An Econometric Evaluation of All-Cause Graft Failure: A Population-Based Approach

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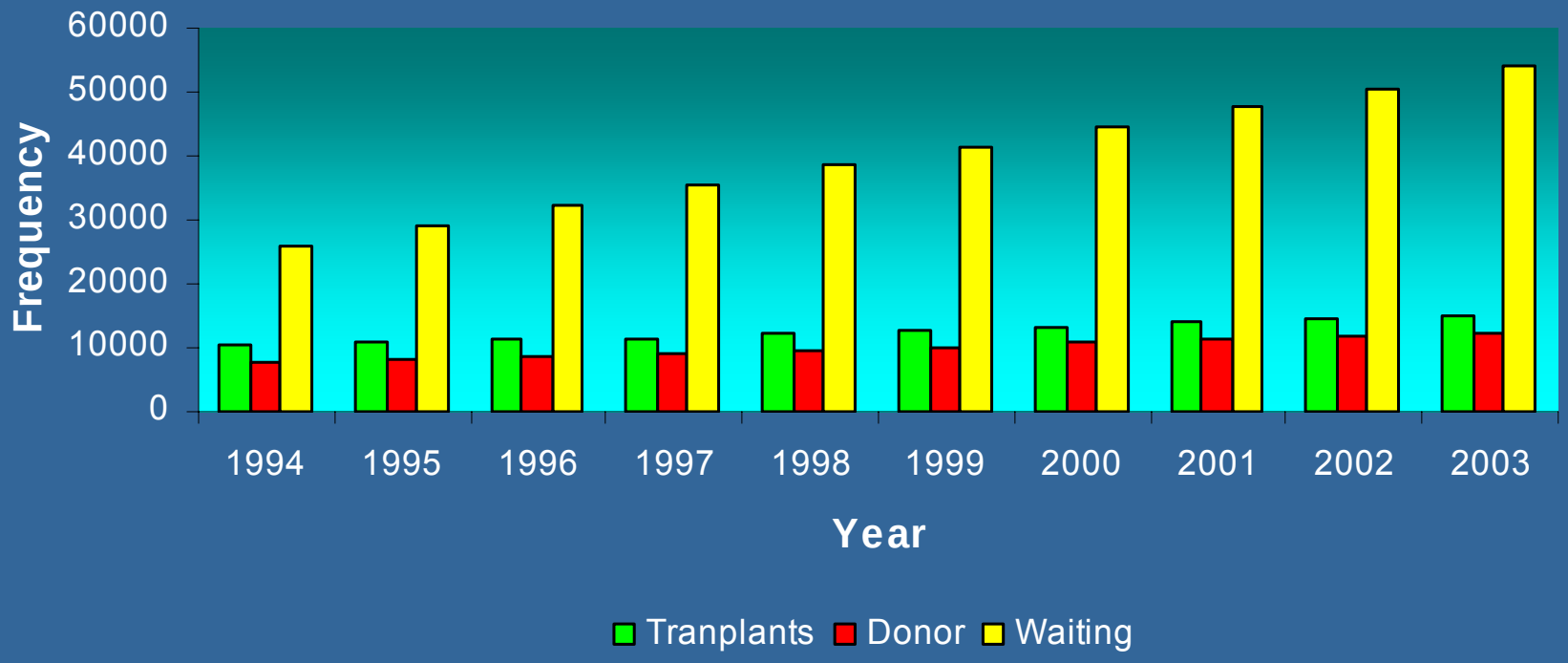
Clinical Motivation

Kidney Transplantation*



* Source: OPTN/SRTR Data as of May 3, 2004

Clinical Dilemma

Solution: Expand the donor pool

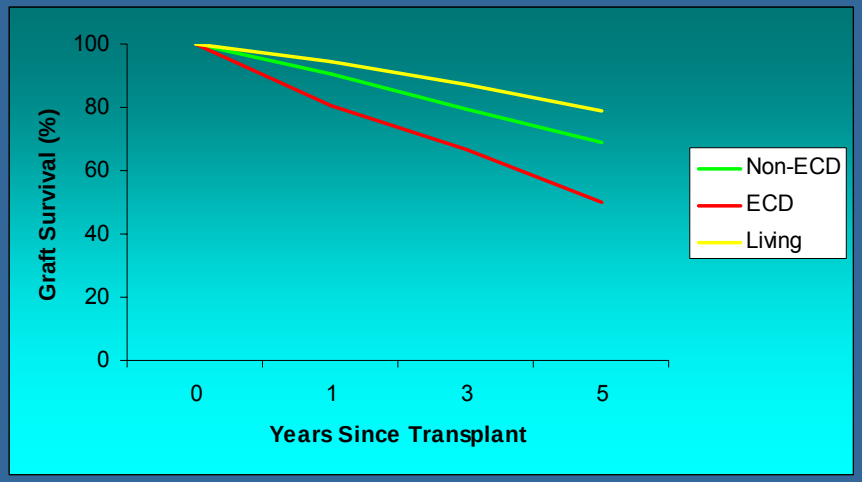
- Expanded criteria donors used more frequently

Downside: Transplant is more likely to fail

- ECD definition: RR of Graft Loss > 1.7*
- Retransplantation accounts for ~ 13% of all kidney transplants

Consequences

- Implications for organ allocation policy
- Effect on health care resource use and cost



OPTN/SRTR: Data as of May 3, 2004

* Transplantation 2002;74:1281-1286.

Study Design

Research Objectives

- Evaluate the cost associated with graft failure following renal transplantation

Study Population

- United States Renal Data System (USRDS)
- Transplant period: 1993 – 1998
- Inclusion criteria
  - Adult ($\geq$ 18 years)
  - First transplant
  - Patient alive with functioning graft 6-months post-transplant
  - Medicare as primary source of payment

Issues

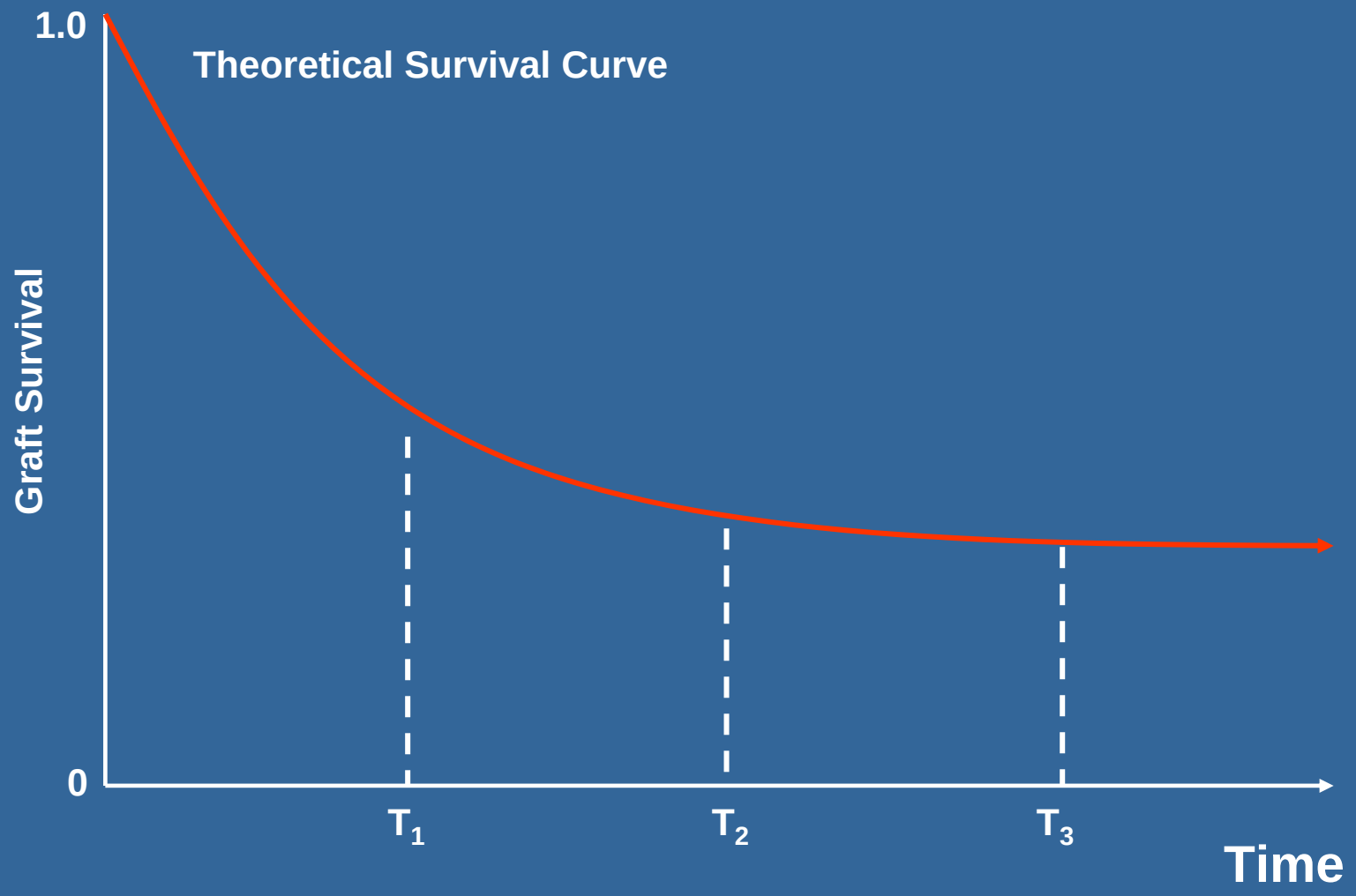
Issues	Requirements
Follow-up time for patients is variable	Estimate costs as of a given timepoint (3 years post-transplant)
Donor and recipient characteristics are significantly associated with outcome, as are treatment choices	Adjust for multiple risk factors (donor & recipient characteristics, treatments)
Patients whose grafts have not yet failed, no claims can be attributed to this specific event	Account for skewness of the data (censored cost data)
Event of interest is not observed on all patients, although all patients are at risk	Want to know expected future costs for whole population – not just for those whose event was observed in the first three years

Analysis Considerations

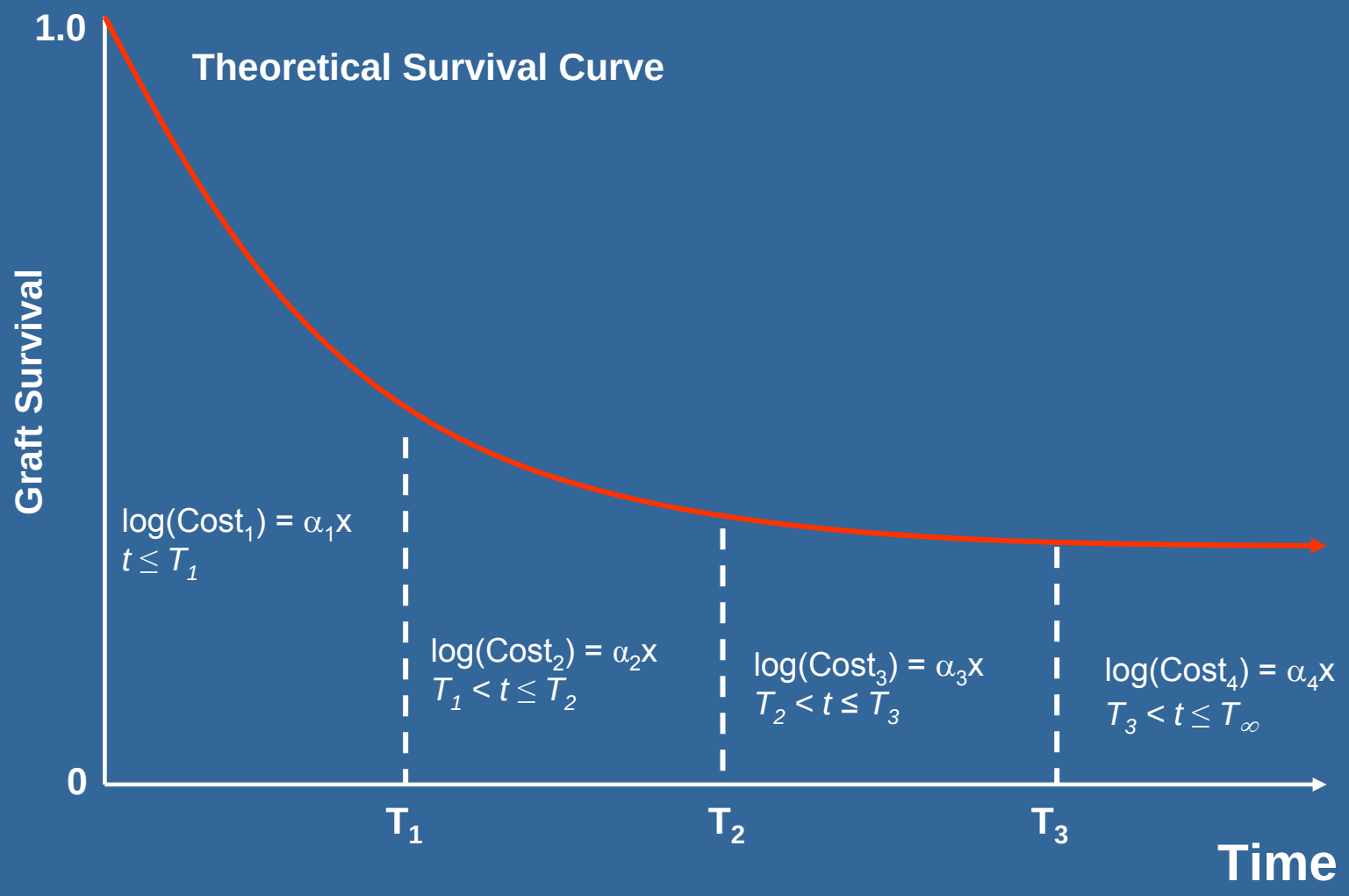
Can we use a simple approach?

Option	Limitations
Multiply known overall rate of failure times cost of hospitalization for failure	▲ Ignores changing rate over time and across different subgroups
Ordinary least-squares regression of log costs against covariates for those who experienced event	▲ Ignores risk profile for patients who have not yet experienced event ▲ Not a population-based estimate
Stratified Kaplan-Meier cost curves	▲ Cannot account for the large number of risk factors and treatment options

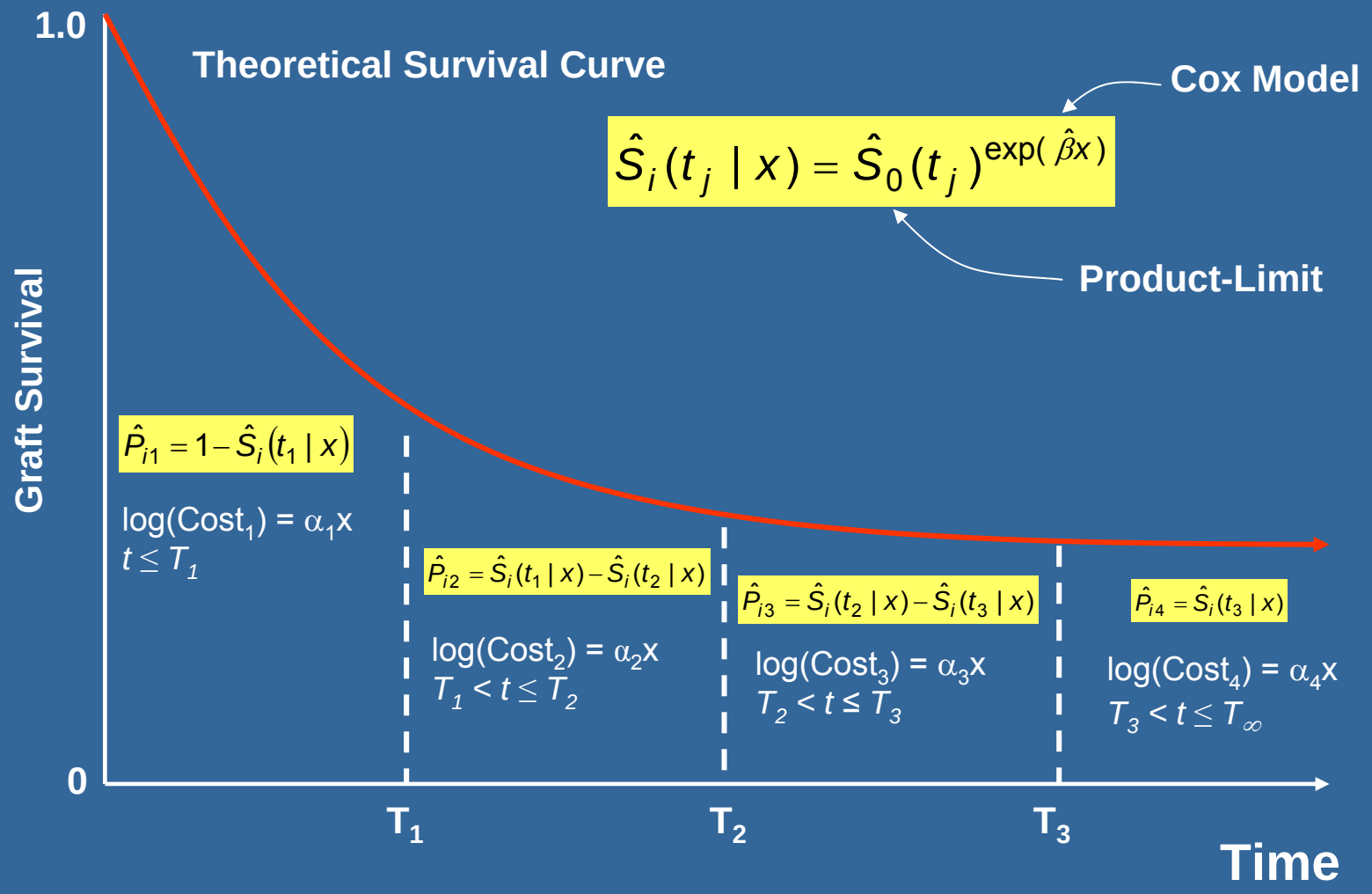
Modified Two-Part Model – Step 1



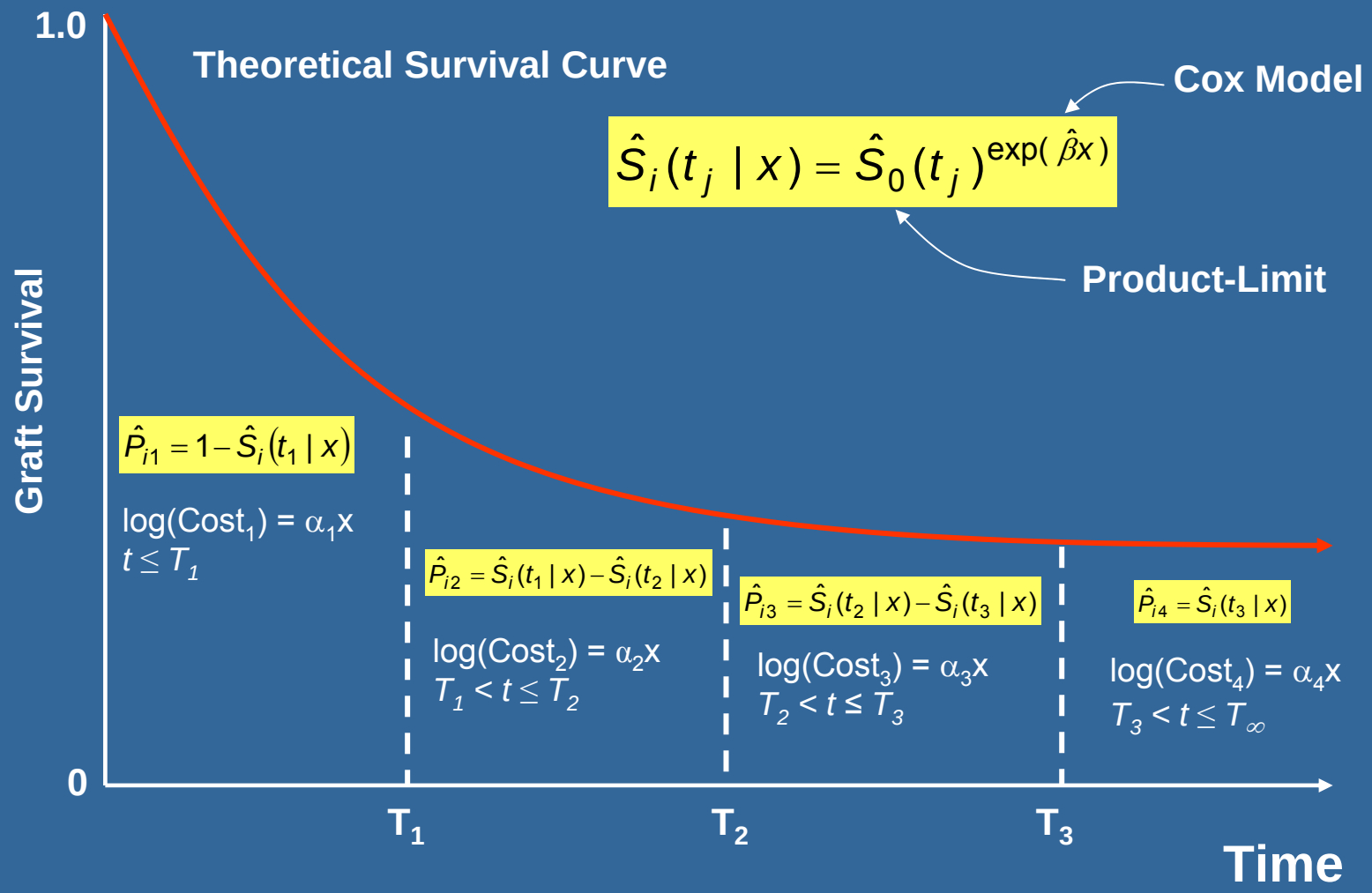
Modified Two-Part Model – Step 1 (cont'd)



Modified Two-Part Model – Step 2



Modified Two-Part Model – Step 3



$$\text{Expected } \log(\text{cost}_i) = \sum_{j=1}^{T_j} \log(\text{cost}_{ij}) \cdot P_{ij}$$

Putting it all together

Example

Probability of Graft Failure - P_j				Predicted cost - log($cost_j$)			
Year 1	Year 2	Year 3	Year 3+	Year 1	Year 2	Year 3	Year 3+
0.05	0.09	0.08	0.78	9.586	10.909	11.257	11.027
Expected Cost = (0.05 * 9.586) + (0.09 * 10.909) + (0.08 * 11.257) + (0.78 * 11.027) = 10.963 or exp(10.963) = $57,700							

Application

Predict individual cost associated with graft failure within 3-years post-transplant

PT #	*Probability of Graft Failure - P_{ij}*				Expected cost ($) log scale (Raw Scale)
	Year 1	Year 2	Year 3	Year 3+	
1	0.019	0.032	0.032	0.917	10.319 (30,236)
2	0.113	0.169	0.141	0.576	12.476 (262,078)

Actual claims were adjusted to year 2000 dollars using health care component of the Consumer Price Index.

Application

Compare the effect of covariates on cost[1]

Characteristic	Cadaveric	Living donor
ECD*: Yes vs. No	$57,463 vs. $50,726	-
Donor Age ≥ 60: Yes vs. No	$58,665 vs. $50,297	$56,738 vs. $46,101
DGF: Yes vs. No	$53,944 vs. $49,901	$52,444 vs. $45,996
Acute rejection: Yes vs. No	$62,749 vs. $47,787	$58,105 vs. $43,809

1. Adjusted for donor, recipient and transplant-related characteristics
* Expanded Criteria Donor: CVA + HTN + Creatinine >1.5 mg/dL
DGF = Delayed Graft Function

Application

Cost-Effectiveness Analysis

Maintenance Immunosuppression	Expected Cost (log scale)	% 3-Year Graft Survival
Cyclosporine	10.8169	85.233
Other	10.8911	84.907

Cost-effectiveness Ratio = (10.8169 – 10.8911) / (85.233 – 84.907)

= -0.22761

20% reduction in cost per 1% increase in 3-year graft survival

Conclusions

- Generation of population-based cost estimates for event-censored data requires a sophisticated approach to account for censoring and changing event rates over time
- The two-part method allows policymakers to assess potential costs of graft failure taking into account the timing of the event and specific characteristics of the entire population at risk
- These estimates provide groundwork for further studies to address the cost-effectiveness of various treatments to delay or prevent graft loss

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