

# ARTICLE

# IMPACT de la déprivation sociale sur les difficultés psychosociales au décours d'un cancer pédiatrique : une étude prospective

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# IMPACT of the Social Deprivation on Psychosocial Difficulties of Pediatric Cancer Survivors: A Prospective Study

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## RÉSUMÉ

La période post-traitement une part fondamental de la prise en charge du cancer pédiatrique. Durant cette période, les difficultés scolaires et psychologiques chez les survivants d'un cancer pédiatriques (SCP) sont connues et peuvent être pronostic sur la bonne réintégration sociale. Cette étude estime l'influence de la déprivation sociale du foyer de l'enfant sur ces difficultés. Notre étude se base sur une base de données multicentrique, et se concentre sur les SCP avant reçu une évaluation psychosociale au cours de leur suivi, de 2013 à 2020. Nous rapportons les données des difficultés scolaires et psychologiques. Le statut socio-économique du foyer de l'enfant a été estimé par un score de déprivation sociale. Nous rapportons les données de 1003 patients. Les difficultés scolaires ont été rapportés chez 22% d'entre eux. Une déprivation sociale plus importante était associée à la survenue de difficultés scolaires.



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La rechute tumorale, le traitement par greffe de cellules souches hématopoïétiques, et les tumeurs du système nerveux central étaient d'autres facteurs de risque. Dans le groupe des patients avec tumeurs du système nerveux central, la déprivation sociale était également un facteur associé à la survenue de difficultés scolaires. Les difficultés psychologiques n'étaient quant à elles pas associées avec le score de déprivation. Il existe un lien entre statut socio-économique et les difficultés scolaires chez les SCP. Des analyses complémentaires doivent être réalisées, notamment chez les enfants avec tumeurs du système nerveux central, qui est la population la plus concernée.

## **MOTS-CLÉS**

Difficultés psychosociales ; contexte socio-économique ; déprivation ; cancer ; pédiatrie

### ABSTRACT

The posttreatment period is a key part of the management of pediatric cancer. During this time, school and psychological difficulties have been described in childhood cancer survivors (CCS) and can be prognostic for the success of social reintegration. This study estimated the influence of the household's socioeconomic status (SES) on these psychosocial difficulties. This study is based on a prospective multicentric database and focused on children who received a psychosocial evaluation during their follow-up from 2013 to 2020. We retrieved data on school and psychological difficulties. Household SES was estimated by a social deprivation score. Data from1003 patients were analyzed. School difficulties were noted in 22% of CCS. A greater social deprivation was significantly associated with school difficulty. Tumor relapse, treatment with hematopoietic stem cell transplantation, and central nervous system (CNS) tumors remained significant risk factors. In the subgroup of CNS tumors, school difficulties were increased and associated with greater social deprivation. Psychological difficulties were not associated with the deprivation score. There is a link between SES and school difficulties in CCS. Further investigations should be carried out for children with CNS tumors, which is the population of the greatest concern.

### **KEYWORDS**

Psychosocial difficulties; contextual socioeconomic status; deprivation; cancer; children

## Introduction

In France, the incidence of pediatric cancer is reported to be 156.6 per million children aged 0-14 years per year and increases to 231.9 cases per million person-years in children aged 15–19 years [1,2]. Over time, a significant improvement in long-term survival rates of pediatric cancers has been achieved. Currently, the 5-year survival rate is reported at 75% in Europe [3]. Therefore, the posttreatment period is a key part of the management. At this period, the main goal is to help the patient return to a normal life. Childhood cancer and its treatments may induce sequalae. Among them, psychosocial affections, i.e., difficulties in educational achievement, and psychological well-being can be a prognosis for the success of the patients' post-cancer reintegration [4,5]. These consequences are mostly described for children with central nervous system (CNS) tumors, with cranial radiotherapy, and with a younger age at diagnosis [4,6-9]. Some of these consequences may be potentiated by the household's socioeconomic status (SES). Therefore, SES can be associated with the probability of having a psychosocial difficulty as well as the ability of the family to be able to deal with it. Associations between school difficulties, psychological wellbeing, and household SES are already known in cancer survivors [10-13]. However, these results mainly focus on the evaluation of these difficulties with important hindsight, when the children's social reintegration is effective [6-8,11,12].

The aim of our study was to estimate the association between SES and psychosocial difficulties in childhood cancer survivors (CCS) during the posttreatment period based on a social deprivation score. We evaluated school and psychological difficulties immediately after the hospital care period, a time when interventions could be possible to avoid the long-term consequences and improve social reintegration.

## Methods

We carried out a retrospective cross-sectional study based on a multicentric database.

### Population

This multicentric study focused on the children from the RECAPGO database (*REcueil des CAncers Pédiatriques du Grand Ouest*) who received a short psychosocial evaluation (described in the variables paragraph). This evaluation was carried out during a dedicated time allowed in a consultation interviewing CCS and their parents. These consultations occurred during years of follow-up (FU) after the end of the child's intense treatment requiring hospital care when the social reintegration is effective. The interviews did not respect a specific structure, all pediatricians were free in how they conducted this evaluation. However, the structure of the interview was suggested by a global questionnaire, which included the evaluation of clinical variables, but also two open questions

about the presence of psychological and school difficulties. Each SE difficulty was reported independently. All the children included in the database were eligible for this evaluation, without difference between children who received the evaluation or not according to their SES (Table 1). We defined the psychosocial FU as completing at least one assessment for these two difficulties at least once during this FU period.

The RECAPGO database results from a collaboration among seven French pediatric oncology hospitals, reported as the French children's oncology study Group GOCE (*Grand Ouest pour les Cancers de l'Enfant*). This prospective database has been open since 01/01/2013 and aims to include all patients aged under 25 years diagnosed with cancer, a hematological malignancy, aplastic anemia, or a Langerhans cell histiocytosis at these participating hospitals. We included patients recorded at diagnosis with a single tumor experience from 01/01/2013 to 08/01/2020. Patients with no known address at diagnosis, those living outside of the GOCE departments, those with no estimated social deprivation score, those aged over 18 years, and those with missing tumor-type data were excluded. One hospital did not complete the psychosocial questionnaire and was excluded from the analysis (Fig. 1).

## Variables

We defined three variables (i) At each consultation during the FU, oncologist pediatricians focused on some items: psychological (global well-being, anxiety, depression,...) and scholarly (marks, attitude at school, socialization,...), collected during the patient interviews without following a specific questionnaire. For some patients already known to be in socio-economic difficulties, the hospital management of the psychosocial FU could be done by a multidisciplinary team involving psychologists and teachers dedicated to social reintegration. Association with scholar and psychological

## TABLE 1

	Total	Patients without a	Patients with a	<i>p</i> -value*
		psychosocial follow-up	psychosocial follow-up	
	N = 1618	N = 615 (38%)	N = 1003 (62%)	
Care center n				p < 0.001
Center 1	377 (23%)	133	244	
Center 2	484 (30%)	173	311	
Center 3	179 (11%)	36	143	
Center 4	178 (11%)	38	140	
Center 5	229 (14%)	114	115	
Center 6	171 (11%)	121	50	
Sex n				p = 0.44
Boys	880 (54%)	342	538	
Girls	738 (46%)	273	465	
Age at diagnosis mean (SD)	7.70 (5.29)	7.61 (5.22)	7.75 (5.29)	p = 0.60
Death n	210 (13%)	18	30	p < 0.001
Relapse n	224 (14%)	128	96	p < 0.001
Type of tumors n				p = 0.29
Blood disorders	765 (47%)	309	456	
CNS tumors	329 (20%)	125	204	
Bone tumors	92 (6%)	33	59	
Solid tumors	319 (20%)	112	207	
Other tumors	113 (7%)	36	77	
Treatment n				
Chemotherapy	1072 (66%)	245	827	p = 0.14
Radiotherapy	316 (20%)	94	222	p < 0.001
Surgery	703 (43%)	159	544	p = 0.62
Stem cell transplantation	125 (8%)	31	94	p = 0.44
EDI mean (SD)	-0.71 (3.42)	-0.57 (3.54)	-0.80 (3.34)	p = 0.18
Total travel time mean (SD)	49.68 (31.58)	51.10 (31.58)	48.80 (29.86)	p = 0.14

Legends: CNS: central nervous system, SD: standard deviation; n: number.

\**p*-value < 0.05 was considered to denote statistical significance.



FIGURE 1. Flow chart of the study.

assistance presented by the patient let clinicians synthesize psychological and scholarly difficulties by a binary response (yes/no) if the difficulty was present or not (for example repeated grades, access to special education, anxiety in socialization, sadness, ...). (ii) The clinical variables were the patients and the characteristics of their tumors. We merged the tumor types into five categories; i.e., blood disorders (leukemia, aplastic anemia, lymphoma), CNS tumors, solid tumors, bone tumors, and other tumors (iii) Two variables evaluated the SES of CCS and their household. First, the European Deprivation Index (EDI) assessed the environment of each socioeconomic patient. This deprivation indicator is constructed by selecting fundamental needs associated both with objective and subjective poverty [14]. This score is determined by an ecological measure using the IRIS scale (Ilôts Regroupés pour l'Information Statistique), which represents the smallest French geographical area for which there is a statistical evaluation to estimate social deprivation. Based on their addresses at diagnosis, each patient can be associated with an IRIS, and thus, their EDI can be established [14,15]. For interpretation, the highest EDI is associated with greater social deprivation. Second, we used the travel time defined as the shortest time to travel by car from the patient's address to the referring hospital to assess geographical disparities. A geographical information system (ArcGIS 10.5®-Esri France) associated with a road map database (Navstreets<sup>®</sup>, provided by HERE and Esri France) was used for this estimation. For our database, each patient's EDI and travel time were estimated from the address at diagnosis.

### Statistical analysis

Baseline characteristics of the population were described as the mean (+/- standard deviation) for quantitative variables numbers (percentages) for qualitative variables. and Quantitative and qualitative variables were analyzed by *t*-tests and chi2 tests, respectively. Two types of analysis were carried out (i) A multivariate analysis by logistic regression model was conducted to estimate factors associated with the probability of declaring a school or psychological difficulty, considering mixed effects for longitudinal data. We defined at the first level each consultation during which the psychosocial evaluation was completed. We defined at the second level the children for which the consultations were conducted. Factors associated with a p-value < 0.10 in the univariate analysis were considered in the multivariate logistic model. Subgroup analyses were carried out according to the tumor type (ii) We evaluated the probability of school and psychological difficulty over time by using Kaplan-Meier failure function curves. We completed a parametric survival regression model based on the same longitudinal data structure with

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two levels. All statistical analyses were performed with STATA software V14 and a p-value < 0.05 was considered to denote statistical significance.

We defined the primary endpoint as the probability of presenting a learning difficulty at school. The secondary endpoint was to assess these difficulties over time. Psychological difficulties were also analyzed for further explorations.

This study was based on a database supported by the *Commission Nationale de l'Informatique et des Libertés* (CNIL) registered under the N° 912302.

## Results

Overall, 1618 patients were included from six hospitals, and 1003 patients (62%) received a psychosocial functioning FU. School and psychological difficulties were evaluated in 2971 and 3320 consultations, respectively. Academic and psychological supports were evaluated in 2625 and 3320 consultations, respectively (Fig. 1). Since the first consultation at FU and the social reintegration, the mean duration of the FU was 34.6 months (+/–20.6). The population who received a psychosocial FU did not differ

from the population who did not receive a psychosocial assessment (Table 1). However, children with a psychosocial FU were less frequently treated with radiotherapy. The rate of children followed differed significantly between hospitals, and also according to vital status and relapse.

## Learning difficulties at school

School difficulties were reported by 224 children (22%) (Table 2). Greater social deprivation was significantly associated with learning difficulty at school; however, the increased geographic distance was not. Tumor relapse, treatment with hematopoietic stem cell transplantation (HSCT), and diagnosis of a CNS tumor remained also significant risk factors. Age expressed continuously (Table 2) or by categories (preschoolers under six years old, schoolaged from six to 15 years old, and adolescents up to 16 years old) was not a significant risk factor. Three-hundred seventy-one children received help with academic support, of which 74% reported difficulties at school. Academic support was mainly provided for children with CNS tumors (p < 0.001). Although learning difficulties were significantly associated with greater social deprivation, the probability of benefitting from support was not. However, there was an

#### TABLE 2

Risk factors associated wit	th school difficulties after	cancer care in children
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	Univariate analysis OR [CI]	Univariate analysis <i>p</i> -value*	Multivariate analysis OR [CI]	Multivariate analysis <i>p</i> -value*
EDI (per one unit)	1.10 [1.02-1.20]	p = 0.02	1.09 [1.01-1.18]	<i>p</i> = 0.04
Total travel time (per one minute)	1.01 [0.99-1.02]	p = 0.17		
Age at diagnosis (per one year)	0.99 [0.93-1.04]	p = 0.65		
Center of care		p = 0.04		p = 0.46
Center 1 (reference)	1		1	
Center 2	0.51 [0.24-1.06]		1.02 [0.47-2.21]	
Center 3	0.18 [0.06-0.55]		0.32 [0.10-1.02]	
Center 4	0.46 [0.18-1.16]		1.11 [0.43-2.91]	
Center 5	0.45 [0.16-1.35]		1.02 [0.34-3.08]	
Center 6	0.23 [0.06-0.92]		1.02 [0.25-4.13]	
Relapse	5.74 [2.26-14.53]	p < 0.001	4.06 [1.65-10.00]	p = 0.003
Chemotherapy	1.26 [0.58-2.73]	p = 0.557		
Radiotherapy	3.33 [1.73-6.39]	p < 0.001	1.24 [0.60-2.55]	p = 0.56
Surgery	1.40 [0.79-2.50]	p = 0.251		
HSCT	4.02 [1.61-10.04]	p = 0.003	2.66 [1.04-6.80]	p = 0.04
Sex	0.48 [0.27-0.85]	p = 0.01	0.60 [0.33-1.10]	p = 0.10
Type of tumors		p < 0.001		p < 0.001
Blood disorders	1		1	
Solid tumors	0.83 [0.37-1.85]		0.73 [0.31-1.76]	
CNS tumors	16.01 [7.59-33.80]		13.64 [6.20-29.99]	
Bone tumors	2.47 [0.79-7.80]		2.41 [0.76-7.76]	
Other tumors	0.17 [0.016-1.74]		0.24 [0.03-2.24]	
Time to consultation (per month)	0.99 [0.99-1.00]	p = 0.81		

<u>Legends</u>: CI: confidential interval; CNS: central nervous system, HSCT: hematopoietic stem cell transplantation, OR: odd ratio.  $\frac{*p}{2}$ -value < 0.05 was considered to denote statistical significance.



**FIGURE 2.** (A) Probability of acquiring a learning disability at school over time according to tumor type. (B) Probability of acquiring a learning disability at school over time according to tumor relapse.

important correlation between the learning disabilities and academic support ( $R^2 = 0.79$ ).

Two factors were significantly associated with the probability of having a school difficulty over time. CNS tumors were a significant risk factor in comparison with the other types, with a hazard ratio of 4.48 (CI: 2.79–7.21) (Fig. 2A). Tumor relapse was also a significant risk factor, with a hazard ratio of 1.80 (CI: 1.05–3.09) (Fig. 2B).

Ninety-two children with a CNS tumor reported a learning difficulty at school (46%). In this CNS group, greater social deprivation, tumor relapse, treatment by chemotherapy, and time were significant risk factors. In contrast, surgical management, alone or in combination with other therapies, remained a protective factor (Table 3). Neither the type of CNS tumor nor its localization had a significant impact on the risk of having a school difficulty. Of these children with CNS tumors who declared learning disabilities, 19% of them did not receive academic support.

Seventy-eight children with blood disorders reported learning difficulty at school (17%). Tumor relapse and management by HSCT were significant risk factors. Time and the female sex were protective.

## Psychological difficulties

Greater social deprivation was not significantly associated with the report of psychological difficulties. However, significant differences were noted between hospitals. A psychological difficulty was reported in 196 children (19.5%), but we did not have precisions about these difficulties. Risk factors associated with psychological difficulty were the relapse and the diagnosis of bone tumors (Suppl. Appendix). Psychological support was reported for 70% of all patients included. Over time, diagnosis of bone tumors was a risk factor for psychological difficulty (HR = 2.04, CI: 1.05–3.96), whereas a solid tumor was a protective factor (HR = 0.53, CI: 0.30–0.93). Greater social deprivation was not a risk factor as such. However, a trend between

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Risk factors associated with school difficulties after CNS cancer care in	children
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	Univariate analysis OR [CI]	Univariate analysis <i>p</i> -value*	Multivariate analysis OR [CI]	Multivariate analysis <i>p</i> -value
EDI (per one unit)	1.15 [1.01-1.32]	p = 0.04	1.15 [1.01–1.32]	<i>p</i> = 0.04
Total travel time (per one minute)	1.01 [0.99-1.02]	p = 0.45		
Age at diagnosis (per one year)	0.91 [0.82-1.01]	p = 0.07	0.95 [0.85-1.06]	<i>p</i> = 0.33
Center of care	p = 0.111			
Relapse	4.04 [0.90-18.23]	p = 0.07	4.55 [1.02-20.26]	p = 0.04
Chemotherapy	7.35 [2.65-20.45]	p < 0.001	4.42 [1.57-12.45]	p = 0.005
Radiotherapy	2.95 [1.07-8.12]	p = 0.04	1.73 [0.57-5.25]	p = 0.34
Surgery	0.27 [0.08-0.91]	p = 0.03	0.21 [0.06-0.78]	p = 0.02
HSCT	2.67 [0.65-10.96]	p = 0.17		
Sex	0.69 [0.26-1.83]	p = 0.45		

(Continued)

## Table 3 (continued)

	Univariate analysis OR [CI]	Univariate analysis <i>p</i> -value*	Multivariate analysis OR [CI]	Multivariate analysis <i>p</i> -value
Metastasis forms	7.68 [1.54-38.42]	p = 0.01	2.61 [0.53-12.83]	p = 0.24
Type of tumors		p = 0.16		
Low grade glioma	1			
Atypical teratoid rhabdoid tumor	1.36 [0.01-128.31]			
High grade glioma	2.12 [0.13-34.62]			
Medulloblastoma	4.46 [1.27-15.72]			
Germline brain tumor	0.08 [0.01-2180.97]			
Ependymomas	0.59 [0.09-4.12]			
Others	1.11 [0.22-5.45]			
Localization		p = 0.49		
Posterior Fossa	1			
Medullar	0.33 [0.03-3.70]			
Meninges	2.41 [0.08-71.06]			
Pineal gland	0.09 [0.00-0.94]			
HH axis and optic chiasm	1.09 [0.27-4.38]			
Multiple initial sites	11.60 [0.06-2085.38]			
Supra tentorial region (except HH axis and pineal region)	0.99 [0.29-3.36]			
Brain stem	0.55 [0.08-3.91]			
Time to consultation (per month)	1.03 [1.01–1.04]	<i>p</i> = 0.002	1.03 [1.01–1.04]	p = 0.001

Legends: CI: confidence interval; CNS: central nervous system; HH: hypothalamo-hypophyseal; HSCT: hematopoietic stem cell transplantation; OR: odd ratio. \*p-value < 0.05 was considered to denote statistical significance.

greater social deprivation and the presence of psychological difficulties could be noted (p = 0.064).

### Discussion

The results of this multicentric study show that greater social deprivation, and therefore poverty, is associated with school difficulties in CCSs.

Learning difficulties were reported in 22% of the children in our study, but higher rates have been noted in the literature [16,17]. CCSs are at risk for learning difficulties with scholarly consequences [7,11,16,17], ultimately leading to a lower overall quality of life (QOL) [18]. School absenteeism induced by cancer is the most common cause of school difficulties [6,19]. Even if we did not evaluate the rate of absenteeism in our cohort, we found that tumor relapse was a risk factor for school difficulties. Indeed, relapse frequently requires extended hospital stays and therefore, induces school absenteeism.

In our study, the probability of declaring a learning difficulty at school was associated with greater social deprivation. Irrespective of the disease status, there is a strong relationship between SES and scholarly achievement [20-22]. This supports our results and those of the literature, even though different methods were used to estimate the SES across studies [10,11,15]. School difficulties may be due to a lack of socialization in the school environment, this parameter being important for academic success [22]. However, our data collection precludes this analysis; but Duan et al.

demonstrated that greater social deprivation negatively influences the relationship between academic socialization and achievement [22]. Therefore, CCSs suffer from poor social integration, potentiated by absenteeism [16,19,19,23]. Among CCSs, children with CNS tumors are the population of greatest concern. Indeed, CNS tumors and their therapies (i.e., cranial radiotherapy, the intrathecal chemotherapy) increase the risk of adverse psychosocial and neurocognitive consequences [5,6,16,17,24]. We did not confirm the inherent risk of radiotherapy in our CNS subgroup analysis, probably due to the low number of children receiving irradiation followed in our cohort. In this CNS subgroup, social deprivation remained a prognostic factor for school difficulties, an observation also noted by Ach et al. [25].

Due to the risk of school difficulties in CCSs, academic support remains necessary. Thirty-six percent of children received such support in our study, a higher rate in comparison to the literature from 20% to 32.5% [19,24,26]. Although greater deprivation was associated with school disabilities, it was not associated with the probability of benefiting from academic support. Academic support seems to be equally shared between children according to the EDI, whereas we showed a higher need in deprived areas.

Our study did not show an association between, psychological difficulties and SES. However, it is well described in the literature that individual SES may participate in causal mechanisms for psychological affections, i.e., low levels of income, education, and employment in adulthood [12]. Indeed, children with high SES may benefit from privileged cultural, social, and economic resources which contribute to good mental health. However, these individual socio-economic parameters were not evaluated in our study, focused on ecological parameters, and may explain the difference in our results. In the literature, children with CNS tumors were reported to be at risk of psychological affections, whereas children with bone tumors were the population of greatest concern in our study [8,14]. Indeed, these last children presented frequently with physical damages induced by the surgery. Therefore, they may suffer from physical performance limitations, diminished ability to attend school, a decreased QOL [27,28]. In our results, differences between hospitals according to the presence of psychological difficulties may be explained by different factors. Indeed, hospitals did not present similar psychological support during the time of intensive treatment, and some units suffered from a lack of financial and human resources to properly carry out this mission. At the time of the reinsertion, psychological support can be continued with the hospital staff. However, new events are usually managed by private health professionals, and some regions suffer from a lack of private psychologists. Plus, these managements "outside the hospital" may not be reported to the pediatrician at the time of psychological evaluation.

#### Limitations

This study is based on a large multicentric prospective cohort in France to evaluate the psychosocial status of survivors after hospital treatment and its evolution over time. However, this study presents some limitations. Our population was based on a database that aims to represent all the children treated for cancer in the GOCE departments. However, one hospital was excluded from the study because it did not participate in patients' psychosocial evaluation, and may expose us to a selection bias (Fig. 1). Each outcome was evaluated during a consultation with the oncologist pediatrician at a time when the clinical evaluation remained the main objective to ensure the remission persistence, monitoring and screening for physical signs of disease. The outcomes were self-reported by children's families, and a subjective part of these reports cannot be ruled out. Additionally, pediatric oncologists did not present a specific background to conduct such interviews, and may not distinguish psychological issues. Indeed, clinicians, patients but also psychologists may have different definitions of well-being, and the subjective part of this evaluation may be shared between these actors. Besides, we did not have precisions about the type of psychological and scholarly difficulties, as well as their intensity. All of these questions the validity and reliability of the data collected, and the use of detailed and standardized questionnaires could have been helpful in clarifying these points.

The data was collected during the posttreatment period with no baseline at diagnosis available. This precludes any analysis to assess the evolution of the difficulties before and after cancer management. This limits our results to an observation of post-treatment difficulties without taking account of some potential predisposed conditions. Indeed, children with CNS tumors can present preexisting predisposition syndromes which can already induce psychosocial effects, as well as the tumor symptoms themselves. However, the evaluation of psychosocial status at diagnosis may be difficult. This time is a period when clinical management remains the absolute priority. This can explain the choice of clinicians to defer the psychosocial evaluation to after treatment.

The measurement of social deprivation using the EDI assesses the environment SES of each patient and can induce an ecological bias. This measurement considers homogeneity between children living in the same IRIS and could induce misclassification and underestimate the effect of the SES. Data on individual deprivation such as the education level of the parents could be a complementary method to precise the SES of children but were not available in the database.

#### Conclusion

Ecological deprivation is a prognosis factor for learning difficulties, particularly for children with CNS tumors. Therefore, our results should alert the professionals involved in children's cancer management, to be attentive to deprived children at risk of learning difficulties. Success at school is important for every child and has an impact on their current and future QOL. Although deprivation did not appear to be a risk factor for psychological difficulties, our rate of reporting poor well-being was high and probably underestimated due to the declarative bias.

Our study suggests further investigations. By focusing on CNS tumor patients, the difficulties of these patients could be detailed to propose adequate support. Plus, evaluation of the SES may integrate individual SES (family structure). Plus, evaluation of the SES may integrate individual SES (family structure, parental profession...) to complete investigations. Therefore, further analysis for attaining solutions to reduce SES-related social inequalities may be carried out.

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# SUPPLEMENTAL APPENDIX

N = 313	Univariate analysis OR [CI]	Univariate analysis <i>p</i> -value	Multivariate analysis OR [CI]	Multivariate analysis <i>p</i> -value
EDI (per one unit)	1.06 [0.99–1.13]	p = 0.08	1.05 [0.99-1.13]	p = 0.09
Total travel time (per one minute)	1.00 [0.99-1.00]	p = 0.98		
Age at diagnosis (per one year)	1.07 [1.02-1.12]	p = 0.005	1.03 [0.99-1.09]	p = 0.18
Center of care		p = 0.02		p = 0.01
Center 1 (reference)	1		1	
Center 2	1.11 [0.61-2.03]		1.30 [0.71-2.40]	
Center 3	0.48 [0.20-1.17]		0.55 [0.23-1.30]	
Center 4	1.15 [0.54-2.42]		1.18 [0.56-2.49]	
Center 5	0.23 [0.07-0.71]		0.24 [0.08-0.71]	
Center 6	0.36 [0.10-1.24]		0.34 [0.10-1.14]	
Relapse	3.15 [1.51-6.56]	p = 0.002	2.48 [1.22-5.02]	p = 0.01
Chemotherapy	2.11 [1.04-4.28]	p = 0.04	2.13 [0.98-4.61]	p = 0.05
Radiotherapy	1.41 [0.81-2.46]	p = 0.22		
Surgery	0.79 [0.49-1.27]	p = 0.33		
HSCT	1.19 [0.54-2.62]	p = 0.67		
Sex	1.14 [0.70-1.85]	p = 0.59		
Type of tumors		p < 0.001		p = 0.01
Blood disorders	1		1	
Solid tumors	0.41 [0.21-0.81]		0.50 [0.24-1.03]	
CNS tumors	0.99 [0.55-1.81]		1.33 [0.65-2.70]	
Bone tumors	2.77 [1.15-6.69]		2.76 [1.15-6.65]	
Other tumors	0.25 [0.07-0.84]		0.43 [0.13-1.42]	
Time to consultation (per month)	0.99 [0.99–1.01]	p = 0.89		

# Risk factors associated with psychological difficulties after cancer care in children

Legends: CI: confidential interval; CNS: central nervous system; HSCT: hematopoietic stem cell transplantation; OR: odd ratio.