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Socioeconomic status and incidence of pediatric leukemia in Canada: 1992–2010

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ABSTRACT

Background: Leukemia is the most common cancer among Canadian children, representing about a third of pediatric cancers in Canada and is responsible for about one-third of pediatric cancer deaths. Understanding the effect of socioeconomic status (SES) on pediatric leukemia incidence provides valuable information for cancer control and interventions in Canada.

Methods: Using a linked data from the Canadian Cancer Registry (CCR), Canadian Census of Population (CCP) and National Household Survey (NHS) we aimed to quantify socioeconomic inequalities in the incidence of pediatric leukemia from 1992 to 2010. We used the concentration index (C) approach to quantify income- and education-related inequalities in the incidence of pediatric leukemia over time.

Results: Though there were fluctuations in incidence over the study period, our results showed that the total incidence of pediatric leukemia in Canada was generally consistent from 1992 to 2010. Incidence rate of 47 per 1,000,000 as at 1992 rose to 57 per 1,000,000 in 2010. The estimated values of the C over the study period failed to show any significant association between pediatric leukemia incidence and household income or education status.

Conclusions: Although pediatric leukemia incidence is not rising significantly, it is not reducing significantly either. The incidence of pediatric leukemia showed no significant association with socioeconomic status. Future cancer control interventions should focus more on mitigating risk factors that are independent of socioeconomic status.

1. Introduction

Leukemia is a malignancy of the blood that is generally classified according to clinical presentation (acute or chronic) and cell lineage of origin (lymphoid or myeloid) [1]. It is the most common cancer in children between 0–14 years of age [2], representing about 32% of pediatric cancers in Canada [3]. Of the different types of leukemia, acute lymphocytic leukemia (ALL) is the most common among children and it represents about 80% of childhood leukemia cases [4–6]. Though modern treatment has improved, with a cure rate as high as 80–90% [2], leukemia is still responsible for about 30% of pediatric cancer deaths [7]. Furthermore, the toxic and traumatic nature of the treatments means that there are short and long-term health consequences for surviving children and their families [8]. As more children survive, the need for long-term monitoring and follow-up care will only continue to increase [2].

The etiology of leukemia is quite complex and not totally understood, with numerous theories proposed over the years. Genetics play a key role in the incidence of leukemia as evidenced by the numerous translocations (e.g. *TEL-AML1* and *BCR-ABL*), copy number alterations (e.g. *CDKN2A* deletion), point mutations (e.g. RAS mutations in AML), and epigenetic modifications that have been identified over the years [2,8–10]. Environmental factors also seem to contribute to the increased incidence of childhood leukemia. Parental exposure to pesticides, benzene, tobacco smoke (both during and after pregnancy), paints and solvents, petroleum products at home or work, organic pollutants as well as traffic emissions have all been associated with an increased risk of leukemia in children [2,11–13]. Pediatric leukemia, particularly ALL has also been associated with delayed exposure to infections at birth [5,8]. This infection theory suggests that delay in exposure of a child to common infections leads to a deficient immune system that is more susceptible to leukemia, especially ALL [5,14].

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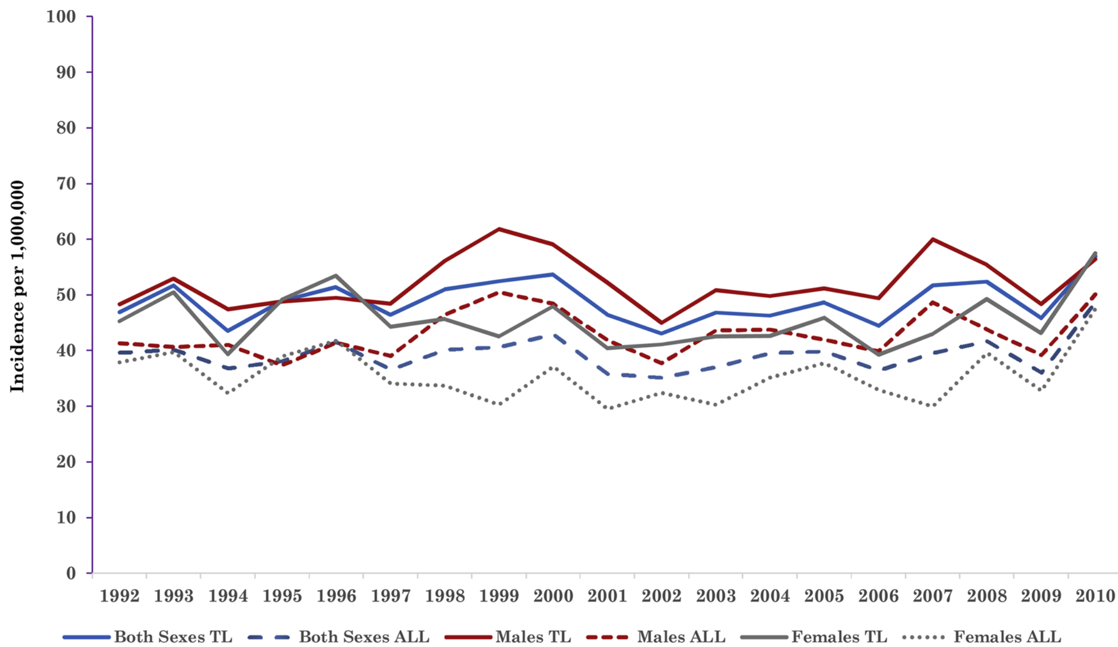

Fig. 1. Incidences of pediatric total leukemia (TL) and pediatric acute lymphocytic leukemia (ALL) per 1,000,000 children (0–14 years old) in Canada by sex from 1992 to 2010.

Table 1
Incidences of total leukemia (TL) and acute lymphocytic leukemia (ALL) per 1,000,000 children (0–14 years old) in Canada from 1992 to 2010.

Year	British Columbia		Prairies		Ontario		Quebec		Atlantic		Canada	
	TL	ALL	TL	ALL	TL	ALL	TL	ALL	TL	ALL	TL	ALL
1992	58	50	46	37	41	37	52	41	41	41	47	40
1993	50	33	37	32	58	39	52	48	51	41	52	40
1994	49	42	41	32	43	36	44	37	43	43	44	37
1995	42	35	46	37	50	36	55	40	54	43	49	39
1996	56	42	41	32	56	45	48	37	54	43	51	42
1997	42	42	46	37	52	38	48	37	32	22	46	37
1998	42	42	46	32	56	43	51	44	43	32	51	40
1999	58	43	38	33	45	34	70	54	73	61	53	40
2000	58	51	52	42	51	42	54	39	61	49	54	43
2001	43	29	47	38	47	34	47	39	49	49	47	36
2002	51	36	42	33	42	36	47	39	24	24	43	35
2003	51	43	57	47	40	31	47	39	61	24	47	37
2004	30	30	34	29	52	45	52	44	55	41	46	40
2005	53	30	48	43	45	38	56	48	41	41	49	40
2006	60	53	57	48	34	29	44	36	41	27	44	36
2007	68	53	48	38	52	41	44	28	55	41	51	40
2008	45	45	57	43	50	38	48	40	68	55	52	42
2009	44	30	36	27	53	44	44	32	43	28	46	36
2010	59	52	45	41	69	60	52	40	43	43	57	48
Trend Coefficients	0.17	0.14	0.33	0.34	0.18	0.35	−0.25	−0.31	0.14	−0.16	0.09	0.09
P-value	0.67	0.70	0.27	0.18	0.60	0.21	0.34	0.21	0.80	0.74	0.60	0.52

Note: Prairies = Alberta, Saskatchewan, Manitoba; Atlantic = New Brunswick, Nova Scotia, Newfoundland and Labrador, Prince Edward Island. †The incidences of pediatric leukemia were combined in the Prairies and in Atlantic Canada to meet the disclosure requirement of the Statistics Canada's Research Data Centre (RDC).

Another infection theory suggests that maternal infection during pregnancy increases the risk of childhood ALL [5,15]. The third well-known theory is Kinlen's population mixing theory which proposes that children in more isolated or less densely populated communities are more likely to possess an immune system that has been exposed to a less variety of infectious agents than their counterparts in less isolated communities. These children are thought to be more likely to develop leukemia upon exposure to new infections from inward migrants [16,17]. Other factors like maternal folate supplementation during pregnancy as well as breastfeeding for more than six months have been observed to reduce the risk of ALL in children [2,8,14], while factors like Down Syndrome, fanconi anemia, hereditary immunodeficiency, exposure to ionizing radiation and caesarean delivery at birth have been observed to show a positive association with pediatric leukemia [2,8,14,17]. It is evident that a plethora of modifiable and non-modifiable risk factors contribute to the incidence of leukemia. Addressing modifiable risk factors at a population level might help reduce the incidence of pediatric leukemia in Canada.

The emphasis on the social determinants of health over the last few decades has led to an increased interest in assessing the impact of social inequalities on health status. In adults, studies have suggested that lower socioeconomic status (SES) is associated with an increased risk of colorectal, lung and cervical cancer while higher SES is associated with increased risk of breast cancer, melanoma and prostate cancer [18–23]. Literature examining the effect of SES on pediatric leukemia reports mixed findings; while some reported childhood leukemia to be more

Table 2
Income-related inequalities in pediatric total leukemia (TL) and pediatric acute lymphocytic leukemia (ALL) incidences in Canada from 1992 to 2010 (average household equivalized income).

Year	The age-standardized C (95% confidence interval)					
	Both Sexes		Male		Female	
	TL	ALL	TL	ALL	TL	ALL
1992	0.04 (-0.041 to 0.122)	0.04 (-0.053 to 0.133)	0.066 (-0.041 to 0.172)	0.064 (-0.051 to 0.179)	0.012 (-0.115 to 0.14)	0.015 (-0.125 to 0.154)
1993	0.019 (-0.062 to 0.1)	−0.006 (-0.08 to 0.068)	0.053 (-0.034 to 0.14)	0.018 (-0.082 to 0.117)	0.001 (-0.139 to 0.142)	−0.017 (-0.147 to 0.113)
1994	0.004 (-0.086 to 0.093)	0.015 (-0.078 to 0.109)	0.014 (-0.102 to 0.129)	0.035 (-0.093 to 0.162)	−0.02 (-0.13 to 0.09)	−0.002 (-0.12 to 0.115)
1995	−0.034 (-0.102 to 0.035)	−0.014 (-0.088 to 0.061)	−0.076 (-0.186 to 0.033)	−0.064 (-0.182 to 0.054)	0.012 (-0.067 to 0.092)	0.041 (-0.057 to 0.138)
1996	0.033 (-0.035 to 0.101)	0.019 (-0.052 to 0.09)	0.046 (-0.045 to 0.136)	0.058 (-0.032 to 0.148)	0.008 (-0.089 to 0.106)	−0.028 (-0.142 to 0.085)
1997	−0.011 (-0.084 to 0.062)	−0.011 (-0.094 to 0.072)	−0.008 (-0.111 to 0.096)	−0.015 (-0.133 to 0.103)	0.009 (-0.125 to 0.144)	0.021 (-0.11 to 0.152)
1998	0.02 (-0.039 to 0.078)	0.023 (-0.048 to 0.093)	0.034 (-0.044 to 0.112)	0.041 (-0.052 to 0.134)	0.013 (-0.078 to 0.105)	0.002 (-0.093 to 0.096)
1999	−0.062 (-0.145 to 0.021)	−0.073 (-0.169 to 0.023)	−0.047 (-0.149 to 0.054)	−0.07 (-0.188 to 0.048)	−0.098 (-0.208 to 0.012)	−0.09 (-0.233 to 0.054)
2000	0.001 (-0.083 to 0.085)	0.034 (-0.06 to 0.129)	−0.057 (-0.147 to 0.032)	−0.027 (-0.122 to 0.069)	0.05 (-0.08 to 0.18)	0.088 (-0.064 to 0.24)
2001	0.072 (-0.044 to 0.188)	−0.002 (-0.115 to 0.111)	0.056 (-0.058 to 0.17)	0 (-0.112 to 0.112)	0.121 (-0.056 to 0.298)	0.024 (-0.142 to 0.19)
2002	0.007 (-0.09 to 0.104)	0.021 (-0.083 to 0.126)	0.079 (-0.024 to 0.182)	0.067 (-0.051 to 0.185)	−0.05 (-0.194 to 0.094)	−0.018 (-0.158 to 0.123)
2003	0.014 (-0.063 to 0.091)	0.026 (-0.058 to 0.109)	0.001 (-0.079 to 0.081)	0.012 (-0.073 to 0.098)	0.02 (-0.108 to 0.148)	0.044 (-0.109 to 0.198)
2004	−0.032 (-0.11 to 0.046)	−0.02 (-0.102 to 0.061)	−0.033 (-0.134 to 0.069)	−0.037 (-0.142 to 0.068)	−0.059 (-0.168 to 0.051)	−0.012 (-0.129 to 0.106)
2005	−0.012 (-0.087 to 0.063)	0.01 (-0.073 to 0.094)	−0.009 (-0.121 to 0.102)	0.011 (-0.117 to 0.139)	−0.031 (-0.128 to 0.066)	−0.003 (-0.102 to 0.096)
2006	−0.003 (-0.098 to 0.092)	0.007 (-0.095 to 0.11)	0.033 (-0.094 to 0.16)	0.045 (-0.095 to 0.186)	−0.024 (-0.139 to 0.091)	−0.015 (-0.125 to 0.095)
2007	−0.005 (-0.075 to 0.064)	0.048 (-0.02 to 0.117)	−0.002 (-0.077 to 0.072)	0.015 (-0.059 to 0.088)	−0.009 (-0.111 to 0.093)	0.126 (0.015 to 0.237)
2008	−0.048 (-0.118 to 0.022)	−0.071 (-0.154 to 0.011)	−0.024 (-0.115 to 0.066)	−0.053 (-0.148 to 0.042)	−0.072 (-0.191 to 0.048)	−0.082 (-0.226 to 0.061)
2009	−0.035 (-0.101 to 0.031)	−0.026 (-0.107 to 0.056)	−0.025 (-0.109 to 0.059)	−0.033 (-0.128 to 0.063)	−0.084 (-0.175 to 0.006)	−0.03 (-0.139 to 0.079)
2010	0.031 (-0.034 to 0.096)	0.055 (-0.023 to 0.133)	0.027 (-0.054 to 0.108)	0.025 (-0.073 to 0.123)	0.073 (-0.011 to 0.157)	0.122 (0.032 to 0.212)
Trend Coefficients	−0.0015	−0.0001	−0.0016	−0.0017	−0.0015	0.0022
P-value	0.2580	0.9330	0.3120	0.3200	0.5280	0.4450

Note: The inverse of the standard errors of the C were used as weights in the trend analysis.

Table 3
Education-related inequalities in pediatric total leukemia (TL) and pediatric acute lymphocytic leukemia (ALL) incidences in Canada from 1992 to 2010.

Year	The age-standardized C (95% confidence interval)					
	Both Sexes		Male		Female	
	TL	ALL	TL	ALL	TL	ALL
1992	−0.004 (-0.098 to 0.09)	−0.019 (-0.125 to 0.086)	−0.03 (-0.156 to 0.095)	−0.036 (-0.174 to 0.102)	−0.009 (-0.135 to 0.118)	−0.027 (-0.163 to 0.109)
1993	−0.012 (-0.097 to 0.073)	−0.033 (-0.12 to 0.055)	0.077 (-0.012 to 0.165)	0.074 (-0.029 to 0.176)	−0.074 (-0.211 to 0.063)	−0.1 (-0.235 to 0.036)
1994	−0.023 (-0.117 to 0.072)	−0.016 (-0.115 to 0.082)	0.003 (-0.12 to 0.125)	0.009 (-0.125 to 0.143)	−0.029 (-0.162 to 0.104)	−0.021 (-0.171 to 0.129)
1995	−0.016 (-0.102 to 0.069)	0.019 (-0.078 to 0.116)	−0.033 (-0.169 to 0.103)	0.025 (-0.116 to 0.167)	0.006 (-0.091 to 0.104)	0.017 (-0.102 to 0.136)
1996	0.054 (-0.028 to 0.135)	0.026 (-0.057 to 0.109)	0.061 (-0.028 to 0.15)	0.061 (-0.025 to 0.147)	0.06 (-0.061 to 0.181)	0.013 (-0.124 to 0.15)
1997	−0.015 (-0.092 to 0.063)	−0.015 (-0.099 to 0.068)	−0.047 (-0.162 to 0.068)	−0.024 (-0.144 to 0.096)	0.049 (-0.105 to 0.203)	0.052 (-0.079 to 0.183)
1998	0.017 (-0.052 to 0.086)	0.031 (-0.055 to 0.116)	0.052 (-0.051 to 0.156)	0.067 (-0.055 to 0.19)	−0.023 (-0.123 to 0.077)	−0.015 (-0.127 to 0.098)
1999	0.009 (-0.072 to 0.091)	0.007 (-0.083 to 0.098)	0.011 (-0.097 to 0.119)	−0.012 (-0.139 to 0.115)	−0.024 (-0.133 to 0.086)	0.011 (-0.126 to 0.149)
2000	0.012 (-0.088 to 0.113)	0.063 (-0.056 to 0.182)	−0.019 (-0.13 to 0.092)	0.016 (-0.103 to 0.135)	0.002 (-0.149 to 0.152)	0.072 (-0.117 to 0.262)
2001	0.131 (0.026 to 0.236)	0.077 (-0.033 to 0.187)	0.187 (0.068 to 0.306)	0.139 (0.011 to 0.267)	0.068 (-0.093 to 0.229)	−0.011 (-0.191 to 0.169)
2002	0.089 (-0.007 to 0.185)	0.093 (-0.005 to 0.191)	0.12 (0.016 to 0.224)	0.104 (-0.003 to 0.211)	0.086 (-0.082 to 0.253)	0.101 (-0.078 to 0.28)
2003	0.074 (-0.024 to 0.173)	0.078 (-0.022 to 0.178)	0.053 (-0.05 to 0.155)	0.05 (-0.068 to 0.167)	0.078 (-0.064 to 0.219)	0.093 (-0.075 to 0.26)
2004	0.041 (-0.041 to 0.122)	0.035 (-0.052 to 0.123)	0.025 (-0.08 to 0.129)	0.016 (-0.095 to 0.127)	0.02 (-0.09 to 0.13)	0.036 (-0.079 to 0.152)
2005	−0.004 (-0.094 to 0.085)	−0.004 (-0.097 to 0.088)	−0.052 (-0.174 to 0.07)	−0.049 (-0.186 to 0.088)	0.044 (-0.064 to 0.153)	0.052 (-0.049 to 0.154)
2006	−0.08 (-0.187 to 0.027)	−0.081 (-0.199 to 0.038)	−0.041 (-0.167 to 0.086)	−0.03 (-0.172 to 0.113)	−0.087 (-0.218 to 0.043)	−0.099 (-0.236 to 0.038)
2007	0.009 (-0.069 to 0.087)	0.027 (-0.05 to 0.103)	0.036 (-0.046 to 0.118)	0.017 (-0.069 to 0.102)	−0.034 (-0.153 to 0.084)	0.067 (-0.06 to 0.193)
2008	−0.055 (-0.133 to 0.023)	−0.071 (-0.162 to 0.021)	−0.087 (-0.188 to 0.014)	−0.113 (-0.222 to -0.004)	−0.016 (-0.139 to 0.107)	−0.008 (-0.155 to 0.139)
2009	0.042 (-0.019 to 0.102)	0.056 (-0.02 to 0.133)	0.057 (-0.019 to 0.133)	0.062 (-0.026 to 0.151)	−0.008 (-0.108 to 0.093)	0.034 (-0.088 to 0.155)
2010	0.058 (-0.001 to 0.116)	0.082 (0.008 to 0.157)	0.075 (-0.011 to 0.161)	0.083 (-0.028 to 0.194)	0.064 (-0.019 to 0.148)	0.104 (0.014 to 0.194)
Trend Coefficients	0.0013	0.0021	0.0002	−0.0009	0.0014	0.0046
P-value	0.4260	0.2800	0.9280	0.7410	0.4620	0.0430

Note: The inverse of the standard errors of the C were used as weights in the trend analysis.

frequent among individuals of low SES, other studies show high SES to be a risk factor for pediatric leukemia [14,24,25]. A Canadian study conducted in 2005 utilized data from the Canadian Cancer Registry (CCR) and demonstrated that higher income is a risk factor for pediatric ALL [26]. A review study by Poole et al. in 2006 observed a negative association when the incidence of childhood leukemia was measured against family income or parental education [27].

Although some of the current literature have investigated the association between childhood leukemia and SES, to the best of our knowledge, no study measures socioeconomic inequalities in the incidence of pediatric leukemias in Canada over time. Using a linked data from the Canadian Cancer Registry (CCR), Canadian Census of Population (CCP) and National Household Survey (NHS) we aimed to quantify income- and education-related inequalities in incidence of pediatric leukemia from 1992 to 2010. Understanding the distribution of the incidence of pediatric leukemia among different SES groups can provide valuable information for cancer control and intervention in Canada.

2. Methods

2.1. Data sources and variables

We used data from the CCR, CCP and NHS to measure socioeconomic inequalities in leukemia incidence among children aged 0–14 years in Canada from 1992 to 2010 (approximately 5.66 million children; 2.90 million males and 2.76 million females in each year). The CCR was used to obtain information about new primary pediatric leukemias diagnosed among residents in Canada. As a population-based registry, the CCR collects and reports new primary cancers by each province/territory. Based on the sex of the individual, the individual's six-digit postal code of residence as well as the age at which the tumor was diagnosed collected from the CCR data, we were able to identify the number of the new cases of leukemia in children (0–14 years old) from 1992 to 2010. We used the third edition of the International Classification of Diseases for Oncology (ICD-O-3) morphology codes (9733, 9742, 9800–9801, 9805–9809, 9811–9818, 9820, 9823, 9826, 9827, 9831–9837, 9840, 9860–9861, 9863, 9865–9867, 9869–9876, 9891, 9895–9898, 9910, 9911, 9920, 9930–9931, 9940, 9945–9946, 9948, 9963–9964) [3] to identify patients with leukemia in the CCR data file. To identify ALL, we used codes from the International Classification of Childhood Cancer, third edition (ICCC-3; 9820, 9826, 9827, 9831–9837, 9940, 9948) [28], after cross-referencing that the codes corresponded to ALL according to ICD-O-3 [29]. The Postal Code Conversion File plus (PCCF+) Version D software was used to identify the Census Division (CD) coordinates of each pediatric leukemia patient in the CCR via their six-digit postal codes. Statistics Canada defines CDs as "a group of neighbouring municipalities joined together for the purposes of regional planning and managing common services" [30]. We then calculated number of new cases of pediatric leukemia in each CD.

The CCR does not contain information on SES of individuals (e.g. income and education); thus, we used SES variables in the CCP 1991, 1996, 2001, 2006 and NHS 2011 to create a new dataset that contains SES (average household income and proportion of individuals with a bachelor's degree and above) and population characteristics of each CD in Canada. As per the Organisation for Economic Co-operation and Development (OECD) publications [31], we equivalized household annual income by dividing it by the square root of household size when we measured the average household income for each CD. Based on CD coordinates, we linked the aggregated CD-level of SES and demographic information of the CCP/NHS data to the CCR (CCP 1992 to CCR 1992–1993, CCP 1996 to CCR 1994–1998, CCP 2001 to CCR 1999–2003, CCP 2006 to CCR 2004–2008, NHS 2011 to CCR 2009–2010) to calculate cancer incidence at the CD level and measure income- and education-related inequalities in pediatric leukemias from 1992 to 2010 in Canada.

2.2. Ethics issues

We accessed and analysed the data via the Statistic Canada's Research Data Centre (RDC). Access to the datasets through the RDC requires strict disclosure protocols in line with Statistics Canada Acts. Studies conducted at the RDC are exempted from the research ethics board review based on the Tri-council policy statement: Ethical conduct for research involving humans (TCPS2) article 2.2 (a).

2.3. Statistical analysis

Several measures have been suggested to assess inequalities in health [32,33], including the index of disparity, index of dissimilarity, Gini coefficient, the relative index of inequality and the concentration index. We used the concentration index (C) to quantify income- and education-related inequalities in the incidence of pediatric leukemia over time. As described by Wagstaff et al. [34], the C is a desired socioeconomic inequality index because it measures health inequalities that originated from the SES characteristics and provides inequality measure which is a representative of the entire population. The C is a modification of the Gini coefficient and is commonly used in health inequality literature and can be estimated from the concentration curve [35,36]. The concentration curve is a plot of the cumulative proportion of a sample (pediatric population) ranked by a SES variable (e.g. income or education), starting from the least advantaged to the most advantaged on the x-axis against the cumulative proportion of the health outcome (pediatric leukemia incidence) on the y-axis [35,36]. The line of equality is a 45° diagonal line that suggests perfect equality between the low and high SES groups. For example, the perfect equality line can illustrate that the least advantaged 30% of children will have 30% of the cases of leukemia incidence. If the concentration curve lies above (below) the line of equality, it indicates that socioeconomic inequality exists and pediatric leukemia incidence is more (less) common in low SES groups [35,36]. The more the concentration curve deviates from the line of equality, the greater the degree of inequality [35,36]. The C can range from −1 to +1, with the value less than zero suggesting that pediatric leukemia is concentrated among lower SES groups and *vice versa*. The value of zero suggests an equal socioeconomic distribution.

We computed the crude C using the following "convenient regression" formula [35]:

$$2\sigma_R^2\left(\frac{y_i}{\mu}\right) = \alpha + \delta R_i + \varepsilon_i, \tag{1}$$

where y_i shows CD i' s pediatric leukemia incidence, μ is the mean incidence rate for pediatric leukemia for all CDs, α is the intercept, R_i is the CD i' s fractional rank in the distribution ($i = 1$ and n for the lowest SES and highest SES CDs, respectively) and is calculated as $R_i = i/n$. The σ_R^2 denotes the variance of fractional rank. The ordinary least squares (OLS) estimate of δ in Eq. (1) and its standard error demonstrates the value and the standard error for the crude C, correspondingly. Age-standardized income/education-related inequality can be calculated using an indirectly standardized concentration index by including the standardizing variables (age-group variables) in the convenient regression as follows [37]:

$$2\sigma_R^2\left(\frac{y_i}{\mu}\right) = \alpha + \delta R_i + \beta_1 Age_{5-9} + \beta_2 Age_{10-14} + \nu_i, \tag{2}$$

where Age_{5-9} and Age_{10-14} denote the proportion of children aged 5–9 years, 10–14 years in each CD (the proportion of children aged 0–4 years in each CD used as a base category in the regression), respectively. β_1 and β_2 are the corresponding coefficients for Age_{5-9} and Age_{10-14}. The OLS estimate of δ in Eq. (2) demonstrates the age-standardized concentration index.

We used the population number of ages 0–14 years in each CD to measure the incidence and as weights in the calculation of Cs. We performed a trend analysis by plotting the C of each inequality measure on the y-axis against time (19 points corresponding to the years from 1992 to 2010) on the x-axis. If the estimated coefficient for the time trend (i.e. the slope of the regression line) is negative (positive), it suggests that the inequality measure is decreasing (increasing) over time while a slope coefficient of zero suggests that there is no linear trend over time.

3. Results

3.1. Trends in pediatric leukemia

The incidence of pediatric total leukemia (TL) and pediatric ALL in Canada from 1992 to 2010 is shown in Fig. 1. Although there were fluctuations over the study period, the total incidence of pediatric leukemia in Canada was consistent from 1992 to 2010 i.e. 47 per 1,000,000 in 1992 to 57 per 1,000,000 in 2010. Similarly, the incidence of pediatric ALL was quite consistent over the study period i.e. 40 per 1,000,000 in 1992 to 48 per 1,000,000 in 2010. For both pediatric TL and ALL, incidence was usually slightly higher in males than in females with an average ratio of 1.2 to 1 over the study period. Male incidence was highest in 1999 at 62 per 1,000,000 and 51 per 1,000,000 for pediatric TL and ALL, respectively, while female incidence was highest in 2010 at 58 per 1,000,000 and 48 per 1,000,000 for pediatric TL and ALL, respectively.

The incidence rates of pediatric leukemia across five Canadian regions are shown in Table 1. Due to very low numbers of pediatric leukemia cases, data from Nova Scotia, Newfoundland and Labrador and Prince Edward Island provinces were merged as the Atlantic region. This was the same case with the Prairies which consists of data from Manitoba, Alberta and Saskatchewan provinces. Although pediatric TL and ALL incidences in Ontario increased from 41 per 1,000,000 in 1992 to 69 per 1,000,000 in 2010 and 37 per 1,000,000 in 1992 to 60 per 1,000,000 in 2010 respectively, there was no significant trend over the years. Across all the other four Canadian regions, there was no significant trend in the incidence of pediatric TL and ALL throughout the study period as the numbers were consistent over time.

3.2. Socioeconomic inequalities in pediatric leukemia

Income-related inequalities in pediatric TL and ALL incidences from 1992 to 2010 are reported in Table 2, while Table 3 shows education-related inequalities in pediatric TL and ALL incidences over time. As reported in Table 2, when we used average household equivalized income as a measure of SES to measure inequality in pediatric TL and ALL incidences, confidence intervals for values of C all contain zero values. Similar results were observed when we used the median household equivalized income to measure inequality in pediatric leukemia incidence (see Table A2 in the appendix). Hence, no significant association was found between household income and pediatric TL and ALL incidences throughout the study period. Similarly, as shown in Table 3, level of education for the most part, showed no significant association with pediatric TL and ALL incidence, except for the years 2001, 2002 and 2010 which showed a higher concentration of TL and/or ALL among higher SES children. The results of the trend analyses did not indicate any significant change in the C over time.

4. Discussion and conclusion

This study aimed to measure income- and education-related inequalities in the incidence of childhood leukemia across Canada from 1992 to 2010 and to determine if there were trends in the inequalities measured over time. Our analysis did not show any significant association between the incidence of pediatric leukemia and household income or level of education.

Although some studies suggest that low SES is associated with increased incidence of childhood leukemia [38,39], others suggest an association with high SES [14,24,26]. Smith et al. in 2006 reported no association between SES and pediatric leukemia in the UK and suggested that small effects reported in some studies might be artefactual [40]. An Australian study in 2012 also found no significant association between SES and incidence rates of pediatric leukemia [41]. Some of the heterogeneity in these results can be explained by the variation in the use of different measures of SES (income, education or occupation) in the studies [25,27,42]. Furthermore, as patterns of SES gradient in cancers can be dynamic, varying according to location and time period, results from individual studies should not be generalised [43] particularly for a cancer like leukemia which has a very complex etiology. In addition, studies that often report the association of pediatric leukemia incidence with higher SES groups as well as those with no association, acknowledge the possibility that leukemia might be underdiagnosed or under-reported in children from lower SES families [14,24,26,40]. For example, the lack of specialist doctors in underprivileged areas could lead to some pediatric leukemia patients dying from an infection without ever being diagnosed, thus resulting in a pseudo-lower incidence rate being observed in these communities. Finally, as Adam et al. summarized in their review, heterogeneous results from both older and more recent large-scale studies could also highlight the fact that there is no conclusive evidence to support an association between SES and incidence of pediatric leukemia [25].

Our findings contradict a previous study by Borugian et al. in 2005 [26] which demonstrated a slightly higher relative risk of pediatric leukemia in the richest income quintile compared to those in the poorest quintile [26]. The difference in the details of methodology and analysis could have contributed to our conflicting findings. Borugian et al. [26] used neighbourhood income quintiles for dissemination areas across Canada to analyse income-related inequalities in pediatric leukemia incidence by measuring rate ratio for the poorest neighborhood income quintile compared with the richest neighbourhood income quintile. Using the rate ratio as a measure of inequality cannot provide a clear picture about the distribution of pediatric leukemia incidence across the entire population as it only uses the incidence information of the poorest and wealthiest quantiles and ignores the incidence among the middle-class population. In order to estimate socioeconomic inequalities which are representative of the entire population, we ranked about 300 CDs across Canada according to their SES and measured income- and education-related inequalities in the incidence of pediatric leukemia using a summary measure of the C [35]. There is evidence that using different measures of inequality can yield contradictory results from the same dataset [32,33].

A major strength of our study is the fact that we have used data from the CCR which has a high coverage rate, thus minimising the challenge of under-reporting. Also, as previous studies [27] argued that using different measures of SES may lead to different conclusions when we attempt to establish the gradient between SES and childhood leukemia, we used two separate measures of socioeconomic inequalities (income and education) to determine if either plays a role in increased incidence of pediatric leukemia. Finally, to provide more clarity on the relationship between SES and childhood leukemia incidence, our study also analysed income and education inequalities in the incidence of ALL and found no significant association between SES and the most common subtype of pediatric leukemia.

Our study is subject to some limitations. First, although studies have observed that area-based SES measures can be comparable with individual-based measures, this may not always be the case due to the risk of ecological fallacy as neighbourhood characteristics do not always reflect individual characteristics [14,44,45]. Second, as childhood cancer is generally rare, rather than using smaller dissemination areas which improve the validity of area-based measures [26,46], we used much larger CDs which are less homogenous compared with smaller area measures [45]. Third, as censuses are not conducted on a yearly basis, as described in the methods section, we had to use the closest census years to our CCR year of interest for getting relevant socioeconomic data. In other words, socioeconomic data might not have been as accurate as possible. Finally, seperate analysis of leukemia incidence according to different age groups (e.g. 0–4, 5–9, 10–14) might have also yielded more clarity as to what ages suffer more from the disease as well as if the inequality in incidence is age-dependent. We could not perform these analyses because of the low incidence rate of pediatric leukemia.

Caveats considered, our study indicated that the incidence of pediatric leukemia has remained steady from 1992 to 2010 in Canada irrespective of income or education status. These results suggest that future cancer control interventions should focus more on mitigating risk factors that are independent of SES.

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Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A

Table A1

Authorship contribution

All authors contributed to the conception and design of the study. Adedeji Ologbenla conceived the study, performed data analysis and wrote the first draft of the paper. Min Hu conceived the study, compiled the data and cleaned data for data analysis. Mohammad Hajizadeh conceived the study, performed data analysis and critically reviewed and revised the draft of the paper. All authors read and approved the final version of the manuscript.

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Table A1
Incidences of total leukemia (TL) and acute lymphocytic leukemia (ALL) per 1,000,000 children (0–14 years old) in Canada by sex: 1992–2010.

Year	Both Sexes		Males		Females	
	TL	ALL	TL	ALL	TL	ALL
1992	47	40	48	41	45	38
1993	52	40	53	41	50	40
1994	44	37	47	41	39	32
1995	49	39	49	37	49	39
1996	51	42	49	41	53	42
1997	46	37	48	39	44	34
1998	51	40	56	46	46	34
1999	53	40	62	51	43	30
2000	54	43	59	48	48	37
2001	47	36	52	42	40	30
2002	43	35	45	38	41	32
2003	47	37	51	44	43	30
2004	46	40	50	44	43	35
2005	49	40	51	42	46	38
2006	44	36	49	40	39	33
2007	51	40	60	49	43	30
2008	52	42	55	44	49	40
2009	46	36	48	39	43	33
2010	57	48	56	50	58	48
Trend Coefficients	0.09	0.09	0.20	0.24	0.03	0.01
P-value	0.60	0.52	0.34	0.18	0.88	0.96

Table A2
Income-related inequalities in pediatric total leukemia (TL) and pediatric acute lymphocytic leukemia (ALL) incidences in Canada from 1992 to 2010 (Median household equivalized income).

Year	The age-standardized C (95% confidence interval)					
	Both Sexes		Male		Female	
	TL	ALL	TL	ALL	TL	ALL
1992	0.034 (-0.043 to 0.111)	0.034 (-0.054 to 0.122)	0.061 (-0.04 to 0.161)	0.06 (-0.049 to 0.169)	0.007 (-0.116 to 0.131)	0.009 (-0.123 to 0.14)
1993	0.021 (-0.058 to 0.099)	0 (-0.072 to 0.072)	0.045 (-0.045 to 0.135)	0.015 (-0.089 to 0.118)	0.009 (-0.127 to 0.145)	−0.006 (-0.13 to 0.119)
1994	−0.001 (-0.091 to 0.088)	0.01 (-0.081 to 0.102)	0.01 (-0.099 to 0.119)	0.028 (-0.091 to 0.146)	−0.037 (-0.147 to 0.072)	−0.013 (-0.126 to 0.101)
1995	−0.023 (-0.09 to 0.043)	−0.012 (-0.084 to 0.059)	−0.071 (-0.168 to 0.026)	−0.069 (-0.175 to 0.036)	0.028 (-0.053 to 0.108)	0.047 (-0.051 to 0.145)
1996	0.03 (-0.036 to 0.095)	0.014 (-0.055 to 0.083)	0.037 (-0.053 to 0.128)	0.04 (-0.052 to 0.133)	−0.001 (-0.091 to 0.09)	−0.032 (-0.137 to 0.073)
1997	0.001 (-0.075 to 0.077)	−0.001 (-0.085 to 0.083)	0.003 (-0.095 to 0.1)	−0.011 (-0.123 to 0.101)	0.022 (-0.108 to 0.152)	0.026 (-0.105 to 0.157)
1998	0.016 (-0.041 to 0.073)	0.019 (-0.049 to 0.087)	0.014 (-0.062 to 0.09)	0.021 (-0.067 to 0.109)	0.03 (-0.058 to 0.118)	0.017 (-0.075 to 0.108)
1999	−0.071 (-0.151 to 0.009)	−0.079 (-0.173 to 0.015)	−0.054 (-0.15 to 0.043)	−0.069 (-0.182 to 0.043)	−0.1 (-0.208 to 0.008)	−0.097 (-0.233 to 0.039)
2000	0.01 (-0.067 to 0.088)	0.04 (-0.048 to 0.128)	−0.036 (-0.118 to 0.046)	−0.001 (-0.087 to 0.085)	0.056 (-0.066 to 0.177)	0.079 (-0.066 to 0.225)
2001	0.05 (-0.058 to 0.159)	−0.015 (-0.121 to 0.091)	0.027 (-0.081 to 0.134)	−0.015 (-0.12 to 0.09)	0.1 (-0.059 to 0.258)	0.008 (-0.145 to 0.16)
2002	−0.013 (-0.103 to 0.077)	−0.004 (-0.1 to 0.093)	0.045 (-0.054 to 0.143)	0.031 (-0.085 to 0.147)	−0.068 (-0.205 to 0.069)	−0.042 (-0.169 to 0.086)
2003	0.008 (-0.06 to 0.077)	0.016 (-0.059 to 0.091)	−0.005 (-0.081 to 0.072)	0.008 (-0.074 to 0.09)	0.023 (-0.093 to 0.139)	0.04 (-0.1 to 0.18)
2004	−0.041 (-0.114 to 0.032)	−0.041 (-0.114 to 0.032)	−0.044 (-0.139 to 0.05)	−0.052 (-0.146 to 0.041)	−0.048 (-0.152 to 0.057)	−0.03 (-0.139 to 0.079)
2005	−0.013 (-0.077 to 0.051)	0.007 (-0.065 to 0.078)	0.002 (-0.099 to 0.103)	0.012 (-0.102 to 0.126)	−0.042 (-0.13 to 0.046)	−0.013 (-0.109 to 0.083)
2006	−0.02 (-0.112 to 0.071)	−0.007 (-0.1 to 0.086)	0.02 (-0.094 to 0.134)	0.024 (-0.098 to 0.146)	−0.064 (-0.174 to 0.047)	−0.037 (-0.143 to 0.068)
2007	−0.003 (-0.069 to 0.063)	0.038 (-0.029 to 0.104)	−0.01 (-0.083 to 0.062)	0.009 (-0.066 to 0.084)	0.01 (-0.082 to 0.103)	0.096 (-0.007 to 0.199)
2008	−0.057 (-0.121 to 0.008)	−0.063 (-0.136 to 0.009)	−0.025 (-0.107 to 0.058)	−0.043 (-0.126 to 0.041)	−0.09 (-0.197 to 0.018)	−0.084 (-0.214 to 0.046)
2009	−0.055 (-0.116 to 0.007)	−0.065 (-0.138 to 0.008)	−0.035 (-0.12 to 0.051)	−0.05 (-0.145 to 0.045)	−0.111 (-0.189 to -0.033)	−0.093 (-0.186 to 0.001)
2010	0 (-0.059 to 0.06)	0.009 (-0.062 to 0.08)	−0.031 (-0.1 to 0.039)	−0.049 (-0.133 to 0.035)	0.075 (-0.007 to 0.157)	0.114 (0.026 to 0.202)
Trend Coefficients	−0.0027	−0.0018	−0.0026	−0.0028	−0.0026	0.0001
P-value	0.0240	0.2060	0.0550	0.0610	0.3760	0.9710

Note: The inverse of the standard errors of the C were used as weights in the trend analysis.

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