

# Population-based Patterns of HIV-related Hodgkin Lymphoma in the Greater San Francisco Bay Area: 1988-98

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# Hodgkin Lymphoma

- Relatively rare lymphoma (3.0 per 100,000)
- Most common cancer of late adolescence
- Infectious precursor suspected
- Associated with Epstein-Barr virus (EBV) in 1/4 - 1/3 of cases
- High survival rate with treatment

# HIV-Hodgkin Lymphoma Association

- Association with HIV first reported in 1984 in small case series
  - Aggressive
  - Advanced stage
  - Virulent histologic subtype
- Association complicated to interpret
  - Hodgkin lymphoma common in young adults
  - HIV population young-adult



# HIV-Hodgkin Lymphoma Association

- HIV-AIDS cohort studies
- Cancer registry-AIDS registry linkages
- Established ~ 10-fold excess of Hodgkin lymphoma given HIV
- Hodgkin lymphoma NOT an AIDS-defining condition



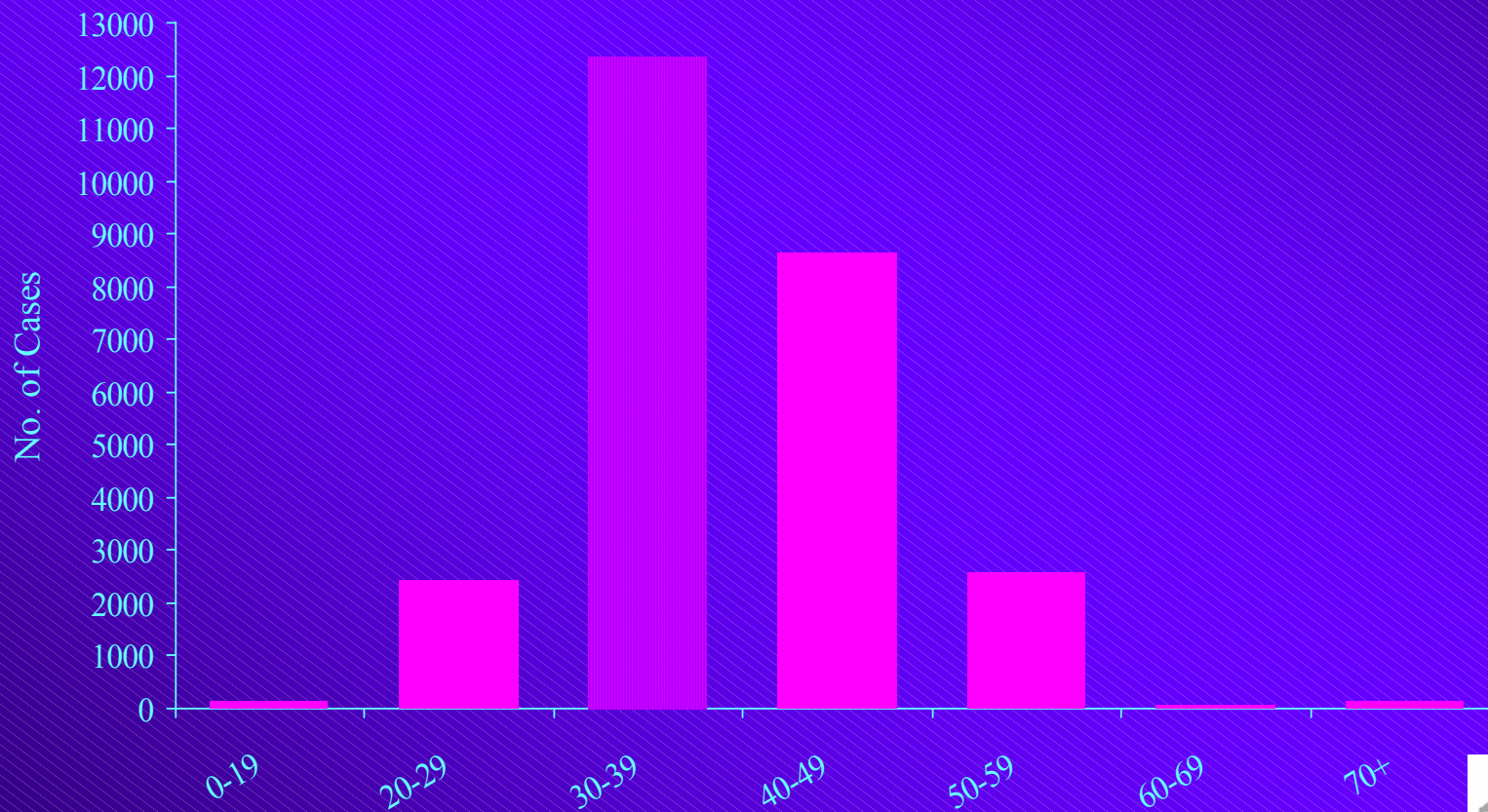
# Cumulative AIDS Cases Greater Bay Area, 1990-2000\*

	Number of cases	%
Male	25,646	91.9
Female	2,277	8.1
Total	27,923	100.0

\*Source: California Department of Health Services—Office of AIDS



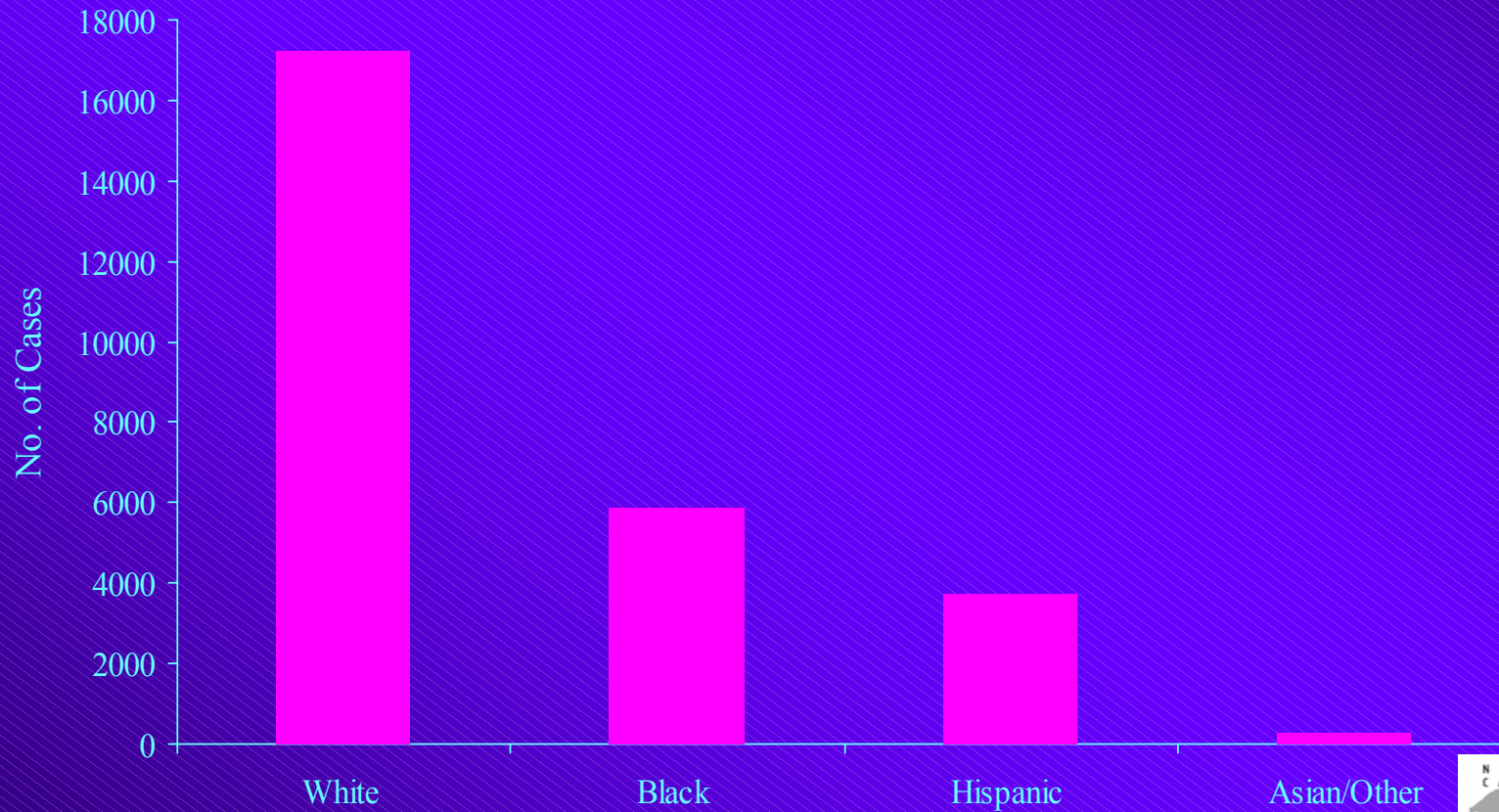
# AIDS Incidence by Age Group Greater Bay Area, 1990-2000\*



\*Source: California Department of Health Services—Office of AIDS



# AIDS Incidence by Race/Ethnicity Greater Bay Area, 1990-2000\*

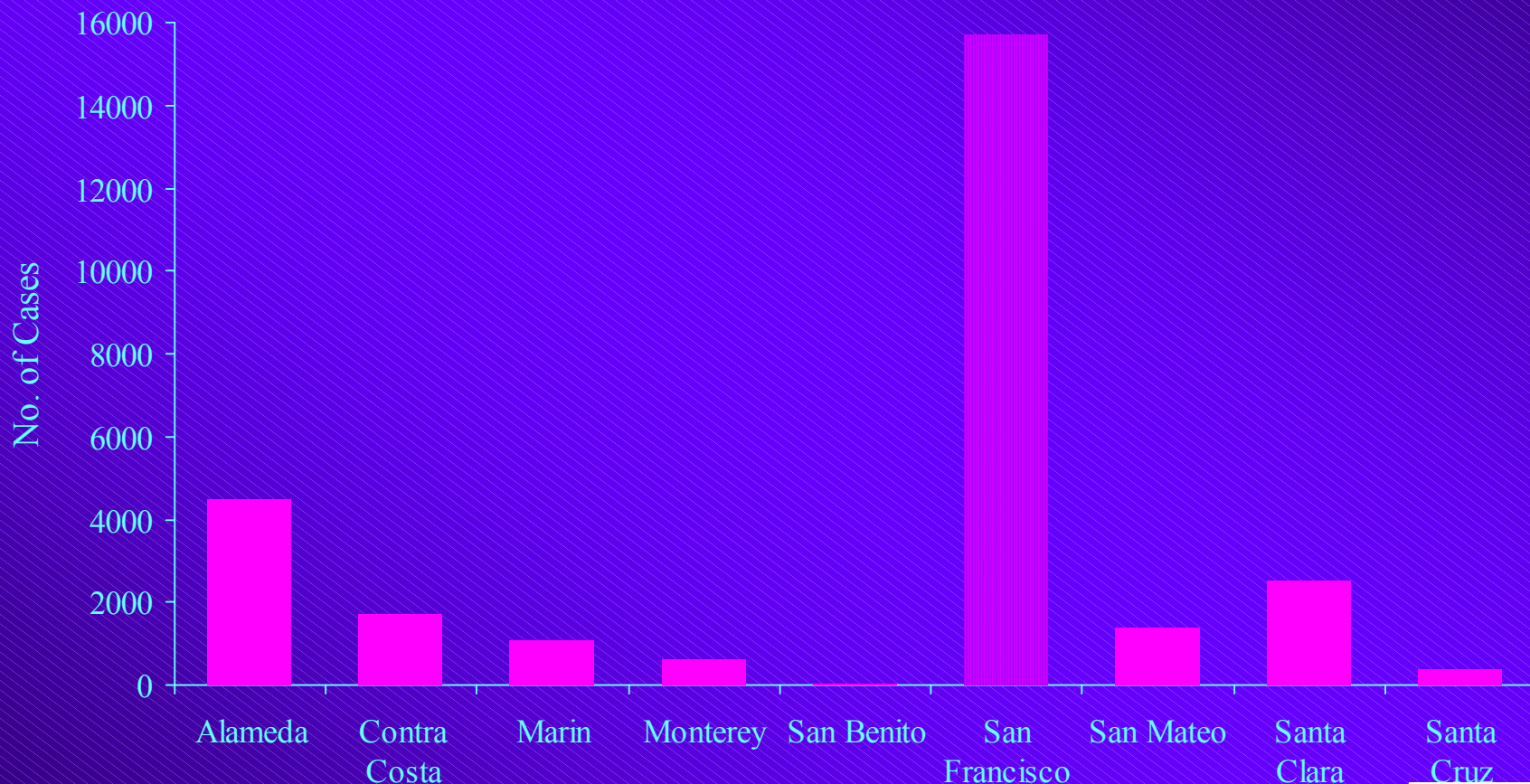


\*Source: California Department of Health Services—Office of AIDS





# AIDS Incidence by County Greater Bay Area, 1990-2000\*



\*Source: California Department of Health Services—Office of AIDS





# Study of HIV-Associated Hodgkin Lymphoma

- Greater Bay Area Cancer Registry
- Study of Hodgkin lymphoma
- All patients with Hodgkin lymphoma
- Diagnosed July 1988 – December 1998
- Residents, 9 Greater Bay Area counties



# Registry Patient Data

- Year of diagnosis
- Age at diagnosis
- Sex
- Race/ethnicity
- County of residence
- Vital status (July, 2001)
- Cause of death

# Registry Tumor Data

- Histologic subtype
- “B-symptoms” (e.g., fever, night sweats)
- Anatomic site (nodal vs extra-nodal)
- Stage of disease
  - Ann Arbor (Stage I-IV)

# Additional Tumor Data (1988-97)

- Histopathologic rereview
- Archival tumor tissues, evaluated for EBV
  - EBER in situ hybridization
  - LMP-1 immunohistochemistry

# Information on HIV/AIDS

- Routinely collected registry variables
  - SEER EOD HIV/AIDS indicator (since 1990)
  - Underlying cause of death
- Relevant text
  - Registry paper abstract
  - Paper death certificate
- Linkage to CA state AIDS registry

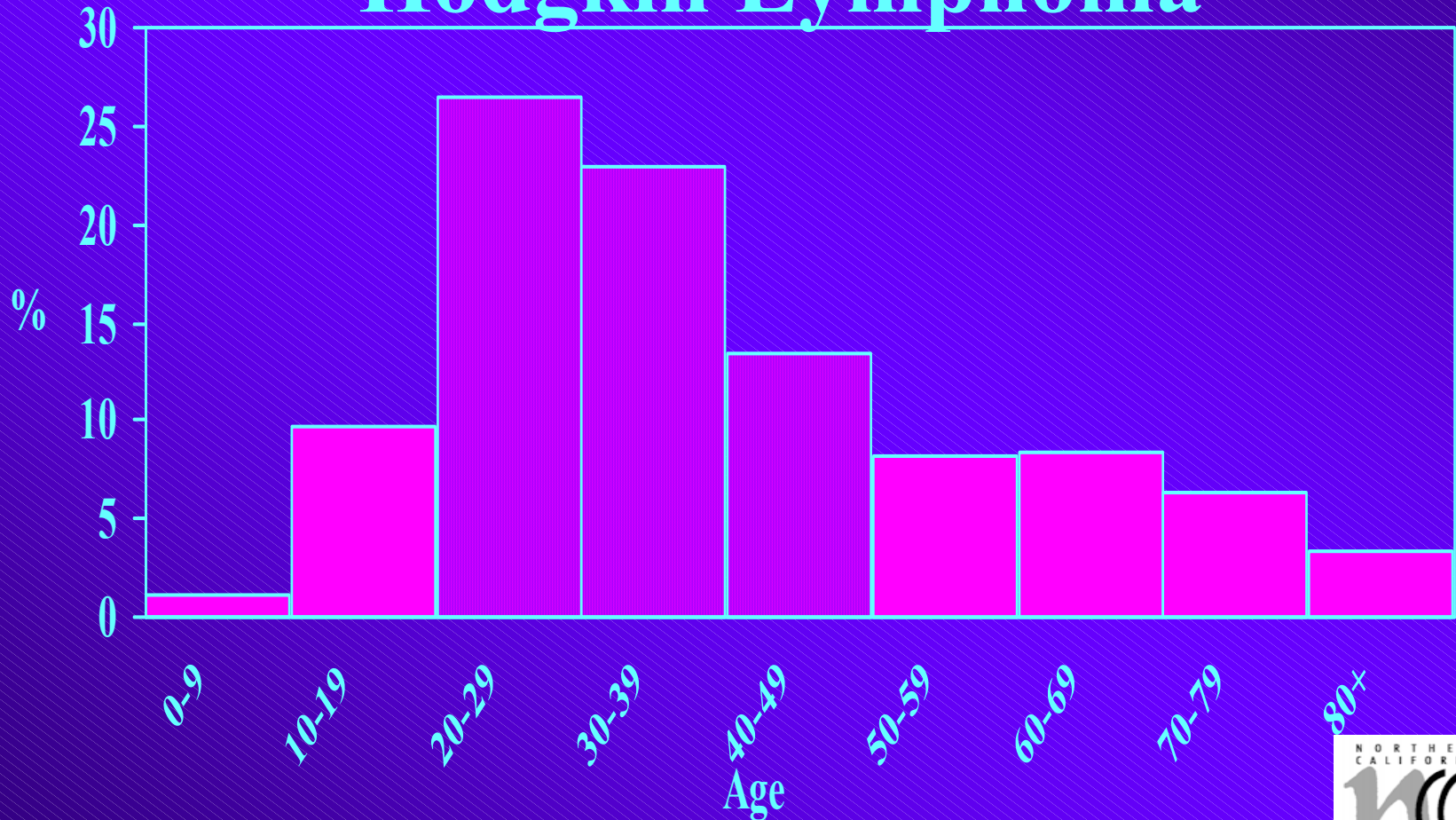


# HIV status

- HIV-positive
  - Positive HIV/AIDS (SEER EOD) indicator, **or**
  - AIDS cause of death, **or**
  - Mention of ARC or HIV or AIDS on registry abstract, **or**
  - Mention of ARC or HIV or AIDS on death certificate
  - Match with AIDS registry
- HIV-negative
  - All other

# Age distribution

## Hodgkin Lymphoma





# Demographic Characteristics Hodgkin Lymphoma

	%
<b>Sex</b>	
Male	56
<b>Race/Ethnicity</b>	
White	70
Black	8
Hispanic	14
Asian/Other	8
<b>Vital Status</b>	
Alive (7/01)	70

# Tumor Characteristics

## Hodgkin Lymphoma

%

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### Histology (Rye Classification)

Nodular Sclerosis	65
Mixed Cellularity	17
Nod. Lymph. Predomin.	2
Lymph. Predominance	3
Lymph. Depletion	2
Not otherwise specified	11

# Clinical Characteristics Hodgkin Lymphoma

	%
<b>No B-symptoms*</b>	<b>54</b>
<b>Nodal disease</b>	<b>68</b>
<b>Ann Arbor stage</b>	
<b>I</b>	<b>19</b>
<b>II</b>	<b>39</b>
<b>III</b>	<b>19</b>
<b>IV</b>	<b>18</b>

\*missing for n=341

# Tumor Specimens

## Hodgkin Lymphoma, 1988-97

	N	%
Not obtained	593	38
Obtained	983	62
EBV-positive	298	30
EBV-negative	685	70

# HIV-AIDS status source

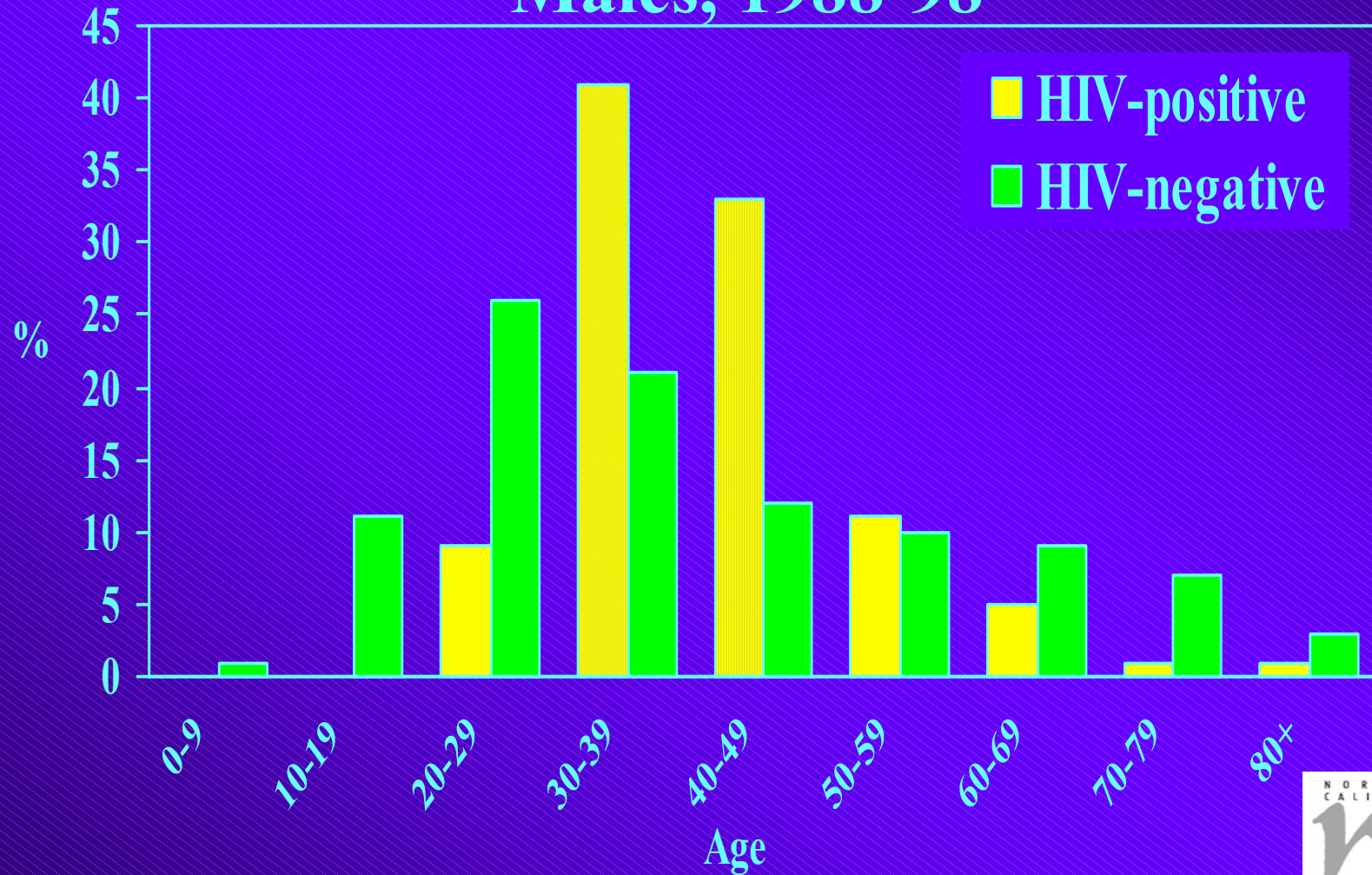
	N	%
All Hodgkin patients	1,726	100
HIV-positive	128	7
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SEER EOD indicator	97	75
Registry abstract mention	76	58
Cause of death	46	35
Death certificate mention	52	40
AIDS registry linkage	70	55

# HIV-positive Hodgkin Lymphoma 1988-98 Greater Bay Area

	N	%
HIV-positive males	122	95
HIV-positive females	6	5

# Hodgkin Lymphoma Patients

## Males, 1988-98





# Patient Characteristics, Males HIV-Associated Hodgkin Lymphoma

%

Race/Ethnicity	HIV-positive	HIV-negative
White	72	70
Black*	13	7
Hispanic	13	12
Asian/Other*	2	10

\* Significantly different from all others at  $p \leq 0.05$

# Patient Characteristics, Males

## HIV-Associated Hodgkin Lymphoma

%

County	HIV-positive	HIV-negative
Alameda*	10	23
Contra Costa*	5	15
Marin	2	4
Monterey	1	6
San Benito	1	1
<b>San Francisco*</b>	<b>62</b>	<b>13</b>
San Mateo	7	11
Santa Clara*	12	25
Santa Cruz	1	4

\* Significantly different from all others at  $p \leq 0.05$



# Clinical Characteristics, Males HIV-Associated Hodgkin Lymphoma

%

	HIV-positive	HIV-negative
<b>B-symptoms*†</b>	77	43
<b>Extra-nodal*‡</b>	80	32
<b>Stage III-IV disease*</b>	58	39

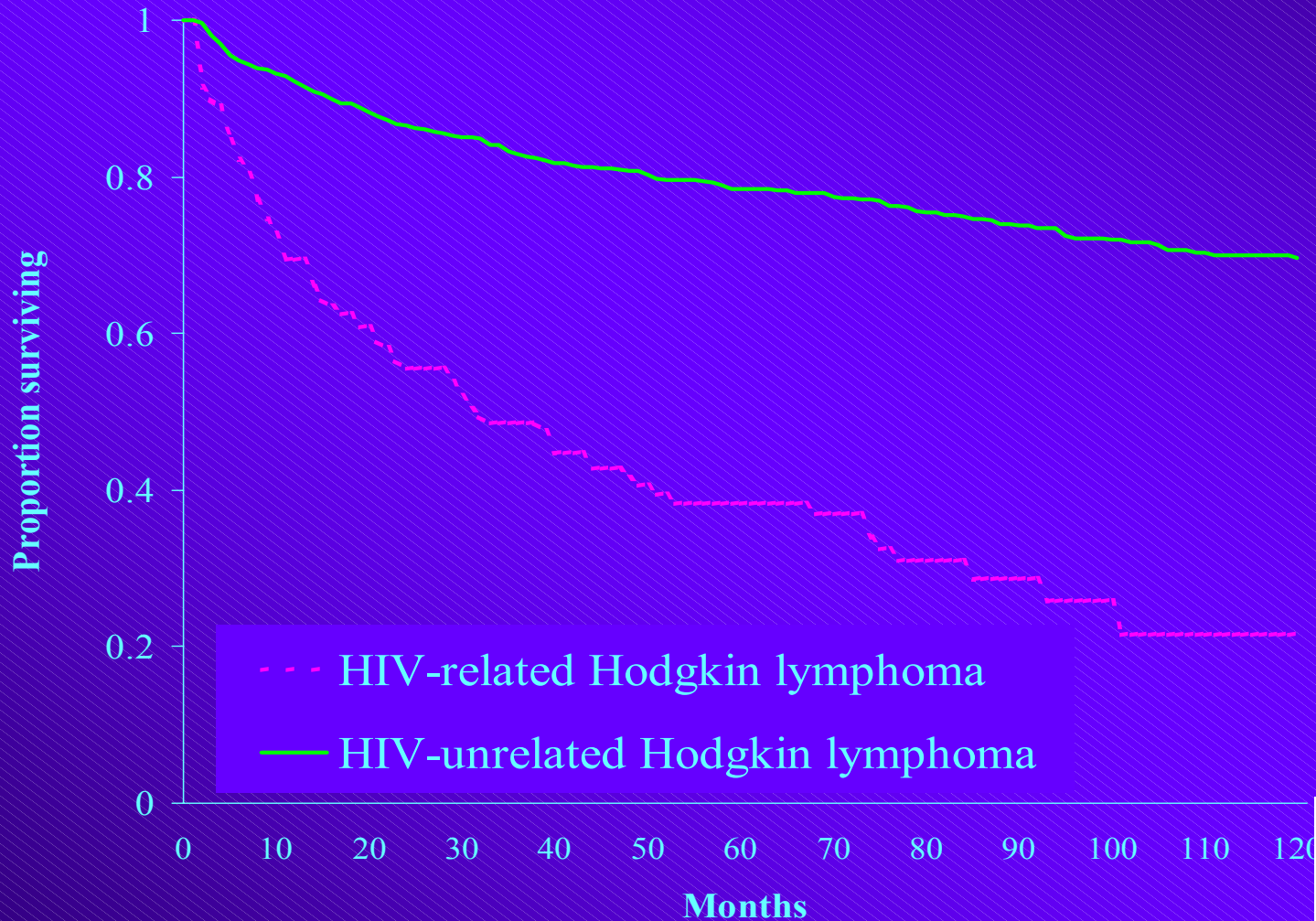
\*Significantly different from all others at  $p \leq 0.05$

†Missing for n=181

‡Missing for n=47



# Overall Survival, Males Hodgkin Lymphoma, as of 7/2001



# Tumor Characteristics, Males HIV-Associated Hodgkin Lymphoma

Histologic subtype	%	
	HIV-pos	HIV-neg
Nodular Sclerosis*	32	61
Mixed Cellularity*	31	19
Nod. Lymph. Predomin.	-	2
Lymph. Predomin.	<1	5
Lymph. Depletion*	8	2
Unspecified*	28	11

\*Significantly different from all others at  $p \leq 0.05$

# Tumor Characteristics, Males HIV-Associated Hodgkin Lymphoma

	%	
	HIV-pos	HIV-neg
<b>EBV-positive*†</b>	<b>90</b>	<b>32</b>

\*Significantly different at  $p \leq 0.05$

† Based on 532 patients



# Predictors of HIV-positive Hodgkin Lymphoma

## Odds Ratios (OR) and 95% Confidence Intervals (CI)

	Age/race-Adjusted		Adjusted†*	
	OR	95% CI	OR	95% CI
30-49 years vs other	5.8	3.8-8.9	19.5	7.3-52.4
SF county vs other	11.5	7.4-17.9	10.6	4.4-25.8
B-symptoms vs none	4.4	2.6-7.4	1.6	0.9-2.8
Stage III-IV vs I-II	7.0	4.3-11.5	5.9	2.3-15.3
LD hist. vs NS hist	13.7	5.2-36.3	9.3	1.1-82.4
Unspec. hist. vs NS	5.5	3.2-9.5	4.3	1.2-15.4
EBV+ vs EBV- cells	29.8	11.9-74.8	25.6	8.5-77.5

\*Adjusted for race, site, mixed cell and lymphocyte predominance histology, and all other variables shown

† Based on 514 of all 877 1988-97 cases





# Impact of HIV on Incidence of Hodgkin Lymphoma

- Incidence rates for Hodgkin lymphoma:
  - Overall patient population
  - HIV-negative patient population
- Compare overall and HIV-negative rates:
  - Difference estimates burden of HIV-related disease

# Age-Adjusted Incidence Rates\* in Males Hodgkin Lymphoma, 1988-98

	HIV-negative		All men		Change
	Rate	95% CI	Rate	95% CI	
<b>All</b>	2.5	2.3-2.7	2.8	2.6-3.0	↑12%
<b>Race/Ethnicity</b>					
Whites	3.1	2.8-3.3	3.4	3.2-3.7	↑11%
Blacks	2.2	1.6-2.8	2.7	2.1-3.3	↑22%
Hispanics	1.9	1.5-2.4	2.2	1.8-2.6	↑14%

\* Average annual, per 100,000, age-adjusted to the 1970 US standard



# Age-Adjusted Incidence Rates\* in Males Hodgkin Lymphoma, 1988-98

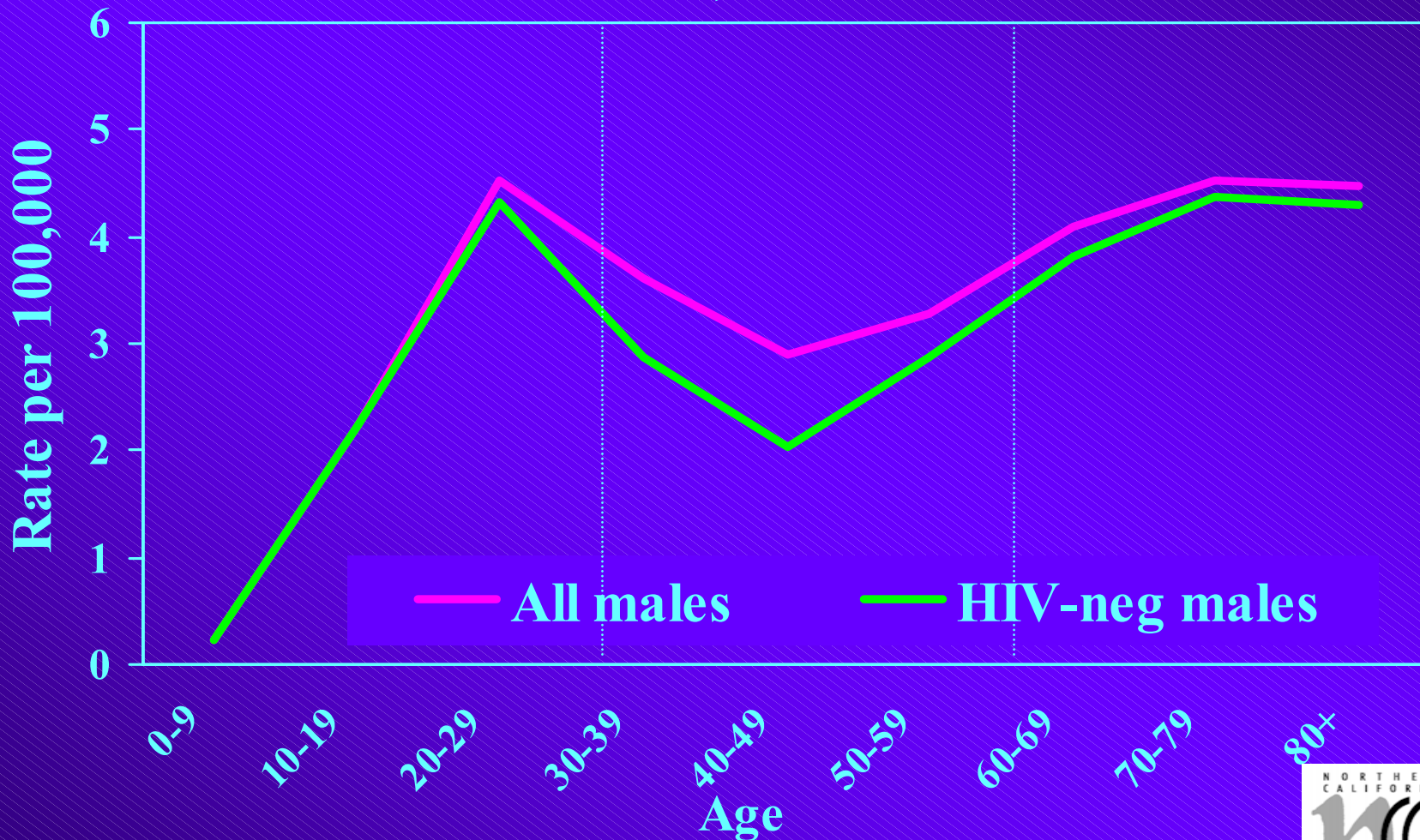
Histologic subtype	HIV-negative		All men		Change
	Rate	95% CI	Rate	95% CI	
Nod. Sclerosis	1.5	1.4-1.6	1.6	1.5-1.8	↑10%
Mixed Cell.	0.5	0.4-0.6	0.6	0.5-0.7	↑16%
Lymph. Depl.	0.04	0.02-.07	0.07	0.04-0.1	↑75%

\* Average annual, per 100,000, age-adjusted to the 1970 US standard



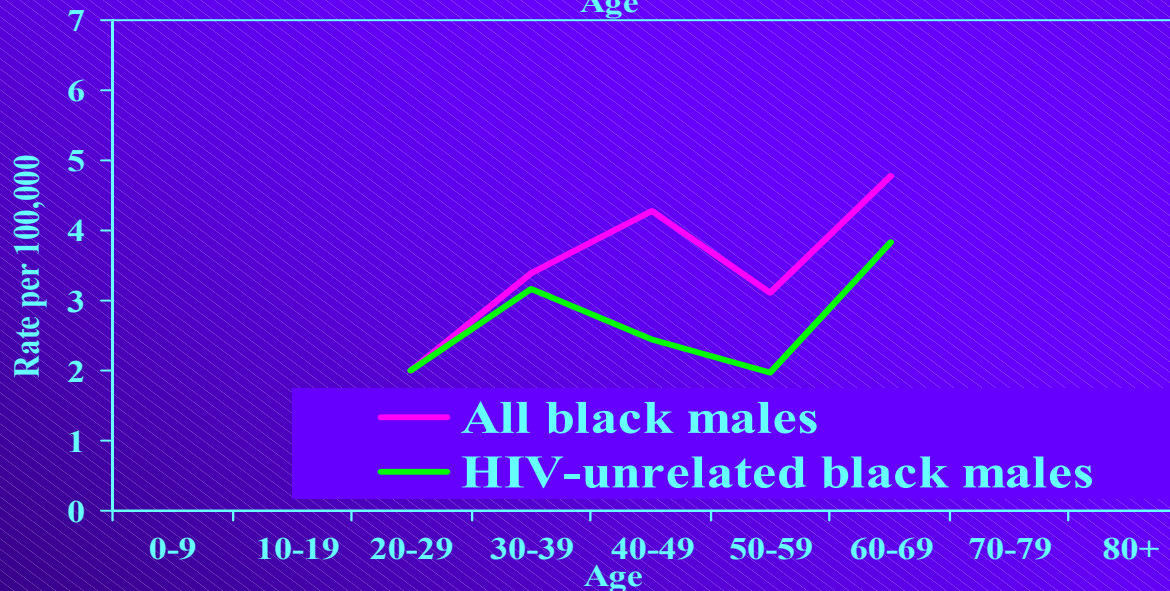
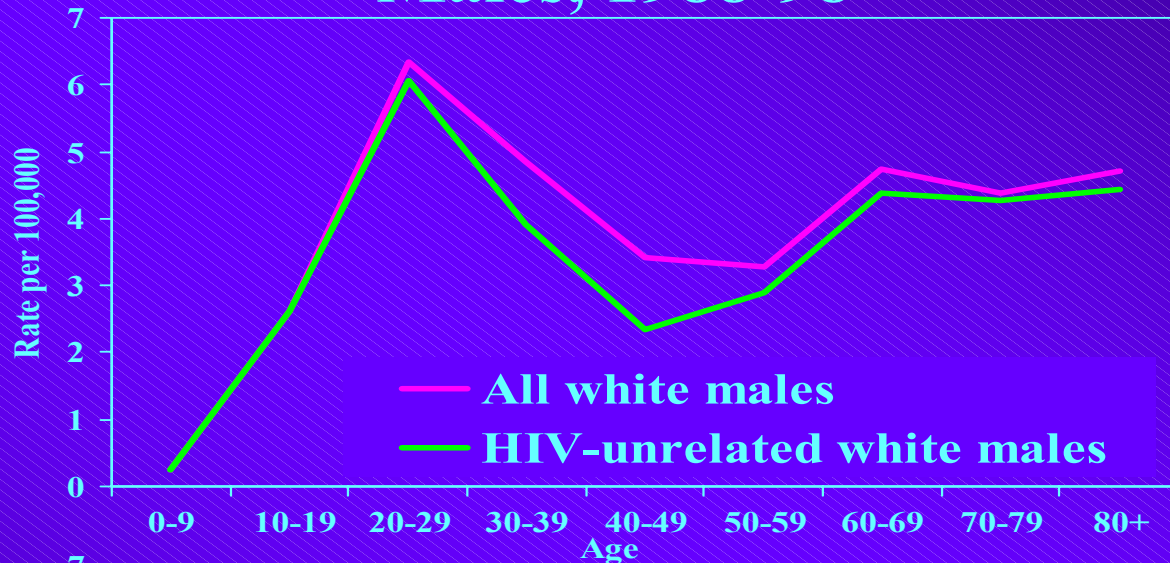
# Hodgkin Lymphoma Incidence Rates

## Males, 1988-98



# Hodgkin Lymphoma Incidence Rates

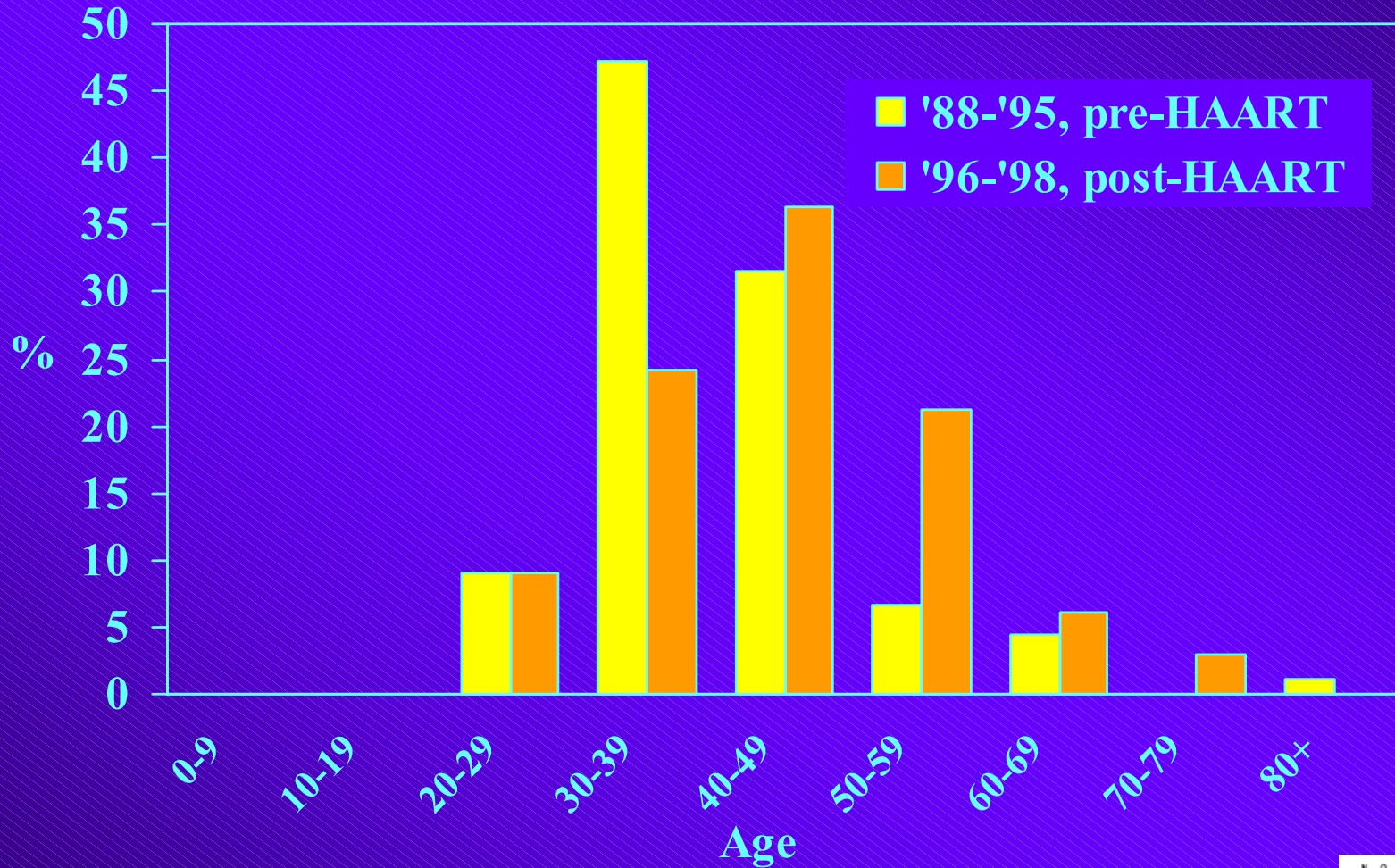
## Males, 1988-98



# HIV-Associated Hodgkin Lymphoma Males Pre- and Post-HAART

Time Period	HIV-pos		HIV-neg	
	n	%	n	%
1988-95 (pre-HAART)	89	13	616	87
1996-98 (HAART era)	33	12	233	88

# HIV-positive Hodgkin Lymphoma, Males





# HIV-positive Hodgkin Lymphoma Males Pre- and Post-HAART

Race/Ethnicity	%	
	1988-95	1996-98
White	74	67
Black	16	6
Hispanic*	8	27
Asian/Other	2	-

\* Significantly different at  $p \leq 0.05$



# HIV-positive Hodgkin Lymphoma Males

## Pre- and Post-HAART

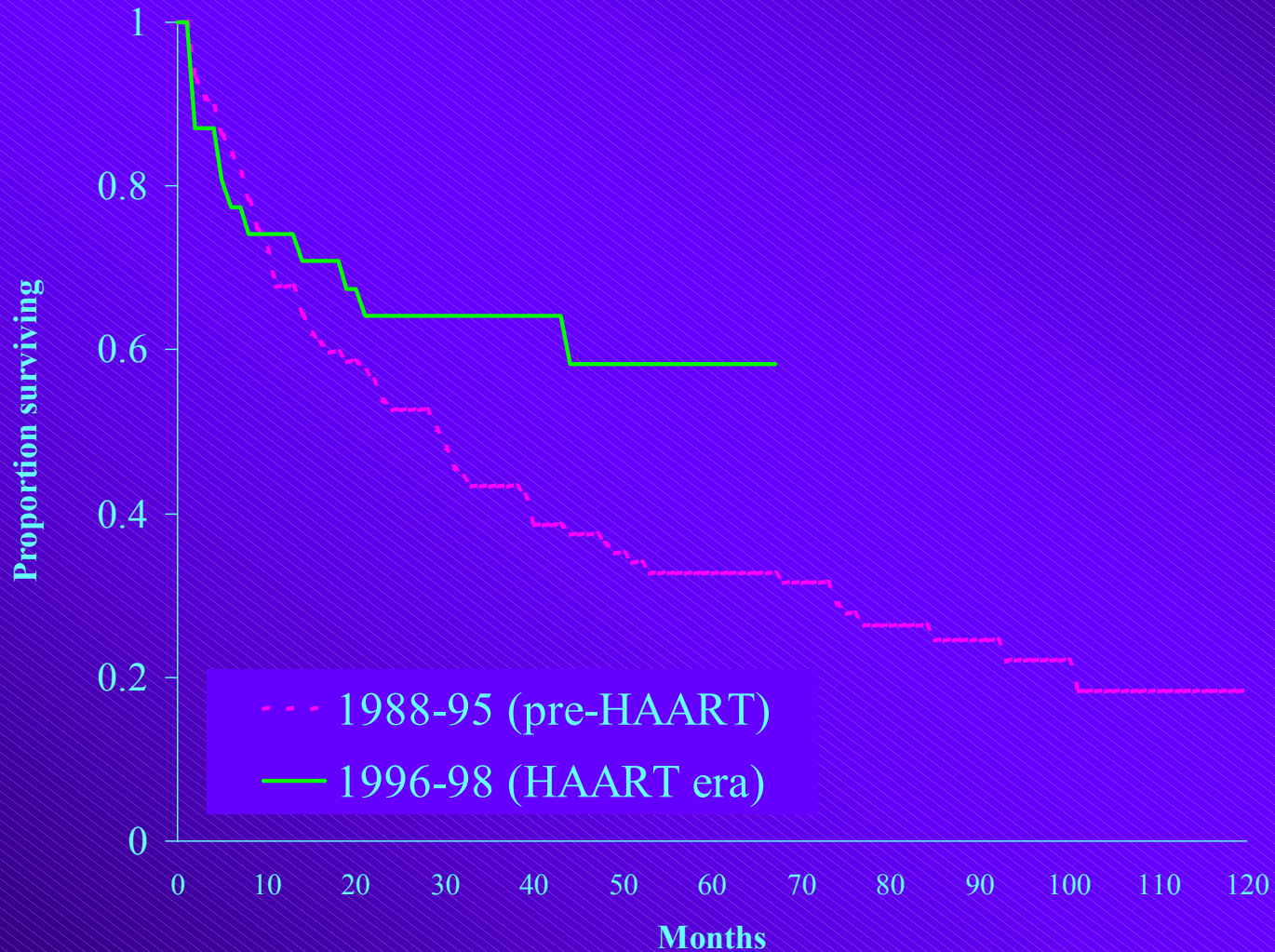
	%	
	1988-95	1996-98
<b>B-symptoms†</b>	80	70
<b>Extra-nodal‡</b>	68	63
<b>Stage III-IV disease*</b>	87	70

† Missing for n=25 ‡ Missing for n=10

\* Significantly different at  $p \leq 0.05$

# Overall Survival, Males

## Hodgkin Lymphoma, 1988-95, 1996-98



# HIV-positive Hodgkin Lymphoma Males

## Pre- and Post-HAART

%

	1988-95	1996-98
<b>Histologic subtype</b>		
Nodular Sclerosis	28	42
Mixed Cellularity	34	24
Nod. Lymph. Predomin		
Lymph. Depletion	9	6
Not otherwise specified	28	27
<b>EBV-positive*</b>	<b>87</b>	<b>91</b>

\* Based on 57 of 111 1988-97 patients



# Study Strengths

- Taken advantage of HIV/AIDS data in regional cancer registry
- First detailed surveillance of HIV-associated Hodgkin lymphoma
  - Regional
  - Population-based

# Study Limitations

- Lack of validation of HIV identification method
- Abstracted medical record data for clinical characteristics
- No individual data on use of HAART
- EBV information on a proportion of patients

# Conclusions

- Consistent findings for HIV-positive Hodgkin lymphoma:
  - Late-stage presentation
  - B-symptoms
  - Non-nodular sclerosis histology
  - Poorer survival
  - Strong association with EBV

# Conclusions

- Impact of HIV on regional incidence rates
  - Reflects characteristics of regional HIV population
  - Importance of considering HIV-related disease in geographic variation
- HAART:
  - Less aggressive
  - Still associated with EBV