Location of Death Among Children with Life-Threatening Conditions: A National Population-Based Observational Study

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ABSTRACT

Background Examining patterns in location of death among children with life-threatening conditions (e.g., cancer, genetic disorders, neurological conditions) may reveal important inequities in access to hospital and community support services. We aimed to identify demographic, socioeconomic, and geographic factors associated with variations in location of death for children across Canada with life-threatening conditions.

Methods We used a retrospective observational cohort design and the Canadian Vital Statistics Database to identify children aged 19 years or younger who died from a life-threatening condition between January 1, 2008 and December 31, 2014. Multivariable logistic regression was used to determine predictors of in-hospital death for two groups: 1) children aged 1 month to 19 years, and 2) neonates less than 1 month old.

Results Of 13,115 decedents less than 19 years of age, 74.2% of children and 98.1% of neonates died in hospital. In children, factors associated with increased odds of in-hospital death included age less than 1 year (OR = 1.73, 95% CI = 1.4 - 2.15), a congenital (OR = 1.74, 95% CI = 1.43 - 2.11) or gastrointestinal cause of death (OR = 5.36, 95% CI = 2.54 - 11.3), and lower income (OR = 1.59, 95% CI = 1.28 - 1.97). Living in British Columbia (OR = 0.43, 95% CI = 0.34 - 0.53) or further from a tertiary pediatric hospital (OR = 0.73, 95% CI = 0.65 - 0.86) were associated with decreased odds of hospital death.

Interpretation In addition to demographics, we identified socioeconomic and geographic disparities in location of death suggesting potential inequities in access to high quality care at end-of-life.

INTRODUCTION

A child's death has a long-lasting and potentially traumatic impact on families, communities, and health professionals providing care.[1,2] Thus, when death in childhood is anticipated – such as when a child is living with a life-threatening condition (e.g., cancer, genetic disorders, neurological conditions)[3] – it is important to provide high quality care to maximize quality of life and facilitate end-of-life care and death in the preferred location.[4] In Canada, provincial studies focused on children highlight the high proportion who die in hospitals.[5-7] Variations in this proportion may reflect variation in child and family preference, but may also be heavily influenced by availability of community services such as pediatric hospice or palliative home care, as well as specialized care through tertiary pediatric hospitals.[4,8,9] Based on research conducted in the United States and other countries, geography and level of income may also impact on where children die.[10-14] From a health equity lens, it is important to identify factors associated with location of death for children with life-threatening condition in Canada.

To date, health administrative data have not been used to study children's location of death across Canada. We therefore examined deaths nationally to identify demographic, socioeconomic, and geographic factors associated with variations in location of death in children who died from life-threatening conditions. Our goal was to identify potential health inequities and opportunities to optimize care across care settings.

METHODS

Population and Cohort

This national observational, retrospective cohort study drew on the population of Canadian residents who died at 19 years of age or younger from January 1, 2008 through December 31, 2014. The cohort was created using the Canadian Vital Statistics Database

(CVSD), a yearly census of all deaths occurring in Canada with relevant demographic and cause of death information coded using the International Classification of Diseases, 10th edition (ICD-10).[15] To identify children who died from a life-threatening condition we first excluded those whose primary cause of death was listed as external, such as accidents, assault, suicide, or drowning (ICD-10 codes from V01 to Y36), or Sudden Infant Death Syndrome (R95). Next, we combined classifications developed in the United Kingdom[16] and United States[17] to create a list of specific ICD-10 codes within 11 categories signifying life-threatening conditions in children (Supplemental File A). Children included in the final cohort had at least one relevant ICD-10 coded listed either as a primary or contributing cause of death. Based on previous research showing the vast majority of neonates die in hospital,[4,7] we stratified the cohort to facilitate separate analysis of children (aged 29 days to 19 years) and neonates (< 29 days of age).

Measures

Outcomes. The primary outcome was location of death, classified as in-hospital (i.e., licensed to operate as hospital under provincial, territorial, or federal government legislation) or out-of-hospital (e.g., private home, freestanding birthing centre, other facility, other specified location).[18]

Predictors. For the child group, age was categorized as: 29 –364 days, 1-4 years, 5-9 years, 10-14 years, and 15-19 years. For the neonate group, age was categorized as < 24 hours and 24 hours to 28 days. Decedents were assigned into 11 categories of life-threatening conditions: neurologic, haematologic, oncologic, metabolic, respiratory, circulatory, gastrointestinal, genitourinary, perinatal, congenital, and other (e.g., systemic lupus).[16,17] For those with causes of death in multiple categories, assignment was based on the primary cause of death. In cases with no relevant primary cause and multiple contributing causes (about 5% of the

sample) we used an *a priori* determined hierarchy (see Supplemental File B) to prioritize diagnoses based on the likelihood they were a unifying cause of death (e.g., oncologic diagnoses were highest priority). Categories were combined as needed to avoid small cell sizes (<6) and preserve anonymity. Similarly, residential province was collapsed into Atlantic (Newfoundland and Labrador, Prince Edward Island, Nova Scotia, and New Brunswick), Quebec, Ontario, Prairies (Manitoba and Saskatchewan), Alberta, British Columbia (BC), and the North (Northwest Territories, Yukon, and Nunavut). Postal code was used to assign income quintiles according to residing neighbourhood and rurality with a population <10,000 classified as rural.[19] Distance from tertiary pediatric hospital was calculated using longitude and latitude data also derived from the decedent's postal code and the location of the nearest of 16 tertiary pediatric hospitals in Canada. Distance was categorized into <50 km, 50-199 km, 200-400 km, and >400 km to represent increasingly complex trips (i.e., easy day trip both ways; substantial day trip both ways; trip likely involving overnight stay; overnight trip possibly involving a plane ride).[20]

Statistical Analysis

All analyses were undertaken using SAS (version 9.4). Demographic characteristics and locations of death among the two groups (children and neonates) were summarized. Multivariable logistic regression was used to model the odds of dying in hospital for each group. Model predictors were selected *a priori* as described above. As full fit was desired, variables were left in each model regardless of p-value.[21] Missing data was minimal (about 2%); thus, complete case analysis was used. Model diagnostics, including tests for multicollinearity, were undertaken prior to selecting the final models for each outcome. All statistical tests were two-sided; p-values <0.05 were considered significant.

RESULTS

Patients

Of the 23,360 Canadian children who died over the seven-year study period, 13,115 (56.1%) had a life-threatening condition (5250 children and 7865 neonates) (Figure 1). Among children aged 29 days to 19 years, 74.2% (95% CI = 73.1 - 75.4) died in hospital and 16.1% died at home (95% CI = 15.1 - 17.1). The remainder died at another healthcare facility (2.9%, 95% CI = 2.4 - 3.3) or another location (6.9%, 95% CI = 6.2 - 7.6). In the neonate group, 98.1% (95% CI = 97.9 - 98.5) died in hospital. The most common causes of death in children were congenital conditions (27.7%) followed closely by oncologic conditions (25.6%). Most neonates (67.2%) died within 24 hours of birth and most (61.9%) died from a perinatal condition. Demographics are summarized in Table 1.

Predictors of Dying in Hospital

Based on multivariable logistic regression, among the child cohort (Table 2), those less than a year of age had higher odds of in-hospital death than those aged 15 - 19 (OR = 1.73, 95% CI = 1.4 - 2.15), while those aged 5 - 9 had lower odds of dying in hospital (OR = 0.66, 95% CI = 0.54 - 0.82). Compared to an oncologic cause of death, all causes of death other than neurologic and metabolic had higher odds of dying in hospital. The increased odds ranged from nearly double for congenital causes (OR = 1.74, 95% CI = 1.43 - 2.11) to more than 5 times for gastrointestinal causes of death (OR = 5.36, 95% CI = 2.54 - 11.3). Compared to Ontario, those residing in BC had lower odds (OR = 0.43, 95% CI = 0.34 - 0.53), while those from Quebec had higher odds (OR = 1.38, 95% CI = 1.14-1.67) of dying in hospital. Compared to the highest income quintile, those in the lowest income quintile had higher odds of dying in hospital (OR = 1.59, 95% CI = 1.28 - 1.97). Finally, those living between 50 and 199 km (OR = 0.73, 95% CI =

0.62 - 0.86) or more than 400 km away (OR = 0.73, 95% CI = 0.65 - 0.86) from the tertiary pediatric hospital had lower odds of dying in hospital than those living <50 km away.

Among neonates (Table 3), those less than 24 hours old had 13 times higher odds of dying in hospital (OR = 13.0, 95% CI = 7.94 - 21.32). Compared to neonates with perinatal conditions, those with congenital (OR = 0.25, 95% CI = 0.17 - 0.36) or other causes of death (OR = 0.47, 95% CI = 0.24 - 0.92) had lower odds of dying in hospital. Finally, those residing in BC had substantially lower odds of dying in hospital (OR = 0.3, 95% CI = 0.19 - 0.49) than those in Ontario.

INTERPRETATION

Our study highlights the high proportion of Canadian children who died from a life-threatening condition in a hospital setting. While not surprising that age and cause of death are significant predictors of location of death, variability based on province, income, and distance from a tertiary pediatric hospital that persist after adjustment for other variables indicate potential inequities in care across the country.

The proportion of children who died in hospitals in our study was higher than reported in other research for children internationally and for adults within Canada. While we found 74.2% of children 29 days to 19 years died in hospital, national studies in England and New Zealand with similar populations of children found 65.7% (15420/23484)[22] and 53.6% (265/494)[10] respectively died in hospital. The proportion of hospital deaths in adult Canadians varies by study (43% to 60%)[23-26] but is considerably lower than our findings in children.

Almost all neonates (98%) died in hospital. Many died within the first 24 hours of life from a perinatal condition such as birth trauma, infection, or asphyxia leaving little opportunity to facilitate end of life care outside the hospital. Neonates with congenital conditions (e.g.,

chromosomal abnormalities, congenital malformations) were more likely to die at home, suggesting that antenatal diagnosis and clearer prognosis may facilitate advanced care planning and out-of-hospital care. Studies have described a link between home death and improved bereavement outcomes such as reduced depression, anxiety, and complicated grief,[4] highlighting the importance of improving access to home end-of-life care even for families of neonates. Increased community support including availability of free-standing hospices may offer additional options to families of neonates for location of care and death.[27]

As described in other research,[10,11,22] children with cancer were more likely to die outside the hospital, possibly due to the more predictable illness trajectory with more opportunities to plan and provide supports to facilitate a home death. Other diagnoses (e.g., congenital illnesses), may have a more unpredictable disease course. Challenges in identifying the terminal phase of an illness may be associated with less opportunity or desire for a home death.[4,11]

While Canada has a publicly funded health care system that is meant to be accessible to all Canadians regardless of where they live, differences in location of death were noted based on province, distance from a tertiary pediatric hospital, and neighborhood income quintiles. Decreased odds of a hospital death in BC (OR = 0.43, 95% CI = 0.34 - 0.53) may reflect implementation of their comprehensive provincial end-of-life care plan prior to our study period.[25] BC is also home to Canuck Place Children's Hospice, North America's first freestanding children's hospice, which opened in 1995 and provides consultation and outreach to infants, children, and youth and their families throughout the province.[28] Other research has noted a trend towards an increased number of home deaths in children when there was a more well-developed system of pediatric palliative care services both in hospitals and within the community setting.[29,30,31] Both palliative care and other specialty services are concentrated in the

16 tertiary pediatric hospitals across Canada. Like others, we found those living further from these tertiary hospitals were less likely to die in hospital.[6,12] Living very close (e.g., <50km) may facilitate relatively easy returns to the hospital where care is provided by healthcare professionals well-known to the family, possibly resulting in reluctance to develop new relationships with community-based providers. Given the challenges of traveling long distances when a child is nearing death, it is possible that those living furthest (e.g., >400 km) from a tertiary hospital may be more likely to remain home if community supports are in place. Further research is needed to examine distance from hospital as a factor in decision-making about location of death.

There are some conflicting findings in previous research about the impact socioeconomic status on location of death.[10,13] However, consistent with our study, a recent metanalysis found those living in neighborhoods with the lowest income quintiles were more likely to die in hospital.[11] Across studies, it is unclear what mechanisms may underlie this disparity. Johnson and colleagues suggested that patient/family preference, system issues, provider biases or some combination of those may be at play.[14] Bona and Wolfe further suggested that underserved populations may have differential access to palliative care supports both in the community and in the hospital and when support is provided there may be differences in the degree of benefit they experience from advanced care planning and efforts to improve quality of life.[32] More research is needed to examine factors underlying socioeconomic status and their contribution to care inequities.

Limitations

Our data do not fully reflect the growth and development of pediatric palliative care in the last eight years and its potential impact on supports available to children and families in their

chosen location of care.[33] However, this study provides an important baseline examination of location of death that can be used to study changes in the future.

Only death record data for decedents was available nationally; more detailed examination of end-of-life care patterns require healthcare data that is not available nationally due to differences in reporting by province. The concerns we raise about potential inequities based on income and geography should be explored in provincial samples to facilitate a more fulsome description of other factors influencing end-of-life care and location of death. Death records are also limited in the specificity of location of death outside of hospital. For example, hospices provide an important alternative to both hospital and home but cannot be examined separately with current data.[9]

In previous work we identified the population of children with life-threatening conditions where death could have been expected by excluding those who died from an external cause.[33] In the current study we also used lists of ICD10 codes for life-threatening conditions in children. This methodology may have resulted in some misclassification given the inability to examine relevant diagnostic codes in the years preceding death,[34] but nonetheless represents a significant advancement compared to previous national work.[33]

Conclusion

Location of death is commonly used as a marker of quality of end-of-life care.[35-37] While not all children or their parents prefer to be at home,[4,8] given the link to potentially improved bereavement outcomes both for parents and siblings,[4] it is important that families of children with life-threatening conditions are given the opportunity to be at home if they so choose. While the Canada Health Act[38] includes the principles of universality, comprehensiveness and accessibility, our study highlighted concerning differences in the likelihood of children's deaths

occurring in hospital across measures of income, province of residence, and distance from tertiary pediatric hospital. These differences may signify a lack of systematic access to both hospital and in the community-based services including specialized pediatric palliative care teams, pediatric hospices, and palliative home care. The geographically dispersed population of Canada means greater efforts are needed to ensure health care principles are applied to all Canadians and particularly to our most vulnerable children and their families.

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KW and SB had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. KW, SB, and SG drafted the manuscript, while remaining authors provided critical revisions. All authors contributed to the study conception and design, were involved in data interpretation, and gave final approval of the manuscript.

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Figure 1. Total number of cases identified and reasons for exclusion

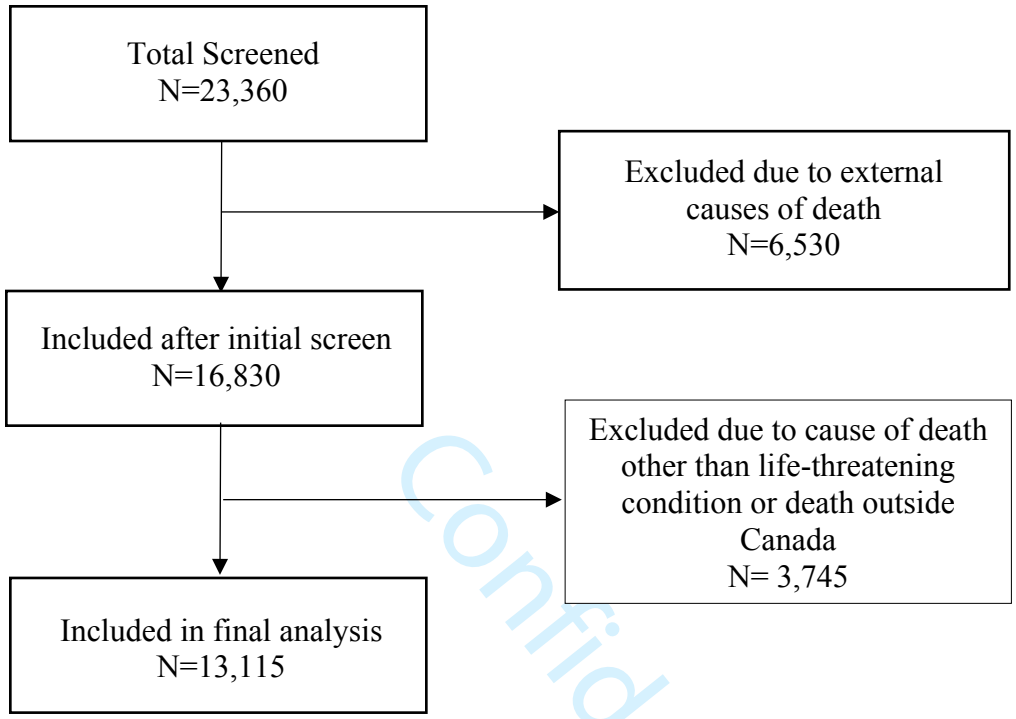

Table 1. Characteristics of study cohort (n=13115). Numbers may not add to total cohort size due to missing data. *Categories combined to avoid small cell sizes.

Characteristic	No. (%) Older Children 29 days-19 years (n=5250)	No. (%) Neonates <29 days (n=7865)
Age		
<24 hours	---	5285 (67.2)
24 hours - 28 days	---	2580 (32.8)
29 - 364 days	1700 (32.4)	---
1 - 4 years	980 (18.7)	---
5 - 9 years	665 (12.7)	---
10 - 14 years	745 (14.2)	---
15 - 19 years	1150 (22.0)	---
Sex		
Female	2810 (46.5)	3595 (45.7)
Male	2440 (53.5)	4270 (54.3)
Cause of Death		
Perinatal	305 (5.8)	4865 (61.9)
Congenital	1455 (27.7)	2690 (34.2)
Oncology	1345 (25.6)	60 (0.8)*
Haematology	120 (2.3)	
Neurology	980 (18.7)	45 (0.6)
Metabolic	345 (6.6)	65 (0.8)
Circulatory	330 (6.3)	40 (0.5)
Respiratory	195 (3.7)	100 (1.3)*
Gastrointestinal	95 (1.8)	
Genitourinary	55 (1.1)	
Other	30 (0.6)	
Province/Region		
Ontario	2055 (39.1)	3240 (41.2)
Quebec	1095 (20.9)	2035 (25.9)
Alberta	675 (12.9)	1015 (12.9)
Prairies	520 (9.9)	600 (7.6)
British Columbia	540 (10.3)	570 (7.3)
Atlantic	320 (6.1)	350 (4.5)
North	45 (0.9)	55 (1.5)
Income Quintile		
1 (lowest)	1210 (23.4)	2055 (26.7)
2	1025 (19.8)	1530 (19.9)
3	1000 (19.3)	1490 (19.3)
4	1050 (20.3)	1520 (19.7)
5 (highest)	890 (17.2)	1110 (14.1)
Rurality		
Urban	4085 (78.3)	6330 (81.7)
Rural	1135 (21.7)	1420 (18.3)

Distance from Pediatric Hospital		
<50 km	2855 (54.8)	4700 (60.7)
50 - 199 km	1460 (28.0)	1910 (24.7)
200 - 400 km	575 (11.0)	645 (8.3)
>400 km	325 (6.2)	485 (6.3)
Location of Death		
Hospital	3895 (74.2)	7715 (98.1)
Home	845 (16.1)	60 (0.8)
Other healthcare facility	150 (2.9)	30 (0.4)
Other location	360 (6.9)	60 (0.8)

Table 2. Multivariable logistic regression examining factors associated with death in hospital among children (29 days – 19 years) (n=5250)

Characteristic	Odds Ratio	95% confidence limits		P value
Age				
15 - 19 years	1.0			
10 - 14 years	0.95	0.77	1.17	0.646
5 - 9 years	0.66	0.54	0.82	0.0001
1 - 4 years	0.88	0.72	1.07	0.198
29 - 364 days	1.73	1.40	2.15	<0.001
Sex				
Male	1.0			
Female	1.06	0.93	1.21	0.408
Cause of Death				
Oncology	1.0			
Congenital	1.74	1.43	2.11	<0.001
Neurology	1.07	0.90	1.28	0.484
Metabolic	1.12	0.86	1.46	0.414
Circulatory	2.73	1.96	3.79	<0.001
Perinatal	2.78	1.84	4.21	<0.001
Respiratory	3.37	2.15	5.31	<0.001
Haematology	2.52	1.49	4.26	0.001
Gastrointestinal	5.36	2.54	11.30	<0.001
Genitourinary	3.44	1.43	8.26	0.006
Other	3.34	1.15	9.68	0.027
Region of Residence				
Ontario	1.0			
Quebec	1.38	1.14	1.67	0.001
Alberta	1.03	0.83	1.27	0.821
Prairies	1.27	0.98	1.63	0.070
British Columbia	0.43	0.34	0.53	<0.001
Atlantic	1.02	0.76	1.37	0.878
North	0.49	0.23	1.05	0.067
Income Quintile				
5 (highest)	1.0			
4	1.08	0.88	1.33	0.475
3	1.07	0.87	1.32	0.533
2	1.23	0.99	1.52	0.057
1 (lowest)	1.59	1.28	1.97	<0.001
Rurality				
Urban	1.0			
Rural	0.98	0.81	1.18	0.806
Distance from Pediatric Hospital				
< 50 km	1.0			
50 - 199 km	0.73	0.62	0.86	<0.001
200 - 399 km	0.87	0.68	1.11	0.269

> 400 km	0.73	0.65	0.86	<0.001

Table 3. Multivariable logistic regression examining factors associated with death in hospital among neonates (<29days) (n=7865)

Characteristic	Odds Ratio	95% confidence limits		P value
Age				
<24 hours	13.01	7.94	21.32	<.0001
24 hours - 28 days	1.0			
Sex				
Male	1.0			
Female	0.75	0.53	1.05	0.097
Cause of Death				
Perinatal	1.0			
Congenital	0.25	0.17	0.36	<.0001
All other causes	0.47	0.24	0.92	0.027
Region of Residence				
Ontario	1.0			
Quebec	1.36	0.79	2.34	0.262
Alberta	0.53	0.31	0.88	0.015
Prairies	0.97	0.49	1.92	0.926
British Columbia	0.30	0.19	0.49	<.0001
Atlantic	1.54	0.53	4.45	0.426
North	0.27	0.05	1.42	0.121
Income Quintile				
5 (highest)	1.0			
4	1.24	0.70	2.18	0.464
3	1.33	0.75	2.35	0.331
2	1.57	0.88	2.83	0.13
1 (lowest)	1.16	0.69	1.94	0.58
Rurality				
Urban	1.0			
Rural	0.73	0.45	1.19	0.206
Distance from Pediatric Hospital				
< 50 km	1.0			
50 - 199 km	0.66	0.43	1.01	0.056
200 - 399 km	1.08	0.56	2.12	0.814
> 400 km	0.89	0.41	1.94	0.771

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3-4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	Report numbers of outcome events or summary measures over time	6-7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Supplemental File A – ICD-10 Codes Signifying a Life-Threatening Condition.[16,17] GI = Gastrointestinal; GU = Genitourinary

Neurology		Hematology	Oncology	Metabolic	Respiratory	Circulatory	GI	GU	Perinatal	Congenital		Other
A17	G60.0	B20-B24	C00-C97	E31.0	E84	I21	K55.0	N17	P10.1	Q00-Q07	Q64.2	H11.1
A81.0	G60.1	D56.1	D33	E34.8	G47.35	I27.0	K55.9	N17	P11.2	Q20.0	Q74.3	H49.8
A81.1	G70.2	D61.0	D43	E70.2	J84.1	I27.82	K72	N18	P21.0	Q20.3	Q75.0	H35.5
F71-F73	G70.9	D61.9	D44.4	E71	J96	I42	K74	N19	P28.5	Q20.4	Q77.2	M31.3
F84.2	G71.0	D70	D48	E72	J98.4	I43	K76.5	N25.8	P29.0	Q20.6	Q77.3	M32.1
G10	G71.1	D76.1		E74		I61.3	K86.8		P29.3	Q20.8	Q77.4	M89.5
G11.1-G11.4	G71.2	D81		E75		I63.30			P35.0	Q21.3	Q78.0	T86.0
G11.8	G71.3	D82.1		E76		I63.50			P35.1	Q23.2	Q78.5	T86.2
G11.9	G72	D83		E77		I81			P35.8	Q21.8	Q79.2	Z51.5
G12	G80.0	D89.1		E79.1					P37.1	Q22.0	Q79.3	
G20	G80.8			E83.0					P52.4	Q22.1	Q80.4	
G21.0	G81.90			E88.0					P52.5	Q22.4	Q81	
G21.1	G82.3			E88.1					P52.9	Q22.5	Q82.1	
G21.8	G82.4								P83.2	Q22.6	Q82.4	
G23.0-G23.2	G82.5								P91.2	Q23.0	Q85.1	
G23.8	G82.90								P91.6	Q23.4	Q85.8	
G24.02	G83.5								P96.0	Q23.9	Q86.0	
G24.8	G83.9									Q25.4	Q87.0	
G25.3-G25.5	G90.1									Q25.6	Q87.1	
G25.81-G25.83	G90.9									Q26.2	Q87.2	
G25.89	G91.1									Q26.4	Q87.8	
G25.9	G93.1									Q26.8	Q91	
G31.01	G93.4-93.9									Q28.2	Q92.0	
G31.09	G94									Q30-Q34	Q92.1	
G31.8	G95.19									Q39.6	Q92.4	
G31.9	G95.89									Q41.0	Q92.7	
G32.89										Q41.9	Q92.8	
G35										Q43.7	Q93.2	
G37.1										Q44.2	Q93.3	
G37.2										Q44.7	Q93.4	
G37.8										Q60.1	Q93.5	
G40.1-40.5										Q60.6	Q93.8	
G40.8										Q61.4	Q95.2	
G40.9										Q61.9		

Supplemental File B – Prioritization of diagnostic categories

In less than 5% of the cohort there was no relevant underlying cause and multiple contributing causes in different categories. Therefore, we developed a hierarchy of categories based on the likelihood that the category was a unifying cause of death. The hierarchy was as follows:

1) oncology
2) metabolic
3) congenital
4) circulatory
5) neurological
6) respiratory
7) haematology
8) gastrointestinal
9) genitourinary
10) other
11) perinatal

Patients were assigned to a category based on having a contributing cause falling into the highest category in the list. Thus, a child with contributing causes of death in both the oncology and circulatory category was assigned to oncology as the cause of death.