

# Recent and Future Changes in Liver and Kidney Allograft Allocation

Update from the AASLD 2017, Washington, D.C.

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Subcommittee

# Disclosures

- I have nothing to disclose

# Goals

- Review recent changes in liver/kidney allocation
  - Share 35
  - Simultaneous Liver Kidney Transplant (SLK)
  - HCC exception points
  - Downstaging Criteria
  - AFP
- Possible Upcoming Changes in liver allocation
  - Redistricting
  - Proximity Points
  - National Review Board
- Alternatives to Increase Donor Supply

# Organ Allocation

- Grouping: **Where**

- Defines the set of candidates available for a given organ
- Currently based on donor service areas and region boundaries
- Balances access to transplantation and transportation burden

- Ordering **Who**

- Defines the sequence in which offers are made to those candidates
- Based on candidate and donor characteristics
- Balances illness severity, age, sensitivity and other factors.

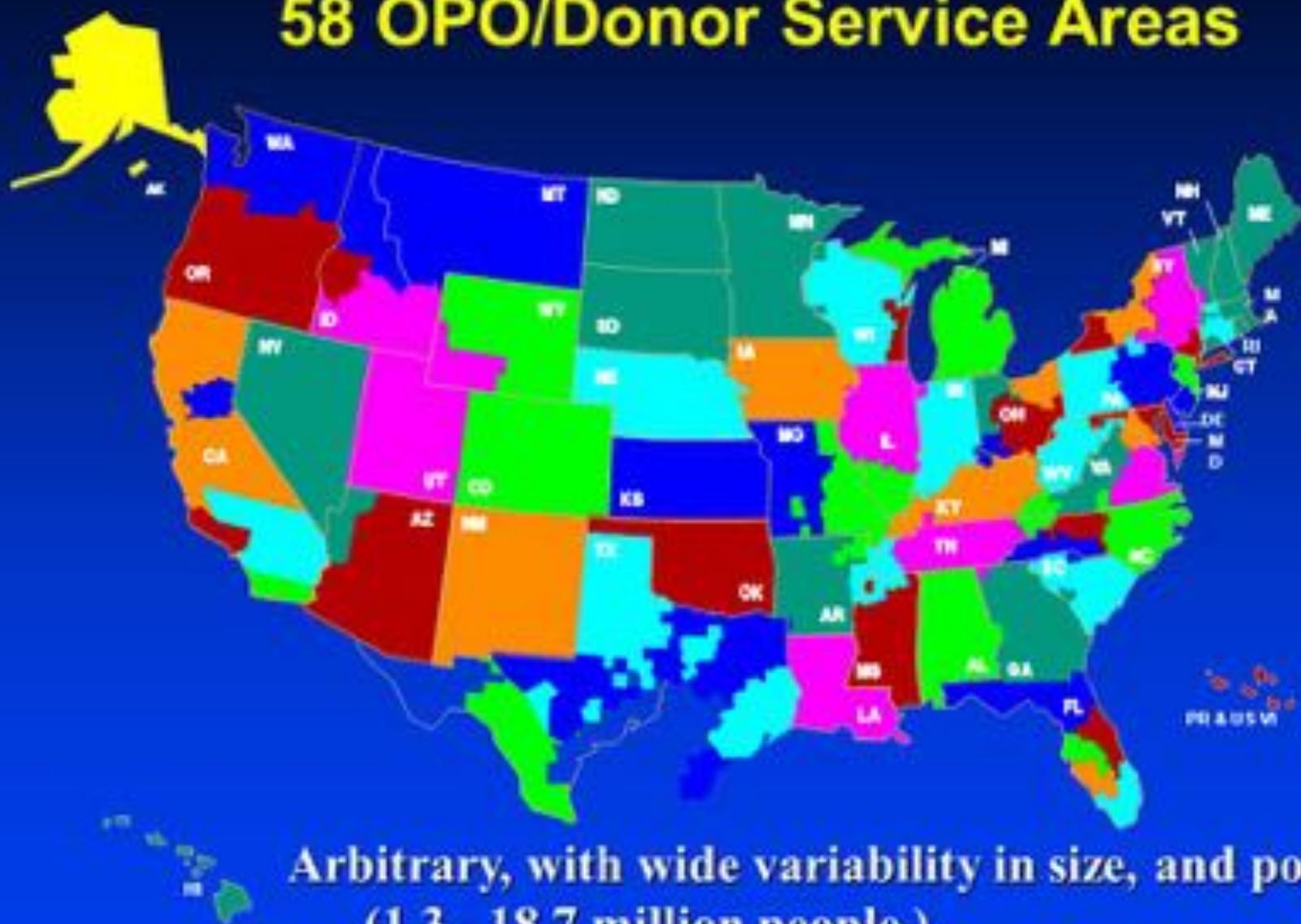
# REGIONAL HIERCHY AND DEFINITIONS

- Local
  - Defined by Organ Procurement Organization (OPO) donor service area (DSA)
- Regional
  - UNOS 11 allocation regions in the United States
- National
  - All remaining patients within the United States



# Current Distribution Unit

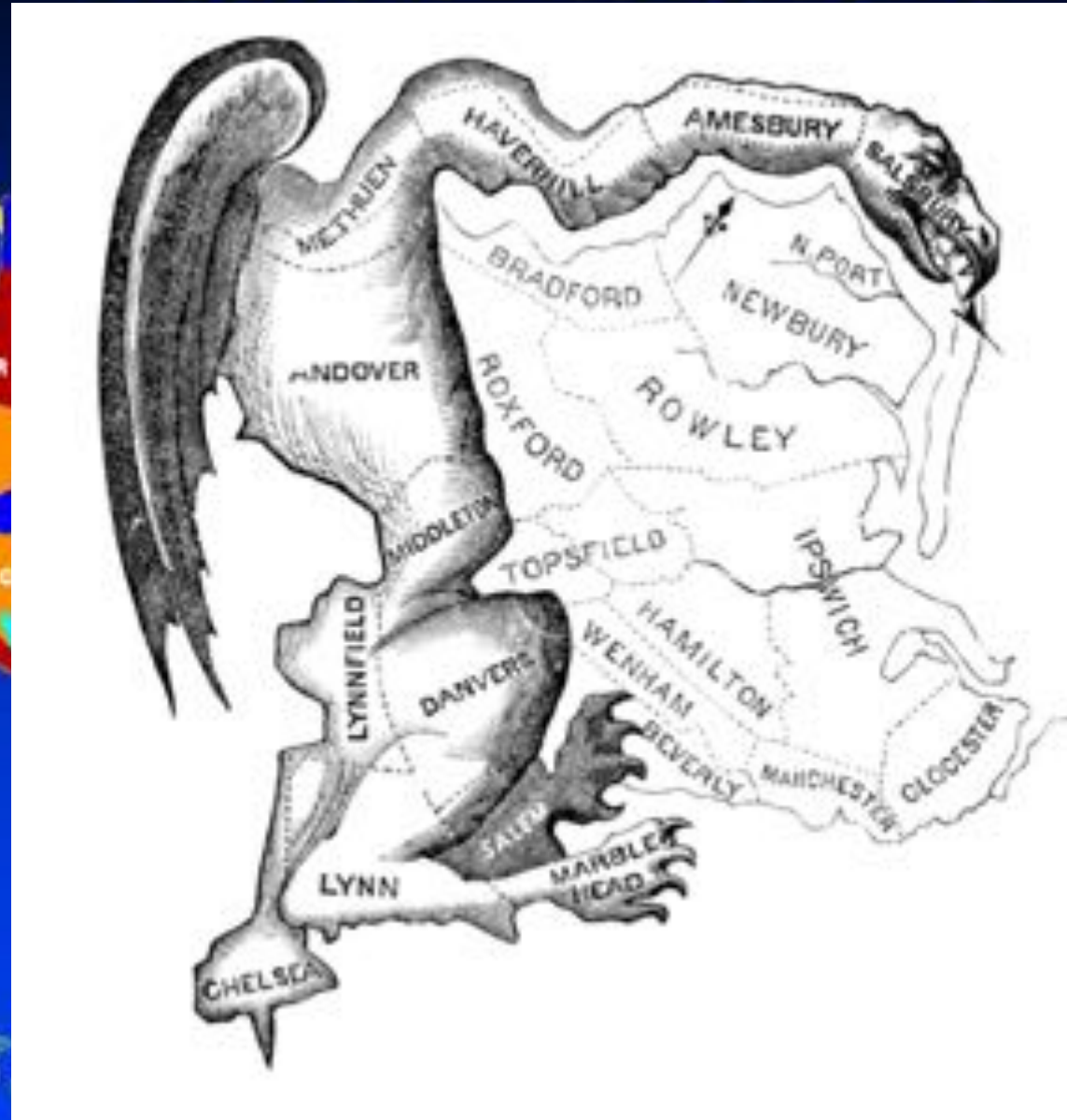
## 58 OPO/Donor Service Areas



Arbitrary, with wide variability in size, and population  
(1.3 - 18.7 million people.)



# Current Distribution Unit



and population



(1.5 - 16.7 million people.)

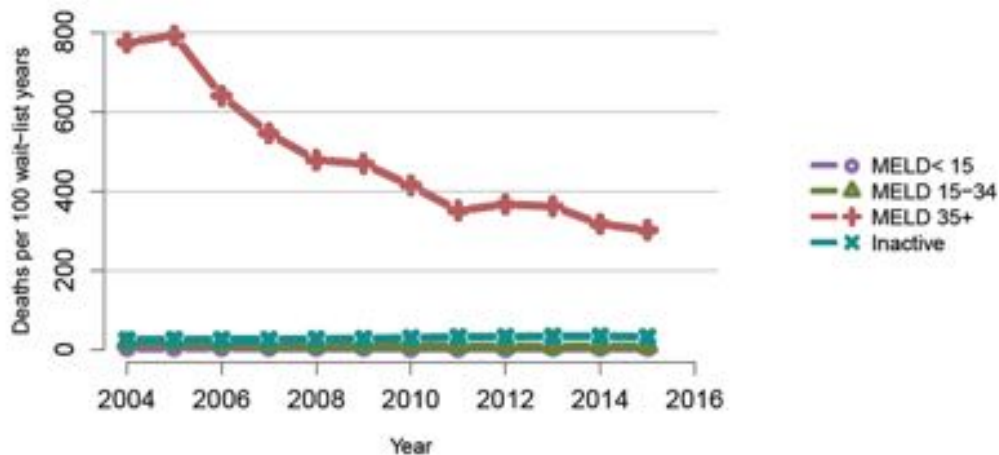
# UNOS Regions



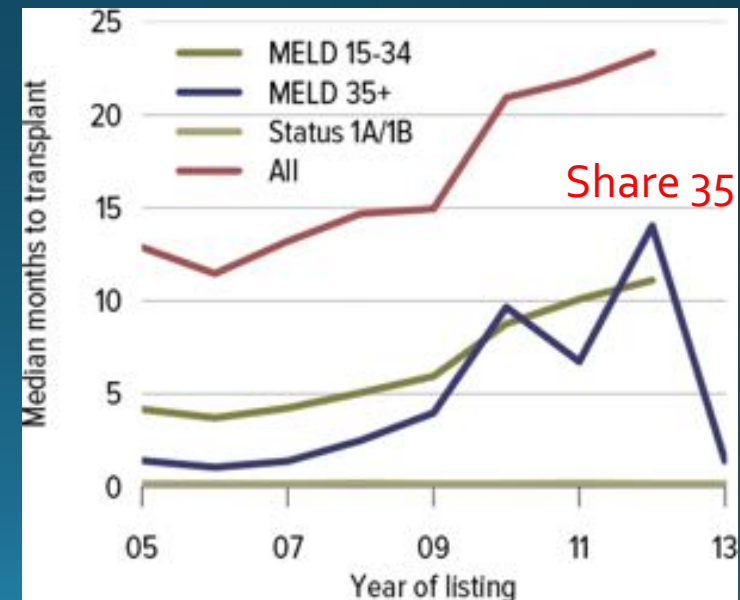


# Shortage of Donor Organs

- Increased Indication
  - More people qualify for life saving therapy. (Expanded HCC criteria, new tumor designation)
  - For many patients liver transplant represents the ONLY life saving option indication for transplant



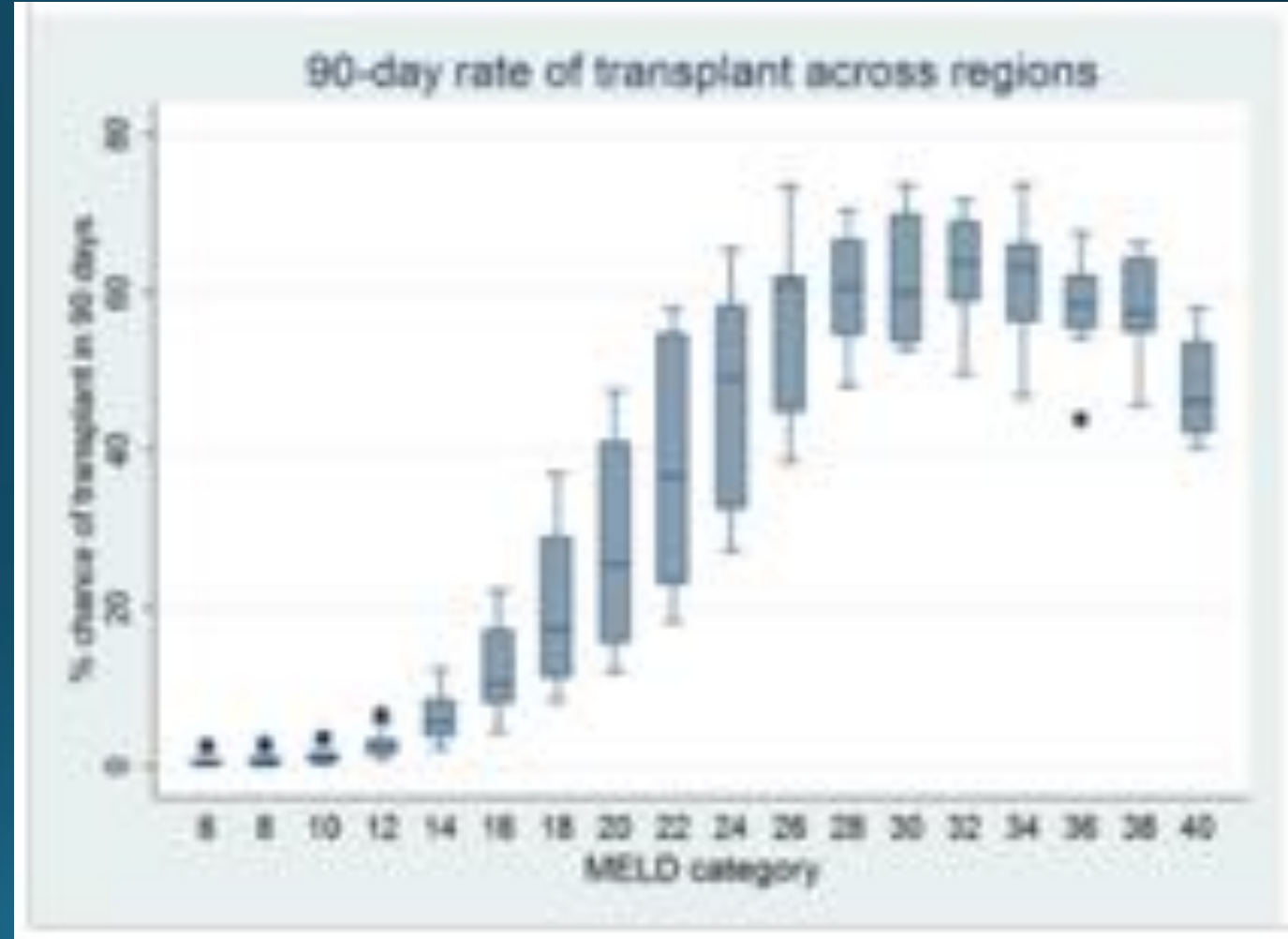
- Decreased Organ Availability
  - Increased competition for an already limited resource
  - Increased wait-list time
  - Decreased wait-list death of sickest patients



Share 35

# Geographic Disparities in Liver Transplant

- 90 day likelihood of transplant or death varies from 14-82% depending on location
- Median MELD score at transplant varied by as much as 12 points (35->23) across the 52 DSA
- Equivalent to a 60% difference in the estimated 3 month mortality without a liver transplant



# Current Liver Allocation Strategy

Combined Local and regional Status 1A
Combined local and regional status 1B
Local/regional MELD/PELD score 35-40 offers made locally then regionally for each MELD score
Local MELD/PELD score 29-34
National Liver-Intestine MELD score >29
Local MELD/PELD score 15-28
Regional MELD/PELD score 15-34
National status 1A or 1B
National MELD/PELD score >15
Local MELD/PELD score <15
Regional MELD/PELD score <15
National MELD/PELD score <15

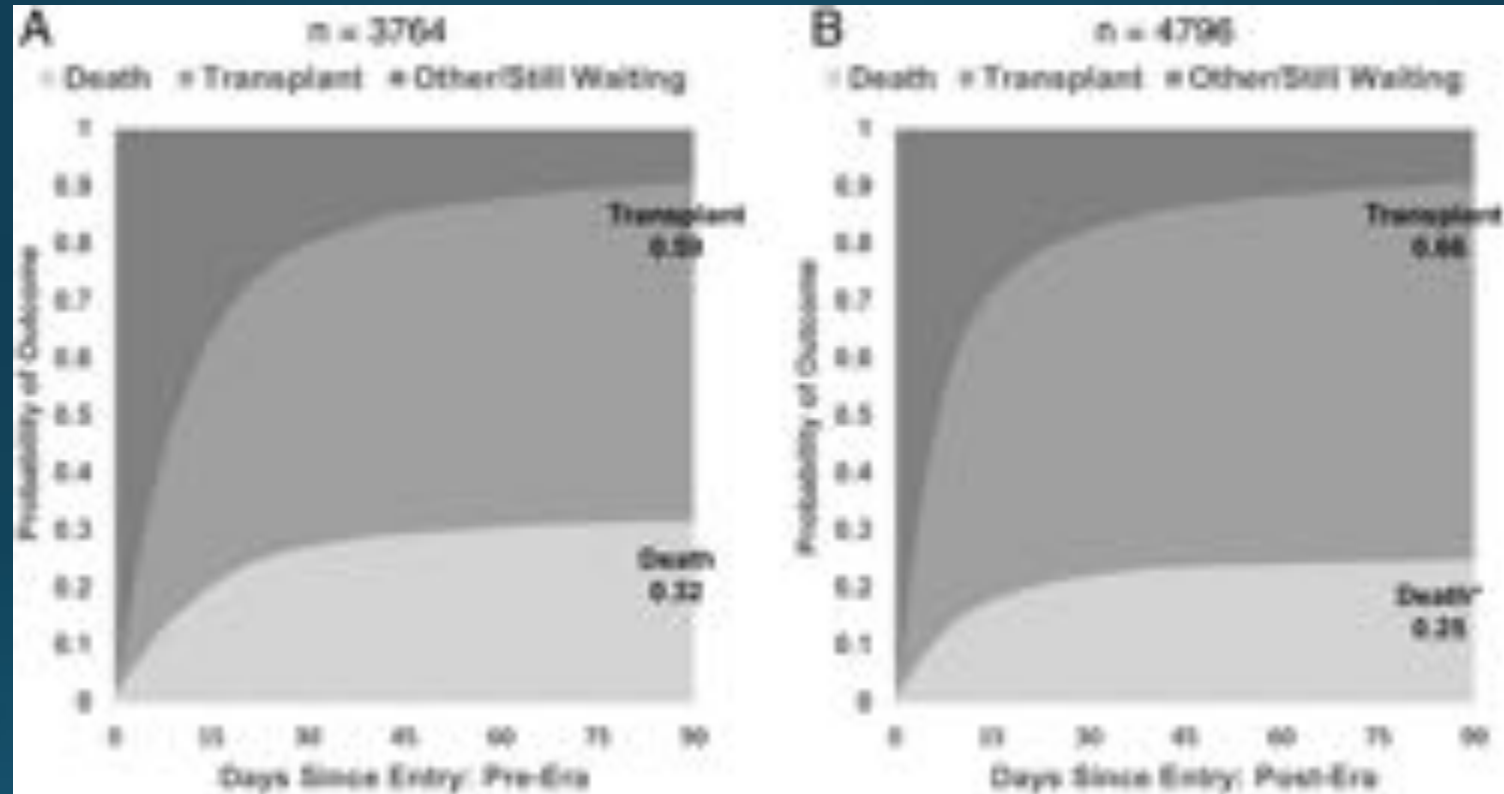
**FIGURE 1.** MELD, Model for End-Stage Liver Disease; PELD, pediatric end-stage liver disease.



# Share 15/35:

- Implemented in June 18, 2013
  - Regional sharing of livers to MELD/PELD 35+ candidates
  - National sharing of livers to MELD/PELD 15+ candidates
  - National sharing of livers and intestines to liver-intestine candidates with MELD > 29+

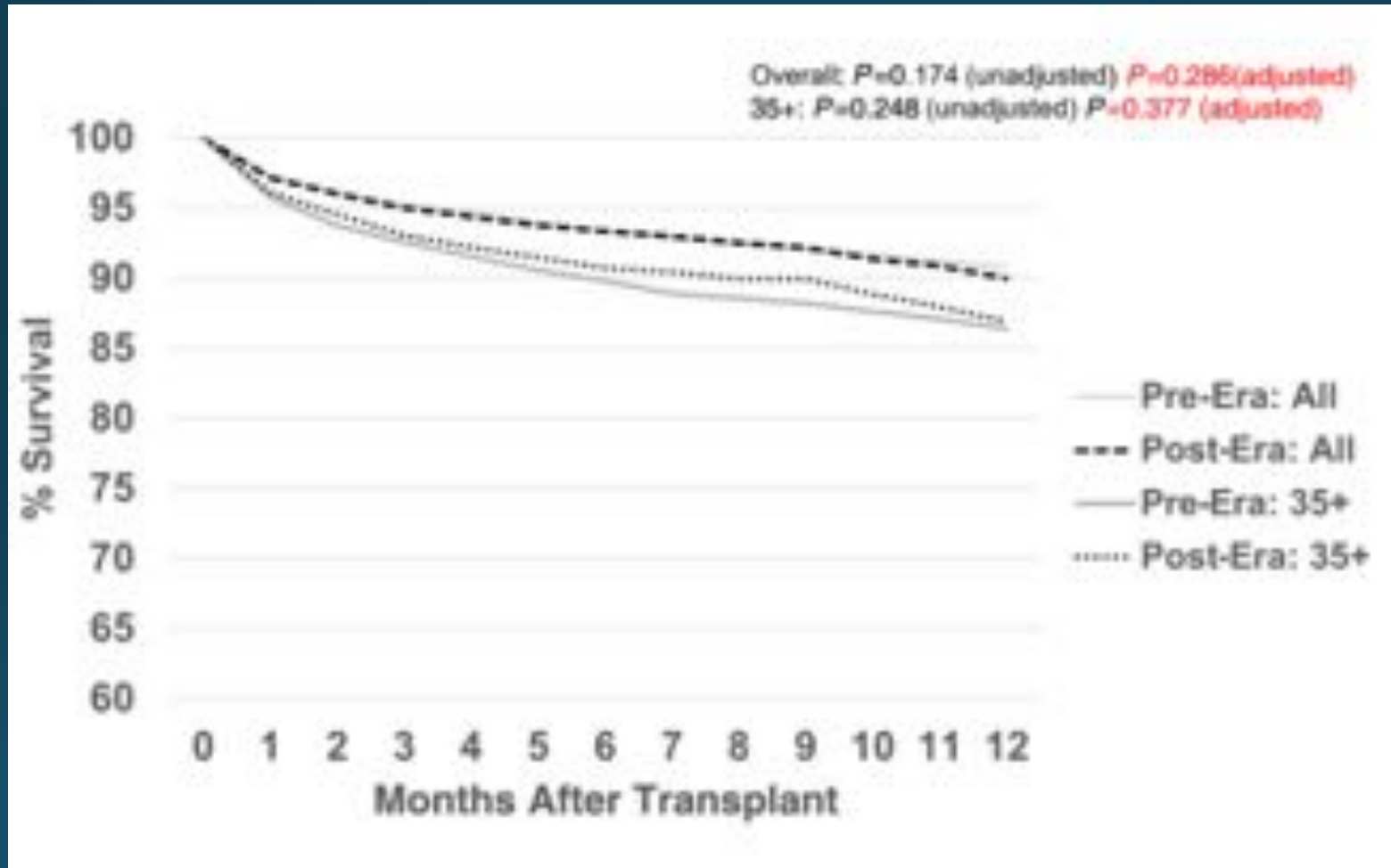
# The impact of broader regional sharing of livers: 2-year results of “Share 35”



## Liver Transplantation

Volume 22, Issue 4, pages 399-409, 28 MAR 2016 DOI: 10.1002/lt.24418  
<http://onlinelibrary.wiley.com/doi/10.1002/lt.24418/full#lt24418-fig-0012>

# The impact of broader regional sharing of livers: 2-year results of “Share 35”



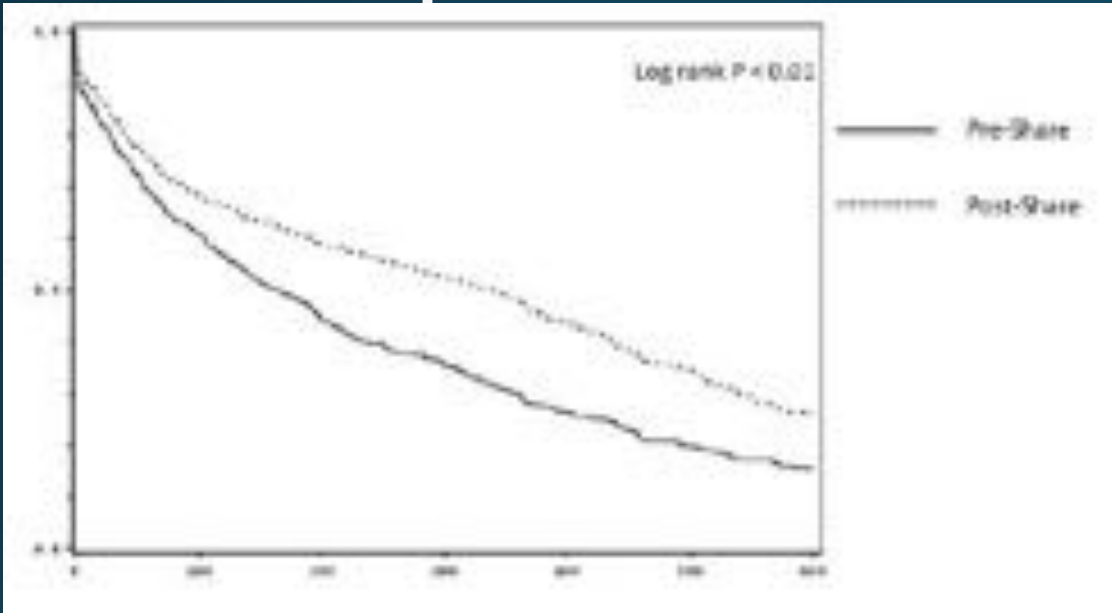


# Implementation of Share 35 Policy has Improved Survival following Liver Transplantation



- Using UNOS data to collect 1- year mortality both pre-share and post-share
- **Excluded** patients with Status 1A, MELD exception transplantation and simultaneous organ transplant

# Implementation of Share 35 Policy has Improved Survival following Liver Transplantation



	Pre Share 35	Post share 35	p
% transplant pts with MELD > 35	28.6	60.6	
1 year survival	85.7	89.4	0.02

- Irrespective of MELD at transplant there was an overall improvement in post liver transplant mortality in the post Share 35 era within this subgroup
- By increasing the sharing of organs with a MELD score greater than 35 locally to regionally we are not only improving waitlist mortality we are improving post-liver transplant survival.

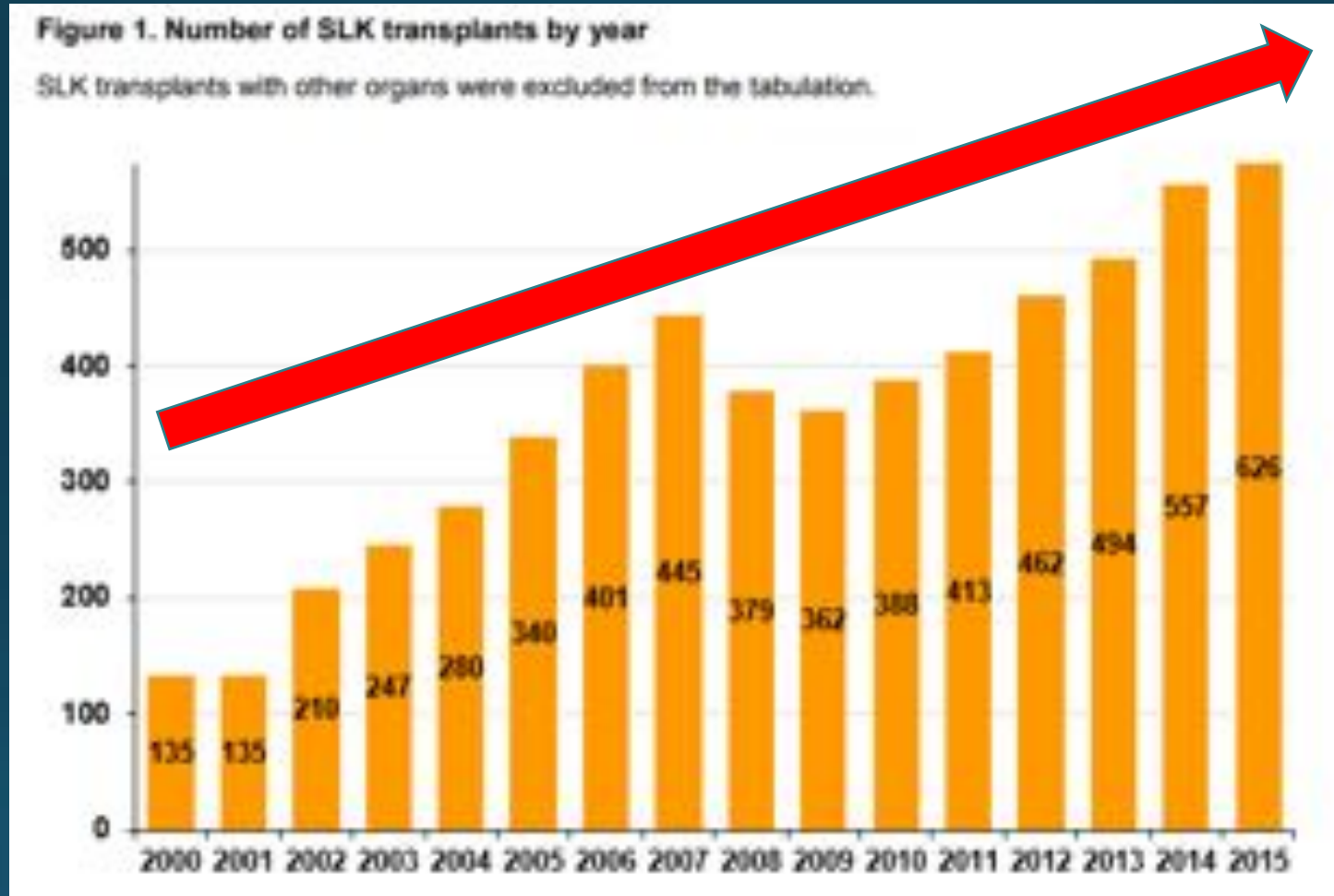
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- Review recent changes in liver/kidney allocation
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  - Simultaneous Liver Kidney Transplant (SLK)
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# Simultaneous Liver Kidney (SLK) Allocation

- Previously SLK allows for kidney sharing based on geography not current kidney function (**Liver** PULLS **Kidney**)
- Violates the OPTN FINAL RULE sound medical judgment and standardized criteria
- Possible return of kidney function in patients post-liver transplant creates debate of need for SLK
- Current absence of regional sharing for SLK

# Increase in Number of SLK by year



# New Simultaneous Liver Kidney Policy

- Policy went into effect 8/10/2017
- Establishes medical eligibility
- Increased clarity of the rules for SLK
- Establishes a “Safety Net” for liver recipient alone who fail to recover kidney function post transplant



# Simultaneous Liver-Kidney Medical Eligibility Criteria

Transplant nephrologist must confirm candidate has one of the following:

And tx hospital must report to UNOS and document one of the following in the medical record:

1. Chronic kidney disease with measured or calculated GFR less than or equal to 60 mL/min for greater than **90 consecutive days**

- Dialysis for ESRD
- Most recent measured or calculated CrCl or GFR is at or below **30** mL/min at the time of registration on kidney waiting list

2. Sustained acute kidney injury

At least *one* of the following or a combination of both for the last 6 weeks:

- Dialysis at least once every 7 days
- Measured or calculated CrCl or GFR at or below 25 mL/min for six consecutive weeks and this is documented in the medical record **every 7 days** beginning with the date of the first test with this value.

3. Metabolic disease

- Diagnosis of:
- Hyperoxaluria
  - Atypical HUS from mutations in factor H or factor I
  - Familial non-neuropathic systemic amyloid
  - Methylmalonic aciduria

# Simultaneous Liver-Kidney Allocation Rules

If a liver-kidney candidate...	And the donor is...	Then the OPO:
is highest on the liver match run, an adult candidate, and meets the SLK medical eligibility criteria	in the same DSA	is <b>required</b> to offer the kidney with the liver before the kidney alone waiting list
is highest on the liver match run, an adult candidate, meets the medical eligibility criteria, and has a <u>MELD of at least 35 or 1A</u>	in the candidate's region	is <b>required</b> to offer the kidney with the liver before the kidney alone waiting list
is highest on the liver match run, meets the medical eligibility criteria, and has a <u>MELD lower than 35</u>	in the candidate's region	may offer the kidney with the liver before the kidney alone waiting list but is not required to do so
is highest on the liver match run, meets the SLK medical eligibility criteria, and has any MELD score	national	may offer the kidney with the liver before the kidney alone waiting list but is not required to do so
is highest on the liver match run, an adult candidate, and does not meet the SLK medical eligibility criteria	in the same DSA, regional, national	must <b><u>not</u></b> offer the kidney with the liver

# Safety Net

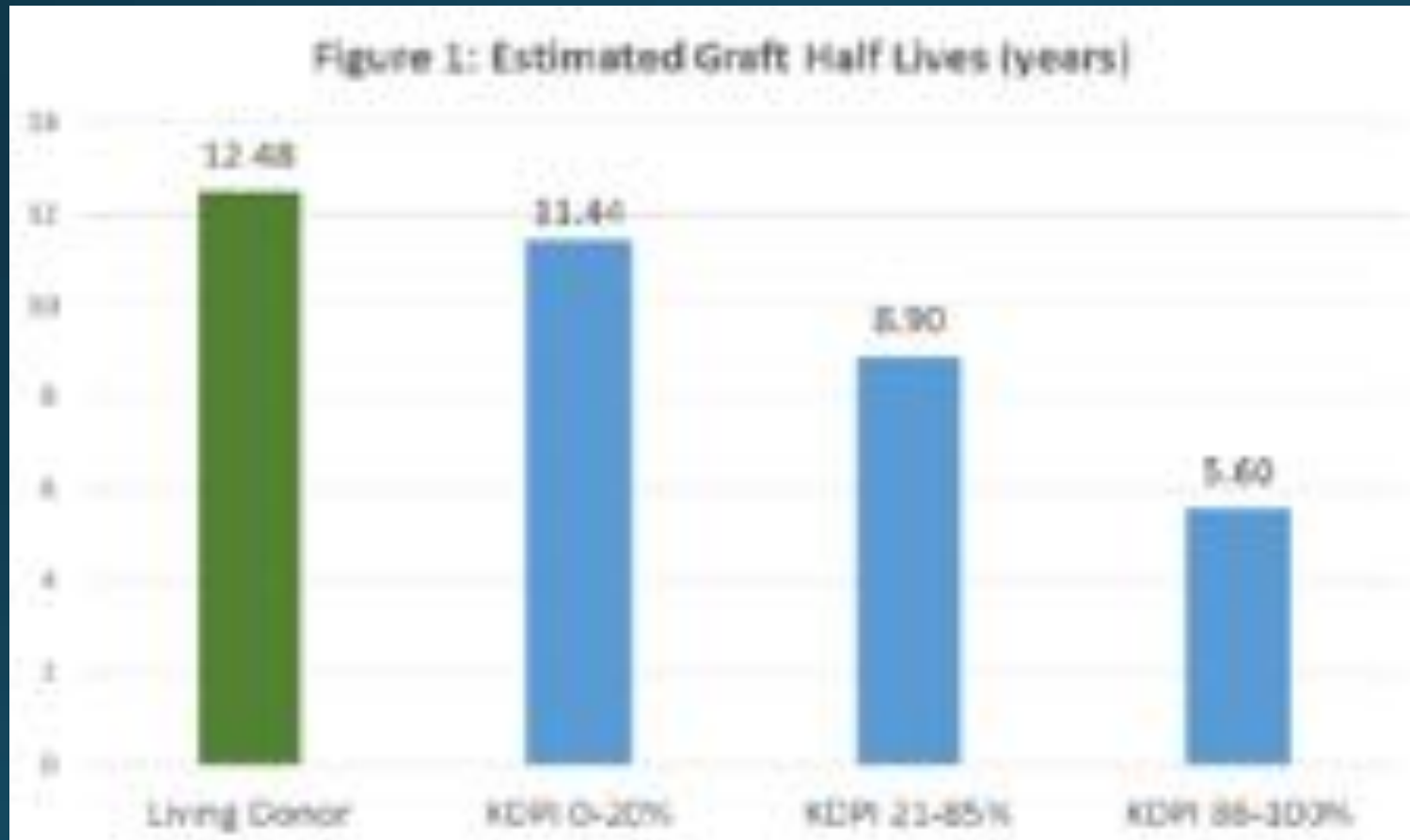
- Patients are eligible for the safety net if:
  - They are listed for kidney transplant BEFORE the 1 year anniversary of most recent liver transplant date
  - On a date that is 6-365 days after OLT, at least one of the following criteria is met:
    - CrCl or GFR < 20 ml/min
    - Candidate is on dialysis



# “Safety Net” Eligibility

- To continue eligibility:
  - Once patient listed with confirmatory information, they keep the safety net designation for 30 days
  - Every 30 days the program has to re-enter information
  - Once this has been confirmed for 3 consecutive periods (90 days), the candidate will be eligible until removed from the kidney wait list
- All liver recipients on the kidney wait list are eligible for priority if they met the medical criteria in the timeframe of days 60-365 after OLT
- If SLK patient experienced immediate and permanent non-function of the kidney then they are eligible for the safety net priority. Otherwise they are not eligible

# Safety Net and KDPI (Kidney Donor Profile Index)



- KDPI combines 10 donor factors into a single number to summarize the quality of the organ
- Lower KDPI = Higher quality graft

# Safety Net

**Safety net: Match classification priority for liver recipients by KDPI sequence**

Sequence A KDPI ≤ 20%	Sequence B KDPI >20% but <35%	Sequence C KDPI >35% but <85%	Sequence D KDPI ≥85%
Highly sensitized	Highly sensitized	Highly sensitized	Highly sensitized
O-ABDR mismatch	O-ABDR mismatch	O-ABDR mismatch	O-ABDR mismatch
Prior living donor	Prior living donor	Prior living donor	Local SLK safety net
Local pediatrics	Local pediatrics	Local SLK safety net	Local +regional
Local top 20% EPTS	Local SLK safety net	Local candidates	National candidates
O-ABDR mismatch (all)	Local adults	Regional candidates	
Local (all)	Regional pediatrics	National candidates	
Regional pediatrics	Regional adults		
Regional (top 20%)	National pediatrics		
Regional (all)	National adults		
National pediatrics			
National (top 20%)			
National (all)			



# SLK Recipients, Jan 2005 – Jun 2015

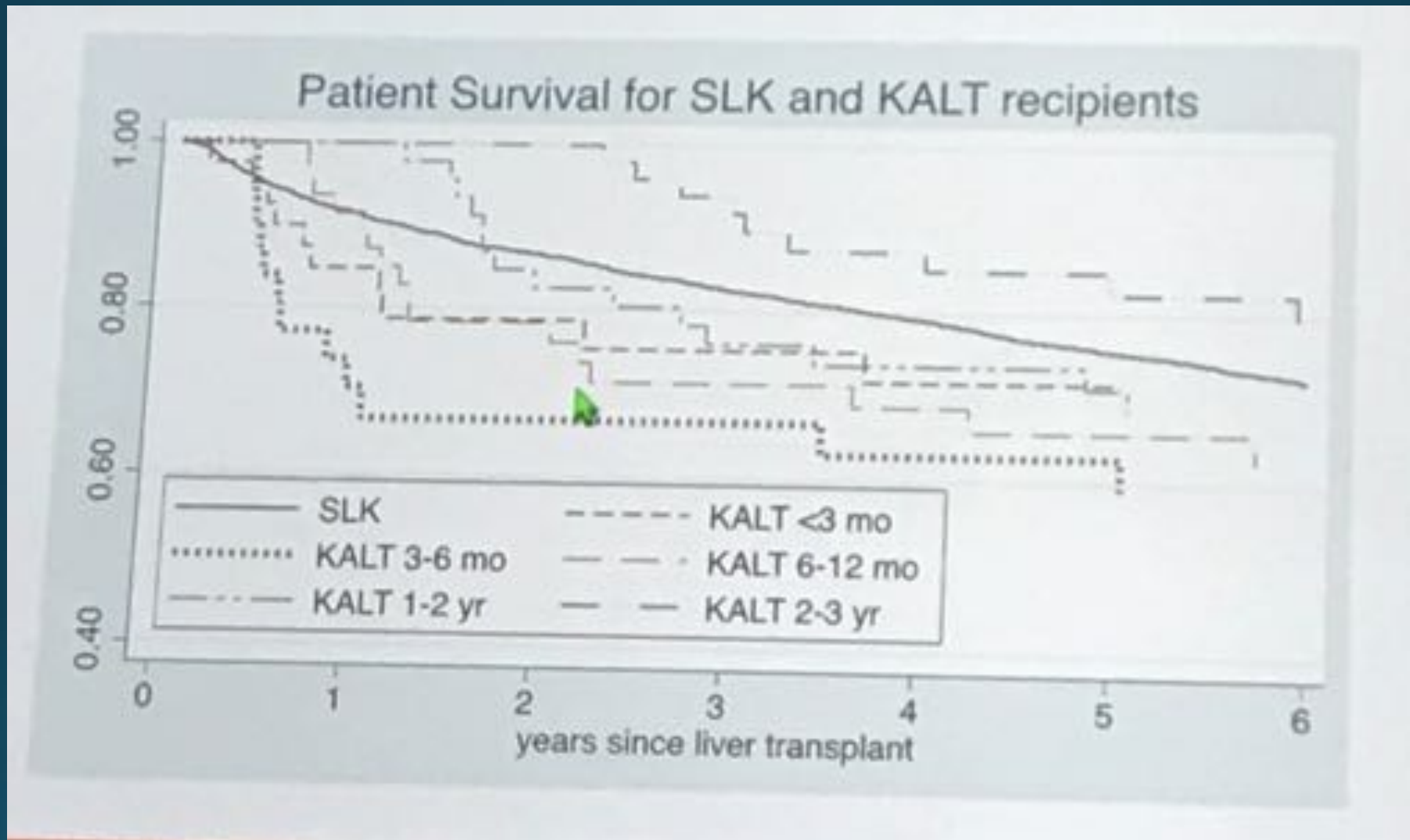
Would SLK recipient have met proposed SLK eligibility criteria?		Total	
		N	%
Chronic kidney disease	On Dialysis for ESRD at Time of Transplant	1,874	41.6
	Not on Dialysis for ESRD, eGFR <21	1,081	24.0
	Not on Dialysis for ESRD, eGFR 21-25	328	7.3
	Not on Dialysis for ESRD, eGFR 26-30	267	5.9
Sustained acute kidney injury	On dialysis for 6+ weeks before transplant <sup>#</sup>	101	2.2
Would not have qualified for SLK	No Dialysis for ESRD or temporary dialysis for 6+ weeks, eGFR 31-35	213	4.7
	No Dialysis for ESRD or temporary dialysis for 6+ weeks, eGFR > 35	636	14.1
Total		4,543	100.0

***Approximately*** 19% of previous SLK recipients would not have qualified under proposed eligible criteria.

# Differences in survival after early kidney after liver transplant (KALT): Evaluating the safety net

Colleen Jay, W. Kenneth Wahsburn, Mark Stegall, Glenn Halff, Greg Abrahamian, Jaqueline Pugh – Abstract 9 – AASLD 2017

- Decisions regarding simultaneous liver kidney transplant (SLK) versus kidney alone after transplant (KALT) are difficult
- New safety net policy allows for prioritization of KALT patients
- Goal was to compare SLK versus KALT survival



	HR	95% CI	P-value
SLK (ref)			
KALT < 1 year	1.51	1.04-2.19	0.007
KALT 1-2 years	1.10	0.63-1.93	0.73
KALT 2-3 years	0.65	0.34-1.22	0.18

Adjusted for KDPI, age at liver transplant, gender, race/ethnicity, MELD, home/hospital/ICU status, HCV and diabetes

# Summary

- “Given imperfections in the ability to predict native renal recovery after liver transplant new guidelines have included a “safety net” to allow for prioritization on the kidney waiting list for those patients who undergo LT alone and have persistent renal failure
- “However, our analysis suggests that early KALT does not have equivalent survival to SLK suggesting continued importance of determining who truly “needs” a SLK
- Additionally, ongoing surveillance of KALT outcomes under safety net criteria is imperative in insuring that policy goals of improving waitlist and transplant outcomes are met”

# Goals

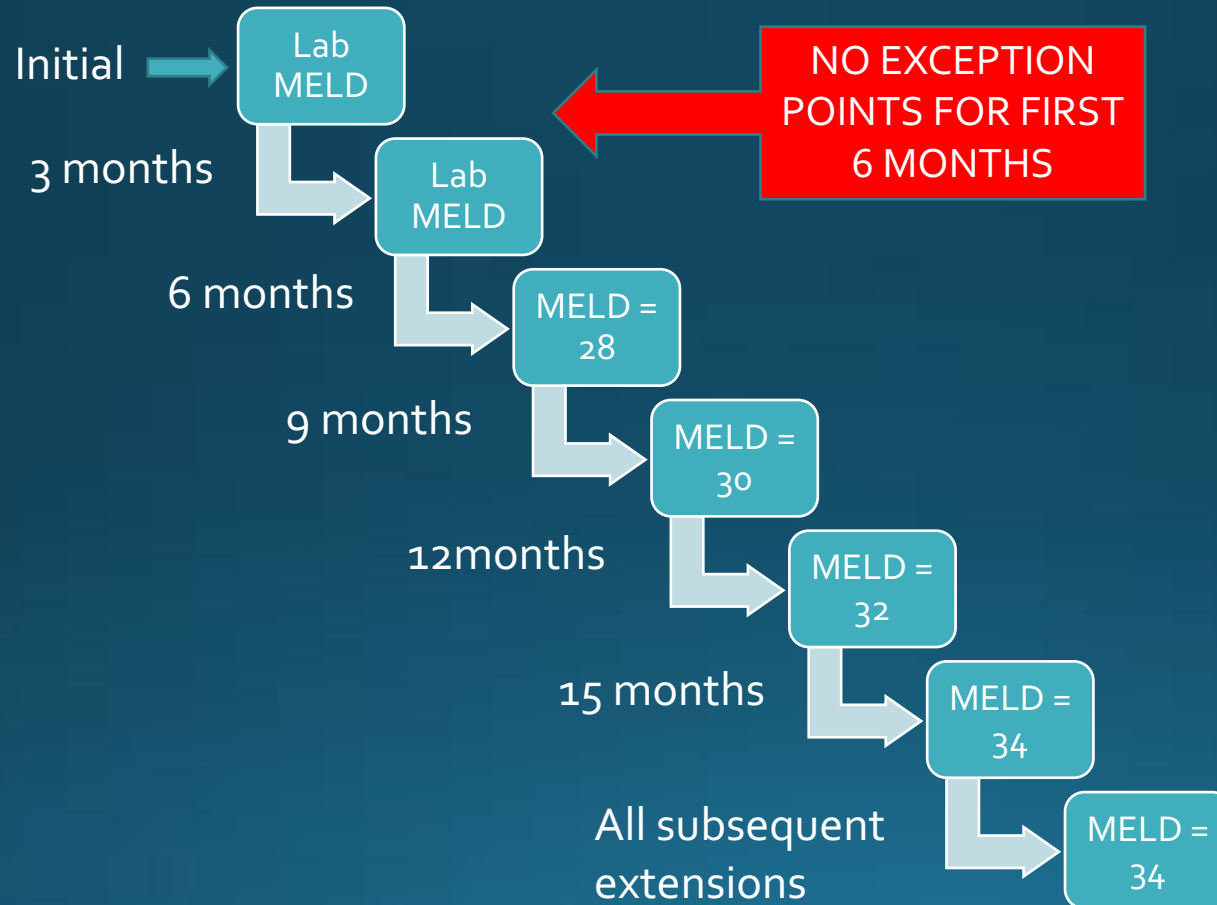
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# HCC Criteria for Auto-Approval

- MELD allocation policy currently provides “exception scores” for patients with HCC
- Exception points = increased priority on the wait-list
- As a result, there may be a disservice to laboratory MELD patients and there must a balance for prioritization between HCC and non-HCC patients
- Fall of 2015 new policy of “Delay and Cap” was implemented

# Schedule for Accruing MELD exception points



# HCC Criteria for Auto-Approval

- Proposal contains two primary policy changes:
  - 1. Candidates with lesions meeting T2 criteria but with an **AFP greater than 1000** are NOT initially eligible for a standardized MELD exception.
    - If these lesions fall below 500 after local-regional therapy, the candidate is eligible for a standardized MELD exception. Candidates with an AFP level greater than or equal to 500 at any time following local-regional therapy will be referred to the review board.
  - 2. The policy addition describes the eligibility criteria for being included in the downstaging protocol. Candidates meeting the criteria will be eligible for automatic priority after they've had locoregional treatment, and if their residual lesions fall within T2 criteria.

# HCC: AFP Greater than 1000

- Data from 2002-2009 comparing 211 patients within Milan
- AFP > 1000 ng/mL was strongest pre-transplant factor predicting vascular invasion (OR = 6.8 95%)
- 5 year survival was 80.3 % if AFP < 1000 and 52.7% if AFP > 1000

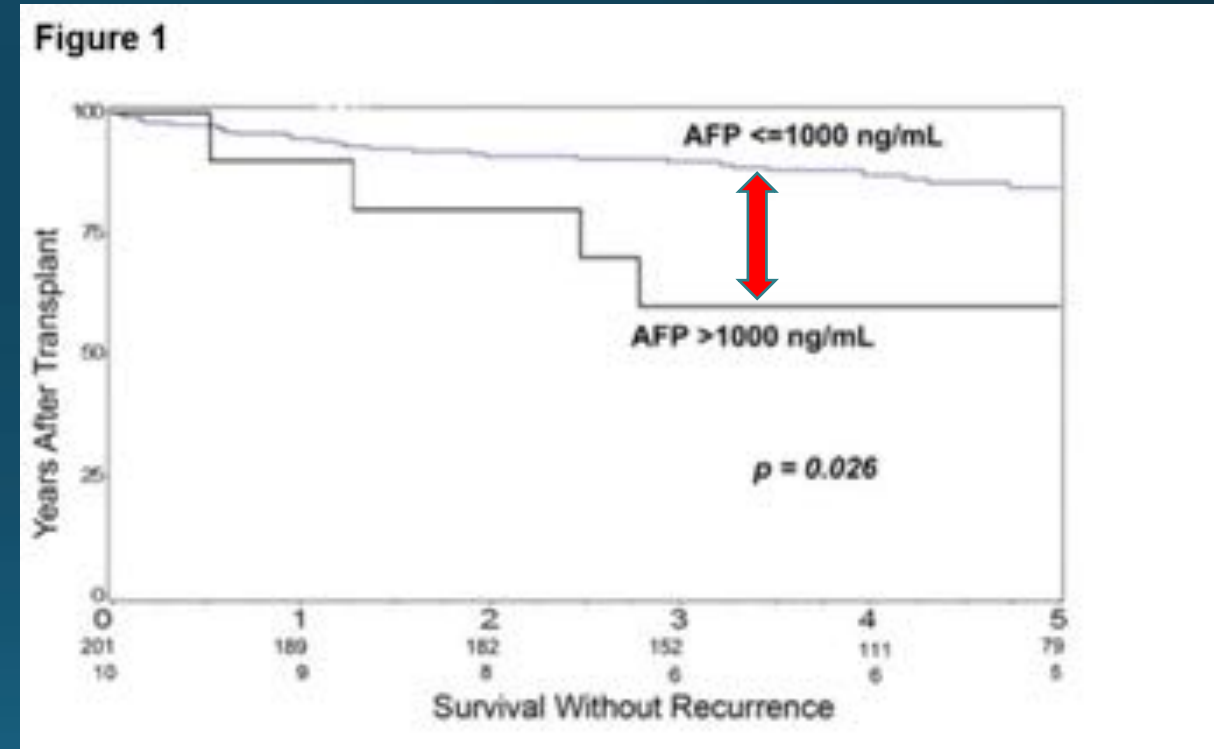


Figure 3. Distribution of AFP at Liver Transplant\*, 2009-2014 (n=8232). \*Primary, non-Status 1 deceased donor liver transplants for HCC.

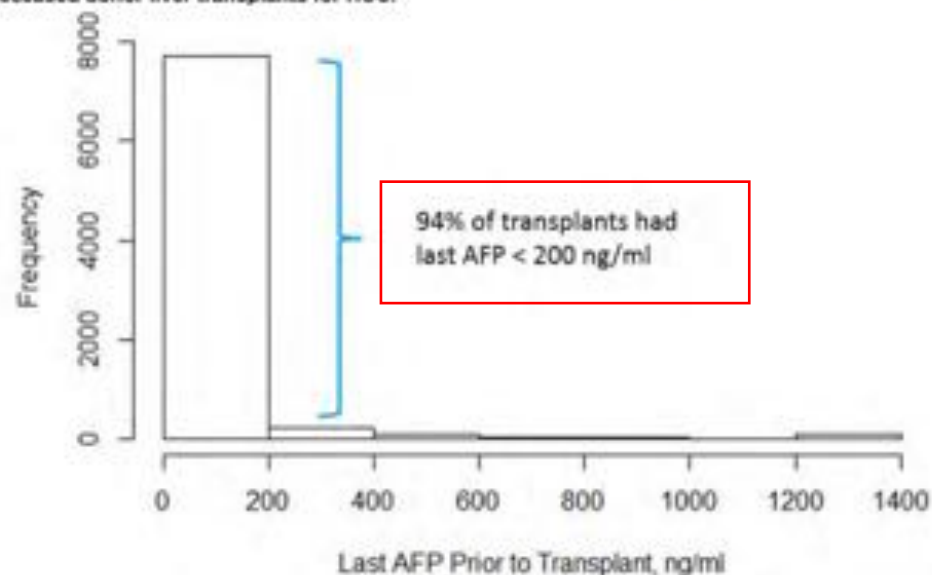
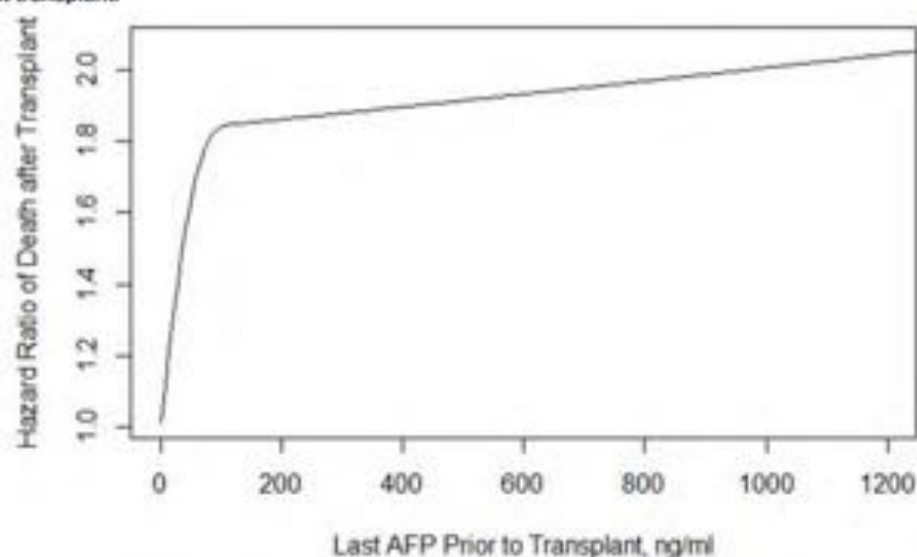


Figure 4. Hazard Ratio of Mortality Following Liver Transplant\* as a Function of AFP, 2009-2014 (n=8232). \*Primary, non-status 1 deceased donor liver transplants for HCC adjusted for lab MELD at transplant.

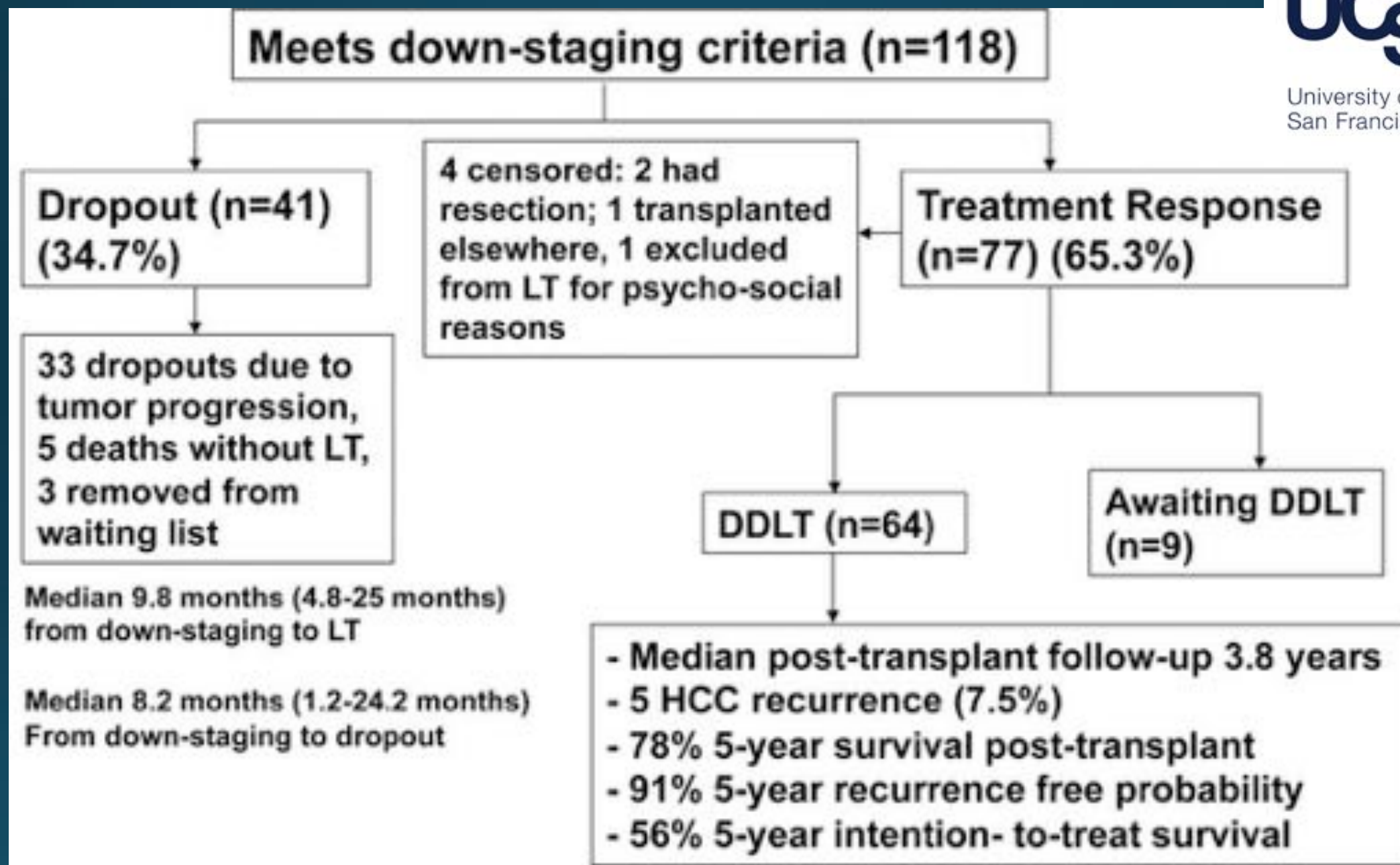


Figures 3 and 4 show the distribution of AFP and its relationship with post-transplant mortality.

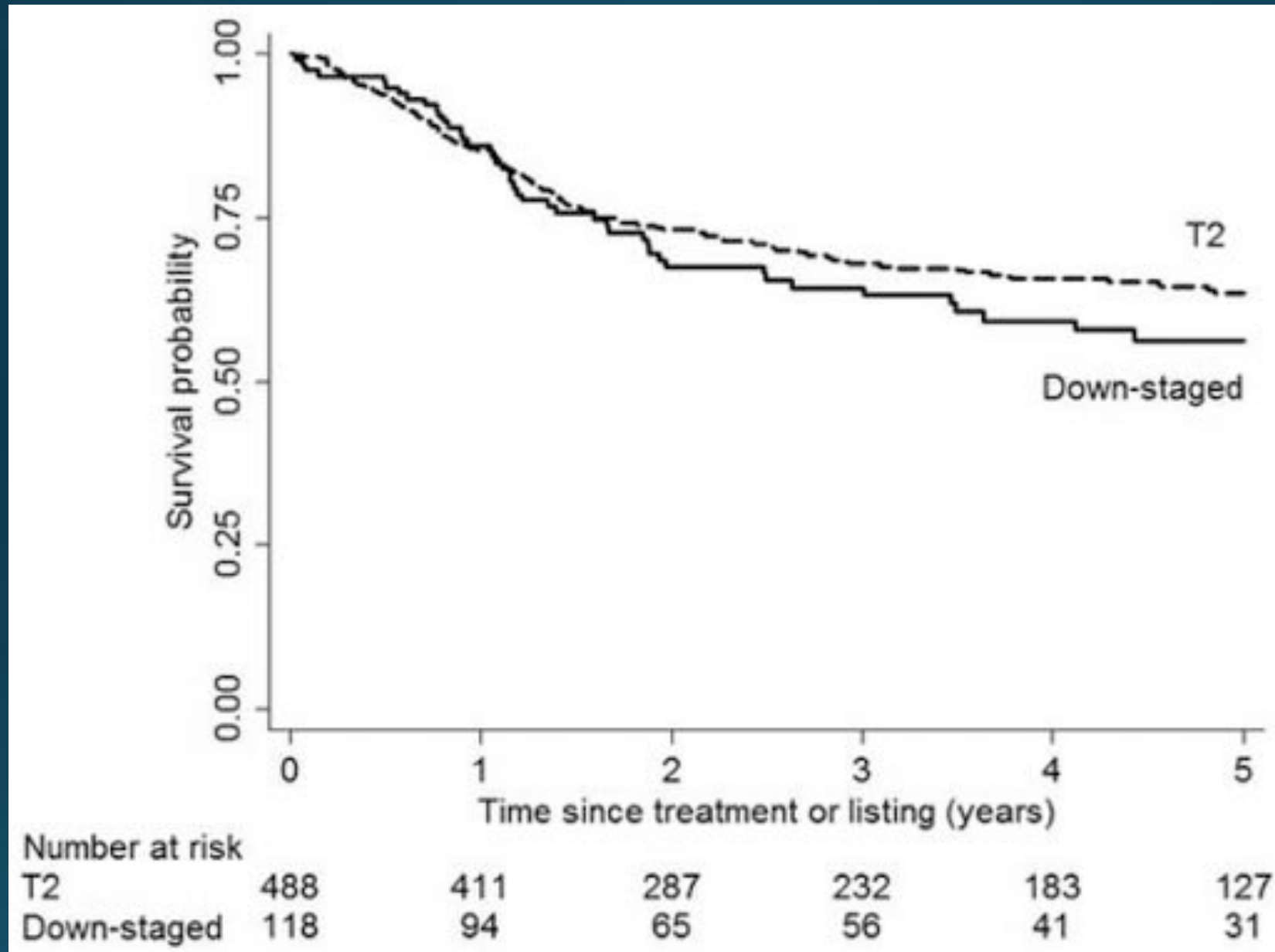
Recipients whose final AFP value prior to transplant exceeded 1000 ng/ml had a hazard ratio of **2.45** [95% CI: 1.83, 3.27] compared to recipients whose AFP values never exceeded 1000 ng/ml.

# Lesions Eligible for Downstaging Protocols

- One lesion greater than 5 cm and less than or equal to 8 cm
- Two or three lesions each less than 5 cm and a total diameter of all lesions less than or equal to 8 cm
- Four or five lesions each less than 3 cm and a total diameter of all lesions less than or equal to 8 cm







# HCC Criteria for Auto-approval

- Candidates who complete loco-regional therapy must then be within the Milan Criteria (T2)
- AFP must remain less than 500 if greater than 1000 at any point
- Patients will then be subjected to the same 6 month delay as outlined previously with the same cap at 34

# Future Changes to HCC Criteria for Auto Approval

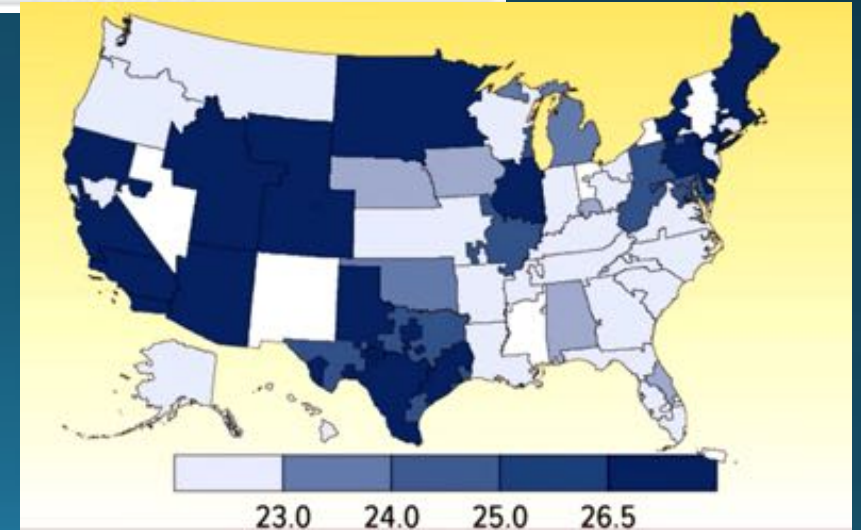
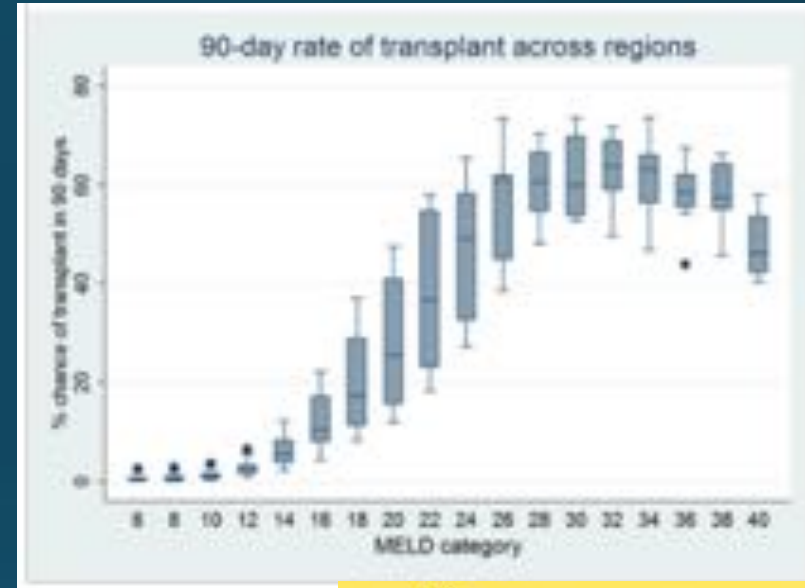
- 1) Criteria for Single Small Lesions
  - Currently there is good data that small HCC lesions which undergo good response to loco-regional therapy have excellent outcomes and therefore will not necessarily benefit from transplant, this was reviewed by the Liver-Intestine Subcommittee, and submitted for public comment
  - Significant negative feedback from regions and public
  - Additionally, recent data reviewing explant data from patients who underwent liver transplant had persistent HCC found on explant suggests that there may still be benefit from liver transplant
  - Overall impression was that it was still “too early” for this policy and further review is required.

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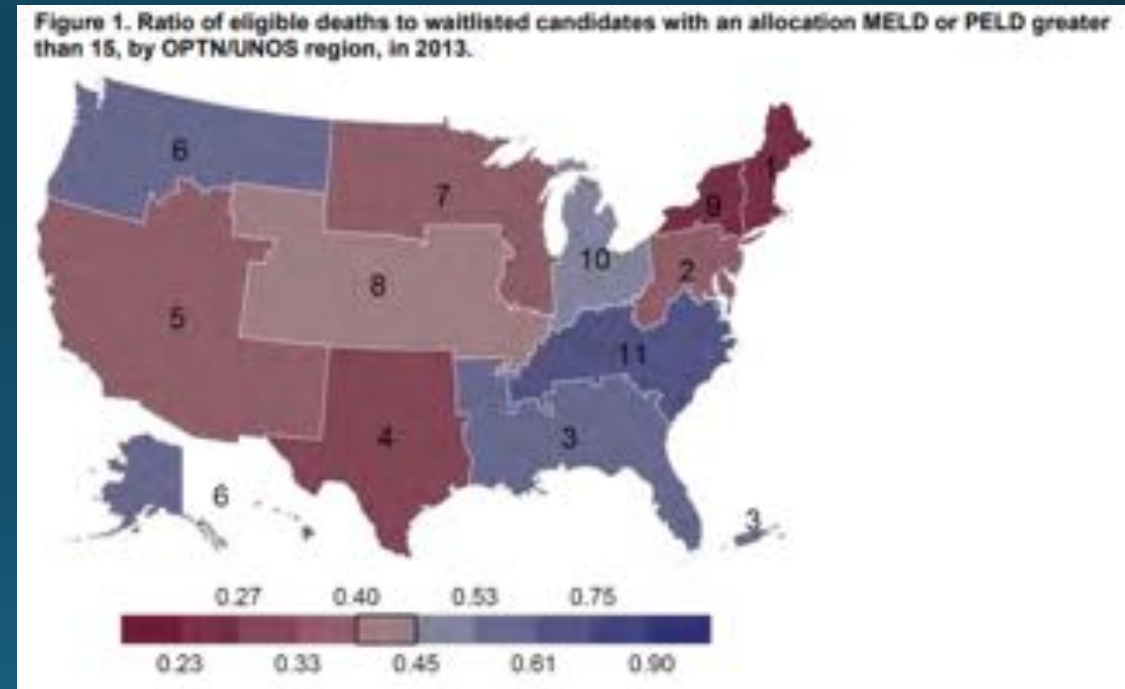
# Geographic Disparities in Liver Transplant

- 90 day likelihood of transplant or death varies from 14-82% depending on location
- Median MELD score at transplant varied by as much as 12 points (35->23) across the 52 DSA
- Equivalent to a 60% difference in the estimated 3 month mortality without a liver transplant

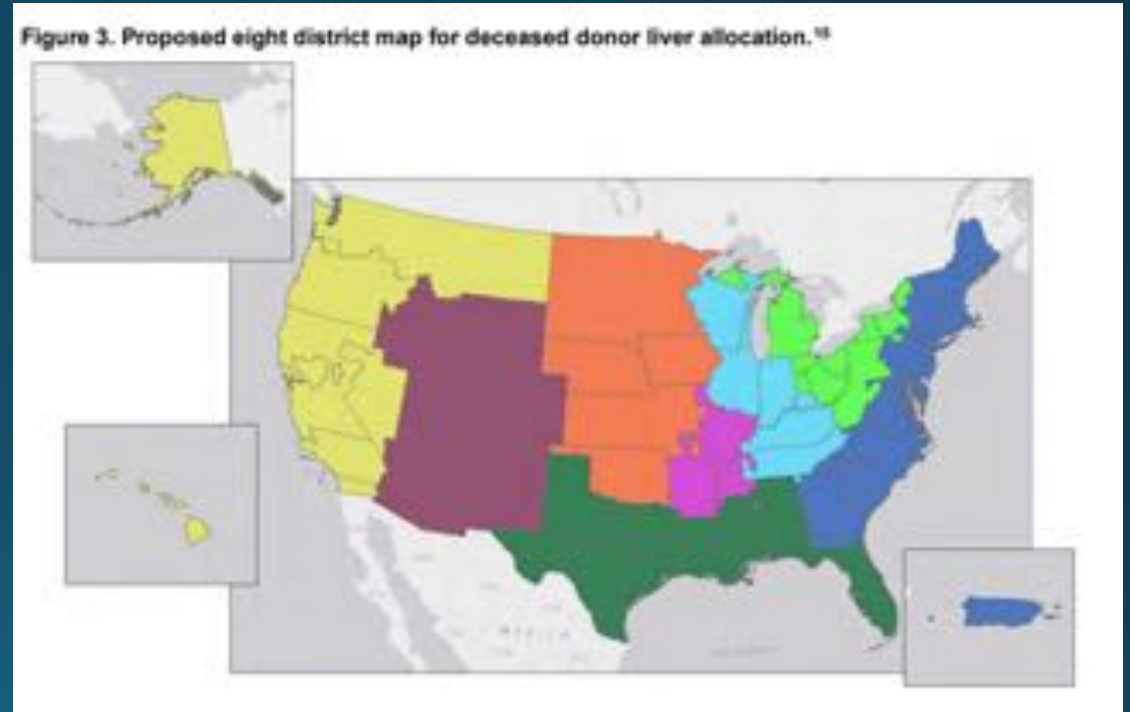


# Reasons for Disparities in Organ Availability

- Local exposures predispose some populations to a greater risk of preventable death
  - In 2015 most common causes of death among organ donors were:
    - Stroke (30.4%)
    - Blunt/vehicular injury (20.4%) ≈
    - CV events (18.2%)
    - Drug use (9.3%)
    - Gunshot wounds (8.4%)
- Many of the above are socially and geographically patterned: access to care, vehicular and guns safety vary widely state to state

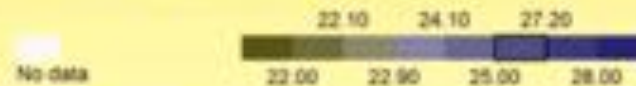
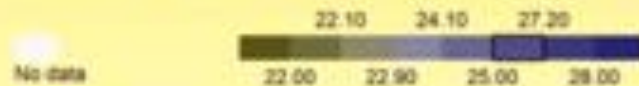


# Proposed Transition from 11 to 8 Districts





# Median MELD/PELD at Transplant



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# OPTN Redistricting Model

## PRO

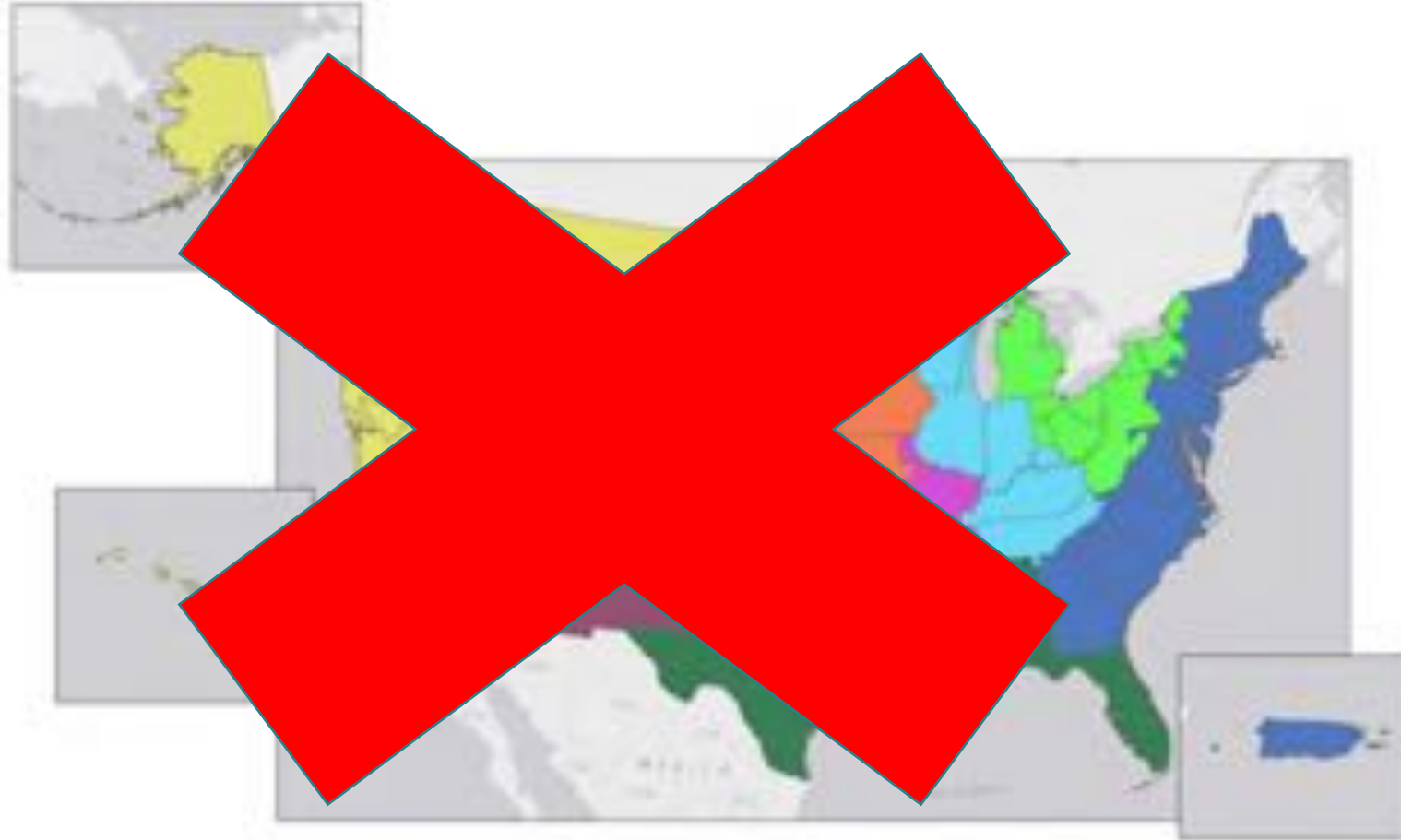
- Fairness (equal entitlement to organs regardless of geography)
- Equality for arbitrary circumstance
- Reduction in waitlist mortality
- Overall cost savings

## CON

- Unfairly disadvantages local recipients
- Increased challenges to patients who are currently underserved
- Increase in logistical complexity
- Increase transport costs
- Increased delivery to health care saturated areas
- Many centers with high MELD at transplant currently have lower rates of wait list death

# Proposed Transition from 11 to 8 Districts

Figure 3. Proposed eight district map for deceased donor liver allocation.<sup>18</sup>



# Thomas E. Starzl Transplant Surgery State-of-the-Art Lecture



- The discussion by the OPTN liver and intestinal committee need to return to what is best for PATIENTS rather than what is best for CENTERS
- The discussion by the OPTN liver and intestinal committee needs to re-focus on truly addressing geographic disparities
- The current proposal that has been sent to the board will do little to address the geographic disparities which are real



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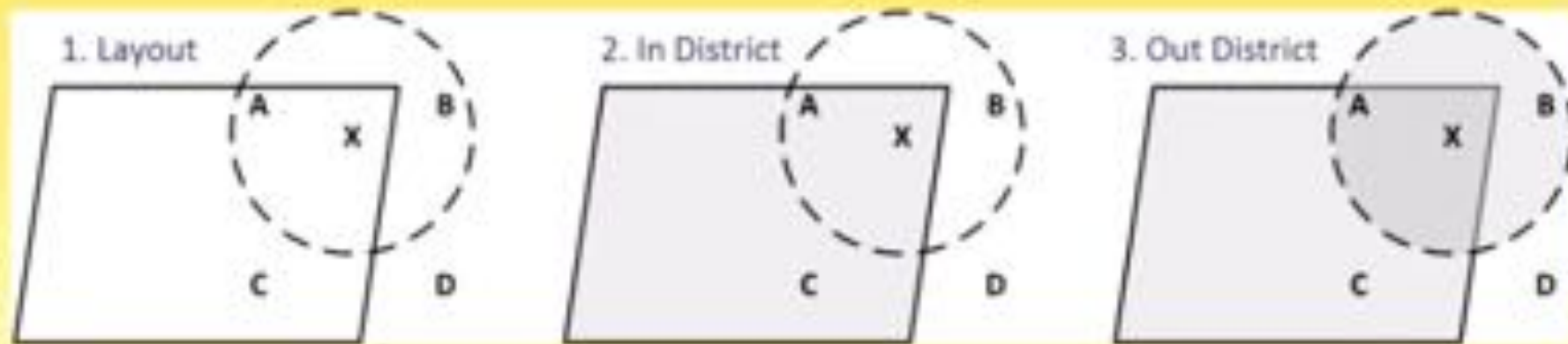
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# Current Proposals Under Evaluation

- DCD and Donors aged > 70 years: Priority given to within DSA MELD candidates over regional candidates
- Proximity points:
  - 5 additional MELD points given to recipients within a certain proximity to the donor
    - Possibilities include:
      - 150 nautical miles of donor hospital
      - 150 nautical miles of donor hospital and DSA
      - Sharing threshold of MELD 29 or above
      - Sharing threshold of MELD 22 or above
  - Additional MELD score (MELD + proximity) is not capped at 40



# Proximity Point Parameters: In/Out District



- Rectangle: region/district
- Circle: proximity radius
- X: donor center
- A-D: transplant centers

Allocation groupings:

1. A + C (A gets points)
2. B + D (B gets points)

Allocation groupings:

1. A + B + C (A, B get points)
2. D

# Variance in Median Allocation MELD/PELD at Transplant by DSA

## Variance in Median Allocation M/P at Transplant by DSA by Exception Status

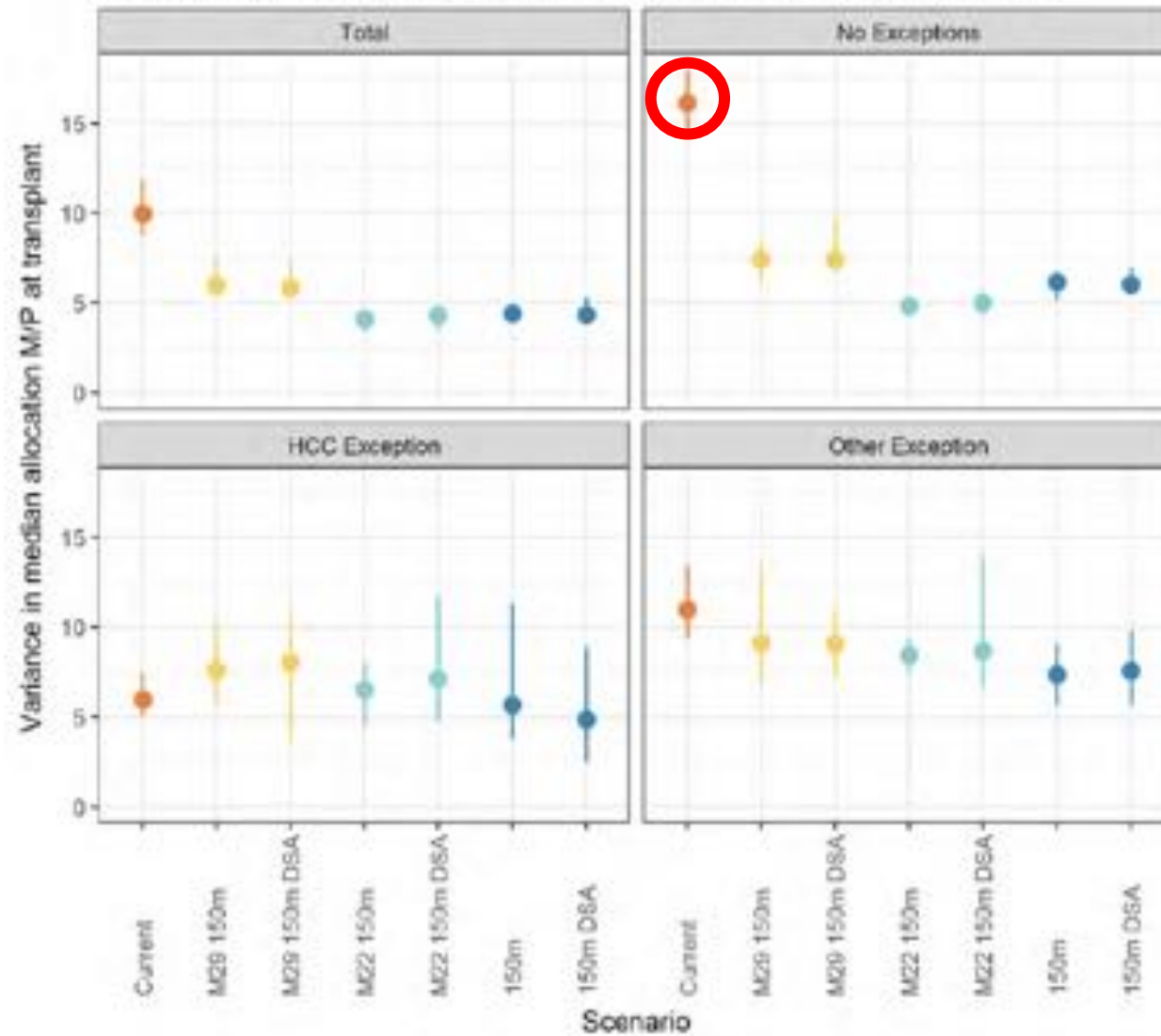


Figure 1 Variance in median allocation M/P at transplant by DSA by exception status



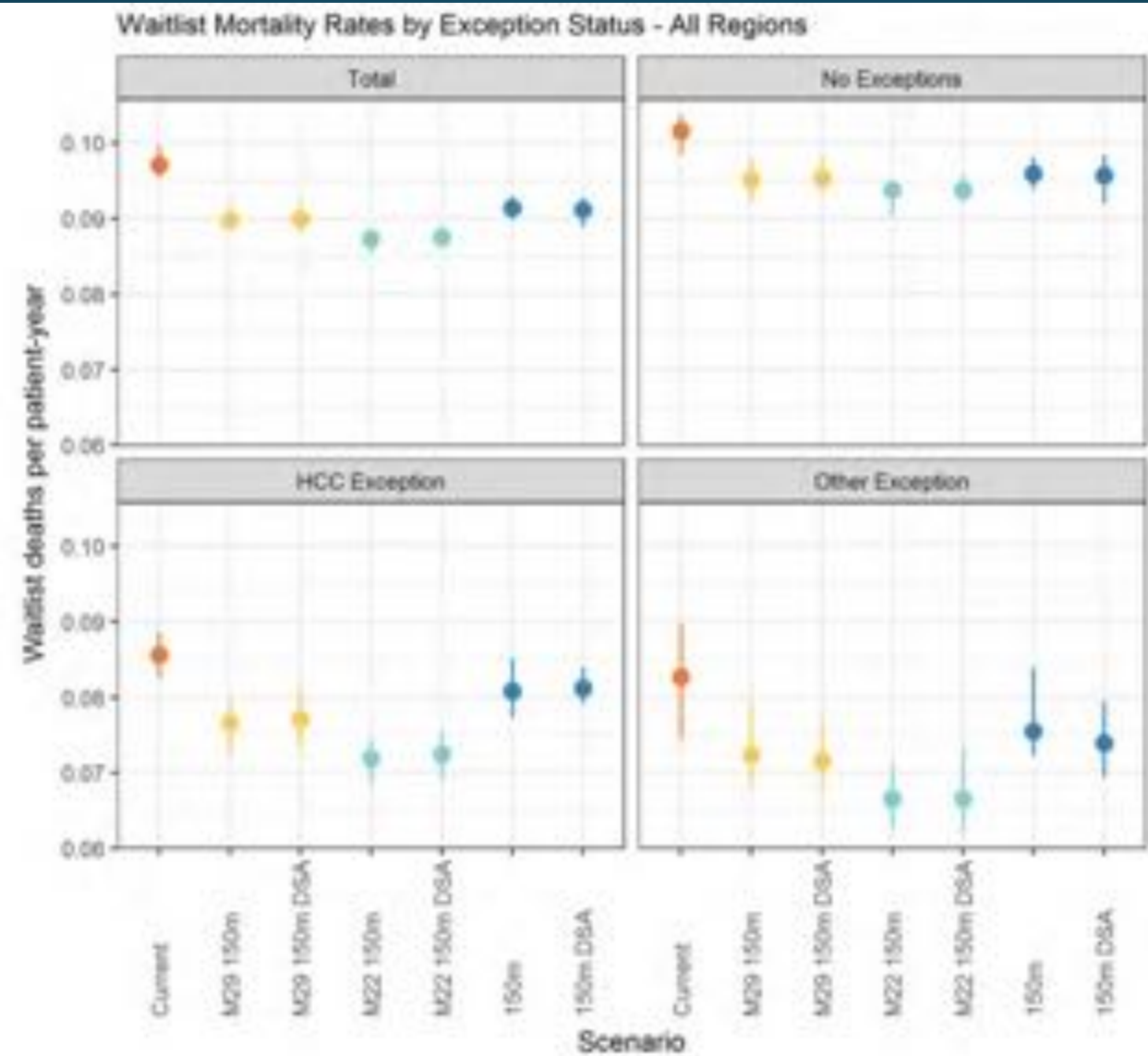


Figure 11 Waitlist mortality rates by exception status - all regions

## Maps of Median Allocation MELD/PELD at Transplant by DSA

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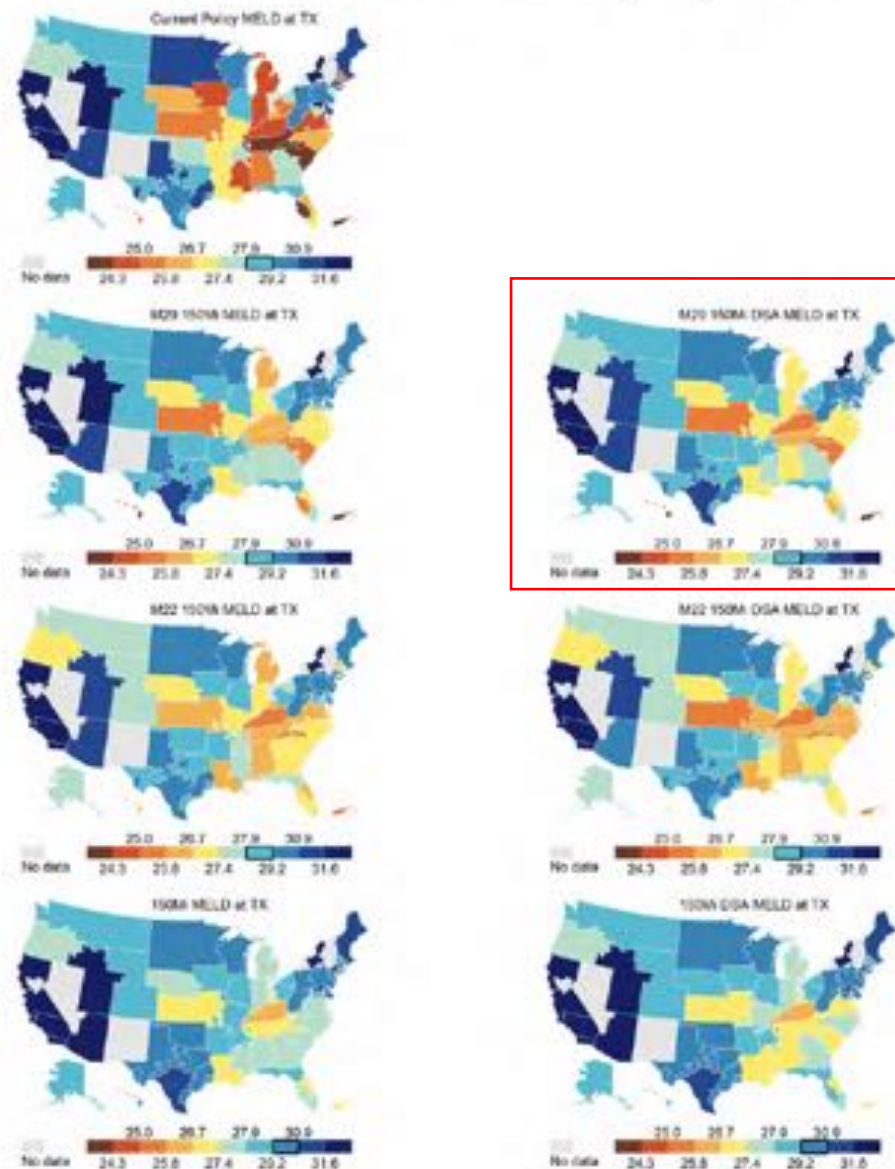


Figure 3 Maps of median allocation MELD/PELD at transplant by DSA

## Maps of Median Calculated MELD/PELD at Transplant by DSA - No Exceptions

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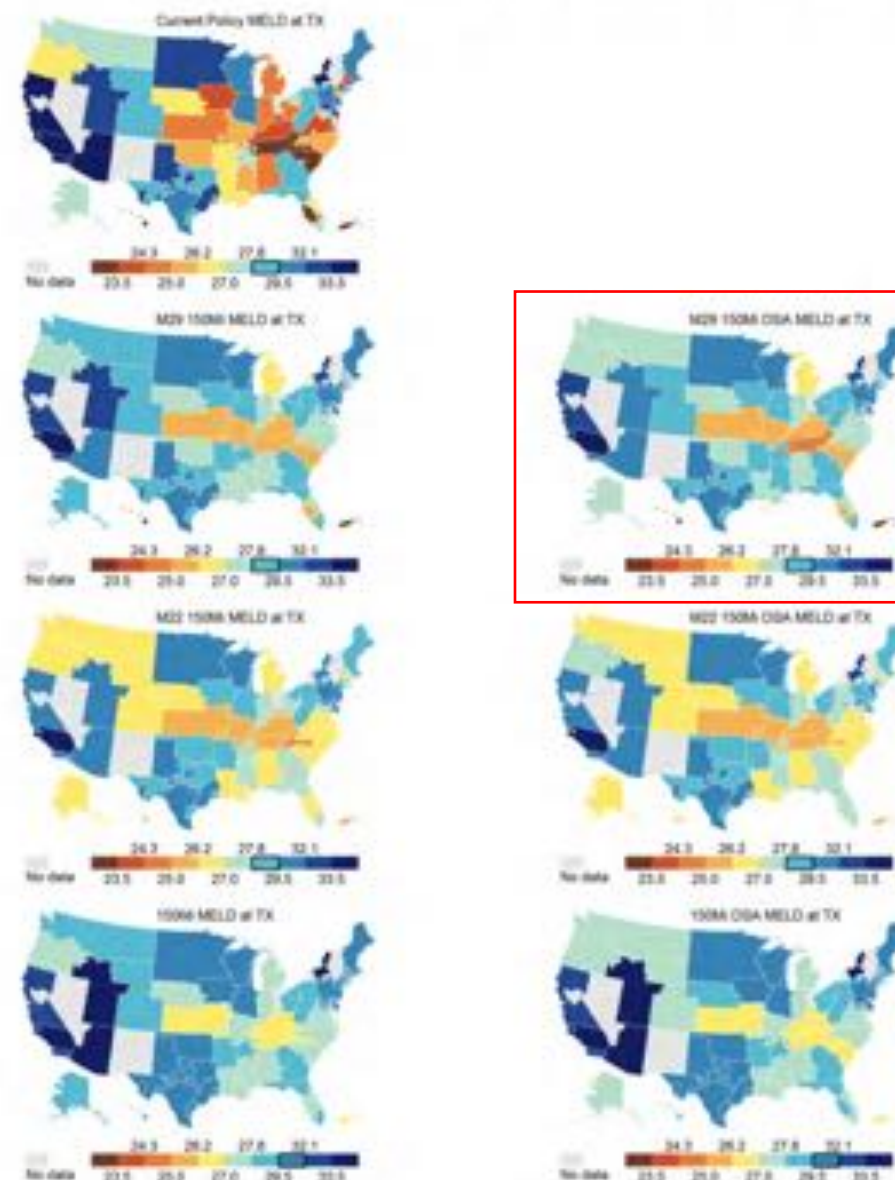


Figure 4 Maps of median calculated MELD/PELD at transplant by DSA - no exceptions





# National Review Board

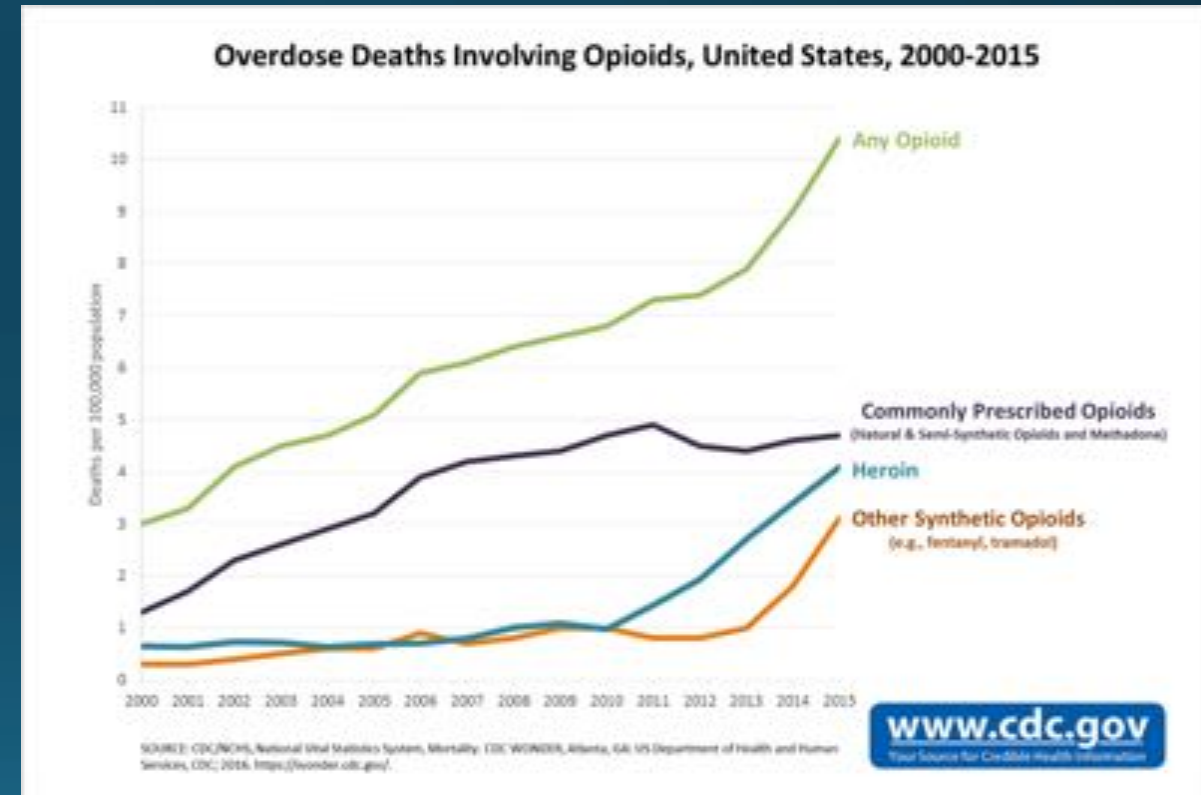
- Accepted June 2017
- Regional review boards (RRB) have different rules regarding representation
- RRB inconsistent in submission and award practices
- Awarding exception scores not correlated with disease severity negatively impacts non-exception candidates
- Complaints have been directed at MELD exception variance as an explanation of regional variability, so this may help increase intraregional variability

# Goals

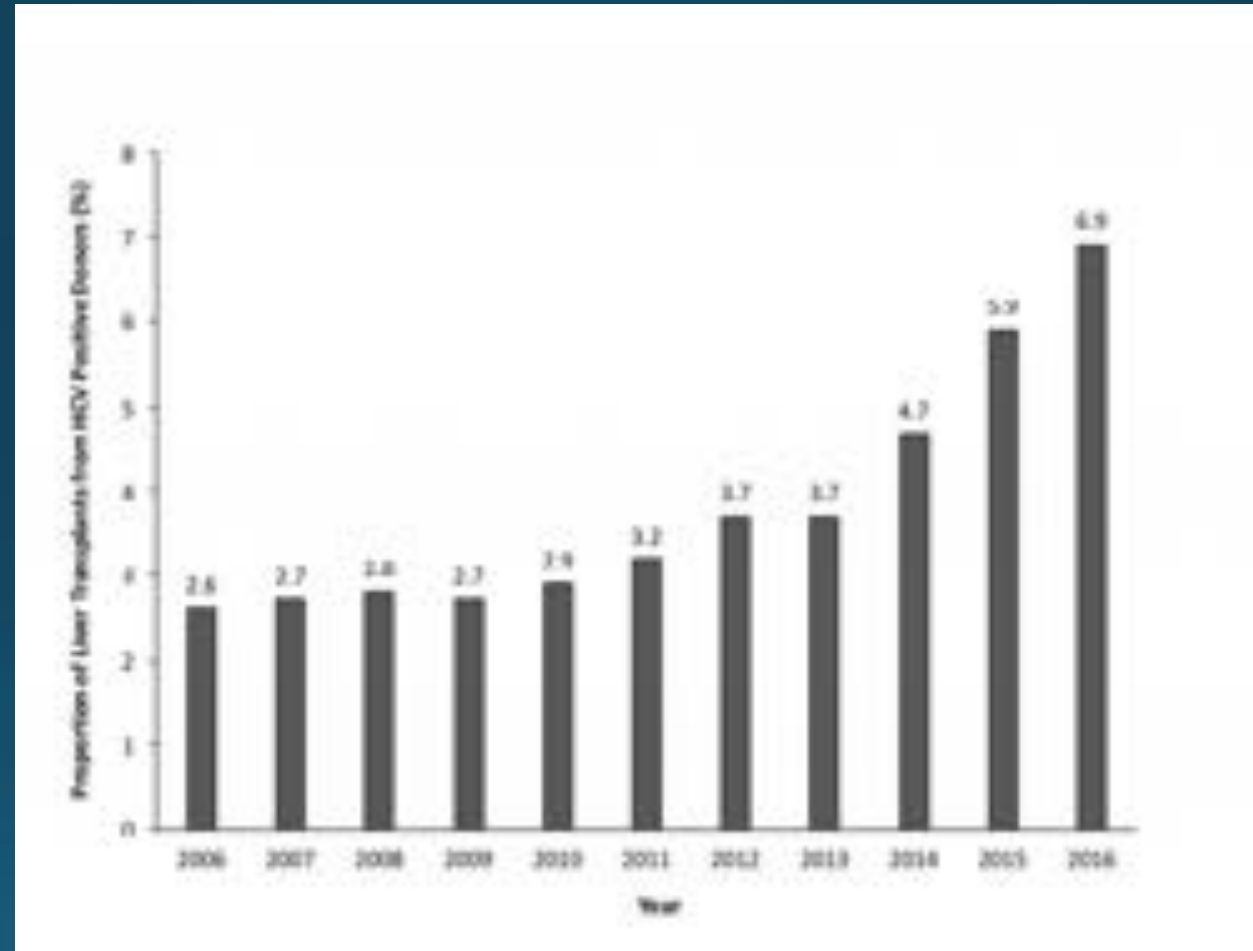
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# Use of HCV Ab + livers

- Over past 2 decades, marked increase in prescription opioid use and abuse
- More commonly rural, poor and more centrally located
- Concurrent increase in heroin use, with abrupt increase in HCV
- Last decade greatest increase in acute HCV has been in Appalachia among those 18-29 years old
- Over past 15 years three fold increase in drug overdose deaths, driven by heroin
- According to OPTN average age of HCV + donor has fallen from 47 to 35 years old



# Use of HCB Ab + Livers

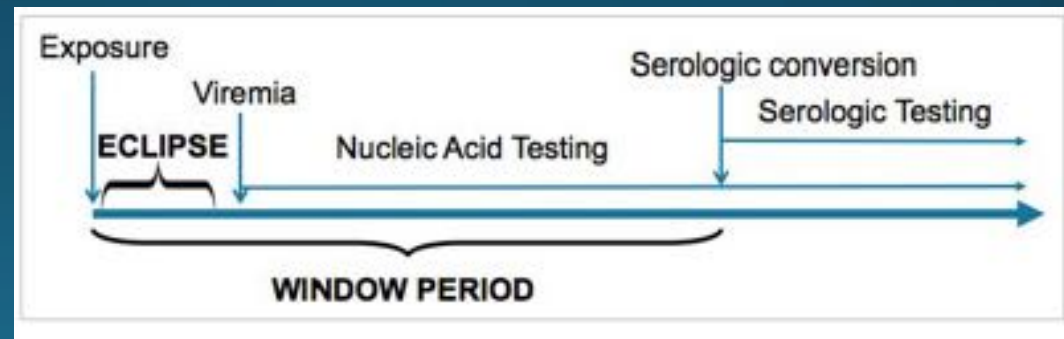


- Increased proportion of donors have been hepatitis C positive



# HCV + Donors

- Prior to 2013 patients were classified as AB + only
- In 2013 UNOS required defining patients not only based on AB +/- but also on Nucleic Acid Testing of Hepatitis C (NAT +/-NAT-)
- Nucleic Acid Testing is a rapid surrogate marker for viremia
- NAT can provide definitive result with false positive rate at less than 1% within 12 hours.

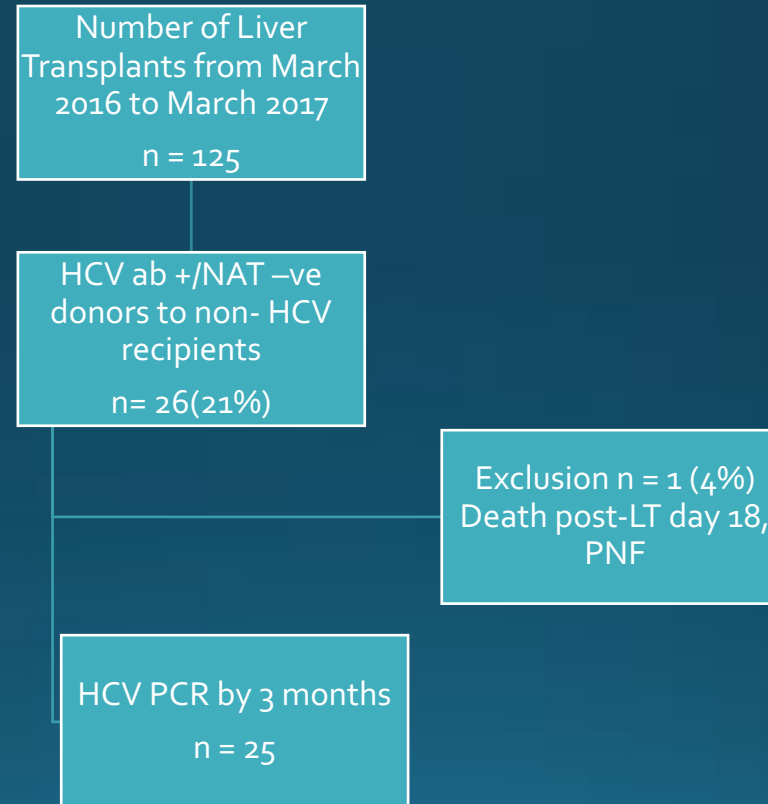


# Risk of Transmission in NAT negative donor

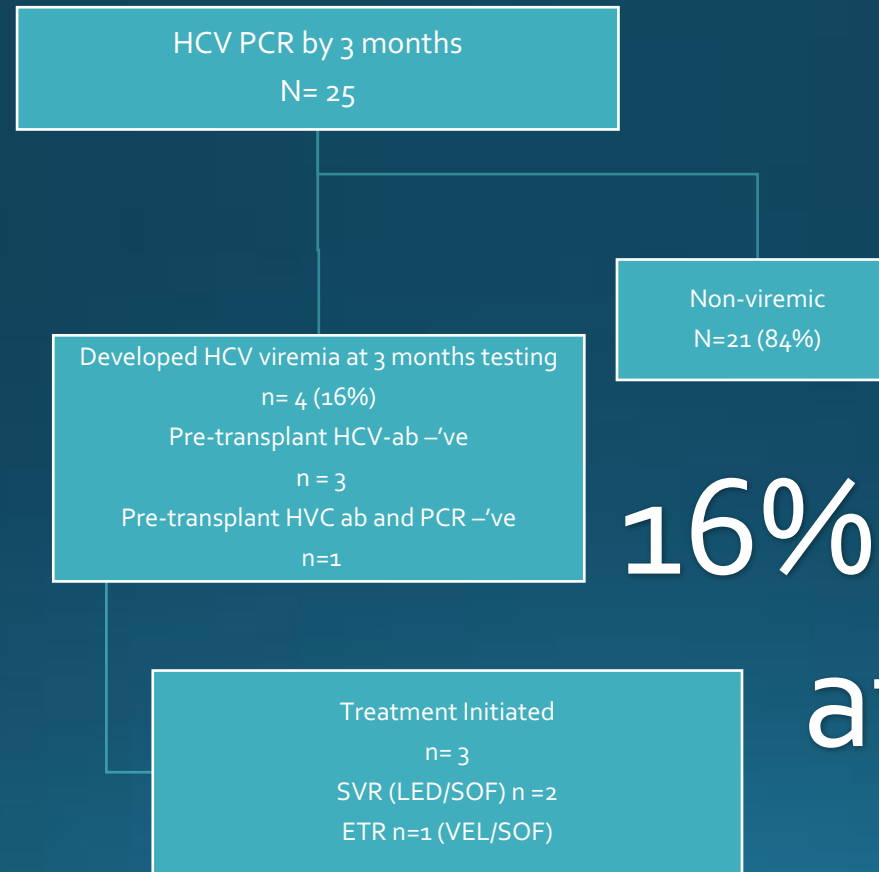


- Non HCV candidates on liver transplant wait list
  - Serum HCV Ab negative
  - OR HCV PCR negative within a 6 month period prior to liver transplantation
- Recipients were counseled on the risk of HCV transmission (estimated to be 5%)
  - Eclipse period transmission
  - Occult hepatitis C infection
- Consent obtained for HCV + NAT – transplant obtained in office and again prior to transplant

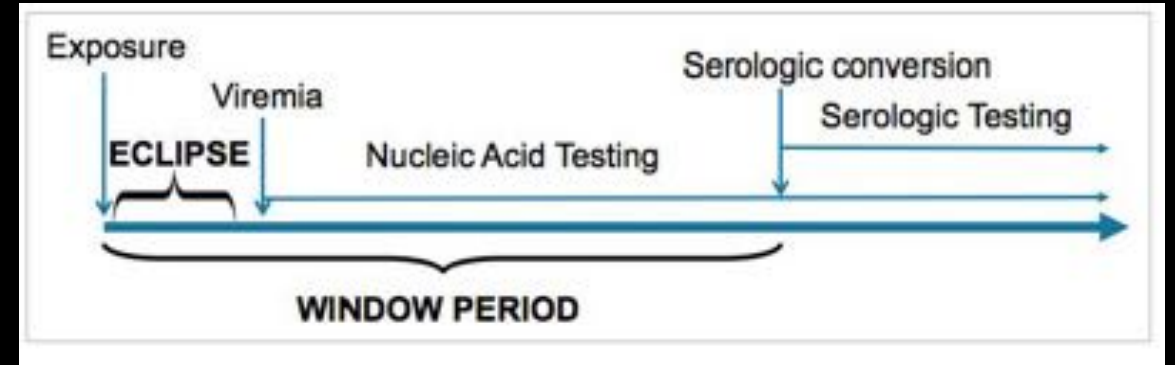
# Results:



# Results:



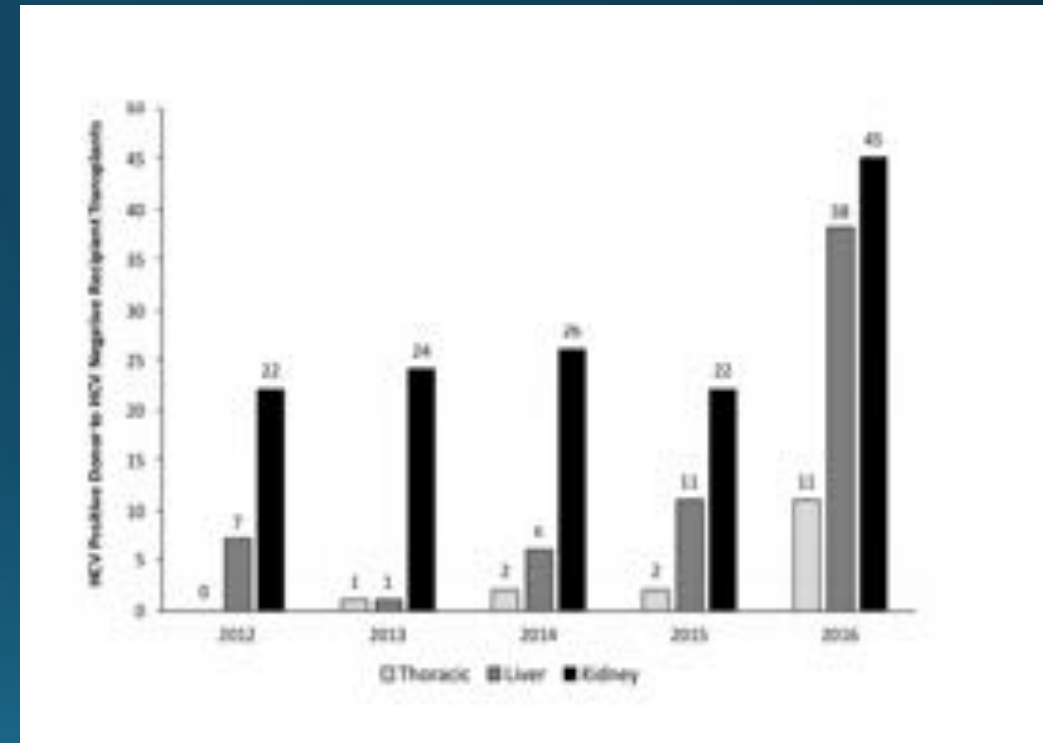
16% NAT- D + PCR  
at 3 months



Beware the Eclipse!!

# HCV ab+ organs to HCV negative patients

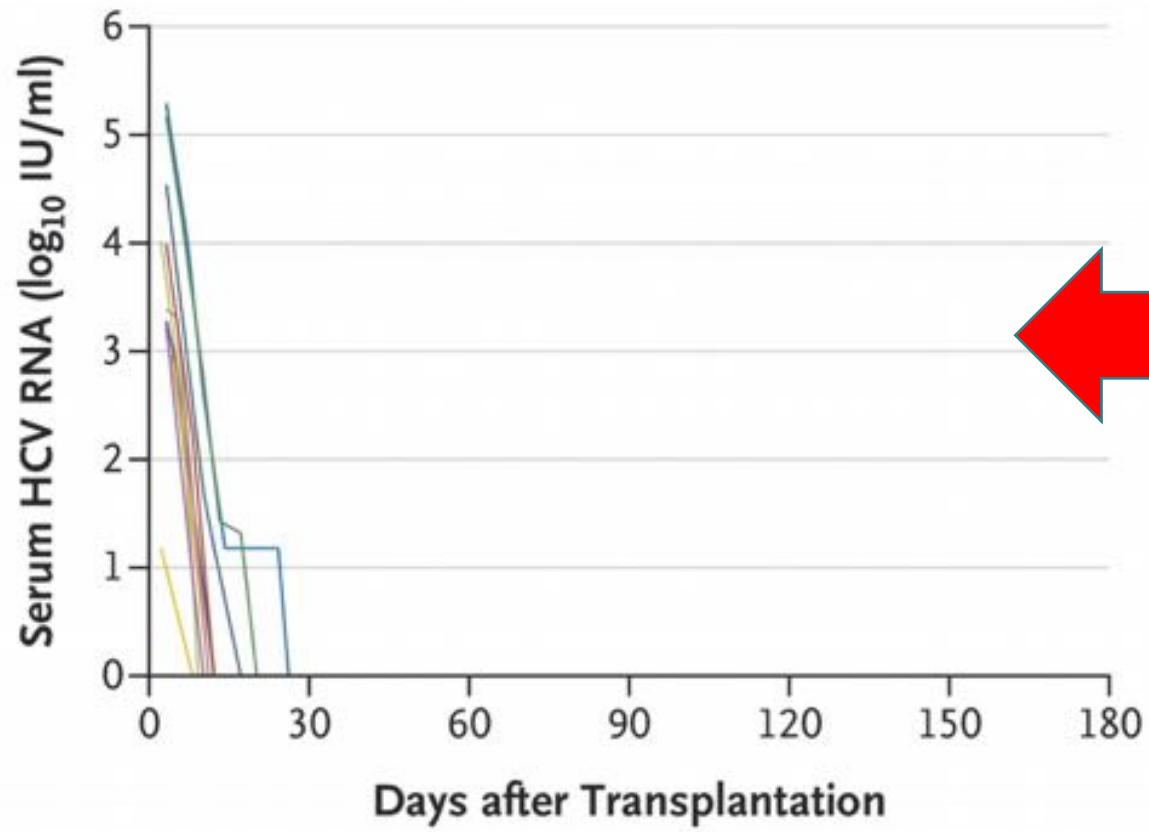
- In the era of highly effective DAA treatment transplant of infected organs to non-infected patients should be considered
- Pros:
  - Reduction of wait list time
  - Reduction of wait list mortality
- Cons:
  - Purposeful infection of a patient with infectious agent
  - Long term implications of infection
  - Risk of rejection
  - Risk of fibrosing cholestatic hepatitis C



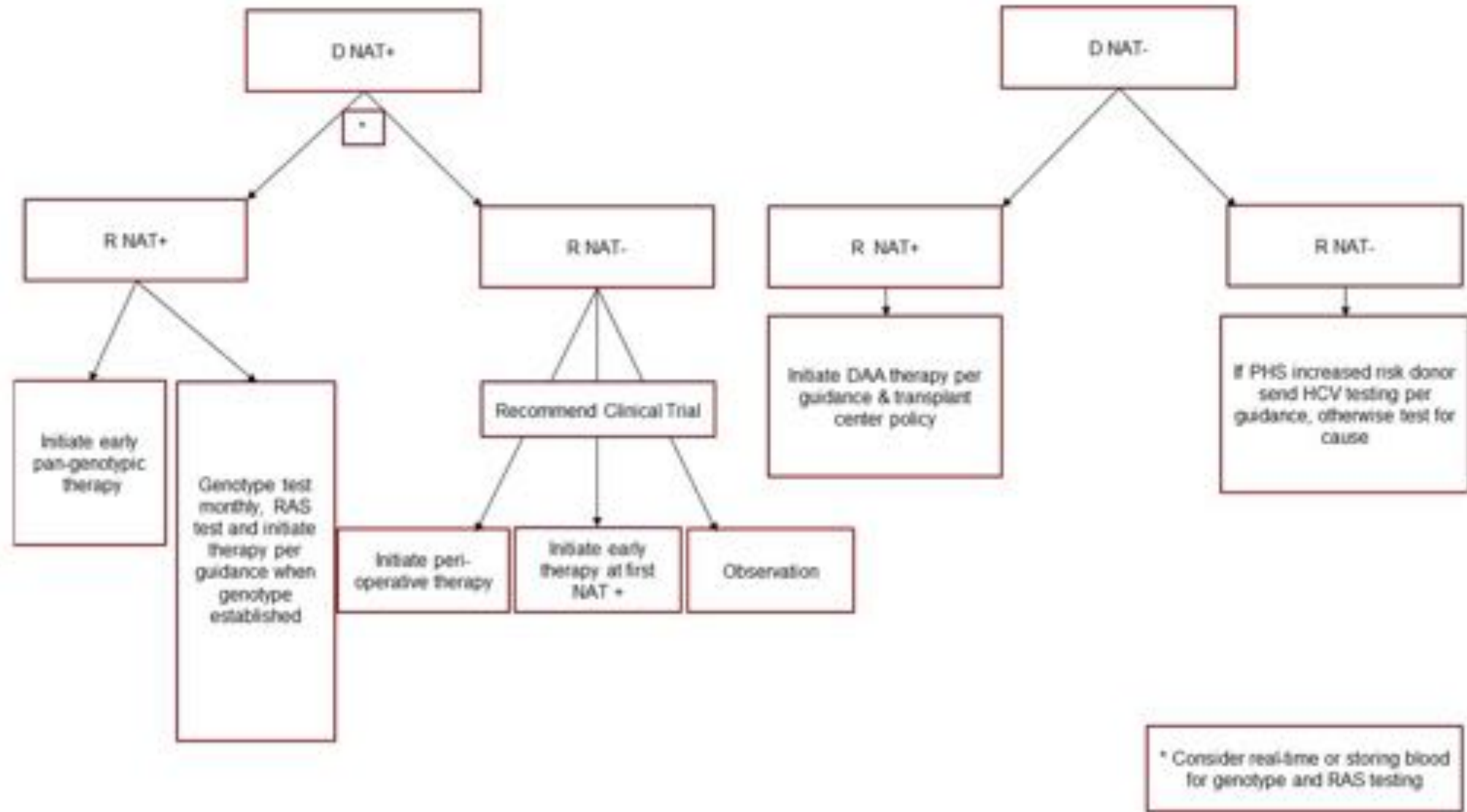
CORRESPONDENCE



Trial of Transplantation of HCV-Infected Kidneys  
into Uninfected Recipients

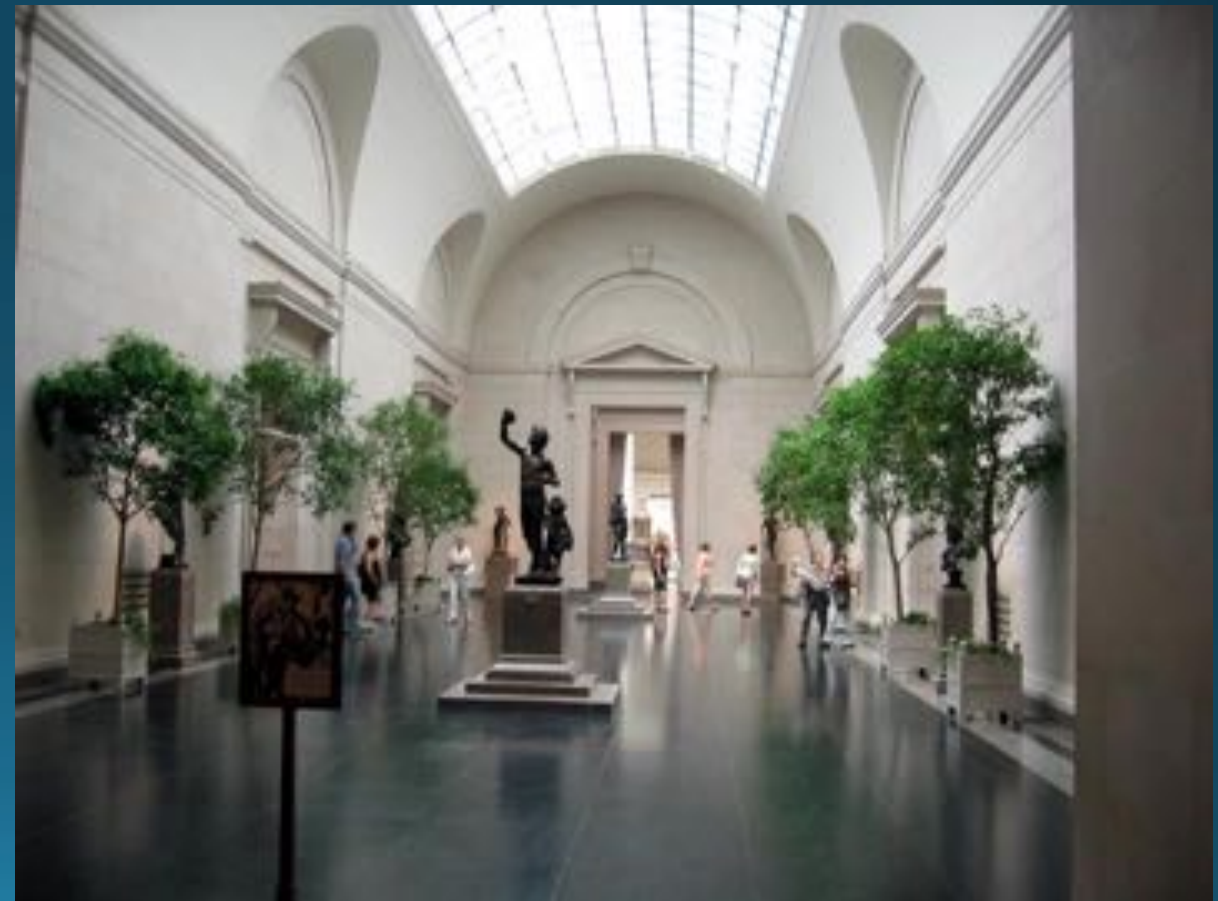






# Summary

- Review recent changes in liver/kidney allocation
  - Share 35 – working well with decreased mortality
  - HCC exception points – 6 months to get them and there is a cap at 34
  - SLK – only for those in need, rapid transplant post with new “safety net”
  - Downstaging Criteria – now national
  - AFP – must be below 1000. If greater than 1000, get it below 500
- Possible Upcoming Changes in liver/kidney allocation
  - Redistricting – Dead for now
  - Proximity Points – currently being debated
  - National Review Board – approved and coming soon
- Alternatives to Increase Donor Supply







The Crippled and Sick Cured  
at the Tomb of Saint  
Nicholas

*Gentile Da Fabriano c. 1370-  
1427*