



Transplant trends: Current data and statistics

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Disclosure Information

- I have no conflicts of interest to disclose.
- My research is funded by the National Institutes of Health. I am also an investigator with the Scientific Registry of Transplant Recipients, funded by the Health Resources Services Administration.



Making sense of transplant data

- Transplantation is one of the most data-rich areas of medicine
 - Organ Procurement and Transplantation Network (OPTN) maintains a national transplant registry: waiting lists, recipients, organ offers, outcomes
 - Records relating to care for end-stage organ failure
 - Insurance claims
 - Pharmacy claims
- Find insights and make recommendations
 - Policy for allocating scarce resources
 - Innovation and excellence in patient care
 - Insurance coverage



Data analytics to help providers, payers, policymakers do the right thing

- Explore current utilization, innovation and donation trends in transplant
- Identify strategies to increase utilization and improve access to organ transplant
- Explain how national data is used to develop strategies to drive improvement and address inequities in transplant
- We use data analytics to
 - increase utilization by urging physicians to use more organs in the right recipients,
 - help caregivers offer the best treatments for each individual patient
 - recommend policies that allocate organs more equitably



Kidney discards and delays in placing organs

 Kidney discard rate is approximately 50% for KDPI > 85 and approximately 20% overall (Bae et al. 2017)

 Long delays can cause usable organs of marginal quality to be eventually discarded (Massie et al. 2010)



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Organ offers: sequential or simultaneous

- Current policy : sequential expiration of offers
 - After a center becomes primary, when all higher-priority candidates have declined, then a 1 hour / 30 minute time limit starts for that center to answer
 - Shorter time limits implemented last year, but still offers expire sequentially
- We propose to make simultaneously expiring kidney offers in batches to multiple centers
 - for post-recovery kidneys at regional and national allocation level



Accelerating kidney allocation: Simultaneously expiring offers

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TABLE 2 Number of kidneys accepted and cumulative acceptance percentage as kidneys progress from local to regional to national offers



Non-ideal kidneys (with higher KDPI) still give survival benefit



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Infectious-Risk Donors

- US Opioid epidemic: almost 30% of donors are IRD
- Discard rates <u>2x</u> higher for IRDs than non-IRD counterparts
- Seems wasteful to discard these: there should be *someone* on the list who would benefit





ORIGINAL ARTICLE

Turn down for what? Patient outcomes associated with declining increased infectious risk kidneys

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AJT

Infectious risk donors are higher-quality (lower KDPI)

Education



Patient Mortality 22.5% 25 **Declined IRD Offer** Accepted IRD Offer Cumulative Mortality (%) 10 15 20 14.0% 5 0 2 3 Years Post-Acceptance/Decline 0 4 5 1 **OPTUM**Health Education

Patients accepting infectious risk donors were less likely to die in 5 years

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doi: 10.1002/ajt.12206

Identifying Appropriate Recipients for CDC Infectious Risk Donor Kidneys

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¹Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD ²Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD ³Division of Health Sciences Informatics, Johns Hopkins University School of Medicine, Baltimore, MD *Corresponding author: Dorry Segev, dorry@jhmi.edu †Both authors contributed equally. donors; NAT, nucleic acid testing; OPTN, Organ Procurement and Transplantation Network; PHS, Public Health Service; PRA, panel reactive antibody; SRTR, Scientific Registry of Program Recipients; T2D, time to death after transplantation with a non-IRD kidney; W2D, time to death from the waitlist; W2T, time to transplant from the waitlist

Received 19 September 2012, revised 23 October 2012 and accepted 19 November 2012

Background



Should candidate accept an IRD kidney? Markov Decision Process Model





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Home LKDPI ESRD Risk Infectious Risk Donors Transplant Candidates older than 65 Pediatric Transplant

transplantmodels.com

The Epidemiology Research Group for Organ Transplantation is a research group focused on organ transplantation at the Johns Hopkins School of Medicine. Below are some of the decision models we have developed.

For more information, please visit our website, www.transplantepi.org

Infectious Risk Donors Living Kidney Donor Risk Index (LKDPI) ESRD Risk Tool for Kidney Donor Candidates This model predicts recipient risk of graft loss after living When a patient with end stage renal disease (ESRD) on This model is intended for low-risk adults considering donor kidney transplantation based on donor the waitlist for a kidney is offered an Infectious Risk Donor characteristics, on the same scale as the KDPI ... living kidney donation in the United States. It provides an (IRD) kidney, they need to decide whether they will estimate of 15-year and lifetime incidence of end-stage accept the IRD kidney and the associated infectious risk, Massie AB, Leanza J, Fahmy LM, Chow EK et al. A Risk Index for Living or if they will decline it and continue to wait for the next renal disease... Donor Kidney Transplantation. AJT 2016 (epub ahead of print) available infectious-risk free kidney ... Grams ME, Sang Y, Levey AS, Matsushita K, Ballew S, Chang AR et al. Continue to model » Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate. Chow, E. K. H., Massie, A. B., Muzaale, A. D., Singer, A. L., Kucirka, L. M., NEJM 2015 (epub ahead of print) Montgomery, R. A., ... & Segev, D. L. (2013). Identifying appropriate recipients for CDC infectious risk donor kidneys. American Journal of Continue to model » Transplantation, 13(5), 1227-1234. Continue to model » Transplant Candidacy for Patients 65+ Pediatric Transplant: Living or deceased

This prediction model is intended for adults with ESRD on dialysis aged 65 and above; it provides the predicted probability of 3-year survival after kidney transplantation (KT). Patients with predicted 3-year post-KT survival in the top guintile are deemed "excellent" candidates ...

Grams, M. E., Kucirka, L. M., Hanrahan, C. F., Montgomery, R. A., Massie,

donor first?

Most pediatric kidney transplant recipients live long enough to require retransplantation. The most beneficial timing for living donor transplantation in candidates with one living donor is not clear ...

Van Arendonk, K. J., Chow, E. K., James, N. T., Orandi, B. J., Ellison, T. A.,



Johns Hopkins IRD Kidney Transplant Calculator

Recipient Characteristics:

Age: (20-75)	50 🔻
Gender:	female 🔻
ABO:	Туре А 🔻
Ethnicity:	White •
BMI: (19-39)	23 🔻
PRA: (0-100)	0 •
Renal failure diagnosis:	diabetes mellitus 🔹
Previous transplant:	no 🔻
Years on waitlist:	0 •
Estimated time remaining until non-IRD transplant *:	48 months V

* This is time in addition to the time the patient may have already waited. eg: if a patient has spent 1 year on the waitlist, and the estimated time remaining until a non-IRD transplant is 18 months, the patient is expected to have waited 30 months since listing, before a non-IRD transplant.

Donor Characteristics:

Infectious Risk Behavior: Serology Testing Used:

Intraver	nou	s drug users	
ELISA	¥		

base-case estimate: mortality risk (if seroconverted) increased by 4.12% HIV, 3.42% HCV per year worst-case estimate: mortality risk (if seroconverted) equivalent to immediate (100% chance) death

www.TransplantModels.com/IRD



Johns Hopkins IRD Kidney Transplant Calculator

base-case estimate: mortality risk (if seroconverted) increased by 4.12% HIV, 3.42% HCV per year worst-case estimate: mortality risk (if seroconverted) equivalent to immediate (100% chance) death **Recipient Characteristics:**

Age: (20-75)	50 🔻
Gender:	female 🔻
ABO:	Туре А 🔻
Ethnicity:	White •
BMI: (19-39)	23 🔻
PRA: (0-100)	0 •
Renal failure diagnosis:	diabetes mellitus
Previous transplant:	no 🔻
Years on waitlist:	0 •
Estimated time remaining until non-IRD transplant *:	3 months V

* This is time in addition to the time the patient may have already waited, eg; if a patient has spent 1 year on the waitlist, and the estimated time remaining until a non-IRD transplant is 18 months, the patient is expected to have waited 30 months since listing, before a non-IRD transplant.

Donor Characteristics:

Infectious Risk Behavior: Serology Testing Used:

Intra	venous drug users	•
ELIS	A 🔻	

www.TransplantModels.com/IRD

Opioid overdose death donors





Durand/Segev, Annals Internal Medicine, 2018

Overdose death donors: 25% HCV+



Durand/Segev, Annals Internal Medicine, 2018



HCV Treatment in Transplantation

- Direct acting antivirals (DAAs) cure HCV in 95-100% of patients
- Effective and tolerated with minimal drug interactions in transplant recipients



HCV+ Donors

- Number of HCV+ donor kidneys exceeds number of HCV+ kidney transplant candidates
 - -> 40% of recovered HCV+ kidneys discarded
 - -4X discard rate compared to HCV-
- Potential pool of HCV+ kidneys may be larger since not all HCV+ kidneys are recovered







EXPANDER: Exploring Transplants Using Hepatitis-C Infected Donor Kidneys for HCV-Negative Recipients

Durand et al, Annals of Internal Medicine, 2018

HCV- patients transplanted with HCV+ kidneys and DAA prophylaxis



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Challenges of HCV+ kidneys to HCV- recipients

- Cost-effectiveness (metabolic, renal advantages)
- Insurance coverage for DAAs
 - Pre-approval for prophylactic treatment
 - Pre-approval without delay for post-tx treatment
 - Approval without requirements for fibrosis
- Larger cooperative trials, longer-term outcomes
- Increased utilization (discard rate still very high)



Kidney and liver transplants for HIV+ recipients increasing



> 100 transplants per year

• > 30 transplants per year

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Estimating the Potential Pool of HIV-Infected Deceased Organ Donors in the United States

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- How many people are we talking about?
- How many lives would be saved?
- How much money would Medicare save?

Received 03 December 2010, revised 24 January 2011 and accepted for publication 09 February 2011



A Push to Let H.I.V. Patients Accept Organs That Are Infected

By PAM BELLUCK

David Aldridge of Los Angeles had a kidney transplant in 2006, but he will soon need another. Like many people living with H.I.V., he suffers from kidney damage, either from the virus or from the life-saving medications that keep it at bay.

Until recently, such patients did not receive transplants at all because doctors worried that their health was too compromised. Now they can get transplants, but organ-donor waiting lists are long. And for Mr. Aldridge, 45, and other H.I.V. patients, a potential source of kidneys and livers is off limits, because it is illegal to transplant organs from donors who test poiother experts are calling for repeal of the provision that bans such transplants, a 23-year-old amendment to the National Organ Transplant Act.

"The clock is ticking more quickly for those who are H.I.V.positive," said Dr. Dorry Segev, transplant surgery director of clinical research at Johns Hopkins and a co-author of a new study indicating that 500 to 600 H.I.V.-infected livers and kidneys would become available each year if the law were changed. "We have a huge organ shortage. Every H.I.V.-infected one we use is a new organ that takes one more person off the list."

Quotation of the Day

"The clock is ticking more quickly for those who are H.I.V.-positive." **DR. DORRY SEGEV**, a co-author of a study indicating that 500 to 600 H.I.V.-infected livers and kidneys would become available each year if the law were changed to allow their use in some patients. SURGICAL PERSPECTIVES

From Bench to Bill: How a Transplant Nuance Became One of Only 57 Laws Passed in 2013

Brian J. Boyarsky, BA,* and Dorry L. Segev, MD, PhD*†

"Tm just a bill, yes I'm only a bill, and I'm sitting here on Capitol Hill. Well it's a long, long journey in capital city, It's a long, long wait while I'm sitting in committee, But I know I'll be a law someday... At least I hope and pray that I will, but today I am still just a bill."

(Schoolhouse Rock)

Ann Surg, 2016; 263:430-433

Organ allocation policy

- The Organ Procurement and Transplantation Network (OPTN) sets and implements policies for allocating organs from deceased donors
- The Kidney Allocation System (KAS)
 - reduced disparities for highly sensitized candidates
 - directed the best 20% of kidneys to the healthiest 20% of recipients
 - took ten years of debate before implementation, and that was after deciding not to address geographic disparity at all
- The OPTN has attempted in recent years to hew more closely to the Final Rule (1998) which demands that "neither place of residence nor place of listing shall be a major determinant of access to a transplant"
- Policies on heart, liver, lung, and kidney allocation all changed but all those changes failed to make a dent in geographic disparity



Local CPRA 100Local CPRA 100Local CPRA 100Local CPRA 100Local CPRA 100Regional CPRA 100National CPRA 100Regional CPRA 100Regional CPRARegional CPRANational CPRA 99Local CPRA 99National CPRA 99National CPRA 100100Local CPRA 99Local CPRA 99Regional CPRA 99National CPRA 99National CPRA 99Local CPRA 98Local CPRA 98Local CPRA 99Regional CPRA 99Regional CPRA 99Zero mismatch (topZero mismatchRegional CPRA 99Regional CPRA 98Local CPRA 9920% EPTS)Prior living donorLocal pediatricsLocal CPLocal CPRA 98Local top 20% EPTSRegional pediatricsLocal CIRegional core matchLocal (all)National pediatricsRegional adultsNational core matchRegional (top 20%)Regional (all)National adultsNationalNational pediatricsNational (top 20%)National adultsNationalNational (all)National (all)National adultsNationalNational (all)National (all)National (all)National (all)	Sequence A KDPI <=20%	Sequence B KDPI >20% but <35%	Sequence C KDPI >=35% but <=85%	Sequence D KDPI>85%
	Local CPRA 100 Regional CPRA 100 National CPRA 100 Local CPRA 99 Regional CPRA 99 Local CPRA 98 Zero mismatch (top 20% EPTS) Prior living donor Local pediatrics Local top 20% EPTS Zero mismatch (all) Local (all) Regional pediatrics Regional (top 20%) Regional (all) National pediatrics National (top 20%) National (all)	Local CPRA 100 Regional CPRA 100 National CPRA 100 Local CPRA 99 Regional CPRA 99 Local CPRA 98 Zero mismatch Prior living donor Local pediatrics Local adults Regional pediatrics Regional pediatrics National pediatrics National adults	Local CPRA 100 Regional CPRA 100 National CPRA 100 Local CPRA 99 Regional (CPA 99 Local CPRA 99 Local CPRA 90 COM 20 COM 90 COM 90 Local CPRA 90 COM 90 COM 90 Local CPRA 90 COM 90 90 COM 90 90 COM 9	Local CPRA 100 Regional CPRA 100 National CPRA 99 Regional CPRA 99 Local CPRA 98 Sismatch Regional nal gories in D to adult

Education



Old policy: 4 points for CPRA>=80%. No points for moderately sensitized. NEW: sliding scale starting at CPRA>=20%

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ORIGINAL ARTICLE

Geographic disparity in kidney transplantation under KAS

Sheng Zhou¹ Allan B. Massie^{1,2} | Xun Luo¹ | Jessica M. Ruck¹ | Eric K. H. Chow¹ | Mary G. Bowring¹ | Sunjae Bae^{1,2} | Dorry L. Segev^{1,2} | Sommer E. Gentry^{1,3}

- KAS was not intended to reduce geographic disparity
- Two candidates with the same kidney allocation score in different donation service areas were expected to have a 1.81-fold difference in transplant rates
 - The healthiest candidates with EPTS score ≤20% had a 1.40-fold increase (IRR = 1.40, P < .01)</p>
 - Three-year dialysis vintage was associated with a 1.57-fold increase (IRR = 1.571, P < .001)
- Geography influences who gets a transplant more significantly than the factors emphasized by KAS

Geographic disparity in kidney transplant rates remained high after KAS

в

Pre-KAS kidney transplant rate per person-year









Original Clinical Science–Liver



Geographic Disparity in Deceased Donor Liver Transplant Rates Following Share 35

Mary G. Bowring, MPH,¹ Sheng Zhou, ScM, MBBS,¹ Eric K.H. Chow, MSC,¹ Allan B. Massie, PhD,^{1,2} Dorry L. Segev, MD, PhD,^{1–3} and Sommer E. Gentry, PhD^{1,4}

- Share35 mandated regional sharing of livers for candidates with MELD > 35
- MIRR measures geographic disparity: Both before and after Share35, two candidates with the same MELD in different donation service areas were expected to have a more-than-two-fold difference in their transplant rates
- Pre-Share35 MIRR was 2.18, and post-Share35 MIRR was 2.16



Geographic disparity in liver transplant rates remained high after Share35

Pre-Share35 liver transplant rate per person-year Post-Share35 liver transplant rate per person-year





DSAs were excluded (white) if they did not have a liver transplant program during the study period (n=6) or included only programs with low transplant volume (n=3).



ORIGINAL ARTICLE

Geographic disparities in lung transplant rates



Patier





Eligible death numbers (supply) vary much more than OPO performance





Optimal Redistricting

- Redistricting uses integer programming to design geographic boundaries that partition an area into smaller areas
 - Redistricting has been applied to design voting districts and school districts, from 1950s to the present
- We use optimization to group the DSAs into new districts



Partition DSAs into districts



Education

not distribute.

Redistricting Objective and Constraints

- Minimize total disparity
 - Disparity = difference between number of donors a district should have (if organs went to highest MELD patient anywhere in the country) and number of donors in a proposed district
 - Minimize sum of these disparities over all districts
- Subject to constraints (the lowest geographic disparity achievable through the allocation system would be national sharing)
- The OPTN Liver Committee requested these constraints:
 - -Exactly 8 districts
 - Minimum number of transplant centers per district is 6
 - The maximum allowable median travel time between DSAs placed in the same district should be 3 hours

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Optimized 8 district map





Simulated redistricting impacts over 5 years





Optimized redistricting can reduce geographic disparity in liver transplant

Median Transplant MELD

Current, MELD at transplant

Redistricting, MELD at transplant





Optimized heterogeneous circle sizes





Optimized heterogeneous circle sizes





Variance in supply/demand: identical circles (blue) versus optimized circles (green star)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Survival Benefit with Kidney Transplants from HLA-Incompatible Live Donors

B.J. Orandi, X. Luo, A.B. Massie, J.M. Garonzik-Wang, B.E. Lonze, R. Ahmed, K.J. Van Arendonk, M.D. Stegall, S.C. Jordan, J. Oberholzer, T.B. Dunn, L.E. Ratner, S. Kapur, R.P. Pelletier, J.P. Roberts, M.L. Melcher, P. Singh,
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OPTUMHealth Education The <u>clinical</u> question is <u>not</u>: "Do recipients of incompatible live donors do better or worse than recipients of compatible live donors?"

The <u>clinical</u> question <u>is</u>: "Is getting an incompatible living donor transplant better or worse than waiting for the next available option?"



The NEW ENGLAND JOURNAL of MEDICINE



Kidney Paired Donation (KPD)





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Kidney Paired Donation and Optimizing the Use of Live Donor Organs

Dorry L. Segev, MD Sommer E. Centry, MS Daniel S. Warren, PhD Brigitte Reeb, MFA Robert A. Montgomery, MD, DPhil

ENAL TRANSPLANTATION HAS emerged as the treatment of choice for medically suitable patients with end-stage renal disease.¹ More than 60 000 patients await kidney transplantation and are listed on the United Network for Organ Sharing **Context** Blood type and crossmatch incompatibility will exclude at least one third of patients in need from receiving a live donor kidney transplant. Kidney paired donation (KPD) offers incompatible donor/recipient pairs the opportunity to match for compatible transplants. Despite its increasing popularity, very few transplants have resulted from KPD.

Objective To determine the potential impact of improved matching schemes on the number and quality of transplants achievable with KPD.

Design, Setting, and Population We developed a model that simulates pools of incompatible donor/recipient pairs. We designed a mathematically verifiable optimized matching algorithm and compared it with the scheme currently used in some centers and regions. Simulated patients from the general community with characteristics drawn from distributions describing end-stage renal disease patients eligible for renal transplantation and their willing and eligible live donors.

Main Outcome Measures Number of kidneys matched, HLA mismatch of matched kidneys, and number of grafts surviving 5 years after transplantation.



The Journal of the American Medical Association

Growth in KPD in the US



*Organ Procurement and Transplantation Network. https://optn.transplant.hrsa.gov/ Accessed 10/31/18

OPTUMHealth Education

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Kidney paired donation (KPD)

- Advantages
 - -Compatible transplants
 - Can be done at any center that does LDKT
 - Outcomes are just like any other transplants
 - Long-term management just like any other transplant
- Disadvantages
 - -Requires a match -- so might have to wait
 - -Requires coordination with other centers (sometimes)



Desensitization

- Advantages
 - Can transplant immediately
 - Does not require coordination with other patients / surgeons / centers
- Disadvantages
 - Requires work and expense
 - Up-front (the desensitization itself)
 - Later (antibody monitoring, protocol biopsies, etc)
 - Magnitude of long-term risks unknown



Desensitization vs KPD = PRA vs DSA

- PRA = ability to match
 - Patient might have very high strength DSA to one particular antigen, but low PRA
 - Blood types also affect ability to match (O donors or AB recipients make a pair easier to match)
- DSA = ability to desensitize
 - Patient with many antibodies (broadly sensitized, very high PRA) might have low strength antibody to a particular donor's particular antigens





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	EASY	HARD
EASY	Try KPD for a few months If match -> KPD If no match -> Desens.	Low PRA High-strength DSA (high-titer positive XM) O donor
KPD HARD	High PRA Low-strength DSA (positive flow or lower) non-O donor (esp AB) O recipient	High PRA High-strength DSA (high-titer positive XM) non-O donor (esp AB) O recipient

OPTUMHealth Education

	EASY	HARD
EASY	Try KPD for a few months If match -> KPD If no match -> Desens.	Wait in KPD
KPD Hard	High PRA Low-strength DSA (positive flow or lower) non-O donor (esp AB) O recipient	High PRA High-strength DSA (high-titer positive XM) non-O donor (esp AB) O recipient

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	EASY	HARD
EASY	Try KPD for a few months If match -> KPD If no match -> Desens.	Wait in KPD
KPD hard	Look in KPD pool <i>Prob. Not Worth Waiting</i> If match -> KPD If no match -> Desens.	High PRA High-strength DSA (high-titer positive XM) non-O donor (esp AB) O recipient

OPTUMHealth[®] Education

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	EASY	HARD
EASY	Try KPD for a few months If match -> KPD If no match -> Desens.	Wait in KPD
KPD		
HARD	Look in KPD pool <i>Prob. Not Worth Waiting</i> If match -> KPD If no match -> Desens.	COMBINE KPD and Desensitization

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Data analytics to help providers, payers, policymakers do the right thing

- Identify opportunities to increase transplants from deceased donors and living donors (deceased donors: use more non-ideal organs from infectious risk and HCV+/HIV+ donors, living donors: desensitization and kidney paired donation)
- Build trust in the transplant system by designing more equitable allocation policies (geographic disparities)



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Thank You.