Organ utilization/risk perception by providers and patients

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With substantial and very appreciated assistance from **Marissa Clark** and **Sarah Taranto, UNOS research**

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RESOLVING THE ORGAN SHORTAGE

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FEBRUARY 25-27, 2016 • PHOENIX, ARIZONA

Conflict of Interest Disclosure

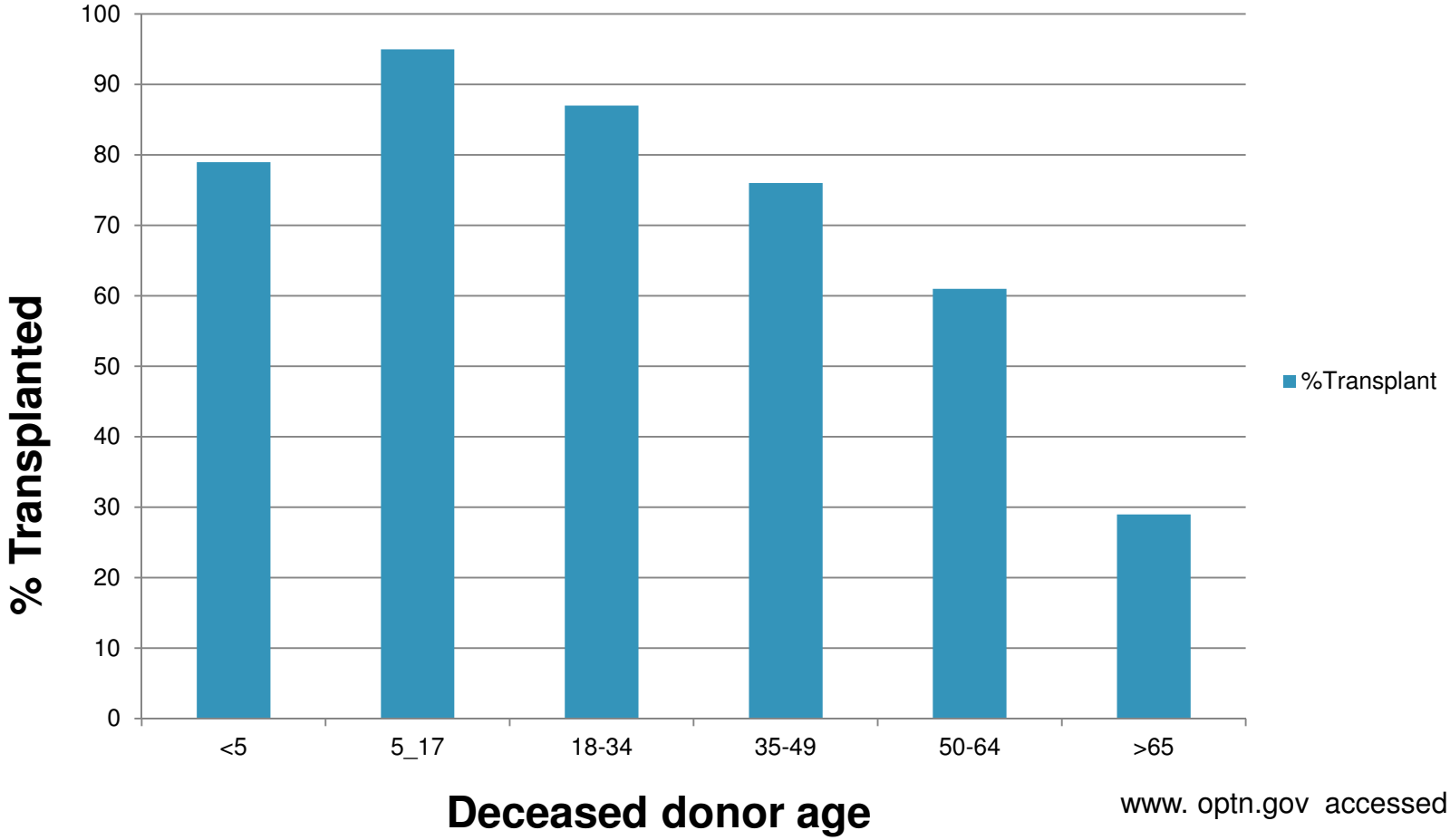
- I have no relevant financial relationships to disclose

Americans want/like/expect the "best": affects decision making

How does it affect organ utilization?

Age matters: younger better

Kidneys transplanted/donor: 2014

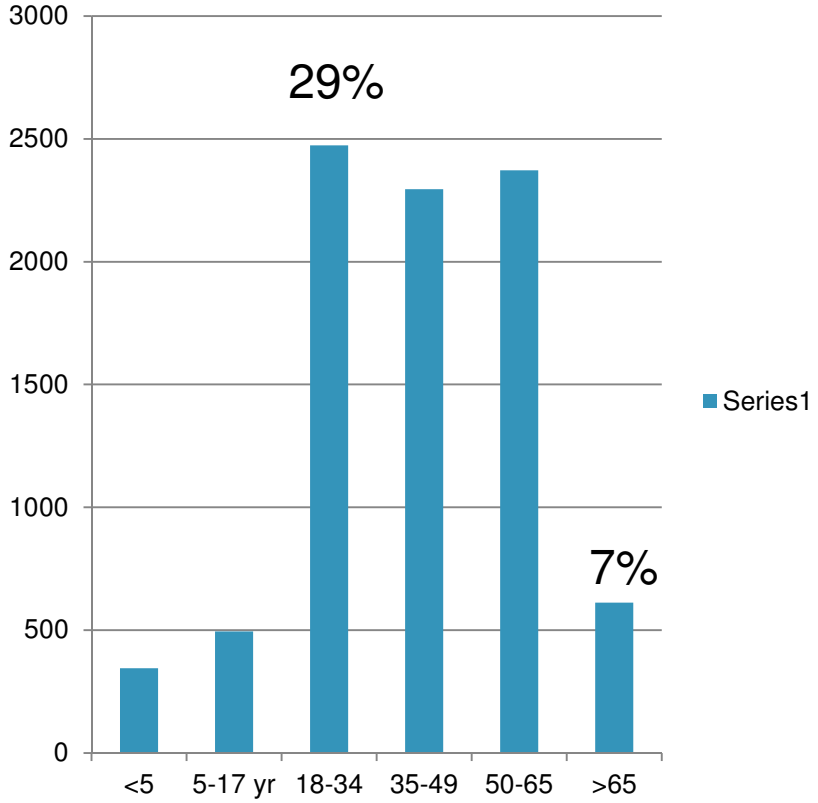


www. optn.gov accessed Jan 2015

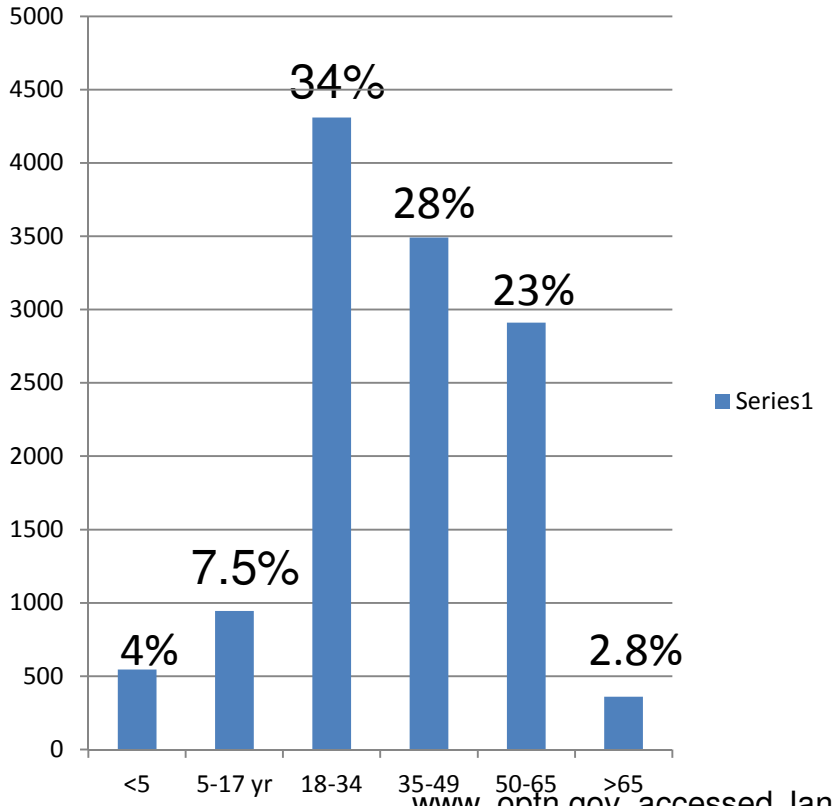
2014 Donor availability ≠ organ usage

making due with what you have

8596 deceased donors



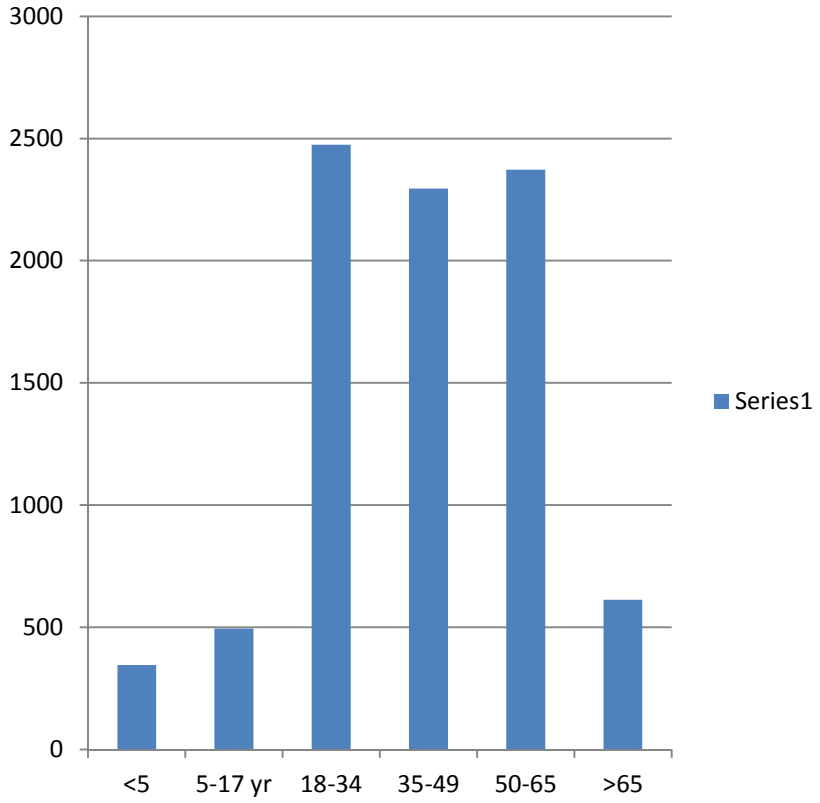
11,570 kidney txp donor age



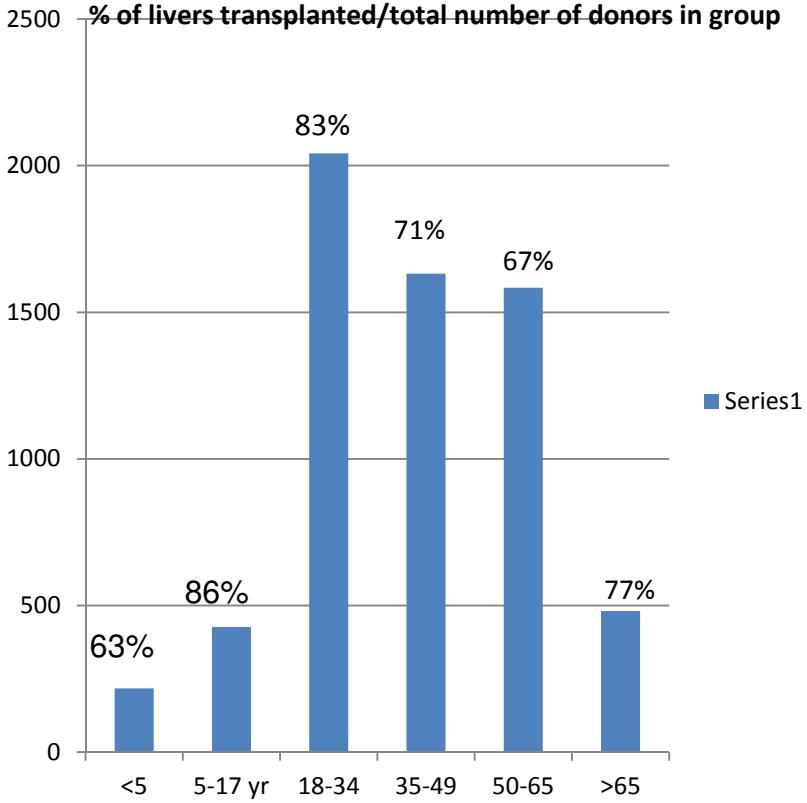
www. optn.gov accessed Jan 2015

Organ utilization differs: organ type is important in decision making

2014 deceased donors



2014 donor age: liver txp



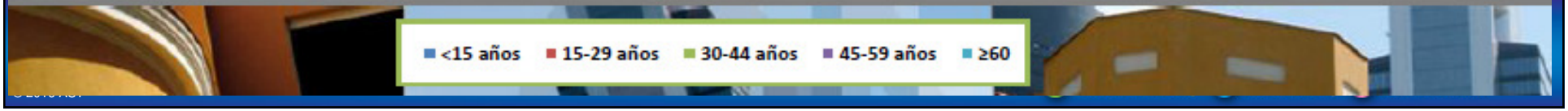
GOBIERNO DE ESPAÑA
MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD
ONT

EVOLUTION OF THE AGE OF THE DONORS IN SPAIN

http://www.ont.es/Documents/Balance_Actividad_2015_English.pdf

SINCE 2011, MORE THAN HALF OF THE DONORS ARE > 60 YEARS OLD

	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
≥60	10	11,5	17	20,5	22	28	27	30,3	31,4	33,9	34,4	34	38,2	38	38,6	42,9	44,3	44,8	46,6	53,6	50,7	52,5	53,9	53,3
45-59 años	21	31,5	28	30	27,6	25,8	27,1	26,5	28,1	28,8	29,8	28,7	29,8	29,1	29	29,2	28,6	29,8	32,4	27,8	28,4	30,5	28,8	31
30-44 años	25	20,5	23	20	19,8	21,9	19,4	19,2	17,1	16,3	15,5	16,2	14,7	15,9	16,7	15,9	15,9	14,8	12,7	12,9	13,4	10,8	11,8	10,2
15-29 años	34	27	23	22,5	22,8	19,5	20,5	19,6	19,7	17,8	15,1	16,6	12,8	13,1	12,5	9,3	8,8	7,2	6,6	4	5,8	3,7	4	4
<15 años	10	9,5	9	7	7,7	5,8	5,7	4,4	3,8	3,2	5,2	4,5	4,5	4	3,2	2,6	2,4	3,4	1,7	1,7	1,7	2,5	1,5	1,6



We (US) have issues in organ utilization and donor availability

The situation

- USA Facts:
  - Over 400,000 people on dialysis
  - Over 100,000 new ESRD/yr
  - Only obtain 14,000 DD kidneys /yr from 8,307 DD
  - Only transplant 11,216 DD kidney (2015).

- Reality: there are not enough organs for everyone on the list.

  “you can’t always get what you want” Mic

The risk-benefit analysis: the reality and perception of risk

People in the US are exposed to infectious agents.

- CMV: 50-85% of US population will have had CMV by the age of 40.
- EBV: about 20% of US population has EBV antibodies.
- HBV: about 0.5% US population, HBV carriers (HBsAg+), but 4-5% are HBcAb+ (indicating past infection and latent HBV in liver). 80% of worldwide HBV cases occur in Asia.
- HCV: 1.8% US population
- HIV: About 1 million people with HIV; 37,000 new cases/yr
- Toxoplasmosis: about 25% have been exposed.
- Syphilis: 70K new cases/yr, untreated/latent <200,000 in US, but not 0.
- Lyme disease (Borrelia): geographic (Northeast, Wisc/Minn, Calif/Ore). 15-20,000 cases/year.
- Tuberculosis: 1998, 18,371 active cases (CDC), 10-15 million with "old" TB (NIAID)
- Miscellaneous: LCMV, babesiosis, rabies, Chagas', Ehrlichia, HTLV ½, atypical tuberculosis, Schistosomiasis, Strongyloides and Coccidiodomycosis and other fungi
- Zika virus

http://www.cdc.gov/diseasesconditions access 2012

Some of these people are going to die and will potentially to be an organ donor. RISK

1. How do you recognize the risk in the donor?
2. What is the risk of transmission to the organ recipient?
3. How does the **perception of risk** affect the (decision-making) of the transplant recipient/surgeon/program?

Organ donor risk assessment of transmissible diseases as written into OPTN policy

- OPOs to determine conditions which may influence donor acceptance (2.2.3), obtain the donor's history. (2.2.4), review the medical chart (2.2.5)
- Perform a physical exam. (2.2.6) and obtain vital signs (2.2.7)
- Policy 2.2.8.1: Assessment of infection mandated by OPTN:
  - Anti-HIV I,II (2.2.2); Hepatitis serology (HBsAg, HBcAb, anti-HCV); VDRL or RPR; anti-CMV, EBV; blood and urine cultures if in hospital >72 hours, urinalysis within 24 hours of cross clamp and chest x-ray.
  - HCV NAT: all donors; HIV NAT or HIV Ag/Ab combo test for increased risk donors (after 2013)
  - Tests should be FDA approved and performed in an approved laboratory facility.

There are known knowns; there are things that we know that we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns, the ones we don't know we don't know.

D. Rumsfeld: 2/2002

Recommendations and Reports

MMWR™

May 20, 1994 / 43(RR-8);1-17

Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs

Chicago Tribune
chicagotribune.com

4 organ patients get HIV Donor's infection is 1st such case in U.S. in 22 years

By Jeremy Manier and Tribune Staff Reporter
November 13, 2007

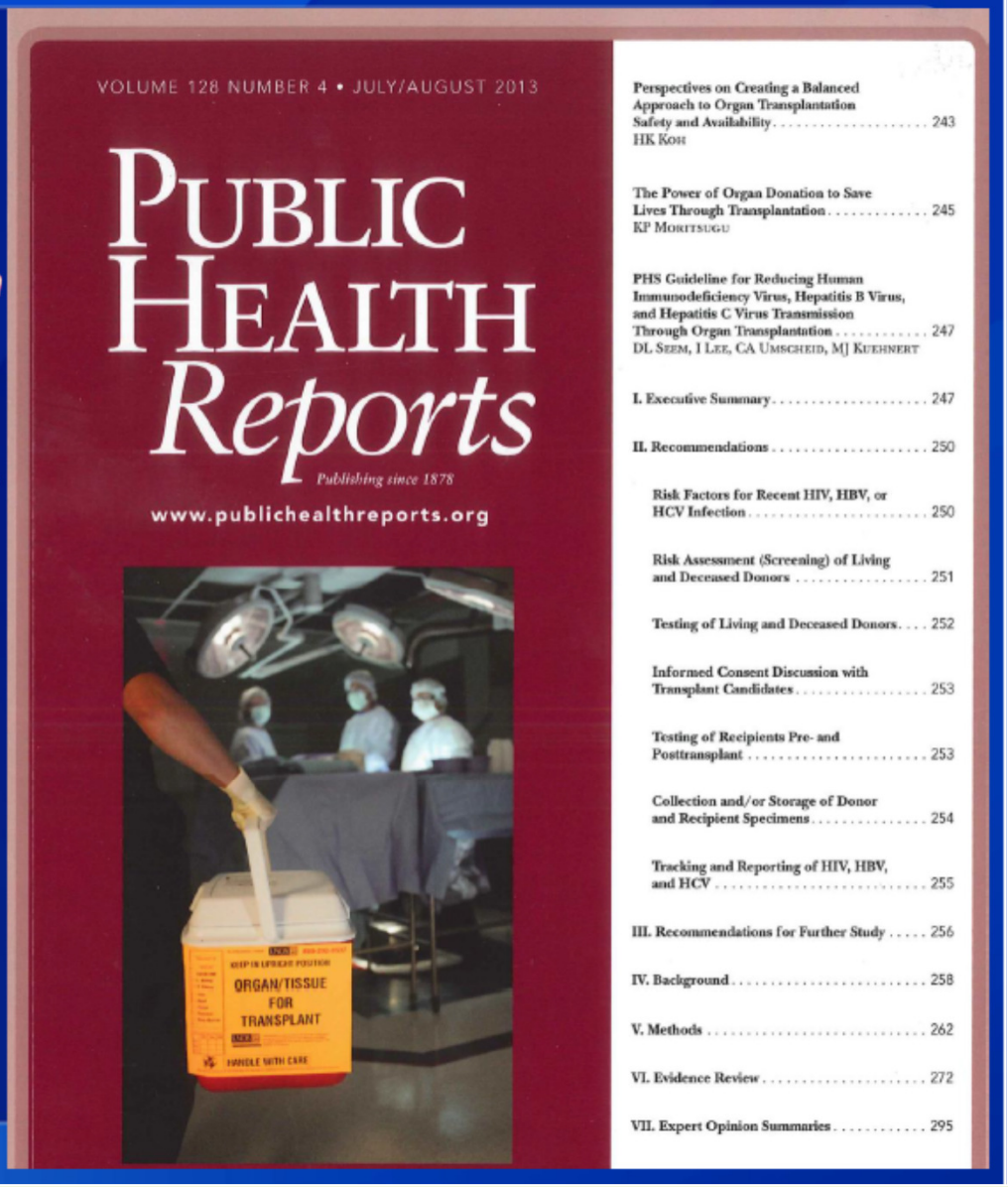
Consequences of the HIV/HCV transmission: 2008

- HRSA instructed UNOS/OPTN that ***recipients must be informed*** when an organ offer comes from a donor with “high risk” behavior.
  - High risk behaviors as defined by CDC in the 1994 PHS guidelines for tissue and organ donors
    - Several vague definitions
    - Definition of informed consent in this setting is not clear.
  - Commercial testing ability was changing. NAT available.
- Formal establishment of a Disease Transmission Advisory Committee in UNOS/OPTN: patient safety

The 2013 PHS Guideline

- *Public Health Service (PHS) Guideline for Reducing HIV, HBV and HCV Infection Transmitted through Organ Transplantation*
  - Transmission of HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV)
  - Organs and blood vessel conduits used for transplantation
  - Developed by USPHS via evidence-based process and expert input

NOW PUBLISHED!



"High Risk" Populations for Transmitting HIV by OPTN Policy 4.1.1 and amended PHS language

- Behavior & History for **increased risk** (not high risk any more)
- 1. Men who have had sex with another man in the preceding 5 (**1**) years.
- 2. Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 (**1**) years.
- 3. Persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates. (**removed**)
- 4. Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 (**1**) years.
- 5. Persons who have had sex in the preceding 12 months with any person described in items 1–4 above or with a person known or suspected to have HIV infection.
- 6. Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, non-intact skin, or mucous membrane.
- 7. Inmates of correctional systems for more than 72 hours in preceding year.
- 8. **Newly diagnosed STD** within prior 12 months.
- 9. HCV only: dialysis within prior 12 months.
- 10. Child <18 mo: born from or at risk for HIV, HBV or HCV mother. Child<18 mo. breast fed by HIV or at risk mother.
- 11. Donor with an inadequate sample to assess for infectious agents

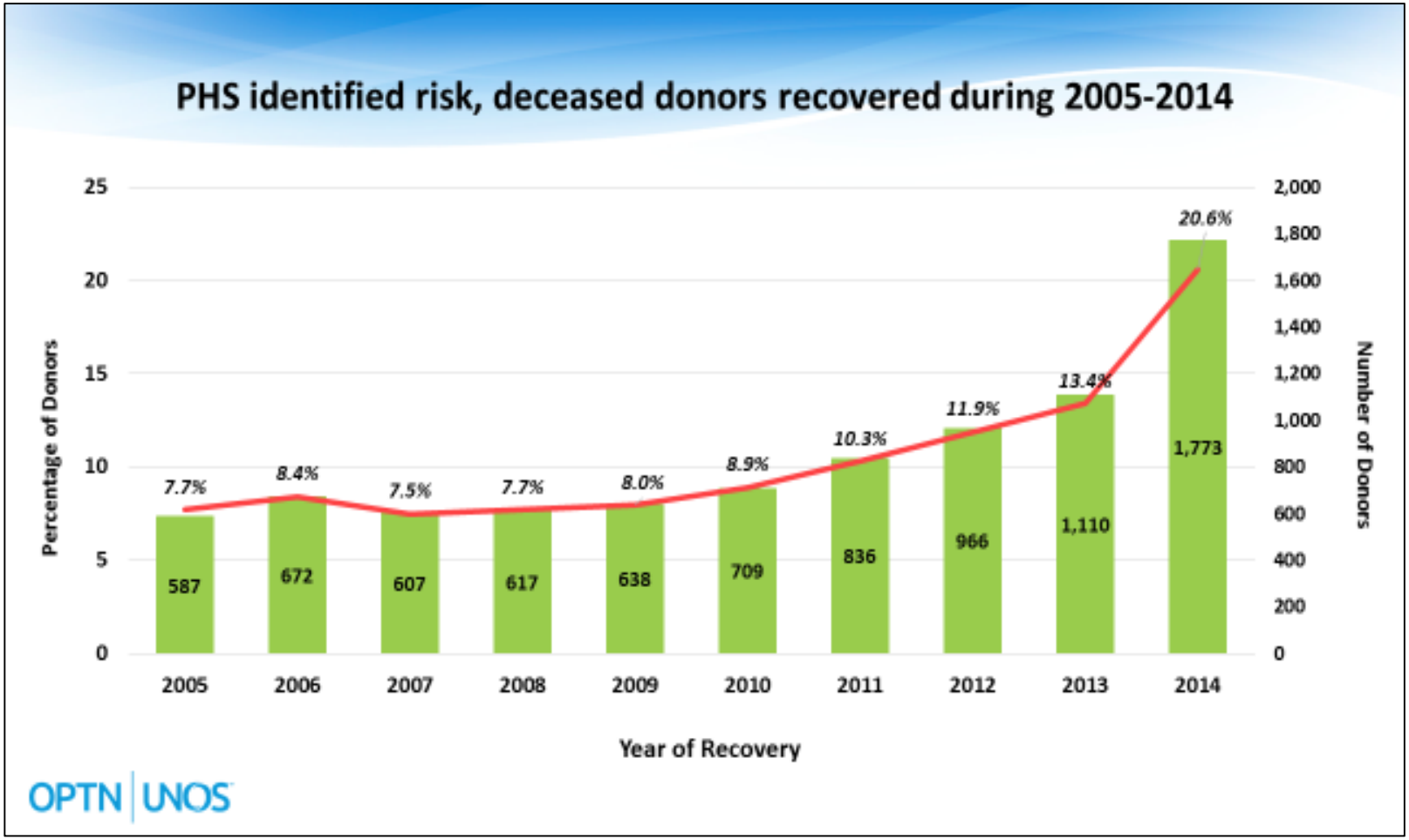
With the caveat that all donors to be assessed by anti-HCV and NAT and all increased risk donors are assessed by anti-HIV and NAT or Ag/Ab combo test.

Who are these PHS identified donors (vs “regular” donors)?

OPTN data to determine differences between PHS and standard risk donors, with specific interest:

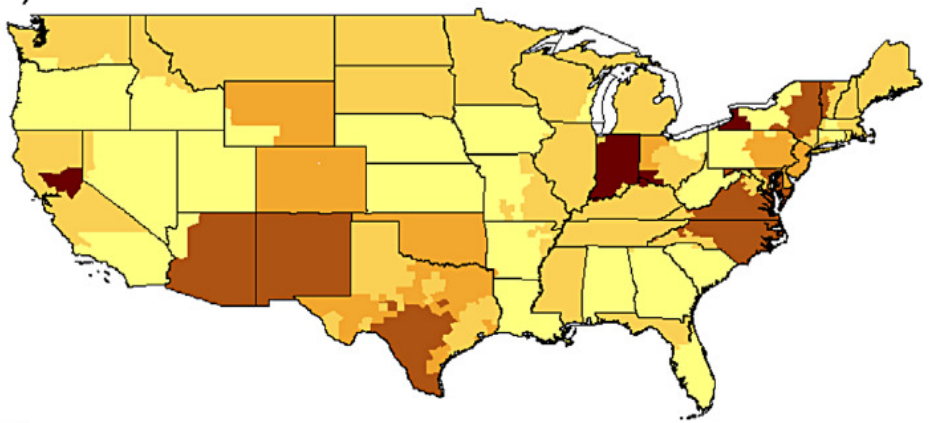
- Donor demographics
- Detection of virus (HIV, HBV, HCV)
- Utilization and outcomes of organ from these donors
- Does disclosure/identification change use?

PHS identified donors a significant portion of donor pool

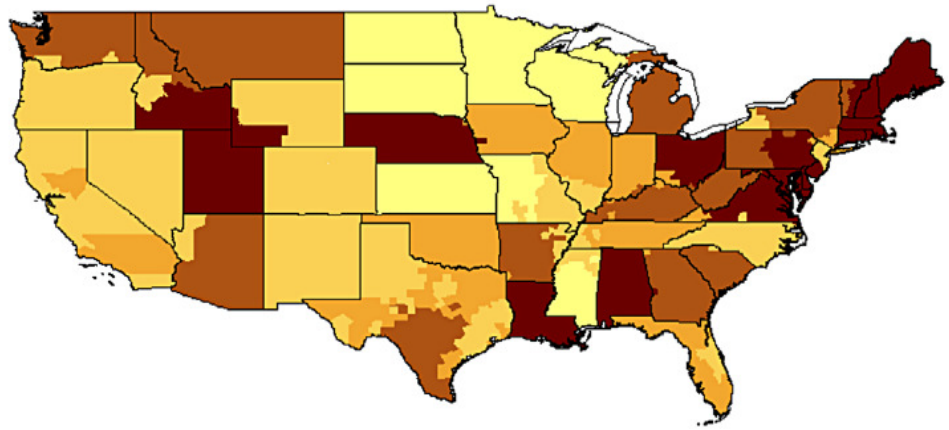


Not surprisingly, donors are unevenly distributed and transplanted across country

(A) Old Guidelines, Percent of Donors Labeled IRDs



(B) New Guidelines, Percent of Donors Labeled IRDs



% Of Donors Labeled IRD

- ≤10
- 11-15%
- 16-20%
- 21-25%
- >25%

American Journal of Transplantation 2015; 15: 3215–3223

Donors with PHS criteria are younger: even more so with the revised criteria

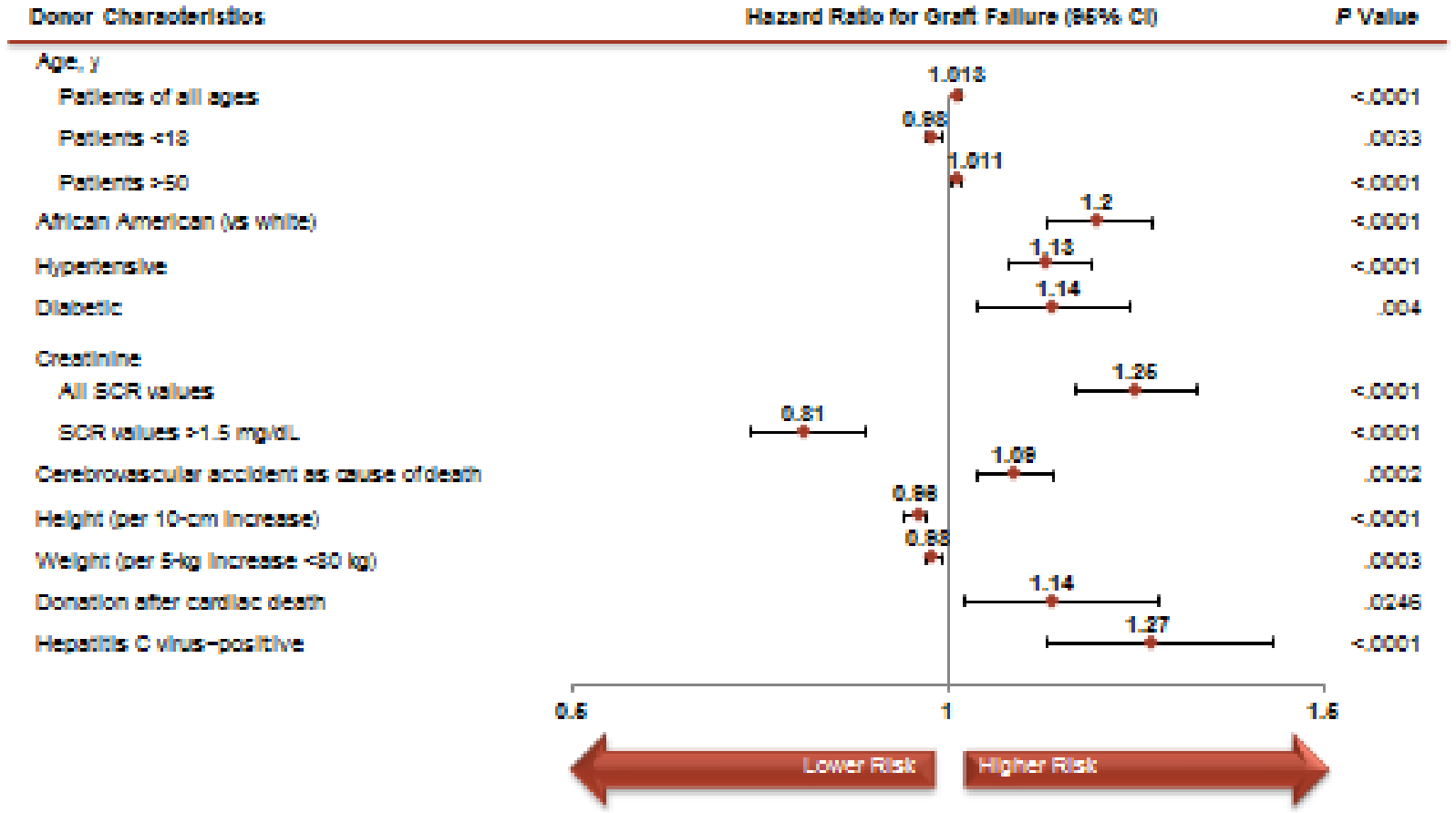
Year of Recovery / Risk Classification		Donor Age									Total	
		0-17			18-34			35+				
		N	Col %	Row %	N	Col %	Row %	N	Col %	Row %	N	Col %
2012	**Standard Risk**	781	91.7	10.9	1,851	79.3	25.8	4,545	91.7	63.3	7,177	88.1
	PHS High Risk	71	8.3	7.3	484	**20.7**	50.1	411	8.3	42.5	966	**11.9**
	Total	852	100.0	10.5	2,335	100	28.7	4,956	100.0	60.9	8,143	100
2014	**Standard Risk**	745	88.6	10.9	1,632	66.0	23.9	4,446	84.2	65.2	6,823	79.4
	PHS Increased Risk	96	11.4	5.4	842	**34.0**	47.5	835	15.8	47.1	1,773	**20.6**
	Total	841	100.0	9.8	2,474	100	28.8	5,281	100.0	61.4	8,596	100
Total	**Standard Risk**	1,526	90.1	10.9	3,483	72.4	24.9	8,991	87.8	64.2	14,000	83.6
	PHS Identified Risk	167	9.9	6.1	1,326	27.6	48.4	1,246	12.2	45.5	2,739	16.4
	Total	1,693	100.0	10.1	4,809	100.0	28.7	10,237	100.0	61.2	16,739	100.0

PHS Donors different in other aspects: male, white, less DM/HTN, non-CVA death

Donor Characteristics	Year of Recovery / Risk Classification									
	2012					2014				
	PHS High Risk		Standard Risk		Chi-Square p-value	PHS Increased Risk		Standard Risk		Chi-Square p-value
	N	%	N	%		N	%	N	%	
Total	966	100.0	7,177	100.0		1,773	100.0	6,823	100.0	
Ethnicity					<0.0001					0.0311
White	728	75.4	4,654	64.8		1,191	67.2	4,522	66.3	
Black	131	13.6	1,238	17.2		296	16.7	1,042	15.3	
Hispanic	88	9.1	945	13.2		224	12.6	922	13.5	
Asian	13	1.3	206	2.9		28	1.6	184	2.7	
Other	6	0.6	134	1.9		34	1.9	153	2.2	
Gender					<0.0001					<0.0001
Male	642	66.5	4,178	58.2		1,185	66.8	3,979	58.3	
Female	324	33.5	2,999	41.8		588	33.2	2,844	41.7	
History of Diabetes					<0.0001					0.0187
Yes	53	5.5	967	13.5		184	10.4	847	12.4	
No/Unknown	913	94.5	6,210	86.5		1,589	89.6	5,976	87.6	
History of Hypertension					<0.0001					<0.0001
Yes	217	22.5	2,656	37.0		492	27.7	2,450	35.9	
No/Unknown	749	77.5	4,521	63.0		1,281	72.3	4,373	64.1	
Cause of Death					<0.0001					<0.0001
Anoxia	412	42.7	2,024	28.2		832	46.9	2,067	30.3	
Cerebrovascular / Stroke	188	19.5	2,645	36.9		331	18.7	2,452	35.9	
Other	366	37.9	2,508	34.9		610	34.4	2,304	33.8	

Stratifying kidney quality

Donor Characteristics in the Kidney Donor Risk Index (KDRI)[1]



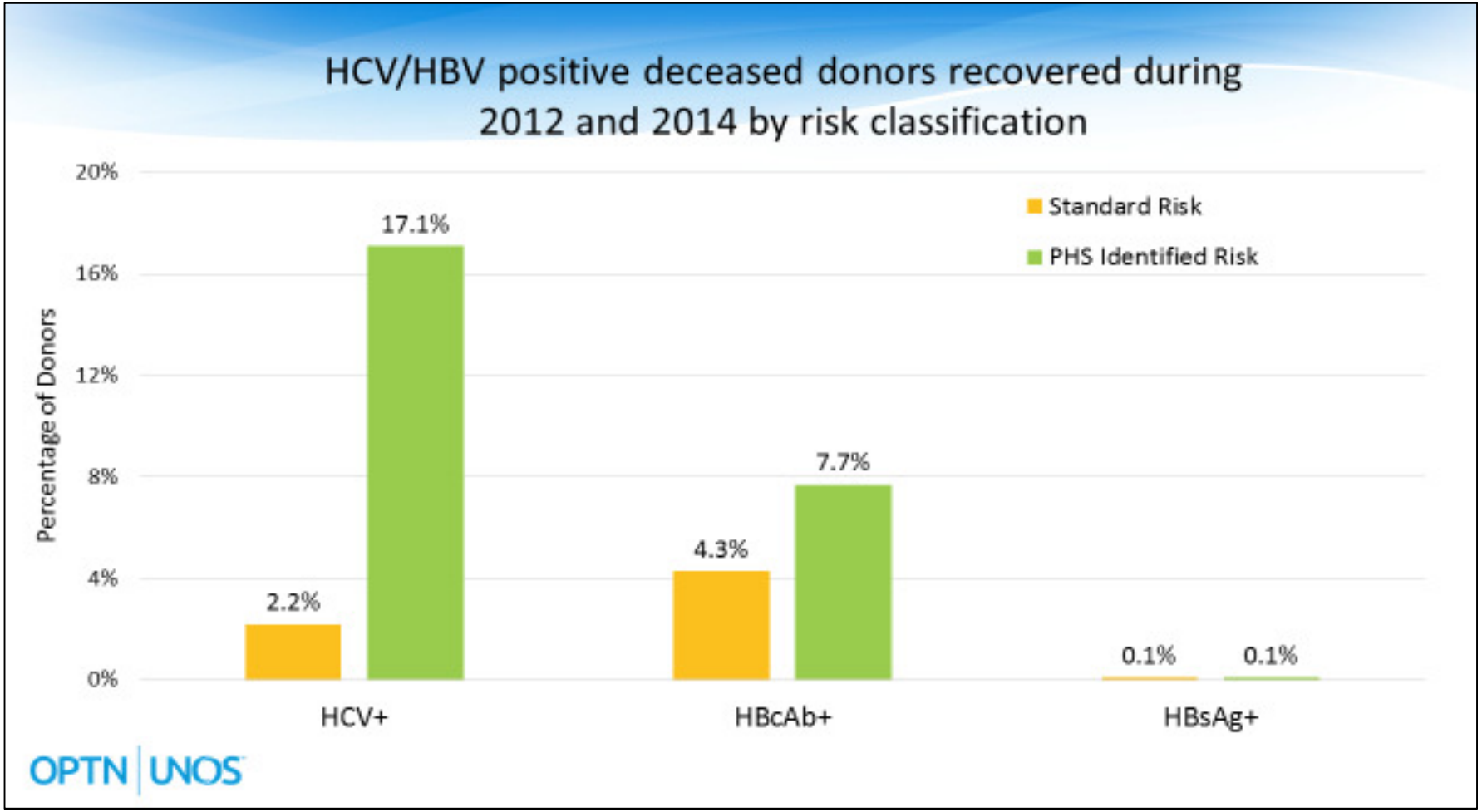
SCR, serum creatinine.

3

Kidneys from PHS donors: KDPI

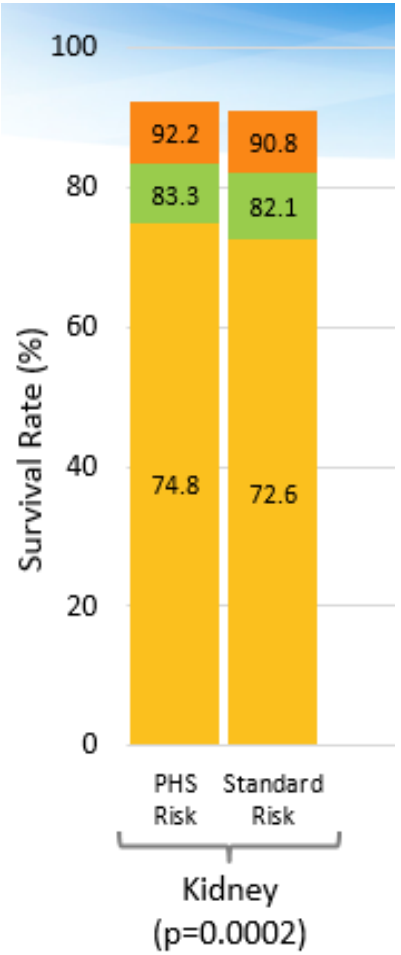
Year of Recovery / Donor Characteristics		Risk Classification								Satterthwaite p-value
		PHS Identified Risk				Standard Risk				
		N	Mean	Std Dev	Std Err	N	Mean	Std Dev	Std Err	
2012	**Age (yrs)**	966	34.0	14.5271	0.4674	7,177	40.6	18.2564	0.2155	<0.0001
	KDPI	930	41.6	27.8457	0.9131	7,141	54.6	30.2292	0.3577	<0.0001
2014	**Age (yrs)**	1,773	35.5	14.1176	0.3353	6,823	41.3	18.2586	0.2210	<0.0001
	KDPI	1,716	46.1	28.6251	0.6910	6,793	55.2	29.6335	0.3595	<0.0001
Total	**Age (yrs)**	2,739	**35.0**	14.2781	0.2728	14,000	**40.9**	18.2602	0.1543	<0.0001
	KDPI	2,646	**44.5**	28.4311	0.5527	13,934	**54.9**	29.9408	0.2536	<0.0001

PHS and standard risk donors differ by infectious risk



Age, HCV and kidney function

- **Youth** wins overall (graph)
  - PHS donor kidneys have a lower KDPI and greater 1,3, 5 yr survival compared to Std risk kidney
- KDPI of 18-34 yr old kidney: effect of **HCV**
  - PHS vs Std risk: **25.6** vs **21.7**
  - HCV-: PHS **21.8** Std risk: **21.3**



2005-2010 kidney txp

HCV+ affects organ acceptance: 18-34 standard risk donors (2014)

- HCV Testing (objective standard)
  - **Kidney** Standard risk donor HCV-/+: 1.84/1.18
  - **Liver** Standard risk donor HCV-/+: 0.84/0.73
- Organ transplantation per donor (18-34): 2014
  - **Standard risk HCV-**: 4.20 vs **HCV+** 1.91
- 2012-2014: no extrarenal/hepatic organ from an HCV+ standard risk donor was transplanted (only one heart was transplanted and that was a PHS identified donor).

Does **labeling** a donor: "**increased risk**" impact upon organ **utilization** and transplant **outcomes?**

- Is organ acceptance impacted by the way the organ is labeled?
- Does the "label" have an impact upon outcomes?
  - Graft function
  - Transmission of HIV, HBV or HCV

Assess outcomes/utilization of good organs (within OPTN data base):

young adult (18-34 y.o.), **no objective risk** for BBP transmission risk (HCV-, HBsAg-, HIV-)

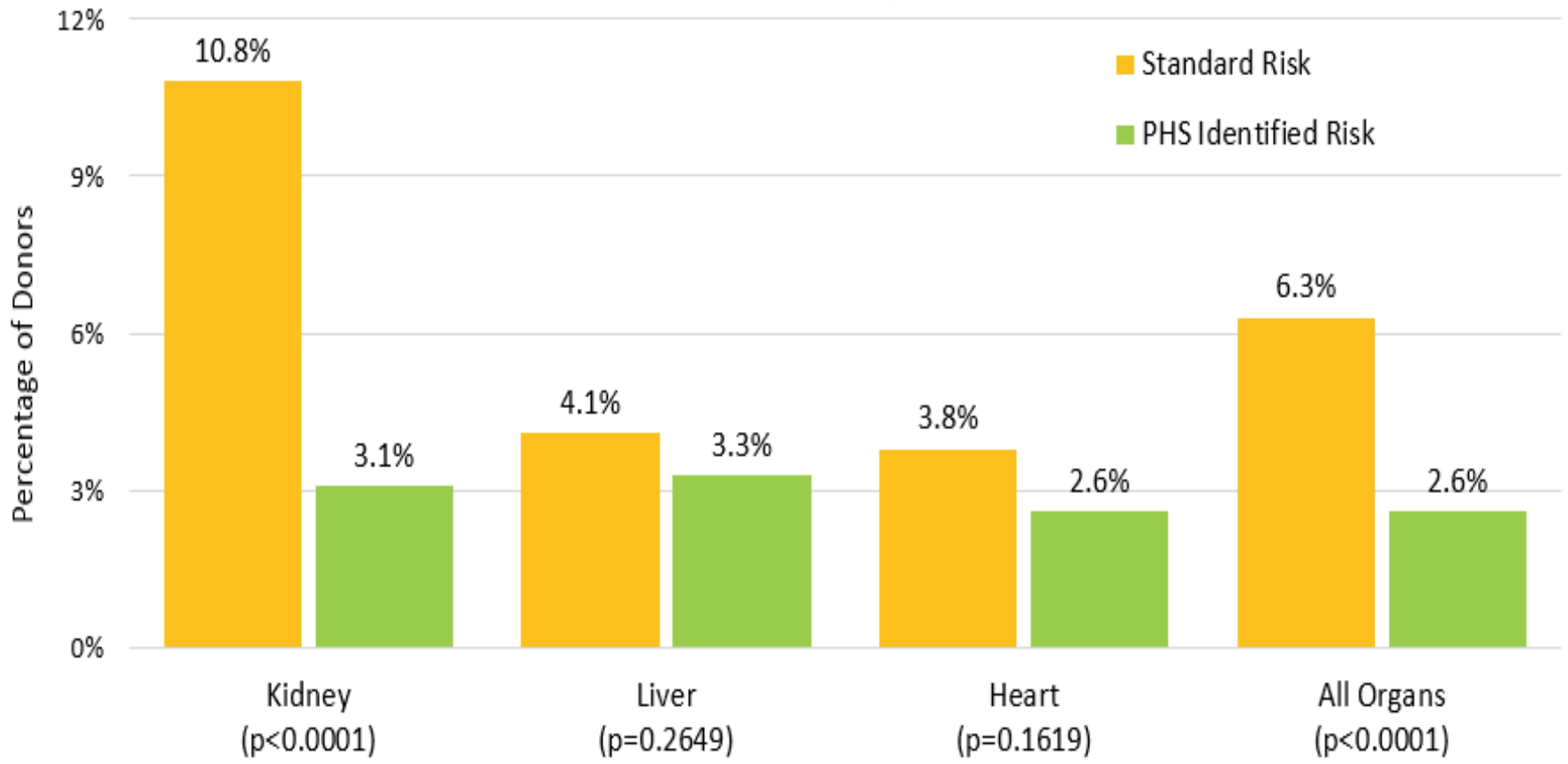
Organs transplanted/18-34 yo, HCV-deceased donor

	2012		2014	
	Standard risk	High risk	Standard risk	Increased risk
Kidney	1.82	1.75	1.84	1.72
Liver	0.84	0.84	0.84	0.82
Heart	0.55	0.44	0.56	0.54
Lung	0.63	0.52	0.65	0.59
Pancreas	0.32	0.21	0.30	0.20
Intestine	0.02	0.00	0.00	0.02
Total	**4.17**	**3.76**	**4.20**	**3.90**

The recipients of “good” kidneys differ from the PHS and regular donors

- PHS recipients were statistically older (but only a few years).
- Necessary to go further down the match list to identify a recipient for the kidney (not sure as to whether candidate or provider driven).

Deceased donor transplants performed during 2012 and 2014 in pediatric recipients from 18-34 year old, HCV negative donors



OPTN | UNOS

* Organ not shown when ≤1 transplant in a risk group.

Short-term (1 year) transplant outcomes: 2012/2014 organs from 18-34 yo, HCV- donors

Survival Type / Organ		Risk Classification				Log-Rank p-value
		PHS Identified Risk		Standard Risk		
		Survival Rate (%)	95% CL of Survival	Survival Rate (%)	95% CL of Survival	
Patient	Kidney	96.54	[95.75,97.33]	97.12	[96.74,97.50]	0.2135
	Liver	92.66	[91.11,94.21]	91.32	[90.45,92.19]	0.0362
	Heart	90.98	[88.76,93.20]	90.69	[89.58,91.79]	0.6663
	Lung	87.78	[84.68,90.87]	88.48	[87.01,89.94]	0.1406
	Pancreas	88.54	[78.61,98.46]	92.28	[89.06,95.49]	0.1594
	Intestine	66.41	[41.17,91.65]	73.91	[63.34,84.49]	0.5649
Graft	Kidney	94.58	[93.62,95.54]	95.05	[94.56,95.53]	0.2371
	Liver	90.90	[89.21,92.58]	89.58	[88.64,90.51]	0.0948
	Heart	90.98	[88.76,93.20]	90.42	[89.30,91.54]	0.9144
	Lung	86.89	[83.72,90.05]	87.53	[86.02,89.04]	0.2508
	Pancreas	74.12	[62.31,85.93]	78.91	[74.41,83.41]	0.0340
	Intestine	57.89	[33.77,82.02]	69.24	[58.37,80.11]	0.1833

5 year survival of HCV-, 18-34 yr old organs transplanted from 2005-2010

Survival Type / Organ		Risk Classification				Log-Rank p-value
		PHS High Risk		Standard Risk		
		Survival Rate (%)	95% CL of Survival	Survival Rate (%)	95% CL of Survival	
Patient	Kidney	86.90	[85.39,88.40]	87.16	[86.61,87.71]	**0.1962**
	Liver	74.87	[72.40,77.33]	76.31	[75.41,77.20]	**0.5418**
	Heart	77.44	[74.11,80.78]	78.14	[77.02,79.26]	**0.6621**
	Lung	55.57	[50.50,60.65]	55.17	[53.49,56.85]	**0.7193**
	Pancreas	80.66	[72.03,89.28]	84.52	[82.20,86.84]	**0.2512**
	Intestine	50.54	[28.73,72.35]	58.07	[50.88,65.26]	**0.6623**
Graft	Kidney	78.35	[76.56,80.14]	77.89	[77.23,78.56]	**0.5583**
	Liver	72.84	[70.35,75.33]	73.19	[72.27,74.11]	**0.9892**
	Heart	75.99	[72.61,79.37]	77.59	[76.46,78.71]	**0.2775**
	Lung	51.78	[46.79,56.77]	52.48	[50.82,54.15]	**0.9515**
	Pancreas	57.04	[48.05,66.03]	58.37	[55.58,61.16]	**0.6489**
	Intestine	41.67	[21.90,61.43]	49.34	[42.29,56.38]	**0.3974**

Risks are not found in survival alone: OPTN Data and DTAC

- OPTN data: Attribution for patient or graft loss: no difference. Special attention to infectious and liver categories.
- DTAC summary, 2008-2011 (over 100,000 txp's)
  - 2800 high risk organs transplanted, 50 PDDTE
  - 0 HIV transmission, 3 HCV transmission (0 recognized PHS risk by OPO: although DTAC attribution 3/3), 1 HBV
- 2012 and 2014 as change years (16,291 deceased donors)
  - 0 HIV transmission
  - 2012: 3 HCV standard risk, 0 PHS high risk
  - 2014: 1 HCV standard risk, 1 PHS increased risk

Summary

- Decision-making for Organ use/txp is multivariate and usually individualized.
- Donor age is highly influential upon organ acceptance (surrogate for quality/potential).
- Pathogen testing dramatically impacts organ utilization (HBsAg: 0.01% organ use, HCV marked effect and HIV: 0 use).
- PHS label affects organ utilization.
- Unexpected HIV, HBV and HCV transmission is infrequent in the pre-NAT and NAT detection eras.

Summary (cont)

- PHS risk stratification:
  - 20% of all deceased donors, 2014
  - 1/3 of the young adult organ donors, 18-34 are increased risk.
  - 17% HCV detection*
    - *Limitation: current database incapable of discerning Ab-/NAT+ (safety for unexpected transmission) or Ab+/NAT- (potential wastage if proves to be cleared virus/non-infectious)
- Outcomes of PHS vs standard 18-34 yo donor organs:
  - Decreased organ utilization of PHS identified donors (0.3-4/donor): HCV-, HBsAg-. > 200 organs fewer from "best" donor (all organs but liver) and at least another 200 from other age groups if they were used commensurately with standard risk donors.
  - Pediatric recipients diminished use of low KDPI kidneys
  - Patient and graft survival statistically similar in organs from young adult, HCV- donors (even though recipients are statistically older for PHS risk donor organs).
  - DTAC attributed rate of unanticipated disease transmission is not significantly different between standard and PHS risk donor organs
  - System attribution for causes of patient and graft loss from kidneys from standard and PHS identified donors: similar

Discussion

In 2014, there were 1,198 HCV- PHS identified donors in the US.

-If organs were txp/donor at same rate as standard donors, over 400 additional transplants with good potential function from deceased donor organs would have occurred.

Does the moniker, “PHS increased risk” have sufficient value to warrant its continued use? Or should we look for a subpopulation with a demonstrated increased risk for disease transmission (ie, [hypothesized] IVDA with a needle in the arm) or possibly move towards universal precautions and eliminate the category?

There is a **price** to calling something “**increased risk**”; decreased utilization. There ***must*** be a **demonstrable benefit** to offset the diminished organ utilization.

The risk-benefit analysis: the reality and perception of risk