Adolescence and Socioeconomic Factors: Key Factors in the Long-Term Impact of Leukemia on Scholastic Performance—A LEA Study

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Objective To evaluate the association between medical and social environmental factors and the risk of repeating a grade in childhood leukemia survivors.

Study design A cross-sectional study of childhood leukemia survivors, recruited through the LEA cohort (Leucémie de l'Enfant et de l'Adolescent [French Childhood Cancer Survivor Study for Leukemia]) in 2014. An adjusted logistic regression model was used to identify variables linked to repeating a grade after the diagnosis among the survivors, and the rates of repeating a grade were compared between the survivors and their siblings using a multilevel logistic regression model.

Results The mean age at inclusion of the 855 participants was 16.2 ± 7.0 years, and the mean duration of follow-up from diagnosis to evaluation was 10.2 ± 6.2 years. After disease onset, 244 patients (28.5%) repeated a grade, with a median interval of 4 years (IQR, 2-8 years). Independent factors associated with repeating a grade were male sex (OR, 1.78; 95% CI, 1.21-2.60), adolescence (OR, 2.70; 95% CI, 1.63-4.48), educational support during the treatment period (OR, 3.79; 95% CI, 2.45-5.88), low parental education level (OR, 2.493; 95% CI, 1.657-3.750), and household financial difficulties (OR, 2.62; 95% CI, 1.607-4.28). Compared with siblings, survivors were at greater risk of repeating a grade (OR, 1.87; 95% CI, 1.48-2.35).

Conclusions The most vulnerable patients seemed to be adolescents and those with parents of low socioeconomic status. Improving the schooling career of leukemia survivors will require that the medical community more carefully consider the social status of patients. *(J Pediatr 2019;205:168-75).*

Children with cancer, among which leukemia is the most frequent, have good overall survival due to improved treatment. Thus, long-term treatment-associated toxicity and functional outcome have become major issues for pediatricians.

Several studies have addressed cognitive and learning impairment and their risk factors in children following cancer.[1,2] As a result, treatment has been adapted to age and relapse risk to minimize neurocognitive toxicity by, for example, less use of cranial irradiation.[3,4] Most studies have been based on neurocognitive tests, but scholastic achievement may be a better measure of long-term effects. Evidence is emerging that scholastic performance is an accurate index of quality of life for children, because absenteeism, social isolation, posttraumatic stress, and physical modifications may affect success at school, even for children with a high IQ.[5]

The effects of various diagnoses and/or treatments on academic results have also been explored. Cerebral tumors, neurotoxic chemotherapies, and cerebral irradiation have been identified as risk factors for failure at school, as they lead to neurocognitive impairment.[6-8] The impact of leukemia on scholastic achievement remains a matter of debate. Zynda et al reported that leukemia survivors obtained a higher level of education than the general population,[9] whereas in a Finnish cohort, a higher proportion of leukemia survivors compared with

AL	Acute leukemia
CNS	Central nervous system
HSCT	Hematopoietic stem cell transplantation
LEA	Leucémie de l'Enfant et de l'Adolescent

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controls had no further education after comprehensive school (9th grade).[10] Buizer et al identified significant behavioral and educational problems in survivors of childhood acute lymphoblastic leukemia in a multicenter study, but no dysfunction for Wilms tumor survivors relative to siblings and general population controls.[11]

The measurement of scholastic achievement is not similar worldwide. In France, repeating a grade (or year) is standard practice for underperforming pupils and a common measure of academic performance. Male sex and low parental socioeconomic/educational status have been identified as risk factors for repeating a grade in the general population. This measure is recognized to affect self-esteem and other psychosocial measures.[12] Comparing the scholastic achievements of patients and their siblings is particularly informative, because siblings and patients share the same familial/educational/social background.

Our first study demonstrated that childhood cancer survivors had a high rate of repeating a grade and that teenagers with cancer (all types) were more vulnerable than younger children to problems at school at a regional level.[13] These results were in contrast to those in the literature in which survivors of cancer during adolescence participated in school and vocational life without major difficulties, except for those with neuropsychological sequelae.[14] Moreover, young age has been previously identified as a risk factor owing to neurologic vulnerability.[15]

Nevertheless, the transferability of results obtained at a regional level can be discussed. Thus, in the present study, we used data collected from the LEA (Leucémie de l'Enfant et de l'Adolescent/French Childhood Cancer Survivor Study for Leukemia) cohort to assess scholastic performance of children suffering from a single type of cancer, acute leukemia (AL), at the national level.

Our first aim was to assess the schooling of long-term leukemia survivors to highlight risk factors, among medical and social environmental factors, for repeating a grade and to further study the school career of teenagers. We then compared the scholastic performance of patients and their siblings.

Methods

The LEA project is a French multicenter prospective long-term follow-up program involving all childhood AL survivors treated before age 18 years in the participating centers (currently 16 academic hospitals) since 1980. The program has been described in detail previously.[16] In brief, patients are included 1 year after the completion of chemotherapy or after hematopoietic stem cell transplantation (HSCT), and assessments are performed every 2 years up to the age 20 years and every 4 years thereafter for a minimal follow-up period of 10 years from diagnosis or last relapse. Clinical information concerning AL history and physical late effects are collected during specific medical visits, and personal data (eg, socioeconomic data, quality of life, work insertion) are collected via a questionnaire completed by the patient at the end of each medical visit. The LEA study has been approved by an Ethical Research Committee (Committee for Personal Protection), and all patients (or their parents, for minors) provided written informed consent.

In 2014, specific items concerning patients' school achievement were incorporated into the questionnaire, with the support of the French League Against Cancer. The present study includes the patients evaluated in 2014 who responded to the school module. Patients with specific comorbidities before the AL diagnosis (psychomotor retardation or cognitive troubles) and those too young to attend school at the time of the evaluation were not included (in France, children typically start school at age 3 years). Patients already requiring specialized school services before the AL diagnosis were excluded as well.

Measures

Clinical data concerning the AL, including the subtype, occurrence of relapse, and history of treatments received, are documented in the LEA cohort and available for all patients included in the present study. The occurrence of physical late effects (ie, second tumor, cataract, metabolic syndrome, late cardiomyopathy, height growth failure, overweight, gonadal dysfunction, dysthyroidism, bone mineral deficiency, osteonecrosis, alopecia, severe neurologic dysfunction, diabetes, and iron overload),[17,18] explored by regular assessment using standardized measurements, was considered at the time of the specific medical visit of 2014.

The school data were self-reported by the participants aged ≥18 years or by their parents of younger participants. Data collected included educational level at time of diagnosis, repeating a grade (before and after the diagnosis), need for special education services, changes in orientation (from a general to a professional orientation), and need for scholastic assistance in the hospital or at home after the diagnosis. The primary endpoint was repeating a grade after the AL diagnosis. Patients who stopped attending school (at an establishment or at home) immediately after the diagnosis were also considered to have repeated a grade because of the very small size of this category (n = 2).[13]

The secondary endpoint took into consideration a broader definition of scholastic difficulties if at least 1 of these events occurred after the AL diagnosis: repeating a grade, changing orientation, or changing to a specialized educational track. In France, specialized education programs for pupils who are disabled or struggling due to a medical or social issue are provided either in the ordinary school or in specialized institutions. School is compulsory in France from age 6 to 16 years, but most children start at 3 years (preschool/kindergarten) and attend for 3 years before then going to primary school for 5 years. They generally attend a 1 (sometimes 2) level class with 1 teacher who changes each year. They then attend middle school for 4 years, starting at age 11. Adolescents then choose between general education (high school for 3 years before going to university) or professional education (2 or 3 years before going to work). From middle school on, they attend classes in which every teacher teaches a single subject. Specialized education for disabled or struggling pupils is included in ordinary schools or provided in specialized institutions. Repeating a grade is

standard practice for underperforming pupils, quite rare before primary school and widespread thereafter. Unlike some European countries, France does not practice automatic promotion. The decision is collective and institutional. In France, access to schooling for all is legislatively protected. Teaching materials for individualized schooling are present in all hospitals that receive children for long periods of hospitalization. Moreover, the French law provides for schooling at home, organized by local institutions. Instructors can be the original teacher or another. Such support must be proposed to every child facing cancer from the moment that traditional schooling is suspended for a long period. However, delays in organizing such specialized schooling or the disease/treatment can lead to differences in schooling between cancer patients and their healthy peers or even among one another.

In addition, data about the family environment at the time of diagnosis were also collected: constitution of the family unit (parents together or separated), education level of the parents, employment status of the parents, household financial difficulties, and availability of at least 1 parent during treatment (homemaker or temporary leave from work).

Comparison Group

The participants (or their parents) were also asked to report information concerning each of their brothers or sisters: age, sex, and whether they had repeated a grade during their schooling (independent of the time of diagnosis of their siblings).

Statistical Analyses

Categorical variables are presented as number and percentage, and continuous variables are reported as mean and SD or median and interquartile range (IQR). Demographic and clinical variables between the participants and nonparticipants were compared using the χ^2 tests (for percentages) and the Student *t* tests (for means) to assess the representativeness of our sample.

An adjusted logistic regression model was used to determine variables that might be associated with repeating a grade after the AL diagnosis (or secondary to school difficulties after the diagnosis) among the survivors. Adjusted ORs (including 95% CIs) were estimated. The variables relevant to the model were selected from univariate analyses (χ^2 or Student *t* test, as appropriate), provided that the variables were associated with repeating a grade (or school difficulties) with $P \leq .05$. The sex of the survivor was included in the model as an adjustment variable.

The univariate exploration of variables potentially associated with repeating a grade was performed for all "school level at diagnosis" categories (too young or age <6 years, primary school for age 6-11 years, and secondary school for age ≥11 years; middle and high school, also called the "adolescent group"). The χ^2 and Kruskal-Wallis tests were used to analyze repeating a grade and the time from diagnosis according to the class at diagnosis, respectively.

Finally, a multilevel logistic regression model was used to compare the rate of repeating a grade between the childhood leukemia survivors and their siblings. We chose this model to consider the hierarchic structure of the data at the individual level (characteristics of the childhood leukemia survivors or their siblings) and the family level (shared characteristics for a survivor and siblings living in the same family). The dependent variable was binary (repeating a grade vs not repeating a grade). The explanatory variable was the profile of the subject (survivor or sibling), and the model accounted for individual covariates (eg, sex, age at diagnosis, schooling completed or not at the time of evaluation) and family covariates (eg, parental education level, parental employment status, household financial difficulties, availability of a parent at the time of treatment). ORs was calculated with 95% CIs.

All tests were 2-sided, and the significance threshold was set at $P < .05$. Statistical analyses were performed using PASW Statistics 17.0.2 (IBM, Armonk, New York) and StataSE 13.1 (StataCorp, College Station, Texas).

Results

Of the 1225 patients evaluated in the LEA cohort in 2014, 22 met at least 1 of the exclusion criteria. Of the 1203 eligible patients, 866 completed the questionnaire (72.0%). The responding and nonresponding groups did not differ with respect to sex, current age and age at diagnosis, type of leukemia, history of relapse, or irradiation received, but a history of transplantation was more common in the nonresponders (24.4% vs 18.2%; $P = .02$). Among the respondents, 11 patients were excluded from our analysis because they reported already needing specialized assistance at school before diagnosis. Finally, a total of 855 participants were included in the analysis (**Figure 1**).

The characteristics of the 855 participating survivors are presented in **Table I**. The mean age at study inclusion was 16.2 ± 7.0 years, and the mean duration of follow-up from diagnosis to evaluation was 10.2 ± 6.2 years. Most of the patients (86.2%) had been diagnosed with acute lymphoblastic leukemia, and 58 patients (6.8%) underwent central nervous system (CNS) irradiation (dose, 9-26 Gy). Among the 153 patients who underwent HSCT, 134 (87.6%) received an allogeneic transplant and 98 (64.1%) received total body irradiation (TBI).

At the time of the LEA consultation, 559 of 855 patients (65.4%) had at least 1 physical late effect.

School Career

At diagnosis, 522 patients were too young to attend school or were in preschool/kindergarten, 195 were in primary school, and 138 were in secondary school. After disease onset, 244 of the 855 patients (28.5%) repeated a grade, at a median of 4 years after the diagnosis (IQR, 2-8 years). The rate of repeating a grade and time between diagnosis and the event differed significantly among patients, depending on their school level at diagnosis. Adolescents (in secondary school at diagnosis) were more likely than younger children to repeat a grade. Their rate of repeating a grade was 48.6% (95% CI, 7.6%-24.6%), compared with 34.9% (95% CI, 28.5%-41.8%) for children in primary school at diagnosis and 20.9% (95% CI, 40.4%-56.8%) for those younger than primary school age at diagnosis ($P < .001$). Adolescents also repeated a grade at a shorter

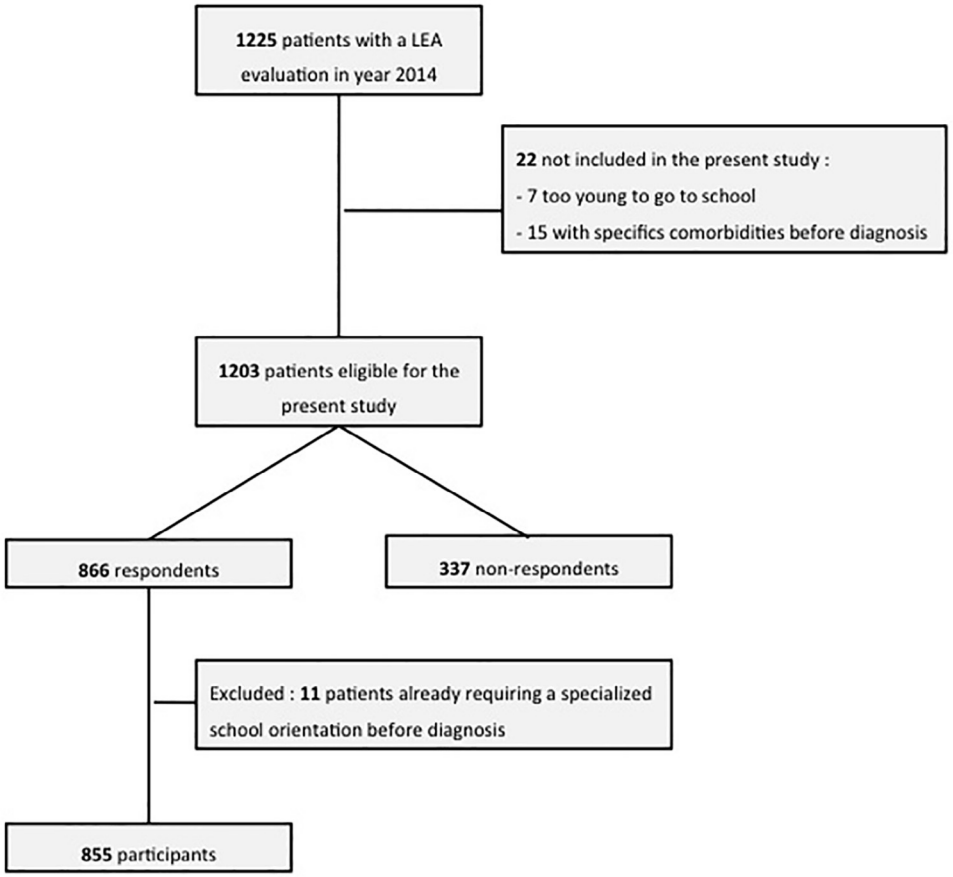

Figure 1. Flow chart of the study.

interval from diagnosis, with a median of 2 years (IQR, 1-4 years) vs 3 years (IQR, 1-8 years) for primary school age patients and 5 years (IQR, 4-10 years) for children younger than primary school age at diagnosis ($P < .001$). Furthermore, the rate of repeating a grade was higher in patients who presented with at least 1 physical late effect compared with those who did not (32.2% vs 21.4%).

Forty-six patients (5.4%) reported changing their educational orientation, and 59 (6.9%) switched to a specialized education program. During the treatment period, 445 patients (53.4%) received educational support at home or in the hospital.

Among the 173 patients who had finished school at the time of the evaluation, 80 (46.2%) followed the professional track. Overall, 73 patients (42.2%) attained an educational level above high school, whereas 52 (30.1%) stopped attending school just after the end of high school, 30 (17.3%) stopped just after the end of a school path resulting in a lower degree than high school, and 16 (9.2%) stopped without obtaining a degree.

Table I. Characteristics of the childhood leukemia survivors (n = 855)

Characteristics	Values
Sex, n (%)	
Female	423 (49.5)
Male	432 (50.5)
Age at assessment, y, mean ± SD	16.2 ± 7.0
Age at diagnosis, y, mean ± SD	6.0 ± 4.3
Leukemia subtype, n (%)	
ALL	737 (86.2)
AML	118 (13.8)
HSCT, n (%)	
No	702 (82.1)
Yes	153 (17.9)
History of relapse, n (%)	
No	772 (90.3)
Yes	83 (9.7)
CNS irradiation (except TBI), n (%)	
No	795 (93,2)
Yes	58 (6,8)
Time since diagnosis, y, mean ± SD	10.2 ± 6.2

ALL, acute lymphoblastic leukemia; *AML*, acute myelogenous leukemia.

Factors Associated with Repeating a Grade

Exploration of the potential determinants of repeating a grade by univariate analysis is presented in **Table II**. In addition to the age at diagnosis (48.2% of children aged 11-17 years and 24.7% of those aged <11 years repeated a grade), several clinical factors were significantly associated with repeating a grade: history of relapse, treatment received (eg, HSCT, CNS irradiation), and time between diagnosis and evaluation. Compared with the other survivors, those who repeated a grade after

Table II. Risk factors for repeating a grade after surviving leukemia: univariate analysis

Risk factors	All patients (n = 855)	Repeating a grade after diagnosis		*P* value
		No (n = 611)	Yes (n = 244)	
Demographic factors				
Sex, n (%)				
Female	423 (49.5)	311 (73.5)	112 (26.5)	.187
Male	432 (50.5)	300 (69.4)	132 (30.6)	
Age at diagnosis, n (%)				
<11 y	716 (83.7)	539 (75.3)	177 (24.7)	<10^-3
11-17 y	139 (16.3)	72 (51.8)	67 (48.2)	
Clinical factors				
Leukemia subtype, n (%)				
ALL	737 (86.2)	532 (72.2)	205 (27.8)	.242
AML	118 (13.8)	79 (66.9)	39 (33.1)	
HSCT, n (%)				
No	702 (82.1)	521 (74.2)	181 (25.8)	<10^-3
Yes	153 (17.9)	90 (58.8)	63 (41.2)	
History of relapse, n (%)				
No	772 (90.3)	563 (72.9)	209 (27.1)	.004
Yes	83 (9.7)	48 (57.8)	35 (42.2)	
Irradiation (CNS), n (%)				
No	795 (93.2)	579 (72.8)	216 (27.2)	.002
Yes	58 (6.8)	31 (53.4)	27 (46.6)	
Time since diagnosis, y, mean ± SD	10.21 ± 6.17	9.36 ± 5.40	12.34 ± 7.35	<10^-3
School factors				
History of repeating a grade before diagnosis, n (%)				
No	816 (95.4)	591 (72.4)	225 (27.6)	.004
Yes	39 (4.6)	20 (51.3)	19 (48.7)	
School support at home and or hospital				
No	388 (45.6)	320 (82.5)	68 (17.5)	<10^-3
Yes	445 (53.4)	280 (62.9)	165 (37.1)	
Family factors				
Living in a traditional family unit at diagnosis, n (%)				
No	95 (11.2)	58 (61.1)	37 (38.9)	.018
Yes	754 (88.8)	548 (72.7)	206 (27.3)	
Parents' education, n (%)				
No diploma	56 (6.8)	26 (46.4)	30 (53.6)	<10^-3
Less than high school	215 (26.2)	123 (57.2)	92 (42.8)	
More than high school	551 (67.0)	442 (80.2)	109 (19.8)	
Parents' employment at diagnosis, n (%)				
Both parents	547 (64.6)	404 (73.9)	143 (26.1)	.13
Only one parent	259 (30.6)	177 (68.3)	82 (31.7)	
No parent	41 (4.8)	26 (63.4)	15 (36.6)	
Financial difficulties at diagnosis, n (%)				
No	669 (84.5)	507 (75.8)	162 (24.2)	<10^-3
Yes	123 (15.5)	66 (53.7)	57 (46.3)	
At least 1 parent at home at diagnosis, n (%)				
No	83 (9.8)	56 (67.5)	27 (32.5)	.292
Yes	746 (87.3)	544 (72.9)	202 (27.1)	

the diagnosis were more likely to have a history of repeating a grade before diagnosis and also were more likely to have received educational support at home or in the hospital after diagnosis.

Parents of the survivors who did not repeat a grade were more likely to be living together at the time of diagnosis, had a higher educational level, and had fewer financial difficulties.

After adjustment, the independent factors associated with repeating a grade were sex of the survivor (higher risk for boys; OR, 1.78; 95% CI, 1.21-2.60; $P = .003$), age at diagnosis (higher risk for adolescents; OR, 2.70; 95% CI, 1.63-4.48; $P < .001$), educational support at home or in the hospital during the treatment period (higher risk if the child received such support; OR, 3.79; 95% CI, 2.45-5.88; $P < .001$), parental educational level (higher risk if no diploma: OR, 4.60; 95% CI, 2.27-9.31 or low level: OR, 2.493; 95% CI, 1.657-3.750; $P < .001$), and the household financial situation (higher risk if parents had financial difficulties; OR, 2.62; 95% CI, 1.607-4.28; $P < .001$) (**Figure 2**).

Univariate analysis found the same significant factors associated with school difficulties when using a broader definition of school difficulties after the diagnosis: not only repeating a grade, but also switching to specialized education or changing the school orientation) (**Table III**; available at www.jpeds.com).

Finally, we explored the factors linked with repeating a grade among adolescents, because this specific subgroup was at elevated risk to repeat a grade compared with younger children

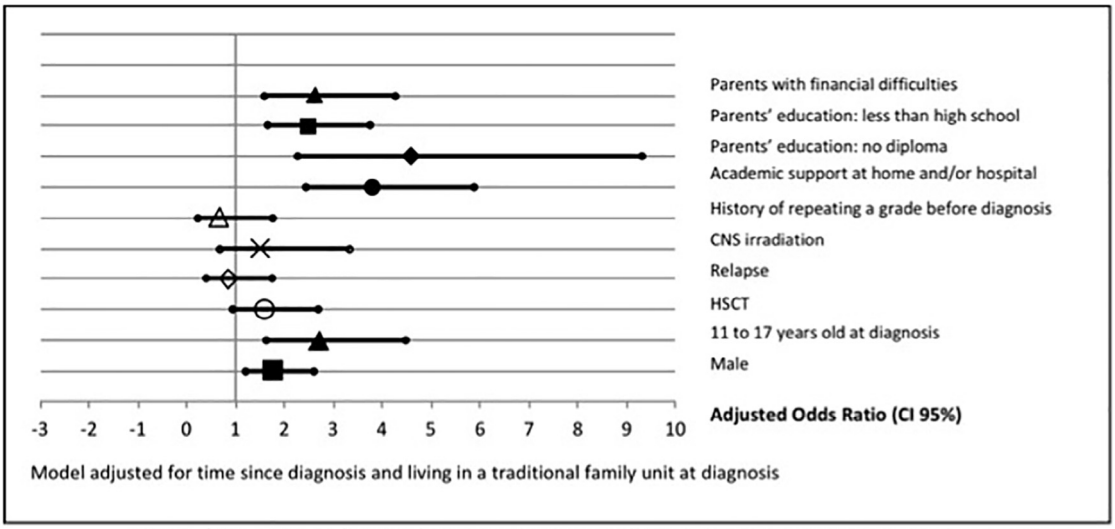

Figure 2. Risk factors for repeating a grade after surviving leukemia: multivariate analysis.

at diagnosis. The sole factor significantly associated with repeating a grade in this subgroup was the household financial situation (42.9% rate of repeating a grade for families without financial difficulties vs 75.0% for families with financial difficulties; $P = .008$) (**Table IV**; available at www.jpeds.com).

Comparison with Siblings

School information was collected for 1304 siblings. Their mean age was 18.5 ± 8.9 years at the time of the report and the male:female sex ratio was 0.98. Among these siblings, 181 (14%) were not yet born when their brother or sister was diagnosed. The mean age of those already born at the time of diagnosis was 9.8 ± 7.0 years. Among the siblings of the survivors, 21.9% repeated a grade during their school career. The grade repeated was kindergarten for 2.1%, primary school for 30.8%, middle school for 31.1%, high school for 26.6%, and unknown for 9.4%.

The multilevel logistic regression model that compared the rate of repeating a grade between childhood leukemia survivors and their siblings adjusted for demographic and family characteristics (ie, equivalent age, sex, family structure, outcome, and parent diploma) also highlighted a significant difference. The risk of repeating a grade was higher for the survivors for all age groups (OR, 1.87; 95% CI, 1.48-2.35; $P < .001$). The same model also revealed a significant difference between adolescent survivors and their adolescent siblings (OR, 2.15; 95% CI, 1.32-3.48; $P = .002$).

Discussion

This study reports long-term schooling of leukemia survivors, whereas previous studies investigating schooling have used a national cohort of cancer survivors (not only leukemia survivors).[1,7] For example, Zynda et al reported German leukemia survivors, but with a lower rate of participation (64%).[9]

In our study, after leukemia, 28.5% of patients repeated a grade, with a median interval of 4 years. This rate was significantly higher than that for their siblings who shared the same socioeconomic environment. Adolescents (age >11 years or in secondary or high school at diagnosis) were highlighted in our study because they were more likely than younger children to repeat a grade (48.6% vs 20.9%) and had a shorter interval from diagnosis (2 years vs 5 years).

Based on the literature, adolescents appear to be more protected from the neurocognitive sequelae than younger children. We did not find any treatment or disease risk factors for repeating a grade in this group. Nevertheless, this population is more likely affected by the psychological state associated with this age, making adolescents particularly vulnerable. Schultz et al reported that survivors between 12 and 17 years of age are more likely than their siblings to have symptoms of anxiety/depression and antisocial behavior, particularly leukemia and CNS tumor survivors.[19] Furthermore, one-third of adolescents and young adults with hematologic malignancies have been reported to experience anxiety, depression, or traumatic stress.[20] The shorter interval before repeating a grade in the adolescent group is likely due to the immediate effect of treatment, such as missing days and psychological stress, which are sufficient to disrupt schooling. It may then be very difficult or impossible to catch up.

Multivariate analysis revealed that in addition to age, demographic and social factors are more closely associated with school difficulties than are treatments or disease. Indeed, male sex, need for educational support at home or in the hospital during the treatment period, low parental educational level, and household financial difficulties were risk factors for

repeating a grade. These socioeconomic risk factors are well recognized in the general population.[12] Similar results were reported by Barrera et al in 2005 for cancer survivors, demonstrating the positive influence of having high self-esteem and parents with postsecondary education.[1]

We compared our population with their siblings to better understand the influence of socioeconomic factors on the scholastic performance of childhood leukemia survivors. We compared the overall rate of repeating a grade among the siblings with the posttreatment rate of the survivors. This approach could underestimate the rate of repeating a grade for survivors and minimize the differences with their siblings. However, the siblings had a significantly lower risk of repeating a grade than the leukemia survivors. In a smaller population of acute myelogenous leukemia survivors, Mulrooney et al reported a lower rate of college graduation in survivors without HSCT compared with their siblings, but a higher rate than in the general population.[21] In contrast, in a study comparing teenage childhood leukemia survivors treated with chemotherapy only with their siblings, Jacola et al that the survivors had an elevated risk of cognitive, behavioral, and academic problems that adversely affected adult education outcomes.[22] The health and well-being of adolescent survivors of early childhood cancer are quite similar to those of their siblings.[23] Facing cancer is a complex event that can influence scholastic results beyond treatment and sequelae.

We also assessed the potential impact of HSCT on scholastic achievement. Indeed, HSCT survivors have a substantially greater burden of serious chronic conditions and impairments, involving virtually every organ system, as well as an overall lower quality of life.[17,18,24-28] However, HSCT with or without TBI entails a minimal risk of late neurocognitive sequelae, except in patients aged <6 years at the time of transplantation, who appear to be at some risk of cognitive decline.[29] Nevertheless, a French study found greater academic difficulties in leukemia survivors who underwent HSCT compared with the general population, independent of irradiation.[30] Conversely, Barrera et al stressed the need to consider personal and familial factors to understand the psychosocial outcomes of HSCT survivors.[31] Our data are consistent with this finding, showing that the correlation between HSCT and repeating a grade by univariate analysis disappeared after the multivariate analysis.

We could not focus on the impact of physical sequelae on schooling because although we had the date of the screening of sequelae, our study design could not confirm whether the sequelae were already present at the time of the repetition of a grade (no link could be established, because a sequela can occur after repeating a grade).

We also found that academic support during treatment did not protect survivors from repeating a grade; the 53.4% of patients who received educational support at home or in the hospital had a greater risk of repeating a grade than those who did not. Although the more vulnerable patients were well identified, they probably did not receive enough aid or the aid they did receive was not well suited to their needs. This result is consistent with our previous study.[13]

Finally, our primary endpoint "to repeat a grade after the AL diagnosis" has limits. In particular, this endpoint does not reflect professional integration. Gerhardt et al reported that although survivors of non-CNS cancer were more likely to report repeating a grade and having more school absences, the proportion of survivors who graduated from high school, were working, or expressed plans to receive postsecondary education or seek employment was similar to that of matched classmates.[32] Nevertheless, repeating a grade may be experienced as a second punishment after the cancer, hurting self-esteem and affecting future plans, probably even more so in the vulnerable population of adolescents who repeated a grade shortly after diagnosis. The care provided to these patients should take into account the significant associations among maintaining peer groups, successfully reintegrating into school, and having a positive view of educational support. Collaborative planning among hospitals, schools, and the home needs to be improved[33] both during and just after the treatment period.

In conclusion, in this large, long-term cohort of childhood leukemia survivors, we found a quite high rate of school difficulties, such as repeating a grade. The more vulnerable patients seemed to be adolescents and those with low parental socioeconomic status. Nevertheless, after adjustment, we reported that survivors have a higher rate of repeating a grade than their siblings who shared the same socioeconomic environment. This suggests that independent of the "medical" event (eg, type of treatment, type of leukemia), it is the "personal" experience of this event that has scholastic consequences, and this event seems particularly difficult to overcome, in terms of schooling, for adolescents and into a difficult socioeconomic context. However, the experience of this event also concerns the siblings in their own lives, who could potentially face more scholastic difficulties than the general population. This merits exploration in future studies.

Improving the school career of leukemia survivors, especially teenagers, will require that the medical community consider the social status of patients. This will require early risk-adapted academic support, with monitoring and adaptation (eg, by changing the policy of the educational system to accept missed days and organize tutoring), throughout the course of treatment and after. ■

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Table III. Risk factors for experiencing school difficulties after surviving leukemia (repeating a grade, specialized education, or changing orientation): univariate analysis

Factors	All patients (n = 848)	School difficulties		*P* value
		No (n = 568)	Yes (n = 280)	
Demographic factors				
Sex, n (%)				
Female	418 (49.3)	290 (69.4)	128 (30.6)	.143
Male	430 (50.7)	278 (64.7)	152 (35.3)	
Age at diagnosis, n (%)				
<11 y	710 (83.7)	506 (71.3)	204 (28.7)	<10^-3
11-17 y	138 (16.3)	62 (44.9)	76 (55.1)	
Clinical factors				
Leukemia subtype, n (%)				
ALL	731 (86.2)	496 (67.9)	235 (32.1)	.178
AML	117 (13.8)	72 (61.5)	45 (38.5)	
HSCT, n (%)				
No	694 (81.8)	490 (70.6)	204 (29.4)	<10^-3
Yes	154 (18.2)	78 (50.6)	76 (49.4)	
History of relapse, n (%)				
No	764 (90.1)	530 (69.4)	234 (30.6)	<10^-3
Yes	84 (9.9)	38 (45.2)	46 (54.8)	
Irradiation (CNS), n (%)				
No	789 (93.3)	540 (68.4)	249 (31.6)	.001
Yes	57 (6.7)	27 (47.4)	30 (52.6)	
Time since diagnosis, y, mean ± SD	10.24 ± 6.18	9.31 ± 5.28	12.11 ± 7.36	<10^-3
School factors				
History of repeating a grade before diagnosis, n (%)				
No	806 (95.5)	555 (68.9)	251 (31.1)	<10^-3
Yes	38 (4.5)	13 (34.2)	25 (65.8)	
School support at home and or hospital				
No	386 (46.6)	303 (78.5)	83 (21.5)	<10^-3
Yes	443 (53.4)	257 (58.0)	186 (42.0)	
Family factors				
Living in a traditional family unit at diagnosis, n (%)				
No	750 (88.9)	512 (68.3)	238 (31.7)	.021
Yes	94 (11.1)	53 (56.4)	41 (43.6)	
Parents' education, n (%)				
No diploma	55 (6.7)	24 (43.6)	31 (56.4)	<10^-3
Less than high school	216 (26.5)	114 (52.8)	102 (47.2)	
More than high school	545 (66.8)	414 (76.0)	131 (24.0)	
Parents' employment at diagnosis, n (%)				
Both parents	546 (65.0)	378 (69.2)	168 (30.8)	.204
Only one parent	255 (30.4)	164 (64.3)	91 (35.7)	
No parent	39 (4.6)	23 (59.0)	16 (41.0)	
Financial difficulties at diagnosis, n (%)				
No	665 (71.1)	473 (71.1)	192 (28.9)	<10^-3
Yes	120 (15.3)	60 (50.0)	60 (50.0)	
At least 1 parent at home at diagnosis, n (%)				
No	84 (10.2)	52 (61.9)	32 (38.1)	.206
Yes	738 (89.8)	507 (68.7)	231 (31.3)	

Table IV. Risk factors for repeating a grade after surviving leukemia for adolescents: univariate analysis

Risk factors	All patients (n = 138)	Repeating a grade		*P* value
		No (n = 71)	Yes (n = 67)	
Sex, n (%)				
Female	79 (57.2)	44 (55.7)	35 (44.3)	.248
Male	59 (42.8)	27 (45.8)	32 (54.2)	
Age at diagnosis, y, mean ± SD	13.94 ± 1.81	13.90 ± 1.79	13.98 ± 1.84	.798
Clinical factors				
Leukemia subtype, n (%)				
ALL	109 (79.0)	56 (51.4)	53 (48.6)	.973
AML	29 (21.0)	15 (51.7)	14 (48.3)	
HSCT, n (%)				
No	106 (76.8)	57 (53.8)	49 (46.2)	.32
Yes	32 (23.2)	14 (43.8)	18 (56.2)	
Relapse, n (%)				
No	123 (89.1)	64 (52.0)	59 (48.0)	.695
Yes	15 (10.9)	7 (46.7)	8 (53.3)	
Irradiation (CNS), n (%)				
No	119 (86.2)	60 (50.4)	59 (49.6)	.545
Yes	19 (13.8)	11 (57.9)	8 (42.1)	
Time since diagnosis, y, mean ± SD	8.83 ± 5.54	8.59 ± 5.20	9.09 ± 5.90	.595
Academic factors				
Academic support at home and/or hospital, n (%)				
No	13 (9.8)	6 (46.2)	7 (53.8)	.664
Yes	120 (90.2)	63 (52.5)	57 (47.5)	
Family factors				
Living in a traditional family unit at diagnosis, n (%)				
Yes	111 (82.8)	55 (49.5)	56 (50.5)	.543
No	23 (17.2)	13 (56.5)	10 (43.5)	
Parents' education, n (%)				
No diploma	7 (5.6)	2 (28.6)	5 (71.4)	.061
Less than high school	42 (33.6)	17 (40.5)	25 (59.5)	
More than high school	76 (60.8)	45 (59.2)	31 (40.8)	
Parents' employment at diagnosis, n (%)				
Both parents	93 (68.9)	46 (49.5)	47 (50.5)	.155
Only 1 parent	37 (27.4)	23 (62.2)	14 (37.8)	
No parent	5 (3.7)	1 (20.0)	4 (80.0)	
At least 1 parent at home at diagnosis, n (%)				
No	26 (19.4)	12 (46.2)	14 (53.8)	.489
Yes	108 (80.6)	58 (53.7)	50 (46.3)	
Financial difficulties at diagnosis, n (%)				
No	105 (84.0)	60 (57.1)	45 (42.9)	.008
Yes	20 (16.0)	5 (25.0)	15 (75.0)	