

Trends in primary central nervous system lymphoma incidence and survival in the U.S.

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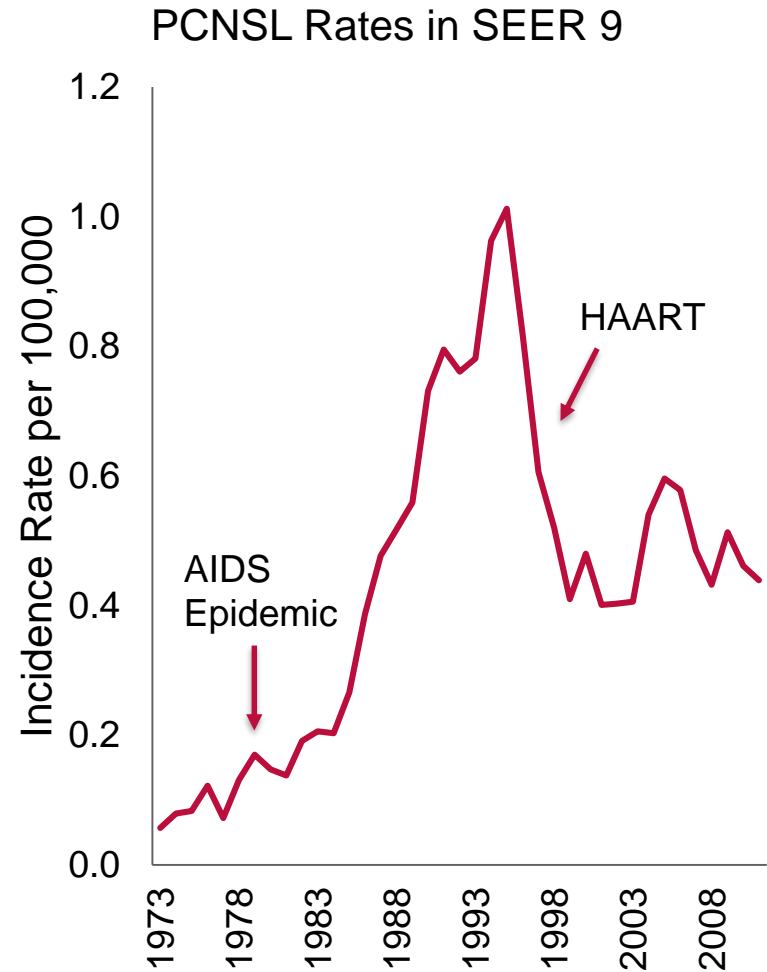
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Primary central nervous system (CNS) lymphoma

- Incidence rate: 7 per million in the U.S.
- Risk increases strongly with immune suppression
 - HIV-infected people: 50-fold increased risk
 - Solid organ transplant recipients: 15-fold increased risk
- Etiology may differ by immune status
 - Most immunocompromised cases are Epstein-Barr virus positive
 - Some suggest that rates of immunocompetent PCNSL are increasing

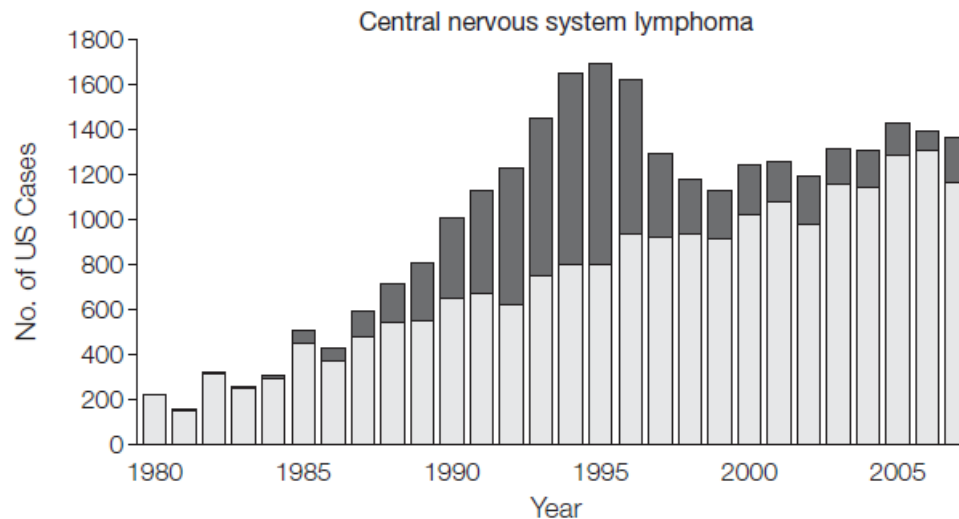
HIV and PCNSL

- Highly active antiretroviral therapy (HAART) was introduced to treat HIV in 1996
 - PCNSL rates decreased by 60% in the post-HAART era
- Impact of HIV epidemic apparent at the population level



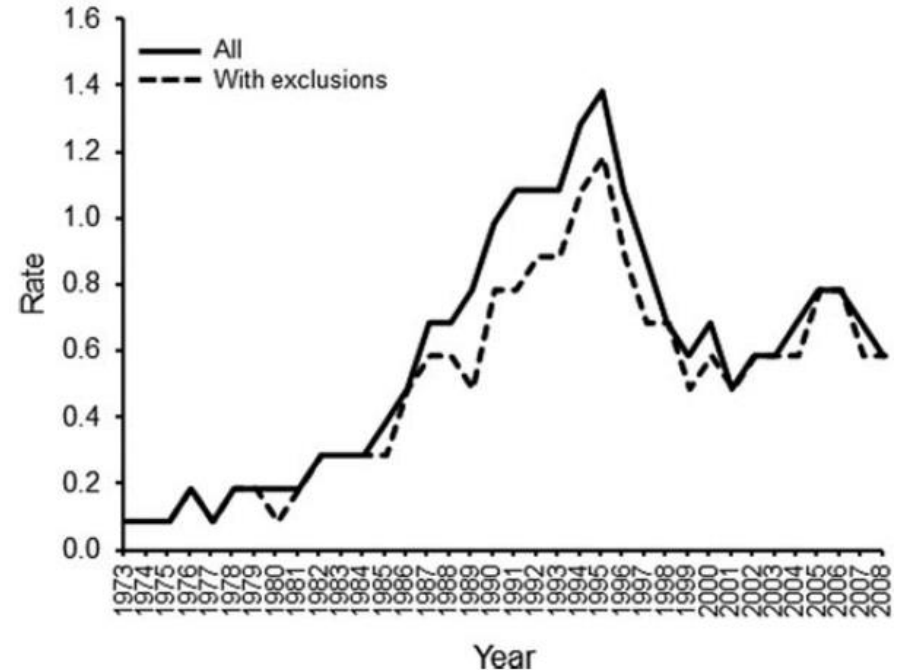
Population-level trends consist of immunocompetent and immunocompromised cases

- National PCNSL trends are highly contaminated by HIV-infected cases (1/4 of cases during 1980-2007).



Approaches used to exclude HIV-infected PCNSL cases

- Excluding populations with higher HIV prevalence
 - San Francisco area residents
 - Never married
 - <65 year-olds
- Exclude deaths due to HIV and other infectious diseases
- Approaches incompletely remove HIV-infected cases and do not address cases among transplant recipients



Study Aims

1. To quantify the fraction of PCNSL that occurred among people who are HIV-infected or transplant recipients
2. To estimate trends in immunocompetent PCNSL over time
3. To compare survival after PCNSL diagnosis among HIV-infected and HIV-uninfected cases

Data sources

- General population rates: 10 SEER registries, 1992-2011
 - CNS lymphoma defined based on SEER site recode (NHL) and topography codes C70.0-C72.9.
- HIV-infected cases: classified as HIV-infected if
 - Positive indicator of HIV status recorded at the time of diagnosis (i.e., “HIV flag”). Unknown values were classified as HIV-negative; or
 - HIV recorded as the cause of death (4.5% of unknown/negative HIV flag).

Estimation of PCNSL in transplant recipients

- Transplant-associated cases:
 - Estimated with data from the Transplant Cancer Match Study
 - Record linkage study of the Scientific Registry of Transplant Recipients (SRTR) and cancer registries
- Calculated IR for transplant-related CNS lymphoma in the TCM Study in strata defined by calendar year, race/ethnicity, sex and age.

$$\frac{\text{\# of CNS lymphoma cases linked to SRTR}}{\text{Person-years in cancer registries in TCM}}$$

- Applied stratum-specific IRs to person-years in SEER -> number of CNS lymphoma cases expected to have occurred among transplant recipients.
- Immunocompetent cases=total-(HIV-infected+transplant)

Characteristics of CNS lymphoma cases in 10 SEER registries, 1992-2011

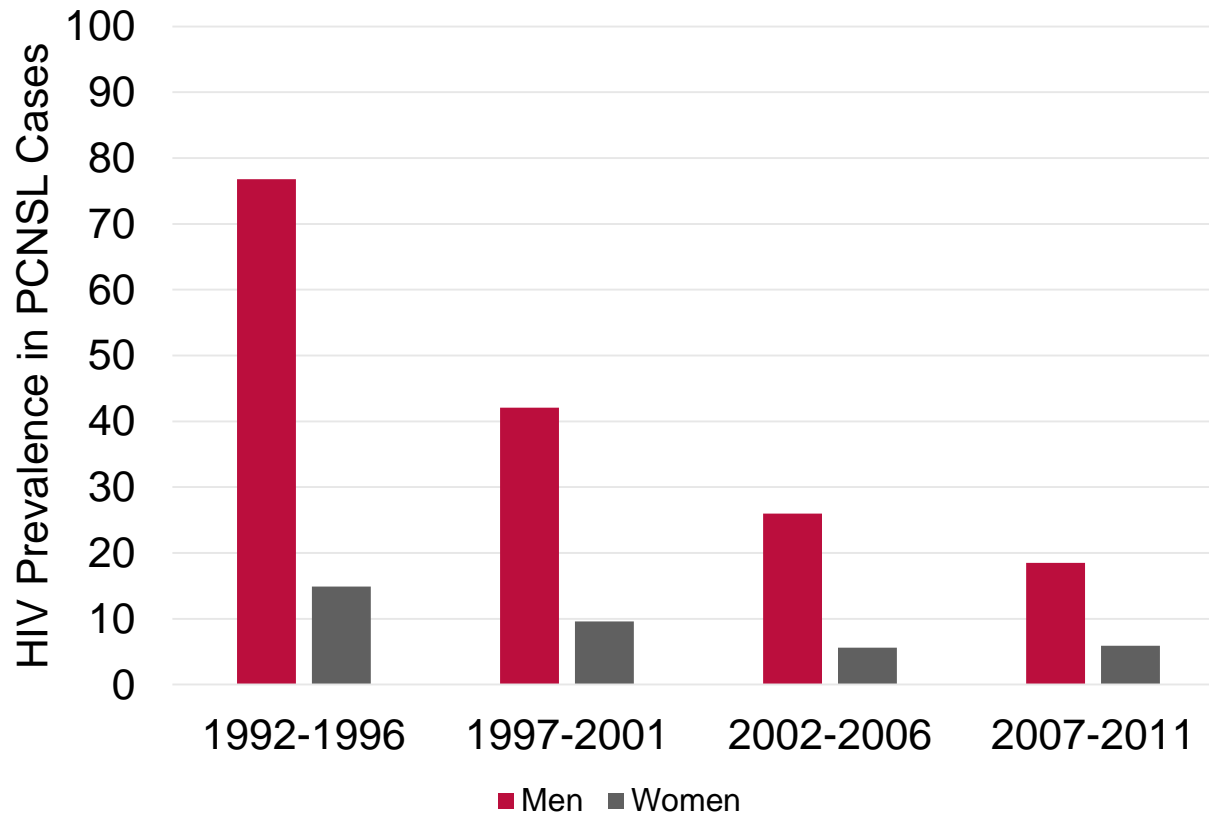
	Immunocompetent <i>N</i> (%)	HIV-infected <i>N</i> (%)	Transplant recipient <i>N</i> (%)
Total	2608	1512	38
Median age, IQR*	67 (52, 77)	37 (32, 42)	52 (42, 62)
Sex			
Male	1318 (50.5)	1388 (91.7)	22 (57.9)
Female	1290 (49.5)	124 (8.2)	16 (42.1)
Race/ethnicity			
Non-Hispanic white	1798 (69.0)	778 (51.5)	19 (50.0)
Other	810 (31.1)	734 (48.5)	19 (50.0)

- 64% B-cell, 1.0% T-cell, 4.8% NHL, unknown lineage and 30.1% NHL, NOS.
- 83.3% occurred in the brain

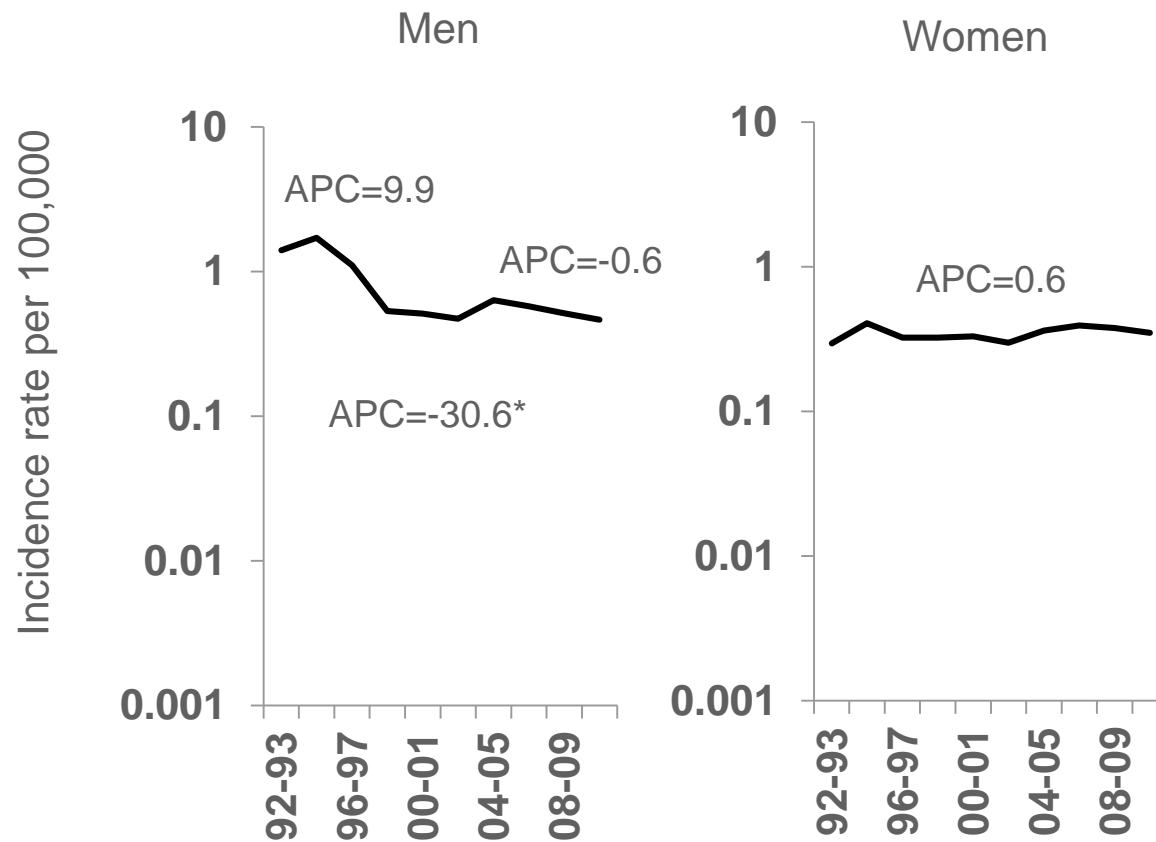
Proportion of total PCNSL cases in HIV+ and transplant populations

	Total (%)	
	HIV+	Transplant
Males and Females		
Total	36.4	0.9
Males		
Total	50.9	0.8
Age (years)		
0–19	4.5	2.6
20–39	88.5	0.5
40–64	50.6	1.2
65+	1.8	0.6
Race/ethnicity		
Non-Hispanic white	44.8	0.6
Non-Hispanic black	84.6	0.8
Hispanic	63.1	0.8
Females		
Total	8.7	1.1
Age (years)		
0–19	5.0	2.5
20–39	54.5	2.1
40–64	8.8	1.6
65+	0.7	0.6
Race/ethnicity		
Non-Hispanic white	3.3	0.9
Non-Hispanic black	44.8	1.9
Hispanic	12.6	0.7

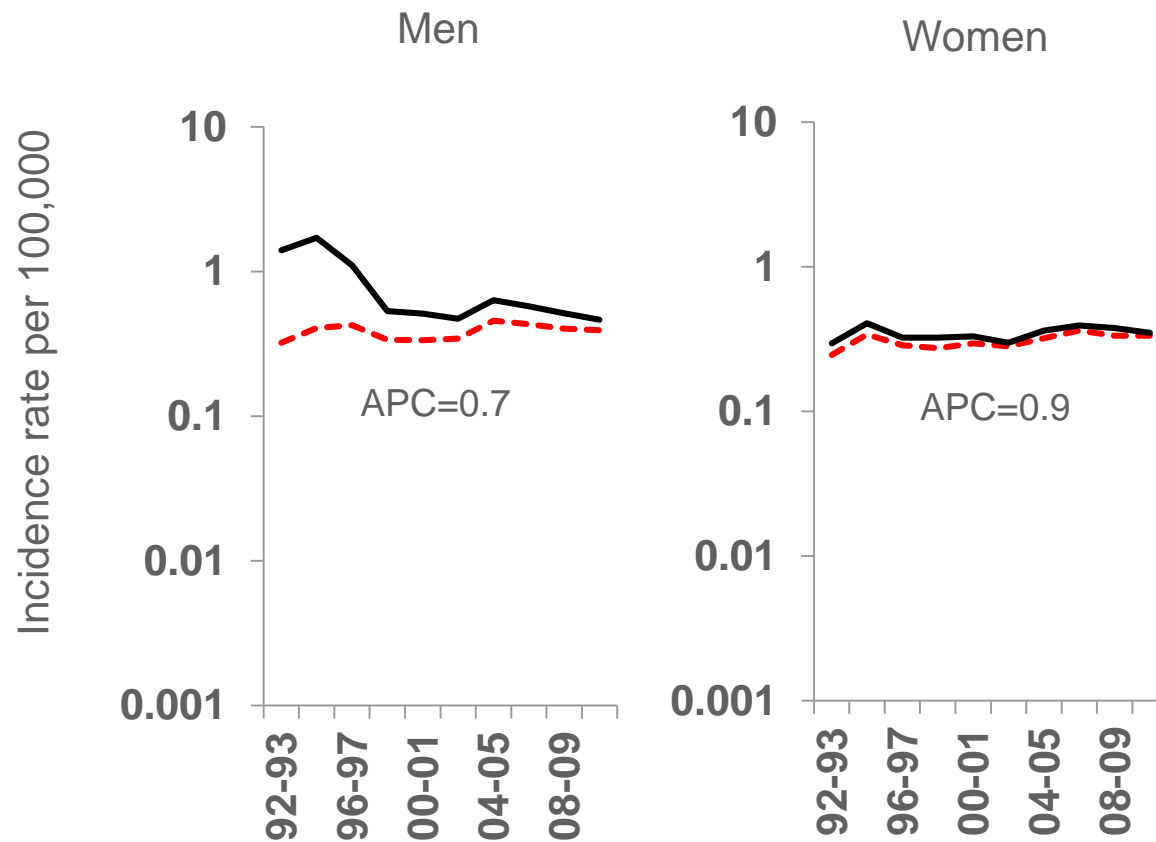
Proportion of total PCNSL cases in HIV+ populations



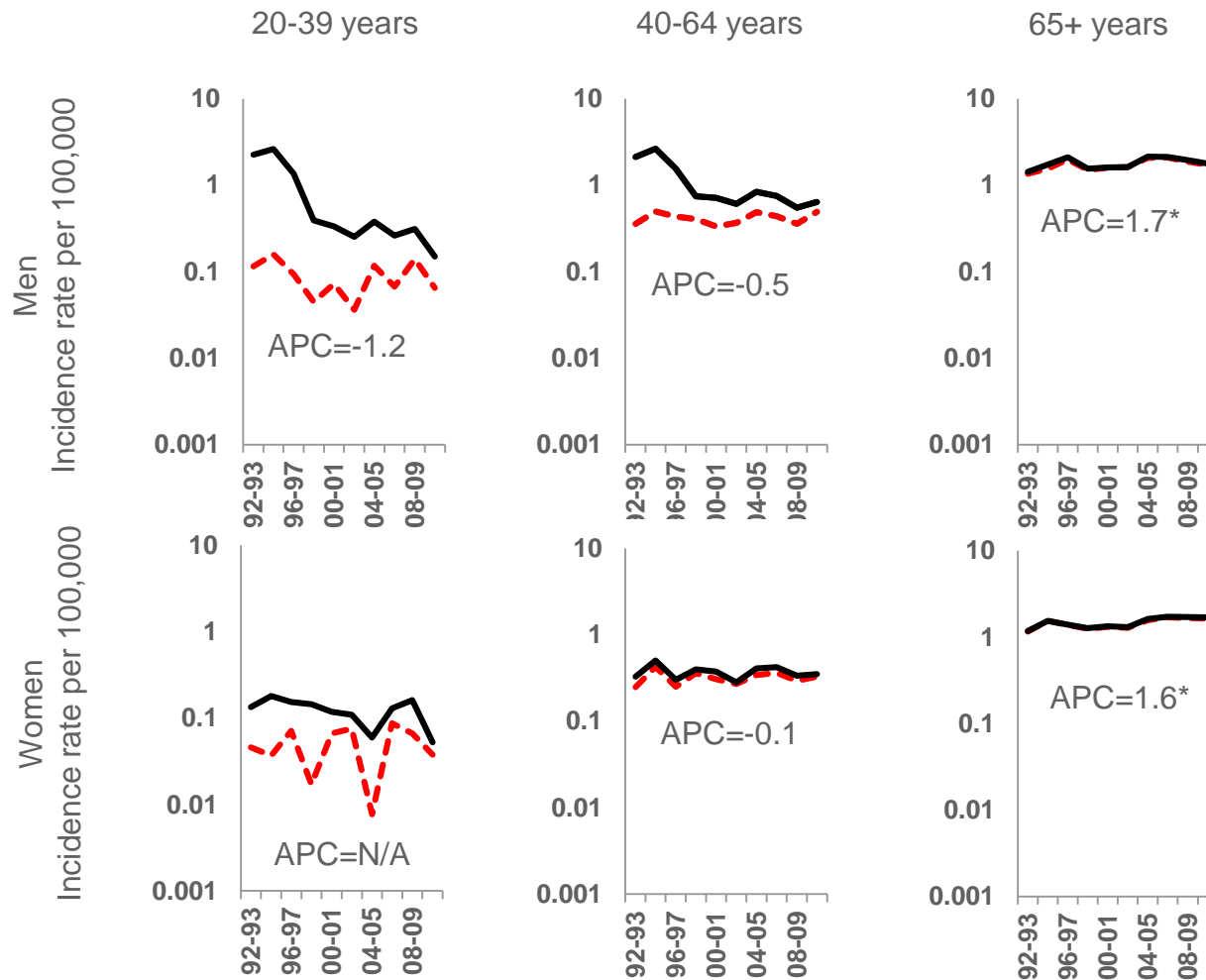
Age-standardized trends in total and immunocompetent PCNSL



Age-standardized trends in total and immunocompetent PCNSL

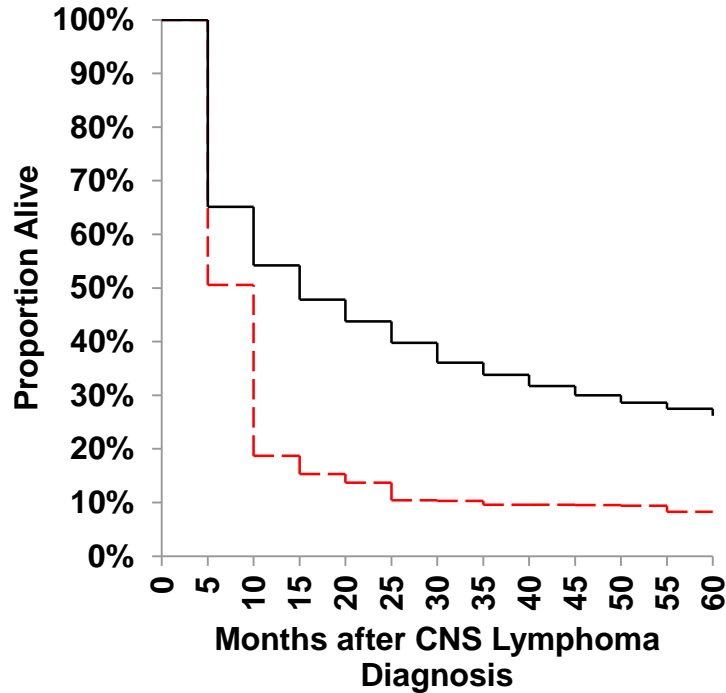


Age-standardized trends in total and immunocompetent CNS lymphoma



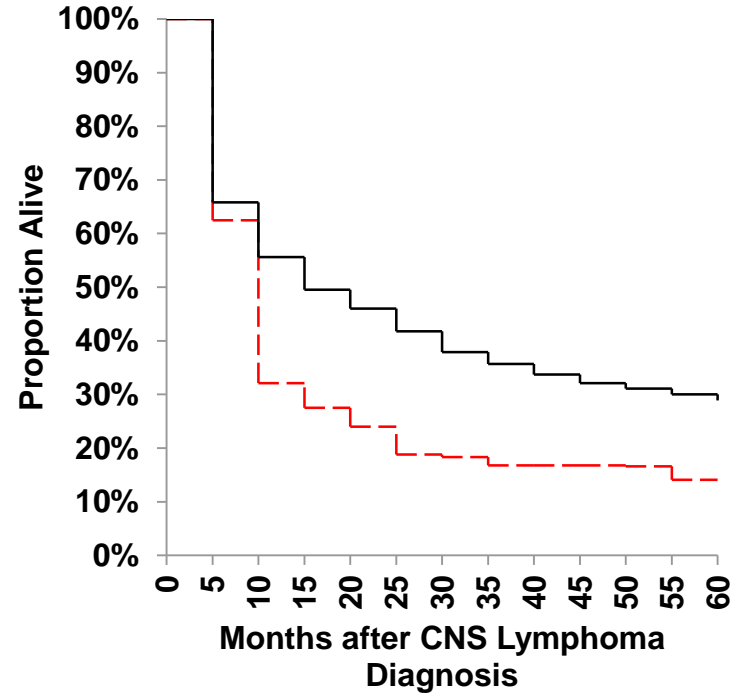
Survival after diagnosis in HIV+ and HIV- cases

1992-2011



5-year survival
HIV+: 8.3%
HIV-: 26.2%

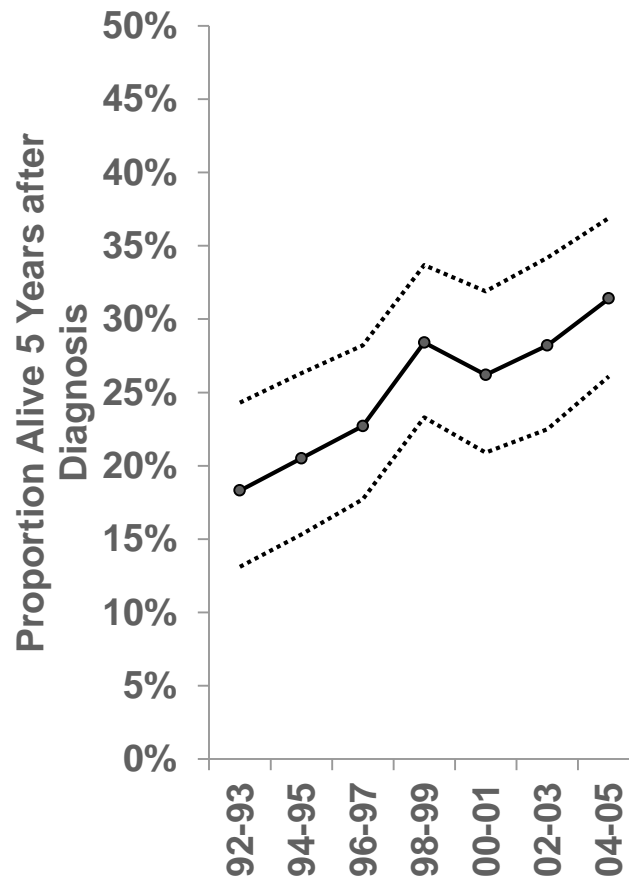
1998-2011



5-year survival
HIV+: 14.1%
HIV-: 28.9%

Changes in 5-year survival in HIV-uninfected cases

- Slight increases in 5-year survival from 20.2% in 1992-1996 to 29.2% in 2002-2006



Study Strengths

- SEER population-based data
- Estimates of transplant-associated cases
- Direct assessment of HIV status through HIV flag

Revisiting approaches used by other studies

- Exclusion of higher HIV prevalence populations in SEER
 - San Francisco registry (HIV prevalence in remaining cases: 33%)
 - Never married men and women (13.1%)
 - People aged <65 years old (1.2%)
- Exclusion of people who died from HIV and other infectious and parasitic diseases (8.0%)

Limitations

- Counts of people living with HIV in SEER areas were not available for all years from CDC
 - Denominators of immunocompetent incidence rates included HIV+ people and transplant recipients
 - Rates are slight underestimates
- HIV flag is incomplete (~50%) and has imperfect sensitivity
- We were unable to remove transplant recipients from survival estimates
 - With only 38 expected cases, transplant recipients were unlikely to have influenced survival estimates
- “Immunocompetent” cases include people with other immune conditions

Conclusions

- Rates of CNS lymphoma increased during 1992-2011 among immunocompetent 65+ year-old men and women
 - Does not reflect trends in overall NHL (rates plateaued in 2004).
 - May reflect improved imaging for diagnosis
 - However, glioma rates have remained stable over the same time period
 - May be due to increased immunosuppressive therapies for autoimmune disease among older people
- Despite recent small improvements, survival among both HIV-infected and HIV-uninfected PCNSL cases remain poor.

Collaborators

- National Cancer Institute
 - Dr. Eric Engels
 - Dr. Ruth Pfeiffer
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- Cancer registries
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