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Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2020;■:■■■-■■■

REVIEW ARTICLE (META-ANALYSIS)

Epidemiology of Cerebral Palsy in Adulthood: A Systematic Review and Meta-analysis of the Most Frequently Studied Outcomes

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Abstract

Objective: To describe the epidemiology of health status, impairments, activities and participation in adults with cerebral palsy (CP).

Data Sources: Embase, MEDLINE, Web of Science, PsycINFO, Cumulative Index to Nursing and Allied Health, Cochrane, and Google Scholar were searched for 3 themes ("cerebral palsy," "adult," and "outcome assessment") in literature published between January 2000 and December 2018.

Study Selection: Full-article peer-reviewed English journal articles on descriptive, observational, or experimental studies describing the most studied outcomes in adults with CP (n≥25, age≥18y) were included. Studies were included in the analyses if frequently studied outcomes were described in at least 3 studies using similar methods of assessment.

Data Extraction: Data were extracted independently by 2 authors from 65 articles (total N=28,429) using a standardized score sheet.

Data Synthesis: Meta-analyses revealed that overall, on average 65.1% (95% confidence interval [CI], 55.1-74.5) of adults with CP experienced pain, 57.9% (95% CI, 51.1-64.6) were ambulant, 65.5% (95% CI, 61.2-69.7) had little or no limitation in manual ability, 18.2% (95% CI, 10.6-27.2) had tertiary education, 39.2% (95% CI, 31.5;47.1) were employed, and 29.3% (95% CI, 9.0-55.3) lived independently. In adults without intellectual disability, proportions of individuals who were ambulant (72.6% [95% CI, 58.8-84.5]) and lived independently (90.0% [95% CI, 83.8-94.9]) were higher ($P=.014$ and $P<.01$, respectively). The Fatigue Severity Scale score was 4.1 (95% CI, 3.8-4.4). Epilepsy (28.8% [95% CI, 20.1-38.4]) and asthma (28.3% [95% CI, 18.7-38.9]) were especially prevalent comorbidities.

Conclusions: The present systematic review and meta-analysis on the epidemiology of adults with CP provided state-of-the-art knowledge on the most frequently studied outcomes. On average, adults with CP are fatigued, and a majority experience pain, are ambulant, and have little or no difficulty with manual ability. On average, 40% are employed and 30% live independently. More uniformity in assessment and reports is advised to improve knowledge on epidemiology and gain insight in more outcomes.

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Cerebral palsy (CP) is an umbrella-term describing "a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behavior, by epilepsy and by secondary musculoskeletal problems"[1(p9)] and it affects 2 to 2.5 per 1000 live births.[1-4] Approximately three-fourths of persons with CP are adults (ie, 18 years or older).[5]

In the past decades, attention for adults with CP in rehabilitation practice and research increased.[6] Aging with CP comes with several issues in health and functioning. Recently, several comorbidities were increased in adults with CP, including asthma

Supported by Rijndam Rehabilitation, Rotterdam, The Netherlands.
Disclosures: none

0003-9993/20/$36 - see front matter © 2020 by the American Congress of Rehabilitation Medicine
https://doi.org/10.1016/j.apmr.2020.01.009

and hypertension.[7,8] Pain and fatigue are common in adults with CP,[9] and pain, mobility, and self-care deteriorate over time.[10,11] In addition, young adults with CP are less often employed or live independently than young adults without CP.[12,13] Moreover, activity limitations and difficulty in participation increase with aging.[10,14]

Common impairments and functional limitations in children with CP were previously studied in a systematic review,[15] but systematic knowledge on adults with CP is scarce. Because differences were found in epidemiology between children and adults with CP,[16] results cannot be extrapolated to the adult CP population. Insight into the prevalence of impairments and level of functioning in adults with CP would be helpful to guide rehabilitation follow-up programs. In addition, such insight would contribute to a better understanding of the effect of CP at adult age. Therefore, this review and meta-analysis aims to describe the health status, prevalence of impairments, and level of activities and participation of adults with CP using published literature. We focused on the most frequently studied outcomes in adults with CP from the literature, which were reported in a recently published review by Benner et al.[6]

Methods

Search strategy

The search strategy, which was developed in consultation with an information specialist, was used in 7 databases (Embase, MEDLINE, Web of Science, PsycINFO, Cumulative Index to Nursing and Allied Health, Cochrane, and Google Scholar) and consisted of 3 themes ("cerebral palsy," "adult," and "outcome assessment"). Key terms were mapped to controlled headings and expanded to include free text terms, tailored to the specific database. See Benner et al for the complete search strategy.[6] Literature was searched from 2000 through 2018 because the search used in Benner et al was updated with publications from 2017 and 2018. After deduplication, all publications were screened for eligibility on title and abstract and subsequently full text by 2 independent reviewers (J.B., S.N. for publications in 2000-2016; M.vG., S.H. for 2017-2018), disagreements were discussed and resolved between the 2 reviewers. If disagreement remained this was discussed with a third reviewer (M.R.) to reach consensus.

Eligibility criteria

Studies were included if they met the following criteria: (1) They reported on the most frequently studied outcomes according to the systematic review of Benner et al.[6] From this list of outcomes single-item outcomes (eg, pain) were selected if at least 10 studies provided information on this outcome; multi-item outcomes (eg, Fatigue Severity Scale [FSS]) were selected if at least 5 studies provided information. (2) At least 3 studies reported on an outcome using similar methods of assessment, enabling comparison and meta-analysis. (3) Study design was descriptive, observational, or experimental. Meta-analyses, reviews, case studies, qualitative studies, comments, and study protocols were excluded. (4) They were full-article peer-reviewed journal articles written in English. (5) They described individuals with CP only or in case-control design. (6) They described ≥25 adults who were 18 years or older at the time of the first measurement or at follow-up. Studies describing both children and adults with CP were included when at least 50% of the sample were adults. (7) They reported on outcomes of functioning, excluding studies reporting on evaluations of services, for example, evaluation of transition services or complications and adverse events during or after surgery. (8) Study samples were population based or rehabilitation based, or samples addressed a substantial subgroup of individuals with CP (eg, Gross Motor Function Classification System [GMFCS] I-III, bilateral spastic CP, dyskinetic CP). Nonrepresentative samples that consisted of adults selected because of having specific impairments (eg, pain, fatigue, incontinence) or because of previous operations (eg, selective dorsal rhizotomy, constructive hip operations) were excluded. For intervention studies, only baseline observations were included. When outcomes were reported in multiple publications on the same study sample, the most recently observed outcome was included.

List of abbreviations:

BMI	**body mass index**
CI	**confidence interval**
CP	**cerebral palsy**
FSS	**Fatigue Severity Scale**
GMFCS	**Gross Motor Function Classification System**
ICF	**International Classification of Functioning, Disability and Health**
ID	**intellectual disability**
MACS	**Manual Ability Classification System**
SF-36	**Short Form-36 Health Survey**

Outcomes

Frequently studied outcomes identified by Benner et al were grouped in line with the International Classification of Functioning, Disability, and Health (ICF) as health status, impairments, or activities and participation, with the first group encompassing outcomes that were not covered by the ICF or were linked to more than 1 component.[6,17] These outcomes are depicted in the first column of Table 1. Health status outcomes addressed weight status (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared], obesity), fat mass (waist circumference), comorbidities, and the domains of the Short Form-36 Health Survey, (SF-36) (scale range 0-100, with the physical health component score on a T score metric with a mean of 50 and SD of 10 for the US general population).[78] Comorbidities included epilepsy, diabetes, hypertension, asthma, stroke, heart disease, and osteoarthritis. The impairments addressed pain (presence of any pain, including the outcomes pain in joints and pain in body part[6]), fatigue (assessed using the FSS, scale range 1-7)[79] and mobility of joints (limited range of motion in knee or hip). Outcomes referring to the level of activities and participation were walking status (ambulant with or without assistive device as primary method of mobility in daily life), which included the outcomes walking or moving around using assistive devices and assistive devices for mobility[6]), fine hand use (Manual Ability Classification System [MACS] level I or II, manual ability),[80] education status (attending or completing tertiary education according to the international standard classification of education; ie, higher education, college and university),[81] employment status (having remunerative employment), living status (living independently), and activities and social roles, assessed using the Assessment of Life Habits questionnaire, Life-H (scale range 0-9).[82] Although frequently studied according to Benner et al,[6] we

Table 1 Characteristics of included studies

Author*	Country†	N	ID (%)	GMFCS I-III (%)	Age (y), Mean (Range)	% Male
Ballester-Plané et al[18]	Spain[a]	52	Mixed	56	25 (7-62)	54
Laporta-Hoyos et al[19]	Spain[a]	39	Mixed	64	21 (6-62)	51
Whitney et al[20]	USA[b]	1395	Mixed	54	18 to >50	48
Whitney et al[8]	USA[b]	452	Mixed	51	24 (18-30)	43
Cremer et al[21]	USA[b]	435	Mixed	54	50 (40-60)	46
Cremer et al a[21]	USA[b]	201	Mixed	55	48 (40-60)	100
Cremer et al b[21]	USA[b]	234	Mixed	53	50 (40-60)	0
Ágústsson et al[22]	Sweden[c]	830	Mixed	57	23 (16-73)	56
Alriksson-Schmidt et al[23]	Sweden[c]	102	Mixed	72	21 (18-24)	62
Rodby-Bousquet et al[24]	Sweden[c]	102	Mixed	72	21 (19-23)	62
van Gorp et al a[25]	The Netherlands[d]	67	31	67	25 (21-27)	67
van Gorp et al b[25]	The Netherlands[d]	54	0	82	32 (29-34)	54
van Meeteren et al[26]	The Netherlands[d]	83	0	87‡	20 (18-22)	59
Nieuwenhuijsen et al[27]	The Netherlands[d]	87	0	90	20 (18-22)	59
Benner et al[10]	The Netherlands[e]	49	22	80	40 (34-45)	55
Benner et al[12]	The Netherlands[e]	49	22	80	40 (34-45)	55
van der Dussen et al[28]	The Netherlands[e]	80	28	71§	21-31	51
Kirk et al a[29]	Denmark[f]	22	Mixed	100	34 (18-57)	68
Kirk et al b[29]	Denmark[f]	22	Mixed	100	37 (18-59)	55
McPhee et al[30]	Canada[g]	42	Mixed	57	34 (18-75)	50
McPhee et al[31]	Canada[g]	42	Mixed	57	34 (18-75)	50
Slaman et al a[32]	The Netherlands[h]	28	0	100	20 (16-24)	43
Slaman et al b[32]	The Netherlands[h]	29	0	98	20 (16-24)	52
Russchen et al[33]	The Netherlands[h]	56	0	100	20 (16-24)	48
Slaman et al[34]	The Netherlands[h]	57	0	98	20 (16-24)	47
Ryan et al[35]	Ireland	55	Mixed	75	38 (18-65)	56
Morgan et al[36]	Australia	34	0	100	44 (26-65)	44
Morgan et al[37]	Australia	25	16	100	41 (30-65)	36
Reddihough et al[38]	Australia	335	50	63	25 (20-30)	51
van der Slot et al[39]	The Netherlands[i]	43	0	95	37 (25-45)	63
van der Slot et al a[39]	The Netherlands[i]	27	0	95	37 (25-45)	100
van der Slot et al b[39]	The Netherlands[i]	16	0	95	37 (25-45)	0
van der Slot et al[40]	The Netherlands[i]	56	0	93	36 (25-45)	63
van der Slot et al[41]	The Netherlands[i]	56	0	93	36 (25-45)	63
van der Slot et al a[41]	The Netherlands[i]	35	0	93	36 (25-45)	100
van der Slot et al b[41]	The Netherlands[i]	21	0	93	36 (25-45)	0
Opheim et al[42]	Norway[j]	149	0	93	40 (24-76)	51
Opheim et al[11]	Norway[j]	149	0	93	40 (24-76)	51
Jahnsen et al[43]	Norway[j]	406	0	78§	34 (18-72)	51
Jahnsen et al[44]	Norway[j]	406	0	78§	34 (18-72)	51
Jahnsen et al[45]	Norway[j]	766	0	Mixed	34 (18-72)	52
Maltais et al[46]	Canada	132	Mixed	60	28 (20-41)	50
Michelsen et al[47]	Denmark[k]	416	20	88§	32 (29-35)	58
Michelsen et al[48]	Denmark[k]	819	20	84§	29 (21-35)	58
Engel et al[49]	USA	100	0	18	38 (19-71)	55
Fortuna et al[7]	USA	229	54	55§	18 to >60	59
Gillet et al[50]	Australia	33	Mixed	100‡	25 (15-51)	55
Lundh et al[51]	Sweden	50	Mixed	100	32 (22-67)	54
Park et al[52]	USA	229	0‖	51	40 (20-69)	60
Peterson et al[53]	USA	2659	Mixed	Mixed	Median (IQR): 36 (25-48)	52
Sienko et al[54]	USA	97	41¶	65	24 (18-30)	48
Smith et al[55]	UK	1705	21	Mixed	33±16	53
Daunter et al[56]	USA	50	0‖	70	27 (18-35)	48
de Albuquerque Botura et al[57]	Brazil	93	Mixed	0	18-57	56
Hayward et al[58]	USA	375	24¶	63	36 (18-76)	0
Park et al[59]	Korea	53	Mixed	63‡	31±14	62
Vukojevic et al[60]	Bosnia and Herzegovina	100	55	Mixed	18-58	62

(*continued on next page*)

Table 1 (*continued*)

Author*	Country†	N	ID (%)	GMFCS I-III (%)	Age (y), Mean (Range)	% Male
Yildiz et al[61]	Turkey	117	26#	74	25 (18-62)	55
Brunton et al[62]	Canada	111	0‖	78	19 (14-31)	50
Peterson et al[63]	USA	1015	Mixed	Mixed	58 (57-60)	66
Peterson et al[64]	USA	112	Mixed	52	34±13	46
Huang et al[65]	Taiwan	279	28	50§	26 (20-40)	61
Nedjad et al[66]	Sweden	156	62¶	27§	37 (19-43)	55
Mesterman et al[67]	Israel	95	35	83§	23 (18-30)	61
Gaskin et al[68]	Australia	51	0	45	38 (19-66)	63
Andersson et al a[69]	Sweden	13	0	100	36 (26-58)	64
Andersson et al b[69]	Sweden	12	0	100	36 (26-58)	64
Sandstrom et al[70]	Sweden	48	20¶	71	33 (20-?)	48
Strauss et al[71]	USA	14,806	Mixed	62§	20-85	53
Andersson et al[72]	Sweden	221	0	Mixed	36 (20-58)	57
Bottos et al[73]	Italy	72	41	76§	33 (19-65)	60
Furukawa et al[74]	Japan	81	Mixed	73§	36 (26-57)	44
Hodgkinson et al[75]	France	234	Mixed	0	28 (15-?)	59
Maruishi et al[76]	Japan	256	43	Mixed	32 (17-83)	55
Murphy et al[77]	USA	101	Mixed	Mixed	43 (19-74)	52

NOTE. Mixed: no exact proportion reported, also no in- or exclusion criteria regarding cognition or mobility.
Abbreviation: IQR, interquartile range.

* Letters a or b after the authors name (ie, Cremer et al a) indicate subsamples of 1 publication.
† Letters indicate publications on the same study sample in a country.
‡ Proportion of GMFCS level I and II.
§ No GMFCS level reported; proportion walking with or without walking aid.
‖ Those unable to complete questionnaires were excluded.
¶ Proportion proxy report.
# Proportion illiterate, but individuals with severe cognitive impairments were excluded.

did not estimate overall results for the following outcomes because these were only reported in 1 or 2 included studies using a similar assessment method: spasticity, muscle power, hip displacement, gait pattern, speech, spinal deformities of thoracic, lumbar and sacral column, Barthel Index,[83] FIM,[84] Gross Motor Function Measure,[85] Functional Mobility Scale,[86] and Japanese Orthopaedic Association Score.[87]

Data extraction

A standardized data extraction record sheet was used to collect study sample characteristics and outcomes. Sample characteristics included country, sample size, sex, age, proportion with intellectual disability (ID), and proportion with level of GMFCS I-III.[88] Studies including any proportion of individuals with ID or those that did not mention exclusion based on intellectual function, suggesting individuals with ID could be part of the sample, were reported as mixed samples. Studies including only individuals without ID are further referred to as no ID samples. With respect to the outcomes, the method of assessment and the outcome (proportion [%], or mean/median scores [SD/interquartile range]) were noted.

Analysis

Overall results with corresponding 95% confidence intervals (CIs) were estimated using meta-analysis models. Overall mean proportions and means were estimated with a random-effects meta-analysis model using the DerSimonian and Laird estimator.[89] The Freeman-Tukey double arcsine transformation was used on proportions.[90,91] Means were analyzed untransformed. Meta-analysis modeling was done using the metaprop and metamean functions of the meta package in R 3.2.5.[a] The random-effects model takes the heterogeneity of samples into account. Statistical heterogeneity was quantified using the I^2 measure, which describes the amount of variation attributed to heterogeneity rather than sampling error across samples.[92] Subgroup analyses of mixed and no ID samples were conducted, if multiple studies of mixed and no ID samples were available, for outcomes on activities and participation because ID is known to be strongly related to these outcomes.[25,93] A random-effect Q test was used to test differences between mixed and no ID samples. Sensitivity analyses excluded specific subsamples of the population with CP from analyses if substantial deviations in the outcome could be explained by sample characteristics. These samples were for manual ability: a no ID sample[25] and a sample with only individuals with dyskinetic subtype,[19] for epilepsy: a no ID sample[52] and a sample with only individuals with GMFCS level IV and V,[57] and for living situation: a young sample (mean age, 20y).[27] Results of sensitivity analyses showed substantial influence of deviating samples, which were therefore excluded in the estimation of overall proportions and means; outcomes of the excluded studies were displayed in the forest plots.

Results

After deduplication, the initial search revealed 6662 publications (fig 1). After screening by title and abstract, 810 full-text articles

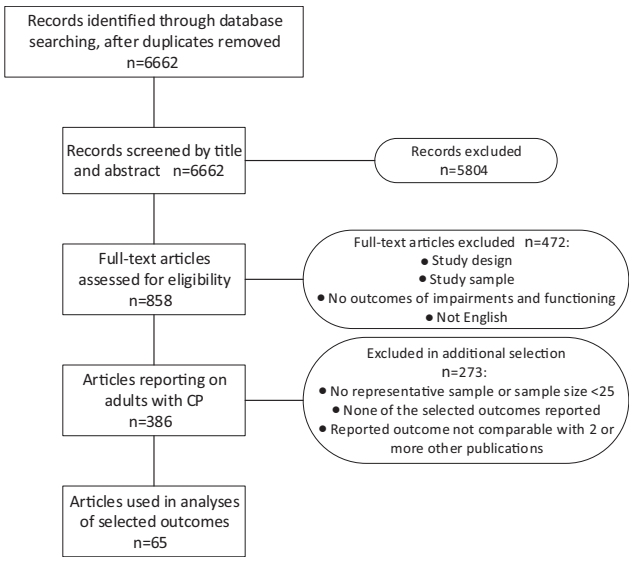


Fig 1 Flow diagram of study selection process.

were assessed for eligibility. Finally, 65 articles (total N=28,429) were included in the meta-analyses, meaning these reported 1 or more of the selected outcomes comparable to at least 2 other studies. Table 1 displays the characteristics of the studies used in the meta-analyses. Of the samples, 73% were mixed and 27% were no ID. The mean age of the study samples was 32 years, samples consisted on average of 68% individuals with GMFCS level I-III and 53% were male. Table 2 shows the overall proportion and/or mean for each of the outcomes, and fig 2 and supplemental appendix S1 (available online only at http://www.archives-pmr.org/) show the forest plots of these analyses. The level of heterogeneity (I^2) was substantial (>75%) for most of the analyses, reflecting considerable variation in results between studies (see fig 2, supplemental appendix S1).

Health status

Mean overall BMI was 25.1 (95% CI, 23.8-26.5), and 22.6% (95% CI, 14.7-31.5) of individuals with CP were obese (BMI>30). Epilepsy (28.8% [95% CI, 20.0-38.4]), asthma (28.3% [95% CI, 18.7-38.9]), and hypertension (21.6% [95% CI: 15.6; 28.4]) were the most prevalent comorbidities. The overall estimated mean SF-36 physical component score was 44.6 (95% CI, 40.7-48.5).

Impairments

Overall presence of pain was estimated at 65.1% (95% CI, 55.1-74.5). For fatigue, the overall estimated mean FSS score was 4.1 (95% CI, 3.8-4.4). Limitations in knee and hip mobility were estimated to be present in 39.5% (95% CI, 21.1-59.5) and 33.4% (95% CI, 15.1-54.6) of adults with CP, respectively.

Level of activities and participation

A majority of adults with CP in mixed samples were estimated to be ambulatory (57.9% [95% CI, 51.1-64.6]) and to have little or no limitation in manual ability (MACS level I or II, 65.5% [95% CI, 61.2-69.7]). The proportion of ambulatory individuals seemed higher in the 2 no ID samples (72.6% [95% CI, 58.8-84.5], Q: 3.60, $P=.058$). Analyses on additional outcomes of those ambulatory included all samples, regardless of ID. Among ambulatory individuals, 31.9% (95% CI, 22.2-42.4) used an assistive device, and 56.2% (95% CI, 37.0-74.5) had reported to perceive a decline in walking function or capacity over time. The overall mean results on the 6-minute walk test of ambulatory adults with CP was 387.9 m (95% CI, 328.5-447.3).

Reports of attendance of tertiary education were remarkably similar between mixed samples and no ID samples (Q: 1.03, $P=0.311$, overall result: 18.2% [95% CI, 10.6-27.2]). The mean estimated proportion of adults with CP with remunerative employment tended to be lower in mixed samples (39.2% [95% CI, 31.5-47.1]) than in no ID samples (56.0% [95% CI, 31.7-78.9], Q: 1.64, $P=.200$). A large difference (Q: 22.11, $P<0.01$) was found in the proportions living independently between mixed samples (29.3% [95% CI, 9.0; 55.3]) and no ID samples (90.0% [95% CI, 83.8; 94.8]). Only used in no ID samples, the overall estimated mean Life-H activities score was 8.0 (95% CI, 7.5-8.4), and the social roles score was 8.2 (95% CI, 7.9-8.4).

Discussion

This systematic review and meta-analysis estimated overall health status, and rates of impairments, activities, and participation of adults with CP for the most studied outcomes in the available literature according to a recent systematic review by Benner et al.[6] This provides state-of-the-art knowledge for this population on a range of topics, such as pain, walking status, living situation, and comorbidities based on large accumulated samples combined from studies across the globe.

Health status

Body composition and comorbidities that are known to be associated with lifestyle, such as obesity, hypertension, and diabetes, vary strongly across regions and age. The overall proportions estimated in the present review are therefore difficult to compare with general population data irrespective of age. Still, the overall estimates that we provided for adults with CP provide a robust indication of the occurrence of several comorbidities in the CP adult population. Epilepsy is a known comorbidity of CP and is included in its definition.[1] The overall occurrence of 28.8% is similar to that reported in a previous review of adults with CP and the more recent review in children with CP.[2,15] In addition, the overall estimated occurrence of asthma in adults with CP (28.3%) exceeds prevalence rates that were reported across the globe in general populations (ranging from 1.0%-21.5%),[94] suggesting that asthma may be a common comorbidity in CP.

Impairments

Pain is the most frequently studied outcome in adults with CP.[6] The estimated occurrence of pain (65%) is in line with another recent review in adults with CP focusing on pain using individual patient data (70%; 95% CI, 62-78)[95] and seems to be more prevalent compared with the general US population (56%).[96] For fatigue we estimated an overall score on the FSS over 4.0, which is often used as a cutoff score indicating fatigue, implying that on average adults with CP experience fatigue.[97] A Swiss study found a similar mean score for patients with a recent stroke and a lower mean score (3.0) for healthy subjects without CP.[97] Prevention and

Table 2 Meta-analyses results

Outcome	Studies (n) (Reference nos.)	Cases in Analysis (N)	Overall Proportion or Mean (95% CI)
Health status			
Body composition			
Waist circumference (mean, in cm)	5 ([31,34,35,39,64])	266	84.0 (82.2-85.7)
BMI (mean)	6 ([21,31,33,35,39,64])	743	25.1 (23.8-26.5)
Obese (% BMI≥30)	7 ([7,21,30,35,39,59,64])	968	22.6% (14.7-31.5)
Comorbidities (%)			
Epilepsy	6 ([7,10,18,55,60,73])	2189	28.8% (20.0-38.4)
Diabetes	7 ([7,8,30,39,52,53,55,63])	6594	6.7% (3.8-10.3)
Hypertension	8 ([7,8,30,39,52,53,59,63])	4646	21.6% (15.6-28.4)
Asthma	4 ([7,8,21,63])	2076	28.3% (18.7-38.9)
Stroke	3 ([8,21,63])	1847	2.0% (0.0-6.8)
Heart disease	3 ([55,63,73])	2792	9.5% (5.1-15.0)
Osteoarthritis	3 ([8,21,55])	2537	11.4% (2.0-26.9)
SF-36 (mean)			
Samples without ID			
Physical component	3 ([36,41,42])	239	44.6 (40.7-48.5)
Physical function	4 ([32,36,41,68])	197	53.9 (34.0-73.7)
Role physical	4 ([32,36,41,68])	197	72.6 (67.7-77.6)
Role emotional	4 ([32,36,41,68])	197	82.7 (77.9-87.5)
Vitality	4 ([32,36,41,68])	197	56.9 (53.3-60.5)
Mental health	4 ([32,36,41,68])	197	73.8 (71.6-76.0)
Social functioning	4 ([32,36,41,68])	197	80.6 (76.5-84.6)
Bodily pain	5 ([32,36,41,44,68])	599	70.3 (63.5-77.2)
General health	4 ([32,36,41,68])	197	70.6 (67.2-73.9)
Impairments			
Pain (%)			
Presence of any pain	16 ([10,24,40,44,49,51,54,56,57,59,62,66,70,72,74,76])	1836	65.1% (55.1-74.5)
Fatigue (mean)			
Fatigue Severity Scale	5 ([11,33,40,51,56])	352	4.1 (3.8-4.4)
Mobility of joints (%)			
Limited knee mobility	3 ([22,51,70])	928	39.5% (21.1-59.5)
Limited hip mobility	3 ([22,51,70])	928	33.4% (15.1-54.6)
Activities and participation			
Walking status			
Ambulatory (%) - subgroup analysis:			
Mixed samples	9 ([7,10,46,65,67,71,73,74,77])	15839	57.9% (51.1-64.6)
Samples without ID	2 ([43,72])	627	72.6% (58.8-84.5)
Ambulatory with assistive devices of those ambulatory (%)	5 ([43,65,72-74])	689	31.9% (22.2-42.4)
Perceived walking decline (%)	4 ([11,36,37,46])	293	56.2% (37.0-74.5)
6MWT (mean, in m)	4 ([29,37,50,69])	127	387.9 (328.5-447.3)
Manual ability (%)			
No or little limitation (MACS level I or II)	3 ([23,25,58])	485	65.4% (61.1-69.6)
Education (%)			
Tertiary education (all samples)	8 ([28,38,45,48,65,72,73,77])	2635	18.2% (10.6-27.2)
Employment (%)			
Remunerative employment - subgroup analysis:			
Mixed samples	9 ([12,23,38,48,65,67,73,74,77])	1845	39.2% (31.5-47.1)
Samples without ID	4 ([11,27,41,72])	437	56.0% (31.7-78.9)
Living status (%)			
Living independently - subgroup analysis:			
Mixed samples	7 ([23,38,47,67,71,73,77])	15927	29.3% (9.0-55.3)
Samples without ID	3 ([11,41,72])	426	90.0% (83.8-94.8)

(*continued on next page*)

Table 2 (*continued*)

Outcome	Studies (n) (Reference nos.)	Cases in Analysis (N)	Overall Proportion or Mean (95% CI)
Activities and social roles (mean score Life-H)			
Activities domain			
Samples without ID	3 ([26,32,41])	198	8.0 (7.5-8.4)
Social roles domain			
Samples without ID	3 ([26,32,41])	198	8.2 (7.9-8.4)

Abbreviation: 6MWT, 6-minute walk test.

treatment of pain and fatigue are high priorities on a recent patient-centered research agenda[98] because literature on pain and fatigue management and lifestyle strategies for this population is scarce.[32,99,100] Using insights from previous studies as a starting point, such as discussing pain and fatigue management with adults with CP and applying a multidimensional lifestyle intervention program, future studies should aim to determine the effectiveness of interventions reducing pain and fatigue.

We found that 1 in 3 adults with CP experience limited knee and hip mobility. However, variation of these proportions were very large, and few population-based studies were available that reported joint mobility in adults with CP. Systematic knowledge of joint mobility seems to be under-reported in current literature. Similarly, other impairments that frequently occur in individuals with CP, such as spasticity, hip displacement and spinal deformities, were not often reported on in population-representative samples or lacked standardized assessments.[2,15,22]

Activities and participation

A majority of adults with CP were ambulatory (58%) and experienced little or no difficulty with manual ability (65%). However, the proportion of ambulant individuals is lower than that previously reported in children with CP (72%).[15] This is likely explained by a decline in walking function as individuals with CP get older, which we found to be experienced by half of the ambulant adults with CP. The proportion of adults with CP who experienced little or no limitation with manual ability (65%) was very close to that reported in a population-based study of children with CP (64%).[101] This suggests that although walking ability declines in individuals with CP, manual ability remains relatively stable in adulthood.

The overall proportions of adults with tertiary education (18%), having remunerative employment (39%), and living independently (29%) seem low but are very difficult to compare with reference values because of regional differences and age-specific participation rates, for example. Additionally, the variation between CP samples is also large, as shown by large statistical heterogeneity (92%-99%), a very large 95% CI for living situation, and substantially higher proportions of participation in samples without adults with ID. Importantly, in individuals without ID, proportions of living independently were very high (90%). Surprisingly, regarding tertiary education and remunerative employment there were no significant differences between mixed samples and samples without ID, which may indicate that adults with CP without ID may still be disadvantaged in these life areas. Although the sample from the study of Murphy et al used in the meta-analyses of the outcomes walking, education, employment status, and living situation was not reported to be selected based on intellectual disability (ie, it was considered a mixed sample), the results were deviant.[77] This might be explained by a large proportion of the sample classified as dyskinetic (50%), which usually represent smaller parts of the population.[2] Individuals with dyskinetic CP may have different levels of participation than those with spastic CP, causing results of this sample to differ.

Overall scores on daily activities and social roles (Life-H) were close to the cutoff for experiencing difficulty.[102,103] These scores are only estimated based on Dutch samples without ID, which may limit generalization. Similarly, overall domain scores for physical functioning and role limitations because of physical health (SF-36) were low compared with reference values reflecting limitations in activities and participation.[104]

Heterogeneity in samples and studies

The high level of statistical heterogeneity, indicating substantial variation between study results, and the wide confidence intervals in some of the analyses may partly be explained by sample differences. These differences in samples reflect the heterogeneity of the population with CP, of which the definition is an umbrella term.[1] Previous studies found associations between CP severity and many of the described outcomes.[8,12,14,95] Because of the available information, we were unable to disentangle differences in outcomes for other determinants (eg, level of motor function, age, or region) than mixed samples and samples without ID. We recommend future studies to systematically report overall results for subgroups of adults with CP to improve clinical interpretation. Moreover, we strongly recommend to further standardize assessments in future research and clinical care for adults with CP. Examples of presently ongoing standardization in this field are improving the uniformity of registries[105,106] and extending them into the adult population,[23] developing core outcome sets for specific outcomes,[107] and creating an overarching ICF core set for adults with CP.[6]

Study limitations

The literature search we conducted was very comprehensive, with 386 English-language publications on adults with CP reporting outcomes of functioning identified by screening more than 6000 records from the database searches. However, some publication bias may be present because we omitted non-English language publications, which comprised less than 10% of the eligible publications. Another source of publication bias might be inconclusive trials that were not published. We expect this source of publication bias to be negligible because the outcomes we studied were non-comparative,[108] and intervention trials in adults with CP are very

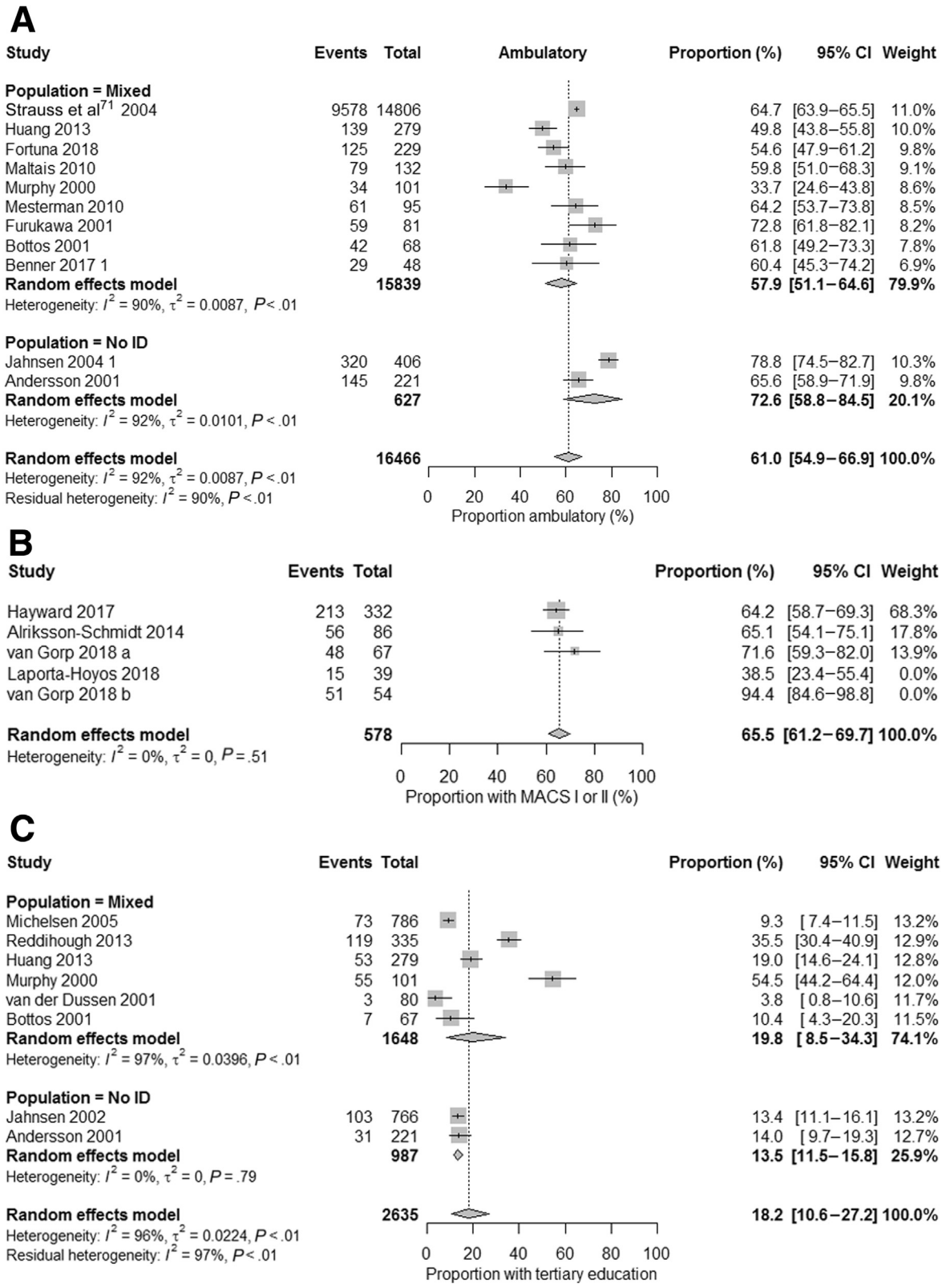
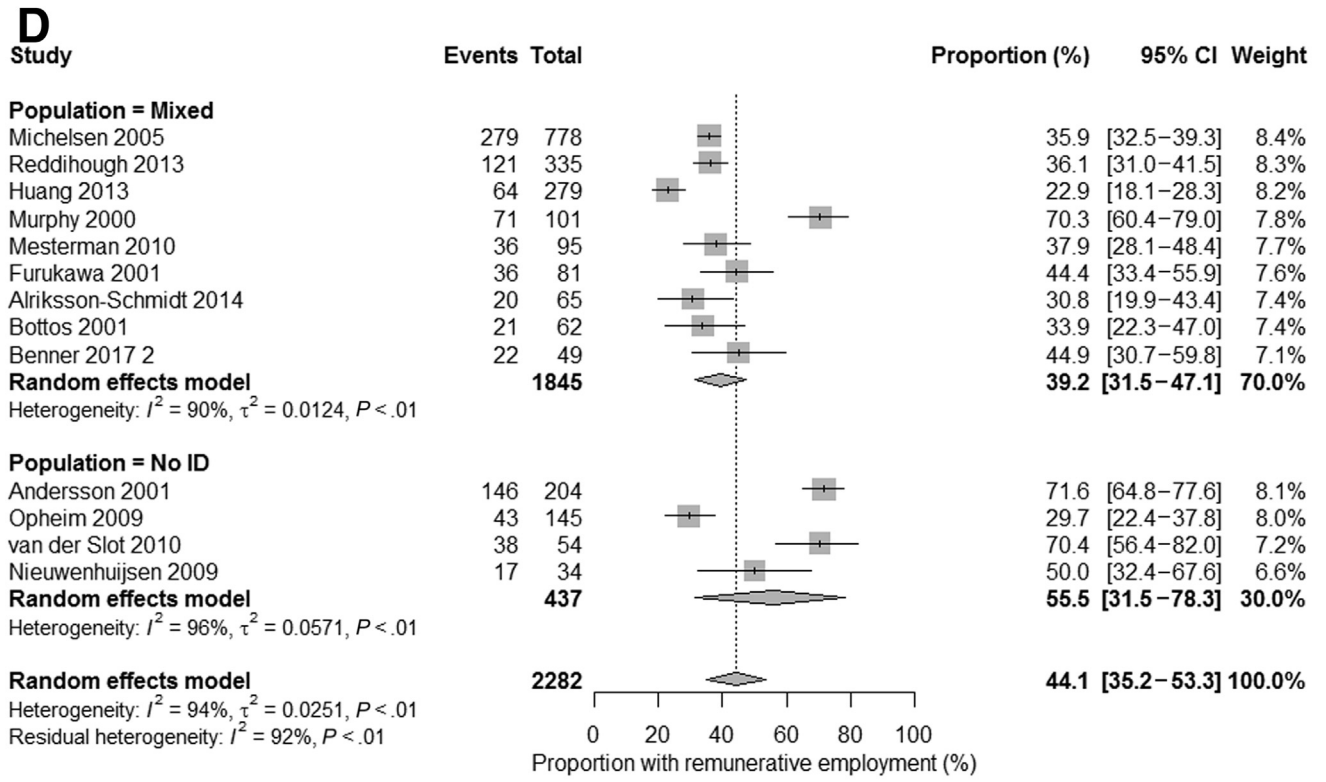


Fig 2 Forest plots of main outcomes of activities and participation. (**A**) Walking status; (**B**) manual ability; (**C**) education status; (**D**) employment status; (**E**) living situation.



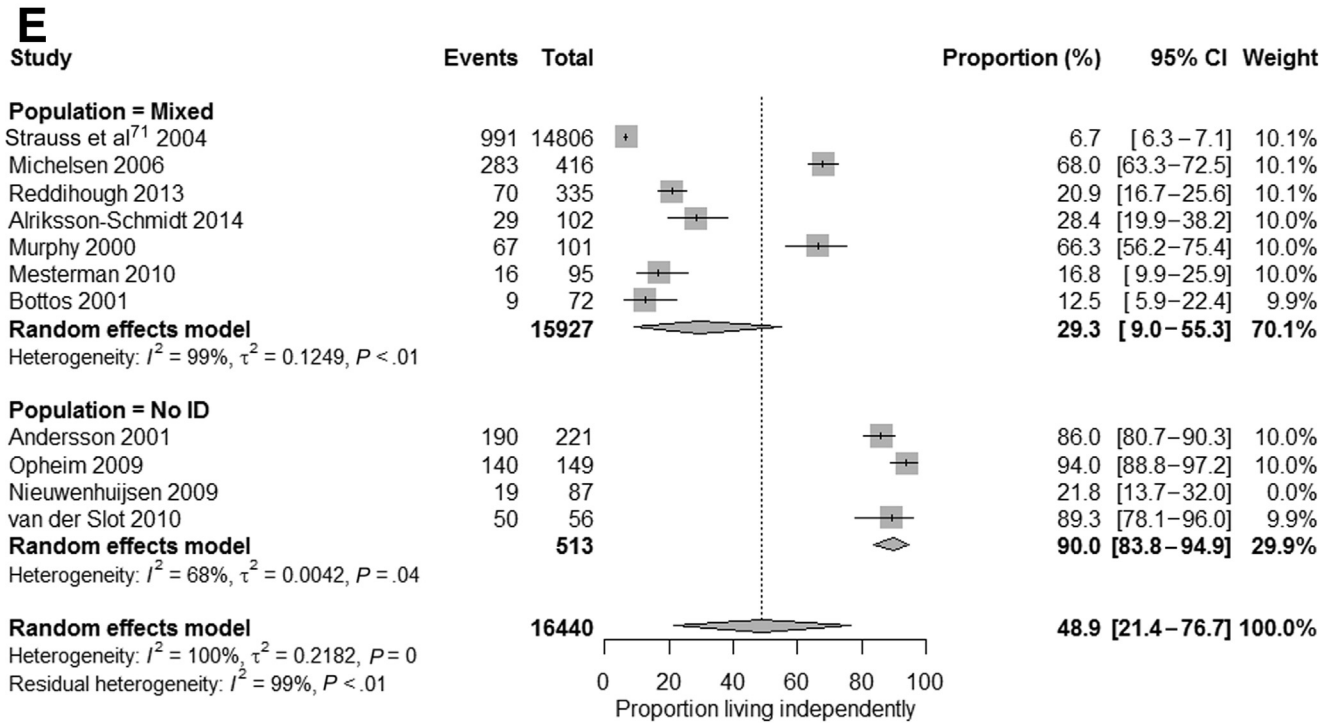


Fig 2 Continued.

scarce, addressing only 5% of the included studies.[6] Notably, most of the included studies were conducted in North America, Western Europe, Asia, or Australia (see table 1), limiting generalizability of the results to other regions, for example, those with lower resources. Because of limited availability of population-based studies (eg, registry studies)[15] in adults with CP compared with children, we were unable to restrict the selection of articles to population-based samples, causing substantial variability in severity of motor and intellectual disability between samples (see table 1). However, the total of all study samples included is considered representative for the population of adults with CP with the majority male and with GMFCS I-III and including both mixed and no ID samples. The mean age of samples was 32 years, indicating the included articles mainly studied younger adults, and the results may not be applicable to older adults with CP. Note that we excluded nonrepresentative samples that were specifically selected

in original studies on having a certain impairment. Still, by including all representative study samples with at least 25 adults with CP who were relatively representative of (a subgroup of) the population with CP, we provided the best available knowledge on the most often studied outcomes in adults with CP. Another limitation of the study may be that we only focused on results that were reported as outcomes in the original studies, in line with the review on most studied outcomes of Benner et al,[6] thus not including information that was originally reported on as sample characteristics, such as level of gross motor functioning, educational level, or employment status.

Conclusions

The present systematic review and meta-analysis provided state-of-the-art knowledge of the epidemiology of the most studied outcomes of health status, impairments, activities, and participation in adults with CP. Epilepsy and asthma are comorbidities that occur often in adults with CP. Overall, a majority of adults with CP experience pain, and on average adults with CP are fatigued. A majority of adults with CP are ambulant and have little or no difficulty in manual ability. A minority of the total population are employed or live independently, with much higher proportions living independently for individuals without ID. More uniformity in assessment and reporting is advised to enable more specified data synthesis on a wider range of outcomes.

Supplier

a. R 3.2.5; R Foundation for Statistical Computing.

Keywords

Adult; Cerebral palsy; Epidemiology; Health; Meta-analysis; Rehabilitation; Systematic review

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Acknowledgment

We thank Wichor Bramer, PhD, for Rijndam Rehabilitation, Rotterdam his support in developing and conducting the literature search.

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