

# **Association between Early Acute Rejection and All-Cause Kidney Allograft Failure Has Increased While the Incidence of AR Has Decreased over a Recent Decade in the US.**

**Jon J. Snyder, PhD, MS**  
**Melissa A. Skeans, MS**  
**Bertram L. Kasiske, MD, FACP**

**United States Renal Data System**

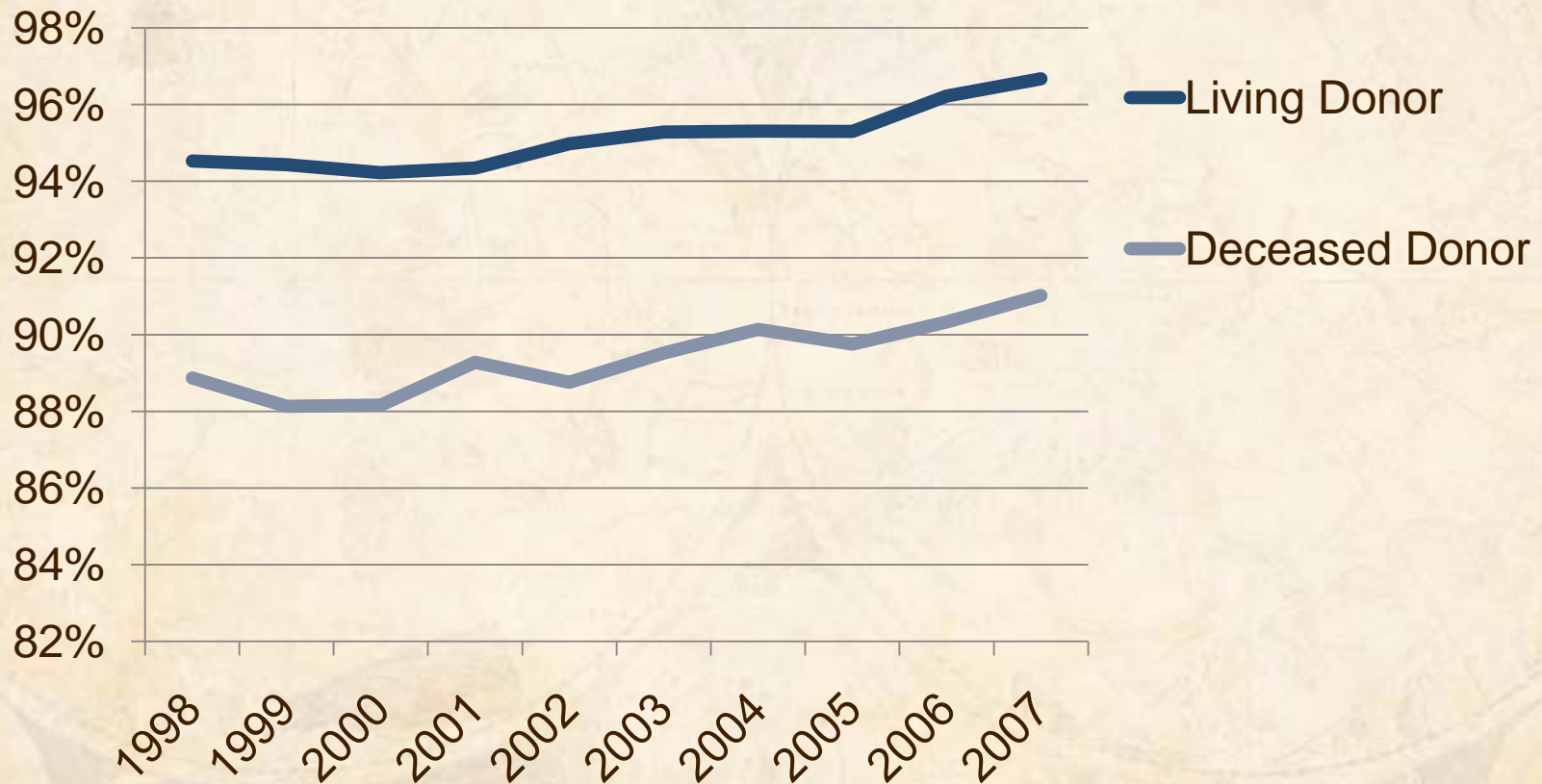
**USRDS**

# Background

- **Acute rejection (AR) is a well known risk factor for allograft failure.**
- **We explored changes in the incidence of AR during the first post-transplant year over a ten-year period and concurrent changes in the hazard for all-cause graft failure associated with having an AR.**

# First-Year All-Cause Graft Survival

USRDS 2010 ADR, Vol. 2, Tables F.2 & F.8



# First-Year Probability of Graft Survival Necessitating Dialysis or Retransplant

USRDS 2010 ADR, Vol. 2, Tables F.14 & F.20



## **Population & Methods**

- **We used USRDS data to construct a population of first-time kidney-alone transplants in patients aged 18+, 1998-2007, who were discharged from the transplant hospitalization with a functioning allograft (N=121,055).**
- **Acute Rejection, defined as at least one reported episode or indication of AR treatment in the first post-transplant year, were identified from Organ Procurement and Transplantation Network (OPTN) recipient follow-up data during year 1 post-transplant.**

# Incidence of At Least 1 Acute Rejection Episode Reported to UNOS During The First-Year Post-Transplant

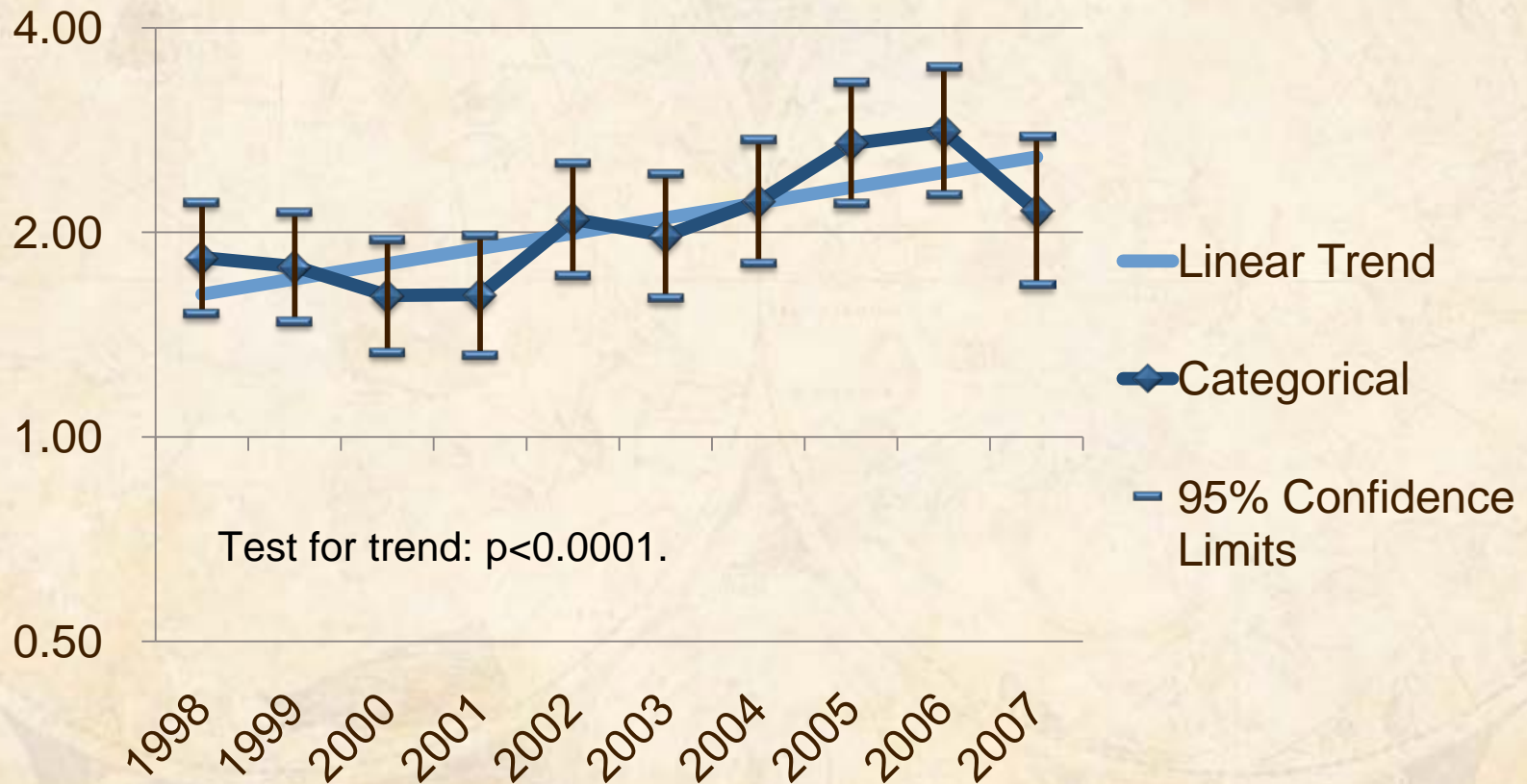
USRDS 2010 ADR, Vol. 2, Figure 7.25



# Estimating the Effect of AR on Outcomes

- The effect of AR on subsequent all-cause graft failure during year 1 post-transplant was estimated using a time-dependent Cox proportional hazards model.
- Reported AR was treated as time dependent covariate.
- The RR associated with having an AR within year 1 was estimated within each year and a linear time trend was also estimated over the decade.
- Models were adjusted for donor type, age, gender, race, primary cause of kidney failure, and year of transplant.

# Adjusted Hazard Ratios for All-Cause Graft Loss within 1 Year: AR vs. No AR





# Possible explanations:

## Possible Explanations for lower rate of AR:

- Better drugs to prevent rejection
- Better CMV prophylaxis
- Better other (unmeasured) care
- Greater use of biopsy (e.g. protocol biopsies) leading to fewer “spurious” AR

## Possible Explanations for increased RR of AR for GF:

- We have eliminated only “treatable AR” that do not have much an effect on GF
- More potent treatments of AR may increase mortality risk
- We are transplanting higher risk “frail” patients (not adequately measured by covariates)

# Possible Explanations...

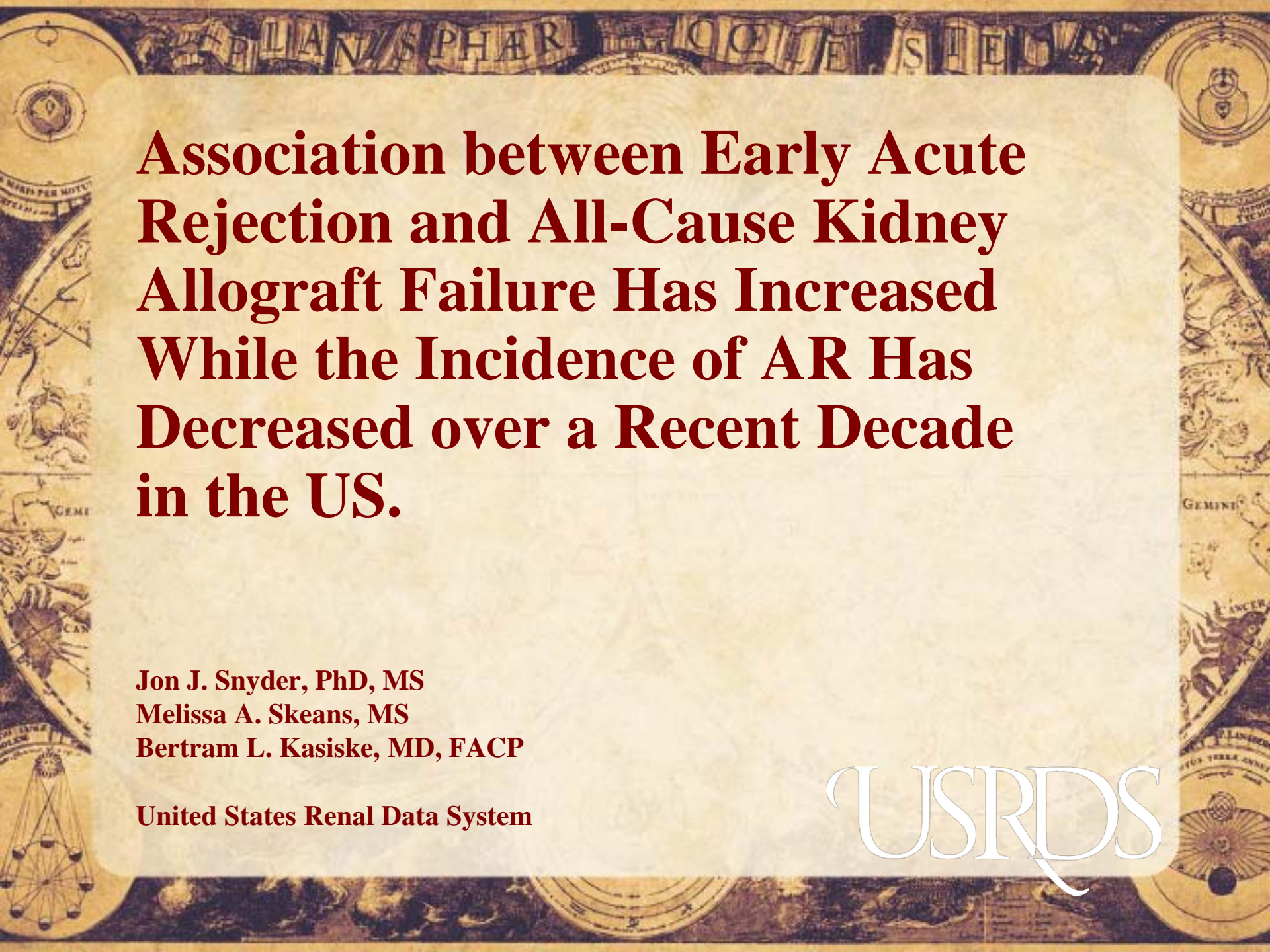
1. **Possible Truth #1: Rejection episodes are becoming less frequent, but are more detrimental when they do occur.**
2. **Possible Truth #2: “Mild/treatable” acute rejections are no longer occurring... only more severe rejection episodes are occurring, resulting in a decreased incidence of AR and increasing hazard associated with AR.**
3. **Reporting Bias: Replace “occurring” with “being reported” in the above explanation.**
4. **Statistical anomaly: observed trend is significant by chance... future data will demonstrate that this trend does not continue.**
5. **Other?**

## Effect on Survival Statistics

- **Increasing Hazard associated with AR offsets the effect of decreasing incidence of AR on graft survival statistics. For example:**
  - **25% reduction in AR events should equate to a 2.4% increase in first-year graft survival probability if the risk associated with AR remained constant over time.**
  - **Given the risk increased from 1.62 to 2.58, the 25% reduction in incidence translates to only a 1.7% increase in first-year graft survival probability... cutting the relative increase in half.**

## Conclusions

- The adjusted hazard ratio for all-cause graft failure during year one for those with AR vs. no AR increased from 1998 through 2007, indicating that while the incidence of AR has declined, the risk associated with having an AR has increased, thereby offsetting the effect of declining incidence of AR on improved graft survival statistics.
- While the incidence of AR has declined over a recent decade, remaining AR episodes are associated with greater hazard for graft loss.



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