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Factors associated with caregiver burden among family caregivers of children with cerebral palsy: A systematic review

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Abstract

Objectives: To identify caregiver and children factors associated with caregiver burden on primary caregivers of children with cerebral palsy.

Design: Systematic review

Data sources: Seven electronic databases, including PubMed, Cochrane Library, Scopus, PsycINFO, Web of Science, CINAHL and Embase, were systematically searched up to August 2021.

Eligibility criteria: Original observational studies reporting caregiver burden and related factors among caregivers of children with cerebral palsy.

Data abstraction and synthesis: Two reviewers independently screened results and assessed the quality of studies. Title, abstract, full-text screening and data abstraction were done independently by two reviewers. Risk of bias was assessed using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies. The quality of evidence for factors was rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results: 15 articles were included in the review. All studies were cross-sectional and examined caregiver-reported burden measures. The Zarit Burden Interview was the most commonly used questionnaire. Anxiety, depression, mental health and physical health of caregiver, gender and severity of illness in children with CP were moderate to high quality of evidence for factors contributing to caregiver burden.

Conclusions: Higher caregiver burden is associated with more depressive feelings and worse life quality of the caregiver, and with more severe physical disability of the children. Future studies should focus on high-quality longitudinal research and appropriate assistance to reduce caregiver burden and improve the quality of caregiving for children with CP.

Key words: caregiver burden, cerebral palsy, systematic review

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Introduction

With the development of domestic perinatal medicine and obstetric technology, the perinatal mortality rate has gradually decreased, but the incidence of cerebral palsy has gradually increased (1). Cerebral palsy (CP) is defined as a group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, behaviour, and by a seizure disorder (2). CP is the most common paediatric disability, seriously affecting the children's self-care ability and social activities (3-4). Thus, Children with CP often require lifetime extensive care and rehabilitation training, which will bring heavy psychological, physical and economic burden to their families (5-6).

Parents, as the primary caregivers of children with disabilities, bear the arduous caregiving burden. Not only do they have to help the children’s daily activities, but they also need to pay close attention to their changing health conditions, which directly leads to changes in the caregivers’ lifestyle and a decline in their quality of life (7-8). Caregiver burden has been defined as a multidimensional response to physical, emotional, psychological, and financial stressors that are associated with caregiving experience (9). Studies have shown that a high level of caregiving burden for children with CP negatively affects the mental and physical health, family functions and social interactions of caregivers, resulting in low quality of care and unmet patient needs (10-13). Paying attention to the burden of caregivers is of great significance.

Relevant factors that affect caregiver burden should be studied in order to propose interventions to support caregivers. In the last decade, there has been an increasing number of studies on the care burden for children with CP, but a comprehensive review of caregiver factors and patient factors influencing caregiver burden is lacking. Therefore, the objective of this study was to systematically review published literature to identify caregiver and patient factors of caregiver burden among primary caregivers of children with CP.

Methods

This systematic review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Appendix 1). The protocol has been registered with PROSPERO 2021 CRD 42021268284.

Search strategy

The electronic databases PubMed, Cochrane Library, Scopus, PsycINFO, Web of Science, CINAHL and Embase were systematically searched from inception to August 2021. The search string contained four groups of combinations of medical subject headings and text words: Caregiver (MeSH term), care*, parents or mother; Caregiver burden (MeSH term), stress, strain or burnout; Cerebral palsy (MeSH term), CP, disability* or neurodev* disorder*; Children (MeSH term), child* or paediatr* (Appendix 2). Additionally, we also searched for grey literature using the first 500 hits from Google Scholar and Open Grey. References for relevant publications were checked to make sure that no relevant papers had been missed.

Inclusion &Exclusion criteria

Original observational studies reporting burden and related factors of caregivers of children with

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CP were taken as the primary focus of the research; Study participants need to be primary caregivers (over 18 years old) of children (0-18 years old) with cerebral palsy. Burden had to be assessed with a total caregiver burden construct; Full-text articles published in English or with an English translation in peer-reviewed journals were included. Studies where caregivers of children with different diagnoses and children with adults are grouped together were excluded, unless results were reported separately for caregivers of children with CP. Intervention studies, reviews, non-original research papers, qualitative research studies were not eligible for this review.

Data extraction and Quality assessment

The titles/abstracts of citations retrieved using the search strategy were independently assessed by two reviewers. The full text articles of potentially relevant studies were then independently screened by two reviewers, and any discrepancies were resolved through discussion. The number of studies excluded during each screening phase, and the reasons for full-text exclusion will be described in a PRISMA flow diagram. A pre-specified form will be used for the extraction of the data from the included studies. This procedure will be completed by one reviewer, and verified by a second reviewer, with any disagreements being resolved through discussion with a third-party reviewer. We extracted the following data from each included study independently by two researchers: first authors, year of publication, sample size, study design, relevant participant demographics, key predictor and outcome variables, self-administered tools used for measurement, results and associations.

Risk of bias was assessed using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies (Appendix 3) by the two researchers independently. The checklists include 8 questions to evaluate the overall quality of the studies from the research object, disease, measurement of influencing factors and confounding factors, data analysis, etc. The choices of answers were ‘yes’, ‘no’, ‘unclear’ or ‘not applicable’. The overall appraisal of ‘include’, ‘exclude’ or ‘seek further information’ were presented in the last section of the checklist.

Data synthesis

Due to the diversity of outcome measures and factors included in the study, a meta-analysis was not possible. Bivariate associations were described in terms of correlation coefficients (*r*) or student statistics or F-statistics. Multivariate associations were described in terms of standardized or Unstandardized coefficients (β *or* b). In studies that applied a logistic regression, the odds ratio (*OR*) was presented. Factors were grouped into caregiver and children characteristics subsequently thematically categorized.

Quality of evidence

We assessed the quality of evidence for each factor measured in at least three studies using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Appendix 4). Two researchers rated the factors based on the study limitations in risk of bias, inconsistency, imprecision, indirectness and publication bias. Certainty of the evidence cannot be rated up for “dose effect” or “large effect”. GRADE has four levels of evidence: very low, low, moderate, and high.

Patient and public involvement

Patients or public were not involved in the conduct of this systematic review.

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Results

Search and screening

The search identified a total of 14511 possibly relevant articles. After the removal of duplicates and the abstract screening, a total of 68 studies were selected for full-text review. Finally, 15 studies were left for full inclusion in the review. There were no additional articles met the inclusion criteria when searching the references of the 15 articles. The PRISMA flow diagram for search and screening results are shown in Figure 1.

Risk of bias

Risk of bias scores for studies ranged from 4 to 7 out of a maximum of 8 points. Some articles lacked clear information in items: study subjects and the setting, exposure factors, and confounding bias. The methodological quality assessment list was listed in supplementary Appendix 5.

Characteristics of the included studies

The 15 included studies reported on overall caregiver burden and related factors of children with CP. Studies were conducted in ten different countries between 2011 and 2021, involving in 1919 caregivers (not inclusive of controls). Of these, 13 studies investigated univariate associations; 8 studies were explored in multivariate associations. Caregivers were predominantly female, and 4 of the 15 articles had samples made up exclusively of mothers. 6 articles involved fathers. The mean age of caregivers varied from 31 to 42 years. Four studies involved control populations, two of four had caregivers of healthy children as the control group. All studies were cross-sectional surveys. The most used sampling method was convenience sampling. The key characteristics of each study are presented in Table 1.

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Table 1. The summary of included studies

Authors (Year)	Country	Design	Caregiver sample size	Caregiver relation to child	Mean age of Caregivers M(SD)	Age of children (range)	Measures tool
Carona et al. (2013)[14]	Portugal	Cross-sectional Study	93	Mothers (83.8%)	42.34(5.72)	8-18	BM
Bella et al. (2011)[15]	Brazil	Cross-sectional Study	38	Mothers (-)	33.3(7.7)	4-11	BI
Whittingham et al. (2013)[16]	Australia	Correlational survey study	94	Mothers (90.4%)	-	2-12	DPC Burden
Farajzadeh et al. (2021)[17]	Iran	Cross-sectional study	160	Female (84.4%)	35.47(6.59)	2-14	CDS
Boztepe et al. (2019)[18]	Turkey	Cross-sectional Study	69	Mothers (100%)	34.6(7.3)	1-18	ZBI
Omole et al. (2019)[19]	Nigeria	Cross-sectional Study	209	Female (91.9%)	34.6(9.2)	1-12	CDS
Terathongkum et al. (2020)[8]	Thailand	correlational research	75	Female (88.0%)	-	0-18	VQ burden
Farajzadeh et al. (2020)[20]	Iran	Cross-sectional Study	203	Mothers (100%)	34.48(6.74)	4-14	CDS
Wijesinghe et al. (2015)[21]	Sri Lanka	Cross-sectional Study	375	Mothers (97%)	32.4(7.2)	1-12	CDS
Barutcu et al. (2021)[22]	Turkey	Cross-sectional Study	109	Mothers (98.2%)	38.53(9.62)	1-18	ZBI
Ozkan et al. (2018)[23]	Turkey	Cross-sectional Study	120	Mothers (100%)	-	2-18	ZBI
Gugała et al. (2021)[24]	Poland	Cross-sectional Study	190	Female (72.6%)	40.6(9.1)	2-18	CBS
Marrón et al. (2013)[25]	Spanish	Cross-sectional Study	62	Mothers (88.7%)	41.98(5.64)	1-17	ZBI
Albayrak et al. (2019)[12]	Turkey	Cross-sectional Study	101	Mothers (100%)	34.93(8.7)	0-18	ZBI
Santos et al. (2012)[26]	Brazil	Cross-sectional Study	21	Female (100%)	31(-)	1-12	ZBI

BM: The Revised Burden Measure; BI: The Burden Interview; DPC Burden =Daily Parenting Tasks Checklist-Parenting Burden; ZBI: Zarit Burden Interview; CDS: Caregiver Difficulties Scale; CBS: Caregiver Burden Scale; VQ burden: Thai version Viriyaprasart's questionnaire about burden of care

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Measures of burden

Seven instruments were used to measure caregiver burden including Zarit Burden Interview (n= 6) (12,18,22-23,25-26); Caregiver Difficulties Scale (n= 4) (17,19,20-21); Caregiver Burden Scale (n= 1) (24); The Revised Burden Measure (n= 1) (14); The Burden Interview (n= 1) (15); Daily Parenting Tasks Checklist-Parenting Burden (n= 1) (16); Viriyaprasart's questionnaire about burden of care (n= 1) (8).

Studied factors in relation to caregiver burden

Overviews of caregiver and children characteristics as factors of caregiver burden are presented in Tables 2 and 3. The criteria for compelling evidence is that each factor was measured in at least three studies reported significant relationships. The detailed description is described as follows.

Caregiver factors

Caregiver factors were grouped into five categories, including caregiver demographics, emotional functioning, physical functioning, overall health and social functioning. Caregiver demographical factors included age (8,12,18-19,21-22), gender (19,22), educational level (18-19,21-22), monthly income (18-19,21-22), number of caregiver (22), socioeconomic status (19), geographic area (21), additional helper (18), daily caring time (12). Emotional functioning factors included anxiety (17,22,24), depression (12,17-18,20,22,24-25), Mental health (12,14-15,20), perceived stress (15,17), beliefs of rehabilitation (8), perceived self-efficacy (8,25), experiential avoidance (16). This category was included in eleven of the 15 studies. Physical functioning factors included sleep quality (12), pain (12,15), fatigue (12,20), Physical health (12,15,20). Overall health factors included quality of life (8,14). Social functioning factors included social functioning (15,20), environment health (20), social support (8,14), coping (16,21).

Children factors

Children factors were grouped into five categories, including children demographics, disease-related, behavioural functioning, overall health and social environment. Children demographical factors included age (8,12,18-19,21-22), gender (18,19,21), birth order (19), number of children (18,21-22), number of disabled child (22), body mass index (12). Disease-related factors included type of CP (19,21), severity of CP (12,18,19,25), etiology (19), additional physical illness (18), associated conditions (19,21), functional impairments (21). This category was included in five of the 15 studies. Behavioural functioning factors included functional status (22), behavioural problems (14,16). Overall health and social environment factors included quality of life (14,23), social support (14) and environment (26).

Evidence for factors related to caregiver burden

Caregiver factors

The results of evidence synthesis for caregiver factors using the GRADE criteria were that "anxiety" and "depression" were the high quality of evidence for factors of caregiver burden, "mental health" and "physical health" were the moderate quality of evidence for factors of caregiver burden. Low quality of evidence was found for the relationship between caregiver burden and "age" "education" and "monthly income" of caregivers (see Table 4). Factors within the categories social functioning of the caregiver, were studied in fewer than three studies and

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could not be rated with the GRADE.

Children factors

The synthesis of the evidence for children factors resulted in high quality of evidence between caregiver burden and “severity of illness”. The factors for “gender” of children were the moderate quality of evidence caregiver burden. “Age” of children and “number of Children” were respectively very low and low quality of evidence for the relations with caregiver burden. Few of the included studies have explored children factors, and fewer factors have been able to perform evidence synthesis.

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Table 2. Associations between caregiver factors and caregiver burden

	Factor	Measure factor	Outcome caregiver burden	Bivariate analysis	Bivariate association r/t/F/β	Multivariate association β/b (95%CI)	N	Ref
Demographics	Age	Years	VQ burden	P	ns	-	75	8
		Years	ZBI	P or S	0.20*	-	101	12
		Years	ZBI	-	-	ns	69	18
		Years	CDS	S	ns	-	209	19
		Years	CDS	R	ns	-	375	21
		Years	ZBI	nr	ns	-	109	22
	Gender	Male/female	CDS	T	-2.01*	-	209	19
		Mother/father/both	ZBI	nr	ns		109	22
	Education	0-4 level	ZBI	-	-	ns	69	18
		0-2 level	CDS	A	4.95**	2.61**(1.97-14.09)	209	19
		Low education	CDS	R	ns	-	375	21
		0-5 level(mother)	ZBI	nr	ns	-	109	22
	Monthly income	TL	ZBI	-	-	ns	69	18
		0-4 level	CDS	A	ns	-	209	19
		Low income	CDS	R	8.65***	3.69*(-)	375	21
		0-2 level	ZBI	nr	4.45*	-	109	22
	Number of caregiver	1/2	ZBI	nr	ns	-	109	22
	Socioeconomic status	0-4 level	CDS	A	ns	-	209	19
	Geographic area	Rural area	CDS	R	6.27**	5.35**(-)	375	21
	Additional helper	None or present	ZBI	-	-	ns	69	18
	Daily Caring time	Hours	ZBI	P or S	ns	-	101	12
Emotional functioning	Anxiety	HADS-A	CDS	P	0.47***	0.14***(nr)	160	17
		BAI	ZBI	nr	0.29**	-	109	22
		HADS-A	CBS	P	0.51****	-	190	24
	Depression	BDI	ZBI	P or S	0.70***	-	101	12
		HADS-D	CDS	P	0.51***	0.17***(nr)	160	17
		BDI	ZBI	-	-	0.48***(nr)	69	18
		BDI-II	CDS	P	0.64***	-	203	20
		BDI-II	ZBI	nr	0.41****	-	109	22
		HADS-D	CBS	P	0.38****	-	190	24
		BDI-II	ZBI	-	-	0.36**(0.17-0.73)	62	25
	Mental health	SF-36-MCS	ZBI	P or S	ns	-	101	12
		MHI-5	BM	nr	-0.51**	-0.20*(nr)	93	14
		SF-36-RE	BI	S	ns	-	38	15
		SF-36-MH	BI	S	-0.62*	-	38	15
		WHOQOL-BREF-PsyH	CDS	P	-0.68***	-	203	20
	Perceived stress	PSQ	BI	S	0.65***	-	38	15

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		PSS-4	CDS	P	0.43***	0.10***(nr)	160	17
	Beliefs of	RBQ	VQ burden	P	ns	-	75	8
	Perceived	PSQ	VQ burden	P	-0.25*	-	75	8
		RSCSE	ZBI	-	-	-0.19**(-0.31~-0.06)	62	25
	Experiential	AAQ-16	DPC Burden	nr	0.42****	0.31**(0.52-1.21)	94	16
Physical functioning	Sleep quality	PSQI	ZBI	P or S	0.39***	-	101	12
	Pain	NRS	ZBI	P or S	0.36***	-	101	12
		SF-36-BP	BI	S	-0.40*	-	38	15
	Fatigue	CIS	ZBI	P or S	0.66***	-	101	12
		FSS	CDS	P	0.40***	-	203	20
	Physical health	SF-36-PCS	ZBI	P or S	-0.21*	-	101	12
		SF-36-PF	BI	S	ns	-	38	15
		SF-36-RP	BI	S	ns	-	38	15
		SF-36-GH	BI	S	-0.44*	-	38	15
		SF-36-VT	BI	S	-0.54*	-	38	15
		WHOQOL-BREF-PH	CDS	P	-0.59***	-	203	20
Overall health	Quality of life	VQ well-being	VQ burden	P	-0.50**	-	75	8
		WHOQOL-8	BM	nr	-0.39**	-0.16*(nr)	93	14
Social functioning	Social functioning	SF-36-SF	BI	S	-0.61*	-	38	15
		WHOQOL-BREF-SR	CDS	P	-0.68***	-	203	20
	Environment health	WHOQOL-BREF-E	CDS	P	-0.63***	-	203	20
	Social support	SSS	BM	nr	-0.35**	-0.41**(nr)	93	14
		SSQ	VQ burden	P	ns	-	75	8
	Coping	CHIP	DPC Burden	nr	ns	ns	94	16
		Individual coping	CDS	R	ns	-	375	21
		Seeking social support	CDS	R	-8.99***	ns	375	21
		Spouse support	CDS	R	-7.44***	-5.67**(nr)	375	21

HADS: Hospital Anxiety and Depression Scale; HADS-A: HADS-Anxiety Scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; HADS-D: HADS-Depression Scale; BDI-II: Beck Depression Inventory-II; SF-36: 36-Item Short Form Health Survey; SF-36-MCS: SF-36-Mental component summary; MHI-5: Mental Health Inventory-short form; SF-36-RE: SF-36-Emotional Role; SF-36-MH: SF-36-Mental health; WHOQOL-BREF: World Health Organization's Quality of Life Questionnaire; WHOQOL-BREF-PsyH: WHOQOL-BREF-Psychological health; PSQ: Perceived self-efficacy in the care questionnaire; PSS-4: Perceived Stress Scale-4 item; RBQ: Adapted rehabilitation belief questionnaire; RSCSE: Revised Scale for Caregiving Self-Efficacy; AAQ-16: Acceptance and Action Questionnaire; PSQI: Pittsburgh sleep quality index; NRS: Numerical rating scale; SF-36-BP: SF-36-Bodily pain; CIS: Multidimensional checklist individual strength; FSS: Fatigue Severity Scale; SF-36-PCS: SF-36-Physical component summary; SF-36-PF:SF-36-Physical functioning; SF-36-RP: SF-36-Physical Role; SF-36-GH: SF-36-General health; SF-36-VT: SF-36-Vitality; WHOQOL-BREF-PH: WHOQOL-BREF-Physical health; VQ well-being: Thai version Viriyaprasart's questionnaire about well-being; WHOQOL-8: The World Health Organization Quality of Life Assessment 8 item index; SF-36-SF: SF-36-Social functioning; WHOQOL-BREF-SR: WHOQOL-BREF-Social relationships; WHOQOL-BREF-E: WHOQOL-BREF-Environment; SSS: Satisfaction with social support scale; SSQ: Adapted social support questionnaire; CHIP: Coping Health Inventory for Parents.

S: Spearman's linear correlation coefficient/ Spearman's Rho correlation; P: Pearson correlation coefficient; A: One-way analysis of variance (ANOVA); T: Independent Student's t-test; R: Univariate regression analysis; nr: not reported; ns: not significant.

****P< 0.0001, ***P < 0.001, **P < 0.01, *P < 0.05.

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Table 3. Associations between children factors and caregiver burden

	Factor	Measure factor	Outcome caregiver burden	Bivariate analysis	Bivariate association r	Multivariate association β/b (95%CI)	N	Ref
Demographics	Age	Years	VQ burden	P	ns	-	75	8
		Years	ZBI	P or S	ns	-	101	12
		Years	ZBI	-	-	ns	69	18
		Years	CDS	S	ns	-	209	19
		Years	CDS	R	ns	-	375	21
		1-5/6-12/>12	ZBI	nr	ns	-	109	22
	Gender	Male/female	ZBI	-	-	ns	69	18
		Male child	CDS	T	3.02**	0.18**(1.56-8.34)	209	19
		Male child	CDS	R	3.60*	3.50*(-)	375	21
	Birth order	$1^{st}/2^{nd}/3^{rd}$ or greater	CDS	A	NS	-	209	19
	Number of Children	3 or higher	ZBI	-	-	ns	69	18
		1/2/3	CDS	R	ns	-	375	21
		1/2/3/4 or more	ZBI	nr	0.20*	-	109	22
	Number of disabled children	1/2 or more	ZBI	nr	ns	-	109	22
	Body mass index	BMI	ZBI	P or S	ns	-	101	12
Disease-related	Type of CP	5 types	CDS	A	3.15*	-	209	19
		Spastic quadriplegia	CDS	R	10.62***	-	375	21
	Severity of illness	GMFCS	ZBI	P or S	0.30**	-	101	12
		Severity of illness scale	ZBI	-	-	0.29*(nr)	69	18
		GMFCS-ER	CDS	A	6.87***	0.29***(4.42-11.23)	209	19

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		nr	ZBI	-	-	0.28*(0.04-0.35)	62	25
	Etiology	7 types	CDS	A	2.49*	-	209	19
	Additional physical illness	Absent/present	ZBI	-	-	ns	69	18
	Associated conditions	0/1/2/3/4 or more	CDS	A	3.21*	-	209	19
		0/1 or more	CDS	R	12.75***	ns	375	21
	Functional impairments	Number of functional deficits	CDS	R	3.97***	2.64***(nr)	375	21
Behavioural functioning	Functional status	FIM	ZBI	nr	ns	-	109	22
	Behavioural problems	SDQ	BM	nr	0.24*	0.29**	93	14
		SDQ	DPC Burden	nr	0.38****	0.27**(0.06-1.43)	94	16
Overall health	Quality of life	KIDSCREEN-10	BM	nr	ns	-	93	14
		PedsQL	ZBI	P	0.40***	-	120	23
Social environment	Social support	SSSS	BM	nr	ns	-0.19*(nr)	93	14
	Environment	Space for child locomotion	ZBI	P	nr*	-	21	26

BMI: Body mass index; GMFCS: Gross Motor Function Classification System; GMFCS-ER: Gross Motor Function Classification System- Expanded and Revised; FIM: Functional Independence Measure; SDQ: Strengths and Difficulties Questionnaire; KIDSCREEN-10: The shortest version of Kidscreen questionnaires; PedsQL: Pediatric Quality of Life 4.0 Generic Core Scales; SSSS: Satisfaction with social support scale for children and adolescents.

S: Spearman's linear correlation coefficient/ Spearman's Rho correlation; P: Pearson correlation coefficient; A: One-way analysis of variance (ANOVA); T: Independent Student's t-test R: Univariate regression analysis; nr: not reported; ns: not significant.

****P< 0.0001, ***P < 0.001, **P < 0.01, *P < 0.05.

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Table 4. Adapted GRADE table for potential factors

Potential factors	Participant (n)	NO. of studies	Bivariate			Multivariate			Grade factors					
			+	0	-	+	0	-	Study limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality
Caregiver														
Age	938	6	1	4	0	0	1	0	√	√	√	×	√	Low
Education	762	4	1	2	0	1	1	0	√	×	√	×	√	Low
Monthly income	762	4	2	1	0	1	1	0	√	×	√	×	√	Low
Anxiety	459	3	3	0	0	1	0	0	√	√	√	×	√	High
Depression	894	7	5	0	0	3	0	0	√	√	√	×	√	High
Mental health	435	4	0	2	3	0	0	1	√	√	√	×	√	Moderate
Physical health	342	3	0	2	4	0	0	0	√	√	√	×	√	Moderate
Children												×		
Age	938	6	0	5	0	0	1	0	√	√	√	×	√	Very low
Gender	653	3	2	0	0	2	1	0	√	√	√	×	√	Moderate
Number of Children	553	3	1	1	0	0	1	0	√	√	√	×	√	Low
Severity of illness	441	4	2	0	0	3	0	0	√	√	√	×	√	High

For bivariate and multivariate analyses: +: number of significant associations with a positive value; 0: number of non-significant associations; -: number of significant associations with a negative value; For GRADE factors: ✓: no serious limitations; ×: serious limitations. For overall quality of evidence: very low, low, moderate, high.

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Discussion

Caring for children with CP is a stressful and difficult task for primary caregivers, especially for their parents. Caregivers of children with CP were under higher pressure than caregivers of healthy children (12,27,28). There were many factors that affect the caregiving burden for children with CP. In our systematic review, we focused on both caregiver characteristics and children characteristics as factors of caregiver burden. There are fewer studies involving children-related factors than caregiver-related factors, possibly because caregiver-related factors are more likely to modify. This review revealed that anxiety, depression, mental health and physical health of caregiver, gender and severity of illness in children with CP were moderate to high quality of evidence for factors contributing to caregiver burden. But our ability to draw conclusions on remaining caregiver and children characteristics as factors is limited because of low to very low quality of evidence.

We found high quality of evidence for the association between caregiver burden and anxiety, depression symptoms of the caregiver. Feelings of anxiety and depression are positively correlated with caregiver burden. The factor for mental health of caregiver as moderate quality of evidence is also a predictor of psychological well-being of the caregiver. Caregivers, who experience poor psychological condition, are more likely to experience high caregiver burden. This correlation between mental health of caregiver and caregiver burden is consistent with the findings in other children with neurodevelopmental diseases, such as epilepsy and autism spectrum disorder (29,30,31). Mother caregivers constitutes the majority of caregiving. Long-term care of children with CP and restricted social activity for the mother caregiver pridict more psychological conditions such as depression, distress and stress in them (32). Caregivers who feel depressed experience a greater burden of care, thereby affecting CP children's quality of life (23). A study revealed that psychological interventions such as Stepping Stones Triple P therapy (SSTP), Acceptance and Commitment Therapy (ACT) could improve parental mental wellbeing of parents of children with CP. It is crucial to develop more interventions that focus primarily on the psychological wellbeing of the parents (33).

Moderate quality of evidence was found for the relationship between caregiver burden and physical health of the caregiver. Physical conditions are negatively related to caregiver burden. The worse the physical conditions, the greater the caregiver burden. Children with CP are often accompanied by intellectual and physical disabilities. Daily life care and assistance with rehabilitation exercises mean more physical strength and energy for the caregiver, so that caregivers often experience problems such as body pain, fatigue and sleep problems (12,34,35,36,37), which seriously affect the physical well-being and reduce the quality of life of the caregiver (38,39). Few studies have focused on interventions for caregivers' physical conditions. We should actively pay attention to the physical health of the caregiver and take feasible interventions to improve the physical functioning of caregivers of children with CP.

Many previous studies have explored the correlation between social support and parenting stress in caregivers of children with CP. Negative associations were found between the levels of stress among parents and social support perceived by them (40,41,42,43). Many families faced financial difficulties and restricted access to healthcare services (44,45). Social support from spouses, social organization and medical institution help prevent and decrease the stressful situation of the family's experience in providing care to children with CP (42,46). Although parenting stress and caregiver burden have similar meanings, this review focuses on caregiver burden and involves

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fewer relevant articles about the association between social support and care burden, so more evidence is needed to determine their relevance.

The factor for severity of illness in CP children as high quality of evidence is positively correlated with the burden of caregiver. GMFCS score is most commonly used to measure the severity of disability of children with CP. Children with more severe disabilities require the more support of their caregivers to carry out the activities of daily living. Caregivers will spend more time and physical strength to meet the caregiving demands (47,48), and the caregiver burden will be heavier. In addition, moderate quality of evidence was found for the relationship between caregiver burden and gender of children with CP. The burden of care for male child is greater than that of female child, probably because of the greater mobility of male children. At present, there are many researches on motor function intervention for children with CP. A guideline synthesized approaches to functional exercise in walking ability and hand mobility in children, indicating whole-task practice combined with assistive devices could increase independence and reduce caregiver burden (49).

This systematic review offers insight into factors related to caregiver burden and guides the supportive interventions aiming to reduce caregiver burden, but more additional research into factors associated with caregiver burden is needed.

Strengths and Limitations

This review was the first one to provide a comprehensive overview of caregiver burden of children with CP. The protocol was registered on the PROSPERO database (CRD42021268284) and was carried out based on the PRISMA guidelines. The quality of evidence for factors was judged by the GRADE approach. There were also some limitations of the review. First, the included literatures used different measurement tools for the burden of care, and the survey details of the total care burden with/without the burden of each dimension were different. Secondly, due to the uneven quality of the included studies, the quality of the literature is at a medium level, and convenience sampling is often used, which has many methodological limitations.

Conclusion

Caregivers of children with CP generally have a heavy burden of caregiving, which has affected the physical, psychological, social and economic conditions of the caregivers. We summarized factors related to caregiver burden from the aspects of caregiver factors and children factors. The results revealed that anxiety, depression, mental health and physical health of caregiver, gender and severity of illness in children with CP were moderate to high quality of evidence for factors contributing to caregiver burden. At present, the relevant literature on the factors affecting the caregiver burden of children with CP are mostly cross-sectional studies, and lack of longitudinal studies with high demonstration efficiency. In the future, we should focus on carrying out high-quality longitudinal research, and verifying the relevant influencing factors of caregiver burden of children with CP. Moreover, by identifying all of the factors, healthcare professionals can provide appropriate assistance to relieve caregiver burden and improve the quality of caregiving for children with CP.

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Contributor statement

This study was conceived and designed by FL and QS. FL developed the search strategy and performed the literature search. FL and QS performed full-text reviews and extraction of data. FL and MH conducted the statistical analysis with input from QS. FL wrote the first draft. All authors reviewed all drafts and approved the final submitted manuscript. Data extraction and quality assessment adhered to PRISMA guidelines.

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Competing interests

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

Data sharing statement

All data relevant to the study are included in the article or uploaded as supplementary information.

Ethics statements

Patient consent for publication

Not applicable.

Ethics approval

This realist synthesis included literature that is available in the public domain and did not involve the collection of personal data.

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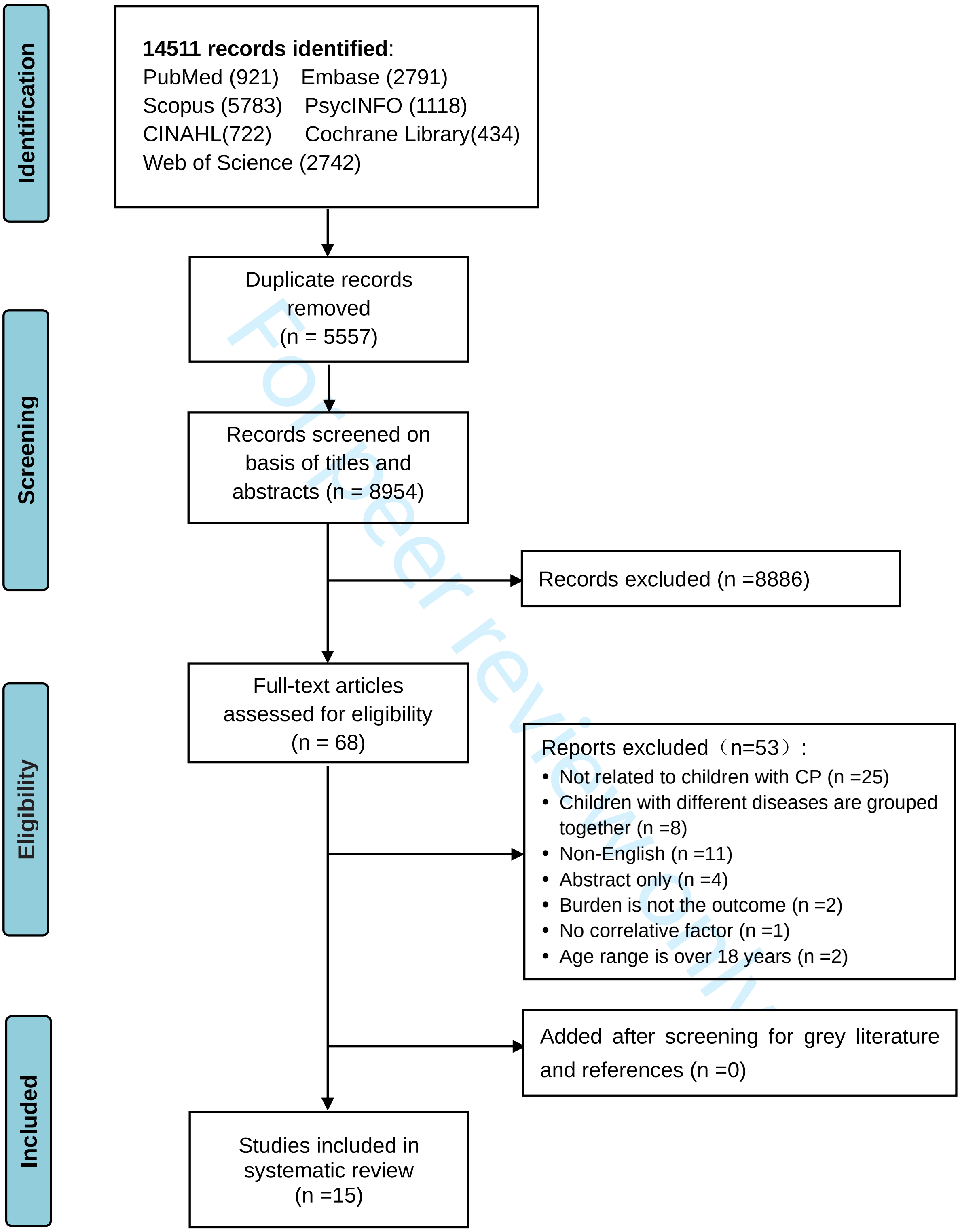

Figure 1. Flow diagram for a systematic literature review on caregiver burden in children with cerebral palsy

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Appendix 1-1 PRISMA Checklist

Section and Topic	Item #	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See table below
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3-4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable

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Section and Topic	Item #	Checklist item	Reported on page #
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	4
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	4
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix 5
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not applicable
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Table 2 and 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Table 4
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	16-17
	23b	Discuss any limitations of the evidence included in the review.	17
	23c	Discuss any limitations of the review processes used.	17
	23d	Discuss implications of the results for practice, policy, and future research.	17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not described
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not described
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	18
Competing interests	26	Declare any competing interests of review authors.	18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	18

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Appendix 1-2 PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

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Appendix 2 Literature Search

Medline (via PubMed) search strategy August 2021

("caregiver"[MeSH Terms] OR "parents"[Title/Abstract] OR "mother"[Title/Abstract] OR "care*"[Title/Abstract]) AND ("caregiver burden"[MeSH Terms] OR "stress"[Title/Abstract] OR "strain"[Title/Abstract] OR "burnout"[Title/Abstract]) AND ("cerebral palsy"[MeSH Terms] OR "CP"[Title/Abstract] OR "disability*"[Title/Abstract] OR ("neurodev*"[All Fields] AND "disorder*"[Title/Abstract])) AND ("child"[MeSH Terms] OR "child*"[Title/Abstract] OR "paediatr*"[Title/Abstract])

Embase search strategy August 2021

('caregiver burden'/exp OR 'caregiver burden':ti,ab,kw OR stress:ti,ab,kw OR 'strain':ti,ab,kw OR 'burnout':ti,ab,kw) AND ('caregiver'/exp OR caregiver:ti,ab,kw OR care*:ti,ab,kw OR parents:ti,ab,kw OR mother:ti,ab,kw) AND ('cerebral palsy'/exp OR 'cerebral palsy':ti,ab,kw OR 'neurodev* disorder*':ti,ab,kw OR disability*:ti,ab,kw) AND ('child'/exp OR children:ti,ab,kw OR child*:ti,ab,kw OR paediatr*:ti,ab,kw)

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Appendix 3:

JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies

Item	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
2. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were objective, standard criteria used for measurement of the condition?	☐	☐	☐	☐
5. Were confounding factors identified?	☐	☐	☐	☐
6. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Comments (Including reason for exclusion)

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Appendix 4: GRADE factors

Item	GRADE factor	Criteria (No serious limitation = ✓, serious limitation=✕)
1.	Study limitations	No serious limitation, if at least 75% of the studies are moderate- (total score 3-5) to high quality (total score 6-8) studies based on the JBI Critical Appraisal Checklist.
2.	Inconsistency	No serious limitation, if the point of effect estimates are not on either side of the line of no effect.
3.	Indirectness	No serious limitation, if at least 75% of the studies used a study sample that fully represents the review question.
4.	Imprecision	No serious limitation, if 75% of the studies applied the rule of thumb: univariate ratio [n:K] exceeds [20:1] and if multivariate ratio [n:K] exceeds [10:1]. In which n represents the sample size and K the number of studied factors.
5.	Publication bias	No serious limitation, if the factor is investigated in 3 or more studies.

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Appendix 5: Quality Assessment List

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Total
Carona (2013) [14]	1	1	0.5	1	1	1	0.5	1	7
Bella (2011) [15]	1	1	0.5	1	1	1	0.5	1	7
Whittingham (2012) [16]	1	1	1	1	0.5	0.5	1	1	7
Farajzadeh (2021) [17]	1	1	1	0.5	0.5	1	1	1	7
Boztepe (2018) [18]	1	1	1	0.5	1	1	1	1	7.5
Omole (2017) [19]	1	1	0.5	1	0.5	1	0.5	1	6.5
Terathongkum (2020) [8]	1	0	1	0.5	0.5	0.5	1	1	5.5
Farajzadeh (2020) [20]	1	1	1	0.5	0.5	1	1	1	7
Wijesinghe (2015) [21]	0.5	0	1	0.5	0.5	0	1	1	4.5
Barutcu (2021) [22]	1	1	1	1	0.5	0	1	1	6.5
Ozkan (2018) [23]	1	1	0.5	1	0.5	0	0.5	1	5.5
Gugała (2021) [24]	1	1	1	1	0.5	1	1	1	7.5
Marrón (2013) [25]	1	0	0.5	0.5	0.5	1	0.5	1	5
Albayrak (2019) [12]	1	1	0.5	0.5	1	1	0.5	1	6.5
Santos (2012) [26]	1	0	0.5	0.5	0.5	0	0.5	1	4

1= Yes; 0= NO; 0.5= Unclear

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Factors associated with caregiver burden among family caregivers of children with cerebral palsy: A systematic review

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Abstract

Objectives: To identify caregiver and children factors associated with caregiver burden on primary caregivers of children with cerebral palsy.

Design: Systematic review

Data sources: Seven electronic databases, including PubMed, Cochrane Library, Scopus, PsycINFO, Web of Science, CINAHL and Embase, were systematically searched up to February 1, 2023.

Eligibility criteria: Original observational studies reporting caregiver burden and related factors among caregivers of children with cerebral palsy.

Data abstraction and synthesis: Two reviewers independently screened results and assessed the quality of studies. Title, abstract, full-text screening and data abstraction were done independently by two reviewers. Risk of bias was assessed using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies. The quality of evidence for factors was rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results: 16 articles were included in the review. All studies were cross-sectional and examined caregiver-reported burden measures. The Zarit Burden Interview was the most commonly used questionnaire. Depression of caregiver and severity of illness in children with CP were moderate quality of evidence for factors contributing to caregiver burden.

Conclusions: Higher caregiver burden is associated with more depressive feelings and worse life quality of the caregiver, and with more severe physical disability of the children. Future studies should focus on high-quality longitudinal research and appropriate assistance to reduce caregiver burden and improve the quality of caregiving for children with CP.

Key words: caregiver burden, cerebral palsy, systematic review

PROSPERO 2021 CRD: 42021268284

Strengths and limitations of this study:

- This review was the first one to provide a comprehensive overview of caregiver burden of children with CP.
- The protocol was registered on the PROSPERO database (CRD42021268284) and was carried out based on the PRISMA guidelines.
- The quality of evidence for factors was judged by the GRADE approach.
- Many survey factors of the total care burden were scattered and failed to provide reliable evidence.
- The uneven quality of the included studies resulted in many methodological limitations.

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Introduction

With the development of perinatal medicine and obstetric technology, the birth prevalence of cerebral palsy in high-income countries had declined to 1.6 per 1000 live births, while the prevalence in low- and middle-income countries was as high as 3.4 per 1000 live births (1). Cerebral palsy (CP) is defined as a group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, behaviour, and by a seizure disorder (2). CP is the most common paediatric disability, seriously affecting the children's self-care ability and social activities (3, 4). Thus, Children with CP often require lifetime extensive care and rehabilitation training, which will bring heavy psychological, physical and economic burden to their families (5, 6).

Parents, as the primary caregivers of children with disabilities, bear the arduous caregiving burden. Not only do they have to help the children’s daily activities, but they also need to pay close attention to their changing health conditions, which directly leads to changes in the caregivers’ lifestyle and a decline in their quality of life (7, 8). Caregiver burden has been defined as a multidimensional response to physical, emotional, psychological, and financial stressors that are associated with caregiving experience (9). Studies have shown that a high level of caregiving burden for children with CP negatively affects the mental and physical health, family functions and social interactions of caregivers, resulting in low quality of care and unmet patient needs (10, 11, 12, 13). Paying attention to the burden of caregivers is of great significance.

Relevant factors that affect caregiver burden should be studied in order to propose interventions to support caregivers. In the last decade, there has been an increasing number of studies on the care burden for children with CP, but a comprehensive review of caregiver factors and patient factors influencing caregiver burden is lacking. Therefore, the objective of this study was to systematically review published literature to identify caregiver and patient factors of caregiver burden among primary caregivers of children with CP.

Methods

This systematic review was checked through the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Appendix 1). The protocol has been registered with PROSPERO 2021 CRD 42021268284.

Search strategy

The electronic databases PubMed, Cochrane Library, Scopus, PsycINFO, Web of Science, CINAHL and Embase were systematically searched from inception to February 1, 2023. The search string contained four groups of combinations of medical subject headings and text words: Caregiver (MeSH term), care*, parents or mother; Caregiver burden (MeSH term), stress, strain or burnout; Cerebral palsy (MeSH term), CP, disability* or neurodev* disorder*; Children (MeSH term), child* or paediatr* (Appendix 2). Additionally, we also searched for grey literature using the first 500 hits from Google Scholar and Open Grey. References for relevant publications were checked to make sure that no relevant papers had been missed.

Inclusion &Exclusion criteria

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Original observational studies reporting burden and related factors of caregivers of children with CP were taken as the primary focus of the research; Study participants need to be primary caregivers (over 18 years old) of children (0-18 years old) with cerebral palsy. Burden had to be assessed with a total caregiver burden construct; Full-text articles published in English or with an English translation in peer-reviewed journals were included. Studies where caregivers of children with different diagnoses and children with adults are grouped together were excluded, unless results were reported separately for caregivers of children with CP. Intervention studies, reviews, non-original research papers, qualitative research studies were not eligible for this review.

Data extraction and Quality assessment

The titles/abstracts of citations retrieved using the search strategy were independently assessed by two reviewers. The full text articles of potentially relevant studies were then independently screened by two reviewers, and any discrepancies were resolved through discussion. The number of studies excluded during each screening phase, and the reasons for full-text exclusion will be described in a PRISMA flow diagram. A pre-specified form will be used for the extraction of the data from the included studies. This procedure will be completed by one reviewer, and verified by a second reviewer, with any disagreements being resolved through discussion with a third-party reviewer. We extracted the following data from each included study independently by two researchers: first authors, year of publication, sample size, study design, relevant participant demographics, key predictor and outcome variables, self-administered tools used for measurement, results and associations.

Risk of bias was assessed using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies (Appendix 3) by the two researchers independently. The checklists include 8 questions to evaluate the overall quality of the studies from the research object, disease, measurement of influencing factors and confounding factors, data analysis, etc. The choices of answers were ‘yes’, ‘no’, ‘unclear’ or ‘not applicable’. The overall appraisal of ‘include’, ‘exclude’ or ‘seek further information’ were presented in the last section of the checklist.

Data synthesis

Due to the diversity of outcome measures and factors included in the study, a meta-analysis was not possible. Bivariate associations were described in terms of different statistical analysis. Multivariate associations were described as standardized or Unstandardized coefficients (*β or b*). In studies that applied a logistic regression, the odds ratio (*OR*) was presented. Factors were grouped into caregiver and children characteristics subsequently thematically categorized.

Quality of evidence

We assessed the quality of evidence for each factor measured in at least three studies using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Appendix 4). GRADE has four levels of evidence: very low, low, moderate, and high. Evidence from observational data starts at low quality. For each of study limitation in risk of bias, imprecision, inconsistency, indirectness, and publication bias, researchers have the option of rating down their level of certainty in evidence. Quality of evidence also can be rated up for “large effect” or “dose effect”.

Patient and public involvement

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Patients or public were not involved in the conduct of this systematic review.

Results

Search and screening

The search identified a total of 16754 possibly relevant articles. After the removal of duplicates and the abstract screening, a total of 80 studies were selected for full-text review. Finally, 16 studies were left for full inclusion in the review. There were no additional articles met the inclusion criteria when searching the references of the 16 articles. The PRISMA flow diagram for search and screening results are shown in Figure 1.

Risk of bias

Risk of bias scores for studies ranged from 4 to 7 out of a maximum of 8 points. Some articles lacked clear information in items: study subjects and the setting, exposure factors, and confounding bias. The methodological quality assessment list was listed in supplementary Appendix 5.

Characteristics of the included studies

The 16 included studies reported on overall caregiver burden and related factors of children with CP. Studies were conducted in eleven different countries between 2011 and 2022, involving in 3109 caregivers (not inclusive of controls). Of these, 14 studies investigated univariate associations; 9 studies were explored in multivariate associations. Caregivers were predominantly female, and 5 of the 16 articles had samples made up exclusively of mothers. 6 articles involved fathers. The mean age of caregivers varied from 31 to 42 years. Four studies involved control populations, two of four had caregivers of healthy children as the control group. All studies were cross-sectional surveys. The most used sampling method was convenience sampling. The key characteristics of each study are presented in Table 1.

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Table 1. The summary of included studies

Authors (Year)	Country	Design	Caregiver sample size	Caregiver relation to child	Mean age of Caregivers M(SD)	Age of children (years)	Measures tool
Carona et al. (2013)[14]	Portugal	Cross-sectional Study	93	Mothers (83.8%)	42.34(5.72)	8-18	BM
Bella et al. (2011)[15]	Brazil	Cross-sectional Study	38	Mothers (-)	33.3(7.7)	4-11	BI
Whittingham et al. (2013)[16]	Australia	Correlational survey study	94	Mothers (90.4%)	-	2-12	DPC Burden
Farajzadeh et al. (2021)[17]	Iran	Cross-sectional study	160	Female (84.4%)	35.47(6.59)	2-14	CDS
Boztepe et al. (2019)[18]	Turkey	Cross-sectional Study	69	Mothers (100%)	34.6(7.3)	1-18	ZBI
Omole et al. (2019)[19]	Nigeria	Cross-sectional Study	209	Female (91.9%)	34.6(9.2)	1-12	CDS
Terathongkum et al. (2020)[8]	Thailand	correlational research	75	Female (88.0%)	-	0-18	VQ burden
Farajzadeh et al. (2020)[20]	Iran	Cross-sectional Study	203	Mothers (100%)	34.48(6.74)	4-14	CDS
Wijesinghe et al. (2015)[21]	Sri Lanka	Cross-sectional Study	375	Mothers (97%)	32.4(7.2)	1-12	CDS
Barutcu et al. (2021)[22]	Turkey	Cross-sectional Study	109	Mothers (98.2%)	38.53(9.62)	1-18	ZBI
Ozkan et al. (2018)[23]	Turkey	Cross-sectional Study	120	Mothers (100%)	-	2-18	ZBI
Gugała et al. (2021)[24]	Poland	Cross-sectional Study	190	Female (72.6%)	40.6(9.1)	2-18	CBS
Marrón et al. (2013)[25]	Spanish	Cross-sectional Study	62	Mothers (88.7%)	41.98(5.64)	1-17	ZBI
Albayrak et al. (2019)[12]	Turkey	Cross-sectional Study	101	Mothers (100%)	34.93(8.7)	0-18	ZBI
Santos et al. (2012)[26]	Brazil	Cross-sectional Study	21	Female (100%)	31(-)	1-12	ZBI
Moriwaki et al. (2022)[27]	Japan	Cross-sectional Study	1190	Mothers (100%)	37.97(5.28)	1-12	ZBI

BM: The Revised Burden Measure; BI: The Burden Interview; DPC Burden =Daily Parenting Tasks Checklist-Parenting Burden; ZBI: Zarit Burden Interview; CDS: Caregiver Difficulties Scale; VQ burden: Thai version Viriyaprasart's questionnaire about burden of care; CBS: Caregiver Burden Scale.

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Measures of burden

Seven instruments were used to measure caregiver burden including Zarit Burden Interview (n= 7) (12,18,22-23,25-27); Caregiver Difficulties Scale (n= 4) (17,19,20-21); Caregiver Burden Scale (n= 1) (24); The Revised Burden Measure (*n*= 1) (14); The Burden Interview (*n*= 1) (15); Daily Parenting Tasks Checklist-Parenting Burden (*n*= 1) (16); Viriyaprasart's questionnaire about burden of care (*n*= 1) (8).

Studied factors in relation to caregiver burden

Overviews of caregiver and children characteristics as factors of caregiver burden are presented in Tables 2 and 3. The detailed description is described as follows.

Caregiver factors

Caregiver factors were grouped into five categories, including caregiver demographics, emotional functioning, physical functioning, overall health and social functioning. Caregiver demographical factors included age (8,12,18-19,21-22), gender (19), educational level (18-19,21-22), monthly income (18-19,21-22), number of caregiver (22), socioeconomic status (19), geographic area (21), mother employment (27), additional helper (18), daily caring time (12). Emotional functioning factors included anxiety (17,22,24), depression (12,17-18,20,22,24-25), mental health (12,14-15,20), perceived stress (15,17), beliefs of rehabilitation (8), perceived self-efficacy (8,25), experiential avoidance (16). This category was included in eleven of the 15 studies. Physical functioning factors included sleep quality (12), pain (12,15), fatigue (12,20), physical health (12,15,20). Overall health factors included quality of life (8,14). Social functioning factors included social functioning (15,20), environment health (20), social support (8,14,27), coping (16,21).

Children factors

Children factors were grouped into five categories, including children demographics, disease-related, behavioural functioning, overall health and social environment. Children demographical factors included age (8,12,18-19,21-22), gender (18,19,21-22), going to nursery/school (27), residence (27), birth order (19), number of children (18,21-22), number of disabled child (22), body mass index (12). Disease-related factors included type of CP (19,21), severity of CP (12,18,19,25), tube/intravenous nutrition (27), etiology (19), additional physical illness (18), associated conditions (19,21), functional impairments (21). This category was included in five of the 15 studies. Behavioural functioning factors included functional status (22), behavioural problems (14,16). Overall health and social environment factors included quality of life (14,23), social support (14) and environment (26).

Quality of evidence for potential factors

Quality of evidence for potential factors of caregiver burden are presented in Supplementary Table. The criteria for compelling evidence are that each factor was measured in at least three studies reported significant relationships. The details are as follows.

Caregiver factors

The results of evidence synthesis for caregiver factors using the GRADE criteria were that

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“depression” was the moderate quality of evidence for factor of caregiver burden. “Age”, “anxiety” and “fatigue” of caregivers was the low quality of evidence for factors of caregiver burden. Very low quality of evidence was found for the relationship between caregiver burden and “education”, “monthly income”, “mental health”, “physical health” and “social support” of caregivers.

Children factors

The synthesis of the evidence for children factors resulted in moderate quality of evidence between caregiver burden and “severity of illness”. The factors for “age” and “gender” of children, “number of Children” were the low quality of evidence for the relations with caregiver burden. Few of the included studies have explored children factors, and fewer factors have been able to perform evidence synthesis.

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Table 2. Associations between caregiver factors and caregiver burden

	Factor	**Measure factor**	**Outcome caregiver burden**	**Bivariate analysis**	**Bivariate association** r/t/F/β/Z	**Multivariate association** β/b (95%CI)	**N**	**Ref**
Demographics	Age	Years	VQ burden	P	ns	-	75	8
		Years	ZBI	P or S	0.20*	-	101	12
		Years	ZBI	-	-	ns	69	18
		Years	CDS	S	ns	-	209	19
		Years	CDS	R	ns	-	375	21
		Years	ZBI	P or S	ns	-	109	22
	Gender	Male/female	CDS	T	-2.01*	-	209	19
	Education	0-4 level	ZBI	-	-	ns	69	18
		0-2 level	CDS	A	4.95**	2.61**(1.97-14.09)	209	19
		Low education	CDS	R	ns	-	375	21
		0-5 level(mother)	ZBI	P or S	ns	-	109	22
	Monthly income	TI	ZBI	-	-	ns	69	18
		0-4 level	CDS	A	ns	-	209	19
		Low income	CDS	R	8.65***	3.69*(-)	375	21
		0-2 level	ZBI	P or S	4.45*	-	109	22
	Number of caregiver	1/2	ZBI	P or S	ns	-	109	22
	Socioeconomic status	0-4 level	CDS	A	ns	-	209	19
	Geographic area	Rural area	CDS	R	6.27**	5.35**(-)	375	21
	Mother employment	Yes/No	ZBI	U	ns	-	1190	27
	Additional helper	None or present	ZBI	-	-	ns	69	18
	Daily Caring time	Hours	ZBI	P or S	ns	-	101	12
Emotional functioning	Anxiety	HADS-A	CDS	P	0.47***	0.14***(nr)	160	17
		BAI	ZBI	P or S	0.29**	-	109	22
		HADS-A	CBS	P	0.51****	-	190	24
	Depression	BDI	ZBI	P or S	0.70***	-	101	12
		HADS-D	CDS	P	0.51***	0.17***(nr)	160	17
		BDI	ZBI	-	-	0.48***(nr)	69	18
		BDI-II	CDS	P	0.64***	-	203	20
		BDI-II	ZBI	P or S	0.41****	-	109	22
		HADS-D	CBS	P	0.38****	-	190	24
		BDI-II	ZBI	-	-	0.36**(0.17-0.73)	62	25
	Mental health	SF-36-MCS	ZBI	P or S	ns	-	101	12
		MHI-5	BM	nr	-0.51**	-0.20*(nr)	93	14
		SF-36-RE	BI	S	ns	-	38	15
		SF-36-MH	BI	S	-0.62*	-	38	15
		WHOQOL-BREF-PsyH	CDS	P	-0.68***	-	203	20
	Perceived stress	PSQ	BI	S	0.65***	-	38	15
		PSS-4	CDS	P	0.43***	0.10***(nr)	160	17
	Beliefs of rehabilitation	RBQ	VQ burden	P	ns	-	75	8
	Perceived self-efficacy	PSQ	VQ burden	P	-0.25*	-	75	8
		RSCSE	ZBI	-	-	-0.19**(-0.31~-0.06)	62	25
	Experiential avoidance	AAQ-16	DPC Burden	nr	0.42****	0.31**(0.52-1.21)	94	16
Physical	Sleep quality	PSQI	ZBI	P or S	0.39***	-	101	12

functioning	Pain	NRS	ZBI	P or S	0.36***	-	101	12
		SF-36-BP	BI	S	-0.40*	-	38	15
	Fatigue/ Vitality	CIS	ZBI	P or S	0.66***	-	101	12
		FSS	CDS	P	0.40***	-	203	20
		SF-36-VT	BI	S	-0.54*	-	38	15
	Physical health	SF-36-PCS	ZBI	P or S	-0.21*	-	101	12
		SF-36-PF	BI	S	ns	-	38	15
		SF-36-RP	BI	S	ns	-	38	15
		SF-36-GH	BI	S	-0.44*	-	38	15
		WHOQOL-BREF-PH	CDS	P	-0.59***	-	203	20
Overall health	Quality of life	VQ well-being	VQ burden	P	-0.50**	-	75	8
		WHOQOL-8	BM	nr	-0.39**	-0.16*(nr)	93	14
Social functioning	Social functioning	SF-36-SF	BI	S	-0.61*	-	38	15
		WHOQOL-BREF-SR	CDS	P	-0.68***	-	203	20
	Environment health	WHOQOL-BREF-E	CDS	P	-0.63***	-	203	20
	Social support	SSS	BM	nr	-0.35**	-0.41**(nr)	93	14
		SSQ	VQ burden	P	ns	-	75	8
		Family support	ZBI	U	ns	-	1190	27
		Others support	ZBI	U	nr**	-	1190	27
		Home-visit nursing	ZBI	C	nr**	-	1190	27
		Home care	ZBI	C	nr*	-	1190	27
		Home-visit rehabilitation	ZBI	C	nr**	-	1190	27
		Training & treatment	ZBI	C	ns	-	1190	27
		Short stay	ZBI	C	ns	-	1190	27
		Mobility support	ZBI	C	nr*	-	1190	27
		Transportation services	ZBI	C	ns	-	1190	27
		No social support usage	ZBI	C	nr*	-	1190	27
		Satisfaction with home-visit nursing	ZBI	C	ns	-	1190	27
		Satisfaction with home care	ZBI	C	nr*	ns	1190	27
		Satisfaction with home-visit rehabilitation	ZBI	C	nr**	ns	1190	27
		Satisfaction with training & treatment	ZBI	C	nr**	ns	1190	27
		Satisfaction with short stay	ZBI	C	nr**	−0.29*	1190	27
		Satisfaction with mobility support	ZBI	C	ns	-	1190	27
		Satisfaction with transportation services	ZBI	C	ns	-	1190	27
	Coping	CHIP	DPC Burden	nr	ns	ns	94	16
		Individual coping	CDS	R	ns	-	375	21
		Seeking social support	CDS	R	-8.99***	ns	375	21
		Spouse support	CDS	R	-7.44***	-5.67**(nr)	375	21

HADS: Hospital Anxiety and Depression Scale; HADS-A: HADS-Anxiety Scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; HADS-D: HADS-Depression Scale; BDI-II: Beck Depression Inventory-II; SF-36: 36-Item Short Form Health Survey; SF-36-MCS: SF-36-Mental component summary; MHI-5: Mental Health Inventory-short form; SF-36-RE: SF-36-Emotional Role; SF-36-MH: SF-36-Mental health; WHOQOL-BREF: World Health Organization's Quality of Life Questionnaire; WHOQOL-BREF-PsyH: WHOQOL-BREF-Psychological health; PSQ: Perceived self-efficacy in the care questionnaire; PSS-4: Perceived Stress Scale-4 item; RBQ: Adapted rehabilitation belief questionnaire; RSCSE: Revised Scale for Caregiving Self-Efficacy; AAQ-16: Acceptance and Action Questionnaire; PSQI: Pittsburgh sleep quality index; NRS: Numerical rating scale; SF-36-BP: SF-36-Bodily pain; CIS: Multidimensional checklist individual strength; FSS: Fatigue Severity Scale; SF-36-VT: SF-36-Vitality; SF-36-PCS: SF-36-Physical component summary; SF-36-PF:SF-36-Physical functioning; SF-36-RP: SF-36-Physical Role; SF-36-GH: SF-36-General health; WHOQOL-BREF-PH: WHOQOL-BREF-Physical health; VQ well-being: Thai version Viriyaprasart's questionnaire about well-being; WHOQOL-8: The World Health Organization Quality of Life Assessment 8 item index; SF-36-SF: SF-36-Social functioning; WHOQOL-BREF-SR: WHOQOL-BREF-Social relationships; WHOQOL-BREF-E: WHOQOL-BREF-Environment; SSS: Satisfaction with social support scale; SSQ: Adapted social support questionnaire; CHIP: Coping Health Inventory for Parents.

S: Spearman's linear correlation coefficient/ Spearman's Rho correlation; P: Pearson correlation coefficient; A: One-way analysis of variance (ANOVA); T: Independent Student's t-test; R: Univariate regression analysis; U: Mann-Whitney U; C: Chi-squared test; nr: not reported; ns: not significant.

****P< 0.0001, ***P < 0.001, **P < 0.01, *P < 0.05.

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Table 3. Associations between children factors and caregiver burden

	Factor	**Measure factor**	**Outcome caregiver burden**	**Bivariate analysis**	**Bivariate association** r/t/F/β/Z/H/X^2	**Multivariate association** β/b (95%CI)	**N**	**Ref**
Demographics	Age	Years	VQ burden	P	ns	-	75	8
		Years	ZBI	P or S	ns	-	101	12
		Years	ZBI	-	-	ns	69	18
		Years	CDS	S	ns	-	209	19
		Years	CDS	R	ns	-	375	21
		1-5/6-12/>12 years old	ZBI	P or S	ns	-	109	22
		Years	ZBI	U	ns	-	1190	27
	Gender	Male/female	ZBI	-	-	ns	69	18
		Male child	CDS	T	3.02**	0.18**(1.56-8.34)	209	19
		Male child	CDS	R	3.60*	3.50*(-)	375	21
		Male/female	CBS	P or S	ns	-	109	22
	Going to nursery/school	Yes/No	ZBI	U	ns	-	1190	27
	Residence	Urban/Rural	ZBI	U	nr****	-	1190	27
	Birth order	1st/2nd/3rd or greater	CDS	A	ns	-	209	19
		First/or not	ZBI	U	ns	-	1190	27
	Number of Children	3 or higher	ZBI	-	-	ns	69	18
		1/2/3	CDS	R	ns	-	375	21
		1/2/3/4 or more	ZBI	P or S	0.20*	-	109	22
		1/or not	ZBI	U	ns	-	1190	27
	Number of disabled	1/or not	ZBI	P or S	ns	-	109	22
	Body mass index	BMI	ZBI	P or S	ns	-	101	12

Disease-related	Type of CP	5 types	CDS	A	3.15*	-	209	19
		Spastic quadriplegia	CDS	R	10.62***	-	375	21
	Severity of illness	GMFCS	ZBI	P or S	0.30**	-	101	12
		Severity of illness scale	ZBI	-	-	0.29*(nr)	69	18
		GMFCS-ER	CDS	A	6.87***	0.29***(4.42-11.23	209	19
		nr	ZBI	-	-	0.28*(0.04-0.35)	62	25
		3 levels	ZBI	H	nr**	ns	1190	27
	Tube/intravenous nutrition	Yes/No	ZBI	C	nr*	ns	1190	27
	Etiology	7 types	CDS	A	2.49*	-	209	19
	Additional physical illness	Absent/present	ZBI	-	-	ns	69	18
	Associated conditions	0/1/2/3/4 or more	CDS	A	3.21*	-	209	19
		0/1 or more	CDS	R	12.75***	ns	375	21
	Functional impairments	Number of functional deficits	CDS	R	3.97***	2.64***(nr)	375	21
Behavioural functioning	Functional status	FIM	ZBI	P or S	ns	-	109	22
	Behavioural problems	SDQ	BM	nr	0.24*	0.29**	93	14
		SDQ	DPC Burden	nr	0.38****	0.27**(0.06-1.43)	94	16
Overall health	Quality of life	KIDSCREEN-10	BM	nr	ns	-	93	14
		PedsQL	ZBI	P	0.40***	-	120	23
Social environment	Social support	SSSS	BM	nr	ns	-0.19*(nr)	93	14
	Environment	Space for child locomotion	ZBI	P	nr*	-	21	26

BMI: Body mass index; GMFCS: Gross Motor Function Classification System; GMFCS-ER: Gross Motor Function Classification System- Expanded and Revised; FIM: Functional Independence Measure; SDQ: Strengths and Difficulties Questionnaire; KIDSCREEN-10: The shortest version of Kidscreen questionnaires; PedsQL: Pediatric Quality of Life 4.0 Generic Core Scales; SSSS: Satisfaction with social support scale for children and adolescents.

S: Spearman's linear correlation coefficient/ Spearman's Rho correlation; P: Pearson correlation coefficient; A: One-way analysis of variance (ANOVA); T: Independent Student's t-test R: Univariate regression analysis; nr: not reported; ns: not significant; U: Mann-Whitney U; H: Kruskal-Wallis H; C: Chi-squared test; nr: not reported; ns: not significant.

****P< 0.0001, ***P < 0.001, **P < 0.01, *P < 0.05

Discussion

Caring for children with CP is a stressful and difficult task for primary caregivers, especially for their parents. Caregivers of children with CP were under higher pressure than caregivers of healthy children (12, 28, 29). There were many factors that affect the caregiving burden for children with CP. In our systematic review, we focused on both caregiver characteristics and children characteristics as factors of caregiver burden. There are fewer studies involving children-related factors than caregiver-related factors, possibly because caregiver-related factors are more likely to modify. This review revealed that anxiety and depression of caregiver, severity of illness in children with CP were moderate quality of evidence for factors contributing to caregiver burden. But our ability to draw conclusions on remaining caregiver and children characteristics as factors is limited because of low to very low quality of evidence.

Moderate quality was found for the association between caregiver burden and depression symptoms of the caregiver. Feelings of depression are positively correlated with caregiver burden of the caregiver. But the factor for mental health predicting psychological well-being of the caregiver as well was rated as very low quality of evidence. This may be due to the limited number of studies that did not yield reliable evidence. Three studies included in this review revealed that caregivers, who experience poor psychological condition, are more likely to experience high caregiver burden. This correlation between mental health of caregiver and caregiver burden is consistent with the findings in other children with neurodevelopmental diseases, such as epilepsy and autism spectrum disorder (30, 31, 32). Mother caregivers constitutes the majority of caregiving. Long-term care of children with CP and restricted social activity for the mother caregiver predict more psychological conditions such as anxiety, depression, and distress in them (33). Caregivers who feel depressed experience a greater burden of care, thereby affecting CP children's quality of life (23). A study revealed that psychological interventions such as Stepping Stones Triple P therapy (SSTP), Acceptance and Commitment Therapy (ACT) could improve parental mental wellbeing of parents of children with CP. It is crucial to develop more interventions that focus primarily on the psychological wellbeing of the parents (34).

Low quality of evidence was found for the relationship between caregiver burden and fatigue of the caregiver. Fatigue of caregivers are positively related to caregiver burden. Children with CP are often accompanied by intellectual and physical disabilities. Daily life care and assistance with rehabilitation exercises mean more physical strength and energy for the caregiver, so that caregivers often experience problems such as body pain, fatigue and sleep problems (12, 35, 36, 37, 38), which seriously affect the physical well-being and reduce the quality of life of the caregiver (39, 40). Few studies have focused on interventions for caregivers' physical conditions. We should actively pay attention to the physical health of the caregiver and take feasible interventions to improve the physical functioning of caregivers of children with CP.

In our systematic review, it is not sufficiently concluded that social support for caregivers is a positive factor in reducing the burden. But many previous studies have explored the correlation between social support and parenting stress in caregivers of children with CP. Negative associations were found between the levels of stress among parents and social support perceived by them (41, 42, 43, 44). Many families faced financial difficulties and restricted access to healthcare services (45, 46). Social support from spouses, social organization and medical institution help prevent and decrease the stressful situation of the family's experience in providing

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care to children with CP (43, 47). Although parenting stress and caregiver burden have similar meanings, this review focuses on caregiver burden and involves fewer relevant articles about the association between social support and care burden, so more evidence is needed to determine their relevance.

The factor for severity of illness in CP children as moderate quality of evidence is positively correlated with the burden of caregiver. GMFCS score is most commonly used to measure the severity of disability of children with CP. Children with more severe disabilities require the more support of their caregivers to carry out the activities of daily living. Caregivers will spend more time and physical strength to meet the caregiving demands (38, 48), and the caregiver burden will be heavier. In addition, there was no significant correlation between the age of CP children and the caregiver burden. And the gender of children with CP may affect the caregiver's burden. The burden of care for male child is greater than that of female child, probably because of the greater mobility of male children. At present, there are many researches on motor function intervention for children with CP. A guideline synthesized approaches to functional exercise in walking ability and hand mobility in children, indicating whole-task practice combined with assistive devices could increase independence and reduce caregiver burden (49).

This systematic review offers insight into factors related to caregiver burden and guides the supportive interventions aiming to reduce caregiver burden, but more additional research into factors associated with caregiver burden is needed.

Strengths and Limitations

This review was the first one to provide a comprehensive overview of caregiver burden of children with CP. The protocol was registered on the PROSPERO database (CRD42021268284) and was carried out based on the PRISMA guidelines. The quality of evidence for factors was judged by the GRADE approach. There were also some limitations of the review. First, the included literatures used different measurement tools, and the survey factors of the total care burden with/without the burden of each dimension were scattered. Secondly, due to the uneven quality of the included studies, the quality of the literature is at a medium level, and convenience sampling is often used, which has many methodological limitations.

Conclusion

Caregivers of children with CP generally have a heavy burden of caregiving, which has affected the physical, psychological, social and economic conditions of the caregivers. We summarized factors related to caregiver burden from the aspects of caregiver factors and children factors. The results revealed that depression of caregiver and severity of illness in children with CP were moderate quality of evidence for factors contributing to caregiver burden. At present, the relevant literature on the factors affecting the caregiver burden of children with CP are mostly cross-sectional studies, and lack of longitudinal studies with high demonstration efficiency. In the future, we should focus on carrying out high-quality longitudinal research, and verifying the relevant influencing factors of caregiver burden of children with CP. Moreover, by identifying all the factors, healthcare professionals can provide appropriate assistance to relieve caregiver burden and improve the quality of caregiving for children with CP.

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Contributor statement

This study was conceived and designed by FL and QS. FL developed the search strategy and performed the literature search. FL and QS performed full-text reviews and extraction of data. FL and MH conducted the statistical analysis with input from QS. FL wrote the first draft. HyZ was responsible for project administration and supervision on revised paper. All authors reviewed all drafts and approved the final submitted manuscript. Data extraction and quality assessment adhered to PRISMA guidelines.

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Competing interests

No competing interest.

Data sharing statement

All data relevant to the study are included in the article or uploaded as supplementary information.

Ethics statements

Patient consent for publication

Not applicable.

Ethics approval

This realist synthesis included literature that is available in the public domain and did not involve the collection of personal data.

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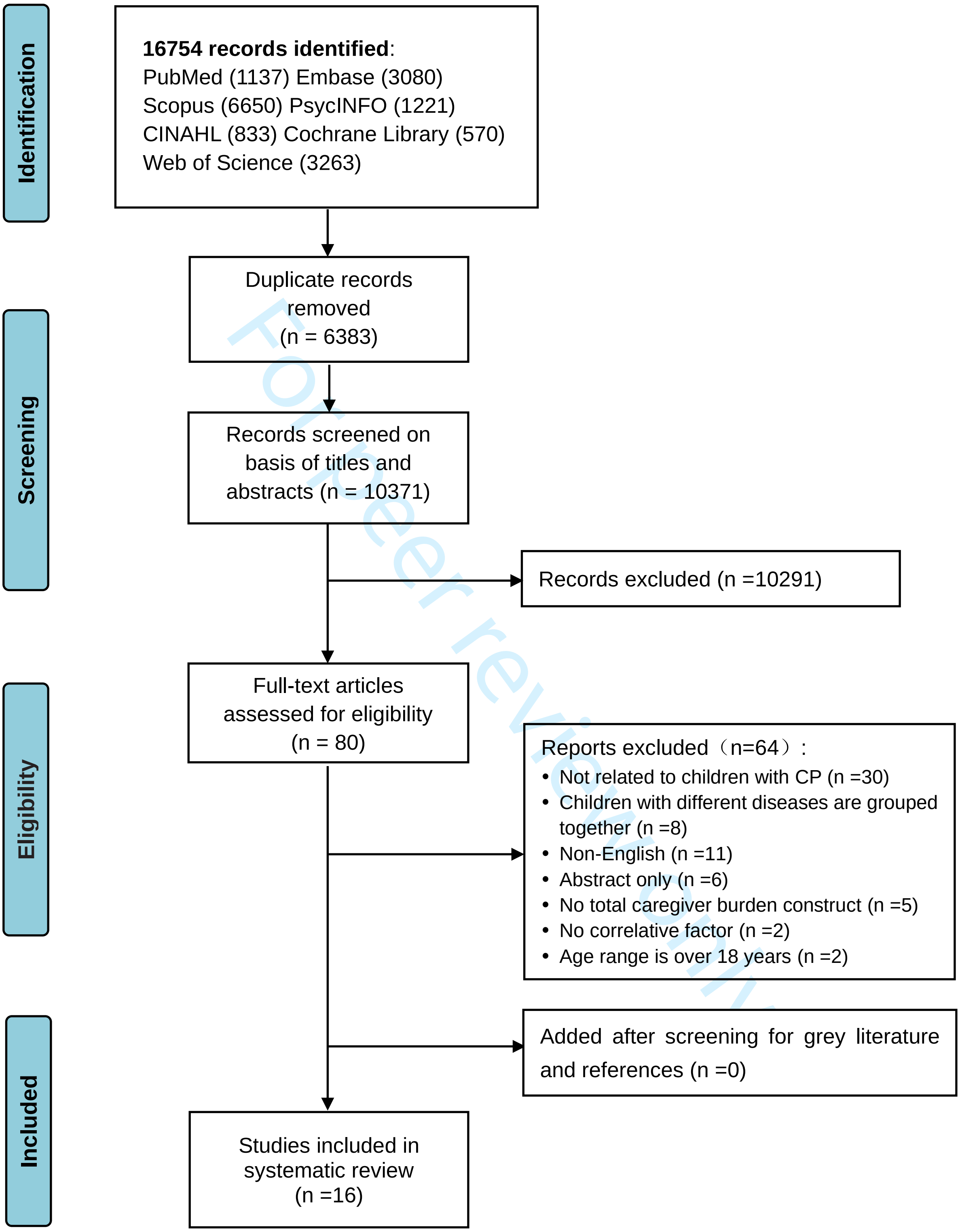

Figure 1. Flow diagram for a systematic literature review on caregiver burden in children with cerebral palsy

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Supplementary Table. Quality of evidence for potential factors

Potential factors	Participant (n)	NO. of studies	Bivariate			Multivariate			Grade factors					
			+	0	-	+	0	-	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality
Caregiver														
Age	938	6	1	4	0	0	1	0	√	√	√	√	√	Low
Education	762	4	1	2	0	1	1	0	√	×	√	√	√	Very low
Monthly income	762	4	2	1	0	1	1	0	√	×	√	√	√	Very low
Anxiety	459	3	3	0	0	1	0	0	√	√	√	√	√	Low
Depression	894	7	5	0	0	3	0	0	√	√	√	√	√	Moderate
Mental health	435	4	0	2	3	0	0	1	√	×	√	√	√	Very low
Fatigue	342	3	3	0	0	0	0	0	√	√	√	√	√	Low
Physical health	342	3	0	2	3	0	0	0	√	×	√	√	√	Very low
Social support	1358	3	0	8	11	0	3	2	√	√	√	√	√	Very low
Children												√		
Age	2128	7	0	6	0	0	1	0	√	√	√	√	√	Low
Gender	762	4	2	1	0	2	1	0	√	√	√	√	√	Low
Number of Children	1743	4	1	2	0	0	1	0	√	√	√	√	√	Low
Severity of illness	1631	5	3	0	0	3	0	0	√	√	√	√	√	Moderate

For bivariate and multivariate analyses: +: number of significant associations with a positive value; 0: number of non-significant associations; -: number of significant associations with a negative value; For GRADE factors: ✓: no serious limitations; ✕: serious limitations. For overall quality of evidence: very low, low, moderate, high.

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Appendix 1-1 PRISMA Checklist

Section and Topic	Item #	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See table below
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3-4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable

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Section and Topic	Item #	Checklist item	Reported on page #
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	4
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	4
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix 5
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not applicable
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Table 2 and 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Table 4
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	16-17
	23b	Discuss any limitations of the evidence included in the review.	17
	23c	Discuss any limitations of the review processes used.	17
	23d	Discuss implications of the results for practice, policy, and future research.	17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not described
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not described
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	18
Competing interests	26	Declare any competing interests of review authors.	18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	18

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Appendix 1-2 PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

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Appendix 2 Literature Search

First search: no filters

Supplementary search: filters applied from 2021/7/24—2023/2/1

The rest are not specifically qualified for retrieval.

CINAHL search strategy

((SU caregiver) OR (AB parents) OR (AB mother) OR (AB care*)) AND ((SU caregiver burden) OR (AB strain) OR (AB stress) OR (AB burnout)) AND ((SU cerebral palsy) OR (AB CP) OR (AB disability*) OR (AB neurodev* disorder*)) AND ((SU children) OR (AB child*) OR (AB paediatr*))

PsycInfo search strategy

((SU caregiver) OR (AB parents) OR (AB mother) OR (AB care*)) AND ((SU caregiver burden) OR (AB strain) OR (AB stress) OR (AB burnout)) AND ((SU cerebral palsy) OR (AB CP) OR (AB disability*) OR (AB neurodev* disorder*)) AND ((SU children) OR (AB child*) OR (AB paediatr*))

PubMed search strategy

(((((caregiver[MeSH Terms]) OR (parents[Title/Abstract])) OR (mother[Title/Abstract])) OR (care*[Title/Abstract])) AND ((((caregiver burden[MeSH Terms]) OR (stress[Title/Abstract])) OR (strain[Title/Abstract])) OR (burnout[Title/Abstract]))) AND ((((cerebral palsy[MeSH Terms]) OR (CP[Title/Abstract])) OR (disability*[Title/Abstract])) OR ((neurodev* disorder* [Title/Abstract]))) AND (((child[MeSH Terms]) OR (child*[Title/Abstract])) OR (paediatr*[Title/Abstract]))

Embase search strategy

('caregiver'/exp OR caregiver:ti,ab,kw OR care*:ti,ab,kw OR parents:ti,ab,kw OR mother:ti,ab,kw) AND ('caregiver burden'/exp OR 'caregiver burden':ti,ab,kw OR stress:ti,ab,kw OR strain:ti,ab,kw OR burnout:ti,ab,kw) AND ('cerebral palsy'/exp OR 'cerebral palsy':ti,ab,kw OR CP:ti,ab,kw OR 'neurodev* disorder*':ti,ab,kw OR disability*:ti,ab,kw) AND ('child'/exp OR children:ti,ab,kw OR child*:ti,ab,kw OR paediatr*:ti,ab,kw)

SCOPUS search strategy

(TITLE-ABS-KEY ("caregiver") OR TITLE-ABS-KEY ("parents") OR TITLE-ABS-KEY ("mother") OR TITLE-ABS-KEY ("care*")) AND (TITLE-ABS-KEY ("burden") OR TITLE-ABS-KEY ("stress") OR TITLE-ABS-KEY ("strain") OR TITLE-ABS-KEY ("burnout")) AND (TITLE-ABS-KEY ("cerebral palsy") OR TITLE-ABS-KEY ("CP") OR TITLE-ABS-KEY ("disability*") OR TITLE-ABS-KEY

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("neurodev* disorder*")) AND (TITLE-ABS-KEY ("children") OR TITLE-ABS-KEY ("child*") OR TITLE-ABS-KEY ("paediatr*"))

Web of science search strategy

(TS=(caregiver OR parents OR mother OR care*)) AND (TS=(caregiver burden OR strain OR stress OR burnout)) AND (TS=(cerebral palsy OR CP OR disability* OR neurodev* disorder*)) AND (TS=(children OR child* OR paediatr*))

Cochrane Library search strategy

#1 (caregiver):ti,ab,kw OR (parents):ti,ab,kw OR (mother):ti,ab,kw OR (care*):ti,ab,kw (Word variations have been searched)

#2 MeSH descriptor: [Caregivers] explode all trees

#3 #1 OR #2

#4 (burden):ti,ab,kw OR (stress):ti,ab,kw OR (strain):ti,ab,kw OR (burnout):ti,ab,kw (Word variations have been searched)

#5 MeSH descriptor: [Caregiver Burden] explode all trees

#6 #4 OR #5

#7 (cerebral palsy):ti,ab,kw OR (CP):ti,ab,kw OR (disability*):ti,ab,kw OR (neurodev* disorder*):ti,ab,kw (Word variations have been searched)

#8 MeSH descriptor: [Cerebral Palsy] explode all trees

#9 #7 OR #8

#10 (children):ti,ab,kw OR (child*):ti,ab,kw OR (paediatr*):ti,ab,kw (Word variations have been searched)

#11 MeSH descriptor: [Child] explode all trees

#12 #10 OR #11

#13 #3 AND #6 AND #9 AND #12

Grey literature:

[OpenGrey | The Online Library (london.ac.uk)]

[Google Scholar (beds.ac.uk)]

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Appendix 3:

JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies

Item	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
2. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were objective, standard criteria used for measurement of the condition?	☐	☐	☐	☐
5. Were confounding factors identified?	☐	☐	☐	☐
6. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was appropriate statistical analysis used?	☐	☐	☐	☐

Overall appraisal: Include☐ Exclude☐ Seek further info ☐

Comments (Including reason for exclusion)

____

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EXPLANATION OF ANALYTICAL CROSS SECTIONAL STUDIES CRITICAL APPRAISAL

How to cite: Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk . In: Aromataris E, Munn Z (Editors). *JBI Manual for Evidence Synthesis*. JBI, 2020. Available from https://synthesismanual.jbi.global

Analytical cross sectional studies Critical Appraisal Tool

Answers: Yes, No, Unclear or Not/Applicable

1. Were the criteria for inclusion in the sample clearly defined?

The authors should provide clear inclusion and exclusion criteria that they developed prior to recruitment of the study participants. The inclusion/exclusion criteria should be specified (e.g., risk, stage of disease progression) with sufficient detail and all the necessary information critical to the study.

2. Were the study subjects and the setting described in detail?

The study sample should be described in sufficient detail so that other researchers can determine if it is comparable to the population of interest to them. The authors should provide a clear description of the population from which the study participants were selected or recruited, including demographics, location, and time period.

3. Was the exposure measured in a valid and reliable way?

The study should clearly describe the method of measurement of exposure. Assessing validity requires that a 'gold standard' is available to which the measure can be compared. The validity of exposure measurement usually relates to whether a current measure is appropriate or whether a measure of past exposure is needed.

Reliability refers to the processes included in an epidemiological study to check repeatability of measurements of the exposures. These usually include intra-observer reliability and inter-observer reliability.

4. Were objective, standard criteria used for measurement of the condition?

It is useful to determine if patients were included in the study based on either a specified diagnosis or definition. This is more likely to decrease the risk of bias. Characteristics are another useful approach to matching groups, and studies that did not use specified diagnostic methods or definitions should provide evidence on matching by key characteristics

5. Were confounding factors identified?

Confounding has occurred where the estimated intervention exposure effect is biased by the presence of some difference between the comparison groups (apart from the exposure investigated/of interest). Typical confounders include baseline characteristics, prognostic factors, or concomitant exposures (e.g. smoking). A confounder is a difference between the comparison groups and it influences the direction of the study results. A high quality study at the level of cohort design will identify the potential confounders and measure them (where possible). This is difficult for studies where behavioral, attitudinal or lifestyle factors may impact on the results.

6. Were strategies to deal with confounding factors stated?

Strategies to deal with effects of confounding factors may be dealt within the study design or in data analysis. By matching or stratifying sampling of participants, effects of confounding factors can be adjusted for. When dealing with adjustment in data analysis, assess the statistics used in the study. Most will be some form of multivariate regression analysis to account for the confounding factors measured.

7. Were the outcomes measured in a valid and reliable way?

Read the methods section of the paper. If for e.g. lung cancer is assessed based on existing definitions or diagnostic criteria, then the answer to this question is likely to be yes. If lung cancer is assessed using observer reported, or self-reported scales, the risk of over- or under-reporting is increased, and objectivity is compromised. Importantly, determine if the measurement tools used were validated instruments as this has a significant impact on outcome assessment validity.

Having established the objectivity of the outcome measurement (e.g. lung cancer) instrument, it's important to establish how the measurement was conducted. Were those involved in collecting data trained or educated in the use of the instrument/s? (e.g. radiographers). If there was more than one data collector, were they similar in terms of level of education, clinical or research experience, or level of responsibility in the piece of research being appraised?

8. Was appropriate statistical analysis used?

As with any consideration of statistical analysis, consideration should be given to whether there was a more appropriate alternate statistical method that could have been used. The methods section should be detailed enough for reviewers to identify which analytical techniques were used (in particular, regression or stratification) and how specific confounders were measured.

For studies utilizing regression analysis, it is useful to identify if the study identified which variables were included and how they related to the outcome. If stratification was the analytical approach used, were the strata of analysis defined by the specified variables? Additionally, it is also important to assess the appropriateness of the analytical strategy in terms of the assumptions associated with the approach as differing methods of analysis are based on differing assumptions about the data and how it will respond.

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Appendix 4: GRADE factors

Item	**GRADE factor**	**Criteria** **(No serious limitation = ✓, serious limitation=✕)**
1.	Risk of bias	No serious limitation, if at least 75% of the studies are moderate- (total score 3-5) to high quality (total score 6-8) studies based on the JBI Critical Appraisal Checklist.
2.	Inconsistency	No serious limitation, if the point of effect estimates are not on either side of the line of no effect.
3.	Indirectness	No serious limitation, if at least 75% of the studies used a study sample that fully represents the review question.
4.	Imprecision	No serious limitation, if 75% of the studies applied the rule of thumb: univariate ratio [n:K] exceeds [20:1] and if multivariate ratio [n:K] exceeds [10:1]. In which n represents the sample size and K the number of studied factors.
5.	Publication bias	No serious limitation, if the factor is investigated in 3 or more studies.

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Appendix 5: Quality Assessment List

References	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Total
Carona (2013) [14]	1	1	0.5	1	1	1	0.5	1	7
Bella (2011) [15]	1	1	0.5	1	1	1	0.5	1	7
Whittingham (2012) [16]	1	1	1	1	0.5	0.5	1	1	7
Farajzadeh (2021) [17]	1	1	1	0.5	0.5	1	1	1	7
Boztepe (2018) [18]	1	1	1	0.5	1	1	1	1	7.5
Omole (2017) [19]	1	1	0.5	1	0.5	1	0.5	1	6.5
Terathongkum (2020) [8]	1	0	1	0.5	0.5	0.5	1	1	5.5
Farajzadeh (2020) [20]	1	1	1	0.5	0.5	1	1	1	7
Wijesinghe (2015) [21]	0.5	0	1	0.5	0.5	0	1	1	4.5
Barutcu (2021) [22]	1	1	1	1	0.5	0	1	1	6.5
Ozkan (2018) [23]	1	1	0.5	1	0.5	0	0.5	1	5.5
Gugała (2021) [24]	1	1	1	1	0.5	1	1	1	7.5
Marrón (2013) [25]	1	0	0.5	0.5	0.5	1	0.5	1	5
Albayrak (2019) [12]	1	1	0.5	0.5	1	1	0.5	1	6.5
Santos (2012) [26]	1	0	0.5	0.5	0.5	0	0.5	1	4
Moriwaki et al. (2022)	0.5	0	1	0.5	1	1	0.5	1	5.5

1= Yes; 0= NO; 0.5= Unclear

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