Time Trends in Allogeneic Stem Cell Transplantation for Multiple Myeloma:

A CIBMTR Analysis

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Background

- Autologous hematopoietic stem cell transplants (HCT) is a standard therapy for myeloma
- Allo-HCT associated with high TRM
- Continued use of allo-HCT due to
  - Poor outcome in patients with aggressive disease
  - Incurable nature of MM despite new drugs
- Not clear how use of allo-HCT has changed over years

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Objectives

- Examine the trends over time among patients undergoing allo-HCT for myeloma in terms of:
  - Demographics
  - Disease characteristics
  - Rates of GVHD and treatment related mortality (TRM)
  - Disease free and overall survival

Patients

Allo-HCT for MM between 1989 and 2005, reported to the CIBMTR (n=**1211**)

1989-1994 (n=**346**)

1995-2000 (n=**285**)

2001-2005 (n=**580**)

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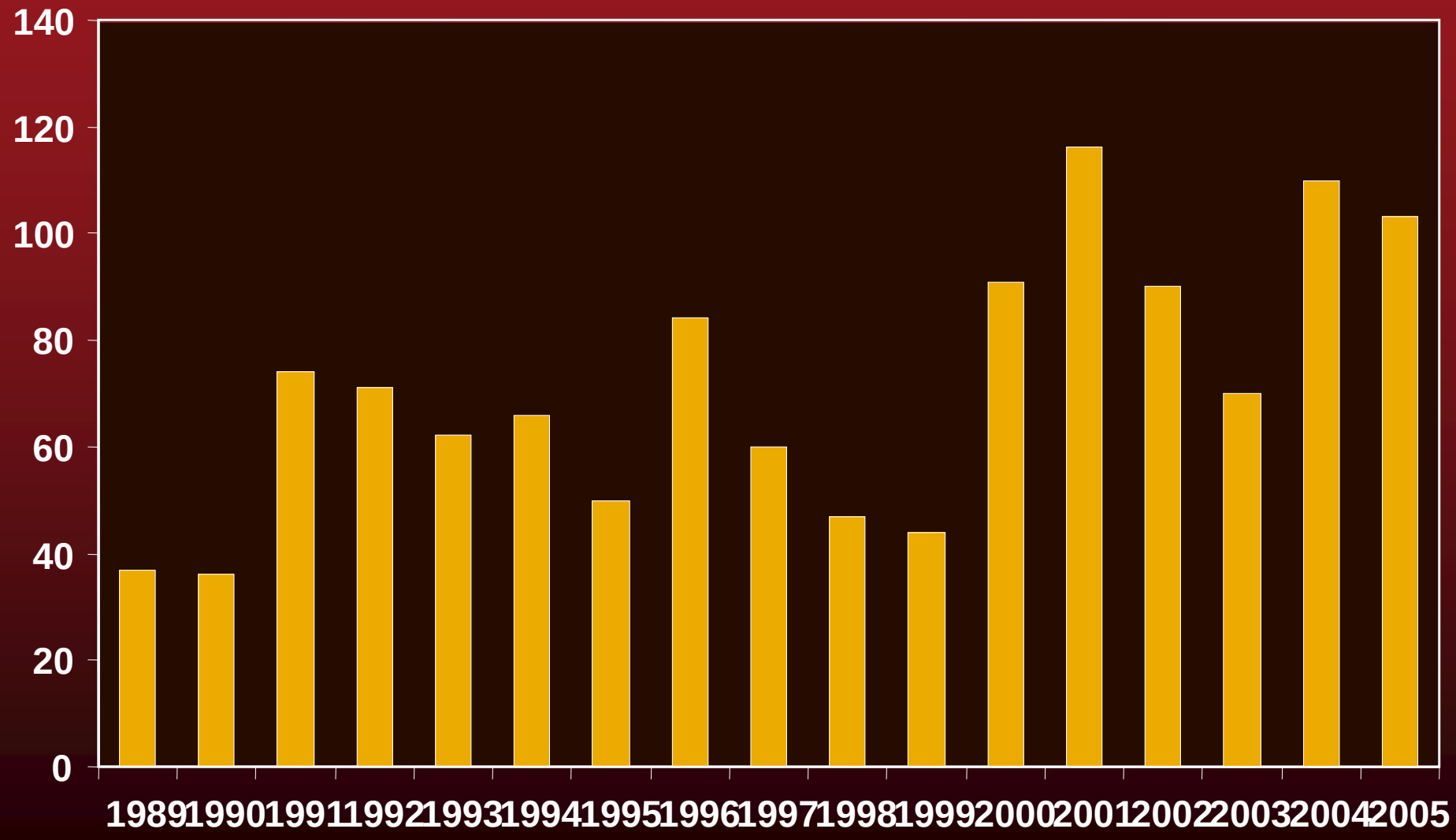
Statistical Analysis

- Cumulative incidence of acute and chronic GVHD, TRM and relapse/progression
- Kaplan-Meier estimator for probabilities of progression-free survival and overall survival
- Univariate analyses of Relative Risks

Patient Characteristics:
Distribution by Year of Transplant



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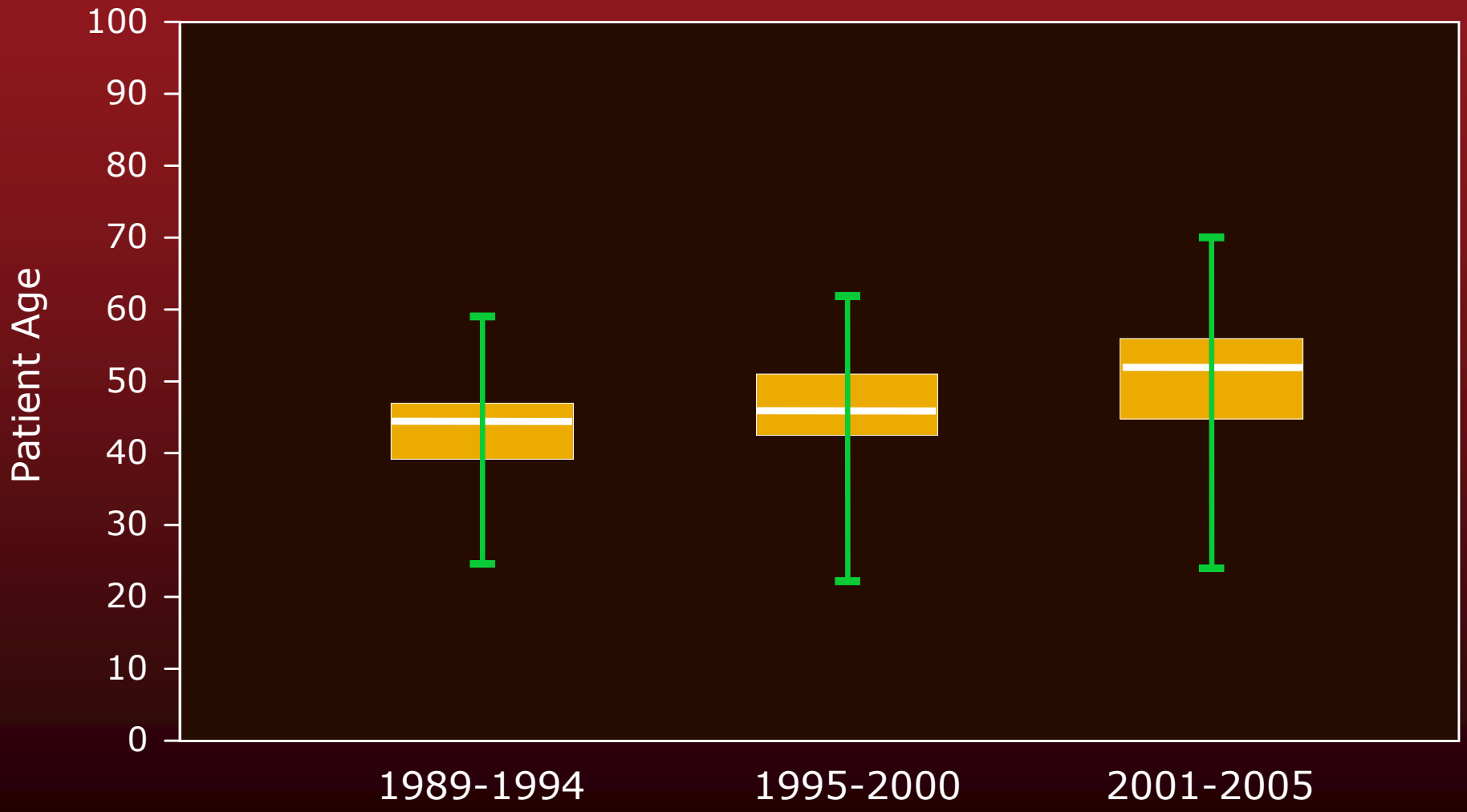
Patient Characteristics:
Patient Age at Transplant



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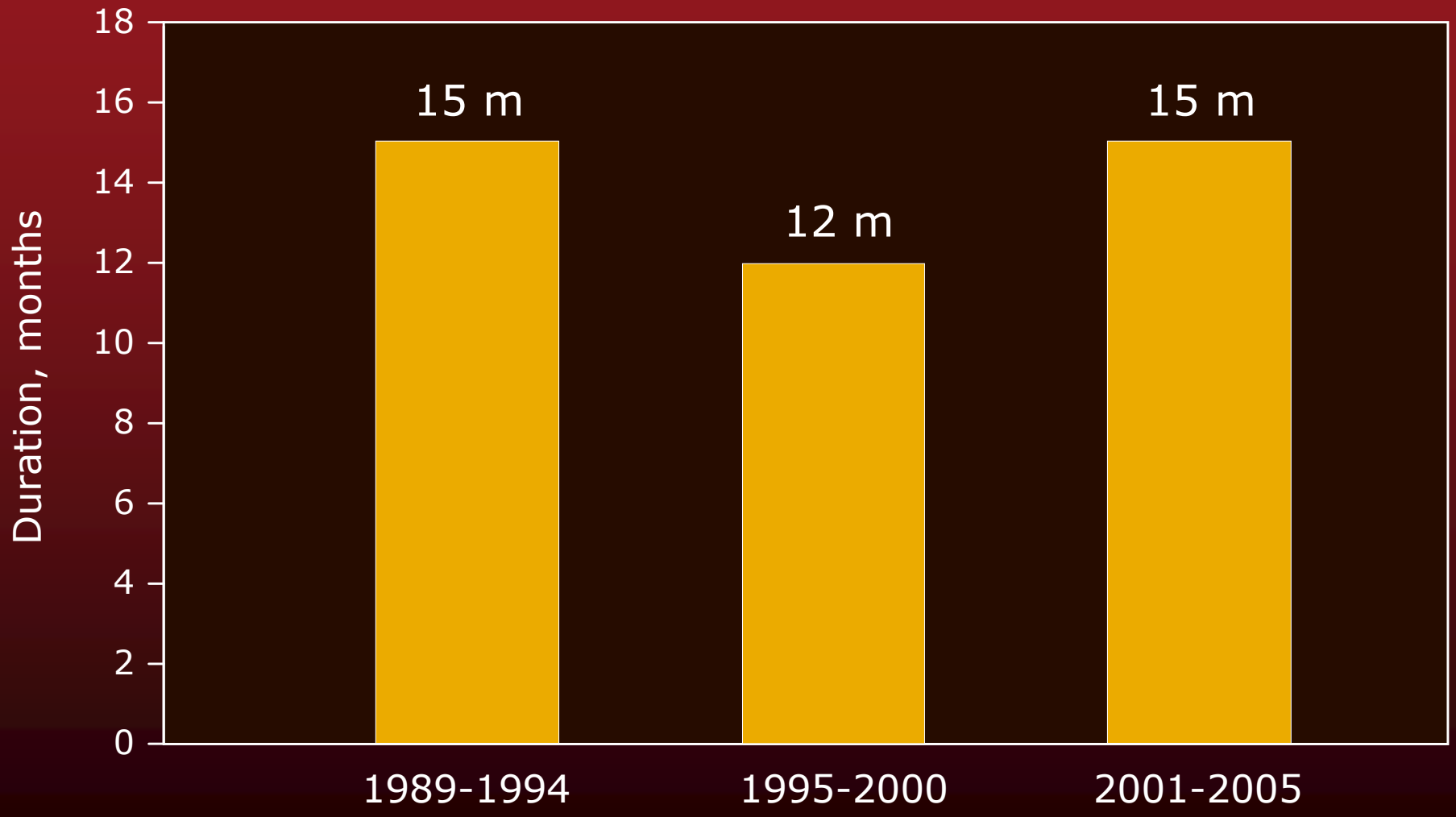
Patient Characteristics

- Proportion of patients ≥ 50 yrs 12% in early cohort to 53% in latest
- Similar gender distribution across the three periods
- Performance score similar across the years with 62-64% of patients having a Karnofsky score ≥ 90

Disease Characteristics

- Similar distribution of M protein type across the groups
- ISS data missing in a large proportion of patients
- The disease status at transplant and sensitivity to prior chemotherapy similar across the groups

Transplant Characteristics:
Time from Diagnosis to Transplant



p < 0.01

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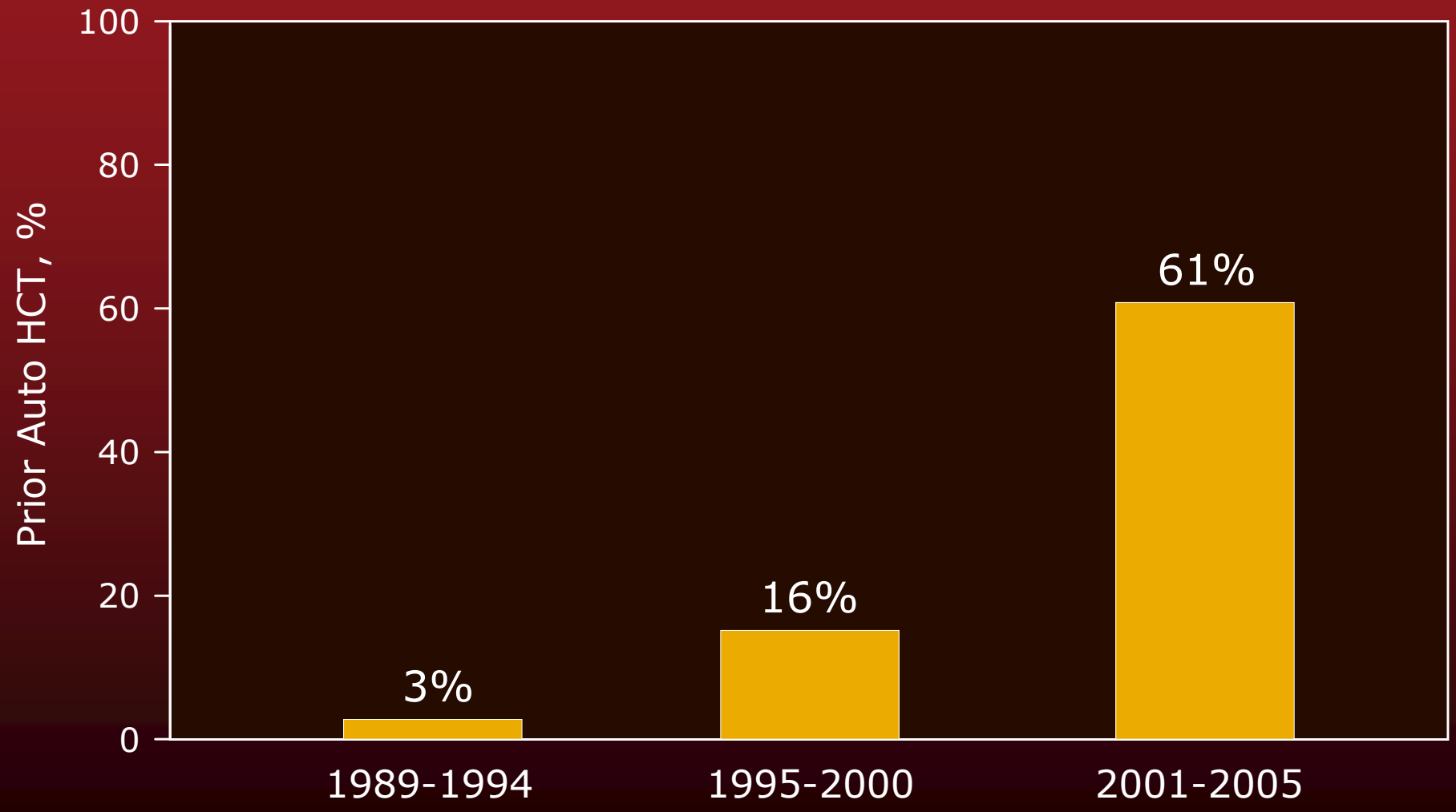
Transplant Characteristics:
Prior Auto HCT



$p < 0.01$

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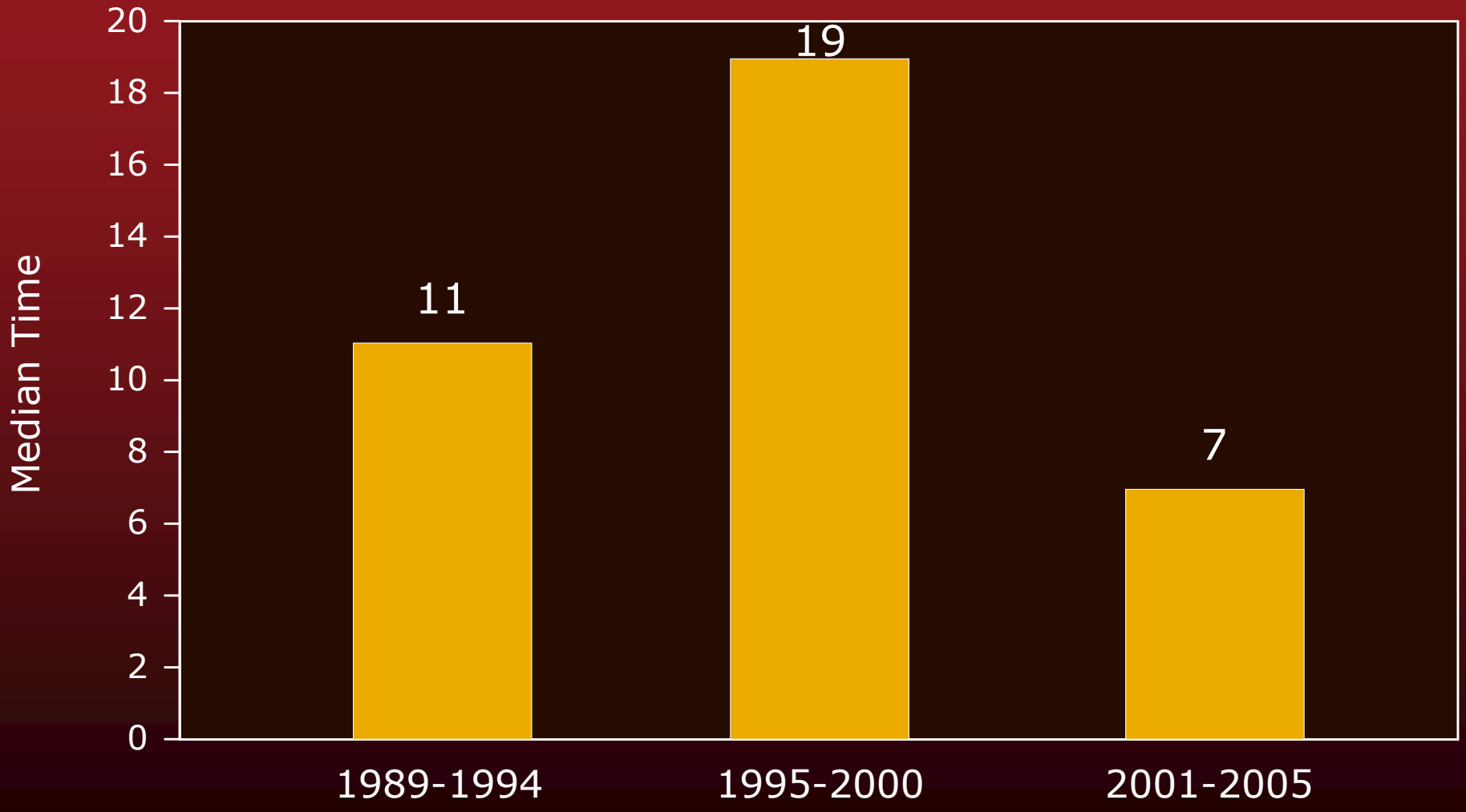
Transplant Characteristics:
Median Time from Auto to Allo HCT



$p < 0.01$

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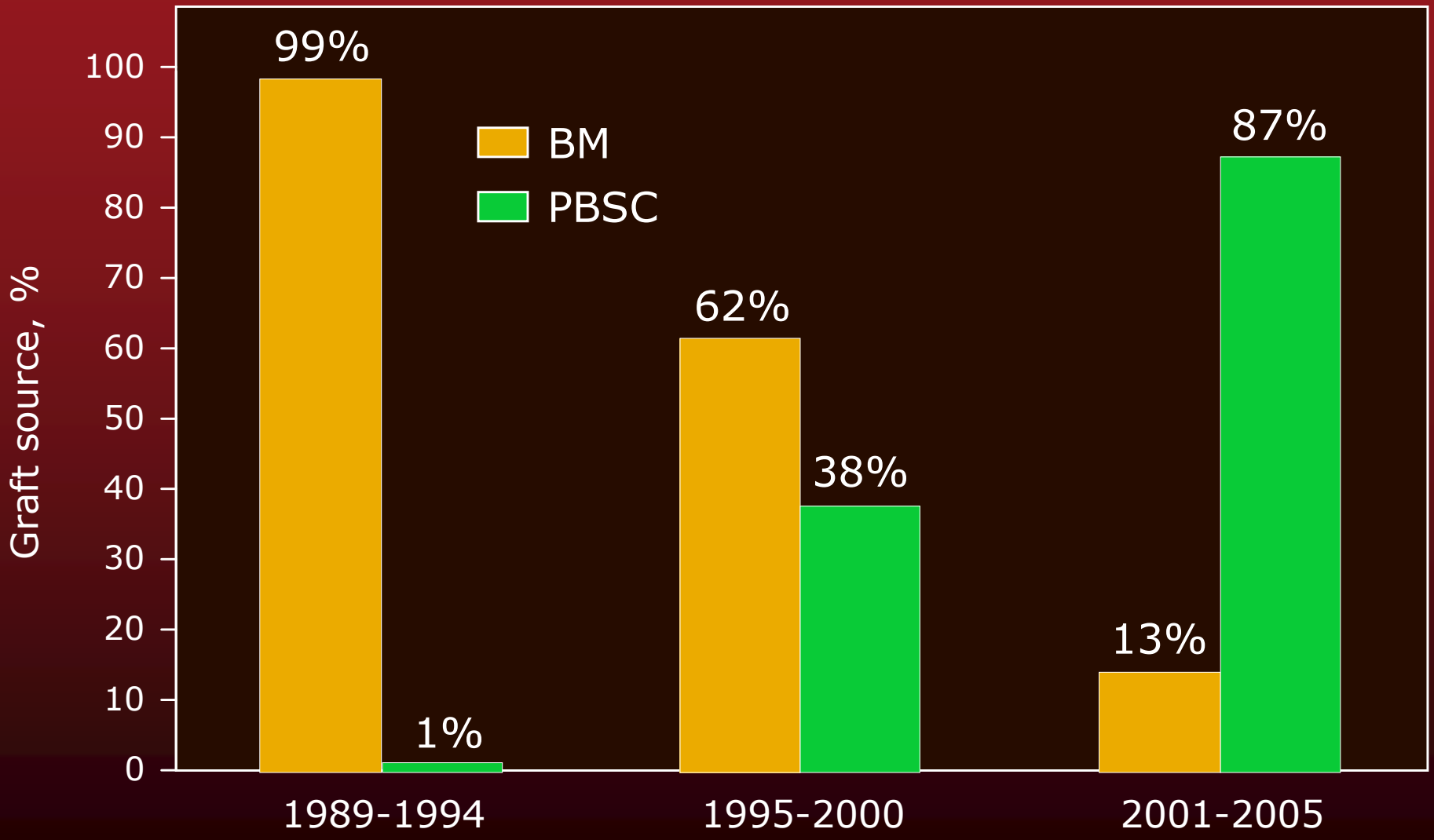
Transplant Characteristics:
Graft source



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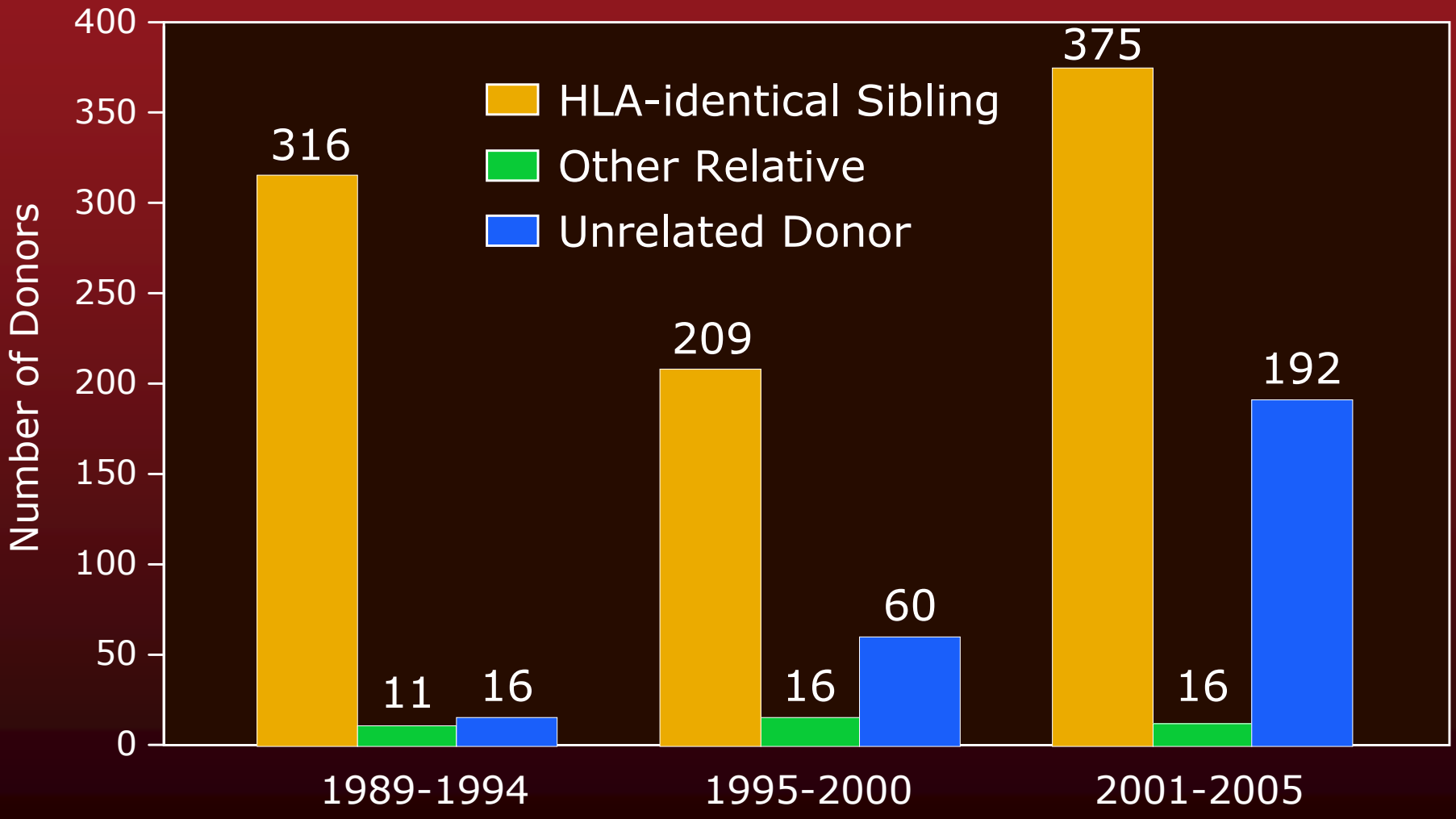
Transplant Characteristics:
Type of Donor



$p < 0.01$

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Transplant Characteristics:
Conditioning Regimen

- There was decreasing use of myeloablative regimens (82% vs. 62% vs. 9%)
- Cy-TBI or Bu-Cy most common regimens in the earlier 2 cohorts (pre 2001)
- Melphalan < 150 mg/m2 (22%), Fludarabine + 200 cGy TBI (16%) and TBI 200 cGy (10%) were the most common regimens in the latest cohort

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Transplant Characteristics:
GVHD Prophylaxis

	1989-1994	1995-2000	2001-2005
CSA/FK506 + MTX	**69%**	**58%**	**37%**
CSA ± other*	12%	12%	43%
FK506 ± other*	1%	5%	12%
T-cell depletion	**17%**	**23%**	**5%**
Other	1%	2%	3%

* includes mycophenolate (MMF)

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GVHD

	1989-1994	1995-2000	2001-2005	P
Acute	29 (25-34)	33 (28-39)	35 (31-40)	0.21
Chronic				
@1yr	31 (27-36)	28 (23-34)	43 (38-47)	<0.01
@3yrs	32 (28-37)	30 (25-36)	46 (41-50)	<0.01
@5yrs	32 (28-37)	30 (25-36)	47 (42-51)	<0.01

Cumulative Incidence of Treatment-related Mortality for Allotransplant - by Year Group -

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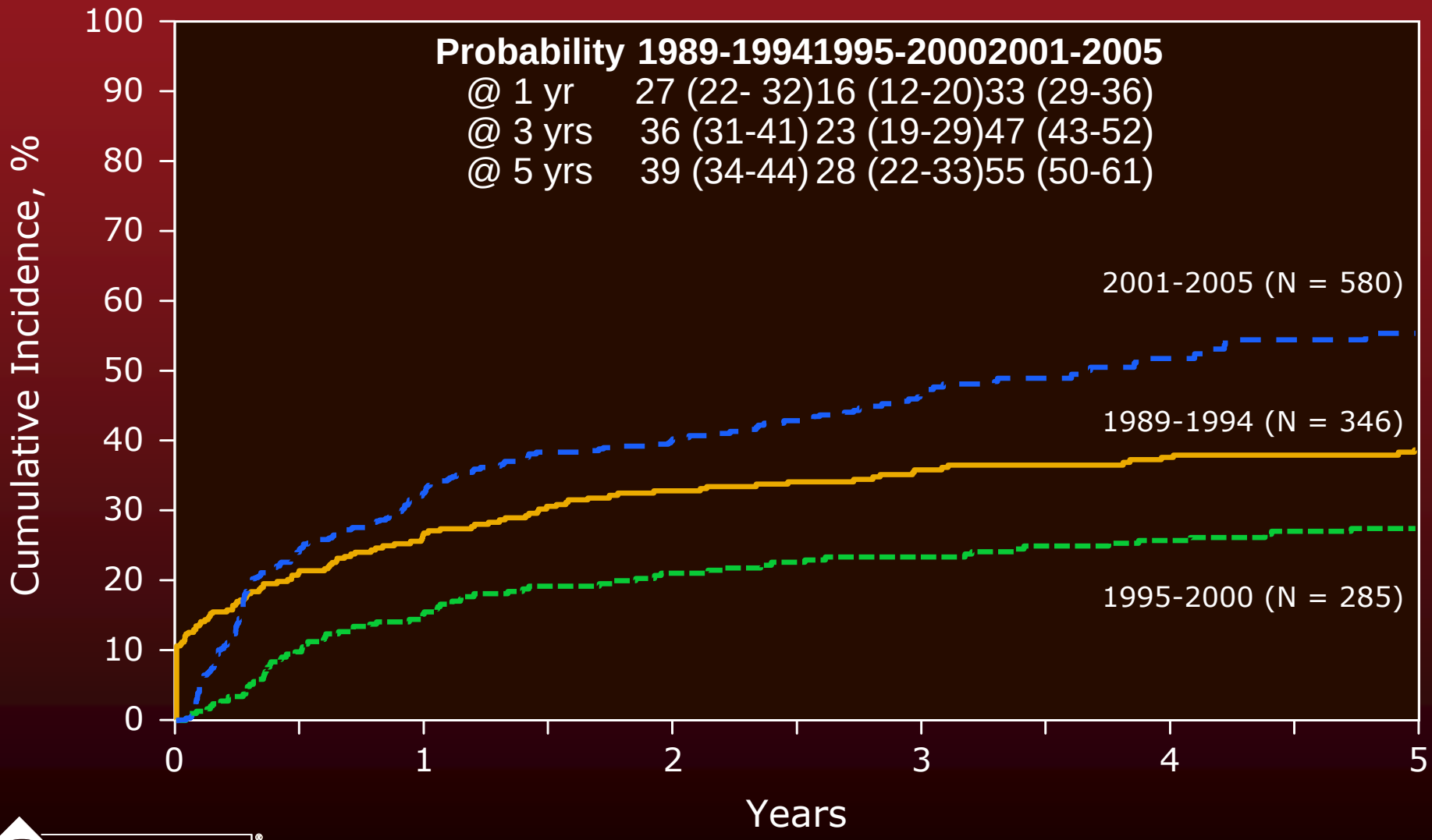
Cumulative Incidence of Relapse for Allotransplant - by Year Group -



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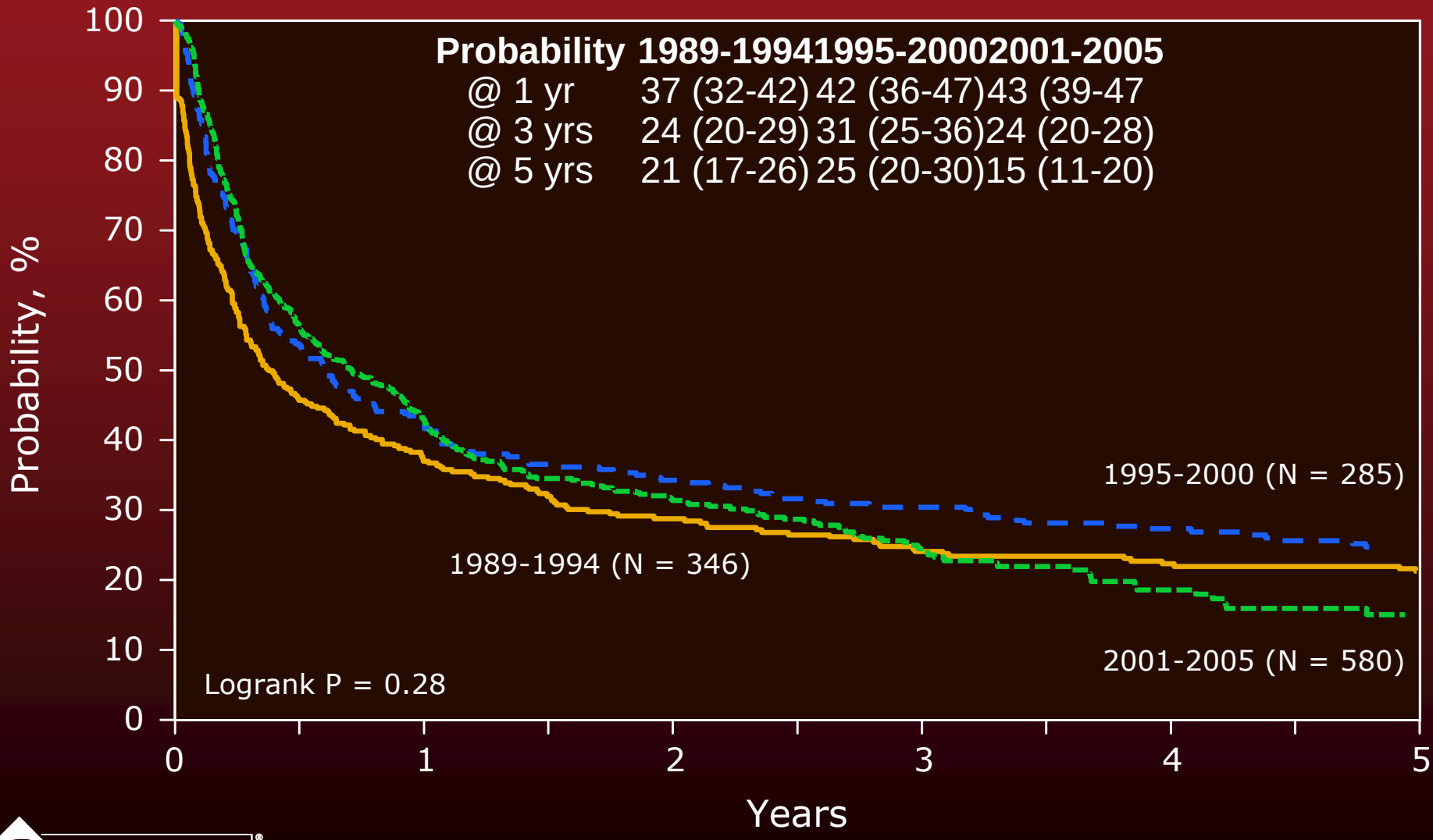
Probability of Progression-free Survival - by Year Group -



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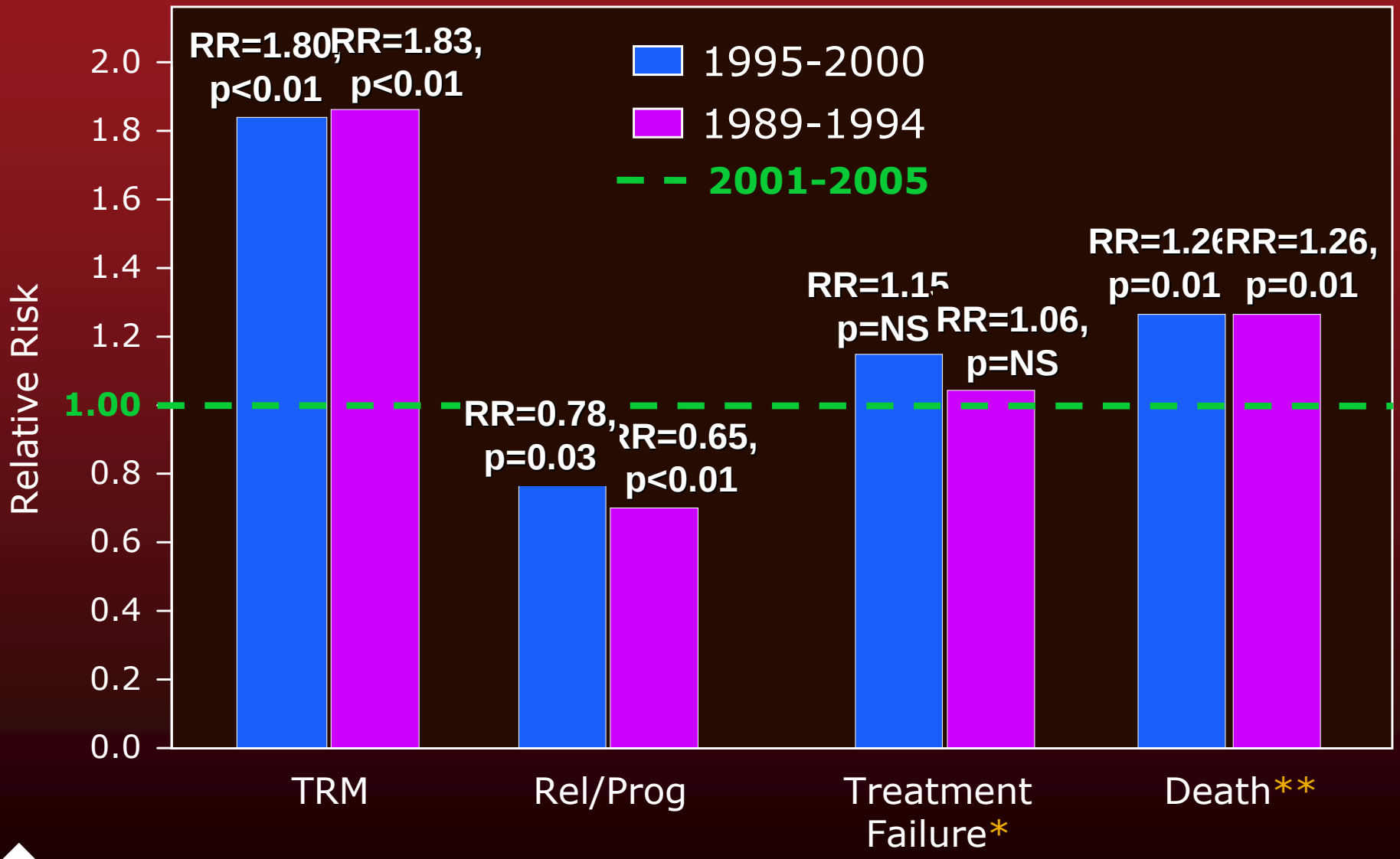
Relative Risk of Outcomes



* Inverse of PFS, ** Inverse of OS

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Causes of Death

	1989-1994	1995-2000	2001-2005
Number of deaths	252/346	204/285	342/580
Progressive myeloma	45%	26%	41%
Infection	15%	17%	17%
Pulmonary syndrome	7%	4%	3%
Organ failure	8%	15%	9%
GVHD	6%	10%	5%
Other/unknown	19%	28%	25%

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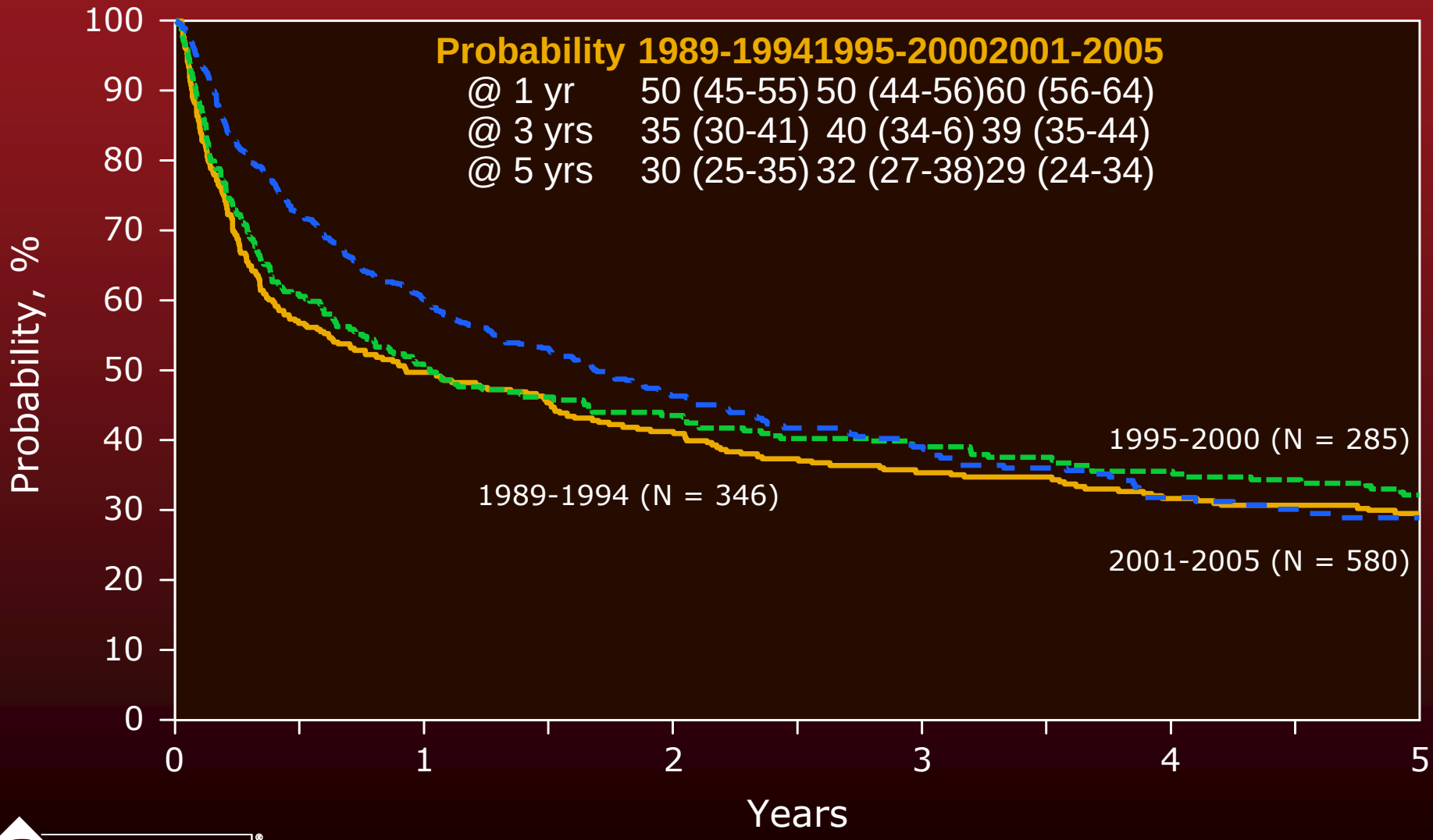
Probability of Overall Survival after HCT
- From Date of HCT -



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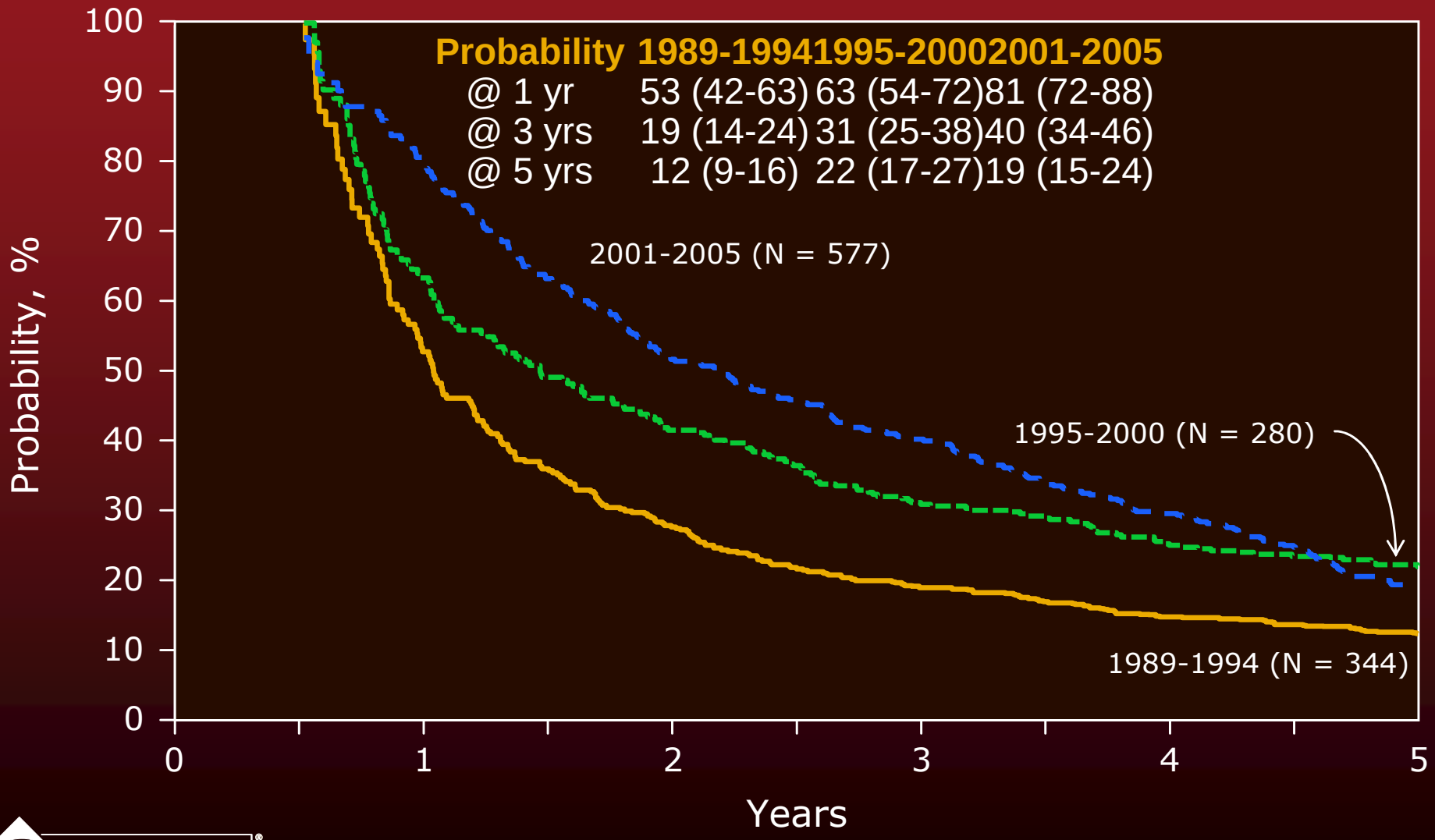
Probability of Overall Survival after HCT
- From Date of Diagnosis -



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Conclusion

- Clear trend towards more of:
  - Reduced intensity conditioning
  - Unrelated donor SCT
  - Use of PBSC grafts
  - Selection of older patients
  - Tandem auto-allo and patients with prior auto-HCT
- While TRM has decreased this did not translate into an improvement in survival because of increased risk of relapse

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Center for International Blood and Marrow Transplant Research (CIBMTR)