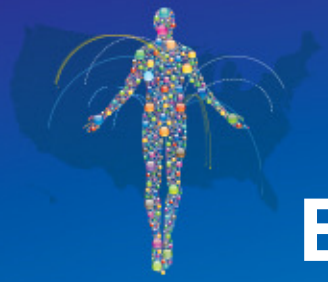

Brain Dead Donor Heart Management:
Maintenance of Hemodynamics with What Drugs?

Darren Malinoski, MD, FACS
Assistant Chief of Surgery
Portland VA Medical Center
Associate Professor of Surgery
Oregon Health & Science University

CEOT
CUTTING EDGE OF TRANSPLANTATION
RESOLVING THE ORGAN SHORTAGE
PRACTICE | POLICY | POLITICS
FEBRUARY 25-27, 2016 • PHOENIX, ARIZONA

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DONATE LIFE

Conflict of Interest Disclosure

Grant funding:

-NIH

-Laura and John Arnold Foundation

*My views may not represent those of the U.S. Government

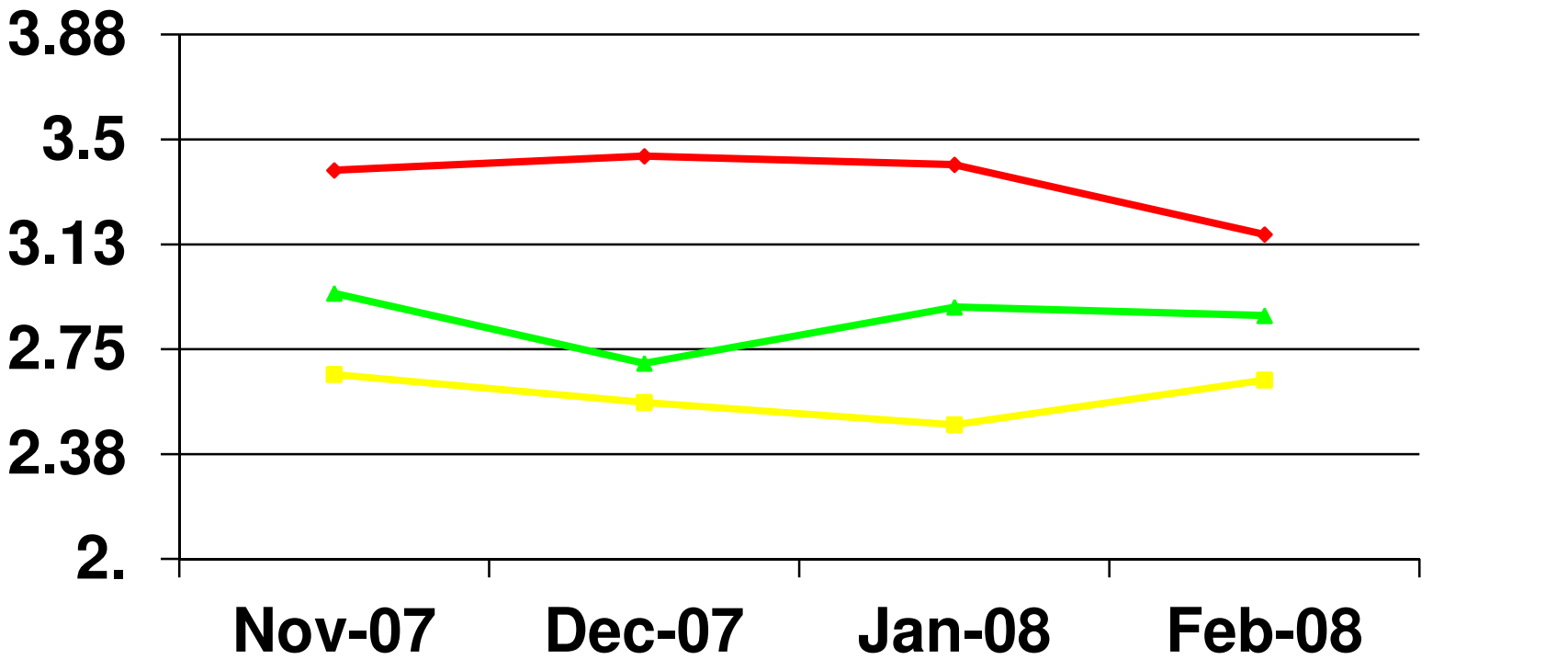
BACKGROUND

- Shortage of organs for transplantation
- National average of three organs transplanted per donor (OTPD)
  - 30% of hearts utilized
- Inconsistent donor management and organ acceptance practices

BACKGROUND

- Checklists have demonstrated utility in several arenas
- Standardized critical care endpoints
- Donor Management Goals (DMGs)

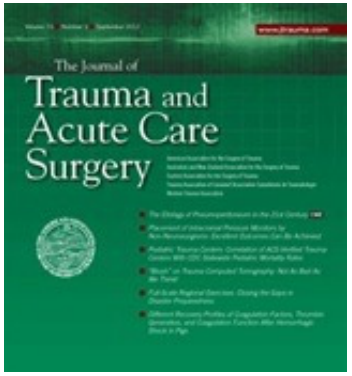
OTPD and DMGs



- HRSA, 2008

UNOS Region 5 DMGs

- Step 1 – retrospective – 2007-2008
- Achieving Donor Management Goals (DMG) Prior to Deceased Donor Procurement is Associated with More Organs Transplanted per Donor
  - Primary outcome measure: ≥ 4 OTPD



Achieving Donor Management Goals Before Deceased Donor Procurement Is Associated With More Organs Transplanted Per Donor

Darren J. Malinoski, MD, Michael C. Daly, MSc, Madhukar S. Patel, ScM, Chrystal Oley-Graybill, Clarence E. Foster III, MD, and Ali Salim, MD

TABLE 1. Donor Management Goals

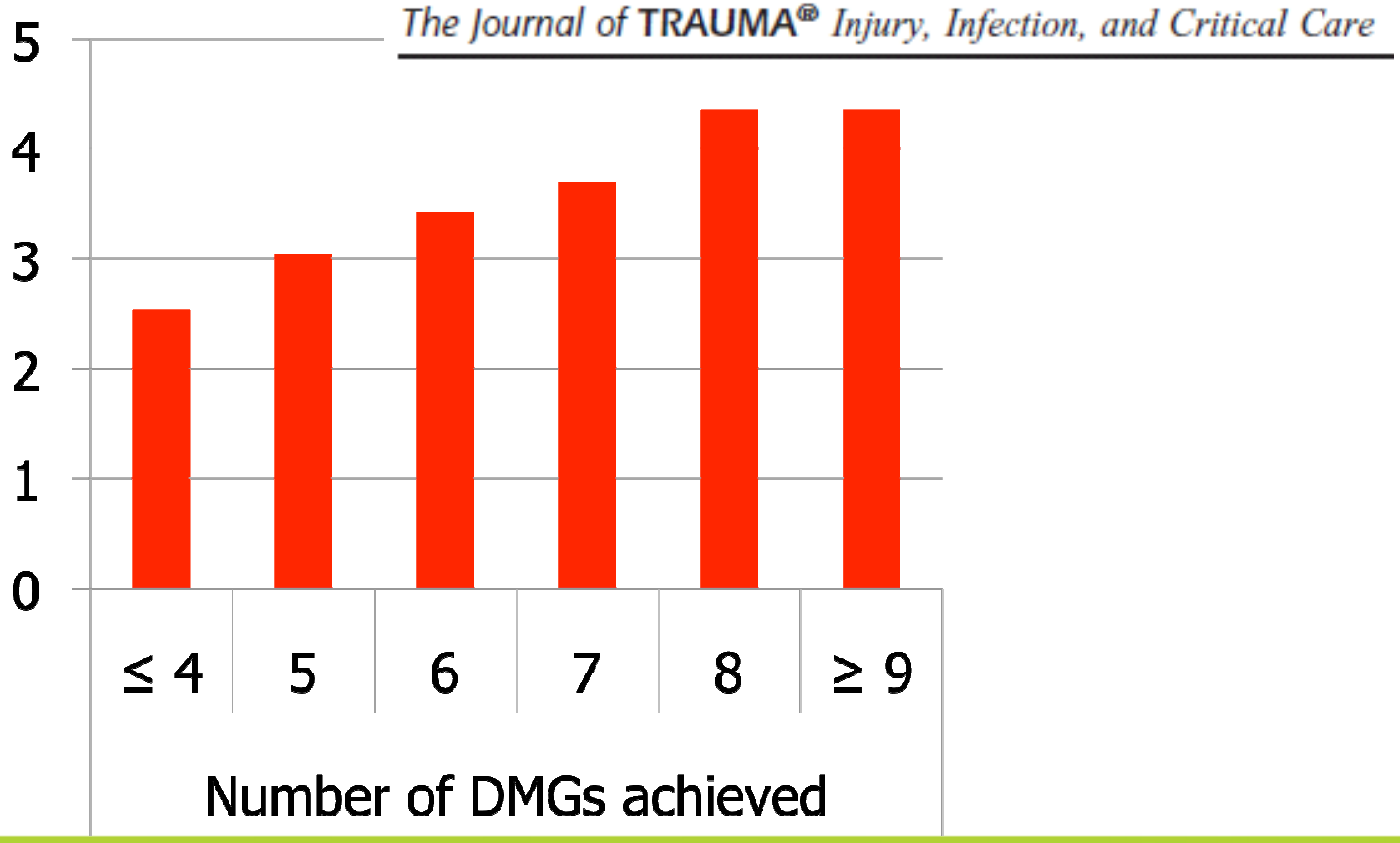
Critical Care End Points	DMG	Proportion of Donors Meeting DMGs (%)
Mean arterial pressure	60–100 mm Hg	83
Central venous pressure	4–10 mm Hg	60
Ejection fraction	>50%	50
Pressors	≤1 and low dose*	75
Arterial blood gas pH	7.3–7.45	70
P_{AO_2}:FIO_2	>300 on PEEP = 5 cm H_2O	43
Serum sodium	135–160 mEq/L	89
Blood glucose	<150 mg/dL	43
Hemoglobin	>10 mg/dL	59
Urine output	1–3 mL/kg/h for preceding 4 h	73

SD, standard deviation

Achieving Donor Management Goals Before Deceased Donor Procurement Is Associated With More Organs Transplanted Per Donor

Darren J. Malinoski, MD, Michael C. Daly, MSc, Madhukar S. Patel, ScM, Chrystal Oley-Graybill, Clarence E. Foster III, MD, and Ali Salim, MD

The Journal of **TRAUMA®** *Injury, Infection, and Critical Care*

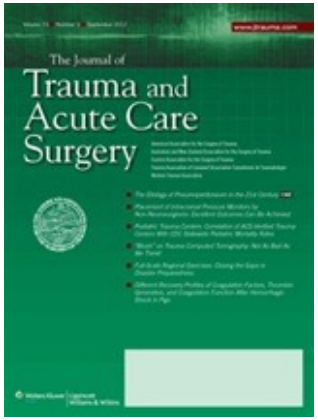


Achieving Donor Management Goals Before Deceased Donor Procurement Is Associated With More Organs Transplanted Per Donor

Darren J. Malinoski, MD, Michael C. Daly, MSc, Madhukar S. Patel, ScM, Chrystal Oley-Graybill, Clarence E. Foster III, MD, and Ali Salim, MD

TABLE 2. Impact of DMGs on Organ Yield

	DMGs Met	DMGs Not Met	*p*
% SCDs with ≥4 OTPD	70.1%	38.7%	<0.001*
Mean OTPD ± SD	4.35 ± 1.61	3.32 ± 1.56	<0.001†
Transplanted			
Right lung	37.1%	14.3%	<0.001*
Left lung	36.1%	14.3%	<0.001*
Heart	56.7%	30.5%	<0.001*
Liver	93.8%	81.6%	0.005*
Pancreas	40.2%	24.7%	0.005*
Right kidney	95.9%	87.4%	0.021*
Left kidney	94.8%	88.8%	0.088*
Intestine	2.1%	1.3%	0.641‡



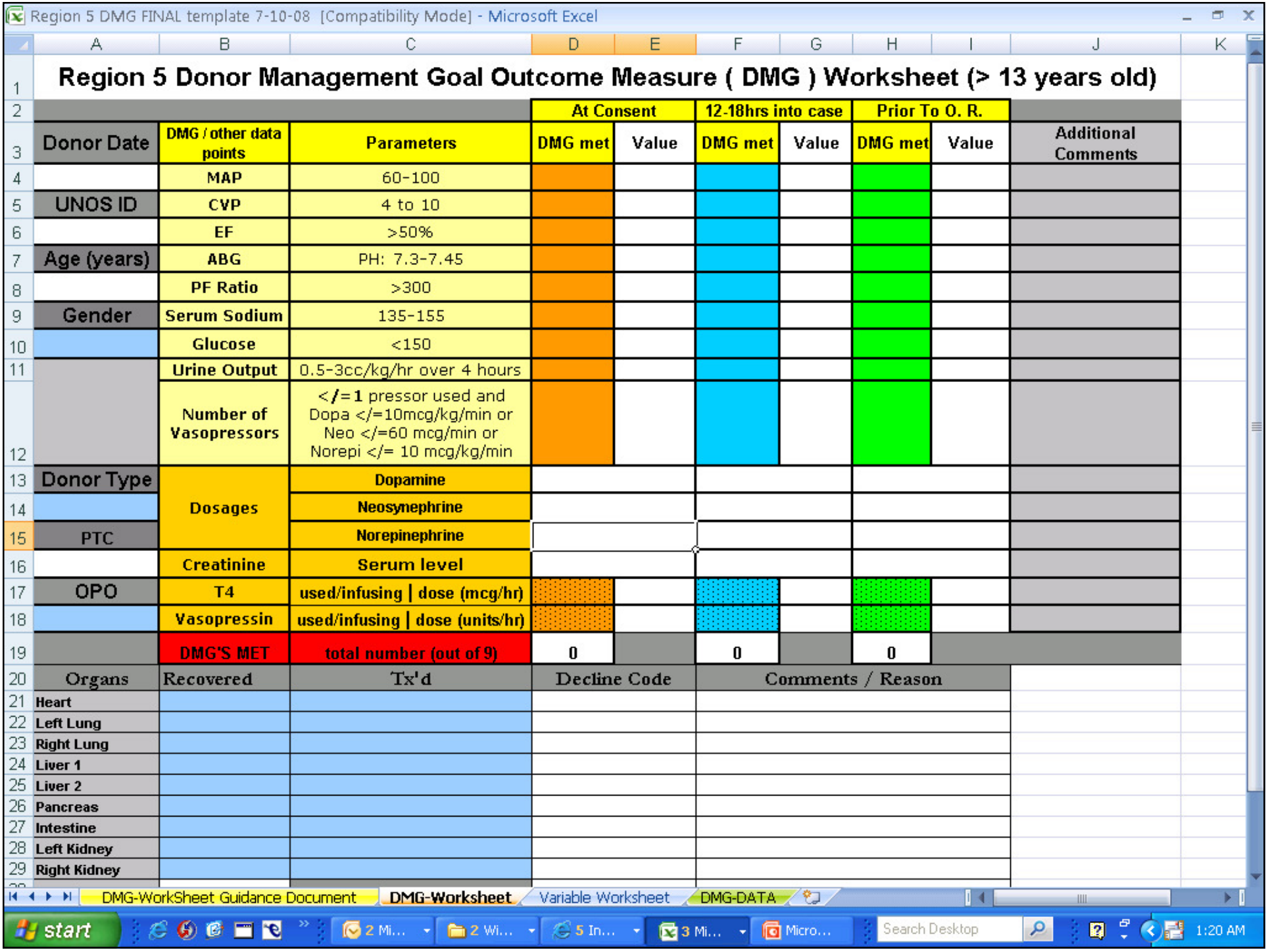
Achieving Donor Management Goals Before Deceased Donor Procurement Is Associated With More Organs Transplanted Per Donor

Darren J. Malinoski, MD, Michael C. Daly, MSc, Madhukar S. Patel, ScM, Chrystal Oley-Graybill, Clarence E. Foster III, MD, and Ali Salim, MD

DMG/Variable	OR	95% CI	p value
Continuous Variables			
Age (years)	0.944	0.923 – 0.966	< 0.001
Creatinine (mg/dL)	0.636	0.409 – 0.987	0.044
Categorical Variables			
Thyroid Hormone use	1.969	1.082 – 3.582	0.026
CVP 4 – 10 mmHg	1.897	1.021 – 3.527	0.043
EF > 50%	3.988	2.095 – 7.592	< 0.001
P:F > 300 on PEEP 5	4.591	2.478 – 8.506	< 0.001
Na 135 – 160 mEq/L	3.352	1.141 – 9.851	0.028
"Goals met"	4.394	2.497 – 7.732	< 0.001

UNOS Region 5 DMGs

- Step 2
  - Prospective
  - Three time points
    - At authorization for donation
    - 12-18 hours later – organ offers are made
    - Prior to organ recovery
  - Modified DMGs
  - June 2008 – January 2009



Region 5 DMG FINAL template 7-10-08 [Compatibility Mode] - Microsoft Excel

Region 5 Donor Management Goal Outcome Measure (DMG) Worksheet (> 13 years old)

				At Consent		12-18hrs into case		Prior To O. R.		
Donor Date	DMG / other data points	Parameters		DMG met	Value	DMG met	Value	DMG met	Value	Additional Comments
	MAP	60-100								
UNOS ID	CVP	4 to 10								
	EF	>50%								
Age (years)	ABG	PH: 7.3-7.45								
	PF Ratio	>300								
Gender	Serum Sodium	135-155								
	Glucose	<150								
	Urine Output	0.5-3cc/kg/hr over 4 hours								
	Number of Vasopressors	</=1 pressor used and Dopa </=10mcg/kg/min or Neo </=60 mcg/min or Norepi </= 10 mcg/kg/min								
Donor Type	Dosages	Dopamine								
		Neosynephrine								
PTC		Norepinephrine								
	Creatinine	Serum level								
OPO	T4	used/infusing | dose (mcg/hr)								
	Vasopressin	used/infusing | dose (units/hr)								
	DMG'S MET	total number (out of 9)		0		0		0		

Organs	Recovered	Tx'd	Decline Code	Comments / Reason
Heart				
Left Lung				
Right Lung				
Liver 1				
Liver 2				
Pancreas				
Intestine				
Left Kidney				
Right Kidney				

DMG-WorkSheet Guidance Document | DMG-Worksheet | Variable Worksheet | DMG-DATA

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UNOS Region 5 DMGs

- Prospective Data
  - 380 SCDs
- The Impact of Meeting Donor Management Goals on the Number of Organs Transplanted per Donor
  - Primary outcome measure: $\geq$ 4 OTPD

The impact of meeting donor management goals on the number of organs transplanted per donor: Results from the United Network for Organ Sharing Region 5 prospective donor management goals study

Darren J. Malinoski, MD, FACS; Madhukar S. Patel, MD, MBA, ScM; Michael C. Daly, MSc; Chrystal Oley-Graybill; Ali Salim, MD, FACS; on behalf of the UNOS Region 5 DMG workgroup

Variable	OR	95% CI for OR	p value[a]
Analysis using DMGs "met"			
Donor age	**0.948**	**0.932-0.963**	**<0.001**
DMGs "met" at time of consent	**2.034**	**1.066-3.881**	**0.031**
DMGs "met" 12-18 hours later	1.481	0.888-2.470	0.132
DMGs "met" prior to organ recovery	**2.344**	**1.430-3.843**	**0.001**
Creatinine prior to organ recovery	**0.746**	**0.606-0.918**	**0.006**
Analysis using change in DMG's			
Donor age	**0.951**	**0.936-0.966**	**<0.001**
Change in DMG's from consent to 12-18 hours later	**1.130**	**1.001-1.277**	**0.048**
Creatinine prior to organ recovery	**0.727**	**0.595-0.889**	**0.002**

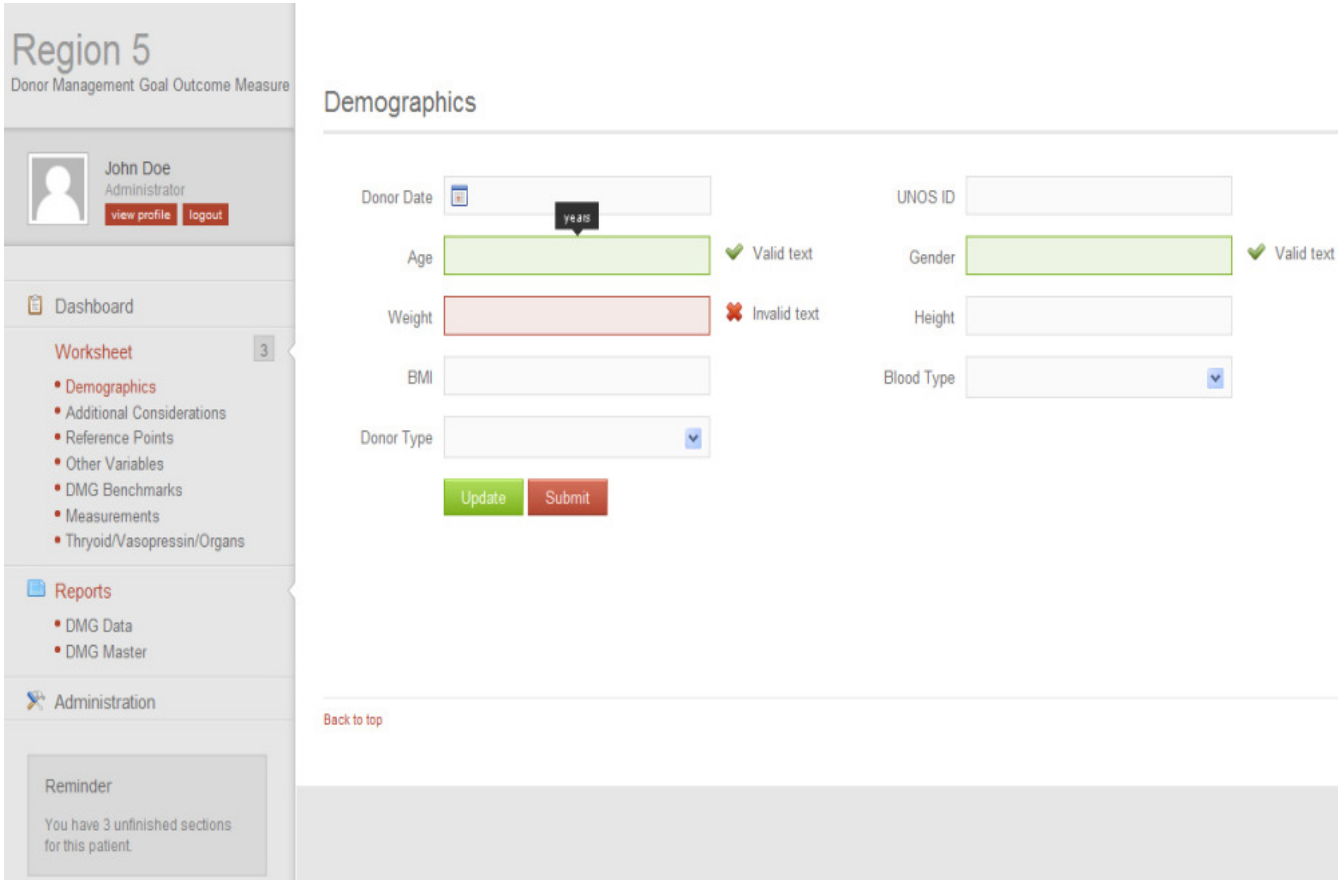
BACKGROUND

- Organs transplanted per donor is not an ideal outcome measure

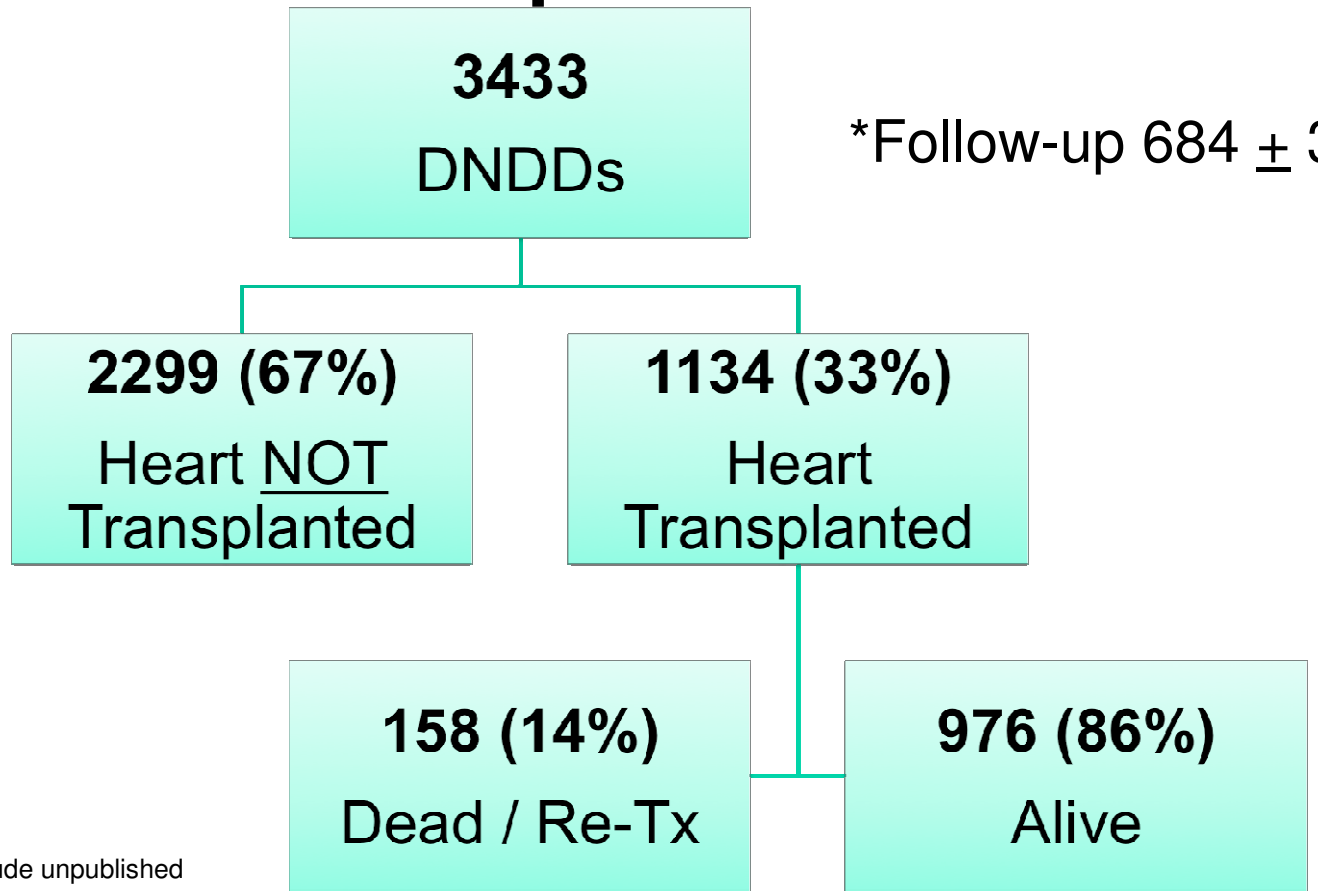
- Graft function / survival are better endpoints

UNOS DMG Web Portal
Launched in March 2012 – supported by Tii

- Forced field entry
- Linked to UNet
- Recipient data added
- Fields for study data
- Funded by OPOs
- SRTR SAF merger



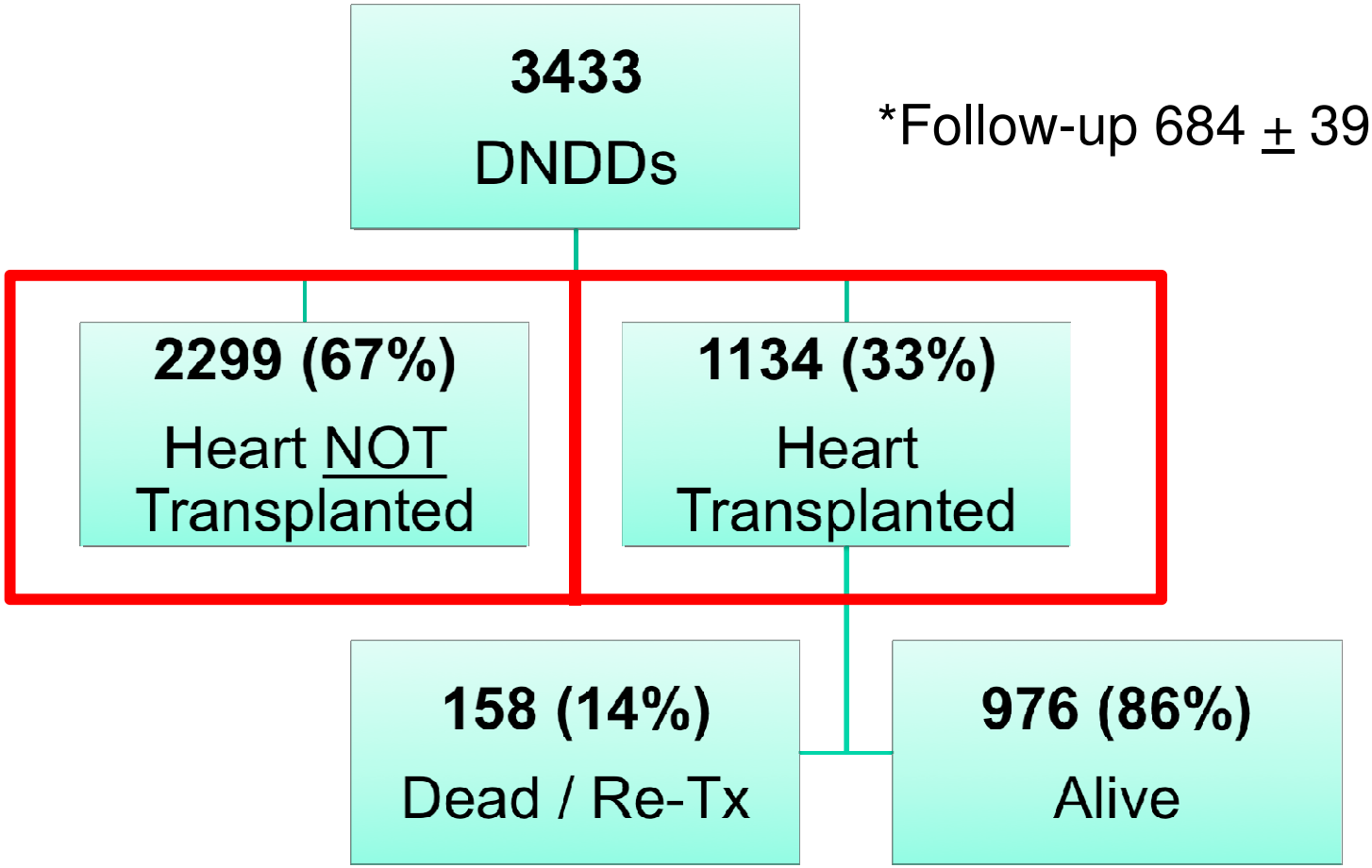
Impact of Donor Demographics and Critical Care Endpoints on Cardiac Transplantation and Recipient Survival



*Follow-up 684 ± 392 days

The remaining slides include unpublished data from our research group

Impact of Donor Demographics and Critical Care Endpoints on Cardiac Transplantation and Recipient Survival



*Follow-up 684 ± 392 days

Univariate Analysis: Predictors of Heart Transplantation

	Authorization: Percent of Hearts Transplanted			**12-18 hours after Auth:** Percent of Hearts Transplanted			**Prior to Organ Recovery:** Percent of Hearts Transplanted		
Variables	Not Met	Met	*p*	Not Met	Met	*p*	Not Met	Met	*p*
Gender (Male)									
Donor Type (Standard Criteria Donor)									
BMI (<30 kg/m^2) [a]									
Donor Management Goals Bundle Met									
Mean Arterial Pressure (60-110 mmHg)									
Central Venous Pressure (4-12 mmHg)									
Ejection Fraction (≥50%)									
Arterial Blood Gas pH (7.30-7.50)									
PaO_2/FiO_2 (≥300)									
Serum Sodium (≤155mEq/L)									
Blood Glucose (≤180mEq/L)									
Urine Output (≥0.5ml/kg/h)									
Vasopressors (≤1 and low dose)[b]									
Dopamine used (>0 mcg/kg/min)[c]									
Neosynephrine used (>0mcg/min)[d]									
Norepinephrine used (>0 mcg/kg/min)[e]									
Epinephrine used (>0mcg/min)[f]									
Thyroid Hormone used (>0 mcg/hr)[g]									
Vasopressin used (>0 units/hr)[h]									

Univariate Analysis: Predictors of Heart Transplantation

	Authorization: Percent of Hearts Transplanted			**12-18 hours after Auth:** Percent of Hearts Transplanted			**Prior to Organ Recovery:** Percent of Hearts Transplanted		
Variables	Not Met	Met	*p*	Not Met	Met	*p*	Not Met	Met	*p*
Gender (Male)	**24%**	**39%**	***<0.001***	-	-	-	-	-	-
Donor Type (Standard Criteria Donor)	**4%**	**42%**	***<0.001***	-	-	-	-	-	-
BMI (<30 kg/m^2) [a]	**25%**	**37%**	***<0.001***						
Donor Management Goals Bundle Met	**32%**	**36%**	***0.045***	**28%**	**39%**	***<0.001***	**28%**	**37%**	***<0.001***
Mean Arterial Pressure (60-110 mmHg)	34%	33%	*0.774*	33%	33%	*0.914*	30%	33%	*0.173*
Central Venous Pressure (4-12 mmHg)	32%	35%	*0.084*	32%	34%	*0.134*	**30%**	**35%**	***0.008***
Ejection Fraction (≥50%)	33%	34%	*0.828*	**29%**	**40%**	***<0.001***	**24%**	**41%**	***<0.001***
Arterial Blood Gas pH (7.30-7.50)	33%	33%	*0.500*	**27%**	**34%**	***0.005***	29%	34%	*0.111*
PaO_2/FiO_2 (≥300)	**31%**	**36%**	***0.004***	**30%**	**37%**	***<0.001***	**29%**	**37%**	***<0.001***
Serum Sodium (≤155mEq/L)	32%	33%	*0.533*	**30%**	**34%**	***0.031***	33%	33%	*0.901*
Blood Glucose (≤180mEq/L)	33%	33%	*0.740*	31%	34%	*0.116*	31%	34%	*0.120*
Urine Output (≥0.5ml/kg/h)	**29%**	**34%**	***0.035***	**28%**	**34%**	***0.009***	30%	34%	*0.114*
Vasopressors (≤1 and low dose)[b]	32%	34%	*0.295*	**31%**	**35%**	***0.020***	**30%**	**35%**	***0.004***
Dopamine used (>0 mcg/kg/min)[c]	33%	34%	*0.544*	**34%**	**30%**	***0.039***	32%	36%	*0.083*
Neosynephrine used (>0mcg/min)[d]	33%	34%	*0.470*	34%	30%	*0.096*	**34%**	**24%**	***<0.001***
Norepinephrine used (>0 mcg/kg/min)[e]	33%	33%	*0.733*	**34%**	**27%**	***0.008***	**34%**	**20%**	***<0.001***
Epinephrine used (>0mcg/min)[f]	**33%**	**21%**	***0.022***	33%	22%	*0.129*	33%	26%	*0.477*
Thyroid Hormone used (>0 mcg/hr)[g]	33%	35%	*0.356*	34%	32%	*0.475*	**35%**	**30%**	***0.005***
Vasopressin used (>0 units/hr)[h]	33%	32%	*0.534*	32%	35%	*0.143*	33%	34%	*0.656*

Univariate Analysis: Predictors of Heart Transplantation

	Authorization: Percent of Hearts Transplanted			**12-18 hours after Auth:** Percent of Hearts Transplanted			**Prior to Organ Recovery:** Percent of Hearts Transplanted		
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Gender (Male)	**24%**	**39%**	***<0.001***	-	-	-	-	-	-
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Central Venous Pressure (4-12 mmHg)	32%	35%	*0.084*	32%	34%	*0.134*	**30%**	**35%**	***0.008***
Ejection Fraction (≥50%)	33%	34%	*0.828*	**29%**	**40%**	***<0.001***	**24%**	**41%**	***<0.001***
Arterial Blood Gas pH (7.30-7.50)	33%	33%	*0.500*	**27%**	**34%**	***0.005***	29%	34%	*0.111*
PaO_2/FiO_2 (≥300)	**31%**	**36%**	***0.004***	**30%**	**37%**	***<0.001***	**29%**	**37%**	***<0.001***
Serum Sodium (≤155mEq/L)	32%	33%	*0.533*	**30%**	**34%**	***0.031***	33%	33%	*0.901*
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Norepinephrine used (>0 mcg/kg/min) [e]	33%	33%	*0.733*	**34%**	**27%**	***0.008***	**34%**	**20%**	***<0.001***
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Vasopressin used (>0 units/hr) [h]	33%	32%	*0.534*	32%	35%	*0.143*	33%	34%	*0.656*

Multivariate Analysis: Predictors of Heart Transplantation

Table 3A (B). Multivariate Analysis: Independent Predictors of Heart Utilization with p<0.05 in Univariate Analysis (N=2552/3433)			
Variables	Odds Ratio	95% CI of OR	p-value
Donor Type -SCD(Cat)	**4.100**	**2.594-6.480**	**<0.001**
Age (Cont)	**0.938**	**0.930-0.946**	**<0.001**
BMI <30 (Cat)	**0.796**	**0.640-0.989**	**0.039**
Gender - Male (Cat)	**1.664**	**1.350-2.050**	**<0.001**
Donor Management Goals Bundle			
Authorization (Cat)	0.953	0.753-1.207	0.692
12-18 Hours After Authorization (Cat)	**1.450**	**1.158-1.817**	**0.001**
Prior to Organ Recovery (Cat)	1.239	0.978-1.570	0.075
Creatinine at 12-18 Hrs (Cont)	**0.830**	**0.770-0.894**	**<0.001**
Epinephrine at Auth (Cat)	**0.505**	**0.265-0.964**	**0.038**
Dopamine at 12-18 Hrs (Cat)	1.057	0.844-1.324	0.627
Norepineprhine at 12-18 Hrs (Cat)	0.839	0.611-1.151	0.276
Neosynephrine Prior to OR (Cat)	0.781	0.589-1.035	0.085
Thyroid Hormone Prior to OR (Cont)	**0.985**	**0.974-0.996**	**0.006**
Hosmer=0.316, CI=0.819			

Multivariate Analysis: Predictors of Heart Transplantation

Table 3A (B). Multivariate Analysis: Independent Predictors of Heart Utilization with p<0.05 in Univariate Analysis (N=2552/3433)			
Variables	Odds Ratio	95% CI of OR	p-value
Donor Type -SCD(Cat)	**4.100**	**2.594-6.480**	**<0.001**
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Gender - Male (Cat)	**1.664**	**1.350-2.050**	**<0.001**
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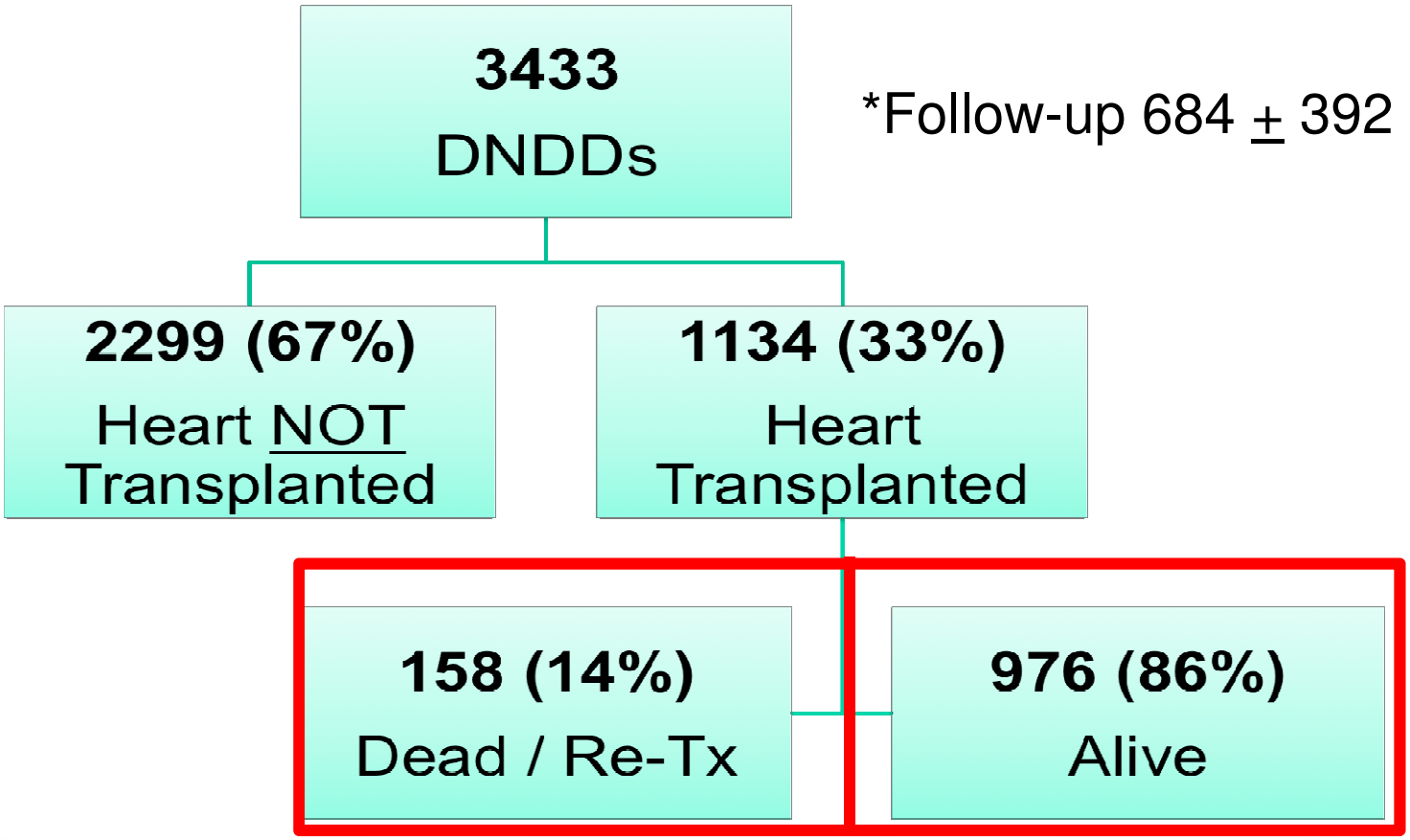
Neosynephrine Prior to OR (Cat)	0.781	0.589-1.035	0.085
Thyroid Hormone Prior to OR (Cont)	**0.985**	**0.974-0.996**	**0.006**
Hosmer=0.316, CI=0.819			

Multivariate Analysis: Predictors of Heart Transplantation

12-18 Hours after Authorization:			
Ejection Fraction met (Cat)	**1.655**	**1.351-2.028**	**<0.001**
Arterial Blood Gas met (Cat)	1.161	0.825-1.633	0.392
PiO_2:FiO_2 Ratio met (Cat)	**1.034**	**1.068-1.593**	**0.009**
Sodium met (Cat)	1.102	0.860-1.413	0.442
Urine Output met (Cat)	1.103	0.801-1.519	0.548
Vasopressors ≤1 and low dose (Cat)	1.069	0.786-1.454	0.672
Prior to Organ Recovery			
Central Venous Pressure met (Cat)	1.055	0.854-1.303	0.618

Impact of Donor Demographics and Critical Care Endpoints on Cardiac Transplantation and Recipient Survival



*Follow-up 684 ± 392 days

SRTR Data Added:

Elements of risk-adjusted 1-year Recipient Survival Model

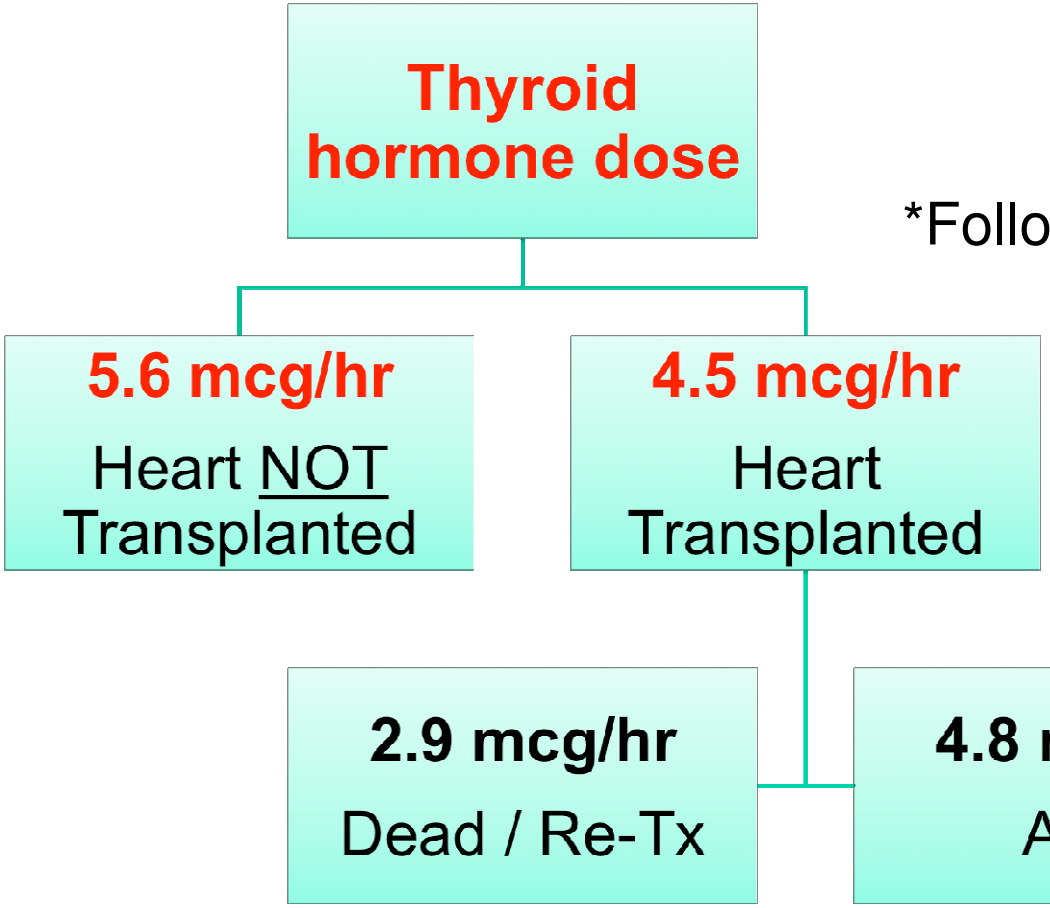
Bilirubin at Transplant
Dialysis at Transplant
Donor Age years (Cont)
Donor Cause of Death (CVA/Stroke vs Others)
Drug-Treated HTN at Listing
Ischemic Time (Cont)
Medical Condition (Cat)
Not Hospitalized
In ICU
Hospitalized Not in ICU
Pulmonary Artery Systolic Pressure mmHg (Cont)
Previous Heart Transplant (Cat)
Recipient Age at Transplant (Cat)
65+
<50
50-64
Recipient Diagnosis (Cat)
Coronary Artery Disease
Cardiomyopathy
Congenital Heart Disease
Other/Missing
Recipient Height cm (Cont)
Recipient Race/Ethnicity
White
Black
Hispanic/Latino
Asian
Multi-Racial/others/missing
Recipient Serum Creatinine (>1.5) (Cat)
Recipient on Life Support: ECMO (Cat)
Recipient on Life Support: VAD (Cat)
Recipient on Life Support: Ventilator (Cat)
Sudden Death at Listing (Cat)

Multivariate Analysis: Predictors of Heart Recipient Survival*

Table 11C. Multivariate Analysis: Independent Predictors of Heart Graft Survival with variables with p<0.05 from univariate analysis and from adjusted risk ratio model (N=914/1134)

Variables	Odds Ratio	95% CI for OR	p-value
Age	0.985	0.967-1.004	0.132
Authorization			
Mean Arterial Pressure (Cont)	0.993	0.981-1.006	0.300
12-18 Hours after Authorization:			
Glucose (Cat)	1.197	0.789-1.814	0.398
Vasopressors ≤1 and low dose (Cat)	1.481	0.977-2.246	0.064
Thyroid Hormone use at 12-18 hours after Auth (Cont)	**1.039**	**1.009-1.071**	**0.011**
Norepinephrine use Prior to Organ Recovery (Cat)	3.729	0.487-28.546	0.205

Impact of Donor Demographics and Critical Care Endpoints on Cardiac Transplantation and Recipient Survival

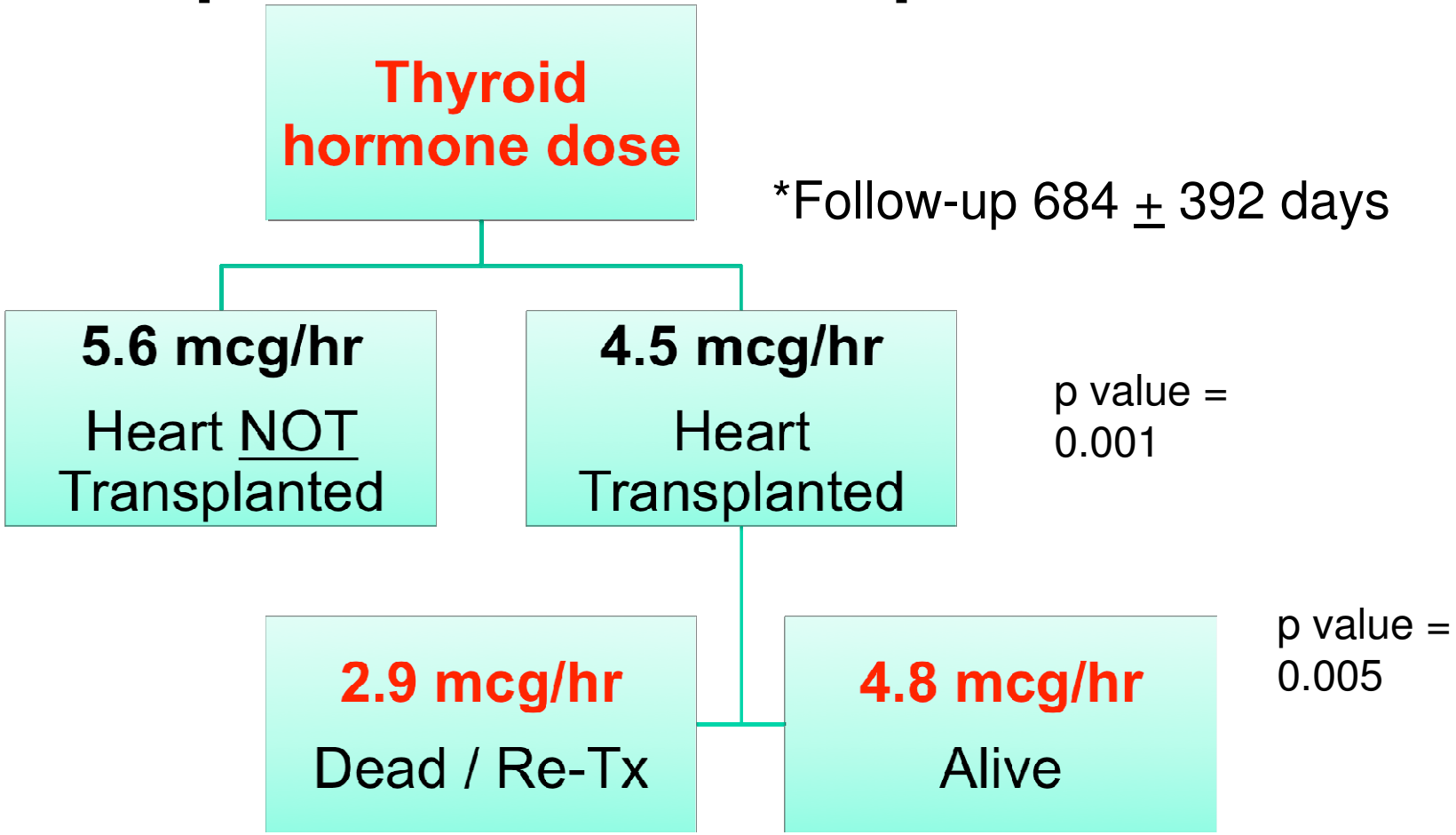


*Follow-up 684 ± 392 days

p value = 0.001

p value = 0.005

Impact of Donor Demographics and Critical Care Endpoints on Cardiac Transplantation and Recipient Survival



Summary

- Predictors of Heart Utilization:
  - Positive: meeting the DMG Bundle, EF $\geq$ 50%, and PaO2:FiO2 $\geq$ 300
  - Negative: serum creatinine, Epinephrine use, and thyroid hormone dose
- Predictors of heart survival
  - Positive: thyroid hormone dose

Summary

- Predictors of Heart Utilization:
  - Positive: meeting the DMG Bundle, EF $\geq$ 50%, and PaO2:FiO2 $\geq$ 300
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- Predictors of heart survival
  - Positive: thyroid hormone dose → RCT needed

Thank You

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