Chronic widespread pain in children and adolescents presenting in primary care: prevalence and associated risk factors

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Summary

A significant proportion of children/adolescents have chronic widespread pain (CWP) status in primary care. Many risk factors are pain based, suggesting potential pain development pathways.

Abstract

A significant proportion of children/adolescents report Chronic Widespread Pain (CWP), but little is known about clinically relevant CWP or what factors lead to onset in this population. Objectives were to report the primary care consultation prevalence of CWP, and investigate risk factors associated with onset. A validated algorithm for identifying CWP status from primary care electronic healthcare records, was applied to a child/adolescent population (aged 8 to 18 years). The algorithm records patients who have recurrent pain consultations (axial skeleton and upper or lower limbs), or those with a non-specific generalised pain disorder (e.g. fibromyalgia). Prevalence was described, and a nested case-control study established to identify risk factors associated with CWP onset using logistic regression producing Odds Ratios (OR) and 95% Confidence Intervals (95%CI). 271 children/adolescents were identified with CWP, resulting in a five-year consultation prevalence of 3.19%. Risk factors significantly associated with CWP onset were; mental health (e.g. anxiety/neurosis consultations), neurological (e.g. headaches), genitourinary (e.g. cystitis), gastrointestinal (e.g. abdominal pain) and throat problems (e.g. sore throats). Children/adolescents with one or two risk factors (OR 2.15, 95% CI 1.6 to 2.9) or three or more risk factors (OR 9.17, 95% CI 5.9 to 14.3) were at significantly increased odds of CWP onset compared to those with none. Findings show a significant proportion of the child/adolescent primary care population have CWP. The majority of risk factors involved pain-related conditions, suggesting potential pathways of pain development. Further work is now needed to better understand the development of CWP in children and adolescents.

Keywords

Chronic Widespread Pain; Primary Care; Risk; Children; Adolescents; Electronic Healthcare Records.

Introduction

Chronic widespread pain (CWP) is defined as pain that lasts for three months or more, located above and below the waist on both sides of the body and within the axial skeleton [66]. Prevalence of CWP is estimated at approximately 10%-12% within adult populations [4,23,44]. The etiology and prognosis of CWP is complex and thought to involve interactions between biological (genetic, sensitisation, stress response, fatigue), psychological (self-esteem, coping, mood), and social (social support, isolation, deprivation) factors [2,6,8,59]. CWP has a substantial impact on the individual (e.g. physical and psychological function), it often persists for many years, and as a consequence has significant bearing on healthcare (e.g. high healthcare use) and the wider society [6,11,39,45,62].

There is growing interest within pain research to understand life course perspectives, in particular how pain conditions such as CWP develop over time and throughout life. Studies have shown that adolescents have “emerging” trajectories for pain compared to more stable patterns found in adults [19,42], along with an increasing prevalence of CWP with age within adolescent populations [22]. In contrast, adult studies show relative stability in trajectories of pain over time for regional pain conditions (notably low back pain) [17,18,40,42]. Furthermore, the presence of CWP in adolescence has been shown to be a risk factor for later adult CWP [28,32]. Research evidence suggest that there may be important earlier life points which may trigger future pain trajectories, with a key life stage being childhood and adolescence [33,37]. Information on the development of and early detection of CWP is important because treatment and management can be more effective at the earliest stages [63].

However, our present knowledge of CWP in child and adolescent populations is limited [20,33]. Current evidence is largely based on general population cohorts (inclusive of adults) which often employ generic measurements that may be less optimal for child and adolescent populations. Such approaches can also lack clinical relevance by including participants with self-limiting pain [33,48]. In addition, research on regional musculoskeletal conditions in children and adolescents show differences in both how children and adolescents present about their pain, as well as differences in associated risk factors, when compared with adults [31,34,38,48,60]. Greater understanding is needed on how children and adolescents develop complex pain disorders such as CWP. One potential

mechanism is that individual risk factors may act accumulatively through the concept of allostatic load [24], whereby repeated stressors increase the physiological stress response in individuals. Such elevation of stress responses then contributes to the development of widespread pain [58], with some supportive evidence that childhood stressors may contribute to developing pain pathways [65].

There is a clear need to understand more about CWP in children and adolescents, in particular CWP of clinical relevance. The aims of this study are to: i) report the prevalence of CWP, ii) describe the characteristics of children and adolescents with CWP, iii) identify risk factors associated with CWP, and iv) ascertain the accumulative risk for CWP based on identified risk factors, within a primary care consultation population.

Methods

Setting and population

The study was carried out using data from the Consultations in Primary Care Archive (CiPCA) database. CIPCA is a high quality, validated, medical record database of anonymised General Practitioner (GP) consultation records from nine practices (covering approximately 90,000 patients) in North Staffordshire, UK. CiPCA has ethical approval from the North Staffordshire Ethical Committee (ref 03/04). CiPCA has been shown to have comparability to other national and international electronic healthcare record (EHR) databases, with similar prevalence figures for musculoskeletal conditions across age and sex groups [29,30], and has previously been used to develop a method of identifying patients with CWP [43]. GP practices within CIPCA receive ongoing training and regular auditing to ensure consultation information (e.g. clinical coding) is entered to a high standard [53].

The identified child and adolescent cohort for this study included all registered children and adolescents aged 8 years to 18 years old within the CiPCA GP practices. All those included were required to have a continual registration period with no breaks (e.g. not moving out of the area and then returning) for a continuous period of five years (from 1/1/2011 to 31/12/2015). This period of five years continual registration was required as five years is the maximum time required to fulfil the criteria for CWP identification [43], see case definition paragraph below. The lower age band of 8 years was based on the earliest age (3 years) that a child can reliably report and understand pain [64]

plus the additional five years required for CWP identification as specified within the algorithm methodology [43]. The upper limit of age 18 years was chosen to correspond with the UK NHS definition of the end period of transition from child and adolescent services to adult services [10].

CWP case/control definition

CWP cases were identified within the cohort population using a validated algorithm developed to identify relevant Read codes [43]. Read codes (codes that denote the reason for consultation inclusive of diagnosis, symptoms, procedures, referrals) are commonly used in UK primary care and are cross-referenced to the ICD version 9 (now version 10) classification system [5]. The method of using Read codes within EHR is widely accepted within clinical based health research [13,15]. For information on Read codes used to define CWP cases and risk factors please access Supplementary File 1 that accompanies this paper.

The algorithm developed by Mansfield et al [43] uses a two-part approach. Firstly, recurrent regional pain consulters (RRPC) are identified by including patients who have at least one consultation for musculoskeletal pain within the axial skeleton (neck, back), and at least one consultation for pain in an upper or lower limb, and also have evidence of recurrence by consulting for musculoskeletal pain in at least three separate years, with a minimum of four relevant musculoskeletal pain consultations within a five-year period. Secondly, the algorithm identifies patients who have consulted for a non-specific generalised pain (NSGP) disorder by identification of Read codes considered as proxy markers of CWP (Read codes for NSGP and RRPC can be found within Supplementary File 1). This current study applied the algorithm to identify both groups (RRPC, NSGP) within the child and adolescent population and then combined them to form a CWP cohort. Patients who qualified for both RRPC and NSGP were only counted once within the CWP cohort. The date on which the patient achieved CWP status was classified as their “index date”; this was the earliest date of either a Read code for NSGP or the date on which the RRPC criteria was fulfilled. Controls were identified as patients who had not fulfilled the criteria above for CWP during the entire five-year time period of the study. To ensure that the lack of presence of RRPC or NSGP in controls was not due to non-attendance at primary care (i.e. if child/adolescent did not attend primary care then they could not be coded), all controls had to have at least one active electronic health care entry (e.g. consultation) within the time period of the study.

For the nested case/control analysis a total of four controls were then matched (matched for age, sex, primary care practice) with each case.

Risk factors

A scoping search of the literature (PubMed, plus contact with relevant experts in the field) was undertaken to identify potential risk factors for CWP and regional pain conditions within children and adolescent populations (see Appendix 1 for full search criteria and detailed description of risk factors). The search was supplemented by the addition of factors clinically considered to convey risk via a potential relationship to central sensitisation. The research team, inclusive of epidemiological experts and GPs with experience of EHR Read coding, reviewed all risk factors and assessed the feasibility of identifying appropriate Read codes that capture (directly or by proxy) each risk factor. Those not feasible for capture (e.g. information on parental pain status) were excluded. Appropriate Read codes were then examined and agreed via consensus of the research team. Finally, the codelists for individual risk factors were then grouped under broader risk factor domains (for example "depression" housed within the broader domain of "mental health") with binary (yes/no) variables created for each participant based on these domains. All associated Read codes and terms are available within the Supplementary File 1.

Table 1. Potential risk factors for the development of chronic widespread pain in children/adolescents

Risk factor domain	**Example risk factors***	**EHR Read Code example#**	**Read code description**
Mental Health Disorders	Anxiety and neurosis	E2004	Chronic anxiety
Adverse Life events	Single Read code used	13lld	On child protection register
Sleep and fatigue problems	Sleep problems	1B1B.11	Insomnia
Neurological problems	Headache	1BA2.	Generalised headache
Genitourinary problems	Cystitis	K15..	Cystitis

Throat problems	Sore throat	1C92.	Has a sore throat
Diabetes	No further subgroups	66A5.	Diabetic on insulin
Skin disorders	Eczema	M112.	Infantile eczema
Palpitations	Non-specific arrhythmias	812	Palpitations
Gastrointestinal symptoms	Abdominal colic and pain	1971	Upper abdominal pain

*Eight risk factor domains were comprised of a number of subgroups

#Full details of Read codes contained within each risk factor domain and individual risk factor are available on request

Confounding variables

Consideration was also given to control for potential confounding variables within the analysis of the association of risk factors with CWP. Socio-economic deprivation was considered as this has been previously shown to be to be associated with chronic pain and multimorbidity [41]. Whilst deprivation could be considered as a risk factor, there is also evidence of association with other modifiable risk factors (e.g. psychological problems, smoking, sedentary lifestyle and drug misuse) and therefore assessment of these risk factors whilst adjusting for deprivation is more informative and results will be presented prior to and after adjustment of deprivation for clarity. The English Indices of Deprivation is based on a combination of weighted multiple indices (i.e. domains of income, employment, health and disability, education, skills and training, crime, housing and services, and living environment) used to produce the Index of Multiple Deprivation (IMD) which is an overall measure calculated for every Lower-layer Super Output Area (neighbourhood) as provided by the UK Government Department for Communities and Local Government (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015). This IMD score was assigned to each child/adolescent dependent on their neighbourhood residence and then categorised into three sub-groups reflecting a 20%, 60%, 20% distribution across the total denominator population following previous methodology [9,49].

Further statistical adjustment was carried out for a potential confounding effect of healthcare surveillance bias. RRPC status required a minimum of four relevant consultations to qualify for CWP, therefore it was also possible that those who consult more often in general were more likely to have RRPC status. To account for this potential effect an analysis with adjustment for overall consultation frequency was carried out. Consultation frequency was calculated as a count of single time point of recorded healthcare entries (i.e. all entries made on the same day and time were only counted once) during the full-time period of 1/1/2011 to 31/12/2015. From this an annual rate of healthcare consultation frequency was calculated for each participant.

Analysis

Chronic widespread pain prevalence

The CWP population was described by percentages for age group, sex, and deprivation levels in comparison to the denominator population. Age groups (8 to 11, 12 to 14 and 15 to 18 years) were created to reflect pre, mid, and post pubertal stages following previous methodology [43,49]. Statistical difference testing (Chi square, Mann Whitney) was used to firstly test for difference ($p < 0.05$) between the CWP cohort and the denominator population for age group, sex, deprivation levels and annual consultation frequency, and secondly between the CWP cohort and the matched controls cohort for deprivation and annual consultation frequency. Five-year prevalence figures for CWP with 95% confidence intervals (CIs) were then calculated for the full CWP cohort and also for each of the three age groups.

Association of risk factors with CWP

CWP case and control cohorts were used to test the association of risk factors with CWP outcome. To determine an approximate temporal risk (i.e. risk factor occurs in the period prior to case status) for the association analysis, the first three-years (1/1/2011 to 31/12/2013) was chosen as the risk factor period based on the calculation that it takes a minimum of three calendar year periods for CWP status using the RRPC methodology [43]. However, the above analysis does also include those with NSGP codes and so CWP status for this particular group could occur at any time including the first three-year period or a risk factor could occur in year one but outcome (via NSGP) at year five. Therefore, a

sensitivity analysis was undertaken that encompassed both temporal risk and recurrence by including only those with RRPC status who would have an index date after the “risk period” of three years.

Due to the anticipated low number of patients reporting some risk factors, for example the inclusion of relatively uncommon disorders such as diabetes, related risk factors were placed in overarching “risk domains” (see Table 1 for the domains). Analysis tested the association of these broader risk domains with CWP using logistic regression to produce odds ratios (OR) with 95% Confidence Intervals (95%CI). A stage analysis approach was applied to give account of each domains’ relationship with the outcome, how each significant domain then independently predicts in the presence of other significant domains (explanation of potential of shared variance with other domains), and finally adjustment for potential confounding variables. Specifically, three stages were applied, i) each domain was tested separately in a univariable analysis, ii) each risk factor domain shown to be statistically significant within the univariable analysis was included in multivariable analysis along with other significant domains, and iii) testing all significant domains adjusting for deprivation with calculation of pseudo R2 (Nagelkerke) to indicate percentage explained variance of CWP from this model. The effect of consultation frequency was also similarly calculated. The three analysis stages described above were repeated within the sensitivity analysis using the restricted RRPC cohort. Power calculation indicated that for a two-sided 95% confidence at 80% power with a < 10% difference in exposure to detect an OR 1.5 or above using a (1:4) ratio of cases and controls sample size would require > 1280 participants [35]. SPSS version 21 software was used to perform analysis.

Accumulative risk

In order to investigate potential accumulative risk in support of an allostatic load hypothesis, CWP cases and controls were assigned a score relating to the number of risk factor domains present for each participant. To assist in interpretation, categories of accumulative risk were created; low (0 risk factor domain), medium (1 to 2 risk factor domains) and high (3 or more risk factor domains), using the low accumulative risk category as the comparator. Analysis employed univariable Logistic Regression producing ORs with 95% CIs.

Results

In total. 21,651 children and adolescents (aged 8 to 18 years old) were registered in CiPCA on the 31/12/2015, and of these 8507 (39%) individuals had full registration during the study period of 1/1/2011 to 31/12/2015 and were identified as the denominator population (those at potential risk). Application of the algorithm [43] identified a total case number of 271, comprising of 147 (54.2%) individuals classified as CWP status via RRPC criteria, 104 (38.4%) individuals via NSGP classification, and 20 (7.4%) individuals who qualified for both RRPC and NSGP. The CWP cohort had a mean age of 14.4 years (SD 2.7) and 47.2% female (see Table 2 for further description of the CWP cohort, the denominator population, and the matched controls cohort).

Results show significant differences in age between the CWP cohort and the denominator population (higher proportion of CWP cohort in older age categories) and in deprivation (greater percentage of the CWP cohort within the least deprived group), but no significant difference was seen between sexes. Testing for differences between the CWP cohort and the matched controls cohort revealed a significant difference (Mann Whitney test) for annual consultation frequency (higher level in CWP cohort) but no significance difference was found for age, sex, or deprivation, though the control cohort had higher representation within the most deprived category (difference of 1.7%).

Table 2. Descriptive characteristics of denominator population, and chronic widespread pain and matched control cohorts

	Denominator Population (n=8507)	**CWP cohort (n=271)**	**Matched controls cohort (n=1084)**
Age Group			
8 to 11 years, n (%)	3214 (37.8%)	48 (17.7%)	226 (20.8%)
12 to 14 years, n (%)	2212 (26.0%)	77 (28.4%)	315 (29.1%)
15 to 18 years, n (%)	3081 (36.2%)	146 (53.9%)	543 (50.1%)
Sex			
			572 (52.8%)
			512 (47.2%)

Male, n (%) Female, n (%) Indeterminate, n (%)	4344 (51.1%) 4162 (48.9%) 1 (<0.0%)	143 (52.8%) 128 (47.2%) 0 (0.0%)	0 (0%)
Level of socioeconomic deprivation*			
Least deprivation, n (%) Medium deprivation, n (%) Most deprivation, n (%) Not available¥	1696 (19.9%) 5089 (59.8%) 1696 (19.9%) 26 (0.3%)	83 (30.6%) 143 (52.4%) 45 (16.6%) 0 (0%)	328 (30.3%) 557 (51.4%) 198 (18.3%) (0%)
Annual consultation frequency (mean and SD)	Not calculated on denominator population	10.28 (7.3)	4.77 (4.7)
Results are expressed as total number and frequency (%) with the exception of annual consultation frequency which is expressed as the mean with +/- SD ¥ 26 children and adolescents had missing deprivation data *Controls were matched on practice rather than on the exact weighted deprivation index number			

Prevalence

As Table 3 outlines, over five-years, CWP prevalence was 3.19% (95% CI 3.12 to 3.23), and by age group: 8 to 11 years of 1.49% (95% CI 1.13 to 1.97), 12 to 14 years of 3.48% (95% CI 2.77 to 4.35) and 15 to 18 years of 4.74% (95% CI 4.03 to 5.57).

Table 3. Five-year prevalence of chronic widespread pain; total and by age group

Age	**Denominator population (n)**	**Chronic widespread pain (n)**	**Five-year prevalence * (95% CI)**
All ages (8 to 18)	8507	271	3.19% (3.12 to 3.23)

8 to 11 years 12 to 14 years 15 to 18 years	3214 2212 3081	48 77 146	1.49% (1.13 to 1.97) 3.48% (2.77 to 4.35) 4.74% (4.03 to 5.57)
* Five-year prevalence expressed as % frequency with 95% Confidence Intervals (95% CI)			

Association of risk factors with CWP

At the first stage of analysis (univariable analysis of each domain separately) results showed that all domains were associated with an increase in odds for CWP (see first column Table 4). However, the domains; adverse life events, diabetes, skin problems, and palpitations were not significantly associated with CWP and were therefore removed from further analysis. The domains; mental health, sleep and fatigue, neurological, genitourinary, throat problems, and gastrointestinal were entered to the second stage multivariable model. This multivariable model (see second column Table 4), where significant domains from the univariable analysis were adjusted for each other, showed an overall attenuation in the odds ratio for each domain in relation to CWP, notably showing that the domain sleep and fatigue as non-significant. At the third and final stage of analysis (multivariable model adjusted for deprivation, see third column Table 4), results show no attenuated effect of deprivation across all domains. From this final model a calculation of pseudo R^2 indicated that 22% of the variance for CWP outcome is explained by this model.

Table 4. Estimates of association of risk factor domains with chronic widespread pain outcome

Risk factor domain[#] (total n, cases, controls)	**Univariable model Odds ratio (95% CI)**	**Multivariable model Odds ratio (95% CI)**	**Adjusted** multivariable model Odds ratio (95% CI)**
Mental Health n=85 (29,56)	2.20 (1.36 to 3.52)	1.81 (1.08 to 3.02)	1.82 (1.07 to 3.03)
Adverse Life Events n=11 (3,8)	1.51 (0.40 to 5.71)	-	-

Sleep & Fatigue n=67 (21,46)	1.90 (1.11 to 3.23)	1.61 (0.89 to 2.90)	1.60 (0.89 to 2.89)
Neurological n=149 (65,84)	3.76 (2.63 to 5.37)	2.83 (1.93 to 4.16)	2.82 (1.92 to 4.14)
Genitourinary n=142 (60,82)	3.48 (2.41 to 5.00)	2.23 (1.49 to 3.31)	2.24 (1.50 to 3.33)
Throat Problems n=377 (120, 257)	2.56 (1.94 to 3.38)	2.16 (1.61 to 2.90)	2.16 (1.61 to 2.90)
Diabetes n=9 (3,6)	2.01 (0.50 to 8.10)	-	-
Skin Problems n=145 (36,110)	1.31 (0.88 to 1.97)	-	-
Palpitations n=11 (4,7)	2.31 (0.67 to 7.93)	-	-
Gastrointestinal n=229 (80,149)	2.63 (1.92 to 3.60)	1.81 (1.28 to 2.54)	1.81 (1.28 to 2.54)

[#]Results expressed as total participants with risk factor (and those in the cases and control cohorts respectively)

** Adjusted for deprivation

- Domain not included in multivariable model as not statistically significant in the univariable model

Sensitivity Analyses (selected results presented here, full results of the sensitivity analyses can be found within Appendix 2)

Consultation frequency

The multivariable model (previously adjusted for deprivation) was then also adjusted for consultation frequency. This showed that in addition to the sleep and fatigue domain (OR 0.94, 95% CI 0.50-1.77), a further two domains were no longer statistically significant; mental health (OR1.24, 95% CI 0.71-2.14) and gastrointestinal (OR 1.26, 95% CI 0.87-1.82), whereas three domains retained statistical significance; neurological (OR 1.81, 95% CI 1.19-2.75), genitourinary (OR 1.54, 95% CI 1.00 to 2.37) and throat problems (OR 1.81, 95% CI 1.33 to 2.37)

Temporal risk

A sub-group of those who fulfilled RRPC criteria was determined from the CWP cohort (n=167). Further refinement was applied to identify only those with more than three calendar years before RRPC status (n=124) to ensure outcome (CWP) after the three-year risk period. Results indicate a similar pattern of effect for the domains within the univariable analysis (increase in odds across all domains), however only neurological (OR 2.94 95% CI 1.73 to 4.97), genitourinary (OR 5.31 95%CI 3.01 to 9.40), throat problems (OR 2.60 95%CI 1.71 to 3.86), and gastrointestinal (OR 2.52 95%CI 1.58 to 4.03) were significant. The multivariate analysis performed showed similar results with again an increase in odds across all domains, with statistically significant results seen for neurological problems (OR 2.19 95% CI 1.22 to 3.93), genitourinary problems (OR 3.60 Cl 1.95 to 6.65) and throat problems (OR 2.23 95% CI 1.45 to 3.42), though gastrointestinal domain was not significant (OR of 1.46 95% CI 0.86 to 2.47). Adjustment for deprivation showed no tangible change (maximum change of 0.02 in ORs).

Accumulative risk

Further exploratory analysis tested the accumulative number of domains as a risk for CWP (potentially supporting an allostatic load hypothesis) and results showed that in comparison to those with no domains, those with 1 to 2 domains had over double the odds of CWP outcome (OR 2.15 95% CI 1.57 to 2.94) and this increased to 9 times the odds for those with 3 or more domains (OR 9.17 95% CI 5.88 to 14.28), full details can be seen in Table 5.

Table 5. Association of accumulative risk factor domains with chronic widespread pain (CWP) outcome

Number of domains present	Total Participants with domain count, n	CWP cases n, (%)*	Controls, n, (%)*	Odds Ratios with 95% CI
0 (LOW)	601	69 (11.48%)	532 (88.52%)	Referent
1 to 2 (MODERATE)	638	139 (21.79%)	499 (78.31%)	2.15 (1.57 to 2.94)
3 or more (HIGH)	116	63 (54.31%)	53 (45.69%)	9.17 (5.88 to 14.28)
*Results expressed as total number along with frequencies				

Discussion

This study describes the epidemiology of CWP within a child/adolescent UK primary care population. Five-year prevalence of CWP is 3.19%, with an increasing prevalence with rising age. Risk factors associated with CWP include mental health, neurological, genitourinary, throat problems, and gastrointestinal issues, with accumulative presence further elevating risk, highlighting both variation and complexity of risk in this population.

To our knowledge there are no directly comparable studies within primary care consultation populations, but similarities are present with other population-based cohorts. One study, using an identical age group, reported a point prevalence of 4.2% for child/adolescent fibromyalgia [3], and three UK based studies (in adolescents) report similar point prevalence of 4.1% to 4.5% for CWP [16,27,51]. Differences in prevalence rates between population cohort studies and this current primary care consultation study may be due to an under-ascertainment of CWP cases, there is potential for confounding by indication as children/adolescents who consult may have greater levels of severity. Furthermore, comparisons are also complicated by different prevalence periods (i.e. period prevalence in this current study compared with point prevalence within population cohorts), however these differences aside, our findings do suggest that many children/adolescents with CWP are also consulting in primary care. Our results demonstrated a clear rise in the prevalence of CWP as age

increased; concurring with previous research [50] and with the developmental process for CWP onset [22]. However, in contrast to adult and older adolescent general population studies where CWP is consistently more prevalent in females [4,16,27,51], our study showed male/female equivalence in distribution of CWP. Recent research, on similar child/adolescent musculoskeletal consultation populations, have greater consensus with our findings. These show patterns of transition, with males more likely to consult at earlier ages and females more at adolescence [54], or parity between sexes [61], suggesting differences in those who report pain (i.e. in the general population) and those who consult about pain (i.e. in primary care). Results also show that CWP was not distributed evenly across deprivation categories, with evidence of greater prevalence in those less deprived; a comparable finding was reported for knee pain in a similar consulting population [48]. This finding is again in contrast to the adult literature, where CWP is seen more commonly in those with greater deprivation [4,64]. Reasons for the difference between adults and children/adolescents are likely to be complex and multifactorial, but may include risk factors associated with deprivation (e.g. employment type, health behaviour) that have not had time to exert an influence on CWP development, and differing patterns of healthcare engagement associated with deprivation; with evidence that adults tend to present more and children less [21,56].

There are a number of strengths of this current study. Over 95% of the UK population are registered with a primary care general practice [7], and whilst the CiPCA database is limited to the region of North Staffordshire, there is evidence of comparability to UK national primary care databases in terms of demographics (age, sex) and to some extent, similarities in musculoskeletal and pain-based consultations [29]. It is one of a small number of studies looking exclusively at CWP in children/adolescents, and importantly reports on a broad age range (ages 8 to 18 years) compared to previous literature predominantly focused on adolescents. A further strength is the use of a scoping review to identify a broad range of potential risk factors and the ability to match the majority of these risk factors to consultation data. Another strength is the use of consultation records as this likely excludes children/adolescents with only self-limiting pain, potentially increasing clinical relevance. Furthermore, the use of consultation records reduces recall bias as the data is collected in real time. Additionally, the use of consultation records reduces response bias found in more traditional research

methodology, an issue that is particularly noted in the recruitment of children/adolescents who consult about musculoskeletal pain [47].

Some limitations are also present. This study required each patient to be registered continually for a period of five years, restricting results to 39% of the full primary care population. Due to the data extraction method (i.e. algorithm), it is unknown whether those not included were more or less likely to consult about CWP. Research has shown previously that children/adolescents who have increased residential mobility are at a heightened risk of poorer health [25]. It may be that those not included are at an increased risk, and the results presented here underestimate both risk and prevalence. Another consideration is whether the methodology identified only recurrent regional pain consulters and those with non-specific pain codes rather than 'true case' CWP, as per accepted criteria [66]. The algorithm used in this study has some validity; the original study by Mansfield et al [43] compared primary care consultation records to a large self-report survey and found that almost all (97%) identified as CWP reported pain, and that concordance with CWP status was 50%. However, this validation study was carried out within an older adult population, therefore currently validity within a child/adolescent population is unknown and potential for misclassification is present. A further issue relates to the use of Read codes within the CWP algorithm that denote injury, as it was possible that multiple injuries rather than multi-site pain are counted within the algorithm. This is important for this study's population as children/adolescents are more likely to report injury compared to adults [14,55]. There are some general limitations in the use of EHR; it was not possible to adjust for lifestyle information (e.g. physical activity, BMI), information may only be contained within free text (not included within this analysis) or not recorded at all because it was not the primary reason for the consultation. Another general issue is the time frame chosen to identify CWP within this study. Selection was arbitrary and based on available data and the time required to fulfil CWP status. A potential limitation concerns those identified as only RRPC who make up 54.2% of the CWP cohort. This criterion involves the necessity of recurrence of consultations over time to qualify for CWP status, there will be children/adolescents who at the beginning and end of the timeframe partially qualify. A further consideration is that this study is reliant on consultation data, and consultation patterns may be more reflective of parental or guardian behaviour rather than the child or adolescent themselves, and is a known issue for non-specific symptoms such as CWP [57]. Finally, the analysis approach has

limitations. A staged analysis model was chosen to allow for the understanding of prediction (stage 1) and explanation of change in the presence of other variables (stages 2 and 3), however the removal of non-significant variables before inclusion in a full model (as was the case here) could preclude "suppression" effects whereby the presence of other variables can add strength to the relationship between the risk factor and outcome. Furthermore, inspection of the variables removed at stage 1 (adverse life events, diabetes, palpitations) show that these had low cell counts (< 12 participants) and therefore could have been removed due to low power.

This study has identified a sizable proportion of children/adolescents within primary care who have CWP or are recurrent regional pain consulters, and also consult for a number of other related factors; information valuable in planning future population healthcare services. There is now a need for further follow-up studies to establish future consequences, for example whether those with child/adolescent CWP are more represented in adult populations who have pain and high healthcare engagement. This study highlights that CWP is a relatively common condition that is under-recognised in primary care and reveals the complexity of children/adolescents who have a classification of CWP. Findings show that a broad range of risk factors are associated with CWP outcome, with many children/adolescents who consult for more than two of these domains being highly likely to have pain. This finding gives some support to an allostatic load hypothesis for the development of CWP in adults [46,58] and raises the issue of whether GPs should enquire about pain in those who consult for these related factors. Research is now required to establish whether the accumulative presence of these risk factors leads to changes in physiological response (as per allostatic load) and is further related to later adult CWP. Another finding of clinical interest is on the risk factor domains that retained statistical significance; neurological, genitourinary, throat problems and gastrointestinal. Each of these domains were predominantly driven by pain-based risk factors (via inspection of the frequency of Read codes used), with three of these risk factors (headaches, cystitis and abdominal pain) being also widely associated with pain syndromes [1,12,67]. Single site musculoskeletal pain appears to be capable of triggering widespread pain [26,36,52,64], however our data also suggests that pain triggers may not be limited to just musculoskeletal pain. It may be that pain pathways of the CWP patient develop early, consequently early interventions focused on the management of pain and the consequences of pain may help prevent the development of CWP.

In conclusion this study has applied a method for identifying CWP within primary care to a child and adolescent population and identified a number of risk factors associated with onset of CWP. Future studies are now needed to understand how these risk factors contribute to the development of CWP.

Conflict of interest statement

The authors of this manuscript have no competing or conflict of interest.

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The datasets generated and/or analysed during the current study are not publicly available as they refer to individual consultation records. However summarised data is available from the corresponding author on reasonable request. Consent for publication from participants is not applicable as CiPCA is an anonymised dataset at point of use.

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