Survival Variability by Race and Ethnicity in Childhood Acute Lymphoblastic Leukemia

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Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy in the United States, comprising 25% of all cancers in individuals younger than 20 years. Over the past several decades, ALL has been transformed from a uniformly fatal disease to one that is associated with a 5-year survival probability of greater than 80%. This remarkable progress is largely because of the adoption of risk-based therapy determined by patient characteristics and leukemia phenotype at disease presentation. Characteristics consistently identified from epidemiological studies to infer higher risk and require more intensive therapy include age at diagnosis (<1 year or ≥10 years), peripheral white blood cell (WBC) count greater than 50000/µL, T-cell immunophenotype, hypodiploidy, and certain chromosomal abnormalities.

Variability in survival outcome across racial and ethnic groups (hereafter referred to as race/ethnicity) also has been identified in some, but not all, clinical research. Based on a study of St Jude's Children's Research Hospital data, Pui et al concluded that survival in black children with ALL was comparable with that of white children with ALL in recent treatment eras, which are associated with more intensive, risk-based therapy. In contrast, Bhatia et al reported that black and Hispanic children enrolled in Children's Cancer Group cooperative trials in the modern treatment era had worse survival than did white children, who in turn had worse survival than children of Asian descent, even after adjusting for other risk factors. The conclusions by Bhatia et al are similar to those of Pollock et al, who found that black children and children with a Spanish surname enrolled in Pediatric Oncology Group cooperative trials had worse outcomes than white children.

Population-based studies are needed to further delineate the role of race/ethnicity in the risk classification of children with ALL. Past clinical studies were vulnerable to participation bias because they were restricted to children at a single medical center or those

See also pp 2001 and 2061.
enrolled in a clinical therapeutic trial, which generally precludes representation from the full spectrum of the disease and/or of individuals with the disease. Trial participation has been shown to vary by racial and ethnic groups. In addition, many past studies have focused primarily on the comparison of black and white children, without considering potential survival differences among Hispanic, Asian, and Native American children.

Using population-based cancer data, the purpose of this study was to compare survival rates of children with ALL within and across racial/ethnic groups and to evaluate secular trends across treatment eras.

**METHODS**

Survival data were analyzed for children diagnosed with ALL for the period 1973-1999 from the 2002 public use database of the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. Our analysis was limited to the 9 population-based SEER cancer registries comprising the states of Connecticut, Hawaii, Iowa, New Mexico, and Utah, and the metropolitan areas of San Francisco/Oakland, Calif, Detroit, Mich, Seattle/Puget Sound, Wash, and Atlanta, Ga. These 9 SEER sites have a case ascertainment of 98%, and they represent approximately 10% of the US population. Individual information about any new incident malignancy is included in the registry by state and federal mandate, regardless of therapy status or any decision to enroll in research therapeutic trials. To ensure complete ascertainment and serve public health needs, accession of basic tumor and demographic information was conducted without consent of the individual. Data were made available to the public stripped of personal identifiers.

For this analysis, we defined cases of childhood ALL as those diagnosed at younger than 20 years with a morphology code of 9821 (acute lymphoblastic leukemia) according to the *International Classification of Diseases for Oncology, Second Edition.* The disease outcome for ALL was examined as overall survival, with rates measured from the date of diagnosis to either the date of death from any cause or the date of last contact. SEER does not contain data on induction failures or relapses, which are necessary to determine event-free survival. Conditional survival probabilities for overall survival were calculated using the life-table method and illustrated using the Kaplan-Meier method. Associated 95% confidence intervals (CIs) were calculated with Greenwood's formula. Survival probabilities were calculated separately for each of the 5 categories of race/ethnicity and further stratified by age at diagnosis, treatment era, and sex. 

Race/ethnicity was, for the purpose of analysis, designated and analyzed in mutually exclusive categories of black, white, Asian/Pacific Islander, American Indian/Alaskan Native, or Hispanic. Race was classified as black, white, Asian/Pacific Islander, American Indian/Alaskan Native, or unknown from the "race record Y" variable in the SEER dataset. The SEER program assigns race/ethnicity in these categories by medical record abstraction. Asian/Pacific Islander is referred to as Asian, and American Indian/Alaskan Native is referred to as Native American, in the remainder of the text. Hispanic ethnicity was categorized using the "origin recode" variable from the SEER database, which is determined by each SEER registry using documented (medical record) self- or guardian-report of Spanish origin, or by using a computer algorithm that searches both surnames and maiden-names of the reported case to determine Spanish origin. An individual designated as Hispanic was considered in the Hispanic race/ethnicity category regardless of his or her racial background.

Age at diagnosis was analyzed as younger than 1 year, 1 to 9 years, and 10 to 19 years, consistent with the National Cancer Institute's risk classification. Peripheral WBC count at diagnosis, the other criterion necessary to assign risk, is not available from the SEER database. Consistent with previous work in this field, treatment era was divided into 3 periods: 1973-1982, 1983-1989, and 1990-1999. Although immunophenotype is a data category collected by the SEER registries, we could not effectively examine this factor in the analysis because 76% of the case records listed immunophenotype as “unspecified.”

Multivariate Cox regression analysis was used to calculate proportional hazard ratios (HRs) for relative comparisons of survival across race/ethnicity categories. The regression models were adjusted for sex, age at diagnosis, and diagnosis era so that the risk measures associated with race/ethnicity would be independent of these known ALL prognostic factors. The assumption of proportionality was tested and met in the Cox analysis (P = .51). SEER Stat Version 4.2 was used to extract case level data from the SEER Cancer Public-Use Database, 1973-1999, November 2001 Submission. SAS version 8.2 was used for data analyses. P < .05 was considered statistically significant.

**RESULTS**

**Characteristics of the Study Population**

From 1973 through 1999, 4976 cases of childhood ALL were ascertained by the SEER program. The study base for this analysis included the 4952 (99.5%) children with recorded race/ethnicity. The median follow-up was 26 years, and 1608 deaths were observed as of November 1999. The racial/ethnic distribution of the study base was 73% white, 10% Hispanic, 8% Asian, 7% black, and 1% Native American.

**Table 1** displays patient and disease characteristics by race/ethnicity. Overall, ALL cases were most likely to be male and to be diagnosed in the 1- to 9-year age range. The sex distribution was similar across racial/ethnic groups. Black children had a slightly higher frequency of being diagnosed at 10 to 19 years than did white children (33% vs 25%; P = .002). Hispanic children were slightly more likely than white children to be diagnosed at younger than 1 year (5% vs 3%; P = .02). Although not explicitly displayed in
Table 1. Characteristics of the Study Population of 4952 Children Diagnosed With Acute Lymphoblastic Leukemia (ALL)

<table>
<thead>
<tr>
<th>Age at diagnosis, y</th>
<th>Sample size</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Native American</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>162 (3)</td>
<td>111 (3)</td>
<td>15 (4)</td>
<td>10 (2)</td>
<td>0</td>
<td>26 (5)</td>
</tr>
<tr>
<td>1-9</td>
<td>3541 (72)</td>
<td>2590 (72)</td>
<td>224 (63)</td>
<td>325 (79)</td>
<td>47 (77)</td>
<td>365 (71)</td>
</tr>
<tr>
<td>10-19</td>
<td>1249 (25)</td>
<td>920 (25)</td>
<td>117 (33)</td>
<td>75 (18)</td>
<td>14 (23)</td>
<td>123 (24)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis era</th>
<th>Sample size</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Native American</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973-1982</td>
<td>1580 (32)</td>
<td>1254 (35)</td>
<td>93 (26)</td>
<td>107 (26)</td>
<td>17 (28)</td>
<td>109 (22)</td>
</tr>
<tr>
<td>1983-1989</td>
<td>1347 (27)</td>
<td>974 (27)</td>
<td>106 (30)</td>
<td>113 (28)</td>
<td>22 (36)</td>
<td>132 (26)</td>
</tr>
<tr>
<td>1990-1999</td>
<td>2025 (41)</td>
<td>1393 (38)</td>
<td>157 (44)</td>
<td>190 (46)</td>
<td>22 (36)</td>
<td>263 (52)</td>
</tr>
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</table>

<table>
<thead>
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<th>Sex</th>
<th>Sample size</th>
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<th>Black</th>
<th>Asian</th>
<th>Native American</th>
<th>Hispanic</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>2827 (57)</td>
<td>2067 (57)</td>
<td>190 (53)</td>
<td>240 (58)</td>
<td>34 (56)</td>
<td>296 (59)</td>
</tr>
<tr>
<td>Female</td>
<td>2125 (43)</td>
<td>1554 (43)</td>
<td>166 (47)</td>
<td>170 (42)</td>
<td>27 (44)</td>
<td>208 (41)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ALL phenotype</th>
<th>Sample size</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Native American</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cell</td>
<td>269 (6)</td>
<td>175 (5)</td>
<td>32 (9)</td>
<td>21 (5)</td>
<td>2 (3)</td>
<td>39 (8)</td>
</tr>
<tr>
<td>B-cell</td>
<td>862 (17)</td>
<td>581 (16)</td>
<td>56 (16)</td>
<td>87 (22)</td>
<td>17 (28)</td>
<td>121 (24)</td>
</tr>
<tr>
<td>Null cell</td>
<td>166 (3)</td>
<td>121 (3)</td>
<td>23 (6)</td>
<td>13 (3)</td>
<td>0</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>3855 (74)</td>
<td>2744 (76)</td>
<td>245 (69)</td>
<td>289 (70)</td>
<td>42 (69)</td>
<td>335 (66)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Survival status</th>
<th>Sample size</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Native American</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deceased</td>
<td>1608 (33)</td>
<td>1135 (31)</td>
<td>146 (41)</td>
<td>122 (30)</td>
<td>27 (44)</td>
<td>178 (35)</td>
</tr>
<tr>
<td>Alive</td>
<td>3344 (67)</td>
<td>2486 (69)</td>
<td>210 (59)</td>
<td>288 (70)</td>
<td>34 (56)</td>
<td>326 (65)</td>
</tr>
</tbody>
</table>

Table 1, white children comprised 79% of accrued cases during the 1973-1982 period, but only 69% during the more recent era of 1990-1999. The largest relative increase among the non-white children was observed for Hispanics, who represented 6.8% in the earliest period compared with 13.0% in the most recent.

Survival Probabilities

Table 2 shows survival probabilities at 5 and 10 years after diagnosis of ALL, conditioned on surviving and not being censored in any year before the 5- or 10-year analysis date, respectively. The overall survival percentage over the entire study period was 69% at 5 years and 64% at 10 years. It is apparent that children diagnosed with infant ALL (age <1 year) had markedly worse survival (34%) than did children diagnosed at ages 1 to 9 years (76%) or ages 10 to 19 years (52%). Female children tended to have better survival probabilities than male children. This table also demonstrates a trend of improved 5-year survival in each succeeding time period, from 55% during the 1973-1982 period to 81% in the 1990-1999 period. The overall survival percentages are strongly weighted, however, by the white children in the study. Black, Hispanic, and Native American children fared considerably worse in survival probability than did white or Asian children in almost every category.

Kaplan-Meier Survival Curves

Figure 1 and Figure 2 extend the life table analyses of survival by race/ethnicity throughout the 26-year follow-up period, stratified by time period of diagnosis and treatment using the Kaplan-Meier method. These curves illustrate the poorer survival experience of black, Hispanic, and Native American children, compared with white and Asian children, in each treatment era, including the most recent. Figure 3 concentrates on differences between white and black children by age at diagnosis. The largest racial disparity in survival is seen among those diagnosed in the 1- to 9-year age category. In fact, no statistical differences in white-black survival were observed for infant ALL (log-rank test, $P=0.78$) or for children diagnosed between ages 10 and 19 years ($P=0.26$), in contrast to those diagnosed between ages 1 and 9 years ($P<0.001$).

Hazard Ratios

After adjusting for age at diagnosis, treatment era, and sex, the risk of death among each racial/ethnic group, relative to that of white children, is shown in Table 3. Averaged over the study period of 1973-1999, Native American children had an 80% higher adjusted risk of death than did white children ($P=.002$). Black children (49%, $P<.001$) and Hispanic children (39%, $P<.001$) also had higher risks of death, compared with white children. In the period of 1990-1999, a similar risk pattern was evident. Black, Hispanic, and Native American children had increased risks of death, and Asian children had similar risk, relative to white children.

COMMENT

Contrary to other reports, the results of our study suggest that black children with ALL in the modern treatment era have worse outcome than white children, at least those who are diagnosed between the ages of 1 and 9 years when ALL incidence peaks. Our results further highlight that racial/ethnic disparities in survival outcome are apparent not only in black children, but also in Hispanic and Native American children. In contrast to the other minority groups studied, Asian children had similar survival probabilities to that of white children. We found that Native Americans had the worst ALL survival probability of any race/ethnic group, but with only 61 Native American children in the analysis this finding must be viewed with considerable caution. Still, our study is the largest to date that highlights the particularly poor prognosis for ALL experienced by Native American children. In the only other known report to focus on Native American children, Foucar et al summarized the University of New Mexico experience between 1969 and 1986, which included 28 children of Native American descent with ALL. The authors concluded that Native Americans did not differ from other ethnic groups in terms of clinical and disease features.
Customized therapy based on risk stratification is a central strategy that has led to substantially improved outcomes for children diagnosed with ALL. However, because of the conflicting evidence and uncertainty of the importance, clinical therapeutic protocols have not considered race or ethnicity in risk stratification algorithms for treatment modality. This study examined ALL survival patterns across race/ethnicity groups using population-based data over the longest study period to date. These data provide a better reflection of the full disease spectrum of ALL, and children with ALL, and avoid the limitations inherent in specialized clinical populations who are enrolled in therapeutic trials.

The inclusion of all newly diagnosed ALL cases is particularly critical when examining racial and ethnic differences because participation in clinical trials varies by this factor. According to Bhatia et al,7 74% of Hispanic children, 51% of Asian children, and only 36% of black children were enrolled in the Children’s Cancer Group cooperative trials for ALL. In contrast, 60% of white children participated in these trials. Pollock et al8 reported the

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Table 2. Survival Probabilities Among the Study Population of 4952 Children Diagnosed With Acute Lymphoblastic Leukemia

<table>
<thead>
<tr>
<th>Survival Probability (95% Confidence Interval)</th>
<th>All Children Combined</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Native American</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>5-Year Survival</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>0.69 (0.67-0.70)</td>
<td>0.70 (0.69-0.72)</td>
<td>0.57 (0.52-0.63)</td>
<td>0.71 (0.67-0.76)</td>
<td>0.54 (0.41-0.67)</td>
<td>0.63 (0.58-0.68)</td>
</tr>
<tr>
<td>Age at diagnosis, y&lt;1</td>
<td>0.34 (0.26-0.41)</td>
<td>0.32 (0.23-0.41)</td>
<td>0.26 (0.04-0.49)</td>
<td>0.53 (0.19-0.88)</td>
<td>NA</td>
<td>0.41 (0.22-0.61)</td>
</tr>
<tr>
<td>1-9</td>
<td>0.76 (0.74-0.77)</td>
<td>0.79 (0.76-0.80)</td>
<td>0.65 (0.59-0.72)</td>
<td>0.77 (0.72-0.82)</td>
<td>0.61 (0.46-0.76)</td>
<td>0.71 (0.66-0.76)</td>
</tr>
<tr>
<td>10-19</td>
<td>0.52 (0.49-0.55)</td>
<td>0.54 (0.51-0.57)</td>
<td>0.46 (0.36-0.56)</td>
<td>0.50 (0.37-0.62)</td>
<td>0.32 (0.06-0.57)</td>
<td>0.45 (0.36-0.54)</td>
</tr>
<tr>
<td>Diagnosis era 1973-1982</td>
<td>0.55 (0.53-0.58)</td>
<td>0.56 (0.53-0.59)</td>
<td>0.43 (0.33-0.53)</td>
<td>0.61 (0.52-0.70)</td>
<td>0.47 (0.23-0.71)</td>
<td>0.52 (0.43-0.62)</td>
</tr>
<tr>
<td>1983-1989</td>
<td>0.69 (0.67-0.71)</td>
<td>0.73 (0.70-0.76)</td>
<td>0.50 (0.41-0.66)</td>
<td>0.69 (0.61-0.78)</td>
<td>0.45 (0.25-0.66)</td>
<td>0.59 (0.51-0.68)</td>
</tr>
<tr>
<td>1990-1999</td>
<td>0.81 (0.79-0.83)</td>
<td>0.84 (0.82-0.86)</td>
<td>0.75 (0.67-0.83)</td>
<td>0.81 (0.73-0.88)</td>
<td>0.72 (0.51-0.93)</td>
<td>0.72 (0.66-0.78)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.66 (0.64-0.67)</td>
<td>0.67 (0.65-0.69)</td>
<td>0.56 (0.48-0.64)</td>
<td>0.67 (0.60-0.73)</td>
<td>0.54 (0.26-0.71)</td>
<td>0.61 (0.55-0.67)</td>
</tr>
<tr>
<td>Female</td>
<td>0.72 (0.70-0.74)</td>
<td>0.74 (0.72-0.76)</td>
<td>0.59 (0.51-0.67)</td>
<td>0.78 (0.71-0.85)</td>
<td>0.55 (0.34-0.75)</td>
<td>0.66 (0.58-0.73)</td>
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<tr>
<td><strong>10-Year Survival</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>0.64 (0.62-0.65)</td>
<td>0.66 (0.64-0.67)</td>
<td>0.54 (0.48-0.60)</td>
<td>0.67 (0.61-0.71)</td>
<td>NA</td>
<td>0.58 (0.53-0.63)</td>
</tr>
<tr>
<td>Age at diagnosis, y&lt;1</td>
<td>0.30 (0.23-0.38)</td>
<td>0.29 (0.19-0.38)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>0.33 (0.12-0.54)</td>
</tr>
<tr>
<td>1-9</td>
<td>0.71 (0.70-0.73)</td>
<td>0.73 (0.71-0.75)</td>
<td>0.63 (0.55-0.69)</td>
<td>0.72 (0.67-0.78)</td>
<td>NA</td>
<td>0.66 (0.60-0.71)</td>
</tr>
<tr>
<td>10-19</td>
<td>0.47 (0.44-0.50)</td>
<td>0.49 (0.45-0.52)</td>
<td>0.43 (0.33-0.54)</td>
<td>0.44 (0.32-0.57)</td>
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<td>0.43 (0.33-0.52)</td>
</tr>
<tr>
<td>Diagnosis era 1973-1982</td>
<td>0.50 (0.48-0.53)</td>
<td>0.51 (0.49-0.54)</td>
<td>0.39 (0.29-0.49)</td>
<td>0.53 (0.44-0.63)</td>
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<tr>
<td>1983-1989</td>
<td>0.65 (0.63-0.68)</td>
<td>0.69 (0.66-0.72)</td>
<td>0.50 (0.40-0.59)</td>
<td>0.67 (0.58-0.76)</td>
<td>NA</td>
<td>0.55 (0.48-0.63)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.61 (0.59-0.63)</td>
<td>0.62 (0.60-0.65)</td>
<td>0.52 (0.44-0.60)</td>
<td>0.60 (0.54-0.68)</td>
<td>NA</td>
<td>0.55 (0.49-0.62)</td>
</tr>
<tr>
<td>Female</td>
<td>0.68 (0.66-0.71)</td>
<td>0.70 (0.67-0.72)</td>
<td>0.57 (0.49-0.65)</td>
<td>0.76 (0.69-0.83)</td>
<td>NA</td>
<td>0.63 (0.56-0.71)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

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Figure 1. Overall Kaplan-Meier Survival Curves by Race

Survival probabilities were significantly different across strata of race/ethnicity for each time period (log-rank χ² test: P<.001).
The rate of enrollment by children with a Spanish surname in Pediatric Oncology Group trials varied by the individual trial. Because the reason for non-entry on clinical trials is not known, previous studies based on cooperative trials cannot directly take into account disproportionate enrollment by race/ethnicity.

Past authors have commented on the poorer prognosis experienced by black children with ALL. Past authors have commented on the poorer prognosis experienced by black children with ALL.5,8,10,26-29 In a report of a single-institution experience at St Jude’s Hospital, Pui et al4 concluded that black children diagnosed between 1984 and 1992 achieved survival rates comparable with their white counterparts. The authors concluded this was because of improved access to health care and more aggressive therapy in the more recent treatment era. Our analysis confirms that black children have demonstrated improved survival with more contemporary therapy. However, our data, continuing into the 1990-1999 diagnostic era, suggest that black children diagnosed between the ages of 1 and 9 years still have a poorer overall survival outcome than do white children of similar age. Our conflicting findings are possibly due to the specialized referral base of the unique practice of St Jude’s Hospital, which attracts patients from an 8-state area and provides therapy at no cost to the patient’s family.

Our finding of worse outcome in black children compared with white children in the recent treatment era (adjusted HR, 1.50; 95% CI, 1.0-2.2; \( P = .03 \)) is consistent with the results of 2 recent studies based on Children’s Cancer Group and Pediatric Oncology Group Cooperative trials. These studies had the advantage over ours of adjusting for many of the poor prognosis patient and leukemia characteristics thought to occur disproportionately among black children, but still yielded similar magnitudes of risk. Bhata et al reported a relative risk (HR) of 1.4 (95% CI, 1.1-1.6) for black children compared with white children, after adjusting for age at diagnosis, WBC count, initial platelet count, sex, liver size, spleen size, and treatment era. Pol-

![Figure 2. Kaplan-Meier Survival Curves by Race and Era of Treatment](image-url)

Survival probabilities were significantly different across strata of race/ethnicity for each time period (log-rank \( \chi^2 \) test: \( P<.001 \)).
lock et al calculated an almost identical HR of 1.42 (95% CI, 1.12-1.80) for black children compared with white children after adjusting for WBC at diagnosis, age at diagnosis, sex, deviation from treatment protocol (as a surrogate for noncompliance), treatment era, and DNA index. These similar results across 3 studies, including our own, suggest that unidentified factors exist in the tumor biology or treatment response of black children that confers worse outcome. Previous investigators have speculated that differences in pharmacokinetics could relate to an altered drug metabolism with lower effective chemotherapy levels in black children. 

If this is the case, the lower effective chemotherapy levels in late to an altered drug metabolism with differences in pharmacokinetics could re-activate for noncompliance), treatment from treatment protocol (as a surrogate for noncompliance), treatment era, and DNA index. These similar results across 3 studies, including our own, suggest that unidentified factors exist in the tumor biology or treatment response of black children that confers worse outcome. Previous investigators have speculated that differences in pharmacokinetics could relate to an altered drug metabolism with lower effective chemotherapy levels in black children. 

If this is the case, the more aggressive therapy of the most recent treatment era has not entirely overcome these differences.

Our results showing comparable survival between Asian and white children differ from those of Bhatia et al, who observed that Asians had superior survival. This difference in our findings remains unexplained. However, our sample is based on a larger proportion of Asians in the study base (8% vs 2%). Studies based in Great Britain, where Asians from the Indian subcontinent comprise about 10% of the minority population, also suggest that Asians and whites have similar ALL survival in the recent treatment era. 

Several limitations of this study must be considered. Even though there is 98% ascertainment at the participating SEER sites, the selected sites only comprise 10% of the US data base. In addition, we used SEER data to determine mutually exclusive categories of race/ethnicity. Race/ethnicity is not really a mutually exclusive variable. Persons may have mixed racial/ethnic ancestry. In addition, the SEER program uses Spanish surnames to define Spanish ethnicity, an approach that is not without error. Not every person of Latin or Hispanic origin has a Spanish sounding surname and not all persons with Spanish or Spanish sounding surnames are of Latin or Hispanic ethnicity.

Data regarding certain patient and disease characteristics were not available.

The SEER program does not ascertain peripheral WBC count at diagnosis, hepatosplenomegaly, cerebrospinal disease, cytogenetic/molecular features, or compliance with therapy. Therefore, we could not adjust for these factors, which are known to be associated with prognosis and may vary with race/ethnici-

**Figure 3. Kaplan-Meier Survival Curves by Age Group at Diagnosis for White and Black Children**

<table>
<thead>
<tr>
<th>Age at Diagnosis</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 y</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-9 y</td>
<td>0.80</td>
<td>0.75</td>
</tr>
<tr>
<td>10-19 y</td>
<td>0.65</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Survival probabilities significantly differed between black children and white children among those aged 1 to 9 years at diagnosis (log rank χ² test: *P*<.001), but not among those diagnosed younger than 1 year (*P*=.78) or 10 to 19 years (*P*=.26).

**Table 3. Multivariate Cox Regression Analysis for Risk of Death, by Diagnosis Period**

<table>
<thead>
<tr>
<th>Diagnosis Years</th>
<th>HR (95% CI)</th>
<th><em>P</em> Value</th>
<th>HR (95% CI)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973-1999 (N = 4952)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.49 (1.2-1.8)</td>
<td>&lt;.001</td>
<td>1.50 (1.0-2.2)</td>
<td>.03</td>
</tr>
<tr>
<td>Asian</td>
<td>1.10 (0.9-1.3)</td>
<td>.32</td>
<td>1.28 (0.9-1.9)</td>
<td>.21</td>
</tr>
<tr>
<td>Native American</td>
<td>1.80 (1.2-2.6)</td>
<td>.002</td>
<td>1.90 (0.8-4.6)</td>
<td>.16</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.39 (1.2-1.6)</td>
<td>&lt;.001</td>
<td>1.83 (1.4-2.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>4.00 (3.3-4.9)</td>
<td>&lt;.001</td>
<td>5.34 (3.4-8.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1-9</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>10-19</td>
<td>2.17 (1.9-2.4)</td>
<td>&lt;.001</td>
<td>2.91 (2.3-3.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.26 (1.1-1.4)</td>
<td>&lt;.001</td>
<td>1.31 (1.0-1.7)</td>
<td>.02</td>
</tr>
<tr>
<td>Female</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis era</th>
<th>HR (95% CI)</th>
<th><em>P</em> Value</th>
<th>HR (95% CI)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1973-1982</td>
<td>2.69 (2.4-3.1)</td>
<td>&lt;.001</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1983-1989</td>
<td>1.69 (1.5-1.9)</td>
<td>&lt;.001</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1990-1999</td>
<td>Reference</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio; NA, not applicable.

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of the pharmacokinet- 
ics of chemotherapeutic agents and de- 
tection of polymorphisms for drug de-
toxification and resistance genes. 
Greater attention must be given to 
learning more about the experience of 
nonwhite patients. Depending on the 
results of such studies, it may be rea-
sonable to consider race/ethnicity in 
deciding therapeutic regimens for child-
hood ALL.

Author Contributions: Study concept and design: 
Kadan-Lottick, Gurney. 
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Drafting of the manuscript: Kadan-Lottick, Ness, Bhatia, 
Gurney. 
Statistical expertise: Kadan-Lottick, Ness, Gurney. 
Administrative, technical, or material support: Gurney. 
Study supervision: Kadan-Lottick, Bhatia, Gurney.

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