Data linkage and pain medication in people with cerebral palsy: a cross-sectional study

Title: Exploring a big data approach to investigate pain affecting individuals with cerebral palsy: a cross-sectional study.

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Abstract:
Aim: To explore data linkage and pain medication as a proxy for pain; to assess differences in pain medication between the CP and the general populations; to identify factors associated with pain medication in CP
Methods: This cross-sectional study linked the Northern Ireland CP Register and two administrative health care databases for people resident in Northern Ireland born between 1981 and 2008. Pain medication as a proxy was validated by replicating analyses from the SPARCLE studies. Logistic regression compared pain medication in the CP and general populations. Multi-level regression models assessed factors associated with pain medication in the CP cohort.
Results: Sample size was 701 075 of whom 1430 (0.2%) were people with CP. The validation exercise produced results similar to the SPARCLE studies. More people with CP received pain medication (61% vs. 50.9%) and had twice the odds of being prescribed opioid analgesics (OR=2.81, 95% CI 2.32-3.40**)**. Among those with CP the odds of being prescribed pain medication were higher for females (OR= 1.34, 95 CI 1.06-1.70), younger age (OR=1.60, 95% CI 1.02-2.51), GMFCS V (OR=2.60, 95% CI 1.52-4.47), seizures (OR=2.55, 95% CI 1.68-3.87) and higher deprivation score (OR=2.06, 95% CI 1.41-3.24).
Interpretation: Pain medication is an effective proxy for pain. More people with CP were prescribed pain medication than the general population. Pain medication for people with CP is not only dependent on physiological and clinical characteristics, but also environmental factors.

What This Paper Adds

- Data linkage using pain medication as a proxy for experiencing pain is a valid method.
- People with CP are more likely to experience pain than the general population.
- People with CP have over twice the odds of receiving opioids compared to the general population.
- The odds of being prescribed pain medication were higher for females with CP.
- Prescription of pain medication among those with CP is not only dependent on clinical characteristics, but also environmental factors.

Abbreviations:
Cerebral Palsy (CP)
Northern Ireland CP Register (NICPR)
National Health Application and Infrastructure Service (NHAIS)
Enhanced Prescribing Database (EPD)
Northern Ireland (NI)
Health and Care Number (HCN)
Northern Ireland Multiple Deprivation Measure 2010 (NIMDM 2010)
Gross Motor Function Classification System (GMFCS)

Pain is a problem commonly affecting those with cerebral palsy (CP).[1] There are various sources of pain in CP, such as spasticity, hip dislocation, neurological pain, gastrointestinal symptoms, as well as treatments and surgery.[1] Pain interferes with sleep, function and activity levels and it is associated with deterioration in quality of life.[1] The subjective nature of pain makes assessment difficult and can be further complicated by motor, cognitive and communication difficulties.[1,2]

There is a growing body of research on pain in CP[1,2] and population-based studies report the most generalisable estimations of pain prevalence.[1] To date, there are seven population-based studies representative of the wider CP population.[3-9]

In recent years attention has been drawn to use of administrative data for the purpose of research.[10] The large scale of these data sets allows to capture events which are relatively unusual. Use of secondary data could be a cost-effective alternative and help overcome some of the limitations of population-based surveys, e.g. potential recruitment/retention bias or recall issues,[11] employing a standardized proxy for all individuals regardless of their motor, cognitive and/or communication problems. This is of particular importance in a population as diverse as that of individuals with CP.

The aims of this study were to [1] explore the potential of data linkage and pain medication as a proxy for experiencing pain; [2] assess differences in levels of pain medication prescription between the CP and general population; [3] identify factors associated with pain medication prescription for those with CP. This project was approved by the North East-York Research Ethics Committee (REC reference 15/NE/0265).

Methods

Study design and procedures

This cross-sectional study uses administrative data by linking the Northern Ireland CP Register (NICPR) to the primary care registration records from the National Health Application and Infrastructure Service (NHAIS), and to the Enhanced Prescribing Database (EPD). Northern Ireland (NI) has a free at the point of service health care system, including free prescriptions. All three databases contained the individuals' unique

Health Care Number (HCN) allowing for one-to-one data linkage. Linkage to the NICPR identified individuals with CP, while linkage to the EPD provided data on dispensation of prescriptions for pain medication. Data were linked by and held within the secure environment of the Honest Broker Service, a data repository launched by the Business Services Organization in 2014.[12] All Honest Broker Service processes are in line with Data Protection, confidentiality requirements and the Information Commissioner's Office's Codes of Practice. The study cohort included all individuals born between 1981 and 2008, i.e. aged 4 to 31years in 2012, registered within NHAIS and alive between 2010 and 2014.

Information on sex, age, area of residence, and Northern Ireland Multiple Deprivation Measure 2010 (NIMDM 2010)[13] was obtained from NHAIS, using postcodes to determine deprivation from Northern Ireland Statistics and Research Agency NIMDM 2010. To anonymise data, only birth years were provided, and age was handled as a categorical rather than continuous variable. Area of residence was defined as rural if the population size in the given area was less than 1000 people, intermediate, between 1000 and 74 999 people, or urban, 75 000 people or more. The NIMDM 2010 is an overall multiple deprivation measure comprising a weighted combination of seven domains of deprivation: income, employment, living environment, crime and disorder, health and disability, education skills and training, and proximity to services. Proximity to services takes into consideration health care and scores for this domain and NIMDM 2010 overall score were included in the analyses.

The NICPR[14] is one of the longest standing registers of CP in Europe with over 40 birth year span. The NICPR provided data regarding CP subtype, Gross Motor Function Classification System (GMFCS),[15] intellectual impairment, communication and feeding problems, seizures, gestational age, and birth weight. The disability profile of the comparator population was unknown. The EPD, established in 2009, contains information on all prescriptions dispensed in community pharmacies across NI. Based on advice by Paediatric Consultants and information from previous literature,[16,17] data were retrieved for non-steroidal anti-inflammatories, opioid and non-opioid analgesics, anaesthetics, anxiolytics, and antidepressant medications. Data on anti-epileptic medication were used to identify those individuals who suffered seizures and were

medically managed compared to those who were not. Data on medication were provided using British National Formulary codes[18] and Defined Daily Dose.[19]

Statistical analysis

Descriptive analyses including chi-squared were used to define the demographic characteristics of the study cohort. Data analysis had three stages addressing each study aim. The first stage replicated analyses conducted in the SPARCLE I and II projects[5,6] in order to validate the study's methodology and ascertain if data linkage and pain medication as a proxy for experiencing pain could produce similar results as self-reports and parent/carer's accounts on pain. These analyses included comparisons of pain medication vs. self-reported and parent/carer's accounts on pain across levels of GMFCS, seizures, among other strata only for those with CP in the same age groups as the SPARCLE studies, 8-12 and 13-17 years respectively. The second stage included the full cohort, and it involved descriptive analysis and logistic regression models to identify differences in pain medication prescription between the CP and general populations. Prescription of each medication group was regressed on the CP/general population classification. The third stage involved multi-level regression models including only CP cohort data to determine factors associated with receipt of pain medication in this population. Prescription of pain medication was regressed on socio-demographic factors (age, sex, multiple deprivation, vicinity of services), CP characteristics, and severity of impairments (GMFCS, feeding problems, intellectual impairment, etc.). Models were adjusted for natural clustering of individuals within GP practices and variance partition co-efficient was calculated to determine the amount of variation attributable to GP practices. Analyses focused on pain specific medication: NSAIDs, opioid and non-opioid analgesics. Following clinicians' advice, sensitivity analyses were conducted using a wider classification of pain medication including anaesthetics, anxiolytics, and antidepressants as they could sometimes be used to manage pain affecting individuals with CP.

Results

The initial NHAIS and EPD dataset included 840 292 people. Of those, 139 217 were excluded due to missing data on sex, if they were deceased or had emigrated during 2010

and 2014. Thus, the final cohort consisted of 701 075 individuals. Of the 1 489 cases provided by the NICPR, 1430 were linked to the NHAIS and EPD, resulting in a final cohort of 1 430 individuals with CP (0.2%) and 699 645 individuals in the general population (without CP; see Table 1).CP was more prevalent among males (56.6%); spastic bilateral cerebral palsy was the most common CP subtype (47.1%), and a higher number of individuals with CP had a GMFCS levels I or II (61.6%). There were slight statistical differences between the CP and general populations regarding sex, area of residence, deprivation scores, and proximity to services.

[Table 1 here]

The first stage analyses results were similar to those noted by the SPARCLE consortium.[3,4] Pain medication was most associated with GMFCS (OR=6.20, 95% CI 1.90-20.40 in our model versus OR=3.00, 95% CI 1.80-5.00 in SPARCLE I) and seizures (OR=2.30, 95% CI 1.10-5.30 in our model versus OR=2.10, 95% CI 1.10-4.00 in SPARCLE I) for those aged 8 to 12. Analyses including the older cohort group showed that pain medication was strongly associated with female sex (OR=2.00, 95% CI 1.10-3.50 in our model versus OR=2.10, 95% CI 1.50-3.00 in SPARCLE II) and seizures (OR=2.80, 95% CI 1.30-6.00 in our model versus not association with pain in SPARCLE II).

Results from the second stage analyses showed that 61.0 % of those with CP received pain medication over the study period compared to 50.9% in the general population. Receipt of pain medication was most prevalent in females, those living in deprived and in urban areas and the youngest age group both within the CP and the general populations, although percentages were also high in the eldest age group within the CP population. Higher percentages of people with CP were prescribed medication if they had Bilateral Spastic CP subtype. Percentages were also higher for those with GMFCS levels IV and V, seizures and on epileptic medication, intellectual and communication impairments, and problems with feeding (see Table 2).

[Table 2 here]

Unadjusted logistic regression results for each medication group showed those with CP had higher odds of receiving all medications included in this study except for antidepressants (see Table 3). In particular individuals with CP had over twice the odds of receiving opioid analgesics (OR=2.81, 95% CI 2.32-3.40) and over three times the odds of receiving anxiolytics (OR=3.39, 95% CI 2.94-3.89).

[Table 3 here]

The final analyses included multi-level models adjusting for the clustering of individuals within GP practices. Results showed that females with CP were 1.34 the odds of receiving pain specific medication compared to males (OR=1.34, 95% CI 1.06-1.70; see Table 4). After adjustment for demographic and key CP characteristics, including standardized weight at birth, age (OR=1.60, 95% CI 1.02-2.51 for 4-7 year olds compared to 8-12 year olds), GMFCS level (OR=2.60, 95% CI 1.52-4.47 for GMFCS level V compared to level I), seizures (OR=2.55, 95% CI 1.68-3.87 for those with seizures and on epilepsy medication compared to those with no seizures and no epilepsy medication), and deprivation score (OR=2.06, 95% CI 1.41-3.32 for those living in the most deprived quintile compared to the most affluent) remained positively associated with pain specific medication. Just 2.8% of the variation observed was attributable to GP practice (VPC=2.8; see Table 4). Sensitivity analyses yielded similar results.

[Table 4 here]

Multi-level models indicated interaction between sex and GMFCS on the odds of receiving pain medication (LR test χ^2=11.9, *P*=.0181). For this reason, multi-level regression models were replicated stratifying by sex. Males aged 4-7 years were almost twice the odds of receiving pain medication compared to males aged 8-12 years (OR=1.98, 95% CI 1.08-3.66). The receiving pain medication increased step-wise as GMFCS and NIMDM 2010 indicated more severe CP and deprived areas. In contrast, only GMFCS level V (OR=2.87, 95% CI 1.09-7.54) and average deprivation scores (OR=2.98, 95% CI 1.51-5.90) were associated to an increased in the odds of receiving pain medication among females. GP practice accounted for 0.001% of variance in receiving pain medication in males with CP (VPC=0.001), and 12.2% of variation among females (VPC=12.2).

Discussion

To our knowledge, this study reports for first time analyses of pain among people with CP using linked population-based datasets and medication as a proxy for experiencing pain. The high percentage of cases in the NICPR database that were linked to the NHAIS and EPD show data linkage between disease-specific and administrative databases is a feasible research methodology. Our sample is representative of both the CP and general populations, with characteristics corresponding to well-established epidemiological and census reports.[14,20,21] Differences in sex distribution between the CP and the general population were expected as CP affects more males.[14,20] Differences in the area of residence between CP and the general population were likely due to the higher percentage of cases with missing data among those with CP as a result of incomplete information on residence postcode.

Results from the validation exercise replicating analyses in the SPARCLE studies corresponded with their outputs.[4,5] Although there were differences in levels of significance, they are likely explained by our smaller sample for the same age groups compared to the SPARCLE studies. Overall, results supported the face validity of pain medication as an effective proxy measure for experiencing pain. Recent evidence on the positive association between pain and prescription for analgesics[8] further supports our use of pain medication as a proxy for pain.

A higher percentage of individuals with CP were prescribed pain medication compared to the general population. Our prevalence of 61% is high as per other population-based studies have also reported high prevalence of pain among those with CP,[3-9] although there were some differences, with two studies reporting a lower prevalence and two a higher prevalence.[4,5] While this could be partially due to methodological differences, CP management factors should not be discounted, e.g. surveillance programmes successful in preventing muscoloskeletal complications[7] or under-treatment should not be discounted.

People with CP had higher odds to be prescribed each of the pain medication groups included in this study, except for antidepressants. As people with CP can be at greater risk of mental health problems,[22] our findings could signal unmet needs in this population and a requirement for physicians to be more aware of patients' mental well-being as well

as their physical health. However, it could also be explained by contextual factors as NI experiences the poorest levels of mental health in the UK.[23] Significantly, people with CP had twice the odds to receive opioid medication. While evidence supports opioids short-term pain relief, they are potentially ineffective in managing chronic pain, with concerns about the risk of potential overdose, dependence and addiction.[24] Our results warrant further research into prescription of opioid and anti-depressant medication for those with CP and comparison to other geographical areas.

Our results showed females with CP had higher odds of receiving pain medication than their male counterparts, even after accounting for CP and socio-demographic characteristics. Analyses stratified by sex showed further differences in the patterns of association between pain medication and clinical and socio-economic factors. Among males younger age, more severe GMFCS levels and living in most deprived areas were associated with pain medication, whereas for females it was GMFCS level V and moderate deprivation scores. The amount of variation attributable to GP practice was also different between sexes, 0.001% for males and 12.2% for females.

Differences between sexes seen in our study are consistent with previous studies,[4-7,9] matching typically developing populations.[1] Although these differences could be partially accounted for by physiological factors, the explanation seems to be more complex as seen by the different patterns of association seen in our results. For example, an association between pain medication and age groups during and after puberty would have been expected for females to account for dysmenorrhoea.[25]Patterns of association between pain medications and GMFCS were also different despite the similar distribution of GMFCS levels in both sexes. The difference between sexes in variation attributable to GP practice may be due to differing prescribing cultures in GP practices. Previous research indicates females are more likely to be prescribed pain medication even after accounting for morbidity.[26] It could also be explained by different health care behaviours between males and females. Evidence has shown men are less likely to seek health care help.[27] However, the authors highlighted factors other than sex associated with this complex issue, such as occupation, socio-economic status, and age. Our results thus warrant further work to explore triggers and barriers associated with accessing health support for

those with CP, whether fewer males with CP seek medical support, and whether there is a sex divide in how pain in people with CP is addressed by health care professionals.

Receiving pain medication was also linked to higher GMFCS level, presence of seizures, younger age, and living in more deprived areas. Individuals with a higher GMFCS level and seizures had increased odds of being prescribed pain medication. Evidence appears to be mixed, with some population-based studies reporting similar associations,[4-6,7,9] while others have not,[3,8] and findings varied whether they were based on parents' accounts or self-reports.[4,5] Interestingly, Alriksson-Schmidt and Hägglund (2016) found associations between GMFCS levels and specific pain sites, rather than pain frequency or severity. While severe spasticity and/or abnormal movements can be a source of pain, this is not always the case. Higher GMFCS levels and seizures are indicative of a wider brain damage frequently leading to other symptoms which can also cause pain, e.g. feeding difficulties.[1] Although motor impairment is one of the defining characteristics of CP, this condition has an obvious neurological component and compromised sensation, perception, and somatosensory brain activity could also have a role in pain.[28] Maybe the association between motor impairment and pain is not necessarily linear but a more complex one. Evidence remains unclear.

Previous studies have reported an increase in pain prevalence with older age,[4,6,7,9] reasoning that aged related changes in comorbidities are likely to cause pain.[1] In contrast, our results showed pain medication was associated with younger age. The percentage of those on pain medication decreased during the teenage years, increasing again later in life but not to the same level as the youngest age group. This pattern could be explained by difficulties surrounding transition from child to adulthood, a time when young people with complex conditions like CP may disengage from health care behaviours,[29] and decreased availability of routine and preventative health care for adults with CP.[17]

Our results described a strong association between living in more deprived areas and pain medication. It is possible that those living in more affluent areas could have access to alternative treatments and/or better equipment/adapted housing.[17] It is also possible that those living in deprived areas are exposed to additional economic and social pressures leading to further emotional distress, depression, and anxiety. Previous research has reported an association between pain in children with CP and parental unemployment,

reasoning parents either gave up work to look after more severely affected children who suffered more pain, or they suffered stress due to unemployment which in turn could enhanced their perception of their children's pain.[4] A follow-up study with the same cohort reported an association between pain of children with CP and parents' higher stress levels.[5] Our findings illustrate that pain/medication is not just dependent on physiological and clinical characteristics but also environmental factors.

The methodology used in this study provided some advantages. Previous population-based research exploring pain in CP included children and young people' self-reports, accounts from parents/carers and/or medical records, with conflicting results.[4,5,7,9] Using pain medication as a proxy for experiencing pain provided a standardized source of information for all participants in this study. The inclusion of a wide age range provided the opportunity to explore the effect it could have in the complex problem of pain. However, there were also drawbacks. Our analyses were limited to the presence or absence of pain; information on frequency, severity, or sources of pain was not available. Data on pain medication was limited to dispensation of pain medication prescriptions in the primary care setting and it assumed patient adherence to treatment. We could not account for over-the-counter medication or prescriptions provided by tertiary services, for example botulinum toxin, which by targeting spasticity may alleviate pain. Neither could we convey details on other treatments such as physiotherapy or exercise. Nevertheless, our results showed those with CP higher odds of being prescribed medication that could be obtained over-the-counter, for example NSAIDs. It is likely that those suffering severe and/or frequent pain will seek medical advice at some point rather than manage it only with over-the-counter medication. We did not include medications used to manage pain by treating comorbidities that may cause it, for example muscle relaxants or laxatives used for spasticity and gastrointestinal problems respectively. This is likely to have limited our analysis into the relationship between CP comorbidities and pain. However, we opted to exclude these medications as said comorbidities not always cause pain, and we could not account when medications were prescribed only to treat the comorbidity or also pain, thus controlling for their potential to be a confounding factor. Focus non-population-based studies could be better place to provide more detail insight into the relationship between specific CP comorbidities and pain. Data on pain medication included anti-depressants and anxiolytics which may be used not only to treat pain but

also to manage mental health problems and/or epilepsy, in the case of anxiolytics. These medication groups were only included in our sensitivity analyses, which produced results similar to analyses focused on pain specific medication (NSAIDs, opioid and non-opioid analgesics). We also made attempts to account for this by using data on epileptic medication to identify individuals who suffered seizures and were medically managed and those who were not. Finally, the NICPR collects information only when children are aged 5 years. Thus, information about CP refers to that time in the participants lives. GMFCS levels have been described to deteriorate overtime, especially for those initially classified in GMFCS levels II to IV.[30] It is possible that the association seen in this study between higher GMFCS levels and pain was underestimated.

This study supports data linkage using pain medication as a proxy for pain is a valid research method and illustrates the value of a population-based registry of CP, offering opportunities to further explore at a population level how pain may affect people with CP, for example on education attainment and employment. People with CP are more likely to receive pain medication than the general population. Differences between sexes are one of the main findings and evidence shows the potential role contextual or behavioural factors may play in this. Thinking more severe impairments can be related to pain is intuitive. However, this relationship is not yet fully understood, neither is the effect of age. The association with deprivation illustrates the importance of environmental factors in the experience of pain. Follow up longitudinal assessments will help to further comprehend how pain affects those with CP.

Contributors' Statement:

Dr Elena Guiomar García Jalón conceptualized and designed the study, coordinated the study and took overall responsibility for the delivery of the work and day-to-day administration of the study, was responsible for the data collection, planning of the data analyses, write up of the manuscript and provided final approval of the version submitted for publication.

Dr Aideen Maguire advised on the design of the study, data collection and planning of the data analysis, conducted the data analyses and first draft of the statistical analysis and results sections in the manuscript, critically reviewed and revised the manuscript and provided final approval of the version submitted for publication.

Dr Oliver Perra advised on the design of the study, data collection and planning of the data analysis, critically reviewed and revised the manuscript and provided final approval of the version submitted for publication.

Dr Anna Gavin advised on the interpretation of the data, critically reviewed and revised the manuscript and provided final approval of the version submitted for publication.

Dr Dermot O'Reilly advised on the design of the study, critically reviewed and revised the manuscript and provided final approval of the version submitted for publication.

Professor Allen Thurston advised on the design of the study and planning of the data analysis, coordinated the study and took overall responsibility for the delivery of the work and day-to-day administration of the study, critically reviewed and revised the manuscript and provided final approval of the version submitted for publication.

Staff in the Honest Broker Service provided part of the data included in this study, provided a fully anonymized data set and a safe haven where to store the data as well as data clearance assurance to confirm figures provided in this manuscript do not lead to the identification of individuals included in the sample.

All authors are in agreement in being be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

All authors declare the submitted work and its essential substance have not previously been published and are not being considered for publication elsewhere.

All authors declare the submitted work is their own and that copyright has not been breached in seeking this publication.

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Results from this study have been presented at the Australasian Academy of Cerebral Palsy and Developmental Medicine Conference (March, 2018) and the International Conference for Administrative Data Research (June, 2018).

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Table 1. Study Cohort Demographics (n=701 075).

	General population n= 699 645 (99.8%)	CP population n= 1430 (0.2%)	χ^2 *p* value
Sex			
Male	358 968 (51.3)	810 (56.6)	<.01
Female	340 677 (48.7)	620 (43.4)	
Age group (years)			
4-7	98 250 (14.0)	179 (12.5)	.08
8-12	114 108 (16.3)	245 (17.1)	
13-17	121 315 (17.3)	264 (18.5)	
18-22	123 235 (17.6)	255 (17.8)	
23-27	132 934 (19.0)	293 (20.5)	
28-31	109 803 (15.7)	194 (13.6)	
Deprivation			
Most Affluent	116 182 (16.6)	213 (14.9)	<.01
2	139 233 (19.9)	269 (18.8)	
3	140 832 (20.1)	291 (20.3)	
4	142 574 (20.4)	282 (19.7)	
Most Deprived	155428 (22.2)	332 (23.2)	
Unknown	5396 (0.8)	43 (3.0)	
Urban/Rural			
Rural	188 678 (27.0)	388 (27.1)	<.01
Intermediate	354 839 (50.7)	703 (49.2)	
Urban	150 510 (21.5)	294 (20.6)	
Unknown	5618 (0.8)	45 (3.1)	
Proximity services			
Farthest	160 242 (22.9)	339 (23.7)	<.01
2	139 881 (20.0)	285 (19.9)	
3	131 943 (18.9)	264 (18.5)	
4	123 611 (17.7)	227 (15.9)	
Closest	138 572 (19.8)	272 (19.0)	
Unknown	5396 (0.8)	43 (3.0)	
CP sub-type			
Unilateral spastic		625 (43.7)	n/a
Bilateral spastic		673 (47.1)	
Other		132 (9.2)	
Standardized birth weight			
Male		-0.41	n/a
Female		-0.34	
GMFCS			
1		270 (18.9)	n/a
2		611 (42.7)	
3		222 (15.5)	
4		105 (7.3)	
5		211 (14.8)	

Unknown		11 (0.8)	
Seizures and epilepsy medication			
Seizure + med		211 (14.8)	n/a
Seizure no med		70 (4.9)	
No seizure + med		190 (13.2)	
No seizure no med		898 (62.8)	
Unknown		61 (4.3)	
Feeding problems			
Yes		248 (17.4)	n/a
No		1090 (76.2)	
Unknown		92 (6.4)	
Communication difficulty			
Yes		569 (39.8)	n/a
No		861 (60.2)	
Intellectual impairment			
Yes		557 (39.0)	n/a
No		824 (57.6)	
Unknown		49 (3.4)	

CP: Cerebral palsy; GMFCS: Gross Motor Function Classification System.

Table 2. Percentage of the General and CP Populations experiencing pain using Pain Medication as a proxy (NSAIDs, Opioid and Non-opioid Analgesics; n=701 075).

	General population (n=699 645)		χ^2 *p* value	CP population (n=1430)		χ^2 *p* value
Pain medication	**No (%)**	**Yes (%)**		**No (%)**	**Yes (%)**	
	49.1	50.9		39.0	61.0	
Sex						
Male	54.6	45.4	<.01	41.9	58.2	.01
Female	43.3	56.7		35.3	64.7	
Age group(years)						
4-7	38.4	61.6	<.01	30.7	69.3	.10
8-12	55.7	44.3		42.0	58.0	
13-17	52.7	47.3		43.6	56.4	
18-22	49.2	50.8		40.0	60.0	
23-27	49.4	50.6		38.2	61.8	
28-31	47.4	52.6		36.6	63.4	
Deprivation						
Most Affluent	58.2	41.8	<.01	49.3	50.7	<.01
2	51.3	48.7		42.4	57.6	
3	48.7	51.3		34.4	65.6	
4	46.8	53.2		34.0	66.0	
Most Deprived	42.8	57.2		33.1	66.9	
Unknown	47.9	52.3		76.7	23.3	
Urban/Rural						
Rural	48.9	51.1	<.01	38.4	61.6	<.01
Intermediate	49.5	50.5		39.8	60.2	
Urban	48.4	51.6		32.3	67.7	
Unknown	48.1	51.9		75.6	24.4	
Proximity services						
Farthest	47.1	52.9	<.01	36.3	63.7	<.01
2	49.1	51.0		40.7	59.3	
3	51.3	48.7		39.8	60.2	
4	50.4	49.6		38.8	61.2	
Closest	48.3	51.7		34.2	65.8	
Unknown	47.9	52.2		76.7	23.3	
CP sub-type						
Unilateral spastic				45.1	54.9	<.01
Bilateral spastic				34.5	65.5	
Other				33.3	66.7	
GMFCS						
1				44.1	55.9	<.01
2				43.9	56.1	
3				44.6	55.4	

4				24.8	75.2	
5				19.0	81.0	
Seizures and epilepsy medication						
Seizure + med				18.5	81.5	<.01
Seizure no med				45.7	54.3	
No seizure + med				30.5	69.5	
No seizure no med				45.2	54.8	
Unknown				37.7	62.3	
Feeding problems						
Yes				23.8	76.2	<.01
No				42.1	57.9	
Unknown				43.5	56.5	
Communication difficulty						
Yes				32.9	67.1	<.01
No				43.1	56.9	
Intellectual impairment						
Yes				32.0	68.0	<.01
No				44.3	55.7	
Unknown				30.6	69.4	

CP: Cerebral palsy; GMFCS: Gross Motor Function Classification System; NSIADs: non-steroidal anti-inflammatories drugs.

Table 3. Logistic Regression to Determine the Odds of Use of Pain Medication by Those with CP Compared to the General Population.

Medication	Population group	Odds ratio (CI 95%)	Significance (p <.05)
Non, opioid analgesics	General CP	1.00 1.70 (1.54-1.89)	*p* <.01
Opioid analgesics	General CP	1.00 2.81(2.32-3.40)	*p* <.01
NSAIDs	General CP	1.00 1.13 (1.02-1.26)	*p* <.01
Anxiolytics	General CP	1.00 3.39 (2.94-3.89)	*p* <.01
Antidepressants	General CP	1.00 1.24 (0.91-1.71)	*p*= .183
Anaesthetics*	n/a	n/a	n/a
Any medication	General CP	1.00 2.15 (1.90-2.40)	*p* <.01

* Due to small numbers involved, no results for anaesthetics could be reported.
CI: Confidence interval; CP: Cerebral palsy; NSAIDs: non-steroidal anti-inflammatories drugs.

Table 4. Multi-Level Logistic Regression Analysis: Odds of Pain Medication (NSAIDs, Opioid and Non-opioid Analgesics) Amongst the CP Population. Figures represent OR (95% CI).

		CP population (n= 1430)*	Female CP population (n= 620)**	Male CP population (n= 810)**
Sex	Male	1.00	n/a	n/a
	Female	1.34 (1.06-1.70)		
Age group (years)	4, 7	1.60 (1.02-2.51)	1.14 (0.54-2.44)	1.98 (1.08-3.66)
	8, 12	1.00	1.00	1.00
	13, 17	0.92 (0.62-1.36)	1.05 (0.53-2.08)	0.83 (0.51-1.36)
	18, 22	1.00 (0.67-1.48)	0.66 (0.33-1.29)	1.21 (0.73-2.00)
	23, 27	1.06 (0.72-1.56)	0.96 (0.50-1.81)	1.08 (0.65-1.79)
	28, 31	1.16 (0.75-1.78)	1.18 (0.57-2.45)	1.11 (0.63-1.94)
GMFCS	1	1.00	1.00	1.00
	2	0.96 (0.70-1.31)	1.04 (0.62-1.73)	0.88 (0.58-1.32)
	3	0.97 (0.65-1.43)	1.30 (0.65-2.60)	0.78 (0.47-1.29)
	4	2.23 (1.28-3.89)	1.44 (0.54-3.84)	2.66 (1.30-5.45)
	5	2.60 (1.52-4.47)	2.87(1.09-7.54)	2.34(1.19-4.61)
	Unknown	0.79 (0.19-3.21)		2.52 (0.37-17.12)
Standardized birth weight		1.01 (0.95-1.08)	1.03 (0.92-1.15)	1.02 (0.93-1.13)
Seizures and epilepsy medication	No seizure no med	1.00	1.00	1.00
	Seizure + med	2.55 (1.68-3.87)	2.47 (1.22-5.03)	2.81 (1.64-4.80)
	Seizure no med	0.96 (0.56-1.66)	0.51 (0.22-1.19)	1.39 (0.65-2.96)
	No seizure + med	1.69 (1.18-2.43)	1.32 (0.73-2.39)	1.91 (1.18-3.08)
	Unknown	1.15 (0.64-2.07)	0.58 (0.21-1.57)	1.76 (0.79-3.91)
Feeding problems	No	1.00	1.00	1.00
	Yes	1.39 (0.92-2.08)	1.20 (0.59-2.47)	1.53 (0.91-2.55)
	Unknown	0.72 (0.5-1.16)	0.53 (0.25-1.11)	0.72 (0.37-1.41)
Communication difficulty	No	1.00	1.00	1.00
	Yes	0.87 (0.64-1.19)	0.93 (0.63-1.62)	0.85 (0.58-1.25)
Intellectual disability	No	1.00	1.00	1.00
	Yes	1.07 (0.78-1.46)	1.67 (0.95-2.93)	0.84 (0.56-1.24)
	Unknown	1.30 (0.63-2.69)	1.16 (0.36-3.78)	1.47 (0.53-4.09)
Deprivation	Most Affluent	1.00	1.00	1.00
	2	1.46 (0.98-2.18)	1.42 (0.72-2.81)	1.56 (0.93-2.61)
	3	1.97 (1.32-2.93)	2.98 (1.51-5.90)	1.65 (0.99-2.77)
	4	2.15 (1.43-3.24)	1.70 (0.85-3.40)	2.49 (1.47-4.21)
	Most Deprived	2.06 (1.41-3.32)	1.81 (0.89-3.68)	2.60 (1.49-4.54)
	Unknown	0.58 (0.03-13.05)		8.87 (0.02-35.29)
Urban/Rural	Rural	1.00	1.00	1.00
	Intermediate	1.10 (0.72-1.68)	1.05 (0.50-2.22)	1.37 (0.79-2.37)
	Urban	1.41 (0.81-2.43)	1.74 (0.65-4.66)	1.56 (0.78-3.14)
	Unknown	0.60 (0.03-11.45)		4.22 (0.01-17.28)

Proximity to services	Farthest	1.00	1.00	1.00
	2	0.76 (0.49-1.17)	0.77 (0.36-1.65)	0.62 (0.35-1.10)
	3	0.79 (0.48-1.33)	0.80 (0.32-2.03)	0.64 (0.34-1.23)
	4	0.73 (0.42-1.24)	0.62 (0.24-1.64)	0.69 (0.35-1.36)
	Closest	0.73 (0.41-1.30)	0.92 (0.33-2.59)	0.49 (0.23-1.03)
Variance		0.09649	0.45698	0.0000386
P		0.0849	0.0394	0.9988
VPC		2.8	12.2	0.001

* Adjusted by sex, GMFCS, birth weight, seizures, feeding, communication, intellectual ability deprivation, urbanicity and proximity to services

** Analyses stratified by sex and adjusted by GMFCS, birth weight, seizures, feeding, communication, intellectual ability deprivation, urbanicity and proximity to services

Cerebral palsy; GMFCS: Gross Motor Function Classification System; NSIADs: non-steroidal anti-inflammatories drugs; VPC: variance partition co-efficient.