Primary central nervous system lymphoma (PCNSL) is a rare non-Hodgkin's lymphoma that occurs in immunocompetent and human immunodeficiency virus (HIV) patients. Despite treatment advances, previous reports have produced conflicting information about survival trends over time. Using the Surveillance, Epidemiology, and End Results (SEER) data, 2,557 patients diagnosed with PCNSL between 1973 and 2004 were identified and classified by HIV status. Potential predictors of survival were evaluated using log-rank tests. Hazard ratios and 95% confidence intervals (CIs) were computed using a Cox proportional hazards regression model. The cohort included 1,732 (67.7%) HIV-negative patients and 825 (32.3%) HIV-positive patients. Median overall survival was 12 months (95% CI 10, 13) among HIV-negative patients. In this group, median survival increased over time, from 7.5 months (95% CI 6, 14) for patients diagnosed in the 1970s, to 14 months (95% CI 11, 20) for patients diagnosed in the 2000s. Independent predictors of mortality included older age (hazard ratio [HR] 1.03 [95% CI 1.02, 1.03]), earlier year of diagnosis (HR 0.98 [95% CI 0.98, 0.99]), male sex (HR 1.20 [95% CI 1.08, 1.34]), married status (HR 0.70 [95% CI 0.63, 0.78]), and receipt of radiation therapy (HR 0.69 [95% CI 0.61, 0.77]). HIV positivity was a powerful adverse prognostic factor in the overall cohort (HR 4.55 [95% CI 4.01, 5.16]). Despite treatment advances, survival among PCNSL patients in the United States remains poor. However, in the subset of PCNSL patients who are HIV-negative, survival has improved over time.