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ORIGINAL REPORT

ELEVATED PREVALENCE OF OSTEOARTHRITIS AMONG ADULTS WITH CEREBRAL PALSY

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Objective: **Adults with cerebral palsy have an increased risk of developing osteoarthritis. However, little is known about the epidemiology of osteoarthritis among this vulnerable population. The objectives of this study were to compare the prevalence of osteoarthritis between adults with and without cerebral palsy, and to determine how the prevalence of osteoarthritis changes throughout adulthood for each group.**
Design: **Data were extracted from the 2016 Optum Clinformatics® Data Mart, a nationwide database of de-identified US insurance claims, containing medical and pharmacy information on beneficiaries.**
Subjects: **International Classification of Diseases 10th revision (ICD-10) codes were used to identify adults (18+ years) with ($n = 7{,}348$) and without ($n = 8.7$ million) cerebral palsy.**
Methods: **ICD-10 codes were used to identify osteoarthritis. Prevalence of osteoarthritis was compared between adults with and without cerebral palsy before and after adjusting for age and sex. The prevalence of any type of osteoarthritis was compared between men and women with and without cerebral palsy, stratified by the following age groups: 18–30, 31–40, 41–50, 51–60, 61–70, and >70 years.**
Results: **Adults with cerebral palsy had higher prevalence and adjusted odds of any, poly, hip, knee, and other/unspecified osteoarthritis (odds ratio (OR): 1.3–2.1; $p < 0.001$), but not hand osteoarthritis (OR: 0.86; $p = 0.46$). Men and women with cerebral palsy had a higher prevalence of any osteoarthritis compared with adults without cerebral palsy across all age groups (all $p < 0.05$).**
Conclusion: **Privately-insured adults with cerebral palsy had a higher prevalence of osteoarthritis compared with adults without cerebral palsy across the adult lifespan.**

Key words: osteoarthritis; epidemiology; cerebral palsy.

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LAY ABSTRACT

The aim of this study was to compare the prevalence of osteoarthritis between adults with and without cerebral palsy. Data were collected from the 2016 Optum Clinformatics® Data Mart, a nationwide de-identified US insurance claims database, containing medical and pharmacy information on beneficiaries. International Classification of Diseases 10th revision (ICD-10) codes were used to identify adults (age 18+ years) with and without cerebral palsy. ICD-10 codes were also used to identify osteoarthritis. Prevalence of osteoarthritis was compared between adults with ($n = 7{,}348$) and without ($n = 8.7$ million) cerebral palsy, before and after adjusting for age and sex. The results showed that adults with cerebral palsy had a higher prevalence and adjusted odds of any, poly, hip, knee, and other/unspecified osteoarthritis. Men and women with cerebral palsy had a higher prevalence of any osteoarthritis compared with men and women without cerebral palsy across all age groups. Adults with cerebral palsy had a higher prevalence of osteoarthritis compared with adults without cerebral palsy across the adult lifespan.

Osteoarthritis (OA) is a pathological condition of the synovial joints, characterized by localized articular cartilage damage and loss of tissue. OA is a debilitating condition associated with pain, fatigue, activity-interference (1), frailty (2) and reduced quality of life (3). OA accounts for a considerable economic burden (3). The burden of OA, determined by disability-adjusted life-years, has increased by 35% over recent decades (4); OA is now a leading cause of global disability (5). Risk factors for OA include age, sex, excess body fat, and joint-related stress injury (6). Populations with paediatric-onset biomechanical alterations and musculoskeletal deficits may be at risk for developing early-onset OA, which can negatively impact rehabilitation strategies aimed at improving function and health.

Cerebral palsy (CP) is a neurological syndrome that results from a non-progressive disturbance to the central nervous system around the time of birth, and is the most common paediatric-onset physical disability (7). The majority of individuals with CP have musculoskeletal malformations, muscle spasticity, and flexion contractures, which alter biomechanics and increase localized joint stress. Children with CP also have low levels of physical activity and an underdeveloped musculoskeletal system (8). As a result, the prevalence of musculoskeletal disease in young adults with CP is more than 10 times higher than in those without CP (9). Furthermore, disparities in the prevalence of

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musculoskeletal disease become more pronounced throughout adulthood (10). In addition to altered biomechanics, inadequate development and poor preservation of muscle and bone may increase the risk of OA. However, associations between musculoskeletal mass and function with OA may be influenced by sex (11, 12) and body mass index (11). Previous studies have shown that children with CP have higher total body (13), abdominal (14), and musculoskeletal (8) fat compared with matched typically developing children.

While individuals with CP are at increased risk for early development of OA, the epidemiology of OA for this population is not well characterized. Using medical records, recent studies in adults with CP have reported the prevalence of any type of OA to be 5.4% in 18–30-year-olds (9, 10), and up to 34% among adults >50 years of age (10). The latter estimate is higher than the 13–25% reported for the general population of men and women >65 years of age (15). Moreover, middle-aged women with CP may be at greater risk for OA than middle-aged men with CP (16).

Previous studies on CP and prevalence of OA (9, 10, 16) have significant limitations. Data were taken from a single medical system in the Southeast region of Michigan, USA, and prevalence of OA was not examined by age and sex. Additional research is needed to determine the prevalence of OA in adults with CP across the USA, and to identify age and sex trajectories (16). This knowledge could inform clinical and rehabilitation strategies aimed at improving health and function throughout the adult lifespan for this population. Therefore, the primary objective of this study was to compare the prevalence of OA between adults with and without CP, using a large, nationwide private insurance database. It was hypothesized that men and women with CP would have a higher prevalence of OA compared with those without CP across the adult lifespan.

MATERIAL AND METHODS

Data source

Data were from the Clinformatics® Data Mart Database (OptumInsight™, Eden Prairie, MN, USA). This database is a nationwide de-identified insurance claims database of beneficiaries from a single private payer in the USA, and contains information on beneficiaries with medical and pharmacy coverage. Data are de-identified and patient consent was waived. The University of Michigan Institutional Review Board approved this study as non-regulated.

Sample selection

Data were obtained from 2016, the most recent available year. Beneficiaries who were 18 years of age and older, had 12 full months of continuous enrolment, and had at least one medical service utilization in 2016 (to determine any medical diagnoses) were considered for this study. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes were used to identify all medical conditions. CP was identified by at least one medical claim using the G80 family of ICD-10 codes, covering all diagnostic subtypes of CP (e.g. spastic quadriplegic, tetraplegic). Data regarding severity of CP using common clinical measures (e.g. gross Motor Function Classification System) are not available in administrative claims. Furthermore, over 70% of the cohort had "other" or "unspecified" CP, thus not allowing us to stratify or account for the clinical subtypes of CP (e.g. spasticity/athetoid, hemiplegic) in the current study. Using a single medical claim to identify a paediatric-onset disability using administrative claims data has shown approximately 80% positive predictive value and 99% sensitivity (17). Beneficiaries with no medical claims for CP represented the group without CP (i.e. control subjects). Beneficiaries who had unknown or missing data for sex were excluded ($n=991$, <0.01% of total sample). The final sample consisted of 8,739,803 beneficiaries, including 7,348 adults with CP.

Osteoarthritis

Any OA was defined as a single claim for the following conditions (ICD-10 code): poly OA (e.g. OA in multiple joints; M15 family); hip OA (M16 family); knee OA (M17 family); first carpometacarpal joint OA (herein referred to as "hand OA"; M18 family); and other/unspecified OA (M19 family).

Sociodemographic and socioeconomic variables

Sociodemographic and socioeconomic variables included age, sex, ethnic group, education level, and household annual income. Guided by previous studies of musculoskeletal health among adults with CP (9, 10), age was stratified into the following groups to reflect different stages of the adult lifespan: 18–30, 31–40, 41–50, 51–60, 61–70 and >70 years of age.

Statistical analysis

Data for the entire sample were summarized as mean (standard deviation (SD)) for continuous variables and percentage (frequency) for categorical variables. Multivariable logistic regression analyses were performed with each OA variable as the outcome. CP group (reference: without CP) was included as the primary exposure variable. Age (as continuous) and sex were included as covariates. The interaction between CP group with sex and CP group with age group for each OA outcome was examined. If significant, subsequent analyses were performed after stratifying by that variable. The main effect of CP group was interpreted for all models. Ethnicity, education level, and household annual income were not initially included as covariates due to the extent of missingness/unknown (4.6–30.6%). However, a sensitivity analysis was conducted by further adjusting the multivariable logistic regression model for ethnicity, education level, and household annual income for participants with complete data.

Unadjusted prevalence of any OA was also determined for each age group and sex. We chose to examine any OA because of the extent of "other" or "unspecified" OA, which may bias results for prevalence of location-specific OA (e.g. hip, knee). Unadjusted logistic regression analyses were performed for each age group and sex, with any OA as the outcome and CP group as the primary exposure variable.

Table I. Descriptive characteristics of adults with and without cerebral palsy (CP)

Descriptive characteristics	With CP (n = 7,348) % (n)	Without CP (n = 8,732,455) % (n)
Age, mean (SD)	49.8 (18.2)	55.2 (18.6)
18–30 years	20.0 (1,467)	12.4 (1,083,125)
31–40 years	14.1 (1,034)	13.1 (1,141,701)
41–50 years	14.5 (1,066)	14.5 (1,264,473)
51–60 years	19.6 (1,437)	17.0 (1,486,496)
61–70 years	18.6 (1,364)	18.9 (1,648,551)
> 70 years	13.3 (980)	24.1 (2,108,109)
Sex		
Female	49.2 (3,615)	55.3 (4,826,637)
Male	50.8 (3,733)	44.7 (3,905,818)
Ethnicity		
White	57.0 (4,190)	55.9 (4,882,512)
Black	11.6 (855)	8.0 (698,549)
Hispanic	8.3 (607)	9.0 (781,721)
Asian	1.8 (130)	3.8 (334,945)
Unknown/missing	21.3 (1,566)	23.3 (2,034,728)
Education		
Less than high school	0.5 (35)	0.5 (47,275)
High school diploma	32.1 (2,358)	25.3 (2,209,051)
More than high school	62.9 (4,618)	69.6 (6,074,054)
Unknown/missing	4.6 (337)	4.6 (402,075)
Household annual income		
< 40,000 US$	24.6 (1,810)	16.8 (1,462,452)
40–59,900 US$	11.5 (845)	11.7 (1,019,787)
60–99,900 US$	16.2 (1,191)	21.4 (1,865,676)
≥ 100,000 US$	17.1 (1,253)	28.2 (2,463,266)
Unknown/missing	30.6 (2,249)	22.0 (1,921,274)

SD: standard deviation.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). All assumptions for statistical tests were met. $p \leq 0.005$ (2-tailed) was used to determine statistical significance for this large sample, as recommended by a coalition of methodologists to detect new discoveries (18, 19). Effect estimates were reported as odds ratios (OR) with 99.5% confidence intervals (95% CI).

RESULTS

Descriptive characteristics for adults with CP (n = 7,348) and without CP (n = 8.7 million) are shown in Table I. The proportion of adults aged 18–30 years was higher for CP (20.0%, 12.4%), and the proportion of adults > 70 years of age was lower for CP (13.3%, 24.1%).

The prevalence of OA in adults with and without CP, as well as the adjusted odds for each type of OA, is shown in Table II. After adjusting for age and sex, and compared with adults without CP, adults with CP had higher odds of any OA, poly OA, hip OA, knee OA, and other/unspecified OA (ORs 1.34–2.28; all $p < 0.005$), but not hand OA (OR 0.86; 99.5% CI 0.48–1.54; $p = 0.459$). The group by sex interaction was only significant for hip OA ($p < 0.005$). After stratifying by sex, men with CP had higher age-adjusted odds of hip OA compared with men without CP (OR 2.47; 95% CI 1.87–3.27), and women with CP had higher age-adjusted odds of hip OA compared with women without CP (OR 1.72; 95% CI 1.29–2.30). Of the OA outcomes that were significantly different between groups, the CP group by age group interaction was significant for any OA, hip OA, knee OA, and other/unspecified OA (all $p < 0.005$). After stratifying by age group, the sex-adjusted odds were higher for all age groups for any OA (ORs 1.72–4.09; all $p < 0.005$), hip OA (ORs 1.54–10.93; all $p < 0.005$), and other/unspecified OA (ORs 1.79–4.80; all $p < 0.005$), and were higher for all age groups for knee OA (ORs 1.42–3.33; all $p < 0.005$) except for 61–70 year olds (OR 1.10; $p = 0.277$) or > 70 year olds (OR 0.99; $p = 0.930$). The younger age groups tended to have higher odds than the older age groups for CP (e.g. any OA: 18–30 years, OR 4.09; > 70 years, OR 1.72). Sensitivity analysis including individuals with complete data on all covariates (n = 5,865,485) revealed that, for each of the OA measures, the addition of ethnicity, education level, and household annual income had little impact on the main effect of CP group (Table II) and the conclusions were the same as the primary analysis.

The unadjusted prevalence of any OA across age and sex strata is shown in Fig. 1. There was an increasing trend of any OA for men and women with and without CP. The unadjusted OR for any OA was higher for men and women across all age groups, and tended to be higher for the younger age groups compared with the older age groups (Table III).

Table II. Prevalence and adjusted odds of osteoarthritis (OA) among adults (≥ 18 years) with and without cerebral palsy (CP)

	With CP (n = 7,348) % (n)	Without CP (n = 8,732,455) % (n)	Adjusted odds[a] (ref: without CP) OR (99.5% CI)	Adjusted odds[b] (ref: without CP) OR (99.5% CI)
Any OA	20.3 (1,489)	15.1 (1,314,760)	2.11 (1.93–2.30)	1.88 (1.68–2.11)
Poly OA	3.9 (288)	2.5 (222,199)	2.28 (1.92–2.71)	1.76 (1.38–2.24)
Hip OA	2.8 (205)	1.9 (161,614)	2.05 (1.68–2.51)	1.91 (1.46–2.49)
Knee OA	6.0 (437)	5.8 (510,404)	1.34 (1.16–1.54)	1.36 (1.14–1.63)
Hand OA	0.3 (23)	0.5 (41,037)	0.86 (0.48–1.54)	1.23 (0.64–2.35)
Other/unspecified OA	13.0 (953)	8.5 (740,533)	2.28 (2.06–2.53)	2.07 (1.81–2.36)

[a]Adjusted for age and sex; n = 8,739,803.
[b]Adjusted for age, sex, ethnicity, education level, and household annual income for participants with complete data; n = 5,865,485.
OR: odds ratio; CI: confidence interval.

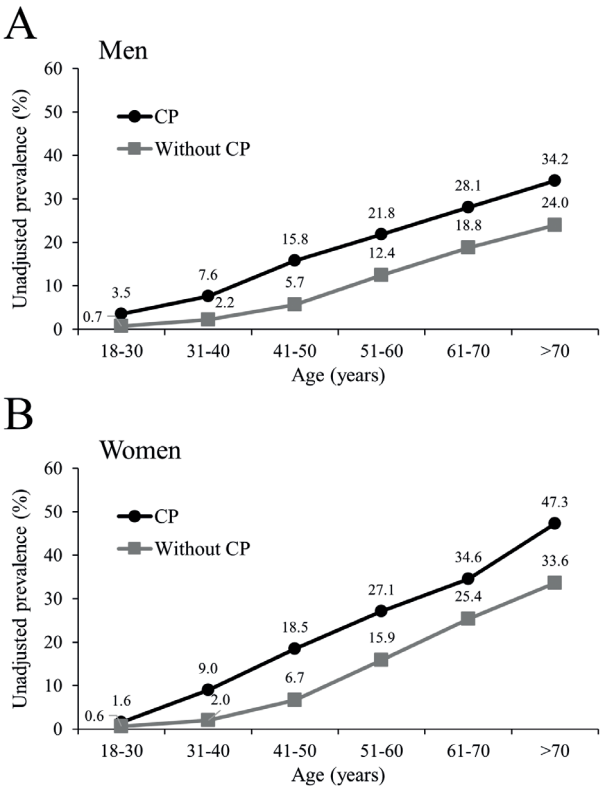

Fig. 1. Unadjusted prevalence of any osteoarthritis (i.e. poly, hip, knee, hand, other/unspecified osteoarthritis) among (A) men and (B) women, with and without cerebral palsy (CP).

DISCUSSION

This study found that privately-insured men and women with CP have higher prevalence of OA compared with men and women without CP across adulthood. The group by sex interaction for hip OA in the entire sample suggests that, while hip OA was higher for men and women with CP compared with men and women without CP, there were disproportionately higher odds in men with CP than would be expected from the privately-insured population without CP. Furthermore, the CP group by age group interaction revealed that, while adults with CP across all age groups had higher odds for OA, the younger age groups had disproportionately higher odds than the older age groups for both men and women, suggesting an early onset of OA for adults with CP. These findings provide large, national-level data to support the need for earlier preventive and health management services for OA and its related health and functional complications among adults with CP. This is important because pharmacological (20), self-management, and exercise (21) interventions have been shown to reduce patient burden of OA in non-CP populations. Whether such interventions would be beneficial for adults with CP requires future research.

The hips and knees are especially debilitating locations for OA, due to weight-bearing and resulting gross motor function limitations. In the current study, the prevalence of hip OA for the entire sample of adults without CP was 1.9%, which is consistent with the Global Burden of Disease prevalence estimate of 1.6% for men and 2.1% for women in high-income North America (5). The prevalence of knee OA for the sample of adults without CP was 5.8%, which is consistent with a previous population-based study in North America (15), but slightly higher than the Global Burden of Disease prevalence estimate of 3.1% for men and 5.0% for women in high-income North America (5). Differences in prevalence estimates are probably due to differences in methodology, with the Global Burden of Disease yielding conservative estimates (5).

Data from the current study represent the largest known sample of claims data for adults with CP evaluated for prevalence of OA. It was found that adults with CP were more likely to have all OA measures, except for hand OA, compared with adults without CP. When stratified by sex, it was found that the prevalence of any OA was higher for men and women with vs without CP throughout the adult lifespan. However, the prevalence of any type of OA among adults with CP from the current study is lower than we have previously published from a clinical sample of adults with CP from the Southeast Michigan region (n=1,395 men and women: 18–30 years, 5.4%; 31–40 years, 13.4%; 41–50 years, 23.1%; >50 years, 33.9%) (9, 10), which may be due to differences in CP sample characteristics. In our previous studies (9, 10), approximately half of the sample had moderate-to-severe forms of CP. In the current study, the sample of adults with CP probably reflects a healthier and higher functioning segment of the CP population (22), although this is speculation, as it is not possible to determine the severity of CP using administrative claims data. To be enrolled with a private health plan, beneficiaries must be able to afford their own insurance or be covered through their employer, parents (up to 26 years of age), or their spouse. Individuals with paediatric-onset disabilities, such as CP, tend to have low employment and marriage rates (23), which may be exacerbated with more severe

Table III. Unadjusted odds of osteoarthritis (OA) among adults (≥18 years) with cerebral palsy (CP) and without CP (reference) stratified by sex and age group

Age group	Men OR (99.5% CI)	Women OR (99.5% CI)
18–30 years	4.98 (2.87–8.65)	2.84 (1.21–6.68)
31–40 years	3.76 (2.35–6.00)	4.79 (3.12–7.36)
41–50 years	3.09 (2.23–4.27)	3.19 (2.31–4.40)
51–60 years	1.96 (1.53–2.51)	1.97 (1.55–2.51)
61–70 years	1.69 (1.34–2.15)	1.55 (1.24–1.95)
>70 years	1.65 (1.24–2.19)	1.77 (1.40–2.26)

OR: odds ratio; CI: confidence interval.

forms of CP. To support this notion, in a previous study leveraging the same database and of the same year, the prevalence of comorbid neurodevelopmental disabilities (i.e. intellectual disabilities, autism spectrum disorders) for adults with CP was lower than expected (24). The presence of comorbid neurodevelopmental disabilities increases the medical needs and complexity of CP (25). Therefore, prevalence estimates are probably conservative, leading to more modest effect sizes reported in this study. Nevertheless, the findings have important implications for public health. The burden of OA, represented as disability-adjusted life years, has substantially increased over recent decades (4). By 2032, predictions have estimated an additional 26,000 per million adults >44 years of age will utilize healthcare services for OA compared with 2012 (26). The adult population with CP is projected to expand over the coming decades (27, 28), and given their early OA profile, this may lead to a disproportionate increase in the disease and economic burden of OA attributable to CP.

Many factors may contribute to the early development of OA for adults with CP, some of which may originate in childhood. The aetiology of CP leads to altered neuromuscular control and gait mechanics (29), low levels of physical activity (8), and a predisposition for inadequate accrual of muscle and bone (8) throughout growth and development. There are also a number of skeletal deformities, malalignments, and problems of the lower extremities present among individuals with CP (30–32), such as greater femoral anteversion, hip subluxation and joint dislocation. The motor function and musculoskeletal pathological phenotype in childhood is confounded by several CP-related factors (33), including the type of CP (e.g. spastic, dyskinetic, ataxic), the anatomical distribution of affected areas (e.g. hemiplegia, diplegia, quadriplegia), and the level of gross motor functional ability (e.g. independent ambulation, use of assistive walking devices or wheelchair). Furthermore, the degree to which muscles are affected (e.g. severity), how they are affected (e.g. spasticity) and the number of affected muscles plays a large, interactive role on joint health by altering articular surface stresses incurred during movement; all of which may lead to localized joint damage and increased risk for OA.

The health and functional problems experienced in childhood increase in severity as these individuals age into their adult years (34, 35). In the first stage of adulthood, 18–30-year-olds with CP have a similar musculoskeletal disease prevalence as the general population of adults ≥50 years of age (36), which becomes more prevalent throughout their lifespan (10). Taken together, long-term altered mechanical loading patterns and insufficient musculoskeletal integrity, function, and structure, especially of regions surrounding lower extremity joints, may impose additive risk for early development of OA (11, 12).

It is also important to note that OA is implicated in the pathogenesis of cardiometabolic diseases (37) and mental health disorders (38) among adults without CP. Adults with CP have elevated cardiometabolic disease prevalence (9), higher incidence of depression and anxiety (39), and 2–3-fold increased risk of cardiovascular mortality (40) compared with adults without CP. While it is unknown how OA associates with non-communicable diseases and mortality among adults with CP, OA has been shown to amplify daily pain levels and negatively affect function and activities of daily living for adults without CP (1). The association of OA with mental health disorders may affect adults with CP to a greater extent than adults without CP, possibly through pathways of lower societal integration at earlier ages. Studies are needed to determine if physical activity-based interventions can slow the onset of OA or reduce the worsening of OA progression for adults with CP, which may also have a positive impact on reducing the burden of other non-communicable diseases.

This study has several limitations. First, it was not possible to determine the severity of CP using administrative claims data. However, the overall CP sample may reflect a healthier and higher functioning segment of the CP population, thus biasing results to be more conservative. Furthermore, the prevalence of CP in this privately insured cohort of adults was 0.84 per 1,000, which is lower than the previously reported 3.1 per 1,000 in children (41); however, no adequately designed or powered epidemiological studies have examined the prevalence of CP among adults. Secondly, we used a single claim to define CP and OA. Previous validation studies have shown that using 2 or more claims for a medical condition tends to improve the accurate identification of that medical condition (17, 42). However, accurately identifying medical conditions depends on the number of years for the study period (43) and the medical condition examined (17, 43, 44). Given the short study period of 12 months, requiring 2 or more claims for OA may have introduced disproportionate risk of biasing estimates to be lower from patients without CP. Adults with CP have complex healthcare needs and are more likely to utilize healthcare resources, which would provide more opportunities to be "flagged" for OA. Taken together, the selected methodology to identify OA is probably sufficient to reasonably detect that the current data is evidence of differences in OA prevalence across groups. Thirdly, administrative claims data are subject to errors, such as inaccurate coding of medical

diagnoses. Fourthly, there was a considerable extent of other/unspecified OA in the Optum database for both groups. The prevalence was 13.0% and 8.5% for adults with and without CP, respectively, which accounted for approximately 64.0% and 56.3% of all OA patients with and without CP, respectively. Therefore, this study was unable to provide reliable age- and sex-stratified prevalence estimates of site-specific OA, such as OA of the hip and knee.

In conclusion, privately-insured men and women with CP have an early onset of OA and higher prevalence of OA across the adult lifespan compared with men and women without CP. These findings highlight the need for earlier screening strategies and preventive services to capture the early OA phenotype present among adults with CP. Future studies are needed to design tailored interventions aimed at preventing the onset of OA, slowing the progression of OA, and managing OA-related health problems (e.g. pain, development of non-communicable diseases) for adults with CP.

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