Transplant Benefit-Based Liver Allocation

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Outline

- Introduction: organ allocation schemes
- Transplant Benefit Score
- Comparison to MELD Score
- Simulation results: LSAM
  - Comparison of deaths, life-years saved, and distance
    - Benefit score vs. MELD
    - Benefit score vs. geographic modifications of MELD
- Conclusions

Background

- Currently, chronic liver failure patients waitlisted for deceased-donor liver transplantation are prioritized with respect to medical urgency in decreasing order of Model for End-stage Liver Disease (MELD) score
- Shortfall in donor livers increases pressure to make the best possible use of available organs
- It has been suggested that post-transplant survival should play a role in liver allocation
- Transplant benefit has been a central component of the allocation system since May, 2005.

Organ Allocation Schemes

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Organ Allocation Policy

- Possible bases for organ allocation:
  1. URGENCY: future wait-list lifetime
  2. UTILITY: post-transplant lifetime
  3. BENEFIT: combines (1) and (2)

Organ Allocation: Example Expected Lifetimes

Patient ID #	Predicted WL Lifetime	Predicted post-LT Lifetime
1	7	10
2	2	3
3	5	9

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Organ Allocation: Example Expected Lifetimes

Patient ID #	Predicted WL Lifetime	Predicted post-LT Lifetime
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- Q: An organ is procured. To which patient should it be allocated?

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Organ Allocation: Example Expected Lifetimes

Patient ID #	Predicted WL Lifetime	Predicted post-LT Lifetime
1	7	10
2	2	3
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- Q: An organ is procured. To which patient should it be allocated?
- A: depends on the allocation rules …..

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Organ Allocation: Example Expected Lifetimes

Patient ID #	Predicted WL Lifetime	Predicted post-LT Lifetime
1	7	10
2	2	3
3	5	9

- **Minimum WL lifetime**:
  - Allocate to: #2

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Organ Allocation: Example
Expected Lifetimes

Patient ID #	Predicted WL Lifetime	Predicted post-LT Lifetime
1	7	10
2	2	3
3	5	9

- Minimum WL lifetime:
  - Allocate to: #2
- Maximum post-LT lifetime:
  - Allocate to: #1

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Organ Allocation: Example
Expected Lifetimes

Patient ID #	Predicted WL Lifetime	Predicted post-LT Lifetime
1	7	10
2	2	3
3	5	9

- Minimum WL lifetime:
  - Allocate to: #2
- Maximum post-LT lifetime:
  - Allocate to: #1
- Benefit (LT - WL):
  - Allocate to: #3

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Organ Allocation: Example

ID #	Future Lifetime (*patient*)		
	WL	LT	Benefit = LT-WL
1	7	10	3
2	2	3	1
3	5	9	4

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Transplant Survival Benefit Score

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Liver Transplant Survival Benefit

- Concept developed in collaboration with OPTN/UNOS Liver Committee since 2006
- Patient-specific and donor-specific
- Separate models for waitlist and post-transplant lifetimes
- Uses available factors other than MELD components
- Difference in area under 5-year survival curves
  - Predicted post-transplant lifetime minus predicted future waitlist lifetime
  - Reflects life years gained through liver transplantation

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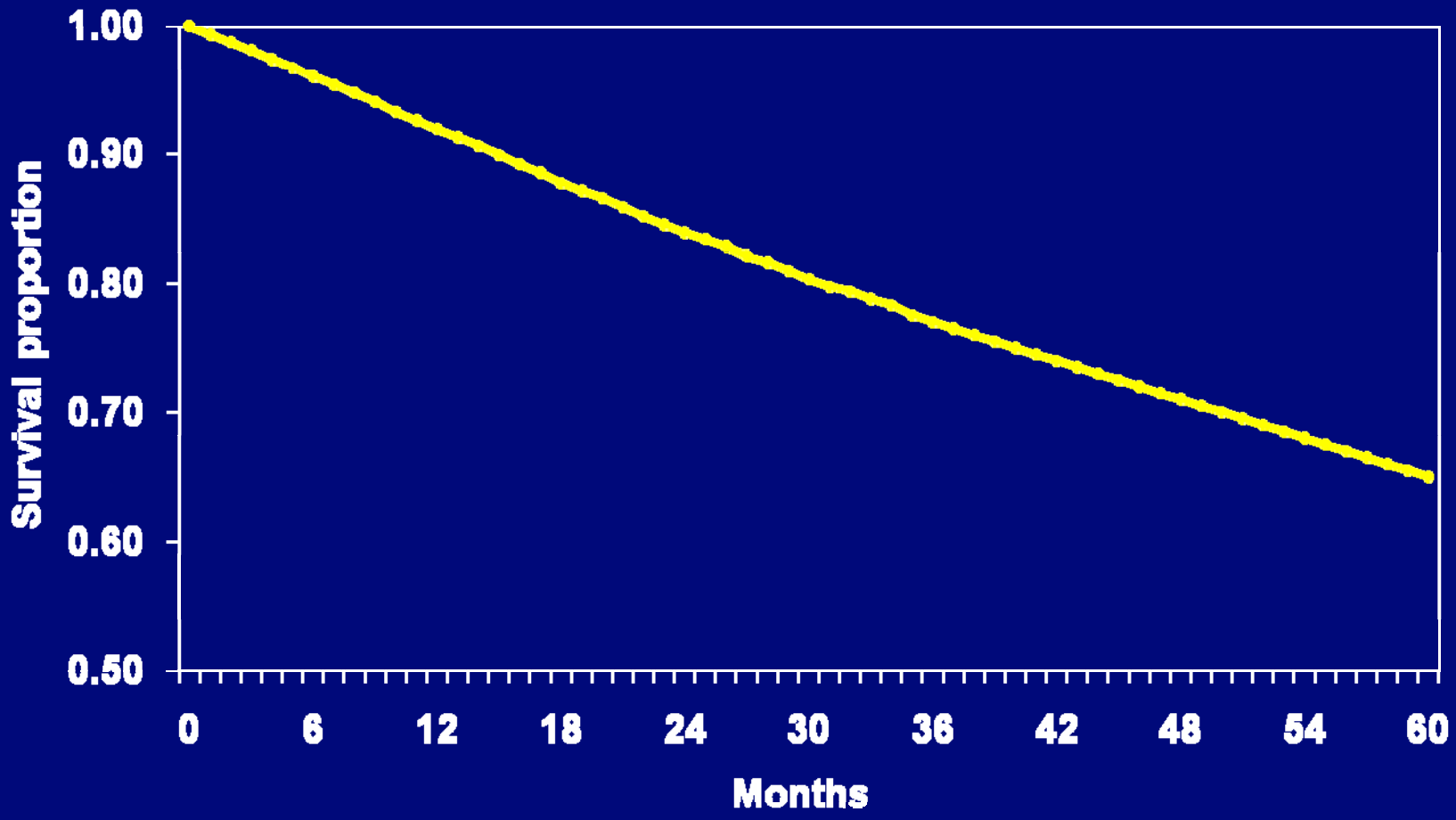
Waitlist Survival Model: Covariates

- Not just MELD
- Creatinine, bilirubin, INR, albumin, sodium, dialysis, age, BMI, diagnosis, HCC, diabetes, hospitalization status, prior malignancy, growth failure, previous time on waitlist, rate of change: creatinine, bilirubin, albumin

Post-Transplant Survival Model: Covariates

- Not just MELD
- Recipient factors:
  - Creatinine, albumin, age, diagnosis, diabetes, dialysis, hospitalization status, previous liver transplant, life support, portal vein thrombosis, previous abdominal surgery, hepatitis C, growth failure
- Donor factors:
  - Age, race, cause of death, donation after cardiac death

Waitlist Survival



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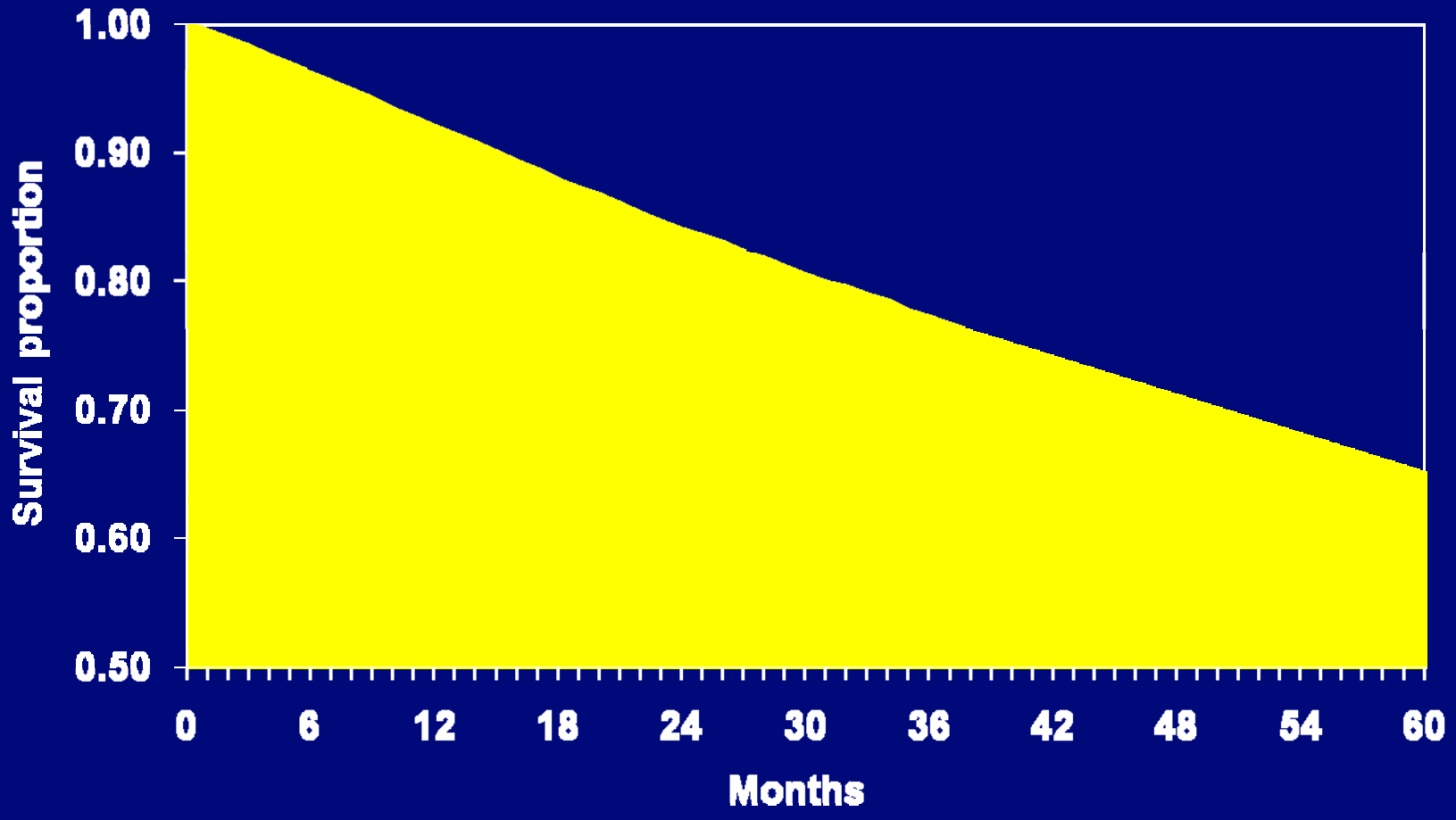
Waitlist 5-Year Expected Lifetime



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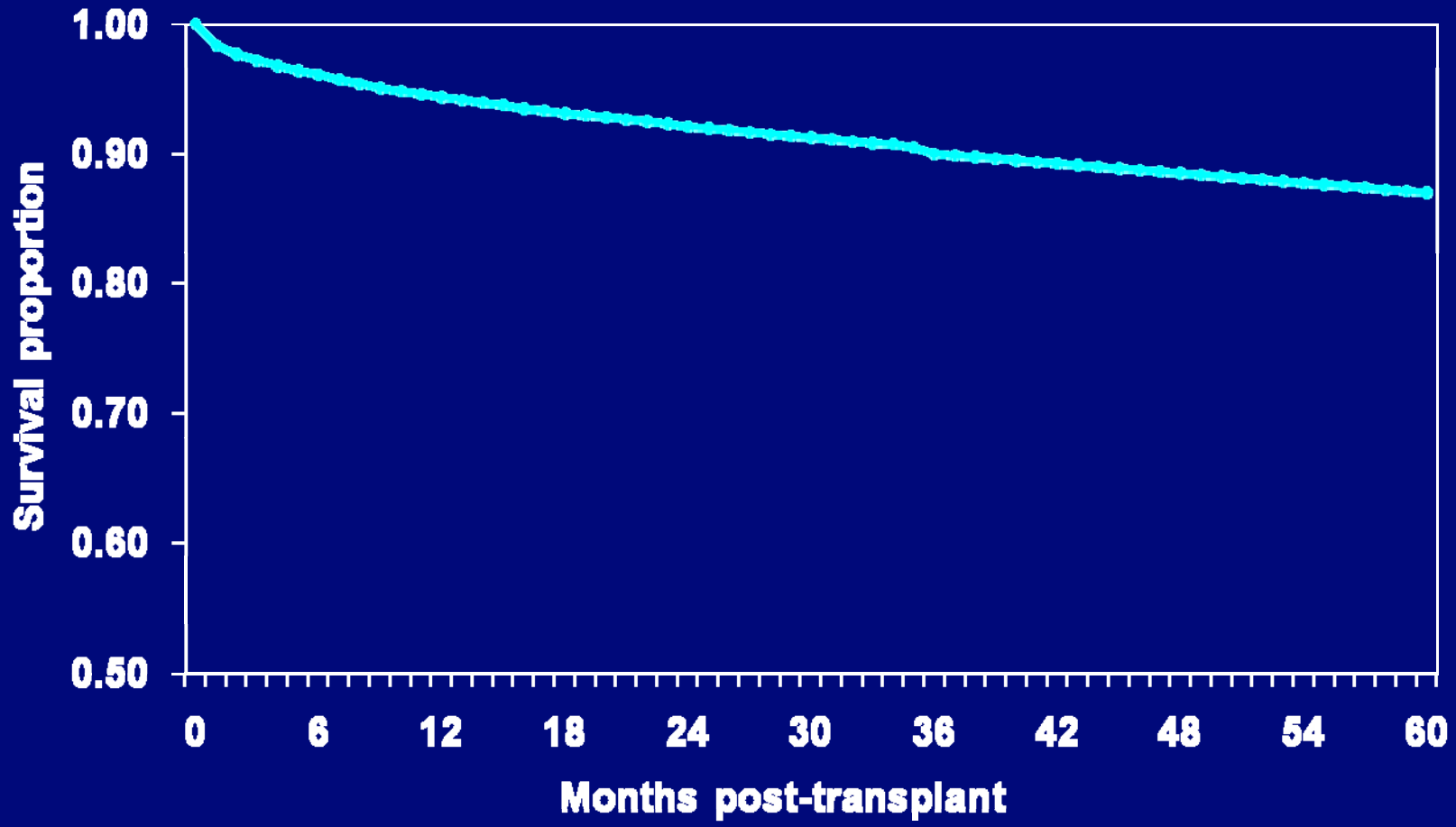
Post-Transplant Survival



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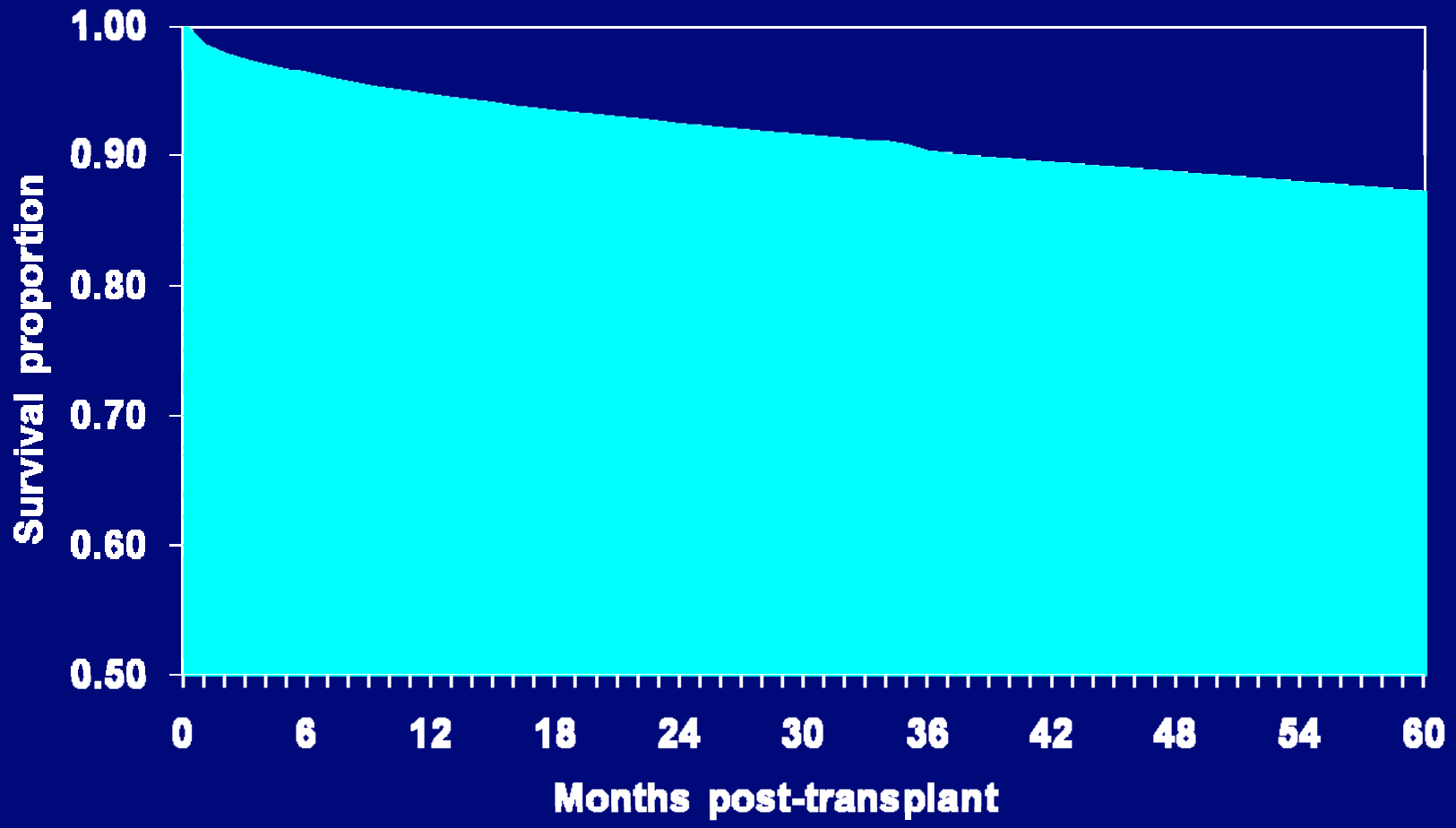
Post-Transplant 5-Year Expected Lifetime



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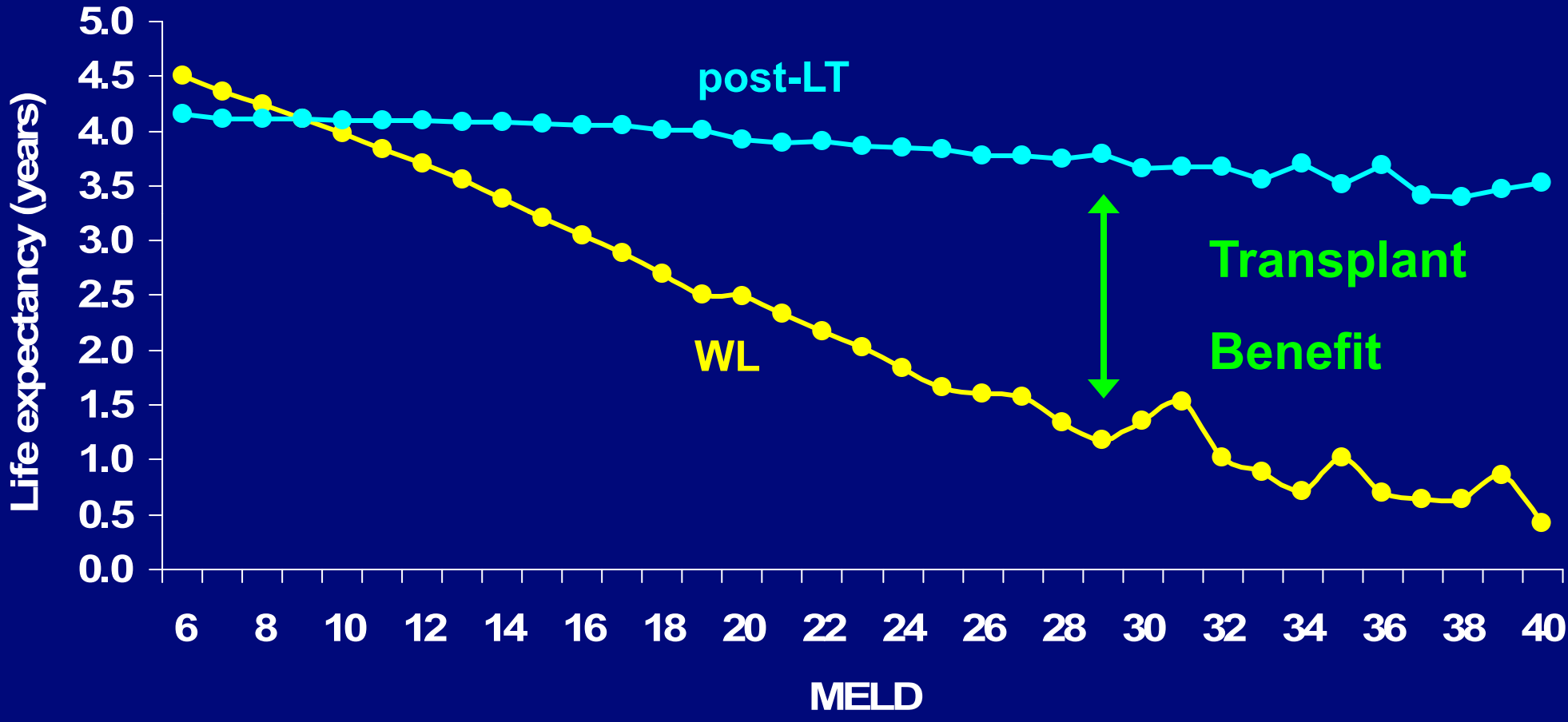
Mean 5-Year Future Lifetime by MELD



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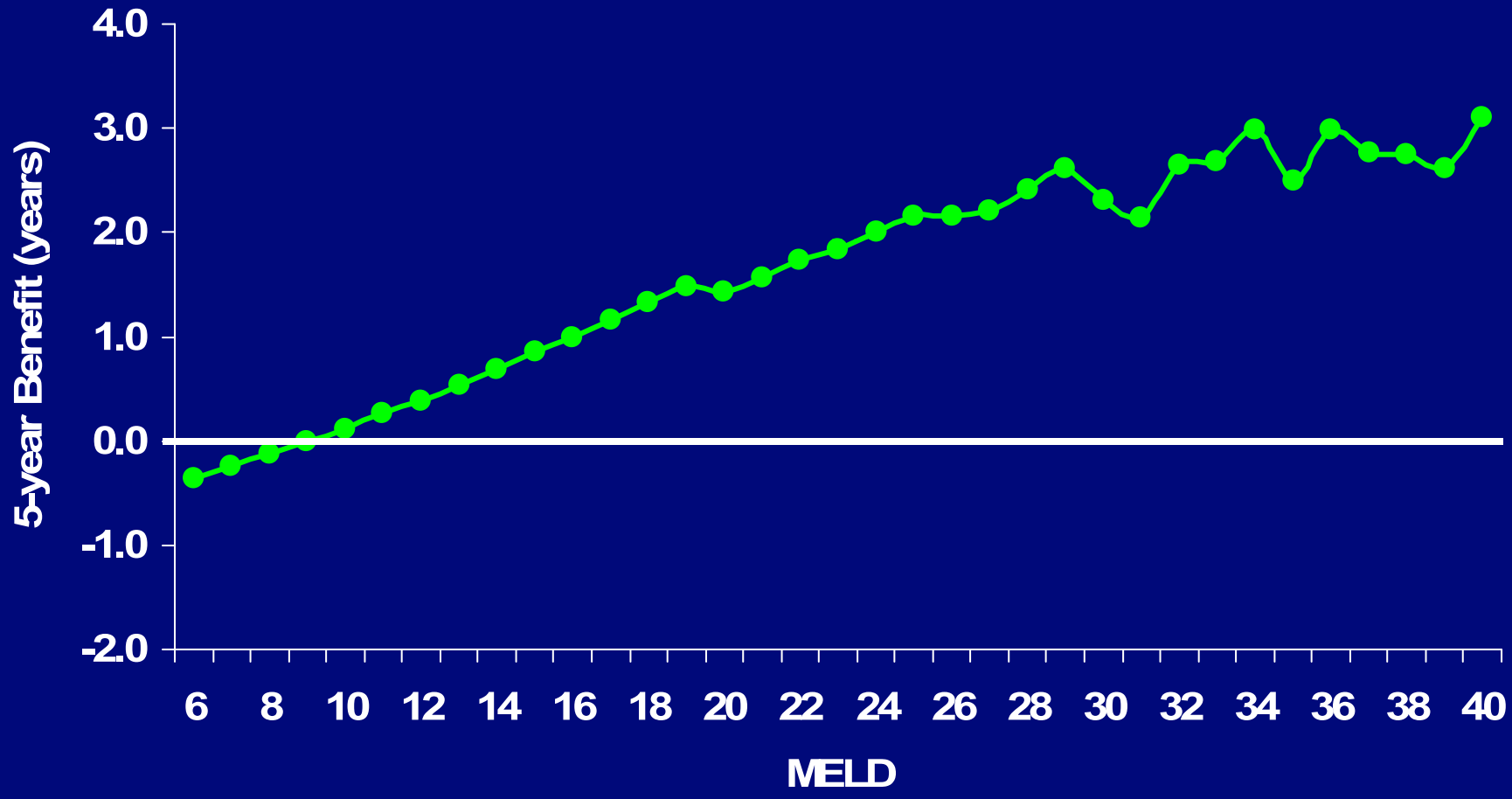
Transplant Benefit by MELD



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Transplant Benefit vs. MELD

- **Q: If average transplant benefit increases with MELD, does allocation by benefit amount to allocation by MELD?**

Transplant Benefit vs. MELD

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Transplant Benefit vs. MELD

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- A: NO!
  - e.g., two patients could have similar (or equal) MELD scores, but very different benefit scores

Transplant Benefit vs. MELD

- Q: If average transplant benefit increases with MELD, does allocation by benefit amount to allocation by MELD?
- A: NO!
  - e.g., two patients could have similar (or equal) MELD scores, but very different benefit scores
  - MELD is not the only factor predicting waitlist and post-transplant survival

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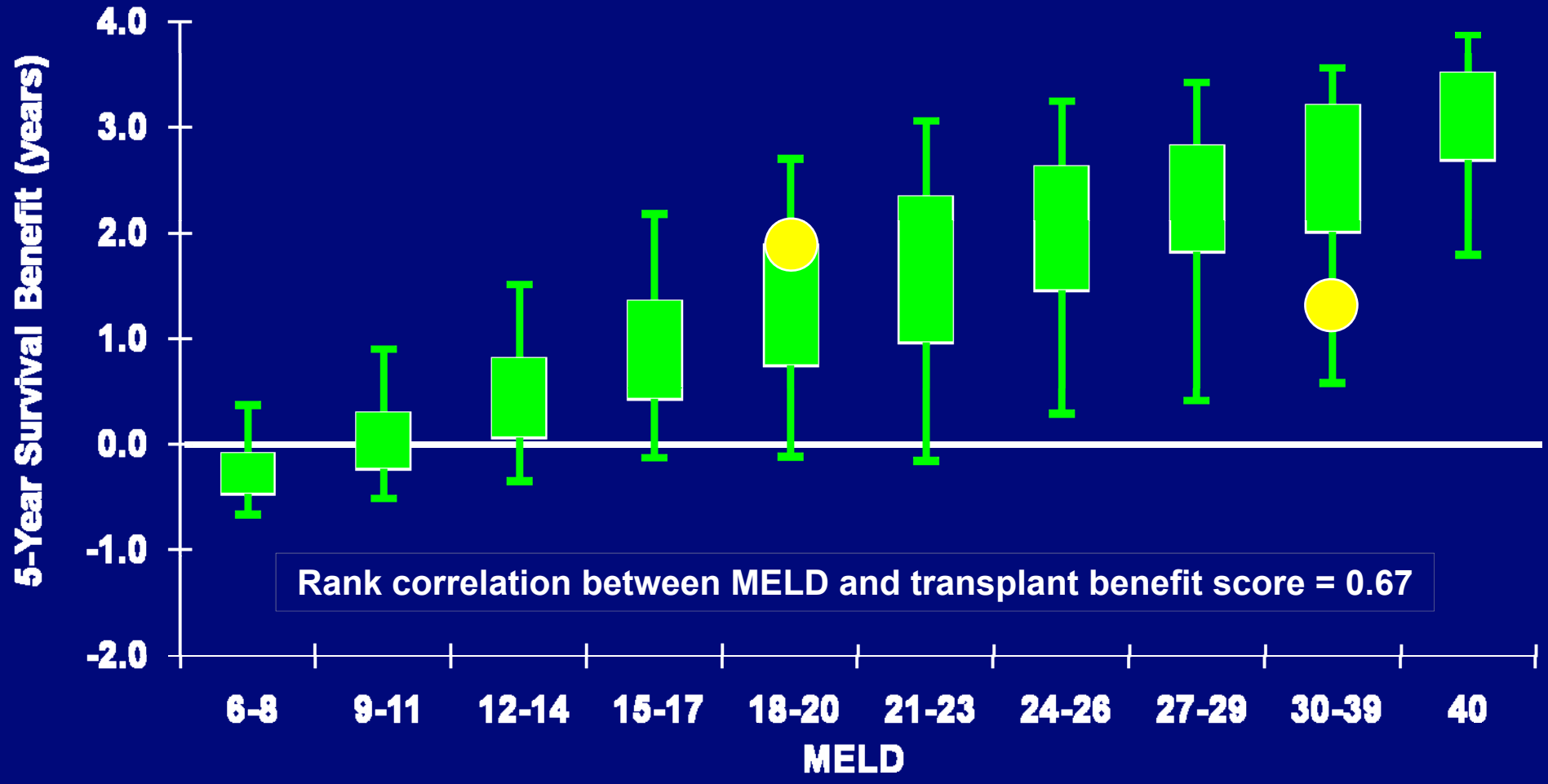
5-Year Transplant Benefit by MELD
Box-Whisker Plots



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Calculation of MELD and Benefit Scores

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MELD: Calculation

Variable	Coefficient
Intercept	0.6431
Not on dialysis: log [min{max(Creatinine,1),4}]	0.957
log (max{Bilirubin,1})	0.378
log (max{INR,1})	1.120
On dialysis	1.326

- Notes:
  - Multiply the score by 10 and round to the nearest whole number.
  - MELD score is bounded by 6 and 40
  - HCC T2 candidates receive an exception score of 22.

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PELD: Calculation

Variable	Coefficient
log (Bilirubin)	0.480
log (INR)	1.857
log (Albumin)	-0.687
Patient is less than 1 year old	0.436
Growth failure	0.667

- Notes:
  - Multiply the score by 10 and round to the nearest whole number.
  - Laboratory values less than 1.0 are set to 1.0 for the purposes of the PELD score calculation.

Benefit Score: Calculation

- Calculation of benefit score by linear approximation is analogous to MELD score
  - more terms
- Comparison to statistically rigorous calculation
  - almost perfect correlation (rank correlation 0.99)
  - used in simulations to reduce computing time
- Linear approximation would be utilized by OPTN/UNOS if incorporated into a future allocation system, just as MELD is currently

Microsimulation to Compare Allocation Systems

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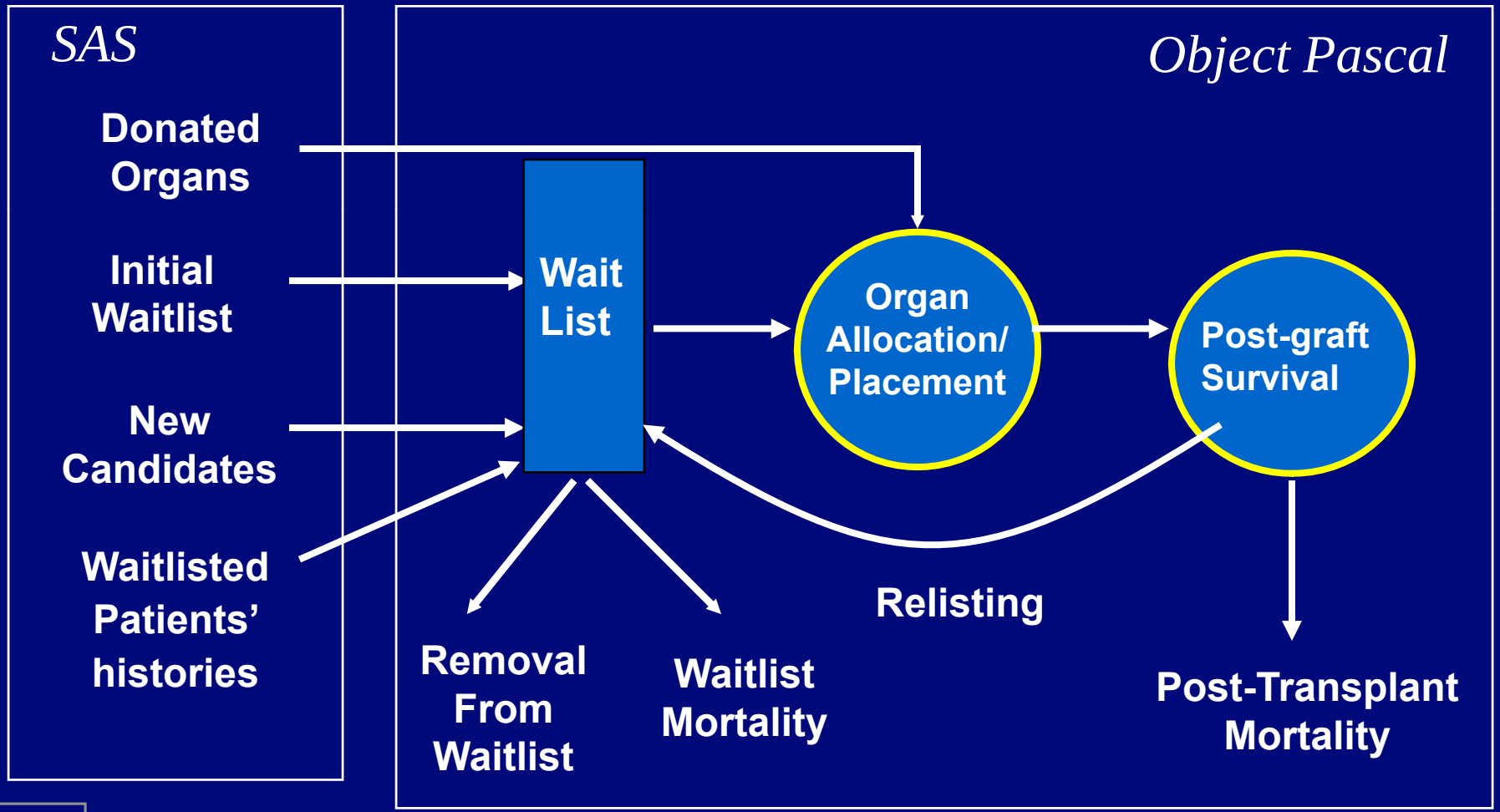
Requests by OPTN/UNOS Liver Committee

- LSAM Simulations Study Population
  - Data from waitlist candidates and donors during 2006 were used for the simulations.
- Compared multiple broader distribution, MELD-based and transplant benefit-based allocation systems to the current allocation system
- For each run, we recorded: number of transplants, mean transplant benefit, life-years saved, total deaths, median distance traveled, percent shared, and percent distance traveled >100 nautical miles.
- Results averaged over 10 iterations

LSAM Event-Sequenced Modeling



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LSAM: Number of Deaths

Deaths	MELD/PELD System	Regional Sharing	Transplant Benefit
Waitlist	1,660	1,602 (-58)	1,519 (-83) 8%
Post-transplant	609	607 (-2)	601 (-6)
Post-removal	407	397 (-10)	384 (-13)
Total	2,675	2,606 (-69)	2,504 (-102) 6%

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(n) Indicates difference vs. prior column; n% indicates difference vs. MELD/PELD system

LSAM: Life Years Gained by Transplant

	MELD/PELD System	Regional Sharing	Transplant Benefit
Mean Extra Years From Transplant	1.56	1.63 (+0.07)	2.01 (+0.38)
∑ Life Years Gained by Transplant	9,875	10,225 (+350)	12,448 (+2,223) 23%

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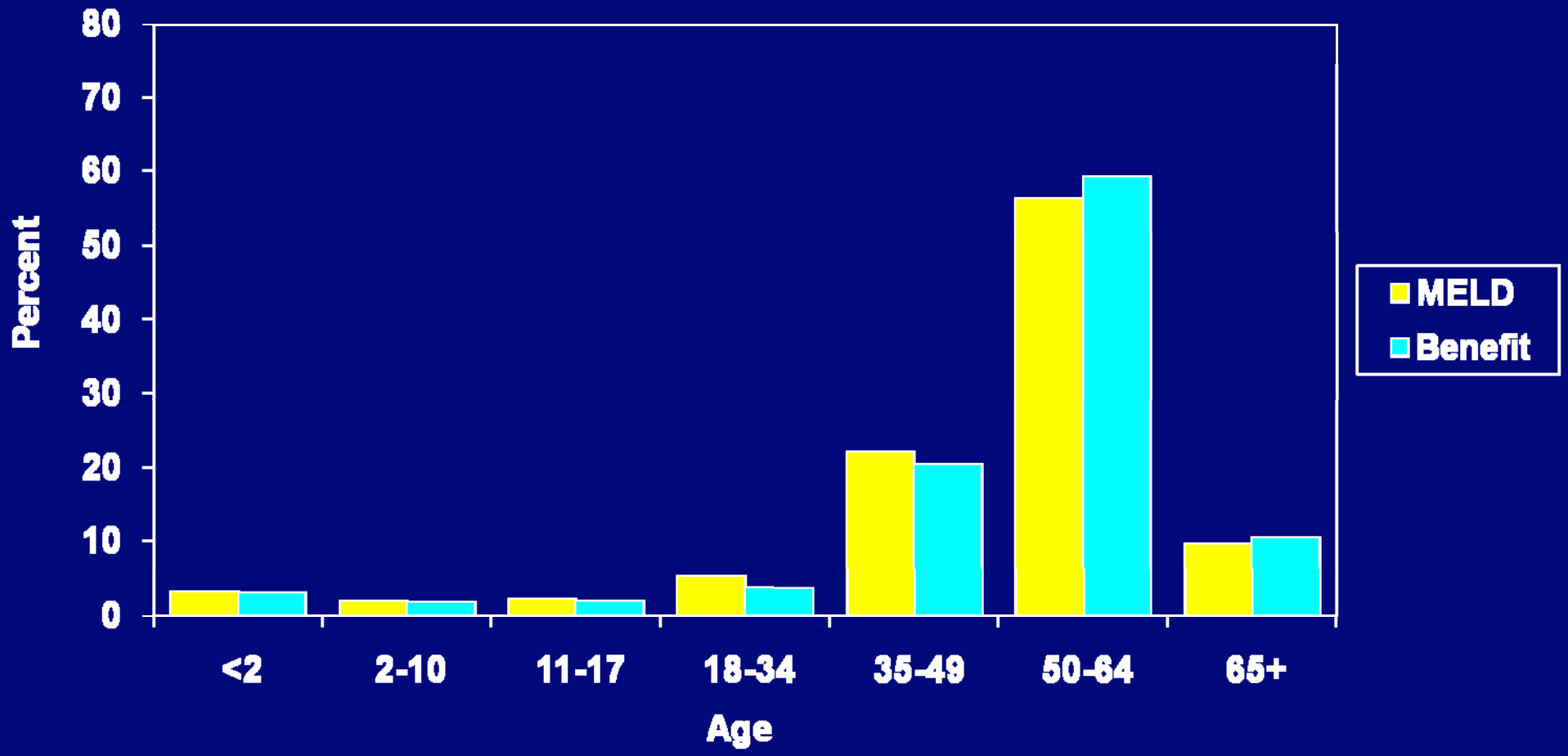
(n) Indicates difference vs. prior column; n% indicates difference vs. MELD/PELD system

Equity: Age of Transplanted Patients



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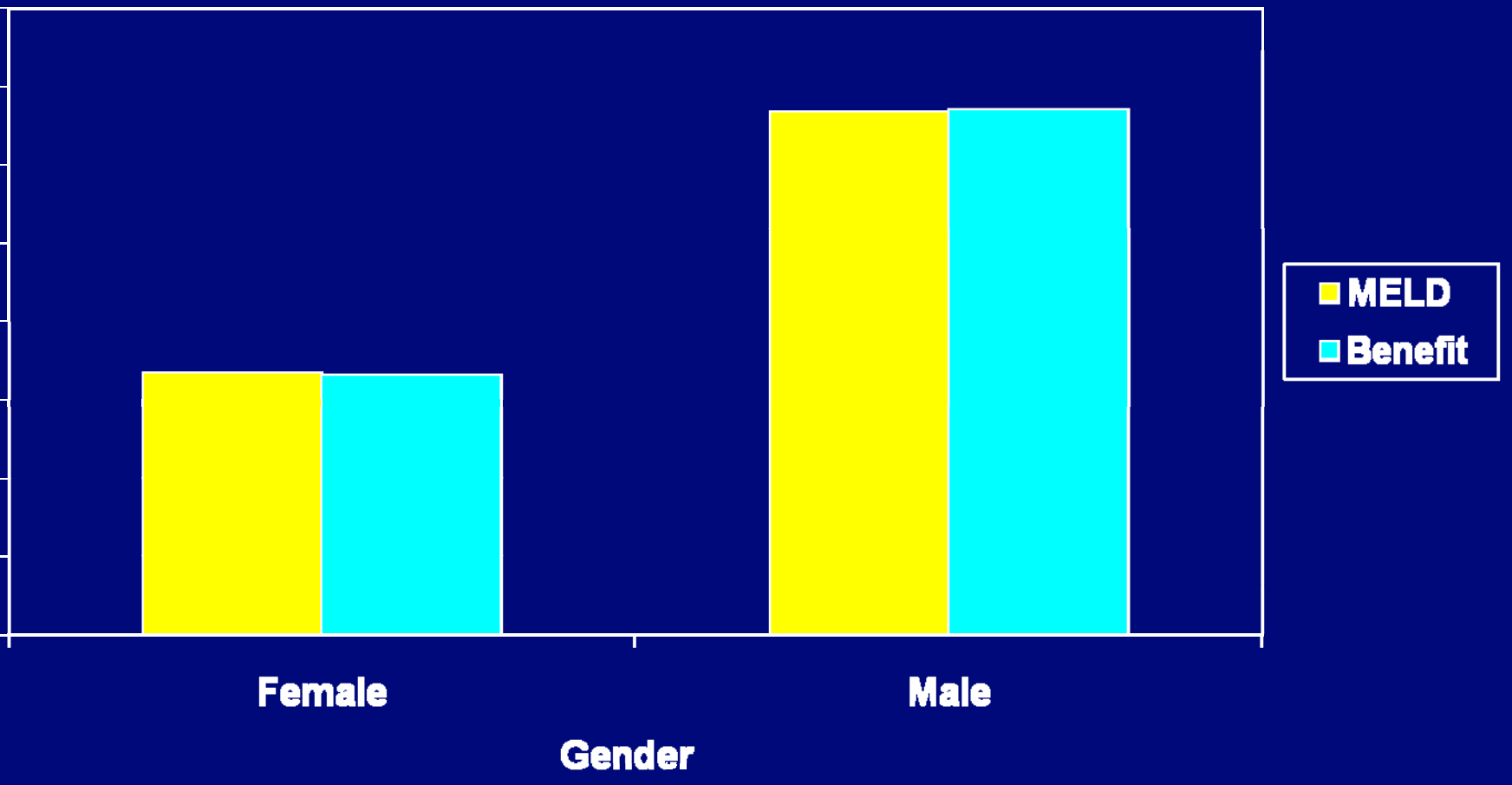
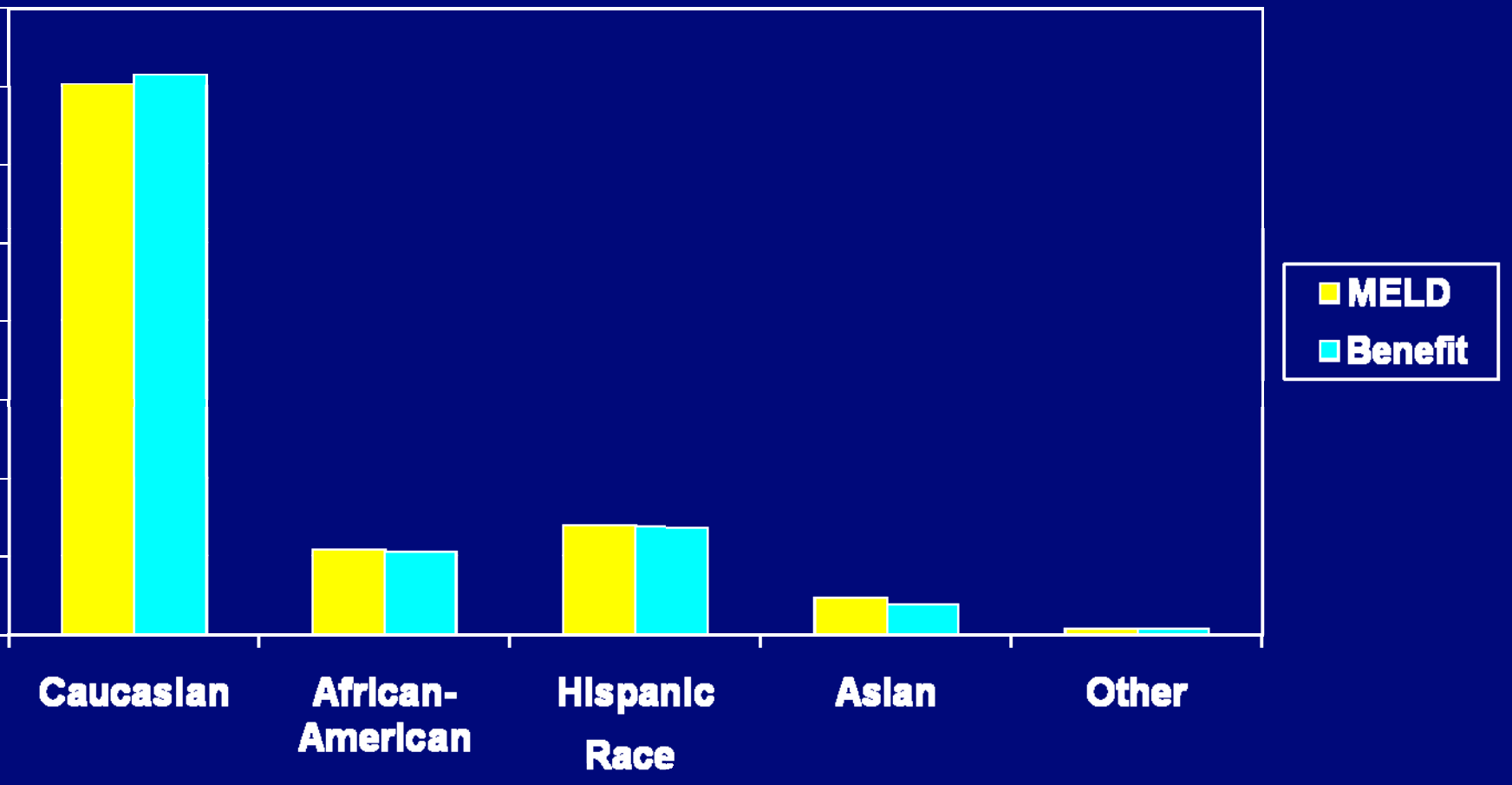
Equity: Gender of Transplanted Patients



Equity: Race/Ethnicity of Transplanted Patients

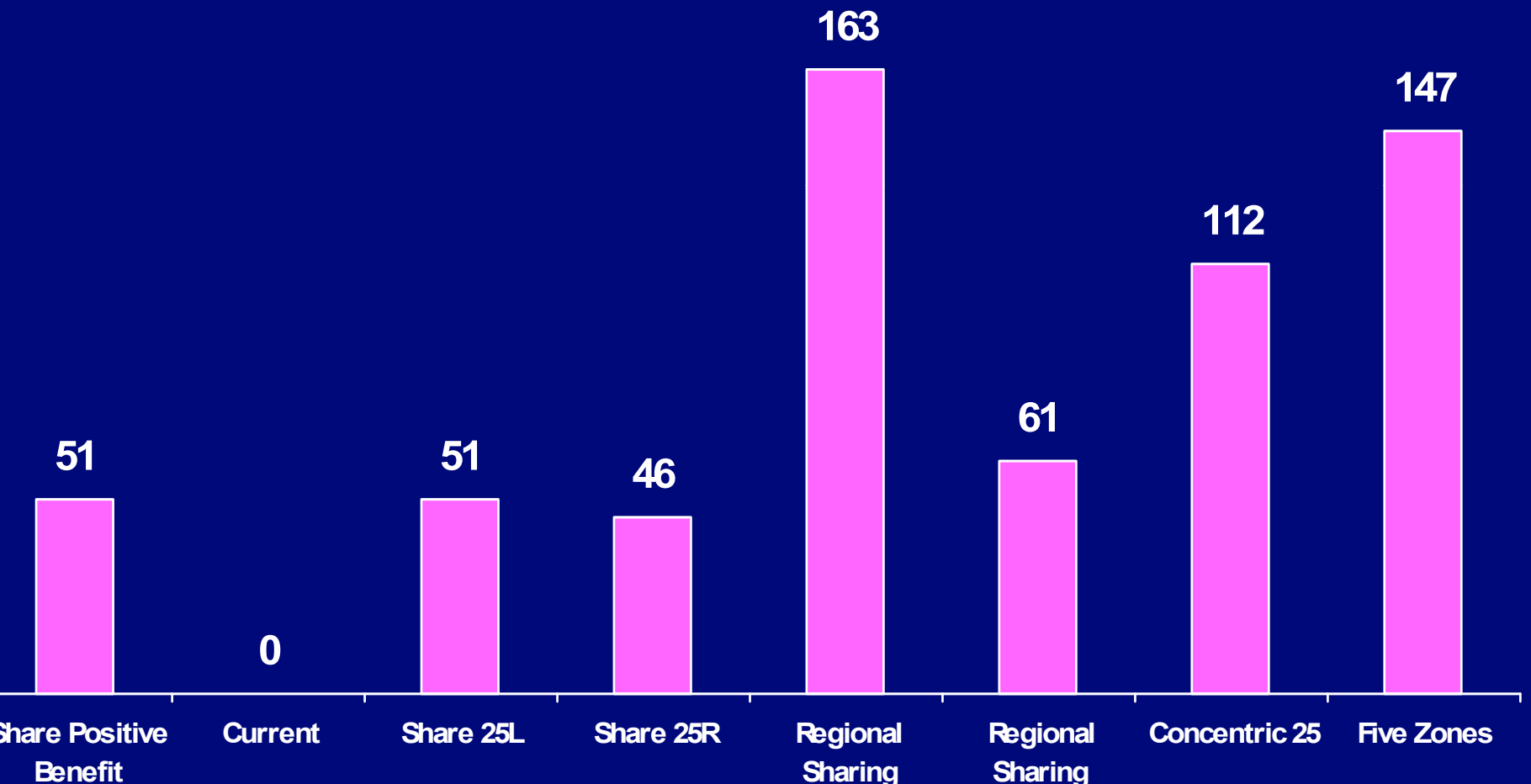


omparison of Allocation Rules for Adult Deceased Donor Livers

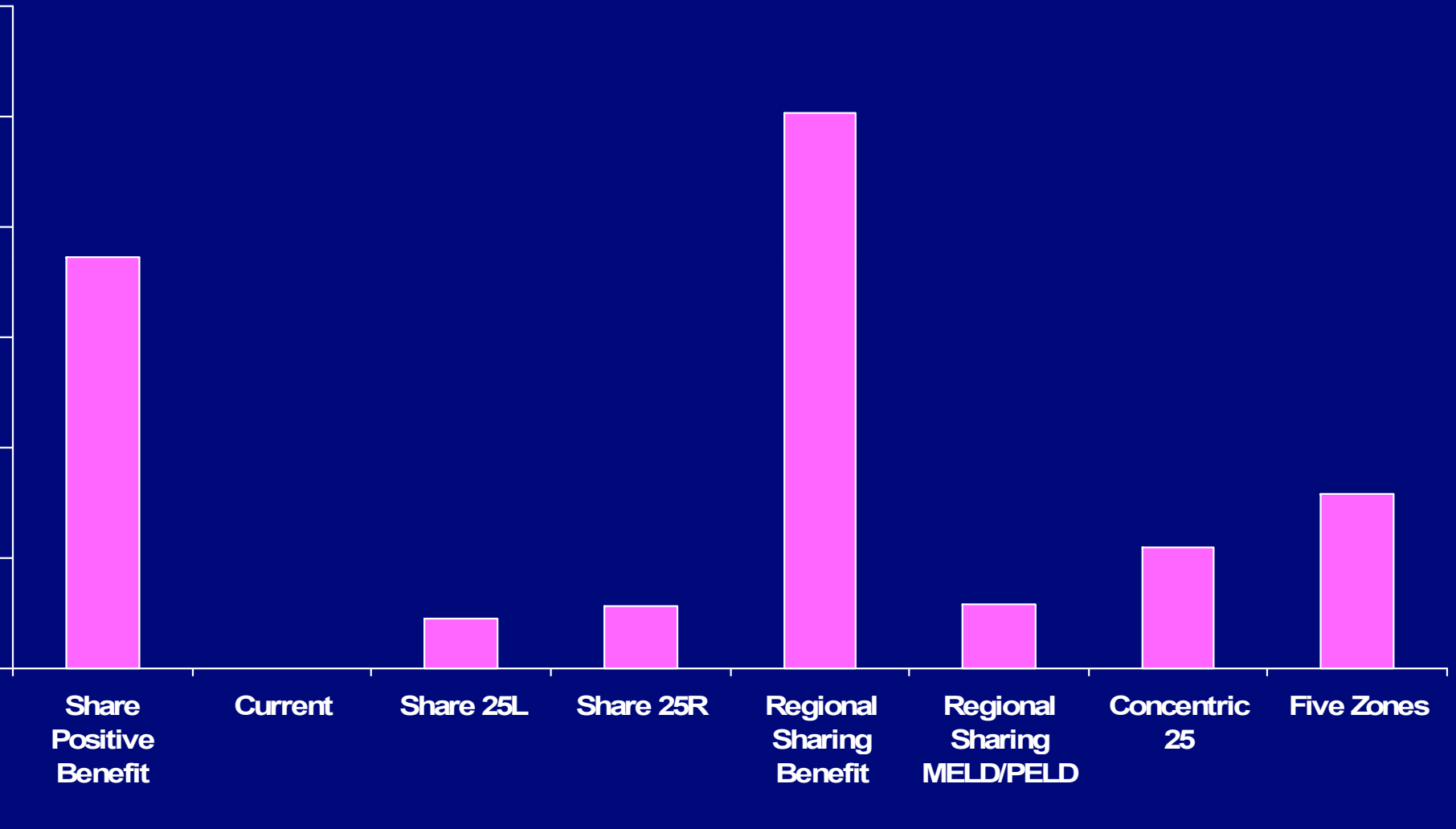
nt System	Share Positive Benefit
– Status 1A	Local – Status 1A
nal – Status 1A	Regional – Status 1A
– Status 1B	Local – Status 1B
nal – Status 1B	Regional – Status 1B
– MELD/PELD ≥ 15	Local – Transplant benefit score > 0
nal – MELD/PELD ≥ 15	Regional – Transplant benefit score > 0
– MELD/PELD < 15	Local – Transplant benefit score < 0
nal – MELD/PELD < 15	Regional – Transplant benefit score < 0
nal – Status 1A	National – Status 1A
nal – Status 1B	National – Status 1B
nal – MELD/PELD	National – Transplant benefit score

Yellow = Unchanged
Blue = Current System

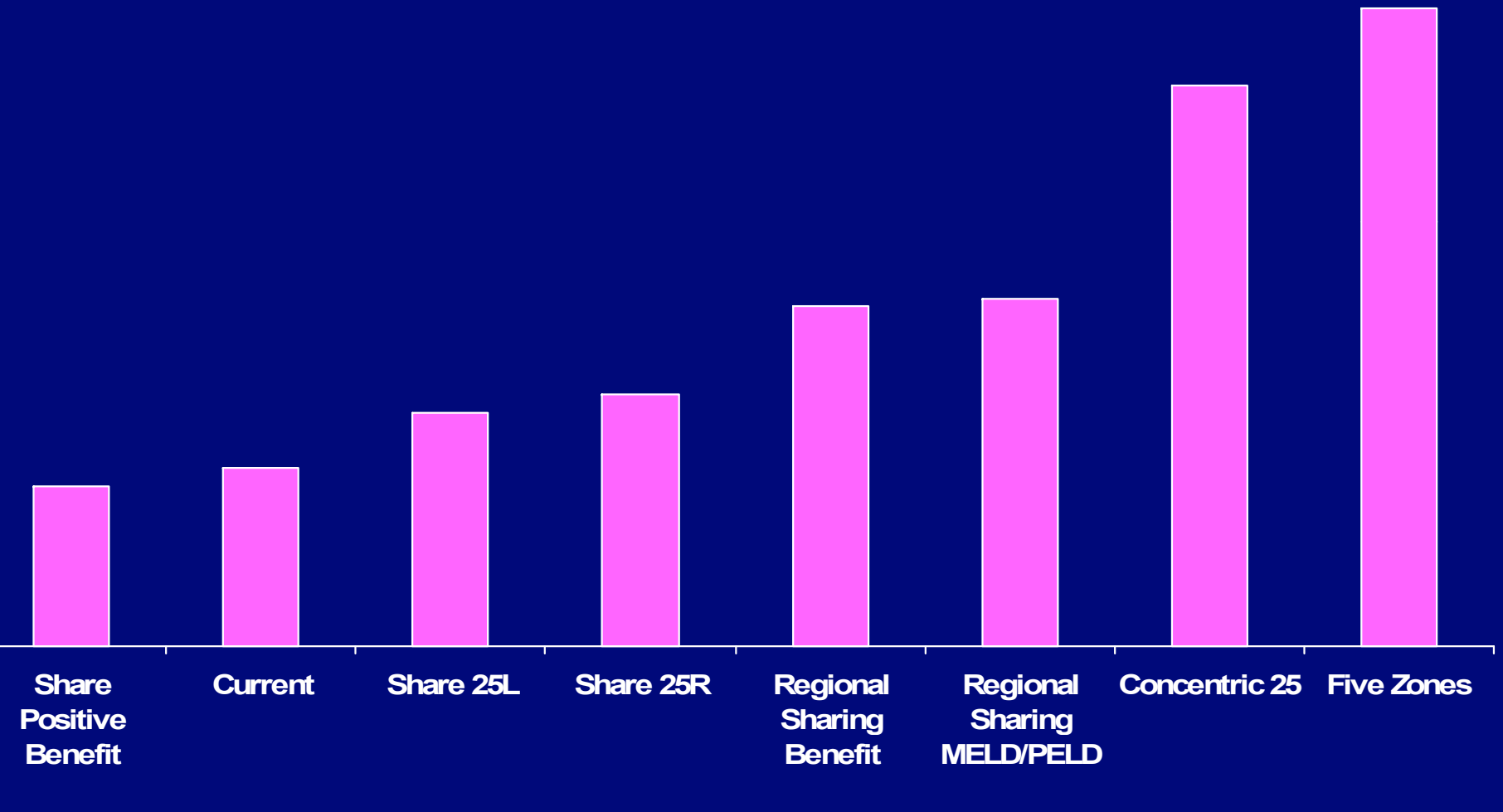
ecrease in Total Deaths (vs. Current)



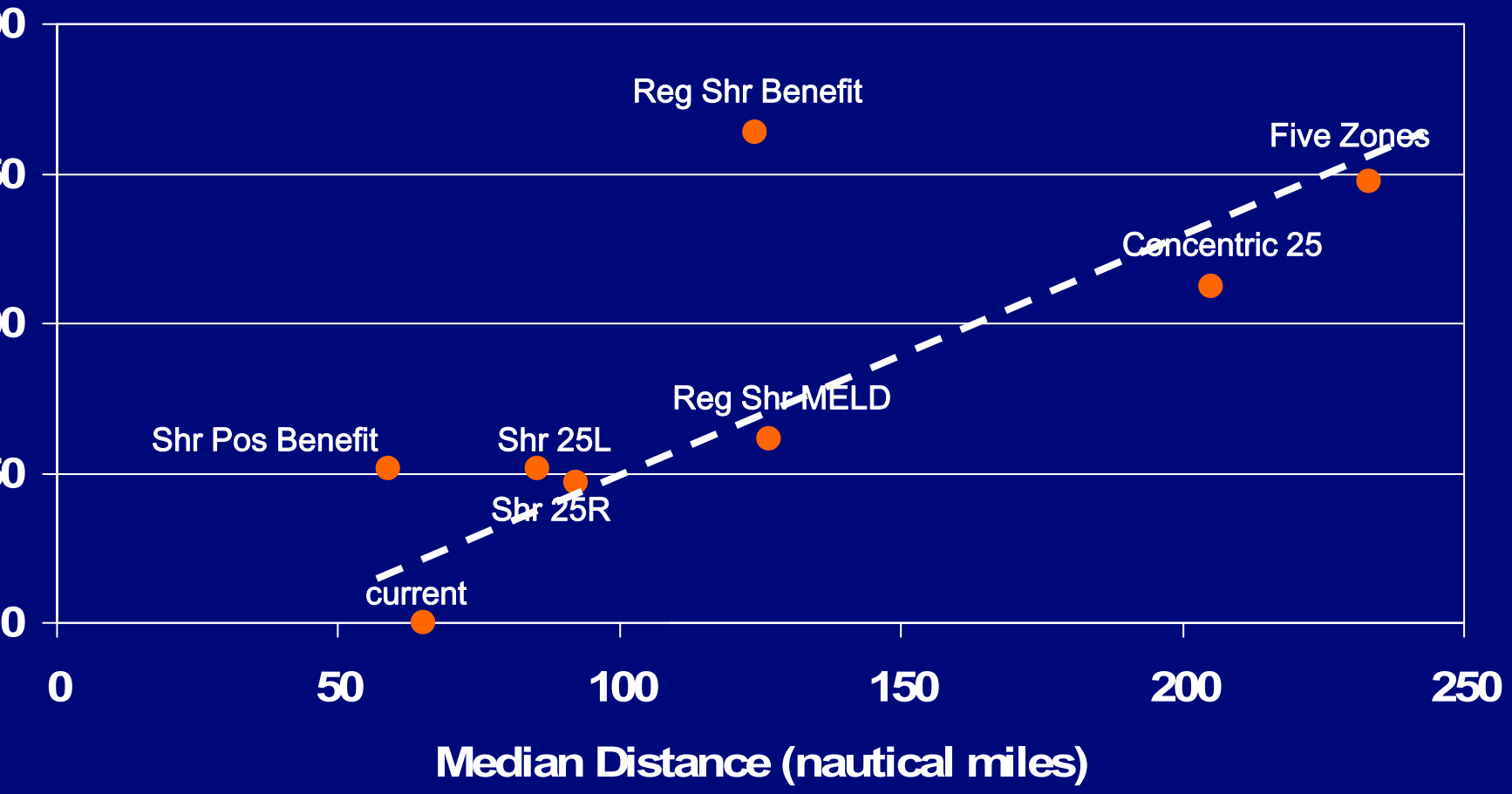
Increase in Life Years Saved via Transplant (vs. Current)



Median Distance Between Donor Hospital and Transplant Center



Median Distance vs. Decrease in Total Deaths



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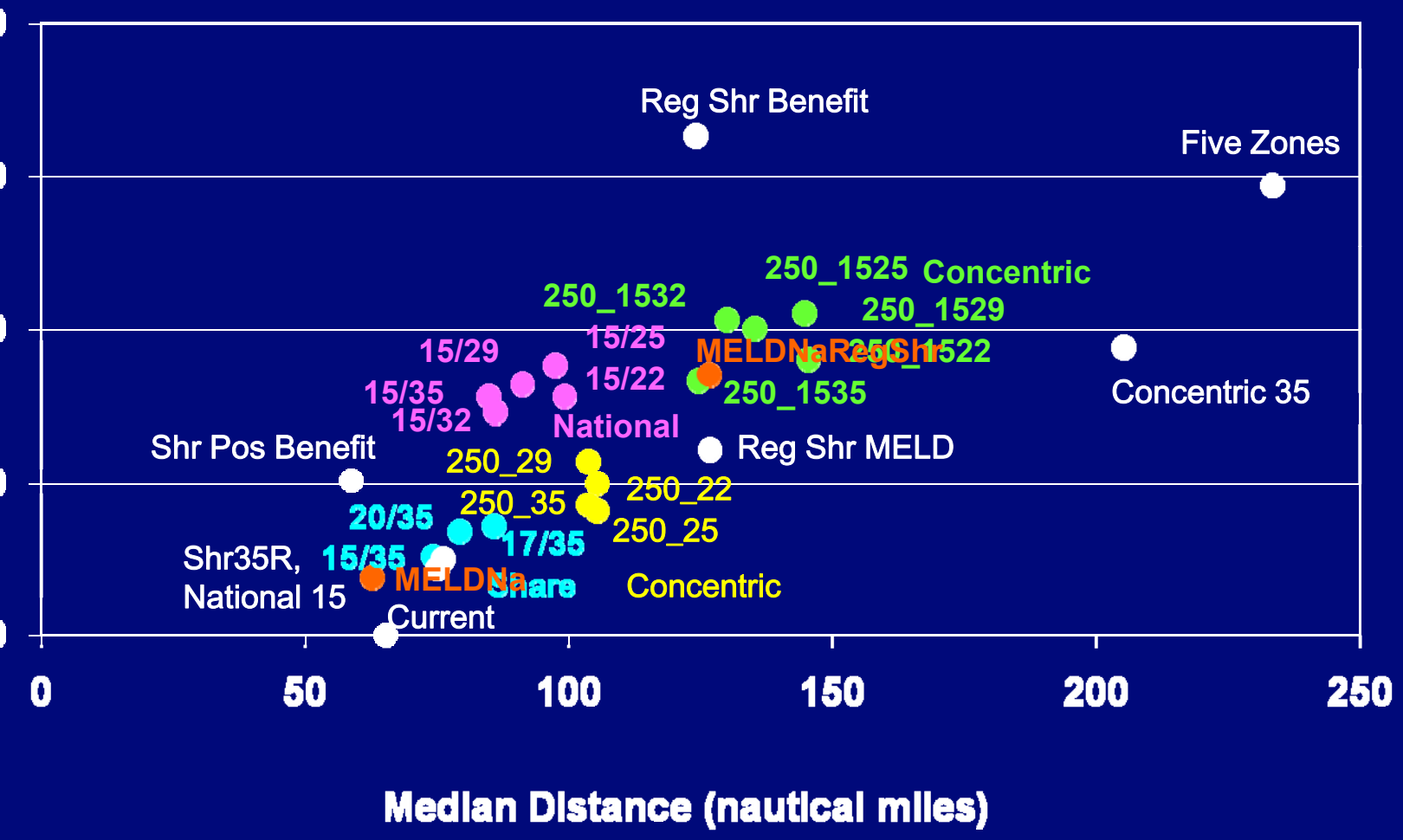
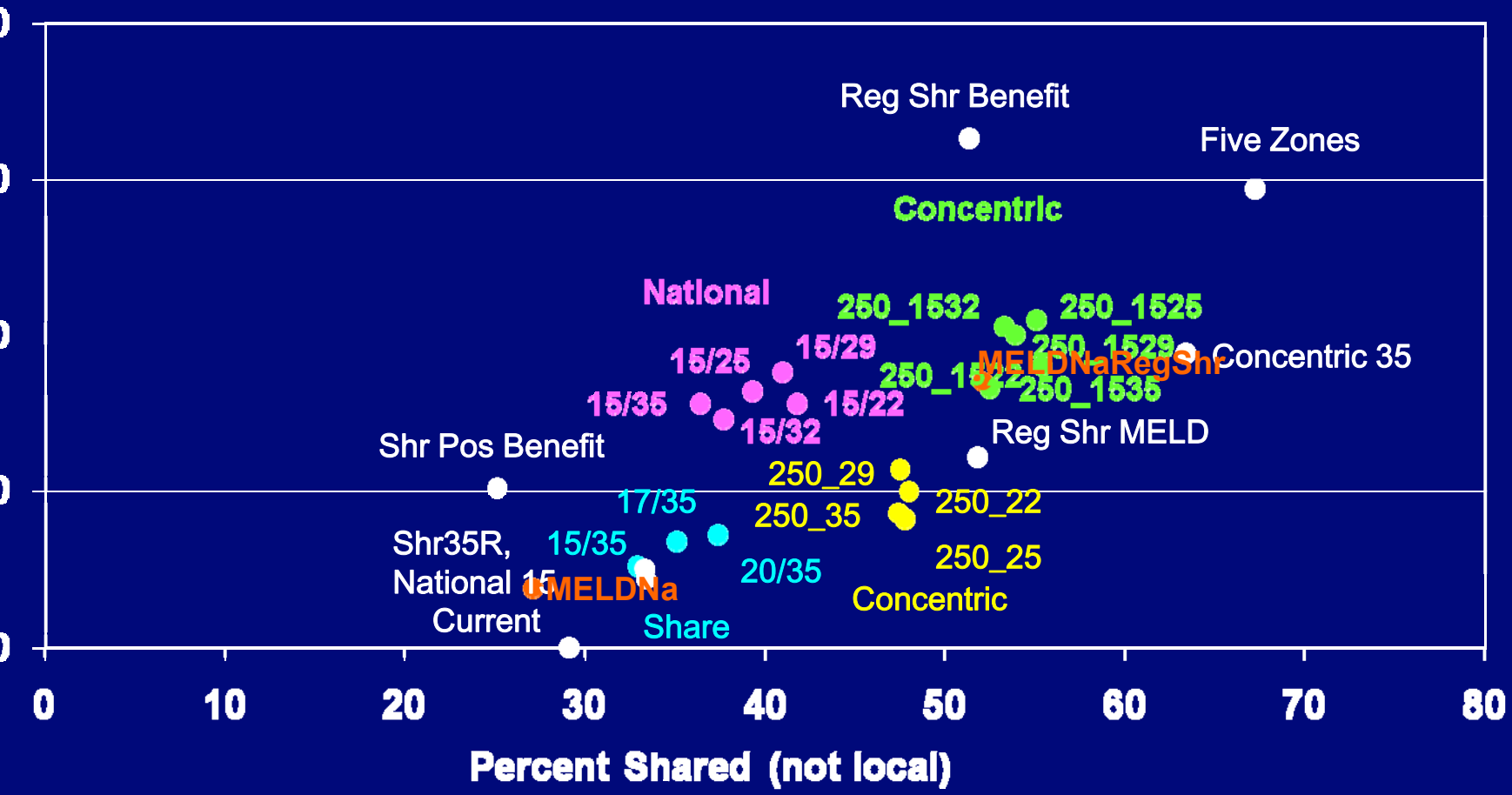


Percent Shared vs. Decrease in Total Deaths



enefit Scores, Life-Years Saved, and Distance Traveled

Allocation System	Mean Benefit Score	Life-Years Saved in 1 Year	Average Distance
onal Sharing Benefit	2.01	12,448	124
e Positive Benefit	1.87	11,794	59
onal Sharing MELD/PELD	1.63	10,217	127
ent	1.57	9,929	65

enefit Score: Reduces Complexity

n a modified benefit score be calculated with fewer tors?

s work is ongoing, and decisions about the deoffs can be made on clinical and statistical unds by examining the effect on the rankings of ndidates under various scenarios with fewer factors

Summary

- orporation of a measure of post-transplant survival o the allocation system is being actively explored
- specific policies or proposals have been put ward
- e role of transplant benefit score as a criterion for er allocation will require further discussion
- ut from the transplant community is extremely portant