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Background and Objectives. Survival after childhood cancer has shown a steady improvement from the late 1970s in most developed countries. Since 1967 the Childhood Cancer Registry of Piedmont has been collecting cases of malignant tumor, diagnosed in children aged 0-14 years, living in Piedmont. This work aims to update survival rates to 31.12.2000.

Design and Methods. This study includes 2,678 children diagnosed between 1970-98. Vital status was assessed at the Registry Office of the town of residence. One thousand four hundred ninety cases were reported to be alive, 1170 dead and for 18 the status was unknown. Thirty-three cases registered with a death certificate only were excluded. Completeness of follow-up was 99.3%. All tumor types were classified according to the Birch-Marsden classification. Histologic verification was available for 94.4% of cases.

Results. Survival at 5 years increased over the period 1970-98 for all tumor types with a statistically significant trend over time (p<0.0001). The 5 year survival rate for acute lymphoblastic leukemia (ALL) increased steadily from 24.7% (95%CI 15.0-34.3) to 87.6% (80.9-94.3), for acute non-lymphoblastic leukemia (ANLL) from 0.0% to 38.1% (17.3-58.9), and for non-Hodgkin's lymphomas from 25.2% (0.6-49.8) to 79.7% (61.9-97.5). Five year survival rates of children with central nervous system tumors increased from 33.4% in 1970-74 to 78.5% in 1990-94 and decreased in 1995-98 to 70.9%. Age <1 year and >50,000×10⁶ cells/L at diagnosis were negative prognostic factors for ALL. Age <1 year was a favorable prognostic factor for neuroblastoma.

Interpretation and Conclusions. Survival of children with all types of tumors improved in Piedmont. This survival improvement is comparable to that reported by other European and North American population-based cancer registries.

Key words: childhood cancer, survival, prognosis, cancer registries, population-based studies.

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Survival after a childhood neoplasm has increased as a consequence of the introduction of both improved protocols and more efficient diagnostic procedures. This increase has been recorded since the early seventies in most developed countries. Positive trends in prognosis have been observed in both population-based studies and clinical trials and for almost all types of tumor. However it would be appropriate to continue survival studies in order to monitor the outcome of new treatments and update results in the cohort of children who first benefited from the new therapies.

The aims of this study, based on population data from the Cancer Childhood Registry of Piedmont (CCRP) in the period 1970-98, were: to update survival rates as of 31.12.2000, and to investigate survival time trends and the role of demographic and clinical prognostic factors. Previous CCRP reports covered children diagnosed up to 1994.

Design and Methods

Since 1967 the CCRP has provided periodic population-based estimates of incidence of cancer and survival in the childhood (age 0-14 years) population of Piedmont Region (North Western Italy) (in 1970-75 data were collected only for children resident in the province of Turin, which accounts for about half the population of Piedmont). Procedures for data collection, follow-up, classification and data processing as well as criteria for inclusion in the CCRP database have been reported elsewhere. The population decreased over the period considered in the present report (1970-1998) from approximately 800,000 in 1975-79 to approximately 500,000 in 1995-98 because of the drop in birth rate.

Cancer site, morphology and behavior were coded according to International Classification of Disease for Oncology (ICD-O) and tumor types were grouped according to Birch and Marsden. Intracranial neoplasms of benign and unspecified behavior were included; angiomias (even if intracranial) and histiocytosis X were excluded.

The database used for the present analysis was formed of 2,678 cases diagnosed during the period 01.01.1970-31.12.1998. The CCRP does in fact include 2,721 incident cases for this period, but we excluded 33 cases documented only by a death certificate, 8 second primary tumors, 1 case with missing follow-up data and 1 case of unknown tumor type; all these were excluded from the
database before survival analyses. Histologic (or cytologic) verification (HV) was available for 93.4% of cases, ranging in the major diagnostic groups from 79.5% for tumors of the central nervous system (CNS) to 99.4% in acute lymphocytic leukemia (ALL) (Table 1).

The life status of each registered case was assessed as of 31.12.2000 at the Registry Offices of the town of residence: 1,490 cases were reported to be alive (55.6%), 1,170 dead (43.7%), while status was unknown for 18 (0.6%). Survival was calculated for all major types of childhood cancer as well as for selected minor categories. Cumulative survival percentages were calculated according to Kaplan and Meier. The statistical significance of the differences in survival among periods were tested using the log-rank statistic for homogeneity and for temporal trends. p-values were considered statistically significant when <0.05. Ninety-five percent confidence intervals (95%CI) were computed for proportions and survival rates. A minimum of 50 cases for each category was the admission criterion for analysis. Details are given in the Appendix.

A multivariate Cox regression was used to compare periods of diagnosis and to investigate prognostic factors. The latter analyses were limited to selected tumor categories. The assumption of proportionality of risk of death in covariate strata was verified by plotting the cumulative hazard function. Hazard ratios (HR) by period were computed adjusting for gender and age at diagnosis, using male gender, age class 0–4 and period 1970–74 as the reference. The HR can be interpreted as a relative risk. The following prognostic factors were included in the multivariate analysis: gender, age at diagnosis and white blood cell count (WBCC). FAB morphological subgroups were included for acute non-lymphocytic leukemia (ANLL) (134 cases) and immunophenotype was considered for ALL (470 cases), limited to cases diagnosed after 1980.

Statistical analysis was performed using SAS software (Release 6.12, by SAS Institute Inc., Cary, NC, USA, 1996).

Table 1. Childhood Cancer Registry of Piedmont 1970-98– Number of cases (0-14 years) and percentages by period, vital status and histologic verification.

<table>
<thead>
<tr>
<th>Diagnostic groups</th>
<th>No. of cases</th>
<th>1970-74 %</th>
<th>1975-79 %</th>
<th>1980-84 %</th>
<th>1985-89 %</th>
<th>1990-94 %</th>
<th>1995-98 %</th>
<th>Life Status</th>
<th>LFU %</th>
<th>HV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lymphocytic leukemia (Ia+Ib)</td>
<td>700</td>
<td>11.0</td>
<td>21.6</td>
<td>19.1</td>
<td>16.1</td>
<td>17.1</td>
<td>15.0</td>
<td>38.0</td>
<td>0.3</td>
<td>99.4</td>
</tr>
<tr>
<td>Acute non-lymphocytic leukemia (Ic)</td>
<td>138</td>
<td>8.7</td>
<td>23.9</td>
<td>19.6</td>
<td>16.7</td>
<td>15.2</td>
<td>15.9</td>
<td>71.0</td>
<td>0.0</td>
<td>99.3</td>
</tr>
<tr>
<td>Hodgkin’s disease (IIa)</td>
<td>125</td>
<td>14.4</td>
<td>25.6</td>
<td>17.6</td>
<td>14.4</td>
<td>11.2</td>
<td>16.8</td>
<td>16.0</td>
<td>0.8</td>
<td>99.2</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphomas (IIb-IIc-IIId)</td>
<td>182</td>
<td>7.1</td>
<td>22.5</td>
<td>19.2</td>
<td>18.7</td>
<td>21.4</td>
<td>11.0</td>
<td>43.4</td>
<td>1.6</td>
<td>98.4</td>
</tr>
<tr>
<td>Ependimoma (IIIa)</td>
<td>66</td>
<td>6.1</td>
<td>9.1</td>
<td>24.2</td>
<td>12.1</td>
<td>24.2</td>
<td>24.2</td>
<td>50.0</td>
<td>3.0</td>
<td>98.5</td>
</tr>
<tr>
<td>Astrocytoma (IIIb)</td>
<td>222</td>
<td>9.9</td>
<td>18.5</td>
<td>14.4</td>
<td>21.2</td>
<td>19.4</td>
<td>16.7</td>
<td>32.4</td>
<td>0.0</td>
<td>95.9</td>
</tr>
<tr>
<td>Medulloblastoma (IIc)</td>
<td>112</td>
<td>9.8</td>
<td>24.1</td>
<td>21.4</td>
<td>16.1</td>
<td>16.1</td>
<td>12.5</td>
<td>65.2</td>
<td>0.9</td>
<td>98.2</td>
</tr>
<tr>
<td>Other gliomas and intracranial/intraspinal neoplasms (IIId+IIIe)</td>
<td>205</td>
<td>11.7</td>
<td>22.0</td>
<td>23.4</td>
<td>19.5</td>
<td>11.7</td>
<td>11.7</td>
<td>47.8</td>
<td>1.0</td>
<td>43.4</td>
</tr>
<tr>
<td>Sympathetic system tumors (IVA-IVb)</td>
<td>202</td>
<td>9.4</td>
<td>19.8</td>
<td>20.3</td>
<td>16.8</td>
<td>18.8</td>
<td>14.9</td>
<td>56.4</td>
<td>1.5</td>
<td>93.6</td>
</tr>
<tr>
<td>Rhabdomyosarcoma (IVA)</td>
<td>64</td>
<td>10.9</td>
<td>18.8</td>
<td>15.6</td>
<td>7.8</td>
<td>23.4</td>
<td>23.4</td>
<td>20.3</td>
<td>0.0</td>
<td>87.3</td>
</tr>
<tr>
<td>Wilms’ tumor (VIA+Vlc)</td>
<td>118</td>
<td>10.2</td>
<td>26.3</td>
<td>21.2</td>
<td>12.7</td>
<td>15.3</td>
<td>14.4</td>
<td>26.3</td>
<td>0.8</td>
<td>89.8</td>
</tr>
<tr>
<td>Osteosarcoma (Villa)</td>
<td>86</td>
<td>14.0</td>
<td>17.4</td>
<td>19.8</td>
<td>30.2</td>
<td>15.1</td>
<td>3.5</td>
<td>55.8</td>
<td>0.0</td>
<td>98.8</td>
</tr>
<tr>
<td>Ewing’s sarcoma (Viloc)</td>
<td>54</td>
<td>5.6</td>
<td>13.0</td>
<td>25.9</td>
<td>22.2</td>
<td>18.5</td>
<td>14.8</td>
<td>51.9</td>
<td>0.0</td>
<td>98.1</td>
</tr>
<tr>
<td>Rhabdomyosarcoma (IVA)</td>
<td>85</td>
<td>4.7</td>
<td>21.2</td>
<td>22.4</td>
<td>22.4</td>
<td>18.8</td>
<td>10.6</td>
<td>41.2</td>
<td>2.4</td>
<td>98.8</td>
</tr>
<tr>
<td>Fibrosarcoma (Ib-Iic)</td>
<td>70</td>
<td>20.0</td>
<td>20.0</td>
<td>10.0</td>
<td>20.0</td>
<td>20.0</td>
<td>10.0</td>
<td>47.1</td>
<td>0.0</td>
<td>94.3</td>
</tr>
<tr>
<td>Other types</td>
<td>249</td>
<td>21.7</td>
<td>21.3</td>
<td>16.8</td>
<td>15.3</td>
<td>14.9</td>
<td>12.4</td>
<td>51.8</td>
<td>0.4</td>
<td>94.4</td>
</tr>
<tr>
<td>All tumor types</td>
<td>2678</td>
<td>11.4</td>
<td>21.1</td>
<td>18.9</td>
<td>17.3</td>
<td>17.0</td>
<td>14.2</td>
<td>43.7</td>
<td>0.7</td>
<td>93.4</td>
</tr>
</tbody>
</table>

LFU: lost to follow-up; HV: histologic verification.; *1970-74: limited to residents in the Turin province.
Results

Survival description and time trends

For all childhood malignancies, survival at 5 years from diagnosis increased over the study period with a clear temporal trend according to periods of diagnosis (log-rank test for trend: $p<0.0001$) (Table 2).

For both ALL and ANLL, the increase of survival over periods of diagnosis was highly significant. ALL survival at 5 years improved between 1970-74 and 1975-79 from 24.7% (95% CI: 15.0-34.3) to 55.6% (47.7-63.6) and reached 87.6% (80.9-94.3) in 1995-98 (Table 2, Figure 1A). The probability of death for children diagnosed in 1995-98 was about one tenth of that for children diagnosed in 1970-74 (Table 3). The trend was statistically significant in all age classes ($p<0.001$), except in the age group of 10-14-year olds in whom the trend was of borderline statistical significance ($p=0.088$). ANLL survival at 5 years increased from 0.0% in 1970-74 to 38.1% (95% CI: 17.3-58.9) in 1990-94, reaching 63.6% (43.5-83.7) in 1995-98 (Table 2, Figure 1b).

For Hodgkin's disease (HD), survival at 10 years was already high in 1970-1974 (66.7%; 95% CI: 51.5-92.9) and improved further in 1975-79 (87.5%; 95% CI: 76.0-99.0), stabilizing thereafter (Table 2, Figure 1c). For non-Hodgkin's lymphomas (NHL) survival at 5 years rose steadily from 25.2% (95% CI 0.6-49.8) in 1970-74 to 79.7% (61.9-97.5) in 1995-1998 (Table 2, Figure 1d).

Unlike most other cancer types, CNS tumors did not show the same constant trend. Survival rates at 5 years improved by approximately 10% in each period compared to the previous one until 1994 (from 33.4% during 1970-74 to 78.5% in 1990-94), but decreased to 70.9% in 1995-98. Nevertheless, the
test for linear trend computed over the entire study period (1970–98) was statistically significant (p < 0.0001). The 95% CI were 70.6–86.5 for 1990–94 and 60.6–81.2 for 1995–98; the difference between periods was not statistically significant (Table 2, Figure 1c).

The trend by period of diagnosis was statistically significant in all age classes (p < 0.01). Relative to children in age class 1–4 years old, the risk of death for children aged 5–9 and 10–14 years old was more than doubled. The decrease observed in the period 1990–94 may be explained as a random fluctuation due to the small number of cases.

Survival of children with osteosarcoma increased from 16.7% at 5 years (95% CI: 0.0–37.8) in 1970–74 to 61.5% (35.1–88.0) in 1990–94 (Table 2). The log-rank test for differences according to period of diagnosis was statistically significant (p = 0.0003) and 5-year survival more than doubled. The decrease observed in the period 1990–94 may be explained as a random fluctuation due to the small number of cases.

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Prognostic factors
The role of prognostic factors was examined in more detail for ALL, ANLL and SST. Regarding ALL (Table 4), the risk of death (hazard ratios - HR) for children aged < 1 year and for females were, respectively, 2.75 (1.43-5.28) and 0.85 (0.66-1.08) relative, respectively, to the 1–4-year old age class and to males. For children diagnosed during 1980–98, age less than 1 year or over 10 years and WBCC > 50 $\times 10^9$ cells/L at diagnosis were negative prognostic
Population-based survival after childhood cancer: report from the Childhood Cancer Registry of Piedmont

Factors with respect to the 1-4-year olds and those with a lower WBC. Period of diagnosis remained the most important predictor of survival. The immunophenotype did not contribute significantly to the fit of the model and was not included in the final one. Multivariate analysis for factors predicting survival in ANLL included period of diagnosis, age, WBC and morphologic subtype. The analysis showed a lower HR (corresponding to a better prognosis) for cases diagnosed after 1980 and a higher HR for children with a WBC > than 50 × 10⁶ cells/L at diagnosis (the reference was the period from 1970-74 and a lower WBC). Age class and morphologic subtype did not contribute to the model fit. However, children with M3, M4, M5 and not otherwise specified ANLL had a higher risk of death (although this was not statistically significant) than children with M1-M2 ANLL (Table 5). The role of gender was opposite for HD and NHL: girls with HD had a 2.88 (1.02-8.16) times higher risk of death than males, whereas if they had NHL, their risk of death was 0.52 (0.29-0.96) that of their male counterparts. Regarding SST, multivariate survival analysis, including period of diagnosis, gender and age group, showed a statistically significant decrease in risk of death for the period of diagnosis (from 0.53 in 1975-79 to 0.26 in 1995-98 compared to 1970-74) and a poor outcome for older children: relative to children aged 1-4 years old, the risk of death was 0.42 (0.24-0.72) for children diagnosed before the first year of age and 2.41 for children aged 5 and older. The trend in decreased risk of death over time was statistically significant (p<0.001) in all age classes.

Females affected by osteosarcoma had a lower survival rate and their risk of death relative to that of males was 2.00 (95% CI 1.08-3.70) while for Ewing's sarcoma neither gender nor age at diagnosis resulted to be significant prognostic factors.

**Discussion**

The analysis of the CCRP survival data confirmed the positive trend for almost all types of tumors, already shown in other developed countries from both hospital and population-based studies.16-30 The improved survival in Piedmont was particularly evident in the 1970s and continued constantly up to 1998. The largest survival improvements were observed in the categories that previously had a poor prognosis, such as ANLL or Ewing's sarcoma. There was little room for further improvement in some types of cancer (e.g. HD, retinoblastoma) that already had high survival rates. The significant improvement in outcome for children with ALL may be due to bet-

| Table 4. Multivariate survival analyses of ALL cases diagnosed in 1980-98 in Piedmont. The Hazard Ratio (HR) of death and the corresponding 95% confidence interval (95% CI) were computed according to the Cox model including: period of diagnosis, gender, age at diagnosis and white blood cell (WBC) count. |
|---|---|---|---|
| N. of cases | HR | 95% CI |
| Period of diagnosis | | |
| 1980-84 | 134 | 1* | -- |
| 1985-89 | 111 | 0.43 | 0.27-0.68 |
| 1990-94 | 120 | 0.44 | 0.28-0.70 |
| 1995-98 | 105 | 0.26 | 0.14-0.48 |
| Gender | | |
| Male | 255 | 1* | -- |
| Female | 215 | 0.80 | 0.56-1.15 |
| Age at diagnosis | | |
| <1 year | 13 | 2.41 | 1.02-5.69 |
| 1-4 years | 231 | 1* | -- |
| 5-9 years | 146 | 1.40 | 0.92-2.14 |
| 10-14 years | 80 | 1.85 | 1.16-2.95 |
| WBC count at diagnosis | | |
| <999 × 10⁶ cells/L | 225 | 1* | -- |
| 1000-49999 × 10⁶ cells/L | 152 | 1.43 | 0.93-2.19 |
| ≥50000 × 10⁶ cells/L | 89 | 2.62 | 1.67-4.09 |
| Missing | 4 | 2.37 | 0.56-10.14 |

*Reference category. Subjects with missing value were retained and included as separate levels in the model.

| Table 5. Multivariate survival analyses of 134 ANLL cases diagnosed in 1970-98 in Piedmont. The Hazard Ratio (HR) of death and the corresponding 95% confidence interval (95% CI) were computed according to the Cox model including period of diagnosis, age at diagnosis, white blood cell (WBC) count and cytological type. |
|---|---|---|---|
| N. of cases | HR | 95% CI |
| Period of diagnosis | | |
| 1970-74 | 12 | 1* | -- |
| 1975-79 | 33 | 0.56 | 0.26-1.20 |
| 1980-84 | 26 | 0.25 | 0.10-0.58 |
| 1985-89 | 21 | 0.19 | 0.08-0.49 |
| 1990-94 | 20 | 0.27 | 0.11-0.68 |
| 1995-98 | 22 | 0.10 | 0.04-0.30 |
| Age at diagnosis | | |
| 0-4 years | 45 | 1* | -- |
| 5-9 years | 45 | 0.81 | 0.47-1.43 |
| 10-14 years | 44 | 1.20 | 0.68-2.11 |
| WBC count at diagnosis | | |
| <5000 × 10⁶ cells/L | 56 | 1* | -- |
| 5000-49999 × 10⁶ cells/L | 35 | 1.45 | 0.82-2.57 |
| ≥50000 × 10⁶ cells/L | 23 | 1.89 | 1.00-3.61 |
| Missing | 20 | 1.47 | 0.75-2.97 |
| Cytological type* | | |
| Acute non-lymphocytic leukemia M1-M2 | 58 | 1* | -- |
| Acute non-lymphocytic leukemia M3 | 23 | 1.99 | 0.97-4.06 |
| Acute non-lymphocytic leukemia M4 | 16 | 1.29 | 0.67-2.48 |
| Acute non-lymphocytic leukemia M5 | 22 | 1.97 | 0.95-4.07 |
| Acute non-lymphocytic leukemia unknown FAB | 15 | 2.11 | 0.99-4.52 |
| Acute lymphoblastic leukemia unknown FAB | 15 | 2.11 | 0.99-4.52 |

*Reference category. The analysis is limited to ANLL with FAB types M1-M5 or FAB type unknown. Three M6-M7 cases and 1 case of hybrid leukemia were excluded.

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*Reference category. Subjects with missing value were retained and included as separate levels in the model.
ter diagnostic techniques and more precise risk-tai-
lored therapeutic approaches. Most of the progno-
stic data are contained in four characteristics at diag-
nosis: age, gender, WBCC and cytogenetics. The val-
ue of these factors has been demonstrated by a vari-
ety of clinical studies and are the basis for the cur-
cent classification of childhood ALL. Among fac-
tors known to predict a better outcome, we con-
firmed the role of a WBCC < 50x10^9 cells/L and age 
at diagnosis being 1–9 years, while the role of im-
munophenotype as an independent prognostic factor is unclear. The poorer prognosis for T-cell ALL might be explained by the link with other unfavorable risk factors such as high WBCC and age over 10 years. New therapeutic strategies for such patients with ALL are needed. We also confirmed that sur-
vival is higher among females (although our results 
were not statistically significant). However, a recent 
large population-based study in Europe showed that 
gender accounts for only a small difference in sur-
vival. The CCRP did not collect information on oth-
er prognostic factors such as cytogenetics, leukemia 
cell burden and response to treatment and socio-
economic status. The outcome of childhood ANLL 
diagnosed during the early 1970s in developed coun-
tries was disappointing: less than 10% survived for 
the first 5 years, although an increase was recorded 
from the late 70s. In the 1980s and 1990s the out-
look improved and higher 5-year survival rates were 
observed, presumably due to more effective chemother-
apy, better supportive therapies as well as 
to bone marrow transplantation. Diagnostic tech-
niques also improved in the study period: cytoge-
etic and monoclonal antibodies became useful tools 
in recognizing ANLL subtypes as well as hybrid or 
bi-phenotypic leukemias. Classification based on these 
techniques, in addition to morphology, may reveal 
subgroups of children with good prognosis. Howev-
er, as yet, few prognostic factors have been consis-
tently identified in ANLL. Prognostic factors may 
also depend on treatment and its intensity and may 
change as new protocols are introduced. The effect 
of WBCC on survival is well known and was statisti-
cally significant in our data. Age, gender and FAB 
classification were not related to prognosis of ANLL 
in this study. The FAB subgroup registered by the 
CCRP personnel were as reported in the clinical 
records, but inter-observer variation is well docu-
mented. Children with M3 have been reported to 
have a good long-term survival but their prognosis is poor when they present disseminated intravascular coagulopathy at diagnosis.

In affluent, Western countries HD is an example of 
childhood cancer which can be cured in over 90% of 
cases with a reasonable burden of sequelae. Litera-
ture data on survival differences according to gen-
der in HD are not consistent.

The differential diagnosis between NHL and ALL is 
not always precise, therefore new treatment pro-
grams are obtained as modifications of the protocols 
for high risk ALL. The survival rates for NHL diag-
nosed during the period 1995–98 increased with a 
trend resembling that observed for ALL. As for 
ALL, the prognosis of children with NHL has improved 
in recent periods due to a better understanding of the 
natural history and heterogeneity of the type of can-
cer and to refinement of treatment plans. Our data-
base showed that females fared better than males, 
but this observation is not consistent with literature 
data. Survival for children with all CNS tumors except 
ependymoma showed a highly significant improve-
ment over the periods of diagnosis, but this picture 
is marred by the decrease in 1995–98. Over the entire 
1970–1998 period we observed a statistically signifi-
cant linear improvement for children with medul-
loblastoma, but survival for cases diagnosed after 
1990 was lower than that for cases diagnosed in 
1985–89. Possible causes for this inverse trend 
include different case-mixes according to prognos-
tic factors or biological features (i.e. age/extent 
of disease at diagnosis) or changes in clinical approach 
(i.e. protocol, surgical removal and radiotherapy tech-
niques) with unexpected results. No information on 
these aspects was available in the data of CCRP and 
an ad hoc study is in progress to investigate their 
role. Random variation cannot be excluded as sur-
vival in Piedmont in the 1980s was much higher than 
in other countries (see below).

The prognosis of SST depends on age, extent of 
disease at diagnosis, and genetic factors, such as 
expression of the N-Myc gene, while gender is not 
related to survival. Prognostic factors or biological features (i.e. age/extent of disease at diagnosis) or changes in clinical approach 
(i.e. protocol, surgical removal and radiotherapy tech-
niques) with unexpected results. No information on 
these aspects was available in the data of CCRP and 
an ad hoc study is in progress to investigate their 
role. Random variation cannot be excluded as sur-
vival in Piedmont in the 1980s was much higher than 
in other countries (see below).
although the last largely mirror those of the CCRP. Substantially similar results have been found for all tumors, ALL, ANLL, NHL, osteosarcoma and rhabdomyosarcoma. The survival rates of patients with CNS tumors, SST and Ewing's sarcoma tend to be higher in Piedmont than in other developed countries. The 5-year survival for children with CNS tumors in Piedmont in 1990-94 was high (78%) in comparison to that in other developed countries in the same period (64% ITACARE, 61% EUROCAR, 65% USA). The survival rates for HD, medulloblastoma, fibrosarcoma and Wilms' tumors seem to be lower. Survival rates for HD in developed countries exceeded 90% in the last decade of the 20th century, whereas they were 83% and 87% (1990-94 and 1995-98) in Piedmont. The decrease in 5-year survival observed in Piedmont in 1990-98 for medulloblastoma is difficult to compare with international rates, both because of the scarcity of data available for this time period and because the decrease must be put in the context of a highly significant improvement from 1970 to 1990 when CCRP survival rates were higher than those in other countries. Two-thirds of the data analyzed in the EUROCAR Study for Italy were from the CCRP, therefore the two observations were not independent.23-25

Non-biological features associated with better prognosis included: treatment plan directed by a tertiary care unit, size of place of treatment and entry in a large trial,44-45 while the role of socio-economic status or parental education was limited.35 Being treated in special centers and according to clinical trials was a well recognized determinant of long-term survival during the decade 1970-1980; thereafter the role of these factors decreased as a result of the use of more standardized treatment in all centers.32,36 The only exception to this is CNS tumors.46

The outcome advantage related to being registered in a trial was still increasing, at least for ALL and ANLL and for selected tumor types, in the 1970s and in 1980s,33,36,46 Since 1970, children resident in our region have mostly been treated in specialized centers according to well-defined clinical protocols;46 this fact hampers survival analysis by entry into a protocol. In conclusion, we confirm the positive trend in survival after childhood cancer in recent years and we emphasize the role of childhood cancer registration as an important method to monitor survival rates in the population.

Appendix

Some minor categories were grouped together: acute lymphocytic leukemia (minor category 01A); with other lymphocytic leukemias (01B); non-Hodgkin's lymphomas (02B) with Burkitt's lymphoma (02C); and unspecified lymphomas (02D) other gliomas (03D) with other and unspecified central nervous system tumors (03E); neuroblastoma (04A) with other tumors of the sympathetic system (04B); Wilms' tumors (06A) with unspecified renal tumors (06C); and fibrosarcoma (09B) with other and unspecified sarcomas (09C). Renal carcinoma (06B), chondrosarcoma (08B), gonadal tumors (10B) with gonadal carcinoma (10C), other and unspecified gonadal tumor (10D), other and unspecified tumor were not included in the analyses. The other minor categories not mentioned in the paper were also excluded.

References

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Contributions
SV: statistical analyses and report writing; GP: conception, design and report writing; MLM: data management; BT: report writing and critical revision; EM: clinical overview; FM: report writing and final approval; CM: report writing, general overview and final approval. Our grateful thanks to Prof. Andrea Pessin and to Prof. Fabrizio Bianchi for their comments and to Mrs. Marinella Nonnato for her careful management of the CCRP data and follow-up. Primary responsibility for the publication: GP; primary responsibility for each Table and Figure: SV.

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