MS CLARE MCKINNON (Orcid ID : 0000-0003-2363-0075)

DR ELAINE M MEEHAN (Orcid ID : 0000-0003-2393-6939)

Article type : Systematic Review

[systematic review: 1 table; 4 figures; 1 online table; 5 appendices; 1 online figure]

Prevalence and characteristics of pain in children and young adults with cerebral palsy: a systematic review

CLARE T MCKINNON[1,2,3]

ELAINE M MEEHAN[2]

ADRIENNE R HARVEY[1,2,3]

GIULIANA C ANTOLOVICH[2,3]

PRUE E MORGAN[1]

1 Department of Physiotherapy, Monash University, Frankston, Victoria; **2** Murdoch Children's Research Institute, Parkville, Victoria; **3** Royal Children's Hospital Melbourne, Parkville, Victoria, Australia.

Correspondence to Clare T McKinnon, Neurodisability and Rehabilitation, Murdoch Children's Research Institute, 50 Flemington Rd, Parkville 3052 Victoria, Australia. E-mail: clare.mckinnon@mcri.edu.au

PUBLICATION DATA

Accepted for publication XXth Month 201X.

Published online XXth Month 201X.

ABBREVIATION

QoL Quality of life

AIM The primary aim of this review is to evaluate the evidence for pain prevalence in children and young adults with cerebral palsy. Secondary aims are to identify pain characteristics and types of pain measurement used in this population.

METHOD Ovid MEDLINE, Embase, CINAHL Plus, and PubMed were searched in October 2016 and updated in November 2017. Two authors independently screened studies according to Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Pain outcomes were categorized within a biopsychosocial pain framework, with pain prevalence extracted for all recall periods and measurement types.

RESULTS One hundred and six publications from 57 studies met inclusion criteria. Pain prevalence varied widely from 14 per cent to 76 per cent and was higher in females, older age groups, and those classified within Gross Motor Function Classification System level V. Pain was most frequent in the lower limbs, back, and abdomen and associated with reduced quality of life or health status. The influence of pain on psychological functioning, interference, and participation was inconclusive.

INTERPRETATION Variation exists in reported pain prevalence because of sampling bias, inconsistent measurement, varying recall periods, and use of different participant age ranges.

What this paper adds:

- Pain prevalence varies from 14 per cent to 76 per cent in children and young adults with cerebral palsy.
- Pain is more prevalent in females, older age groups, and children in Gross Motor Function Classification System level V.

[First page footer]

DOI: 10.1111/dmcn.xxxxx

[Left page footer]

Developmental Medicine & Child Neurology 2018, XX: 000–000

[Right page footer]

Review

[main text]

Cerebral palsy (CP) is a common cause of physical disability in childhood, which occurs in approximately 2.1 per 1000 births.[1] It is a heterogeneous disorder which is characterized by abnormal muscle tone, movement disorder, and multiple medical comorbidities including pain.[2] Pain itself is a complex sensory experience, which can be acute, of short duration, or chronic, constant, or recurrent lasting longer than 3 months.[3] In children with CP, pain is commonly attributed to hip dislocation, scoliosis, muscle spasm, muscle tone, and gastrointestinal dysfunction.[4] It is also reported to be associated with reduced quality of life (QoL), participation, and psychological functioning.[5–8]

Accurate estimates of pain prevalence and broader parameters of pain can influence health care provision, management, and research in childhood CP.[9] Within the CP population, pain is reported to be present in 32 per cent of children and 74 per cent of adolescents.[10,11] Population research, performed in cohorts representative of all children with CP, produce the most generalizable (externally valid) estimates of pain. However, obtaining representative population cohorts is difficult because of the likelihood of non-response bias and need for prospective data collection of pain measures.[12] The inherent limitations of research in pain in CP result in a high proportion of studies with variable results. These discrepancies between studies complicate the interpretation of the body of pain literature, hindering its use to inform clinical and research practice.

Despite frequent reports of pain in childhood CP, pain is typically under identified, under measured, and under treated by clinicians.[13–15] Difficulties in pain identification and measurement in children with CP stem from the presence of multiple pain sources, impaired communication, variable cognitive and physical functioning, and limitations within existing measurement tools.[16] The selection and administration of pain measurement tools is complicated by the varying ability of children to self-report pain across a spectrum of disability and ages.[16] Proxy reported pain is predicted to overestimate pain in comparison to self-reported measures, which are considered to be the criterion standard for pain measurement.[17] Selection of pain measurement tools is further complicated by the ability to quantify pain using a range of physical, psychological, and social parameters. These multifactorial considerations when using pain tools contribute to variable clinical measurement practices, and are likely to compound the failure to recognize and treat pain.

Little is known regarding the influence of CP on childhood pain experiences, leading to a lack of targeted pain management strategies in this population. As children with CP grow, secondary comorbidities, which form underlying pain sources, evolve and change.[10,18–21] In response, various surgical, pharmacological, and rehabilitative interventions are used to manage symptoms. Both the presence of comorbidities and their management have the potential to influence childhood pain experiences. Further influences on pain include the cognitive, emotional, hormonal, and physical maturation which accompany childhood growth and development.[22] Some authors postulate that better pain management in childhood could reduce the incidence of chronic pain into adulthood.[23,24] The unique developmental context of a child with CP, and their pain experience, requires further exploration to assist the timing and focus of pain management strategies.

Pain prevalence has been reported in an increasing number of publications, highlighting the impact of pain on the CP population. A previous systematic review reported that pain was prevalent in 75 per cent of people with CP. However this pooled estimate is likely to overinflate child prevalence (60%) because of higher adult prevalence (78%).[25] Furthermore, this review did not perform in-depth analysis of pain within CP subsets or evaluate broader parameters of pain. Broader pain parameters, aside from prevalence, give insight into the complex multidimensional nature of pain and can be categorized according to bio-psychosocial pain models.[26,27] A bio-psychosocial pain model integrates notions of both disease, an objective biological event involving the disruption of a specific bodily structure or organ, and illness, the subjective response of a child or family to living and responding to symptoms of disability.[27] Using this recognized pain model, this systematic review aims to give a realistic picture of how often and how pain affects children with CP. The primary aim of this review is to synthesize the evidence for pain prevalence in children and young adults with CP. Secondary aims are to identify pain characteristics and summarize outcome measures used in this population.

METHOD

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered with Prospero (registration number: CRD42016046762).[28]

Inclusion and exclusion criteria

Studies were included if they met the following conditions: minimum sample size of 20 participants aged between 2 years and 25 years with a diagnosis of CP, were observational, reported at least one or more pain outcome, and published in English.

Studies were excluded if the participant group included additional diagnoses to CP where outcomes for diagnostic groups were not evaluated separately, the participant group included adult participants aged over 25 years where outcomes of participants from below 25 years were not evaluated separately, they primarily investigated pain in presurgical or postsurgical participants, did not report pain subscales separately from broader health related measures, or were a systematic review.

Childhood was defined as 2 years to 25 years of age, to account for global and institutional differences in the age range for childhood CP. No limits were placed on publication date and conference abstracts were included.

Search strategy

Searches were originally performed in October 2016 and updated in November 2017. A sensitive search strategy targeted articles where pain was the main outcome or where pain subscales were reported as part of broader health-related measures (i.e. QoL). Key words and their synonyms were established for 'population' and 'outcome' categories. The Boolean operator 'or' was used to combine searches within categories and 'and' was used to combine searches between categories. Searches were conducted in Ovid MEDLINE, Embase, CINAHL Plus, and PubMed (see Appendix S1, online supporting information). Keyword searching was performed in PubMed to retrieve e-pubs and articles not indexed in Ovid MEDLINE. Where subject terms could not be mapped to Medical Subject Headings or subject headings they were searched as key words within the title, abstract, and subject or thesaurus terms of articles. Key words searched included 'cerebral palsy', 'child*', 'adolescen*', 'toddler*', 'pre-schooler*', 'paediatric*', 'pediatric*', 'pain', 'quality of life', 'health status', 'participat*', 'school*', and 'attend*'. Two authors (CTM and EMM) screened the reference lists of included publications and performed electronic author citation tracking via Scopus.

Study selection

Two authors (CTM and EMM) removed duplicate articles and reviewed the titles and abstracts of studies for eligibility. Where discrepancies occurred between authors, a third author (ARH) was consulted. Study authors were contacted where more information was required to determine eligibility (e.g. conference abstracts).

Data extraction

Two authors (CTM and EMM) independently performed data extraction for all studies, comparing for discrepancies using a customized table for participant characteristics, study sampling, design, and outcome measurement. A study was defined by the cohort of children from which the data was sourced.[29] All reported pain outcomes were extracted and assigned pain domains extrapolated from relevant pain literature.[30,31] Pain domains were differentiated into 'biological', 'psychological', and 'socio-cultural' categories of the bio-psychosocial framework. Within the biological category, pain domains were defined as 'prevalence', 'intensity', 'frequency', 'bodily location (all)', 'bodily location (single), 'descriptors', and 'diagnoses/causes'. Within the psychological category there was a single 'psychological' pain domain. Within the socio-cultural category, pain domains were defined as 'pain subscales within QoL or health status', 'participation', 'aggravators', 'relievers', 'treatments', 'health

service utilization', and 'interference'. The term 'interference' was used for measures which assessed the influence of pain on all or part of activity, mood, and sleep.[32,33] Studies were differentiated into those with representative and non-representative CP cohorts, to ensure between study-comparison of participants with like characteristics. A representative CP sample was defined as a sample of children with characteristics representative of the wider CP population (e.g. across all Gross Motor Function Classification System [GMFCS] levels, sub types, cognitive abilities), whereas a non-representative CP sample was a sample of children from a defined CP subset (e.g. non-verbal children, GMFCS level IV or V, hemiplegia). Where insufficient detail was available to determine if a study was representative, it was evaluated as non-representative.

Pain prevalence was extracted for all recall periods and measurement types. Pain prevalence evaluated at a single bodily site (e.g. hip pain), was analysed as a bodily location (single). Outcome measures correlated with other pain outcome measures within the bio-psychosocial model (e.g. participation and psychological measures) were also extracted.

Quality and risk of bias assessment

Two authors (CTM and EMM) independently performed quality and risk of bias assessment for all studies. Detailed quality assessment was performed using a modified Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (see Appendix S2, online supporting information).[34] As the STROBE checklist is designed for reporting of observational studies, decision rules were adapted for quality assessment, and criterion rated as 'yes', 'no', or 'partially' achieved. Risk of bias was evaluated separately for sampling (external validity) and outcome measurement (internal validity) using the relevant STROBE criteria. Risk of bias was classified as 'low', 'moderate', or 'high' for sampling and outcome measurement, with an overall risk of bias assigned. For sampling risk of bias, low risk of bias was assigned to population studies which covered at least 80 per cent of the population or had a sample size of more than 500 participants.[25,35] For outcome measurement risk of bias, higher weighting was given to the psychometric properties of the primary outcome for studies reporting multiple pain domains. For studies with multiple publications, each individual publication was separately assessed with an overall quality and risk of bias assessment assigned based on all available information.

Data analysis

All studies meeting the review's eligibility criteria were qualitatively analysed. However, to be considered for meta-analysis, a study was required to be from a representative CP sample

and have a low risk of bias. Where meta-analysis was not possible, a quantitative synthesis of studies with low or moderate risk of bias was performed. When interpreting the data, higher weighting was given to studies with low risk of bias. Authors were contacted where additional data was required for quantitative synthesis.[10,36]

Data analysis was complicated by the high proportion of studies with multiple publications, so the following decision rules were adopted to ensure integrity within the reported results: (1) Where a study had multiple publications reporting the same outcome, the publication with the most comprehensive data set was chosen. (2) Where a study had multiple publications reporting different pain outcomes, each available outcome was extracted. (3) For longitudinal studies, outcomes from the first time point were reported; however, if additional outcomes were reported at the second time point that were not reported at the first time point, these outcomes were also analysed. (4) For cross-sectional studies, where additional pain outcomes were reported in a smaller subset of participants, these outcomes were also analysed. (5) For studies reporting multiple pain outcomes, only measures with low or moderate measurement bias influenced study results.

Data was analysed descriptively using STATA version 14.0 (StataCorp, College Station, TX, USA). Dichotomous outcomes were summarized using proportions and odds ratios (ORs) and 95 per cent confidence intervals (CI). Planned subgroup analysis for prevalence and intensity in representative CP samples included age, GMFCS level, sex, and subtype. Forest plots were used to graphically represent data where possible.

RESULTS

A total of 1964 citations were identified through database searching. One hundred and six publications met inclusion criteria, accounting for 57 studies, because of some studies having multiple publications arising from the same cohort (see Fig. S1 and Appendix S3, online supporting information). Four publications were conference abstracts and one a thesis.[37–41]

Across all 57 included studies, the majority were cross-sectional (75%), with a small proportion of longitudinal (11%), retrospective chart reviews (7%), and cross-sectional with comparison group (7%). Of these, three (5%) utilized a whole population approach. Sample size varied from 21 to 2616 participants, with 54% of studies from representative CP samples. Participants were predominantly recruited from hospitals (32%), registers/surveillance programmes/birth cohorts (26%), community (21%), and a mixture of these sources (18%). Studies had a broad geographical distribution, with the greatest proportion carried out in Europe (37%), North America (23%), and Asia (21%).

Pain measures were categorized predominantly as biological (53%) and socio-cultural (44%), with few psychological (4%) measures reported. Across pain domains, the influence of pain on QoL or health status (60%) and pain prevalence (42%) were most frequently reported (Fig. 1). Table SI (online supporting information) summarizes the participant characteristics, study design, and risk of bias for studies included in the quantitative synthesis while Appendix S4 (online supporting information) summarizes those not included.

Study quality and risk of bias

Of the 57 included studies, only one study had a low (2%) risk of bias while the remaining had a moderate (37%) or high (61%) risk of bias. Conference abstracts (7%) were classified as awaiting classification because of insufficient data for quality and risk of bias assessment. Across studies there was low to moderate quality of evidence with the largest risk of bias found in study generalizability and sample size (Appendix S5, online supporting information). Twenty-two (39%) studies were of sufficient quality to be included in the quantitative synthesis and are discussed below.

DISCUSSION

Studies with representative CP samples – biological

Pain prevalence

Eight studies (one low and seven moderate risk of bias) evaluated pain prevalence, which varied from 14 per cent to 76 per cent in participants aged from 2 to 23 years (Fig. 2).[10,36,43–48] One low risk of bias population study reported prevalence to be 73 per cent (95% CI 69–76) over 4 weeks. Another population study reported prevalence to be 34 per cent (95% CI 32–36%) but used no recall period so had the potential for measurement bias. The wide variance in prevalence across studies was because of non-population sampling, inconsistent outcome measurement, and differing age range of participants. Prevalence measurement was heterogeneous with majority of studies using non-standardized questions, different pain recall periods (0–4 weeks), and variable reporting methods. Pain reporting varied from carer, clinician, to a combination of self and carer report most commonly.

Included subgroup analysis varied across studies. Four studies (one low and three moderate risk of bias) evaluated age as a predictor of pain prevalence.[10,36,44,47] Of these, three reported a positive association between pain prevalence and increasing age.[10,36,47] One population longitudinal study reported that pain increased from childhood (8–12y) into

adolescence (13–17y), while another population cross sectional study demonstrated an upward trend in prevalence in children aged from 2 to 14 years (Fig. 3).[10,36]

Five studies (one low and four moderate risk of bias) evaluated sex as a predictor of pain prevalence.[10,36,43,46,47] There was a trend towards higher pain prevalence in females compared to males reported in three studies.[10,43,47]

Four studies (one low and three moderate risk of bias) evaluated GMFCS level as a predictor of pain prevalence (Fig. 4).[10,36,43,45] Pain prevalence was positively associated with children classified within GMFCS level V compared to I, demonstrated by two population studies.[10,36] Of these studies, one reported a positive association with pain prevalence within GMFCS level III and another within GMFCS level IV compared to level I. Other studies reported no significant differences.[43,45]

Two studies (moderate risk of bias) evaluated CP motor-type as a predictor of pain prevalence, reporting non-significant effects.[10,47] The influence of CP motor-type on pain prevalence is inconclusive, with few studies including this analysis.

Intensity

Five studies (one low and four moderate risk of bias) evaluated pain intensity.[36,43,44,46,47] Of these, three studies evaluated the association between pain intensity and GMFCS level.[36,43,47] There was a trend towards parent-reported pain intensity being higher among children classified within GMFCS levels IV and V compared to lower levels.[36,47] No other trends in predictive factors were detected across studies. Intensity analysis was complicated by variable pain measurement, categorization of severity, and included subset analysis.

Bodily location (all)

Four studies (one low and three moderate risk of bias) evaluated the proportion of painful bodily sites across all body sites.[36,43,44,47] Pain was most frequently reported to be located in the lower limbs (32–82%) and less so in the upper limbs (4–19%). Other common sites of pain were the abdomen (11–32%), head (10–30%), and back (9–25%).[36,44,47]

Studies with representative CP samples – socio-cultural

Pain influence on QoL or health status

Fourteen studies (one low and 13 moderate risk of bias) evaluated the influence of pain on QoL or health status.[36,42–44,46–55] Five studies were not included in this analysis as they did not statistically analyse pain as a predictive factor or compare to a normative sample.[42,51,53–55] Of the remaining nine studies, seven demonstrated that pain had a negative impact on the QoL or

health status on children with CP.[36,44,46–49,52] One longitudinal study reported that childhood pain predicted lower QoL or health status in adolescence.[36]

Social demographics

Two studies (one low and one moderate risk of bias) evaluated the influence of social demographics on pain outcomes.[36,47] One reported a positive association between parental unemployment and higher pain intensity (p=0.003).[36] There were no other significant associations.

Participation

Three studies (one low and two moderate risk of bias) evaluated the influence of pain on participation.[36,47,54] One reported a positive association between pain and reduced participation, while another reported that childhood pain was associated with reduced adolescent participation.[36,47] There were no other significant associations.[54]

Interference

Three studies (all three moderate risk of bias) evaluated pain interference; however, these studies were unable to be analysed because of measurement bias associated with the use of non-standardized, incomplete, or inappropriate measures.[43,44,47]

Psychological

Two studies (one low and one moderate risk of bias) evaluated the influence of pain on psychological functioning.[36,47] One reported a significant association between psychological symptoms in children with higher pain intensity (OR 2.7, 95% CI 1.6–4.6) and another reported peer problems in females with self-reported recurrent musculoskeletal pain (p=0.02).[36,47]

Non-representative CP samples

Across all bio-psychosocial pain domains

Key outcomes of non-representative CP studies are summarized in Table I.[19,56–60]

DISCUSSION

This systematic review found that pain prevalence estimates ranged from 14 per cent to 76 per cent. There was a trend towards pain being more prevalent in females, older compared to younger children, and those within GMFCS level V compared to lower GMFCS levels. Pain

was most frequent in the lower limbs and associated with poor QoL or health status. Evidence for the influence of pain on psychological functioning, participation, and interference were inconclusive with few studies evaluating these outcomes.

Estimates of pain prevalence varied widely between studies because of the complex interaction of multiple influences and sources of bias, which made it difficult to distinguish between predicting factors for prevalence (e.g. age, recall) and compare prevalence estimates between studies. Sampling bias was present in the majority of studies, with only two population studies sourced. Study cohorts including older children had the potential to positively influence prevalence, because of the positive association between pain prevalence and older age groups. Measurement bias was present in a large proportion of studies, with the use of non-standardized questions or questions adapted from health-related tools not designed to detect pain prevalence (i.e. Child Health Questionnaire). Heterogeneity in measurement resulted in prevalence proportions being calculated based on different underlying pain constructs. For example, the study with the lowest prevalence (14%) embedded pain measurement into activity using the Health Utilities Index Mark 3 whilst the study with the highest prevalence (76%) based pain measurement on scores from the Pain Evaluation Scale, a behavioural rating measure.[43,46] Measures used across studies also adopted different pain recall periods and reporting, potentially introducing further bias.[14,17] The inherent limitations of point prevalence proportions result in reduced ability to compare estimates between studies, making them unable to be used to evaluate population strategies which may impact pain (i.e. hip surveillance).[14] Limitations in between-study comparability made the analysis of trends in prevalence according to CP subsets more useful in determining the impact of pain on the CP population.

The co-occurring impact of CP and childhood development on pain was highlighted by comparing this review's findings with typically developing populations. The increased pain prevalence in females and adolescents reported in this review matched typically developing populations. Similarly pain had a negative influence on QoL or health status within both populations.[61–65] However, in children with CP, the lower limbs were found to be the most common site of bodily pain compared to the head in typically developing children, where limb pain is less common.[66,67] The higher prevalence of lower limb pain in children with CP is not surprising considering the impact of musculoskeletal deformity on these joints. These patterns in pain characteristics highlight both the developmental stage of adolescence and lower limbs as important targets for pain management within the CP population.

This review identified CP subsets at risk of developing pain who are likely to require targeted pain management. The higher pain prevalence within GMFCS level V can be explained by the higher proportion of children with pain causing comorbidities such as hip dislocation, scoliosis, gastro-intestinal abnormalities, and movement dysfunction.[10,68–70] Age related changes in comorbidities are likely to further contribute to higher pain prevalence in adolescents and young adults with CP.[20,71,72] Comorbidities were evaluated in detail within non-representative studies, giving greater insight into these distinct pain sources. Studies of children with hip dislocation identified additional risk factors for pain including access to hip surveillance and surgery, poor hip morphology, and hip displacement (>50°).[19,60] Such findings have direct implications for clinical practice, and highlight the need to evaluate pain in both focussed (non-representative) and generalized (representative) CP populations.

The lack of studies which evaluate the impact of pain on psychological functioning, participation, and interference implies that bio-psychosocial pain models are not being consistently adopted in CP pain research. The failure to integrate bio-psychosocial pain models into disability assessment frameworks limits the understanding of complex pain experiences in children with CP. Recent National Institute for Health and Care Excellence guidelines recommend multi-dimensional pain assessment across the heterogeneous CP population which accounts for age, cognition, and functional level.[73] These guidelines also recommend prospective trials evaluating the impact of pain measurement tools on its early identification and treatment. Pain identification using prevalence measures requires further evaluation to determine the optimum type, reporting, and recall period to detect pain in CP.[13] Future consensus around pain measurement across pain domains would assist in streamlining clinical and research practice by minimizing modifiable bias and making future studies more comparable.[31]

Limitations

This review is likely to be limited by publication bias within included studies, which refers to a study's tendency to only report and be published with statistically significant outcomes. Because of the large amount of review data, only risk factors for prevalence and intensity were evaluated to align with review aims. There were limitations in study comparability, so participant cohorts were categorized and only those of sufficient quality were quantitatively analysed.

Future research directions

There needs to be a shift in research emphasis from pain prevalence towards broader pain measures within the bio-psychosocial pain framework. Consistency with pain measurement is of particular importance as more efficacy-based pain research is undertaken. Future research and pain management strategy should target identified at risk CP subgroups and explore the value of extrapolating pain treatments from other chronic pain populations.

Conclusions

This review highlighted the multi-dimensional impact of pain in children and young adults with CP within a bio-psychosocial framework. Risk of bias within prevalence estimates reduces their utility when being used to compare outcomes between populations. However there is moderate quality evidence that pain is likely to be more prevalent in females, older children, and those in GMFCS level V and negatively impacts QoL or health status. More research is required to evaluate the impact of pain on participation, interference, and psychological functioning.

Acknowledgements

We would like to acknowledge the contribution of additional data from the Study of Participation of Children with Cerebral Palsy Living in Europe group and the Swedish CPUP follow-up surveillance programme included in this review.

Clare McKinnon is funded to complete her PhD by the Australian Government Research Training Program Scholarship and Centre for Research Excellence in Cerebral Palsy, Murdoch Children's Research Institute, Top-Up Scholarship. The authors have stated that they had no interests that might be perceived as posing a conflict or bias.

Supporting information

The following additional material may be found online:

Appendix S1: Ovid MEDLINE Search Strategy

Appendix S2: Modified Strobe Checklist

Appendix S3: Table of studies with multiple publications

Appendix S4: Participant, study characteristics, and methodological quality for studies not included in the quantitative synthesis

Appendix S5: Modified Strengthening the Reporting of Observational Studies in Epidemiology Checklist and overall risk of bias for studies included in quantitative synthesis

Figure S1: PRISMA flow diagram of eligible articles

Table SI: Participant characteristics, study design, and risk of bias for studies included in the quantitative synthesis

REFERENCES

1. Oskoui M, Coutinho F, Dykeman J, Jetté N, Pringsheim T. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Dev Med Child Neurol* 2013; **55**: 509–19.

2. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol Suppl* 2007; **109**: 8–14.

3. Merskey H, Bogduk N. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms, Second Edition. Seattle, WA: IASP Press; 1994.

4. Massaro M, Pastore S, Ventura A, Barbi E. Pain in cognitively impaired children: a focus for general pediatricians. *Eur J Pediatr* 2013; **172**: 9–14.

5. Colver A, Rapp M, Eisemann N, et al. Self-reported quality of life of adolescents with cerebral palsy: a cross-sectional and longitudinal analysis. *Lancet* 2015; **385**: 705–16.

6. Dickinson HO, Parkinson KN, Ravens-Sieberer U, et al. Self-reported quality of life of 8–12-year-old children with cerebral palsy: a cross-sectional European study. *Lancet* 2007; **369**: 2171–8.

7. Fauconnier J, Dickinson HO, Beckung E, et al. Participation in life situations of 8–12 year old children with cerebral palsy: cross sectional European study. *BMJ* 2009; **338**: b1458.

8. Parkes J, White-Koning M, Dickinson HO, et al. Psychological problems in children with cerebral palsy: a cross-sectional European study. *J Child Psychol Psychiatry* 2008; **49**: 405–13.

9. Andrusaitis SF, Oliveira RP, Barros Filho TE. Study of the prevalence and risk factors for low back pain in truck drivers in the state of Sao Paulo, Brazil. *Clinics (Sao Paulo)* 2006; **61**: 503–10.

10. Alriksson-Schmidt A, Hägglund G. Pain in children and adolescents with cerebral palsy: a population-based registry study. *Acta Paediatr* 2016; **105**: 665–70.

11. Parkinson KN, Dickinson HO, Arnaud C, Lyons A, Colver A SPARCLE group. Pain in young people aged 13 to 17 years with cerebral palsy: cross-sectional, multicentre European study. *Arch Dis Child* 2013; **98**: 434–40.
12. Delgado-Rodríguez M, Llorca J. Bias. *J Epidemiol Community Health* 2004; **58**: 635–41.
13. Fehlings D. Pain in cerebral palsy: a neglected comorbidity. *Dev Med Child Neurol* 2017; **59**: 782–3.
14. Westbom L, Rimstedt A, Nordmark E. Assessments of pain in children and adolescents with cerebral palsy: a retrospective population-based registry study. *Dev Med Child Neurol* 2017; **59**: 858–63.
15. Morrow AM, Hayen A, Quine S, Scheinberg A, Craig JC. A comparison of doctors', parents' and children's reports of health states and health-related quality of life in children with chronic conditions. *Child Care Health Dev* 2012; **38**: 186–95.
16. Kingsnorth S, Orava T, Provvidenza C, et al. Chronic pain assessment tools for cerebral palsy: a systematic review. *Pediatrics* 2015; **136**: e947–60.
17. White-Koning M, Arnaud C, Dickinson HO, et al. Determinants of child-parent agreement in quality-of-life reports: a European study of children with cerebral palsy. *Pediatrics* 2007; **120**: e804–14.
18. Terjesen T. The natural history of hip development in cerebral palsy. *Dev Med Child Neurol* 2012; **54**: 951–7.
19. Wawrzuta J, Willoughby KL, Molesworth C, et al. Hip health at skeletal maturity: a population-based study of young adults with cerebral palsy. *Dev Med Child Neurol* 2016; **58**: 1273–80.
20. Gu Y, Shelton JE, Ketchum JM, et al. Natural history of scoliosis in nonambulatory spastic tetraplegic cerebral palsy. *PM R* 2011; **3**: 27–32.
21. Bell KJ, Ounpuu S, DeLuca PA, Romness MJ. Natural progression of gait in children with cerebral palsy. *J Pediatr Orthop* 2002; **22**: 677–82.
22. World Health Organization. WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. Geneva: World Health Organization, 2012.
23. Berbrayer D. Are adult cerebral palsy receiving optimal medical care and is there an unmet need for physiatrists input? *Phys Med Rehabil Int* 2015; **2**: 1029.
24. Murphy KP. Cerebral palsy lifetime care – four musculoskeletal conditions. *Dev Med Child Neurol* 2009; **51** (Suppl. 4): 30–7.
25. Novak I, Hines M, Goldsmith S, Barclay R. Clinical prognostic messages from a systematic review on cerebral palsy. *Pediatrics* 2012; **130**: e1285–312.

26. Gatchel RJ. Comorbidity of chronic pain and mental health disorders: the biopsychosocial perspective. *Am Psychol* 2004; **59**: 795–805.
27. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull* 2007; **133**: 581–624.
28. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097.
29. Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions: Version 5.1.0. The Cochrane Collaboration, 2011. Available from: www.handbook.cochrane.org (accessed 2 November 2016).
30. Fillingim RB, Loeser JD, Baron R, Edwards RR. Assessment of chronic pain: domains, methods, and mechanisms. *J Pain* 2016; **17** (9 Suppl): T10–20.
31. McGrath PJ, Walco GA, Turk DC, et al. Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. *J Pain* 2008; **9**: 771–83.
32. Wilson M. Integrating the concept of pain interference into pain management. *Pain Manag Nurs* 2014; **15**: 499–505.
33. Kanstrup M. More than pain – assessment and treatment of pain-related dysfunction in pediatric chronic pain. Stockholm, Sweden: Karolinska Instituet, 2017.
34. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *PLoS Med* 2007; **4**: e297.
35. Reid SM, Modak MB, Berkowitz RG, Reddihough DS. A population-based study and systematic review of hearing loss in children with cerebral palsy. *Dev Med Child Neurol* 2011; **53**: 1038–45.
36. Parkinson KN, Gibson L, Dickinson HO, Colver AF. Pain in children with cerebral palsy: a cross-sectional multicentre European study. *Acta Paediatr* 2010; **99**: 446–51.
37. Hollung S, Vik T, Andersen G. Comparison of young adults with cerebral palsy in Norway with and without epilepsy. *Dev Med Child Neurol* 2017; **59** (Suppl. 3): 40–1.
38. Imms C, Timmers L, Kerr C, et al. Sleep in children with cerebral palsy: a cross sectional-study. *Dev Med Child Neurol* 2017; **59** (Suppl. 2): 64–5.
39. Karlsson P, Galea C, Townsend A, Wallen M. Identifying and monitoring pain and sleep in children with cerebral palsy: early findings from a surveillance program. *Dev Med Child Neurol* 2016; **58** (Suppl. 5): 95.

40. Myklebust G, Jahnsen R, Elkjaer S. Descriptive analysis of a total population of children with dyskinetic cerebral palsy in Norway compared to children with spastic cerebral palsy. *Dev Med Child Neurol* 2016; **58** (Suppl. 5): 46–7.
41. Jiang B. A profile of young adults aged 20 to 30 years with cerebral palsy in Victoria: health, function, pain, quality of life, social participation, and service utilization. Melbourne, Victoria: The University of Melbourne, 2009.
42. Jiang B, Davis E, Walstab J, McLinepi SR, Lanigan A, Reddihough D. Pain experience in young adults with cerebral palsy. *Dev Med Child Neurol* 2009; **51** (Suppl. 5): 10–11.
43. Kennes J, Rosenbaum P, Hanna SE, et al. Health status of school-aged children with cerebral palsy: information from a population-based sample. *Dev Med Child Neurol* 2002; **44**: 240–7.
44. Penner M, Xie WY, Binepal N, Switzer L, Fehlings D. Characteristics of pain in children and youth with cerebral palsy. *Pediatrics* 2013; **132**: e407–13.
45. Rodby-Bousquet E, Czuba T, Hägglund G, Westbom L. Postural asymmetries in young adults with cerebral palsy. *Dev Med Child Neurol* 2013; **55**: 1009–15.
46. Tüzün EH, Guven DK, Eker L. Pain prevalence and its impact on the quality of life in a sample of Turkish children with cerebral palsy. *Disabil Rehabil* 2010; **32**: 723–8.
47. Ramstad K, Jahnsen R, Skjeldal OH, Diseth TH. Characteristics of recurrent musculoskeletal pain in children with cerebral palsy aged 8 to 18 years. *Dev Med Child Neurol* 2011; **53**: 1013–8.
48. Radsel A, Osredkar D, Neubauer D. Health-related quality of life in children and adolescents with cerebral palsy. *Zdr Varst* 2017; **56**: 1–10.
49. Böling S, Varho T, Kiviranta T, Haataja L. Quality of life of Finnish children with cerebral palsy. *Disabil Rehabil* 2016; **38**: 683–8.
50. Vargus-Adams J. Health-related quality of life in childhood cerebral palsy. *Arch Phys Med Rehabil* 2005; **86**: 940–5.
51. Young NL, Rochon TG, McCormick A, Law M, Wedge JH, Fehlings D. The health and quality of life outcomes among youth and young adults with cerebral palsy. *Arch Phys Med Rehabil* 2010; **91**: 143–8.
52. Wake M, Salmon L, Reddihough D. Health status of Australian children with mild to severe cerebral palsy: cross-sectional survey using the Child Health Questionnaire. *Dev Med Child Neurol* 2003; **45**: 194–9.

53. Davis E, Mackinnon A, Waters E. Parent proxy-reported quality of life for children with cerebral palsy: is it related to parental psychosocial distress? *Child Care Health Dev* 2012; **38**: 553–60.
54. Tan SS, van Meeteren J, Ketelaar M, et al. Long-term trajectories of health-related quality of life in individuals with cerebral palsy: a multicenter longitudinal study. *Arch Phys Med Rehabil* 2014; **95**: 2029–39.
55. Şimşek TT, Tuç G. Examination of the relation between body mass index, functional level and health-related quality of life in children with cerebral palsy. *Turk Pediatri Ars* 2014; **49**: 130–7.
56. Houlihan CM, O'Donnell M, Conaway M, Stevenson RD. Bodily pain and health-related quality of life in children with cerebral palsy. *Dev Med Child Neurol* 2004; **46**: 305–10.
57. Jayanath S, Ong LC, Marret MJ, Fauzi AA. Parent-reported pain in non-verbal children and adolescents with cerebral palsy. *Dev Med Child Neurol* 2016; **58**: 395–401.
58. McCullough N, Parkes J, Kerr C, McDowell BC. The health of children and young people with cerebral palsy: a longitudinal, population-based study. *Int J Nurs Stud* 2013; **50**: 747–56.
59. Russo RN, Miller MD, Haan E, Cameron ID, Crotty M. Pain characteristics and their association with quality of life and self-concept in children with hemiplegic cerebral palsy identified from a population register. *Clin J Pain* 2008; **24**: 335–42.
60. Ramstad K, Terjesen T. Hip pain is more frequent in severe hip displacement: a population-based study of 77 children with cerebral palsy. *J Pediatr Orthop B* 2016; **25**: 217–21.
61. Oddson BE, Clancy CA, McGrath P. The role of pain in reduced quality of life and depressive symptomology in children with spina bifida. *Clin J Pain* 2006; **22**: 784–9.
62. Haraldstad K, Christophersen KA, Helseth S. Health-related quality of life and pain in children and adolescents: a school survey. *BMC Pediatr* 2017; **17**: 174.
63. Hunfeld JA, Perquin CW, Duivenvoorden HJ, et al. Chronic pain and its impact on quality of life in adolescents and their families. *J Pediatr Psychol* 2001; **26**: 145–53.
64. Brun Sundblad GM, Saartok T, Engström LM. Prevalence and co-occurrence of self-rated pain and perceived health in school-children: age and gender differences. *Eur J Pain* 2007; **11**: 171–80.
65. Haraldstad K, Sorum R, Eide H, Natvig GK, Helseth S. Pain in children and adolescents: prevalence, impact on daily life, and parents' perception, a school survey. *Scand J Caring Sci* 2011; **25**: 27–36.

66. Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA et al. Pain in children and adolescents: a common experience. *Pain* 2000; **87**: 51–8.
67. King S, Chambers CT, Huguet A, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. *Pain* 2011; **152**: 2729–38.
68. Hägglund G, Lauge-Pedersen H, Wagner P. Characteristics of children with hip displacement in cerebral palsy. *BMC Musculoskelet Disord* 2007; **8**: 101.
69. Soo B, Howard JJ, Boyd RN, et al. Hip displacement in cerebral palsy. *J Bone Joint Surg Am* 2006; **88**: 121–9.
70. Rosenbaum PL, Walter SD, Hanna SE, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. *JAMA* 2002; **288**: 1357–63.
71. Persson-Bunke M, Hägglund G, Lauge-Pedersen H, Wagner P, Westbom L. Scoliosis in a total population of children with cerebral palsy. *Spine (Phila Pa 1976)* 2012; **37**: E708–13.
72. Haak P, Lenski M, Hidecker MJ, Li M, Paneth N. Cerebral palsy and aging. *Dev Med Child Neurol* 2009; **51** (Suppl 4): 16–23.
73. National Institute for Health and Care Excellence. Cerebral palsy in under 25s: assessment and management. London: National Institute for Health and Care Excellence, NICE Guideline 62, 2017.

Table I: Summary of key results for non-representative studies

Study	Country	Defined Subset	Key results
Houlihan et al.[56]	USA	GMFCS level III–V 2–18y	Pain prevalence: 65% (95% CI 58%–71%) Females had more pain compared to males (p=0.03) Higher pain frequency compared to normative values (p<0.001) Higher pain frequency was associated with school days missed (p=0.03) and days in bed (p=0.01) Parents who perceived children to be in pain were emotionally affected by their child's health and emotional well-being (r=0.38, p<0.001)
Wawrzuta et al.[19]	Australia	GMFCS level I–V 15–24y Migration percentage >30%	Hip pain prevalence: 72% (95% CI 63%–80%) Pain intensity was associated with increasing GMFCS level and poor hip morphology (p<0.001) Hip surveillance and access to surgery was associated with less pain
Ramstad et al.[60]	Norway	GMFCS level III–V Bilateral 7–12y	Hip pain prevalence: 29% (95% CI 20%–40%) Worse hip pain intensity was associated with GMFCS level V and spastic quadriplegia Hip pain was more frequent with a migration percentage ≥50% (p<0.001) Hip displacement (>40°) associated with lower scores on comfort and emotions section of the CP CHILD (p<0.001)
Jayanath et al.[57]	Singapore	GMFCS level I–V 2–20y Non-verbal	Pain prevalence: 63% (95% CI 53%–71%) 50% of sample had moderate or severe pain intensity Pain intensity was not associated with parental psychosocial factors Worse pain intensity was associated with older age (p=0.016) and spastic quadriplegia (p=0.020)
Russo et al.[59]	Australia	GMFCS level I–V Spastic hemiplegia 3–16y	Pain prevalence: 48% (95% CI 38%–57%) Pain negatively influenced QoL or health status (effect size 0.8, p<0.001)
McCullough et al.[58]	Ireland	GMFCS I–IV 4–17y Ambulate	Children with CP had significantly lower health status compared to typically developing population (Cohen's effect size 0.2) Bodily pain according to the Child Health Questionnaire

			did not change over time (Cohen's effect size 0.17)

GMFCS, Gross Motor Function Classification System; CI, confidence interval; CP CHILD, Caregiver Priorities and Child Health Index of Life with Disabilities Questionnaire; QoL, quality of life.

[figure legends]

Figure 1: Pain domains (%) reported across studies. QoL, quality of life.

Figure 2: Forest plot of pain prevalence proportions and 95% confidence interval (CI) for representative studies. The age range (y) and pain recall (wks) is listed above each study proportion. Refer to Table SI (online supporting information) for description of study cohorts.

Figure 3: Prevalence and 95% confidence interval (CI) by age for population studies. Refer to Table I for description of study cohorts.

Figure 4: Prevalence odds ratio (OR) by Gross Motor Function Classification System (GMFCS) level and 95% confidence interval (CI). GMFCS level I used as the base group for the OR. Refer to Table SI (online supporting information) for description of study cohorts.