-2014 (n = 38)	P value
Recipient Age	50.5 ± 9.2	54.0 ± 9.3	58.2 ± 7.6	**< 0.001**
Donor Age	35.6 ± 14.1	37.8 ± 11.5	38.8 ± 12.1	0.53
Allocation MELD at TXP	19.5 ± 5.0	20.3 ± 9.0	25.9 ± 6.3	**< 0.001**
CIT (h)	8.0 ± 2.0	6.1 ± 2.2	6.0 ± 1.4	**< 0.001**

UW DCD Liver Transplantation 1994-2014

	1994-2003 (n = 38)	2004-2008 (n = 37)	2009-2014 (n = 38)	P value
Graft Survival (1 year)	63.2 %	64.8 %	76.3 %	0.54
Graft Survival (3 year)	55.2 %	56.8 %	65.3 %	
Ischemic Cholangiopathy (1 year)	23.4 %	0 %	9.1 %	0.02
Post operative Infection (1 year)	54.8 %	61.2 %	49.8 %	0.75

Current DCDD Donor Selection at UW

- Donor age < 65
- Donor WIT < 30 minutes (agonal time)
- Biopsy performed in all cases prior to recovery.
- Exclusion criteria included >20% macrosteatosis based on a baseline protocol biopsy.
- Goal CIT < 6 hours

DCDD Liver Transplantation: Donor Surgery

- Consent is obtained from family members to expose the femoral vessels under local anesthesia prior to withdrawal of support.
- Patient is given 30,000 Units of heparin and Phentolamine (Regitine), prior to extubation.
- Limit DWIT (agonal time: 70-70 rule)
- Femoral vessels are cannulated and UW solution (4-5 liters) flushed through artery.
- IMV/PV and CBD flushed in situ
- Organs are removed *en bloc* (pancreas and liver) and prepared afterward on the back table for transplantation.

DCDD Liver Transplantation: Recipient

- Recipient to the operative suite once organs are explanted from the donor.
- Hepatectomy is performed while organs are in transit. Back table is performed by a second team in order to minimize cold ischemia time.
- tPA given (2 -5 mg) into HA prior to HA reperfusion
- Livers are perfused via the portal vein or through the hepatic artery.

Results

- n=30 DCDD liver transplants since June 2013
  - 4% of UW liver transplant volume in 2011 was from DCDD donors
  - 6.5% of UW liver transplant volume in 2012 was from DCDD donors
  - 10.6% of UW liver transplant volume in 2013 was from DCDD donors
  - 15.5% of UW liver transplant volume in 2014 was from DCDD donors
  - 10 DCDD livers in 2015
- 7 donors were over the age of 55
- 3 out of 28 (10%) incidence of IC within 90 days.
- One re-transplant due to IC; 1 re-transplant due to hepatic artery thrombosis
- 11 of 28 DCDD liver transplants were reperfused through the portal vein

University of Wisconsin Transplant Database Analysis

Summary

- DCDD liver transplant outcomes improving over time
- Selected DCDD liver outcomes better than older DBD livers
- Comparable outcomes in MELD > 35
- Ischemic cholangiopathy rates decreasing
- Strategies to expand pool and improve outcomes
  - Shorter CIT
  - Rapid donor organ removal
  - Induction IS (Thymoglobulin vs. Simulect)
  - t-PA into HA
  - ? HA reperfusion before PV
  - Donor-recipient matching

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