DicData Project

Supplementary report

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Introduction

In May 2012, our research team completed a series of linked research studies that comprised the DicData project. The aim of the project was to explore the impact on families of caring for child with a life limiting condition. We did this by analysing data that had already been gathered over the course of seven years about the families of a cohort of children born in the year 2000; the Millennium Cohort Study (MCS). This kind of secondary analysis had only recently become possible following our team's compilation of a list of the ICD10 codes that, according to the ACT/RCPCH criteria, should be considered life-limiting conditions (LLC). That list is often known, somewhat inaccurately, as the 'Dictionary of LLC'.

In our final report, we explained that in the course of the study we had uncovered an important weakness in the Millennium Cohort Study when considered as a source of data for palliative care research. Namely, in the MCS, ICD10 codes were recorded in less detail than in our ICD10 'dictionary'. The result is that, where a single ICD10 category includes conditions that are LLC as well as those that are not, the MCS cannot distinguish between them. While the effect for most categories is (we think) relatively small, the impact of the category of Pervasive Neurological Disorders (F84) was more significant, since it contained only a small number of genuinely life-limiting conditions. We were concerned that this rendered our data analysis unreliable, particularly in respect of reporting and comparing prevalence.

With that in mind, we excluded those diagnoses and have re-analysed the data. What follows in the supplementary report on the two projects whose conclusions

we have reconsidered in light of these newly analysed data. Reassuringly, the effect of the F84 exclusion was not enough to impact significantly on any of the main conclusions.

The main finding of the first chapter is that in the population of five and seven year olds, the prevalence of LLC is approximately 1.5% (145 per 10,000 population). This is higher than in previous estimates, because it represents the total number of children at any one time with a LLC. It therefore provides an important adjunct to other studies funded by Together for Short Lives (1) that have given an estimate of the numbers already accessing palliative care services. Where those studies show the *minimum* number of children in the population who might need palliative care, ours shows the *maximum*. Our study represents the sum total of all those who can be expected to need to access palliative care services at some point in the trajectory of their condition. Our data show that the number of children potentially needing palliative care is much higher than previous estimates. This provides a target figure for 'penetration' by palliative care services. The two studies thus provide valuable and complementary information for service providers. A rule of thumb has always been that around half of children with LLC will need to access palliative care services at any one time. These two studies suggest the proportion is actually somewhat smaller than that. Only around a quarter of children with LLC are under any kind of hospital service. The proportion who specifically access specialist palliative care services remains unclear. More importantly for the specialty, it is also unclear how many children should access palliative care services but are unable to do so. It is impossible to distinguish between patients who could benefit from them and patients who certainly ought to be referred.

The main message from the second chapter is the strong association of behavioural and developmental problems in children with LLC. At the same time, the study provides evidence that parents are resilient, with high levels of psychological distress but no increase in significant mental illness. Furthermore,

the study suggests that, despite a high level of parental unemployment, families of children with LLC are not struggling financially. This suggests, though it does not prove, that benefit provision to families caring for children with LLC is adequate for many.

The research team in Bangor would like to record once again their thanks to Together for Short Lives for funding this study, and for their understanding in extending the period by further six months to allow for this reanalysis of the data.

Chapter 1

Prevalence of life-limiting conditions in children aged 3, 5 and 7 years: secondary data analysis of the Millennium Cohort Study

Introduction

Establishing the prevalence of life-limiting conditions in children is both important and challenging. Its importance lies in the need to demonstrate to commissioners that development of palliative care services is necessary. Its challenge lies in the difficulty identifying all children who would potentially benefit from the availability of such services. Many of the key terms are difficult to define, and it is problematic in practice to identify all the children who should be recruited to any study.

In this project, we addressed the first of those difficulties by utilising the Together for Short Lives 'Dictionary of LLC conditions' (DLLCC) {Fraser, 2012 #19} which is based on the ACT/RCPCH categories (2). This enabled us to define with some clarity the population of children whose problems we were trying to establish. The second difficulty can only be overcome by utilising a cohort study approach, which is designed to ensure that the population under study is not different from the general population in any way that is significant to the outcome of the study. We performed secondary analysis of data gathered on a cohort of children recruited into the Millennium Cohort Study because of the date of their birth.

Whatever factors influence the likelihood of having or developing a life-limiting condition, it is implausible that they will be different on different days of the year. Since date of birth has no impact on the likelihood of any individual child developing a LLC, a cohort design allows conclusions to be confidently drawn in respect of prevalence in the population at large. Studies of prevalence that have

to rely on identifying patients already known to services provide good estimates of the *minimum* demand for services, because the true prevalence must be that or greater. To establish the *maximum* number of children who could potentially be affected by a LLC and thus benefit from children's care services, however, a cohort study design is essential.

Finally, the unique design of the MCS (a nationally-representative birth cohort with repeated measurements every two years) allowed us to examine the incidence and persistence of life-limiting conditions in the early years.

Materials and methods

This is a secondary analysis of data available in the second, third and fourth surveys (ages 3, 5 and 7) of the Millennium Cohort Study. The MCS was designed to identify a population-representative sample of children in the UK, born in the new millennium and to follow them up prospectively. Participants were identified through the Child Benefit Register. The child benefit is a non-means tested benefit available to all UK children. Participant identification was geographically clustered to include all four countries (England, Wales, Scotland, Northern Ireland), and disproportionately stratified to over-include ethnic minority and disadvantaged children (3, 4). Over-sampling was done to ensure adequate representation of these groups in the survey (3). Children and families were selected from 398 randomly selected electoral wards in the UK.

 At age 3, there were 15,590 children who participated in MCS2; at age 5, 15,246 children were included (MCS3), and at age 7, 13,857 children were followed up (MCS4). All analyses conducted and reported below used appropriate weights to account for the disproportionate stratification of ethnic minority and disadvantaged children along with attrition/non-response.

List of ICD10 codes associated with life-limiting diagnoses
Diagnostic labels among children with life-limiting conditions were collected from two sources. First, diagnoses of children admitted to children's hospices were provided by Children's Hospices Hospice UK (CHUK, now Together for Short LIves), the membership organisation for Children's Hospices in England and Wales. The diagnoses emanated from the five children's hospices that were using a standardised data collection tool developed by Chase Hospice (Esplen, personal communication 2010). Second, diagnoses of children accepted by specialist paediatric palliative medicine services were obtained from tertiary service based at the Children's Hospital in Cardiff. Neither source used any formal disease classification system.

The two lists of diagnoses were merged. The combined list was edited, removing duplicate diagnoses and descriptions that were not truly diagnostic labels. Duplicates occurred either when two diagnoses were exactly the same, or when two or more terms were used to describe the same condition (e.g., trisomy 13 and Patau's syndrome). Non-diagnoses included terms that had led to referral, but were deemed by the investigators to be modes of death rather than diagnosis (e.g., apnoea), were incidental to the life-limiting diagnosis (e.g., anaemia), or were treatments for the life limiting diagnosis (e.g., tracheostomy). Finally, diagnoses were removed if they could not be described by one or more of the ACT/RCPCH categories and therefore, by the definition used for this study, were not life-limiting conditions.

A diagnostic label and code from the International Classification of Disease (ICD10) was assigned by the investigators to each diagnosis on the list (apps.who.int/classifications/apps/icd/icd10online/).

The combined list of LLCs built from evidence in practice was then verified by comparison with aggregated anonymous death certificate data for all deaths in Wales between 0 and 19 years between 2002 and 2007, obtained from Public Health Wales Observatory {Public Health Wales Observatory, 2011 #41}. LLC that did not already appear in the ICD10 list, were added to it. The resulting list has been used in other studies that have already been published {Fraser, 2012 #19;NHS, 2012 #42} and is currently being prepared for publication as the Together for Short Lives 'Dictionary' of LLC.

Analysis

Point Prevalence: Number of children with LLC at one point in time as a proportion of the total number of population at that time point

Persistence: Number of children with an LLC at both time points as a proportion of number of children with LLC at the first time point

New cases: Children with an LLC at Time 2 who did not have an LLC at Time 1 as a proportion of the number of children with available data at both time points (total population for this ratio)

Incidence: Number of new cases, expressed as a proportion of number of children with available data at both time points MINUS number of children who had LLC at start point ('population at risk'). Also known as Cumulative incidence, or incidence proportion (5).

Results

Prevalence

Prevalence of LLC in the three age groups is shown in table 1.1. At age 3, this prevalence corresponds to a weighted count of approximately 297 children, of whom 283 (95%) have one LLC, 13 (4.5%) have two LLCs and 1 (0.5%) has three LLCs. At age 5, the weighted estimate is 226 children of whom 210 have one LLC (93%) and 16 (7%) have two LLCs. At age 7, the weighted count is 199, of whom 194 (97.5%) have one LLC and 5 (2.5%) have two LLCs. The difference in prevalence between cohorts at 5 and 7 years was not significant ($\chi^2 = 0$, p=1), but prevalence at both was significantly lower than at 3 (McNemar, $\chi^2 = 13.83$, p=.0002 between 3 and 5, $\chi^2 = 14.29$, p=.0002 between 3 and 7).

	Unweighted prevalence (95% CIs)	Weighted prevalence (95% CIs)	Weighted number of children with LLC
Age 3	1.74% (1.54%, 1.95%)	1.89% (1.65%, 2.13%)	297
Age 5	1.40% (1.21%, 1.58%)	1.45% (1.21%, 1.68%)	226
Age 7	1.31% (1.12%, 1.50%)	1.44% (1.16%, 1.71%)	199

Table 1.1: Prevalence at ages 3, 5 and 7 years.

Frequency of LLCs by cohort

The ten most frequent LLCs within each time point (ages 3, 5, and 7) were identified. These are presented in Table 1.2 below, accompanied by the corresponding ICD-10 name

ICD-10 code	ICD-10 name	weighted counts	weighted frequencies
Age 3			
Q21	Congenital malformations of cardiac septa	41	14%
G40	Epilepsy	28	9%
G80	Cerebral Palsy	24	8%
J98	Other respiratory disorders	23	8%
Q74	Other congenital malformations of limbs	17	6%
Q60	Renal agenesis and other reduction defects of kidney	16	5%
R06	Abnormalities of breathing	15	5%
F80	Specific developmental disorders of speech and language	15	5%
Q82	Other congenital malformation of skin	13	4%
Q87	Other specified congenital malformation syndromes affecting multiple systems	9	3%
Age 5			
G40	Epilepsy	53	24%
J98	Other respiratory disorders	27	12%
G80	Cerebral Palsy	22	10%
R06	Abnormalities of breathing	19	8%
Q21	Congenital malformations of cardiac septa	16	7%
Q87	Other specified congenital	12	5%

	malformation syndromes affecting multiple systems		
Q82	Other congenital malformation of skin	8	3%
Q79	Congenital malformations of the musculoskeletal system, not elsewhere classified	7	3%
Q85	Phakomatoses, not elsewhere classified	5	2%
Q78	Other osteochondrodysplasias	4	2%
Age 7			
G40	Epilepsy	56	28%
G80	Cerebral Palsy	18	9%
Q21	Congenital malformations of cardiac septa	11	6%
N25	Disorders resulting from impaired renal tubular function	11	6%
F80	Specific developmental disorders of speech and language	9	5%
Q82	Other congenital malformation of skin	9	5%
J98	Other respiratory disorders	7	4%
Q87	Other specified congenital malformation syndromes affecting multiple systems	7	4%
R06	Abnormalities of breathing	5	3%
Q61	Cystic kidney disease	4	2%

Table 1.2: The 10 most frequent LLCs at each cohort (*Description based on current version ICD-10 2010)

Incidence, Persistence and New Cases

Data on incidence, persistence and new cases are shown in table 1.3. There were no differences between three and five and five and seven years of age, either in persistence (McNemar's χ^2 1.17, p=.336) or in the rate of new cases emerging (χ^2=0.35, p=0.556).

	3 to 5 years (95% CIs)	5-7 years (95% CIs)	3-7 years (95% CIs)
Persistence	37.98% (30.06%, 45.89%)	55.62% (44.62%, 66.62%)	35.60% (27.55%, 43.64%)
New cases	0.72% (0.55%, 0.90%)	0.63% (0.47%, 0.79%)	0.76% (0.56%, 0.95%)
Incidence	0.74% (0.56% , 0.92%)	0.64% (0.48%, 0.80%)	0.77% (0.57%, 0.97%)

Table 1.3: Incidence, persistence and percentage of new cases (with 95% confidence Intervals) in each of the three age cohorts.

Following the identification of persistent and new cases, we explored potential predictors of persistence and new cases. Looking at the sociodemographic characteristics at age 3, we examined their association (using odds ratios [OR]) with new and persistent cases at age 5 (Table 1.4), and new and persistent cases at age 7 (Table 1.5).

Age 3 predictor	New cases 3_5	Persistent cases 3_5
	OR (95 CIs)	OR (95 CIs)
Male gender	1.08 (.69, 1.66)	1.21 (.73, 2.02)
White ethnic group	.94 (.56, 1.56)	2.05 (.88, 4.74)
Mixed ethnic group	1.48 (.51, 4.34)	1.41 (.49, 4.02)
Indian ethnic group	.63 (.23, 1.74)	no cases
Pakistani ethnic group	1.30 (.65, 2.58)	.47 (.15, 1.48)
Black ethnic group	.54 (.09, 3.37)	no cases
Many siblings (2+)	1.01 (.63, 1.61)	1.10 (.63, 1.93)
Large family (5+)	1.23 (.72, 2.09)	.91 (.53, 1.55)
Single-parent household	.84 (.43, 1.67)	2.21 (1.31, 3.74)*
Maternal age	1.01 (.98, 1.05)	.96 (.92, 1.00)
Subjective poverty	.71 (.31, 1.58)	1.18 (.60, 2.34)
Area deprivation	1.06 (.65, 1.72)	.74 (.38, 1.43)
Parental unemployment	2.40 (1.24, 4.64)*	.89 (.31, 2.52)
Income poverty	1.19, (.76, 1.88)	1.08 (.63, 1.83)
Deprivation at age 3	1.10 (.88, 1.36)	1.00 (.77, 1.29)
Cumulative deprivation (age 9 months to 3 yrs)	1.07 (.96, 1.20)	1.03 (.09, 1.19)

Table 1.4: Age 3 predictors of new and persistent LLC cases at age 5 years.

Age 3 predictor	New cases 5_7	Persistent cases 5_7
	OR (95 CIs)	OR (95 CIs)
Male gender	.76 (.45, 1.29)	1.29 (.86, 1.94)
White ethnic group	2.61 (.97, 7.03)	1.52 (.69, 3.37)
Mixed ethnic group	.14 (.02, .86)*	1.49 (.52, 4.26)
Indian ethnic group	no cases	.17 (.03, .96)*
Pakistani ethnic group	.57 (.16, 1.99)	.58 (.25, 1.36)
Black ethnic group	.81 (.18, 3.58)	.47 (.08, 2.89)
Many siblings (2+)	1.58 (1.01, 2.49)	1.29 (.82, 2.04)
Large family (5+)	1.09 (.67, 1.78)	1.13 (.70, 1.82)
Single-parent household	1.79 (1.02, 3.14)*	2.03 (1.26, 3.27)*
Maternal age	1.00 (.97, 1.04)	.97 (.93, 1.00)
Subjective poverty	1.81 (.87, 3.76)	.28 (.08, 1.07)
Area deprivation	1.24 (.74, 2.10)	.83 (.48, 1.43)
Parental unemployment	2.50 (1.50, 4.17) **	2.01 (1.10, 3.68)*
Income poverty	1.51 (.93, 2.45)	1.54 (.96, 2.46)
Deprivation at age 3	1.32 (1.11, 1.57)*	1.10 (.93, 1.30)
Cumulative deprivation (age 9 months to 3 yrs)	1.12 (.104, 1.22)*	1.03 (.95, 1.12)

Table 1.5 Age 3 predictors of new and persistent LLC cases at age 7 years.

Discussion

This is the first study to use secondary analysis of cohort data to examine LLC in childhood. Previous studies have had to rely on reporting (6-8), meta-analysis (2, 9), service usage data (1, 10) or a combination of these (11, 12). By analysing the MCS, we were able to study the same population at ages 3, 5 and 7 years. LLC prevalence at age 3 years was estimated at 1.89% of the population of three year-olds. Prevalence significantly reduced at ages 5 and 7, stabilizing at about 1.5% of the population 145/10000 (table 1.1). This is higher than previous estimates(e.g., <1%, Fraser et al., 2012). A cohort study analysed using a disease classification system identifies every possible case in the population. For the purposes of service development, this figure therefore represents the maximum likely prevalence using current definitions of life-limiting conditions based on the ACT/RCPCH categories. This is logically greater than the number of children with a LLC who actually access palliative care services. It needs to be distinguished carefully from the number of children who will need input from palliative care services at any one time. Given the definition used in this study, all the children identified are likely to need palliative care at some time in the course of their condition. It does not follow, however, that they all need it all the time; in fact that is highly unlikely. The figure we have represented here is the maximum number of children who could logically need access palliative care services. The number who will need to do so at any one time is likely to be a fraction of this, meaning that an additional judgment criterion such as the 'surprise' question {Brook, 2008 #43} is required in individual children. In addition, the trend of decreasing prevalence over time is consistent with findings from clinical populatins (Fraser et al., 2012). An important observation from our study (Table 1.1) is that a significant proportion of individual children with one LLC have at least one more (4.5%, 7% and 2.5% at 3, 5 and 7 years respectively). This emphasises the potential complexity for parents and for health professionals in caring for children with LLC.

The results provide evidence of a change in prevalence over the course of childhood. It is intuitively implausible that the prevalence of LLC is constant over the whole range of age groups usually considered in prevalence studies. The diagnosis of an LLC is usually made in the neonatal period, or in the first few months and years of life as delayed developmental milestones become apparent. It would be relatively unusual for most LLC to be diagnosed for the first time in late childhood or adolescence. The number of children living with LLC is also likely to change over the course of childhood. Conditions such as genetic anomalies that are diagnosed in the neonatal period may lead to death within weeks or months, while those with a natural trajectory of many years, such as cerebral palsy, are often diagnosed in infancy and those such as cancer that can be diagnosed at any point in childhood will typically persist for some years.

A further factor contributing to that high prevalence figure relates to a limitation of the Millennium Cohort Study itself. The ICD10 classification offers precise descriptions of individual conditions under chapter subheadings (ie. up to 4-digit ICD-10 codes), grouped together under more general chapter headings. Unfortunately, the MCS does not do this; it records only chapter headings (ie. only 2-digit codes). Within the same chapter, therefore, it is likely that some conditions that are not life-limiting will be grouped for analysis as though they were. Secondary analysis of MCS data will result in overestimation of prevalence, and at present the extent of this methodological limitation across ICD chapters is unknown.

The most frequent LLC present at each cohort (table 1.2) are non-malignant, chronically disabling conditions. At each cohort they include cerebral palsy (G80), epilepsy (G40) and congenital cardiac malformations (Q21). All these present a spectrum of clinical severity, such that some patients with the diagnosis will be expected to survive into adulthood. A disease-based classification alone does not allow those patients to be identified, and, again, this

underlines that some additional judgment criterion is needed to distinguish between a *condition that is potentially life-limiting*, and the need for palliative care services of a *specific child with that condition*.

The second set of conclusions we were able to draw from our data relates to characteristics of families caring to children with life limiting conditions, compared with those who did not. The influences of demographic difference changed with age and were unexpectedly complex.

Ethnic groups

In contrast with the findings of other authors {Fraser, 2012 #19;Fraser, 2012 #44}, in our study there is no difference in the distribution of ethnic groups between families of children with LLC and those without. Being of Indian origin was actually associated with *reduced* odds of LLC at ages five and seven (tables 1.5b-c), but it was also associated with decreased persistence suggesting the cause might be a higher number of deaths before the age of five. Mixed ethnic background was commoner in families with LLC at age five (table 1.5b).

Relationship between LLC and deprivation

In early childhood, there is no systematic indication that children with LLC grow up in families that are more deprived. Deprivation was not systematically associated with prevalence of LLC, and neither deprivation nor cumulative deprivation was associated with increased persistence of LLC.

Parental unemployment

Parental unemployment was more likely among families of children with LLC and (table 1.5b-c). The rate of new diagnosis was consistently predicted by parental

unemployment (table 1.3a-b), probably reflecting the difficulty maintaining employment while caring for a child with a LLC. That difficulty might be the result of a variety of reasons including physical ill-health - as a result of caring, or because of a heritable diagnosis shared with the child - or the practical difficulties of managing time. Subjective poverty, however, was associated with *lower* odds of LLC at age five (table 1.5b), and at age three (table 1.5a) indicators of deprivation were significantly influential only if several were combined ('high deprivation').

An important and interesting finding is that there was an association between deprivation and increased odds of LLC at age three, but not in later cohorts (table 1.3b). This probably reflects a change in the nature of the diagnoses; most metabolic and other neurodegenerative conditions that are essentially unaffected by environment are diagnosed before the age of three. In contrast, by the ages of five and seven a higher proportion of new diagnoses will be those influenced by environmental factors, such as cancer or acute traumatic or infectious brain injury.

Single-parent families

The only consistent association of LLC across all three cohorts was with single-parent household. Children with a LLC are more likely to grow-up in households in which parents are cohabiting or single rather than married. Single-parent household was also associated with persistence of cases between the cohorts (table 1.4). This might be because relationship breakdown is more likely in the early months after a diagnosis is made (that is, before the earliest data captured in the MCS), or because claiming single status is advantageous, for example by allowing access to certain benefits.

New cases

The prevalence was highest at age 3 (table 1.1), but thereafter there was no difference between the cohorts, suggesting that there is a group of conditions in which diagnosis and death are both made in the first few years of life. This would include, for example, conditions causing death in the neonatal period. There was no change in the rate at which new diagnoses were made across the three cohorts, or in persistence of cases already diagnosed, suggesting that over the three cohorts the rate of death from LLC approximated the rate of new diagnosis (table 1.4). Although a number of factors predicted persistence of cases between the cohorts (table 1.3a-b), the only consistent one between all three was single-parent household, suggesting that if relationship breakdown occurred it was likely to be in the first few months after diagnosis and had already happened before the cohort at age 3.

An association between the rate of new cases of LLC with early deprivation - mainly through parental unemployment - was most obvious at age seven. Also, at age seven (table 1.5c), but not before, there was an increased likelihood of LLC among families with more than two siblings. Taken together, these suggest that families of children with LLC have a 'double whammy'; compared with other families, they are more likely both to face deprivation because one or both parents are unemployed, and to be part of a large family.

Importantly, this is the first study to provide information on persistence and incidence of LLCs across the British population. Overall, about 35% of children with a LLC condition at age 3 still have that condition at age 7 (Table 1.3). Persistence was somewhat lower in the earlier years (38% ages 3 to 5 years) compared to the later ones (56% from age 5 to age 7 years), although not significantly so. The increase could perhaps reflect increased survival rates past the age of 5. In general, the longitudinal data suggest a certain stability of LLCs across ages 3 to 7, with persistence, incidence and new case rates being fairly

similar across the two-year periods. Overall incidence (ages 3 to 7) is about 0.8% suggesting that past age 3, fewer than one new LLC cases are identified every two year period. This supports suggestions that LLCs tend to be identified in the neonatal and toddlerhood period.

Our analysis of early life predictors (age 3) of persistent cases indicated that parental unemployment and single parent household were systematically associated with the presence of LLCs. These may possibly highlight the stable nature of household changes that follow a diagnosis of LLC at the beginning of life: if relationships are more likely to break up and parents leave their jobs to care for their children soon after a diagnosis, they are also likely to remain under these conditions for a long period in early childhood. In addition,Indian ethnic group is protective of persistence, reflecting perhaps the decreased odds of having or developing LLCs when of Indian ethnic origin. The most interesting aspect of this analysis is the fact that socioeconomic deprivation, especially poverty, is not significantly associated with persistence. This may be because benefits are made available to these families to counterbalance the loss of income from parental unemployment and single-parent status and keep families out of poverty.

Looking at the early life predictors of new LLC cases, parental unemployment again emerges as a systematic predictor of new cases. One potential explanation is that parents of children who will develop LLCs are also likely to suffer poor health themselves and therefore are unable to work. This might also account in part for the significant association of parental unemployment with persistent cases: If parents of children with ongoing, persistent or emerging LLCs are more likely to suffer physical ill-health, they would be less likely to be employed.

Also of interest is the pattern of associations with deprivation: in the early years, new cases are no more likely amongst those who experience higher deprivation. However, by age 5, increased levels of earlier deprivation (and long-term exposure to deprivation from birth to age 3) are significantly associated with new

LLC cases. One possible explanation for this pattern of findings is that emerging LLC cases after the age of 5 are of a different type, more likely to be associated with environmental risk.

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Conclusions

Our study has shown that a disease-based classification can identify approximately 145/10000 children with LLC among the total population of 5 and 7 year-olds. This number includes but is not limited to all those likely to need to access palliative care services. Such a classification does not, however, replace the need for a further judgment criterion in individual cases. In addition, the present study indicated that approximately 36% of children with a LLC will still present with this LLC at age 7. New cases of LLC past the age of three are limited to less than one child over the time period considered (about 0.77% incidence rate) We found no consistent difference in the overall distribution of ethnic groups between children with LLC and those without. Children with LLC are more likely to grow-up in single-parent households. There was no systematic indication that children with LLC grow up in families that are more deprived, despite a higher likelihood of parental unemployment, perhaps because statutory benefits offset the impact of low income. However, early deprivation affected the rate of new diagnosis in a way that became more pronounced as the cohort grew older.

Secondary analysis of existing cohort data provides opportunity to obtain accurate information to underpin evidence-based service development in palliative care for children. This study has identified both the potential and some of the limitations of using a disease-based classification to carry out such analysis, particularly the need to use cohort studies that record diagnoses as precisely as possible.

Chapter 2

Five-year-old children with a life-limiting condition: Evidence from a British cohort study on children's development and maternal well-being

Introduction

The objective of caring for patients is ultimately to improve their well-being. The concept of well-being itself, however, is difficult to define, still more to measure. As a translation of Aristotle's term *eudaemonia*, it is both more precise and more complex than the traditional alternative 'happiness'. Well-being more faithfully represents Aristotle's concept that *eudaemonia* describes an individual who is fulfilling the purpose for which they were created. It certainly encompasses an individual's capacity to be happy, but also other relevant capacities such as to relate to others, to be able to influence the environment around them, and to have a sense of *telos* - that is, a direction that gives purpose to life experience (13).

With this complex understanding, it becomes clear that well-being can be enhanced by events and circumstances that cause unhappiness, and even by unhappiness itself. In this project, we examine the cognitive and physical development of children with life limiting conditions along with the psychological and physical well-being of their mothers. To do this, we performed a secondary analysis of cohort data available from the MCS at age 5 years, comparing data from families of children with LLC and families with a child without LLC. Our aim was to explore both the behavioural, cognitive and physical development of children with a life-limiting condition, and the psychological and physical well-being of their mothers.

Materials and methods

This is a secondary analysis of data available in the third survey (age 5) of the Millennium Cohort Study (MCS3). The MCS was designed to identify a population-representative sample of children in the UK, born in the new millennium and to follow them up prospectively. Participants were identified through the Child Benefit Register. The child benefit is a non-means tested benefit available to all UK children. Participant identification was geographically clustered to include all four countries (England, Wales, Scotland, Northern Ireland), and disproportionately stratified to over-include ethnic minority and disadvantaged children (3, 4) Over-sampling was done to ensure adequate representation of these groups in the survey (3) . Children and families were selected from 398 randomly selected electoral wards in the UK. In MCS3, 19,422 participants were eligible, of which 15,246 actually participated (79.2% participation rate).

Participants

Among the 15,246 singleton children in MCS3, we identified 226 with a LLC (weighted prevalence 1.45%, 95% CIs: 1.21% to 1.68%; Hain et al, Paper 1). The remaining MCS children without a LLC were used as a comparison group. Approximately 55% of children with a LLC were boys, and 88% were of a white ethnic background (see table 1).Children with LLC were more likely to live in a family where both parents were unemployed compared to the non-LLC group (31% vs 20%), and in a single-parent household (30% vs 20%). Despite these differences however, children with a LLC were no more likely than other children to live in poverty (35% vs 30%), or in deprived areas (20% vs 22%), and as a matter of fact, families of children with LLC were significantly less likely to say that they struggle financially (5% vs 11%). Looking at the overall level of deprivation experienced by families at age 5, children with LLC were experiencing comparable deprivation levels as children without LLC (Table 2.1).

Demographic characteristics	LLC group	non-LLC group	Comparison (*p* value)	Odds Ratio (95% CIs)
Child characteristics				
Child male	55.4%	51.0%	F=1.22, p=.269	1.19 (.87, 1.63)
White	87.9%	86.7%		1.12 (.74, 1.70)
Mixed	6.4%	3.2%		1.97 (1.04, 3.75)*
Indian	0.7%	1.8%		.37 (.16, .87) *
Pakistani/Bangladeshi	3.6%	4.2%		.85 (.50, 1.43)
Black or Black British	0.8%	2.84%		.28 (.07, 1.13)
Other (inc. Chinese)	0.6%	1.2%	F=3.42, p=.009	
Family Characteristics				
2+ siblings	33.6%	35.2%	F=.18, p=.670	.93 (.67, 1.31)
Large family (5+ people in household)	31.3%	34.7%	F=.84, p=.360	.86 (.61, 1.20)
Single-parent household	29.9%	19.7%	F=9.15, p=.003	1.74 (1.21, 2.51) *
If 2- parents, % married	77.9%	76.2%	F=.20, p=.655	.91 (.60, 1.37)
Mum main respondent	97.6%	97.7%	F=.01, p=.970	
Maternal age	33.7 (.44)	33.9 (.12)	t=-.60, p=.546	.99 (.97, 1.02)
Social and Economic indicators				

Subjective poverty (finding it quite/very hard to manage)	4.87%	10.8%	F=5.87, p=.016	.42 (.20, .87) *
Area Deprivation (lowest 20% of IMD)	19.5%	21.9%	F=.66, p=.417	.87 (.61, 1.23)
Both parents unemployed	31.0%	20.0%	F8.64, p=.004	1.79 (1.21, 2.66)*
Income Poverty (<60% median UK equivilised income)	35.4%	30.4%	F=1.97, p=.160	1.26 (.91, 1.73)
High deprivation (2+ adverse SEP indicators)	28.3%	23.6%	F=1.84, p=.174	1.07 (.94, 1.21)

Table 2.1. Exploring differences in demographic characteristics between children with and without a life-limiting condition at age 5 years

Measures

1. Children's LLC status and developmental outcomes

In MCS3, mothers were asked to identify any long-standing illnesses the child may have had, and these were coded (post-interview; up to six illnesses) on the basis of ICD-10 (NatCen, 2006). ICD-10 data in the MCS3 were compared against the ICD-10 codes on life-limiting conditions in the Together for Short Lives Dictionary of LLC, a list of diagnoses and codes drawn from death data and referrals to clinical paediatric palliative care services.   Codes were merged to identify children with *any* life-limiting condition among reported long-standing illnesses. Among the children with a life-limiting condition, 93% had one LLC, whilst 7% had two LLCs.

In the present study, we examined children's cognitive and behavioural development, and their physical health status. Cognitive development was captured using three subscales (picture similarities, naming vocabulary, and pattern construction) of the British Ability Scales or BAS-II; (14). The BAS-II is a standardised measure of intellectual functioning frequently used in clinical, educational practice and research. In MCS3, scores were subjected to a principal components analysis, which confirmed the presence of a factor *g* as an index of general cognitive ability, accounting for about 56% of the overall variance (15, 16). A presence of an intellectual disability (ID) was indicated by a score at or below two standard deviations of the standardised *g* scores (17). This indicated a 3.1% weighted prevalence of ID overall among MCS3 children.

The Strengths and Difficulties Questionnaire (SDQ, (18) measured behavioural and emotional problems at age 5. Due to its ease of use and excellent psychometric properties (19), the SDQ is frequently used in research and clinical practice to assess behaviour problems and indicate potential clinical levels of difficulties. It measures hyperactivity, emotional symptoms, conduct problems, peer relationship problems and prosocial behaviour. A total behaviour problems score is obtained by combining the first four subscales (range 0-40; Cronbach's alpha for these data: .80). Available cut-off scores indicate borderline and abnormal levels of problem behaviours (http://www.sdqinfo.com), and were used in the present study to indicate rates of caseness (borderline and abnormal levels of behaviour problems).

MCS3 interviewers recorded mothers' reports of their child's physical status ND obtained measurements of children's height and weight used to calculate Body Mass Index (BMI). Using age and gender-specific normative indices, MCS3 estimated obesity levels (20).

2. Parental well-being

Information was obtained through interviews with the child's main carer using Computer Assisted Personal Interviewing (CAPI). In 97.14% of cases the main carer was the child's mother (N= 14,810; 396 were male relatives and 40 were another female relative). As only a small proportion of interviews were conducted with non-maternal carers, these were retained in the analyses, and for ease of reference parental outcomes will be referred to as maternal.

Psychological distress was measured using the K6 (21). The K6 is widely used to screen community populations for psychiatric disorders. It includes six items on symptoms present over the past 30 days, which can be summed into a total K6 score (range 0-24) to indicate high levels of psychological distress (α:.88). A cut-off is also available to predict serious mental illness (SMI: at least one 12-month DSM disorder, other than substance use (21).

Physical health was reported by mothers as excellent, good, good, fair or poor in answer to the question 'How would you describe your health'? Similarly, a 1-10 point item rated overall satisfaction with life so far, with higher values indicating higher satisfaction. Satisfaction with partner relationship was assessed using four items from the Golombok Rust Inventory of Marital Satisfaction (GRIMS, (22). They were grouped to indicate overall relationship satisfaction (range 4-20, α: .81), with higher scores suggesting *lower* satisfaction with partner relationship.

3. Family socioeconomic position

A robust index of socioeconomic position (SEP) was created using a variety of economic indicators. Household work status (neither parent working vs at least one working), area deprivation (area in the lowest 20% of the Index of Multiple Deprivation [combining area information on income, education, housing, crime, employment, and health]), subjective poverty poverty (family is finding it quite/very hard to cope financially), and income poverty (income <60 equivilised

median income for the UK) were combined to describe the family's SEP (α: .62), with higher values indicating higher levels of deprivation.

Statistical analysis

MCS data were obtained from the UK Data Archive (http://www.data-archive.ac.uk/). The ethical responsibilities of the present authors included the protection of participants' anonymity and confidentiality. Because of the complex design of the MCS, weights were used throughout all analyses to account for both the disproportionate sampling of particular groups and nonresponse/attrition rates. All analyses were conducted in STATA 11 (StataCorp., 2009) using the survey data analysis environment.

To address the first two research questions, we adopted a two-group design comparing outcomes for children with and without LLC. Where continuous measures had available cut-offs (to indicate clinical caseness as described in Measures above) comparisons were done on both types of outcomes. We estimated the standardised mean difference (*d*) and relative risk (RR) as effect sizes for continuous and binary outcomes, respectively. As with all analyses, effect sizes were estimated on weighted data. For the first research question, we compared levels of behaviour problems, cognitive skills and body mass index (BMI) between the two groups of children. For the second research question, we compared the two groups of mothers on their self-reported health status, psychological distress, life satisfaction and satisfaction with partner relationship.

To explore the association between LLC and children's development, we adopted two modelling approaches. First, we wanted to see whether LLC is significantly associated with development, after controlling for the effect of other important variables. We fitted a multiple regression model in the overall MCS sample, to examine whether the presence of a LLC would be a significant independent predictor for adverse developmental outcomes, after controlling for

potential confounders. One such model was fitted for children's total behaviour problems. Following this, we wanted to identify factors which are associated with high levels of behaviour problems among children with a LLC. For this, we examined the relative risk of sociodemographic, family and child characteristics on high levels of total behaviour problems.

Results

Comparison of children with and without LLC

Table 2 compares developmental outcomes between children with (LLC) and without life-limiting conditions. Socio-behavioural development is associated with consistently worse outcomes among children with a LLC: all types of behaviour problems are higher among children with a LLC, although the differences for some of them (e.g., conduct problems and peer relationship problems) are associated with very small effect sizes. When we examined the proportion of children wit a SDQ score that placed them above the cutoff for borderline and abnormal levels of behaviour problems (Goodman, 2001), it was shown that children with a LLC had significantly higher levels for all types of behaviour problems, except for conduct problems. Likewise, they were significantly more likely to present lower levels of prosocial skills (Table 2).

In relation to cognitive outcomes, the findings on Table 2 suggest small to moderate difference between the two groups on all three measures: apptern construction, picture similarities and naming vocabulary. Unsurprisingly, the overall cognitive score *g* was significantly lower among children with a LLC and an intellectual disability was present in 17.64% of children in the LLC group but only 2.86% of those in the non-LLC group (F: 111.35, p<0.001, Relative Risk 7.27, 95% CIs: 4.73, 11.19).. Another developmental disability, autistic spectrum disorder (ASD) was reported present in 2.1% of children with LLC, whereas it is

present in only 0.9% of children without a LLC. The difference however was not significant (F=2.26, p=.134; RR= 2.34, 95% CI: .74, 7.38).

The only indicator of physical health development that was available related to the BMI, and this suggested that children with LLC have comparable BMIs to children without LLC (Table 2.2).

	LLC children	non-LLC children	Comparison	Effect size (95% CI)
Socio-behavioural development	Mean (SE)	Mean (SE)	t-test (*p*)	Cohen's d
Hyperactivity	4.67 (.22)	3.28 (.03)	6.34 (<.001)	.38 (.25, .51)
Conduct problems	1.86 (.13)	1.50 (.02)	2.65 (.008)	.15 (.01, .28)
Emotional symptoms	2/09 (.16)	1.36 (.02)	4.50 (<.001)	.30 (.16, .43)
Peer relationship problems	1.55 (.17)	1.13 (.02)	2.50 (.013)	.17 (.04, .31)
Total behaviour problems (SDQ)	10.18 (.48)	7.25 (.07)	6.10 (<.001)	.34 (.21, 48)
Prosocial skills	7.95 (.18)	8.38 (.02)	-2.34 (.020)	-.18 (-.31, -.04)
Cognitive Development				
Pattern Construction	64.97 (2.75)	86.13 (.38)	-7.75 (<.001)	-.45 (-.58, -.32)
Naming vocabulary	101.85 (1.55)	108.51 (.34)	-4.31 (<.001)	-.16 (-.30, -.02)
Picture similarities	75.75 (1.27)	81.99 (.21)	-4.92 (<.001)	-.24 (-.38, -.10)
Cognitive score (*g*)	-.53 (.10)	.05 (.02)	-5.77 (<.001)	-.24 (-.37, -.01)
Physical health				
BMI	16.61 (.17)	16.34 (.02)	1.57 (.116)	.11 (-.03, .25)

Table 2.2. Comparing developmental outcomes between children with a life-limiting condition (LLC) and those without

Comparison of mothers' well-being

Table 3 shows a comparison of physical and psychological outcomes betwe
mothers caring for children with LLC and those without. The only signific
difference was that mothers in the LLC group showed higher levels
psychological distress. Using the K6 cutoff for psychiatric disorder (Kessler et
2003), serious mental illness (SMI) was present in 4.38% of LLC mothers a
3.40% of non-LLC, which was not significantly different (F=0.489, p=0.4
Relative Risk=1.30 (0.62-2.73).

	LLC children	non-LLC children	Comparison	Effect s (95% CI)
	Mean (SE)	Mean (SE)	t-test (*p*)	Cohen's
Physical health status	2.47 (.10)	2.40 (.02)	.70 (.486)	.03 (-. .16)
Psychological distress	3.90 (.34)	3.12 (.04)	2.28 (.023)	.16 (. 30)
Life satisfaction	7.44 (.15)	7.48 (.02)	-.31 (.757)	-.02 (-. 12)
Satisfaction with partner relationship	15.64 (.29)	16.07 (.04)	-1.48 (.141)	-.10 (-. 06)

Table 2.3. Maternal physical health and psychological well-being

The association of the presence of a LLC with children's behaviour problems

To examine whether the presence of a LLC is significantly associated with children's behaviour problems after controlling for a range of associated factors, we fitted a multiple linear regression model. The outcome was children's total behaviour problems and we controlled for child male gender, presence of intellectual disability, presence of ASD, family socioeconomic position and maternal psychological distress. The model explained about 20% of the variance in children's behaviour problems. The findings suggested that the presence of a LLC was significantly associated with increases in levels of behaviour problems (beta:.043, p<.001), after accounting for the effects of all other factors.

Exploring associates of high behaviour problems among children with a LLC

The presence of a LLC might be a significant factor associated with behaviour problems, but this does not mean that all children with a LLC will present behaviour problems at clinically significant levels. About 28% of children with LLC presented behaviour problems at borderline or abnormal levels, i.e., levels that would indicate the need for further clinical assessment. To understand better factors that may be associated with elevated levels of behaviour problems in children with a LLC, we fitted a series of univariate logistic regression models to examine the association (using relative risk) between a range of sociodemographic, family and child characteristics with borderline/abnormal levels of behaviour problems. Table 4 presents the results of these analyses.

	Abnormal/Borderline problem behaviours
	Relative risk (RR, 95% CI and p-value)
Family demographics	
Child male gender	.59 (.28, 1.24), p=.165
Child white ethnic group (vs any other)	.09 (.03, .25), p<.001
Single-parent household	1.05 (.53, 2.09), p=.888
Maternal age	.94 (.89, 1.01), p=.118
Subjective poverty	1.40 (.42, 4.65), p=.583
Area deprivation	1.75 (.81, 3.79), p=.154
Parental unemployment	3.41 (1.71, 6.79), p=.001
Income poverty	1.74 (.83, 3.64), p=.141
High overall deprivation	2.26 (1.14, 4.50), p= .020
Child characteristics	
Intellectual disability	3.79 (1.53, 9.40), p<.001
Presence of autism	3.29 (.28, 38.43), p=.340
Obesity	2.40 (.65, 8.89), p=.191
Mothers' well-being	
Physical health status	1.92 (1.43, 2.57), p<.001
Psychological distress	1.19 (1.08, 1.31), p<.001
Life satisfaction	.78 (.60, 1.00), p=.052
Satisfaction with partner relationship	.81 (.71, .93), p=.003

Table 2.4. Factors associated with high levels of problem behaviours among children with a LLC.

Borderline/abnormal levels of behaviour problems are more likely to be present when children have an intellectual disability, their parents are unemployed, and their mothers experience psychological distress and poor physical health. High levels of behaviour problems are less likely among LLC children of a non-white ethnicity, or whose mothers are satisfied with their partner relationship.

Discussion

The aim of this study was to explore the development of children with a life-limiting condition, and the psychological and physical wellbeing of their mothers, and through these to examine the putative impact on a child's development of having a life-limiting condition. For the first time, we were able to interrogate an existing cohort database in order to compare data in the two groups. This was made possible by the development of a 'dictionary' of ICD 10 codes based on the ACT/RCPCH criteria for life-limiting conditions Hain et al, under review, (1). This approach avoided the risk of recruitment bias and allowed us to study a numerically large group, something that is otherwise difficult in children's palliative care.

Children with LLC are likely to live in families that do not report high levels of subjective poverty, and they do not experience greater socioeconomic deprivation than other children, despite the fact that they are more likely to live in families where parents are not employed. It seems likely that this is a result of an effective benefit system in the UK, that adequately offsets the financial impact of parents being unable to look for paid employment while they care for their child. This is not shown by our data, however, and should be explored in future studies.

In considering the impact of a LLC on the child's development, the most striking finding were the consistent differences on socio-behavioural and cognitive development between the two groups (table 2 Children with LLC presented systematically worse outcomes compared to their peers without a LLC: they presented higher levels of overall behaviour problems, lower levels of prosocial skills, and lower levels of both verbal and non-verbal cognitive skills. Although this is the first study to report findings from a nationally representative sample of children with several life-limiting conditions, findings are mostly consistent with

previous studies that reported lower levels of cognitive achievements, social and peer relationships (23-25).

After controlling for a range of factors with an established association with high levels of behaviour problems (e.g., male gender, presence of intellectual disability, autism spectrum disorder, maternal psychological distress and family socioeconomic position), the results suggested that the presence of a LLC is still significantly associated with higher behaviour problems among children. Future longitudinal studies could investigate further whether the presence of a LLC can indeed be a risk factor for the development and maintenance of behaviour problems. Despite the significantly higher behaviour problems in the LLC group, it was obvious that not all children with a LLC present behaviour problems at a level where the condition may require further clinical assessment. About 28% of children with LLC presented such borderline and abnormal levels of overall behaviour problems, suggesting that about two thirds of children with a LLC present behaviour problems within the normal range. In an attempt to explore what factors may make the presence of severe behaviour problems more likely among these children, we explored a range of potential correlates. Higher deprivation seems to be associated with more severe behaviour problems, but it is likely that this association is mostly driven by parental unemployment. Obviously, the presence of an intellectual disability is associated with more severe behaviour problems (19 21), where behaviour problems have a clear communicative function to compensate for children's verbal and social skills. Maternal physical and psychological well-being was also associated with higher levels of behaviour problems. It is likely that mothers who are unwell might struggle more to manage their children's behaviour effectively, and behaviour problems escalate. On the other hand, potentially protective factors may be a non-white ethnic origin (which would indicate a cultural variation in levels of behaviour problems), and mothers' positive psychological well-being (namely, satisfaction with their partner relationship, and, the marginally non-significant, life satisfaction.

Among mothers of children with life-limiting conditions, psychological distress was higher than among those without, but there was no significant difference in general health status (table 2.3). The use of a single self- report item on physical health status, though less robust than a health-related quality of life measure, was nevertheless sufficiently sensitive to have identified any differences between the two groups of mothers in this respect.

Despite the abundance of potential causes for psychological distress, Present findings indicate that although psychological distress might be slightly elevated among these mothers, the probability of experiencing high levels of distress indicative of a psychiatric disorder is no different compared to mothers whose children do not have a LLC. This finding contrasts the majority of the available literature (26, 27) and suggests that we need to be mindful of the way we assess negative psychological adaptation in this population (symptom severity vs clinical disorders).

Perhaps more surprisingly, mothers in the families of children with LLC group did not seem to be any less satisfied with their life than those without. This supports the conclusions of other studies that families caring for children with complex chronic conditions such as developmental disabilities (28) and autism (17) are often resilient and can indeed describe many positive outcomes of their experience (29-32). This suggests preservation of the potential for positive psychological adaptation, and that mothers of children with disabilities can simultaneously experience impacts on mental health that are both positive and negative. Mothers of children with LLC were more no more likely than those without to be dissatisfied with relationships with their partner. There is evidence that working together to care for their child allows some parents to become more effective in their communication and to develop a stronger partnership (33).

Conclusion

In summary, our study suggests that children with LLC do not experience more poverty or socioeconomic deprivation compared with other children, though they are more likely to live in families where neither parent is employed.

Children with LLC have systematically worse cognitive and socio-behavioural developmental outcomes, consistent with the nature of the conditions. The presence of a LLC is independently associated with behaviour problems even after controlling for a range of background factors. High levels of behavioural difficulty are more likely when children with LLC have Intellectual disability, parental unemployment and psychological distress or poor physical health on the part of a child's mother makes high levels of behavioural difficulty more likely, while non-white ethnicity and maternal satisfaction with partner relationship make it less so.

Although they report higher levels of psychological distress, however, mothers of children with LLC are at no greater risk of serious psychopathology than those without. Our study indicates that parents in the MCS3 cohort show a high degree of psychological resilience in caring for children with complex and chronic health conditions for which there is no prospect of cure.

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