Population-level analysis of appropriateness of end-of-life care for children with neurological conditions

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Abstract

Objectives: To measure the appropriateness of end-of-life care for children who died with neurological conditions.

Study design: Based on linked routinely collected databases, we conducted a population-level decedent cohort study of children who died in Belgium with neurological conditions between 2010 and 2017. We measured a set of 22 face-validated quality indicators. The set concerns 12 indicators of potentially appropriate end-of-life care (e.g. specialized comfort medication, physician contact, continuous care) and 10 indicators of potentially inappropriate end-of-life care (e.g. diagnostics, drawing blood). We performed analysis of variance for predictors (age, sex, disease category, nationality, having siblings, year of death) for scales of appropriate and inappropriate care.

Results: Between 2010 and 2017, 139 children died with neurological conditions in Belgium. For potentially appropriate care, in the last 30 days 76% of children received clinical care, 55% had continuous care relationships, 17% had contact with a general physician, 8% of children received specialized comfort medication, and 14% received care from a palliative care team. For potentially inappropriate care, in the last 14 days 45% had blood drawn, and 27% were admitted to ICU.

Conclusions: Our study found indications of appropriate as well as inappropriate end-of-life care for children who died with neurological conditions. Findings seem to imply a substantial margin for quality improvement, for the themes of palliative care provision, multidisciplinary care, financial support, specialized comfort medication, clinical follow-up, general physician contact, diagnostics and blood drawing.

List of abbreviations

None

Body

Introduction

One in five children dying with neurological and neuromuscular complex chronic conditions are reported to suffer a high symptom burden at the end of life.[1] Such conditions, such as cerebral palsy[2] and muscular dystrophy[3], are often incurable and progressive, with treatment focusing on long-term symptom control instead of cure.[4] In the final stages of life, children with neurological and neuromuscular conditions can suffer from muscle tone problems such as spasticity and dystonia, spine and chest deformations, pain and other symptoms such as headaches, sleep problems, respiratory complications, digestive problems, psychological problems (agitation), excessive salivation and convulsions.[5-10] Neurological conditions have been reported in several cohort studies to be the most common diagnoses of children referred to paediatric palliative care teams,[2-3,11-15] and parents of children with neurological conditions report less satisfaction with end-of-life management than parents of children with cancer and heart conditions.[16-17] An extensive evaluation of the quality of end-of-life care for children with neurological conditions at the level of the entire healthcare system is missing.

Prior to this study, we developed a set of quality indicators that measure aspects of care that may indicate potentially appropriate or inappropriate care at the end of life in children with neurological conditions.[18] The quality indicators were developed for a population level, using administrative health data. Appropriate end-of-life care, has been defined as care, such as treatments or medications for which there is more expected health benefit (e.g. improved quality of life, pain relief) than possible negative consequence (e.g. symptom burden, mortality) on a group level. Inappropriate care was seen as the opposite, i.e. more expected negative consequences than benefits on a group level. The term ‘potentially’ is placed the terms appropriateness and inappropriateness to signal that the constructed categories are only indicative and do not provide a definite value judgement for care provision on an individual

level.This study aims to: 1) measure these quality indicators in 6 linked administrative healthcare databases of children who died with neurological conditions in Belgium between 2010 and 2017; and 2) identify risk factors of appropriate and inappropriate end-of-life care (i.e. to identify whether certain clinical or socio-demographic variables show different outcomes for appropriateness – for example, for younger as opposed to older children).

Methods

Study design

We conducted a decedent cohort study of all insured children who died with neurological conditions in Belgium between 2010 and 2017. Health insurance is mandatory in Belgium and, therefore, our data are expected to include practically the full population.

Data sources

We used data from 6 linked Belgian governmental databases. See also Table 1 (Online)x.

Population

Children, 1-17 years old, who died with neurological conditions within the years 2010 to 2017 were selected using death certificate data (see Figure 1). Newborns or children between 0 and 1 were not included, as this age group is treated in neonatology and differs in treatment approach, disease and trajectory. We selected the ICD-10 codes as defined in the framework of complex chronic conditions.[19] Neurological and neuromuscular conditions are defined as brain and spinal cord malformations, intellectual disability, central nervous system degeneration and diseases, infantile cerebral palsy, epilepsy, other conditions of the central nervous system, occlusion of cerebral arteries, muscular dystrophies and myopathies, and movement diseases[19]. We selected neurological conditions for any cause of death – i.e. either underlying, intermediate, immediate or associated cause of death. Therefore, overlap is present for children

with other conditions, such as children with brain tumours who developed a neurological condition. Sensitivity analysis was done for underlying cause of death (see Table 2 (Onlinex).

Context and setting

The Belgian government recognizes 9 neuromuscular reference centres that work to provide multidisciplinary help to children and adults with neuromuscular diseases. Most of these reference centres are connected to a university hospital.

In Belgium, healthcare insurance is mandatory. For most health claims, there is an out-of-pocket amount and an amount that is either reimbursed or covered through third-party payment arrangements. The out-of-pocket amount can vary depending on the characteristics of the insured person or the household – such as socio-economic status, or having an official 'palliative care status'. These reimbursed healthcare expenditures are registered by governmental institutions in large population databases.

Data

We used available data on healthcare use, including data on medication and treatments, admissions to hospitals, and socio-demographic data.

Quality indicators

Based on previously validated quality indicators, we measured 12 indicators for potentially appropriate and 10 indicators for potentially inappropriate end-of-life care.[18] Two other previously developed indicators – 1. having reimbursed prescriptions, and 2. having transfers from a medical-pedagogical institute to intensive care – were not measured, as we could not measure the concepts validly based on the available data. We made slight changes to the original indicator 'paediatric intensive care unit admissions', instead measuring intensive care unit

admissions, as no code was available for the paediatric intensive care unit. A summary table of the measured indicators can be found in Table 3.

Statistical analysis

We used descriptive statistics to describe the characteristics of children who died with neurological conditions and to measure the quality indicators.

The second research aim is to identify risk factors for the indicator results. For this purpose, logistic regressions were performed for all 22 separate indicators, with the identified potential confounders as independent variables and the indicator variables (0 vs 1) as dependent. For a more parsimonious presentation of the findings (the 22 logistic regressions models result in a large table), with the aim of data reduction, factor scales were constructed. This identification was first based on theoretical assumptions about thematic consistency (i.e. appropriateness vs. inappropriateness of care). A principal components analysis limited to one factor was then performed for each scale to verify internal consistency. Items with a component loading below 0.50 were removed from the scale. Cronbach alpha analyses were performed for the scales. The factor scores for the scales were saved, and for each scale and per predictor we performed multi-variable analysis of variance (proc glm) to identify if and which predictors have significantly different scores per scale.

To identify the candidate confounders for this analysis, we built directed acyclic graphs, inspired by the evidence synthesis for constructing directed acyclic graphs (ESC-DAGs)[20], following a non-causal theory-driven approach. Based on predictors identified in previous studies, our own assumptions, and mediator/collider analysis, a set of possible confounders was identified: age, sex, disease category, nationality, having siblings, year of death.

Analyses were conducted with SAS Enterprise Guide, version 7.1, and StataSE, version 17.

Ethics

All data were linked in a secure, ethically responsible manner, guaranteeing anonymity of the deceased. The study was approved by the Belgian Information Safety Committee.

Results

Population characteristics

Between 2010 and 2017, there were 139 children between 1 and 17 years old that died with neurological conditions in Belgium. See Table 4 for socio-demographic and clinical characteristics.

Potentially appropriate care at the end of life

In the last 30 days of life, as shown in Table 5, 34% of the children received prescriptions for physiotherapy, 17% of the children had contact with a family physician, 75% with hospital specialists, 7% received multidisciplinary care (received care from at least 2 categories of care providers – e.g. a physician and a paramedic), 55% received continuous care (physician seen in the last month before death had also been seen in the year before). Increased child benefits – which in Belgium can be assigned to parents with children under 21 with a disability or serious condition and provided certain requirements are fulfilled – were assigned in 8% of cases. A palliative care service was involved in 14% of the children and 13% received palliative status.

Potentially inappropriate care at the end of life

In the last month before death, or prior, none of the children received dialysis, nor old-generation prescriptions for nausea, and none received a new anti-depressant in the last 2 weeks before death (Table 5). But, diagnostics (MRIs, X-rays and CT scans) were carried out in 26% of the children in the last month before death and in 45% of the children in the last

week before death. 4% of the children received a palliative care visit for the first time, or a palliative status, only in the 2 weeks before death. 27% were admitted to an intensive care unit in the last 2 weeks of life.

Risk factors for potentially appropriate and inappropriate care at the end of life

The 2 constructed scales had standardized Cronbach alpha of 0.85 and 0.61, respectively. The multi-variable analysis of variance revealed that disorders of the central nervous system and movement diseases received less potentially appropriate care (Table 6 and 7; online). No associations were found with age, sex, nationality, having siblings, or year of death.

Discussion

Summary of findings

In this decedent cohort study, we evaluated the quality of end-of-life care with population-level quality indicators for potentially appropriate and inappropriate care for 139 children, from 1 to 17 years old, that died with neurological conditions between 2010 and 2017 in Belgium. Indicators for appropriateness of end-of-life care ranged from 0% (e.g. follow-up visits at the hospital) to 76% (clinical care provision). Indicators for inappropriateness of end-of-life care ranged from 0% (e.g. starting dialysis) to 45% (drawing blood in the last week before death). Analyses of variance indicated that disorders of the central nervous system and movement diseases received less appropriate care.

Strengths and limitations

A strength of our study is the use of routinely collected data. In Belgium, health insurance is mandatory, and our database thus includes healthcare use for the full population of insured children who died in Belgium in the studied period. Thus, we avoided a common pitfall in cohort and children's studies: our database includes children that would normally be difficult to recruit for. Furthermore, our quality indicator set was extensively face-validated specifically for the data at hand. Our database is extensive, as 6 different databases were linked, and many clinical and socio-demographic variables are found within the data. To our knowledge, only 1 previous international population-based study has measured similar indicators for children with neurological conditions at the end of life – namely, for dialysis and ICU admissions.[21]

A limitation of the study is that our data do not include certain procedures or non-population-level measures for the children or families, such as consultations with a psychologist or

quality-of-life measures. Variables were not collected with research questions in mind, and therefore they might lack validity. Our indicators centred on the child, but did not take the family's healthcare use into account. For the identification of relevant risk factors for appropriate or inappropriate care, not all variables identified as relevant through the DAG-ECS method were available from the data.

Interpretation of findings

Our results show varying numbers for indicators involving care providers. Continuity of care and the use of professional and specialist care was found to occur in the majority of cases. This is consistent with continuity of care being reported as a priority for Belgian paediatric liaison teams.[22] The involvement of a general practitioner (GP) in the last month of life seemed much lower. Previous studies report general practitioners experience a relatively high distress level during the terminal phase of the death of a child, as well as feelings of sadness and powerlessness around the child's time of death, which may underlie and account for the low percentage.[23] The results also seem to indicate that follow-up consultations at the hospital after receiving a palliative status (an administrative notion indicating that the patient needs palliative care) were non-existent. If the measurements are valid, this could lead to families feeling they "missed out on instructions given by nurses or specialists and on contacts with other families confronted with similar problems"[17], per rationale behind the indicator.[18] However, it could also be possible that visits to the hospital were not registered or charged, and therefore not registered in the databases. Belgian paediatric liaison teams also report incorporating in-hospital consultations in their work, based on some families' preference for hospital support.[22]

The measured indicators carefully seem to signal a low use of palliative care services (14% of the children received reimbursed palliative care provision in the last 2 years before death;

13% received an official palliative status, which entails the removal of several out-of-pocket costs). This seemingly confirms findings from other studies: the specificity of symptoms of children with degenerative disorders has been previously reported to complicate the provision of palliative care.[24] It is possible that the reported numbers are an underestimation, as palliative care for children can also be provided with philanthropic funding and, hence, without any official reimbursement. The small body of evidence for palliative care in children with neurological conditions suggests palliative care could be beneficial: an Indian cohort study of 60 children with cerebral palsy found all children had palliative care needs.[25]Case studies show that palliative care can support children with neurological conditions in a psychosocial, symptomatic, spiritual, and emotional manner, through pharmacologic as well as non-pharmacologic approaches.[26,27]

Additionally, financial support measures – such as being given an official palliative status (13%) and increased child benefits (8%; in Belgium, this can be assigned to parents with children under 21 with a disability or serious condition and provided certain requirements are fulfilled) – seemed to be low. Families of children with complex chronic conditions have previously been reported to require "additional social assistance, financial resources, and support for administrative procedures" due to the high family financial burden.[22] Administrative support for families could be provided, or awareness campaigns could possibly be set up, to increase the use of these measures.

Another finding is that diagnostics, drawing blood and intensive care unit admissions seem to occur often in the final weeks of life. This suggests that a proportion of children potentially receive inappropriate care at the end of life, which perhaps could be avoided. Diagnostics may be highly requested as they are effective for prediction of clinical outcomes (e.g. CT scans in cerebral palsy),[28,29] and deterioration to death can be unpredictable.[24] A 2004 cohort

study on clinical outcomes for children with neuromuscular disease admitted to paediatric intensive care indicated that admissions for children frequently required invasive ventilation,[30] while another cohort study indicated breathing difficulties cause the greatest suffering in children with complex chronic conditions and distress for their parents.[1]

Risk factors

Certain types of neurological diseases were more at risk: disorders of the central nervous system and movement diseases received less appropriate care. This could be caused by the combination of the lesser known or predictable pathology and more erratic symptom pattern for these illnesses. For instance, juvenile Huntington's, classified as a movement disorder within the used complex chronic conditions framework, is relatively rare and therefore a clinician "managing the patient is often doing so for the first time", with few available evidence-based guidelines.[31] Epilepsy is an example of a central nervous system disease symptom that can be unpredictable to manage.[32] Our finding also could be connected to a recent analysis by Lindley et al., who found that the population of children with neurological conditions at the end of life can be divided into two classes, namely one with moderate use of health services, and one with high-intensity use of health services.[33] The latter category included most of the children with central nervous system disorders (89%). These results mirror our findings and further the hypothesis that certain, possibly lesser-known, neurological conditions utilize more health services and clinical settings at the end of life.

Comparison with international findings

Only 1 previous population-level study (in California, on children's deaths between 2000 and 2013) has measured 2 similar indicators for children with neurological conditions at the end of life.[21] Therefore, interpretations about whether findings are low or high remain speculative and based on assumptions. The study in California found that 2.6% of US children with neurological

conditions were reported to receive dialysis in the last month before death, as opposed to none in Belgium, and 39% received ICU admissions, while 27% received such in Belgium. International case studies provide similar indications for healthcare setting use, for instance describing ICU use at the end of life in a child with neurological impairment for symptom control.[26] In contrast, international cohort studies and case studies show differing measurements for some indicators, such as palliative care provision and medication use. For instance, palliative care consultation was observed to be very high for an inpatient US cohort of children with neurological conditions (76,9% for children with neuromuscular disorders), while our numbers indicated low palliative care provision.[34] A Canadian and US cohort study also showed a higher use of comfort medications than our measurements: in this study 57% of children were provided with opioids in the last days of life, and a median of 4 drugs classes was given, while our findings show less than 4% of children received certain specialized comfort medications.[35] Such contrasts may signal important differences between hospital and population samples, and it may be looked into further whether this also indicates a care quality difference. Differences could also be present due to care provision differences per region (US vs Belgium), and/or due to measurement differences (reimbursed vs non-reimbursed medications).

Recommendations for research, practice and policy

Our research provided a broad evaluation of the quality of end-of-life care for children with neurological conditions in Belgium, and it can be used as a starting point for further interventions to improve the end of life for these children and the related research. Further steps could involve the design of interventions to target the potential areas of improvement (e.g. courses to increase comfort medication knowledge), after which the quality indicators could be measured again to measure the interventions' impact. Besides educational efforts, other possible system barriers that might be targeted are the lack of incentives for multidisciplinary

care provision in children at the end of life, and the lack of a proper evidence base (overview) with potential benefits and downsides of medications and treatments for children with neurological conditions' quality of life at the end of life.

Workload indicators and patient-reported outcome measures, amongst others, have been previously suggested for the Belgian context to improve continuity of care for paediatric liaison teams,[22] yet analysis of quality improvement evidence and national system mechanics is advisable before development of further quality improvement initiatives.

Additionally, the indicators are best externally validated in further studies. Due to the absence of similar national and international measurements, it is unknown whether the measured frequencies precisely reflect the true frequencies of the concepts selected for measurement. While some indicators likely provide accurate reflection, other indicators could provide underestimations due to lack of reimbursement, misclassification, or greater concept ambiguity. Highly specialized treatments such as surgeries and specialized comfort medication are likely accurate in measurement as these treatments are always reimbursed in Belgium due to their lack of over-the-counter availability, and free provision based on goodwill of providers is unlikely. On the other hand, care which also could be provided without reimbursement or via goodwill could show undermeasurement, such as palliative care, general physician contact or follow-up by the hospital. Also, concepts which are less concrete and only measurable in part via administrative data, such as multidisciplinary care, could provide undermeasurement. Certain one-time administrative measures, such as palliative status, could have showed low scores due to the availability of data, which was limited to 2 years before death. It is advised that surveys are conducted to measure the indicators in small samples of children at the end of life, in order to further validate the indicators. Parents' and children's evaluation of the quality of end-of-life care might provide further triangulation - previous studies show parents can be highly involved

in the care and decision-making on treatments for children with neurological conditions at the end of life.[36]

Conclusion

This study performed the first evaluation of the quality of end-of-life care for children with neurological conditions, using quality indicators for the appropriateness of end-of-life care for 139 children who died between 2010 and 2017 with neurological conditions in Belgium. Our study found indications of appropriate, as well as inappropriate, end-of-life care for children who died from neurological conditions, with relatively frequent blood drawing and ICU admissions in the final weeks of life and infrequent comfort care, general physician contact, and palliative care service use, but also frequent clinical and continuous care relationships. While further research and international comparison is warranted to develop further interventions, these findings seem to imply a substantial margin for quality improvement in paediatric neurological end-of-life care, especially for the themes of palliative care provision, multidisciplinary care, financial support, specialized comfort medication, clinical follow-up, general physician contact, diagnostics and blood drawing.

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Figure legends

Figure 1: Flow chart describing cohort selection. Step-by-step flow chart describing how cohort selection was performed.

Table 1: Information on databases (based on De Schreye et al.[29])

Institution	**Database**	**Description**
Intermutualistic Agency	Sociodemographic database	Sociodemographic information for all individuals with healthcare insurance, which is legally mandatory in Belgium[29]
	Healthcare database	Outpatient and hospital care provided in Belgium, except medication dispensed in pharmacies, with amongst others date, healthcare provider, setting.[29]
	Pharmaceutical database	Reimbursed medication dispensed in pharmacies in Belgium, with amongst others date of prescription, date of delivery, information on prescriber, setting, for every reimbursed medication delivery[29]
StatBel	Death certificate database	Underlying cause of death, as well as associated and intermediate causes of death on all deaths in Belgium, from Belgian death certificates[29]
	Population registry database	Citizens' household composition and highest attained level of education for every Belgian citizen[29]
	Census database	Data from the last census in Belgium in 2012, such as educational level and housing comfort characteristics[29]

Table 2: Sensitivity analyses

A. For cases excluded based on external cause (ICD S-V)

We conducted a sensitivity analysis on external/acute causes of death, i.e. the cases that were excluded based on ICD-10 codes S to V. This analysis was conducted to verify whether the excluded causes were indeed acute causes and not cases of e.g. palliative sedation or complications of surgeries. Due to privacy reasons, the exact results of this sensitivity analysis cannot be shown, yet sensitivity analysis for causes of death confirmed that the excluded cases all had causes of death related to acute causes, such as traffic accidents, suicide, or drownings, that fell out of the scope of this study.

B. For underlying neurological conditions only as underlying cause of death

We conducted a sensitivity analysis for children who died from neurological conditions, i.e. neurological conditions only as an underlying cause of death (n=67). No large differences in percentages are present for children dying with and children dying from neurological conditions. The results for the indicators with only children dying from neurological conditions are shown below.

Indicators of appropriate care for underlying neurological conditions only as underlying cause of death

	Number of days before death until death							
Indicator	2	7	14	30	120	From palliative status onwards	730 (full period available)	Denominator (n)[b]
Treatment, medication, and monitoring								
Prescriptions of physiotherapy				22 (33%)			34 (51%)	67
(Off-label) prescription of comfort medication	<5 (<8%)	<5 (<8%)	<5 (<8%)	<5 (<8%)			6 (9%)	67
Pain control according to WHO steps					<5 (50%)			<5
Place of care								
Follow-up visits at the hospital						0 (0%)		10
Care services and providers								
Contact with general physician				13 (20%)			44 (66%)	67
Continuous care relationships				40 (60%)				67
Clinical care provision			47 (70%)*	50 (75%)*			56 (84%)*	67
Palliative care team							11 (16%)	67

Multidisciplinarity of care				<5 (<8%)			31 (46%)	67
Involvement of specialist physicians				48 (72%)			55 (82%)	67
Administrative measures								
Palliative status							10 (15%)	67
Increased child benefits							6 (9%)	67

Indicators of inappropriate care for underlying neurological conditions only as underlying cause of death								
	Number of days before death until death							
Indicator	2	7	14	30	120	From palliative status onwards	730 (full period available)	Denominator (n)[b]
Treatment, medication, and monitoring								
Daily diagnostics	<5 (<8%)	<5 (<8%)	0 (0%)	0 (0%)			0 (0%)	67
General diagnostics	9 (13%)	13 (19%)	14 (21%)	16 (24%)			39 (58%)	67
Starting dialysis	0 (0%)	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)	67
Old-generation prescriptions nausea	0 (0%)	0 (0%)	0 (0%)	0 (0%)			0 (0%)	0
Surgeries	0 (0%)						12 (18%)	67
New antidepressant			<5 (<8%)				2 (3%)	67
Late palliative care provision		<5 (<8%)	<5 (<8%)				10 (15%)	67
Drawing blood	25 (37%)	31 (46%)					48 (72%)	67
Place of care and death								
Pediatric Intensive Care Unit admissions	15 (22%)	17 (25%)	17 (25%)				23 (34%)	67
Transfers between care settings	0 (0%)	0 (0%)	0 (0%)	<5 (<8%)			20 (30%)	67

C. For acute vs. chronic trajectory

We conducted a sensitivity analysis for children who died from acute vs. chronic (and therefore known EOL) trajectory. Two variables were taken as proxy for trajectory for these sensitivity analyses: 1. Having received palliative care/palliative status in the last 3 weeks before death (n=5), and 2. Dying at the ICU (n=39). Results from the first proxy contained too many small cells, therefore only the results from the second proxy are shown below, but showed similar results.

Indicators of appropriate care for death at ICU

	Number of days before death until death							
Indicator	2	7	14	30	120	From palliative status onwards	730 (full period available)	Denominator (n)[b]
Treatment, medication, and monitoring								
Prescriptions of physiotherapy				20 (51%)			24 (62%)	39
(Off-label) prescription of comfort medication	0 (0%)	0 (0%)	0 (0%)	0 (0%)			1 (3%)	39
Pain control according to WHO steps					0 (0%)			0
Place of care								
Follow-up visits at the hospital						0 (0%)		10
Care services and providers								
Contact with general physician				5 (13%)			25 (64%)	39
Continuous care relationships				28 (72%)				39
Clinical care provision			34 (87%)	34 (87%)			34 (87%)	39
Palliative care team							0 (0%)	39
Multidisciplinarity of care				<5 (<13%)			17 (44%)	39
Involvement of specialist physicians				34 (87%)			34 (87%)	39
Administrative measures								
Palliative status							0 (0%)	39
Increased child benefits							<5 (<13%)	39

Indicators of inappropriate care for death at ICU

	Number of days before death until death							
Indicator	2	7	14	30	120	From palliative status onwards	730 (full period available)	Denominator (n)[b]
Treatment, medication, and monitoring								
Daily diagnostics	7 (18%)	<5 (<13%)	0 (0%)	0 (0%)			0 (0%)	39
General diagnostics	18 (46%)	23 (59%)	25 (64%)	25 (64%)			30 (77%)	39
Starting dialysis	0 (0%)	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)	39
Old-generation prescriptions nausea	0 (0%)	0 (0%)	0 (0%)	0 (0%)			0 (0%)	0
Surgeries	0 (0%)						7 (18%)	39
New antidepressant			0 (0%)				0 (0%)	39
Late palliative care provision		0 (0%)	0 (0%)	0 (0%)			0 (0%)	39
Drawing blood	31 (80%)ùp 7m	31 (80%)					34 (87%)	39
Place of care and death								
Intensive Care Unit admissions	34 (87%)*	34 (87%)*	34 (87%)*				34 (87%)*	39
Transfers between care settings	0 (0%)	0 (0%)	0 (0%)	0 (0%)			8 (21%)	39

*Measured on admission, while n=39 was measured on admission and dismissal variables, therefore there is a difference of 5.

Table 3. Measured indicators with numerator, denominator, period(s) and operationalization

Nr	Title	Numerator (number of children that died of neurological conditions in which*)	Denominator (*Number of children that died of neurological conditions)	Period(s)
		Potentially appropriate care		
1	Prescriptions of physiotherapy	*Physiotherapy was given	*	30 days before death
2	Prescription of specialized comfort medication	*There were prescriptions for hyoscine butylbromide, dexmedetomidine, fentanyl, gabapentin, ketamine, ketorolac, lidocaine, midazolam, ondansetron, or scopolamine	*	30, 14, 7, 2 days before death
3	Pain control according to WHO steps	*There were prescriptions from the third World Health Organization step, i.e. morphine, fentanyl, methadone, oxycodone, or hydromorphone, and these were preceded, in the last 2 years before death, by prescriptions from the first World Health Organization step, i.e. paracetamol, non-steroidal anti-inflammatory drugs or aspirin, and from the second World Health Organization step, i.e. codeine, tramadol, or buprenorphine	*with prescriptions from the third World Health Organization step, i.e. morphine, fentanyl, methadone, oxycodone, or hydromorphone in the last 3 months before death	90/120 days before death
4	Follow-up visits at the hospital	*There was at least 1 consultation in a hospital, or with a specialist physician	*	From palliative status onwards
5	Contact with general physician	*There were at least 3 house visits of, prescriptions of, or consultations with a general physician	*	30 days before death
6	Continuous care relationships	*There was at least 1 prescription, visit, consultation, or treatment from the same physician (general or specialist) in the last 30 days before death, as in the last year before death	*	30 days before death

7	Clinical care provision	*There were more than 2 prescriptions, house visits, treatments, consultations of physicians or paramedics, or a visit to a care institute	*	30, 14 days before death
8	Palliative care team	*There was at least 1 visit of a palliative home care team	*	730 days before death (full period available)
9	Multidisciplinary care	*There was a total of 5 or more prescriptions, treatments, visits, or advices, from 2 or more of the following care providers: general physicians, pediatricians, specialist physicians or paramedics	*	30 days before death
10	Involvement of specialist physicians	*There was at least 1 prescription, visit of or consultation with at least 1 specialist physician	*	30 days before death
11	Palliative status	*Receiving a palliative status (administrative notion that patient is palliative, hereby qualifying also for a palliative stipend)	*	730 days before death (full period available)
12	Increased child benefits	*There were increased child benefits assigned to the family	*	730 days before death (full period available)
		Potentially inappropriate care		
13	Daily diagnostics	*Received 2 or more X-rays, magnetic resonance imaging scans, or Computed Tomography scans per day	*	30, 14, 7, 2 days before death
14	General diagnostics	*Received 2 or more X-rays, magnetic resonance imaging scans, or Computed Tomography scans	*	30, 14, 7, 2 days before death
15	Starting dialysis	*Dialysis was started	*	30, 14, 7, 2 days before death

16	Old-generation prescriptions nausea	*Domperidone or metoclopramide was prescribed	*with prescriptions for nausea-treating medication	30, 14, 7, 2 days before death
17	Surgeries	*A surgery was performed	*	2 days before death
18	New antidepressant	*At least 1 new antidepressant was started	*	14 days before death
19	Drawing blood	*There was at least 1 blood drawing	*	7, 2 days before death
20	Late palliative care provision	*There was a first registration of a palliative home care team or palliative status	*	14, 7 days before death
21	Intensive Care Unit admissions	*There were 1 or more hospital admissions at the Intensive Care Unit	*	14, 7, 2 days before death
22	Transfers between care settings	*There were 4 or more different care settings (home, hospital or other setting)	*	30, 14, 7, 2 days before death

Table 4. Characteristics of children who died with neurological conditions in Belgium,[a] 2010-2017

Characteristic	Percentage (number)
All	139 (100%)
Sex of the child	
Male	67 (48%)
Female	72 (52%)
Age range of the child	
1-5	44 (32%)
>5-9	31 (22%)
>9-15	40 (29%)
>15-17	24 (17%)
Nationality of the child	
Belgian	125 (90%)
Other	14 (10%)
Type of household in which the child lived	
Two-parent household	102 (74%)
Single-parent or other household	36 (26%)
Comfort of the house in which the child lived	
High	39 (28%)
Average	12 (9%)
Low	13 (9%)
Missing information (None, missing, not known or trailer)	75 (54%)
Highest level of education of the child's parents[b]	
Postsecondary 40-60	45 (32%)
High school 30-34	41 (29%)
Junior high school 20-24	26 (19%)

Primary school 10	17 (12%)
Not known or missing	10 (7%)
Urbanicity of municipality of residence of the child's family[c]	
Very high	37 (27%)
High	44 (32%)
Average	42 (30%)
Low	15 (11%)
Net annual taxable income of the child's family[b]	
High (decile 1-3)	49 (35%)
Average (decile 4-6)	32 (23%)
Low (decile 7-10)	35 (25%)
Missing	23 (17%)
Underlying cause of death of the child according to general ICD-10 category[d]	
Diseases of the nervous system	52 (37%)
Diseases of the respiratory system	19 (14%)
Neoplasms	17 (12%)
Endocrine, nutritional and metabolic diseases	12 (9%)
Diseases of the circulatory system	11 (8%)
Congenital malformations, deformations and chromosomal abnormalities	11 (8%)
Certain infectious and parasitic diseases	6 (4%)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism and Mental, Behavioral and Neurodevelopmental disorders	7 (5%)
Certain conditions originating in the perinatal period	5 (4%)

Categories of neurological and neuromuscular complex chronic conditions[d]	
Brain and spinal cord malformations	11 (8%)
Mental retardation or Movement diseases	10 (7%)
Central nervous system degeneration and diseases	34 (25%)
Infantile cerebral palsy	32 (23%)
Other disorders of central nervous system	47 (34%)
Muscular dystrophies and myopathies	13 (9%)

[a] Due to the use of population-level databases, practically all children who died are expected to be included with sample. However, the number of children who died may be slightly larger than reported as some IDs did not overlap v the relational database, see Appendix 4.;[b]Highest level of education/income of both parents was selected; [c]Based o Eurostat degree of urbanization method; [d]Total number exceeds 139 as neurological or neuromuscular complex ch conditions could surface in more than one cause of death. No children were found with a cause of death for the i categories of epilepsy or occlusion of cerebral arteries.

Table 5: Indicators for potentially appropriate and inappropriate end-of-life care for children who died with neurological conditions in Belgium, 2010-2017[a]

Indicators of potentially appropriate end-of-life care								
Number of days until death	**2**	**7**	**14**	**30**	**120**	**From palliative status onwards**	**730 (full period available)**	**Denominator (n)[b]**
Treatment, medication, and monitoring								
Prescriptions of physiotherapy				47 (34%)			72 (52%)[c]	139[d]
Prescription of specialized comfort medication	<5 (<4%)*	6 (4%)	8 (6%)	11 (8%)			16 (12%)[c]	139[d]
Pain control according to WHO steps					6 (55%)			11
Place of care								
Follow-up visits at the hospital						0 (0%)		18
Care services and providers								
Contact with general physician				24 (17%)			118 (85%)[c]	139[d]
Continuous care relationships				76 (55%)				139[d]
Clinical care provision			100 (72%)	105 (76%)			118 (85%)[c]	139[d]
Palliative care team							20 (14%)	139[d]
Multidisciplinary care				10 (7%)			60 (43%)[c]	139[d]
Involvement of specialist physicians				104 (75%)			117 (84%)[c]	139[d]
Financial measures								

Palliative status	18 (13%)	139[a]
Increased child benefits	11 (8%)	139[a]

Indicators of potentially inappropriate end-of-life care								
Number of days until death	**2**	**7**	**14**	**30**	**120**	**From palliative status onwards**	**730 (full period available)**	**Denominator (n)[b]**
Treatment, medication, and monitoring								
Daily diagnostics	9 (7%)[c]	<5 (<4%)[c*]	0 (0%)	0 (0%)			0 (0%)[d]	139[e]
General diagnostics	24 (17%)	31 (22%)	34 (25%)	36 (26%)			85 (61%)[d]	139[e]
Starting dialysis	0 (0%)	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)[d]	139[e]
Old-generation prescriptions nausea	0 (0%)	0 (0%)	0 (0%)	0 (0%)			0 (0%)[d]	0[f]
Surgeries	<5 (<4%)						23 (17%)[d]	139[e]
New antidepressant			0 (0%)				6 (4%)[d]	139[e]
Drawing blood	51 (37%)	63 (45%)					100 (72%)	139[e]
Care services and providers								
Late palliative care provision		<5 (<4%)	5 (4%)				20 (14%)[d]	139[e]
Place of care								
Pediatric Intensive Care Unit admissions	35 (25%)	38 (27%)	38 (27%)				53 (38%)[d]	139[e]

Transfers between care settings	0 (0%)	0 (0%)	0 (0%)	<5 (<4%)	39 (28%)[d]	139[e]

[a]Empty cells indicate that the indicator was not face-validated for this time period; [b]Some indicators were measure
subset of the population due to the formulation of the indicator, but are still expected to provide an indication
population through this subset measurement; [c]Indicator does not increase with number of days as number of scans
(min. 2) were counted; [d]Indicator was not face-validated for this period, but is shown to provide a comparison; [e]Twe
children did not have health care claims within the database and were therefore counted as not having received the ind
[f] Measured with ATC code A03, no children with prescription for drugs for functional gastrointestinal disorders were
for the full population; *Due to privacy guidelines, it was not possible to report exact details of small cells, i.e. cel
fewer than 5 children

Table 6: Analysis of variance for predictors of scales of appropriateness

	Scale 1: Potentially appropriate care		Scale 2: Potentially inappropriate care	
	Estimate	P value[a]	Estimate	P value[a]
Age				
1-9 (vs. 10-17)	-0.219162833	0.2093	-.1793831182	0.3231
Sex				
Male (vs. female)	0.088207514	0.6130	-.0150202220	0.9340
Disease category				
Mental retardation (vs. Brain and spinal cord malformations)	-0.014641639	0.9797	-.3662769235	0.5406
CNS degeneration and diseases (vs. Brain and spinal cord malformations)	-0.727120281	0.0360*	-.1030144408	0.7734
Infantile cerebral palsy (vs. Brain and spinal cord malformations)	-0.416541655	0.2360	-.2890929301	0.4288
Other disorders of CNS (vs. Brain and spinal cord malformations)	-0.779199074	0.0207*	-.3364073373	0.3329
Muscular dystrophies and myopathies (vs. Brain and spinal cord malformations)	-0.646261797	0.1182	-.2553471636	0.5516
Movement diseases (vs. Brain and spinal cord malformations)	-1.446395263	0.0127*	-.2873778987	0.6302
Nationality				
Other (vs. Belgian)	-0.523262420	0.0648	-.0945328012	0.7470
Having siblings				
No (vs. yes)	-0.039641064	0.8544	0.3155960991	0.1620

Year of death				
2010-2014 (vs. 2015-2017)	-0.105538600	0.5944	-.1616360011	0.4337

[a] Alpha level below 0.05

Table 7: Logistic regressions per separate indicator

Supplemental file 7.a. Appropriateness indicators[a]

	QI1 (Physiotherapy)		**QI2 (Comfort medication)[a]**		**QI3 (WHO Steps)[b]**		**QI4 (Follow-up Visits)[b]**		**QI5 (General physician)[a]**		**QI6 (Continuous care)[a]**	
	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj. OR (95% CI).	N/A	N/A	N/A	N/A	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj .OR (95% CI).
Age												
1-9 (vs. 10-17)	1.24 (0.57-2.70)	1.61 (0.79-3.30)	1.05 (0.32-3.47)	1.01 (0.31-3.35)					1.47 (0.57-3.79)	1.50 (0.61-3.65)	1.54 (0.74-3.21)	1.60 (0.81-3.13)
Sex												
Male (vs.female)	1.37 (0.62-2.99)	1.41 (0.70-2.86)	0.43 (0.13-1.45)	0.35 (0.10-1.30)					0.63 (0.24-1.62)	0.62 (0.26-1.50)	1.32 (0.63-2.76)	1.08 (0.55-2.10)
Disease category												
Mental retardation (vs. Brain andspinal cord malformations)	2.29 (0.17-31.32)	1.71 (0.13-22.50)	0.31 (0.02-5.47)	0.33 (0.02-5.41)					2.30 (0.19-27.62)	2.76 (0.24-31.82)	0.95 (0.07-13.53)	0.89 (0.06-12.25)
CNS degeneration and diseases (vs. Brainand spinal cord malformations)	1.29 (0.29-5.67)	1.00 (0.24-4.13)	1.39 (0.15-12.76)	1.80 (0.20-16.47)					9.47 (1.88-47.78)	7.75 (1.64-36.71)	2.13 (0.47-9.80)	1.73 (0.39-7.76)
Infantile cerebral palsy (vs. Brainand spinal cord malformations)	1.00 (0.22-4.61)	0.94 (0.22-3.94)	0.62 (0.08-5.04)	0.81 (0.10-6.33)					5.69 (1.20-26.98)	5.26 (1.16-23.92)	1.92 (0.41-9.11)	1.63 (0.36-7.48)
Other disordersof CNS (vs. Brainand spinal cord malformations)	1.62 (0.38-7.01)	1.41 (0.35-5.63)	1.87 (0.21-16.59)	2.49 (0.28-22.51)					8.91 (1.93-41.07)	8.70 (1.96-38.58)	3.43 (0.78-15.06)	3.05 (0.72-13.00)
Muscular dystrophies and myopathies (vs. Brainand spinal cord malformations)	1.17 (0.21-6.72)	0.91 (0.17-4.81)	0.63 (0.05-8.69)	1.19 (0.10-14.60)					3.41 (0.55-21.05)	3.55 (0.63-19.94)	5.71 (0.94-34.52)	4.27 (0.75-24.18)
Moveme nt diseases (vs. Brainand spinal cord malformations)	1.83 (0.12-26.99)	1.71 (0.13-22.50)	1.49 (0.04-64.17)	1.29 (0.03-53.23)					9.27 (0.30-289.04)	10.64 (0.33-343.62)	8.77 (0.61-126.47)	8.00 (0.58-110.27)
Nationality												
Other (vs. Belgian)	4.38 (1.23-15.68)	2.94 (0.96-9.05)	1.01 (0.16-6.53)	1.22 (0.19-7.83)					2.84 (0.77-10.50)	2.21 (0.64-7.61)	3.72 (0.94-14.71)	3.39 (0.90-12.72)
Having siblings												
No (vs.yes)	0.20 (0.06-0.68)	0.25 (0.08-0.77)	1.68 (0.44-6.37)	2.44 (0.69-8.60)					1.41 (0.46-4.34)	1.38 (0.50-3.82)	0.89 (0.36-2.23)	0.86 (0.38-1.95)
Year of death												
2010-2014 (vs. 2015-2017)	1.22 (0.51-2.93)	1.03 (0.46-2.31)	6.53 (0.53-80.92)	8.74 (0.48-158.38)					0.79 (0.27-2.28)	0.97 (0.36-2.63)	1.18 (0.51-2.71)	1.19 (0.55-2.57)

[a] Penalized logistic regression was performed due to low counts in the contingency table, [b] Due to low total and cell counts for these indicators, no logistic regression was performed

Supplemental file 7.a. Appropriateness indicators (Continued)

	QI7 (Clinicalcare) [a]		**QI8 (Palliativecare)** [a]		**QI9 (Multidisciplinary care)** [a]		**QI10 (Specialist physicians)** [a]		**QI11 (Palliative status)**	
	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj .OR (95% CI).
Age										
1-9 (vs. 10-17)	1.67 (0.72-3.85)	1.67 (0.77-3.63)	1.28 (0.49-3.35)	1.31 (0.51-3.38)	1.07 (0.32 -3.65)	1.26 (0.36-4.43)	1.80 (0.79-4.11)	1.80 (0.83-3.89)	1.59 (0.58-4.39)	1.77 (0.64-4.91)
Sex										
Male (vs.female)	0.96 (0.41-2.24)	0.81 (0.37-1.76)	0.95 (0.36-2.47)	0.92 (0.36-2.34)	0.88 (0.24-3.16)	1.38 (0.39-4.86)	0.81 (0.35-1.87)	0.76 (0.35-1.63)	0.64 (0.23-1.79)	0.72 (0.27-1.92)
Disease category										
Mental retardation (vs. Brain andspinal cord malforma tions)	0.92 (0.02-38.14)	0.78 (0.02-32.20)	0.76 (0.06-9.55)	0.96 (0.08-11.74)	0.11 (0.01-4.01)	0.10 (0.01-3.90)	0.86 (0.02-36.11)	0.78 (0.02-32.20)	0.76 (0.0 6-9.81)	0.96 (0.08-11.74)
CNS degeneration and diseases (vs. Brainand spinal cord malformations)	2.74 (0.38-19.51)	2.33 (0.33-16.45)	3.04 (0.57-16.25)	2.70 (0.52-13.98)	1.55 (0.06-40.58)	0.94 (0.03-28.01)	3.54 (0.51-24.70)	3.13 (0.45-21.62)	4.63 (0.78-27.44)	3.59 (0.64-20.00)
Infantile cerebral palsy (vs. Brainand spinal cord malforma tions)	2.02 (0.27-15.04)	1.94 (0.26-14.21)	1.76 (0.35-8.75)	1.49 (0.31-7.17)	0.61 (0.03-13.54)	0.48 (0.02-12.18)	1.58 (0.21-12.01)	1.57 (0.21-11.84)	1.68 (0.3 3-8.44)	1.49 (0.31-7.17)
Other disordersof CNS (vs. Brainand spinal cord malformations)	2.52 (0.37-17.20)	2.61 (0.39-17.53)	4.16 (0.79-21.92)	3.80 (0.74-19.39)	0.72 (0.04-14.97)	0.53 (0.02-12.39)	2.33 (0.34 -15.83)	2.61 (0.39-17.53)	5.24 (0.92-29.85)	5.00 (0.91-27.49)
Muscular dystrophies and myopathies (vs. Brainand spinal cord malformations)	3.23 (0.36-29.25)	3.32 (0.39-27.97)	2.18 (0.30-15.97)	1.89 (0.28-12.98)	0.17 (0.01-3.70)	0.13 (0.01-3.24)	3.09 (0.35-27.54)	3.32 (0.39-27.97)	2.02 (0.27-15.02)	1.89 (0.28-12.98)
Moveme nt diseases (vs. Brainand spinal cord malforma tions)	19.0 (1.14-314.70)	16.34 (1.01-265.26)	3.49 (0.11-114.58)	3.71 (0.11-124.68)	0.37 (0.01-25.45)	0.39 (0.01-32.08)	17.48 (1.06-288.99)	16.34 (1.01-265.23)	2.91 (0.09-93.34)	3.71 (0.11 - 124.67)
Nationality										
Other (vs. Belgian)	3.20 (0.55-18.69)	3.26 (0.54-19.55)	1.93 (0.48-7.71)	1.89 (0.50-7.20)	6.40 (1.39-29.46)	4.81 (1.14-20.36)	1.95 (0.44-8.63)	1.81 (0.42-7.80)	2.76 (0.67-11.34)	2.17 (0.56-8.36)
Having siblings										
No (vs.yes)	0.91 (0.32-2.56)	0.99 (0.38-2.54)	1.99 (0.66-6.03)	1.84 (0.65-5.22)	0.42 (0.07-2.62)	0.56 (0.09-3.40)	0.78 (0.29-2.14)	0.83 (0.33-2.08)	1.24 (0.37-4.22)	1.17 (0.37-3.75)
Year of death										
2010-2014 (vs. 2015-2017)	2.33 (0.96-5.66)	2.33 (1.01-5.36)	0.62 (0.21-1.79)	0.73 (0.26-2.03)	0.78 (0.20-3.04)	0.71 (0.19-2.74)	1.88 (0.78-4.56)	1.85 (0.80-4.25)	0.51 (0.17-1.54)	0.61 (0.22-1.75)

[a] Penalized logistic regression was performed due to low counts in the contingency table, [b] Due to low total and cell counts for these indicators, no logistic regression was performed

Supplemental file 7.a. Appropriateness indicatorsa (Continued)

	QI12 (Increased child benefits)	
	Adj. OR (95% CI)	Unadj. OR (95% CI).
Age		
1-9 (vs. 10-17)	0.85 (0.27-2.69)	0.70 (0.21-2.32)
Sex		
Male (vs.female)	1.06 (0.34-3.33)	0.77 (2.55)
Disease category		
Mental retardation (vs. Brain andspinal cord malforma tions)	0.55 (0.04-7.45)	0.61 (0.05-8.16)
CNS degeneration and diseases (vs. Brainand spinal cord malformations)	4.23 (0.52-34.79)	5.70 (0.63-51.90)
Infantile cerebral palsy (vs. Brainand spinal cord malforma tions)	1.42 (0.24-8.44)	1.49 (0.25-8.81)
Other disordersof CNS (vs. Brainand spinal cord malformations)	3.01 (0.49-18.66)	3.20 (0.52-19.83)
Muscular dystrophies and myopathies (vs. Brainand spinal cord malformations)	5.74 (0.25-132.44)	7.16 (0.27-187.09
Moveme nt diseases (vs. Brainand spinal cord malforma tions)	2.73 (0.08-96.78)	2.37 (0.07-84.63)
Nationality		
Other (vs. Belgian)	0.39 (0.03-5.54)	0.34 (0.02-6.77)
Having siblings		
No (vs.yes)	2.30 (0.63-8.40)	2.44 (0.69-8.60)
Year of death		
2010-2014 (vs. 2015-2017)	1.04 (0.26-4.22)	1.33 (0.31-5.77)

[a] Penalized logistic regression was performed due to low counts in the contingency table, [b] Due to low total and cell counts for these indicators, no logistic regression was performed

Supplemental file 7.b. Inappropriateness indicators (Continued)

	QI13 (Daily diagnostics) [b]		**QI14 (General diagnostics)**		**QI15 (Dialysis) b**		**QI16 (Nauseau prescriptions) b**		**QI17 (Surgeries)[a]**	
	N/A	N/A	Adj. OR (95% CI)	Unadj. OR (95% CI).	N/A	N/A	N/A	N/A	Adj. OR (95% CI)	Unadj .OR (95% CI).
Age										
1-9 (vs. 10-17)			1.24 (0.54-2.83)	1,48 (0,68-3.21)					1.69 (0.27-10.78)	2.60 (0.10-66.47)
Sex										
Male (vs.female)			0.88 (0.39-2.01)	0.78 (0.37-1.67)					0.32 (0.05-2.12)	0.31 (0.01-7.81)
Disease category										
Mental retardation (vs. Brain andspinal cord malformations)			3.31 (0.25-44.08)	2.50 (0.19-32.19)					0.46 (0.01-30.66)	0.39 (0.01-32.07)
CNS degeneration and diseases (vs. Brainand spinal cord malformations)			1.79 (0.43-7.54)	1.67 (0.42-6.70)					3.01 (0.09-104.02)	2.91 (0.05-175.12)
Infantile cerebral palsy (vs. Brainand spinal cord malformations)			2.94 (0.63-13.73)	3.19 (0.72-14.15)					0.61 (0.03-12.28)	0.83 (0.03-24.66)
Other disordersof CNS (vs. Brainand spinal cord malformations)			3.17 (0.75-13.40)	3.33 (0.83-13.43)					2.95 (0.09-93.03)	3.96 (0.07-235.14)
Muscular dystrophies and myopathies (vs. Brainand spinal cord malformations)			2.54 (0.40-15.95)	2.78 (0.48-16.03)					0.71 (0.02-29.76)	1.17 (0.02-75.40)
Moveme nt diseases (vs. Brainand spinal cord malformations)			2.71 (0.20-36.86)	2.50 (0.19-32.19)					0.33 (0.01-19.79)	0.39 (0.01-32.07)
Nationality										
Other (vs. Belgian)			1.37 (0.37-5.07)	1.16 (0.34-3.97)					2.66 (0.23-31.04)	2.86 (0.10-80.43)
Having siblings										
No (vs.yes)			0.37 (0.11-1.23)	0.39 (0.13-1.21)					0.66 (0.07-6.70)	1.24 (0.05-32.60)
Year of death										
2010-2014 (vs. 2015-2017)			2.10 (0.76-5.85)	1.96 (0.74-5.20)					1.20 (0.13-11.55)	1.03 (0.04-26.84)

[a] Penalized logistic regression was performed due to low counts in the contingency table, [b] Due to low total and cell counts for these indicators, no logistic regression was performed

Supplemental file 7.b. Inappropriateness indicators (Continued)

	QI18 (New antidepressants) [b]		**QI19 (Drawing blood)**		**QI20 (Late palliative care)** [a]		**QI21 (ICU admissions)**		**QI22 (Care setting transfers)** [a]	
	N/A	N/A.	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj. OR (95% CI).	Adj. OR (95% CI)	Unadj .OR (95% CI).
Age										
1-9 (vs. 10-17)			1.28 (0.61-2.66)	1.60 (0.82-3.15)	1.27 (0.30-5.44)	1.21 (0.23-6.41)	1.73 (0.77-3.88)	1.96 (0.90-4.26)	2.17 (0.32-14.87)	2.60 (0.10-66.47)
Sex										
Male (vs.female)			1.18 (0.56-2.48)	1.17 (0.60-2.29)	2.60 (0.52-13.14)	2.91 (0.44-19.32)	1.22 (0.55-2.72)	1.21 (0.57-2.56)	2.25 (0.33-15.49)	2.83 (0.11-72.43)
Disease category										
Mental retardation (vs. Brain andspinal cord malformations)			0.79 (0.06-10.81)	0.58 (0.04-7.66)	0.28 (0.02-4.84)	0.33 (0.02-5.41)	1.24 (0.09-17.70)	1.13 (0.08-15.51)	0.11 (0.00-3.43)	0.10 (0.00-3.90)
CNS degeneration and diseases (vs. Brainand spinal cord malformations)			2.67 (0.62-11.52)	2.10 (0.51-8.57)	9.42 (0.47-188.85)	9.57 (0.37-272.99)	0.80 (0.17-3.74)	0.75 (0.17-3.40)	3.15 (0.11-91.06)	2.91 (0.05-175.12)
Infantile cerebral palsy (vs. Brainand spinal cord malformations)			1.98 (0.45-8.79)	1.88 (0.45-7.82)	3.51 (0.33-37.04)	2.71 (0.24-31.32)	1.03 (0.21-5.10)	0.98 (0.21-4.67)	4.06 (0.12-139.20)	2.57 (0.04-155.13)
Other disorders of CNS (vs. Brainand spinal cord malformations)			3.53 (0.84-14.77)	3.17 (0.81-12.50)	5.05 (0.47-54.09)	4.24 (0.37-48.08)	1.24 (0.27-5.78)	1.31 (0.29-5.89)	4.28 (0.14-133.82)	3.96 (0.07-235.14)
Muscular dystrophies and myopathies (vs. Brainand spinal cord malformations)			1.78 (0.32-9.99)	1.50 (0.29-7.75)	2.25 (0.18-28.78)	1.19 (0.10-14.60)	1.02 (0.16-6.47)	0.84 (0.41-4.97)	2.13 (0.06-81.57)	1.17 (0.02-75.40)
Movement diseases (vs. Brainand spinal cord malformations)			5.99 (0.42-85.34)	5.25 (0.40-68.95)	1.34 (0.04-51.44)	1.29 (0.03-53.23)	1.14 (0.08-16.78)	1.13 (0.08-15.51)	0.55 (0.01-32.84)	0.39 (0.01-32.08)
Nationality										
Other (vs. Belgian)			3.37 (0.98-11.62)	2.37 (0.75-7.47)	0.89 (0.06-13.37)	0.76 (0.04-15.82)	1.13 (0.32-4.06)	1.07 (0.32-3.64)	3.18 (0.25-39.74)	2.86 (0.10-80.43)
Having siblings										
No (vs.yes)			0.34 (0.12-0.91)	0.38 (0.16-0.93)	2.73 (0.47-15.99)	1.25 (0.18-8.50)	0.57 (0.19-1.70)	0.49 (0.17-1.38)	2.57 (0.30-22.26)	1.24 (0.05-32.60)
Year of death										
2010-2014 (vs. 2015-2017)			1.55 (0.67-3.61)	1.34 (0.61-2.91)	0.41 (0.08-2.01)	0.46 (0.09-2.50)	1.01 (0.42-2.48)	0.92 (0.39-2.16)	0.69 (0.08-6.29)	1.03 (0.04-26.84)

[a] Penalized logistic regression was performed due to low counts in the contingency table, [b] Due to low total and cell counts for these indicators, no logistic regression was performed

Table 8: Validation and reliability verifications for identification of bias

Population
Validity
Our database population was compared to population numbers from Statistics Belgium. Statistics Belgium public documentation* identified 6050 deaths for children between 1 and 25 years old. Our database includes 5098 deaths for children between 1 and 25 years old, which is 84% of the number of deaths reported by Statistics Belgium. Differing selections for death, time and age by the governmental agencies providing the data may account for the differing number of deaths between databases.
Reliability
The unique IDs within our databases that form the relational database were compared to each other to assess reliability of the databases. The majority of IDs provided overlap. However, some IDs did not overlap with the IDs in other databases for the total amount of children (1-25) who died of all causes of death: 91 for the databases of the Intermutualistic Agency, 104 for Statistics Belgium (out of 5344 unique codes in total). However, this concerns all children dying of all cause of death, and is therefore expected not to have a large impact on the identified number of children with neurological conditions that was found. Further investigation confirmed there was no faulty linking at the base of the unlinkable IDs.
Indicators
Validity
To our knowledge, no publications are available to compare the percentages found to verify external validity for the Belgian context.
Reliability
To evaluate reliability, measurements were repeated with a different method or by a different researcher for some indicators. For some indicators (physiotherapy, general physician contact, clinical care provision, specialist physician involvement, surgeries, care setting transfers), two different calculation methods were used to verify reliability. Categorical selection and selective selection were applied. Indicators were originally calculated with a selective method, meaning the researcher screened all nomenclature codes and hand-selected the relevant codes. The categorical selection method was used to validate the selective method, meaning the calculations were repeated while

selecting categories, e.g. following the structure of the nomenclature codes or practitioner categories. For example, for the indicator 'Prescriptions of physiotherapy', the selective method entailed selecting all individual nomenclature codes of which the description referred to physiotherapy. The categorical method entailed selecting all nomenclature codes that were categorized as prescribed by a physiotherapist by the healthcare funds. For most indicators, results of the two methods were similar, which suggests results are internally reliable. For the indicator care setting transfers, use of different variables gave differing results, which suggests results may not be reliable – however, conversations with the database providers indicate that the more reliable variables were used for final analysis.

Some indicators (palliative status, dialysis), were repeated by another researcher. Same result were found by the other researcher for these indicators, which suggests the calculations are reliable.