Quality of Life in Children and Young People with Cerebral Palsy:

A Meta-analytic Review

Tina Marie Makris

This thesis is submitted in partial fulfillment of the Honours degree of Bachelor of Psychological Science

School of Psychology

The University of Adelaide

October 2018

Word count: 8,417

TABLE OF CONTENTS

TABLES AND FIGURES

ABSTRACT

Background: Cerebral Palsy (CP) is a chronic neurodevelopmental disorder that can significantly impact on the quality of life (QoL) of affected children and adolescents. However, inconsistencies in the measurement of QoL confound this literature. *Aims:* To examine QoL ratings in children and adolescents with CP relative to typically developing peers based on measures that are reliable and valid for this cohort. *Methods:* Fourteen eligible studies, comprising a pooled sample of 2,042 children and adolescents with CP and 55,222 controls were identified from a search of the Embase, PsycINFO, PubMed, Scopus and Web of Science electronic databases. The reporting quality of included studies was examined (*QualSyst* tool) and standardised mean group differences (Hedge's *g*), with 95% confidence intervals and fail-safe *N* statistics calculated. Heterogeneity indices included Cochran's χ^2 (*Q*), I-squared (I^2) and tau (*T*). Both random and mixed-effects models were adopted. *Results:* Although QoL ratings indicated greater impairment in physical functioning for those with CP, subjective ratings of psychological and social functioning were comparable to peers without a disability. *Conclusions:* QoL is not necessarily reduced in children and young people with CP. Routine measurement of QoL is important in order to ensure comprehensive care for this cohort. Further research targeting those with a severe degree of physical behavioural and/or emotional impairment also is needed to confirm the generalisability of the present findings and differential impacts of CP on life domains.

DECLARATION

This thesis contains no material which has been accepted for the award for any other degree or diploma in any University, and, to the best of my knowledge, contains no materials previously published except where due reference is made.

I give permission for the digital version of this thesis to be made available on the web, via the University of Adelaide's digital thesis repository, the Library Search and through web search engines, unless permission has been granted by the School to restrict access for a period of time.

Tina Marie Makris
2 October, 2018

ACKNOWLEDGEMENTS

First and foremost, I would like to sincerely thank my relentlessly hard-working, talented, superwoman of a supervisor, Dr. Diana Dorstyn. I would have not been able to get through this year without your guidance, patience and dedication. Your door was always open for any question, either large or small. You truly are an inspiring individual and I am so grateful that I was able to work with you this year. I would also like to thank my external supervisor, Dr. Angela Crettenden. I am so very grateful for your expertise, advice and assistance with any and all enquiries.

I would like to thank the various researchers who responded to my requests for data or enquiries in regards to their work. In particular, I would like to thank Dr. Allan Colver for his extensive help and efforts in retrieving data and his expertise within the field. I would also like to extend this to the SPARCLE group and Dr. Heather Dickinson for extracting unpublished summary statistics from SPARCLE data. I also thank Dr. Kristie Bjornson for providing data so promptly upon request.

A huge thank you to my extremely supportive family and friends. I wouldn't have been able to get through the year without your humour, patience and countless food and coffee breaks. Thank you for always allowing me to talk your ears off – even though it was likely that you all never completely grasped what I was even talking about. You all deserve an award for putting up with my general whining and mood swings, this thesis stands as a testament to your unconditional love and encouragement.

Lastly, thank you to the Honours cohort of 2018. The countless venting sessions and support really helped me through this entire year and I'm so appreciative of all of you.

CHAPTER 1

Introduction

1.1 Cerebral Palsy: Aetiology, Epidemiology and Impairment

Cerebral Palsy (CP) is a neurodevelopmental syndrome involving a heterogeneous group of movement and posture disorders. CP is caused by damage to, or abnormalities inside, the developing fetal or infant brain. To date, there are no specific treatments that can remediate the brain damage responsible for CP. The majority of children and adolescents have congenital forms of CP which develop before or during childbirth. Typical causes of congenital CP include perinatal infection (of the mother or foetus) that directly or indirectly attacks the infant's central nervous system and brain development, gestational age (prematurity), and multiple births (Eunson, 2016; Sankar & Mundkur, 2005). However, approximately 20% of cases are acquired CP (Sankar, & Mundkur, 2005). Acquired causes include head trauma, significant birth asphyxia, blood clotting problems (thrombophilia), and heart complications (Colver, Fairhurt & Pharoah, 2013; Eunson, 2016; Sankar & Mundkur, 2005).

CP not only involves life-long disability but is a highly prevalent disorder. Indeed, CP represents the leading cause of disability in children, with an estimated prevalence of 2 to 2.5 per 1000 live births among industrialised countries, or one new case of CP in every 500 live births (Eunson, 2016; Oskoui, Coutinho, Dykeman, Jette & Pringsheim, 2013). Significant gender differences are also reported: a greater incidence of CP is observed in males (Romeo et al., 2016). Genetic disorders are thought to contribute to this gender pattern (Romeo et al., 2016). Mortality is, however, low in this cohort. Children with CP have an almost normal life expectancy, with 90% individuals expected to survive into adulthood (Jiang, Walstab,

Reid, Davis, Reddinhough, 2016). Notably, this statistic is highly dependent on disorder severity; with life expectancy being proportional to the number of functional motor and associated impairments (Colver, 2016; Eunson, 2016).

While CP has many different manifestations, depending on the site and form of brain abnormality, there are some typical ways in which this disorder impacts on people's movements. These manifestations include: *spasticity* (most common type) whereby the muscles are in a constant state of tension; *athetoid* (or dyskinetic CP) which affects 10-25% of all persons with CP and is characterised by muscle stiffness but also limpness; *ataxic* CP, which affects 5 to 10% of this population and involves poor muscle tone in addition to tremor and gait problems; and *mixed* type, which involves a combination of spasticity and athetoid movements (Du, McGrath, Yiu & King, 2010; Sankar & Mundkur, 2005). CP can be further classified in four main subcategories ranging from least to most severe: monoplegia (i.e. paralysis restricted to one limb or region of the body), hemiplegia (i.e. paralysis to one side of the body), diplegia (i.e. paralysis of corresponding parts on both sides of the body, typically affecting the legs) and quadriplegia (i.e. paralysis to all four limbs; Sankar & Mundkur, 2005; Shevell, 2010).

Epileptic seizures, reduced cognitive ability and intellectual, visual, hearing and/or communicative impairments are also frequent and significant neurological deficiencies for this group (Sankar & Mundkur, 2005). However, not all children with CP will experience these issues, with substantial inter-individual variation noted in the severity of impairments (Mpundu-Kaambwa, Chen, Huynh, Russo & Ratcliffe, 2018). There is also evidence that functional decline can occur as individuals with CP age (Horsman, Suto, Dudgeon & Harris, 2010).

It is important to accurately measure gross motor function in children with CP in order to plan clinical interventions and to monitor progress over time. Motor development is typically assessed with the clinician-based Gross Motor Function Classification System (GMFCS). This universally renown and reliable measure, describes and classifies severity of mobility across a spectrum of activities (e.g. lying, rolling, walking, running, jumping) into one of five ordinal levels (Reid, Carlin & Reddihough, 2011). Children classified at Level I are able to walk without limitations and can perform gross motor tasks (i.e. running, jumping) although may experience limitations in speed, balance and coordination. At GMFCS Level II, children may have difficulty walking long distances and a minimal ability to perform gross motor skills. Children classified as Level III require assistance with walking, from a hand-held mobility device to wheeled mobility for long distances. Self-mobility is limited for children and youth in Level IV therefore primary methods of transport may include a manual wheelchair or powered mobility. Lastly, children classified as Level V require transportation in a manual wheelchair in all settings and are limited in their ability to maintain posture and motor control (i.e. head and trunk postures, leg and arm movements; Rosenbaum, 2003). Notably, most children with CP are classified as level I or II, which is inclusive of mild to moderate impairment (Reid et al., 2011).

Psychosocial issues typically occur during the transition from childhood to adolescence; a period usually characterised by physical, emotional and social change (Davis et al., 2013; Weber et al., 2016). More specifically, children with CP are likely to exhibit heightened levels of hyperactivity and conduct issues in comparison to age-matched peers without a disability (Colver, 2016; Parkes et al., 2008; Yamaguchi, Perry & Hines, 2014). These issues, in turn, can lead to difficulties

interacting with peers, social withdrawal, adjustment problems, and symptoms of depression and anxiety (Janssen, Voorman, Becher, Dallmeijer & Schuengel, 2010).

In addition to altered neurological pathways that regulate emotions and behaviour, several risk factors may explain why children with CP are more likely to have behavioural challenges. This includes being male, having a seizure disorder, having learning disabilities and communication difficulties (Colver, Fairhurst & Pharoah, 2014; Parkes et al., 2008; Romeo et al., 2016). Given the extensive physical and psychosocial impairments associated with CP, it is perhaps not surprising that quality of life (QoL) has been well-researched as a key disability indicator in this cohort. Indeed, QoL is considered one of the most important outcomes of neurological rehabilitation (Chen et al., 2013; Vargus-Adams, 2006).

1.2 QoL in CP: Definition and Empirical Evidence

QoL is a multi-dimensional construct based upon subjective reports of an individual's overall well-being (Vinson, Shank, Thomas, Warschausky, 2010). The World Health Organisation (WHO) provides one of the most comprehensive definitions of QoL. According to WHO (2002), QoL encompasses three key areas or domains, namely an individual's subjective assessment of their physical health status (e.g. daily physical functioning) in conjunction with their overall psychological wellbeing (including emotional functioning), and perceived social status (e.g. social relationships). Each of these domains are equally important to overall QoL (Janssen et al., 2010; Vinson et al., 2010). Moreover, these components are observable and can be measured by others. For example, parental proxy reports of child functioning are often used as a guide in the management of CP (Davis et al., 2013).

The term QoL is often used interchangeably with health-related quality of life. Whilst the latter is concerned specifically with health aspects it is also a broad ranging concept which incorporates general QoL components. Given that there is significant overlap between the two concepts (Karimi & Brazier, 2016), the term QoL will be utilised hereafter in order to broadly capture all aspects of health and wellbeing of the CP population.

The CP literature has demonstrated that QoL, as perceived by children and adolescents with CP, is reduced. For example, Maher, Olds, Williams & Lane (2008) observed that adolescents reported poor physical and psychosocial functioning, as measured by the Pediatric Quality of Life Inventory (PedsQL), in comparison to typically developing peers. Du and colleagues (2010) replicated this finding using the same measure with preschool children with CP. Importantly, this latter study controlled for potential sample confounds by utilising a comparison group of aged-matched peers.

There is also evidence to suggest that children and adolescents with CP may experience a level of QoL commensurate with that of typically developing peers. Janssen and colleagues (2010) found that school-aged children with CP reported comparable QoL ratings to peers, particularly in relation to the severity of physical complaints (e.g. aches, pains, fatigue, dizziness) and general mood (e.g. depression, anxiety). However, this latter finding may reflect a selection bias, in that individuals with severely gross motor or intellectual impairments were excluded from the study. In saying this, Bjornson and colleagues (2008) also reported no significant differences between adolescents with CP and controls on self-reported QoL (assessed with the Youth Quality of Life scale; YQoL), despite parental/proxy reports indicating significant impairments in health status, as per the Child Health Questionnaire-Child

Form (CHQ-CF87). Similarly, Dickinson et al. (2007) reported no significant group differences in KIDSCREEN ratings, a widely utilised and psychometrically sound QoL measure for youth (Ravens-Sieberer et al., 2005), between children with CP and aged-matched peers from the general population in one of the largest studies conducted in their area.

A term often used to explain why children and adolescents with CP do not necessarily perceive their QoL as compromised, despite their circumstances, is the "satisfaction paradox", also coined the "disability paradox" (Albrecht & Delieger, 1999; Olson & Schober, 1993). The suggestion is that children and adolescents with CP possess the ability to re-evaluate and accept their life circumstance, despite experiencing an array of physical and health impairments of varying severities.

1.2.1. Measurement of QoL in CP

Issues with the measurement of QoL itself characterise the CP research. There is complexity in measuring a dynamic, psychological construct such as QoL for a chronic and multifaceted syndrome such as CP. This complexity is reflected in the factor structure of available QoL instruments, all of which vary considerably in their item-content (see Table 1). For example, the KIDSCREEN includes 10 life domains including: Physical (5 items), Psychological Well-being (6 items), Mood and Emotions (7 items), Self-Perception (5 items), Autonomy (5 items), Parent Relations and Home life (6 items), Social Support and Peers (6 items), School Environment (6 items), Social Acceptance/Bullying (3 items), and Financial Resources (3 items) (Ravens-Sieberer et al., 2005). In comparison, research on the factor structure of the Youth Quality of Life-Research version (YQOL-R) has not consistently reported this measure's original four-factor solution (i.e. environmental, self, relationship, general

QoL; Patrick, Edwards & Topolski, 2002; Salum, Patrick, Isolan, Manfro & Fleck, 2012). It follows that global and domain-specific (i.e. physical, psychological, society, environmental domains) QoL measures should be examined separately where possible, in order to accurately capture all aspects of QoL.

Differing QoL perspectives – that is, child reported and parent-proxy reports – must also be considered. In the CP literature, self-reported instruments such as the TNO-AZL Children's Quality of Life-Child Form (TACQOL-CF) are often supplemented with parent/proxy reports (e.g. Child Health Questionnaire-Parent Form; CHQ-PF50). Given that QoL is a subjective concept it should be self-reported, where possible (Rapp et al., 2017). Evidence is accumulating that children with CP as young as five with sufficient cognitive capacity, emotional development and reading level can reliably self-report their QoL, provided that the questionnaire is age-appropriate (Arnaud et al., 2008; Maher et al., 2008). However, in cases of severe CP involving intellectual or communicative difficulties, the ability to self-report may not only be compromised but is unreliable (Arnaud et al., 2008). In such cases, it is necessary that parental/proxy reports of QoL be utilised (Rapp et al., 2017). This may lead to discrepancies in child-parent reporting of emotional and behavioural difficulties, with parents not always identifying problems that a child considers to be important. This is certainly a trend that has been noted in the general population (Van Roy, Groholt, Heyerdahl & Clench-Aas, 2010), although not as widely identified in CP literature.

The reliance on generic QoL instruments may also contribute to inaccurate QoL ratings. There is suggestion that generic measures have a tendency to underestimate the QoL of children and adolescents with CP (Davis et al., 2013). In order to more accurately capture specific aspects of this population (e.g. gross motor

functioning), condition and age-specific QoL measures have been developed (e.g. Cerebral Palsy Quality of Life- Child [CP QOL-Child], CP QOL-Teen). However, whilst condition-specific QoL instruments are appropriate to evaluate the effectiveness of a targeted intervention for individuals with a specific disability, generic instruments are broadly applicable and practical when comparisons between groups and populations are required (Davis et al., 2013).

The use of case-control studies, or matching of groups on potentially important contextual variables, is also critical in order to reduce observed discrepancies in group QoL ratings. For children and young people with a disability, this might include sociodemographic characteristics such as gender, which is considered to be an important confounder in the measurement of QoL. For example lower QoL has been reported by school-aged boys with CP (Bjornson et al., 2008; Türkoglu, Bilgic, Türkoglu & Yilmaz, 2015).

Another methodological issue that may contribute to inconsistencies in QoL outcomes is the reliance on normative data to provide evidence that CP has a significant and detrimental impact. Normative data typically represent the performance of a defined population on a measure at a specific point in time (Kendall, Marrs-Garcia, Nath & Sheldrick, 1999). However, normative data cannot account for changes in population compositions over time. In the case of children and young people with CP, for example, social factors such as the home and school environment may influence self-report of QoL (Kendall et al., 1999). It is vital, then, that the normative population is comparable on such factors. In saying this, a measure such as the TACQOL, which was developed in 1998 and has not been updated or validated in recent years, may not accurately reflect the current population of children and young persons with CP (Vogels et al., 1998).

Table 1. Validated Generic vs CP-specific Measures

Items		Domains	Reference
Generic ($N_{studies}$=13)			
CHQ-PF50	50	Physical functioning, role/social limitations, general health perceptions, bodily pain/discomfort, family activities, role/social limitations – emotional/behavioural, parent impact – time, parent impact – emotion, self-esteem, mental	Landgraf et al., 1996
KIDSCREEN-52	52	Physical wellbeing, psychological wellbeing, moods and emotions, self-perception, autonomy, relationships with parents, social support and peers, school environment, financial resources, social acceptance	Ravens-Sieberer et al., 2005
PedsQL	23	Physical, emotional, social and school function	Varni et al., 2001
SEIQoL-DW	-	Self-identified domains using semi-structured interviews	O'Boyle et al., 1997
TACQOL-CF/PF	56	Physical complaints, motor functioning, autonomous functioning, cognitive functioning, social functioning, positive moods, negative moods	Vogels et al., 1998
YQOL-R	41	Total QoL, sense of self, social relationships, culture and community environment and general QoL	Edwards et al., 2002
CP-specific ($N_{studies}$= 1)			
CP-QOL	66	Social wellbeing and acceptance, feelings about functioning, participation and physical health, emotional wellbeing and self-esteem, access to services, pain and impact of disability, family health	Waters et al., 2005

Abbreviations: CHQ-PF50= Child Health Questionnaire-Parent Form; PedsQL= Pediatric Quality of Life Inventory; SEIQoL-DW= The Schedule for the Evaluation of Individual Quality of Life- Directed Weighted; TACQOL-CF/PF= TNO AZL Children's Quality of Life Child Form/Parent Form; YQOL= Youth Quality of Life Instrument – Research Version; CP-QOL= Cerebral Palsy Quality of Life questionnaire

1.3 Current Study

The impact of CP on QoL of children and adolescent populations remains unclear. This is partly due to CP being a heterogeneous disorder, paired with difficulties in the measurement of QoL as a construct (Vinson et al., 2010). Researching key QoL indicators for children and adolescents with CP including physical, psychological and social limitations which affect daily functioning and activities, is important in order to inform research and future healthcare provision. Important research questions remain: *Which QoL domains differentiate children and young people with CP in comparison to peers?* And, *to what extent is the relationship between QoL and CP moderated by (a) QoL measurements used and (b) sample characteristics?* The current study addresses these research questions by systematically reviewing available empirical studies that have examined QoL of children and adolescents with CP. The tools and methods used to evaluate QoL in this cohort will also be examined. Meta-analytic techniques, considered to be the highest standard of evidence, will be utilised to consolidate the available research and provide a precise and powerful estimate of the effects of CP on the QoL than would otherwise be provided by an individual study (Gopalakrishnan & Ganeshkumar, 2013). Specific aims are to:

1. Examine group differences in QoL between children and adolescents with CP and peers in consideration of the different measures and comparison groups utilised and quality of available studies.

3. Explore potential sources of study heterogeneity, namely differing perspectives (child-reported vs. parent-proxy reports) and various control or comparison groups (normative data vs. typically developing peers – some of which are matched on sociodemographic characteristics).

CHAPTER 2

Method

2.1 Literature Search

Studies examining QoL in persons with CP relative to an independent control or comparison group were identified through the Embase, PsycINFO, PubMed, Scopus and Web of Science databases in addition to the Google search engine. Databases were searched from inception (Embase 1947; PsycINFO 1967; PubMed 1996; Scopus 1960; Web of Science 1900) to May 2018. Bimonthly alerts were activated for each database to ensure that all current results were being captured. Search terms were specified to each database, with assistance from an expert research librarian. This included a broad combination of terms relating to CP (e.g. *'cerebral palsy', 'neurodevelopmental disability'*) and QoL (e.g. *'quality of life', 'life quality'*; see Appendix A for detailed search strategies). Finally, the reference lists of all included studies, in addition to the reference lists of available reviews on the health status and prevalence of CP (Power et al., 2018; Vles, Hendriksen, Kessels, Hendriksen, Vles, 2012; Wake, Salmon and Reddihough, 2003), were hand-searched in order to capture any additional research not retrieved by the electronic search strategy. This process did not identify any additional studies.

2.2 Eligibility Criteria and Study Selection

Eligible studies needed to recruit a sample of children and adolescents (i.e. ages 2-17 years) with clinically diagnosed CP, as determined by parent-reported information (e.g. symptom checklist) or a medical diagnosis (Sankar & Mundkur,

2005). Studies were ineligible if they included children and adolescents with a range of chronic illnesses or disabilities that did not provide the data for participants with CP separately. In addition, studies had to utilise an independent group design, whereby individuals with CP were compared to a non-clinical control group or a comparison group (i.e. typically developing peers, normative data) on a standardised QoL measure (as per Table 1). Studies which used self-report and parental-proxy QoL measures were both eligible. Finally, it was essential that studies provide sufficient quantitative data (e.g. means, standard deviations) to permit the calculation of standardised mean group differences in the form of Hedge's *g*. Studies were also required to be published journal articles (Balshem et al., 2013; Juni, Holenstein, Sterne, Barlett & Egger, 2002) published in the English language.

In total, the systematic search yielded 14,654 potentially relevant studies, of which 5,464 were duplicates. Titles and abstracts of the remaining 9,190 studies were screened against the eligibility criteria, leading to 53 articles to be reviewed in full. Authors from two studies (Bjornson et al., 2008; Dickinson et al., 2007) were contacted for further data, where it was provided upon request. During this screening process, seven studies with overlapping data were identified (Beckung et al., 2008; Bjornson et al., 2008; Bjornson, Belza, Kartin, Logsdon & McLaughlin, 2007; Colver et al., 2015; Dickinson et al., 2007; Mezgebe et al., 2015; Parkes et al., 2009). The article that provided the most comprehensive dataset (i.e. largest sample size) was included. This resulted in a final sample of 14 independent studies (see Figure 1). A second reviewer, a postgraduate psychology student (S. P.), checked a subset of 30 eligible studies randomly selected by the primary researcher (T.M.) against eligibility criteria, with adequate inter-rater agreement of 93% (κ= 87, Cohen, 1968). This review is registered on the PROSPERO database (registration no. CRD42018102466).

2.3 Data Collection and Preparation

Consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher, Liberati, Tetzlaff & Altman, 2009), key information was extracted from all eligible studies using a purposely developed data extraction sheet in Microsoft Excel. This information included: study characteristics (e.g., author, country, recruitment source); demographic characteristics (e.g., age, gender, *N*); methodological factors (e.g. QoL measure) and effect size data. Most studies provided sufficient data (i.e. means, SDs, sample *N*, *t*-tests, one-way ANOVAs or exact *p* values) to allow the calculation of standardised mean differences. Only one study (Russo et al., 2008) required data conversion: 95% confidence intervals (CIs) were converted to standard deviations (SDs) as outlined by the Cochrane Collaboration (Higgins & Green, 2008). For ease of data interpretation and presentation, individual QoL subscales were mapped onto three broad domains as defined by WHO (1998) *physical* (or the ability to perform daily activities, based on degree of physical impairment) *psychological* (a combination of mental health and general emotional functioning) and *social* (relating to social relationships and support).

2.4 Study Reporting Quality

Methodological rigour and reporting bias of all included studies were evaluated using the *QualSyst* tool (Kmet, Lee & Cook, 2004). Items reflect a range of methodological criteria ranging from adequacy of study design and sample size to the proficiency in which results were reported and discussed. For each item, studies were rated as *'Yes'* (score of 2; sufficiently addressed), *'Partial'* (score of 1; partially addressed), *'No'* (score of 0; not addressed) or *'Not applicable'*.

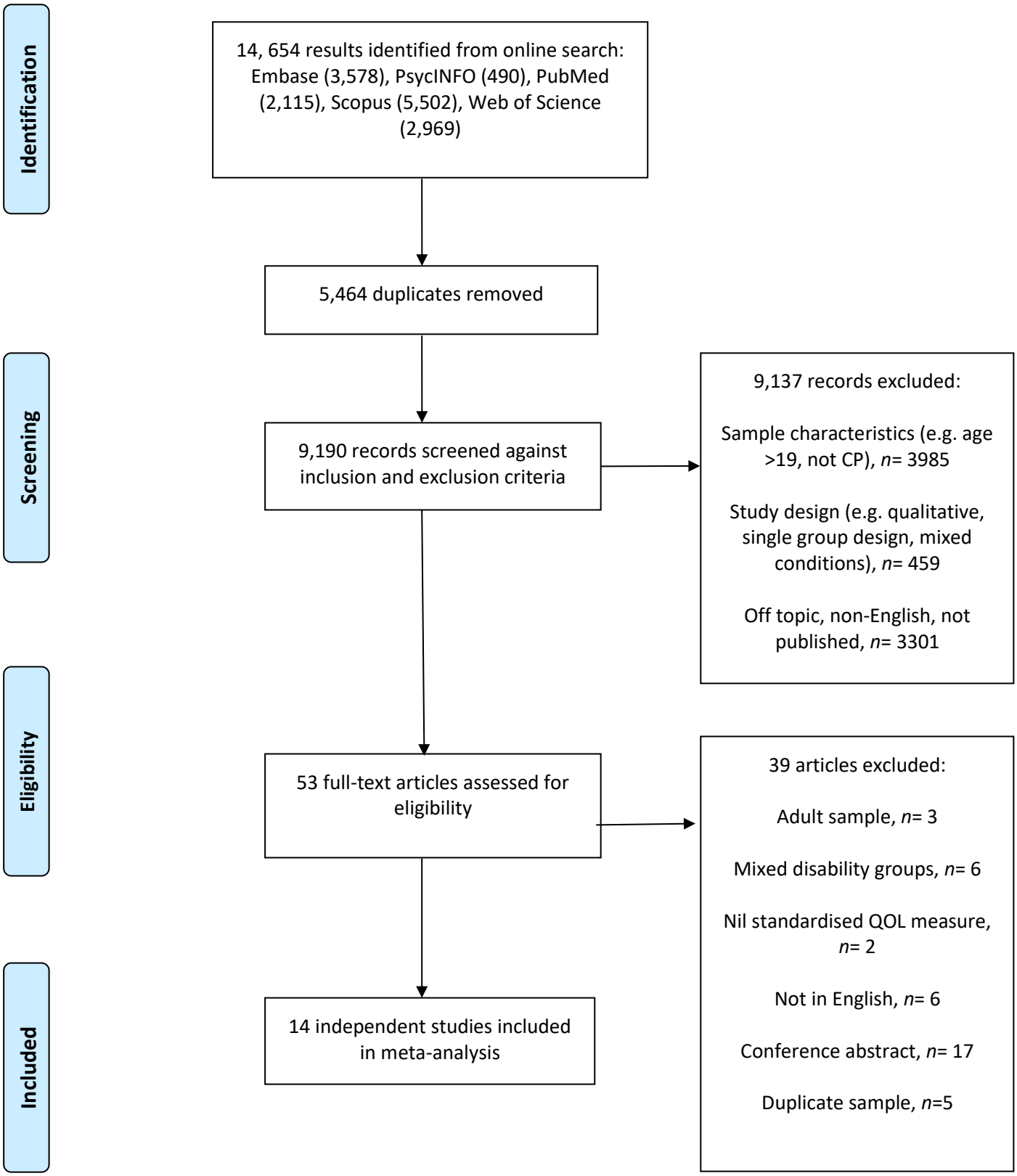

Figure 1: PRISMA flow diagram for study selection process

Two corresponding scores were then calculated: a summary score for each study (possible score ranging from 0-22) reflecting how adequate each study fulfilled the criterion, and the overall proportion of studies receiving scores of 2, 1 and 0 for each item. Creators of the tool have suggested a conservative cutoff of 0.75 (i.e. requirement that a study meet 75% of the specified criteria) as the threshold for including a paper in a review (Kmet, Lee & Cook, 2004). Three criteria appropriate to intervention studies (*random allocation, blinding of investigators, blinding of subjects*) were excluded from the total summary scores. A second reviewer (S. P.) reviewed a subset of five included independent studies selected by the first researcher (T. M.), with adequate inter-rater agreement of 92.73% ($r = 0.96$).

2.5 Statistical Analyses

Data were entered and analysed using Comprehensive Meta-Analysis Software (CMA, Version 3.0, Englewood, NJL Biostat Inc). The extent to which CP and control/comparison groups differed in QoL ratings, was determined by calculating standardised mean differences (Hedges' *g*; Hedges & Olkin, 1985). This effect estimate, which utilises a pooled SD weighted to sample size, was considered to be the most appropriate estimate due to the use of various QoL measures and sample sizes within and between studies (Borenstein, Hedges, Higgins & Rothstein, 2009; Ellis, 2010). Interpretation of *g* followed Cohen's (Cohen, 1988) guidelines: a small effect ≥ 0.2, moderate effect ≥ 0.5, and a large effect ≥ 0.8.

The computation and interpretation of *g* required several stages. First, effect estimates for studies which reported a composite QoL score and/or a QoL subscale score were examined separately. Studies that utilised the same QoL measure or subscale were then pooled and weighted by their inverse variance (g_w). This

weighting gives preference to studies with larger samples thereby accounting for an upward bias that is typically associated with effect estimates based on small sample sizes (Higgins & Green, 2008). Effect sizes for each broad QoL domain – physical, psychological, social – were also pooled and weighted by this same process. Where a study provided more than one subscale score from an individual QoL measure within a single domain, effect estimates for that study were averaged beforehand – this ensured that each study only contributed one single effect estimate to an overall *g* (Lipsey & Wilson, 2001). Similarly, for studies which utilised a longitudinal design (e.g. Janssen et al., 2010; McCullough, Parkes, Kerr & McDowell, 2013; Tan et al., 2014), only baseline data was extracted to ensure data independence (Lipsey & Wilson, 2001). For ease of data interpretation, the direction of *g* was standardised across measures: a negative value indicated lower QoL among individuals with CP in comparison to controls. Lastly, 95% CIs and *p* values were calculated for both individual and pooled effect sizes to determine the statistical significance of *g*. An effect size is considered to be statistically significant if the associated CI does not include the value of zero in addition to a *p*-value that is less than .05 (Cumming, 2012).

Heterogeneity, or the degree of variation in true effect size estimates between studies, was estimated with three statistics: tau (*T*, analogous to the SD of *g*), Cochran's χ^2 test (also known as *Q*) and I^2. A non-significant *Q* is indicative of a homogenous distribution of the effect size whilst the I^2 statistic determines the percentage of between-study variability (Borenstein et al., 2009). An I^2 value greater than 70% is indicative of moderate to substantial heterogeneity (Higgins & Green, 2008). With this in mind a conservative random effects model, which assumes inter-study variation, was applied for these statistical analyses. Such a model is appropriate

given that CP is a syndrome characterised by various subtypes (congenital vs. acquired) and medical comorbidities (Shevell, 2010) in addition to the multidimensional nature of QoL (Mpundu-Kaambwa et al., 2018).

Fail-safe *N*s (N_{fs}) statistics were calculated in order to deal with a significant criticism of meta-analysis: publication bias. Publication bias typically occurs in the published research which, in itself, is characterised by positive and significant results. Any pooled effect estimates based solely on published literature, as was the case in this review, may over-estimate the magnitude of the true effect. N_{fs} accounts for this by providing an index that estimates the number of unpublished studies with non-significant findings that would be required to invalidate the current findings (i.e. reduce an effect size to $g \leq 0.2$ or a small effect) (Lipsey & Wilson, 2001; Zakzanis, 2001). The larger the N_{fs} value, the more likely that g is robust. For this meta-analysis, an N_{fs} value was considered adequate if it exceeded the number of studies contributing to a particular analysis (i.e. $N_{fs} > N_{studies}$).

The conclusions drawn from this meta-analysis were interpreted based on a combination of the above statistics. Differences in QoL ratings between the CP and control groups were considered statistically and clinically relevant if an individual or weighted g: (a) equated to a medium to large difference ($g \geq 0.50$); (b) was statistically significant (i.e. 95% CI $\neq 0$, $p < 0.05$) and (c) the N_{fs} score suggested that the findings were not characterised by publication bias (i.e. $N_{fs} > N_{studies}$).

2.6 Moderator Analyses

Exploratory subgroup analyses were conducted for each QoL domain (i.e. physical, psychological, social) to clarify sources of heterogeneity. This included a comparison of differing perspectives in the measurement of QoL (i.e. child vs

parent/proxy reports), in addition to the use of normative data and the use of controls matched on sample parameters (i.e. age, gender). These analyses involved a *Q*-test based on an Analysis of Variance (ANOVA). A full random effects model (for between subgroups) and a mixed effects model (for within subgroups) was adopted (Borenstein et al., 2009).

CHAPTER 3

Results

3.1 Study Characteristics

Fourteen independent studies published from 2003 to 2015 were included in this review. This included three longitudinal and 11 cross-sectional studies. Studies originated from Australia ($N_{studies}$= 4), China ($N_{studies}$= 1), Ireland ($N_{studies}$= 1), The Netherlands ($N_{studies}$= 3), Turkey ($N_{studies}$= 1) and the United States of America ($N_{studies}$= 3). Dickinson et al.'s (2007) pan-European study recruited individuals across seven countries (see Table B2, Appendix B). Sample sizes were highly varied across studies. The two largest studies (Dickinson et al., 2007; Tan et al., 2014) comprised of 51% of the overall CP sample. Participants were primarily recruited from single sites (e.g. hospital or outpatient clinic) or population-based CP registers (e.g. North Ireland Cerebral Palsy Register, South Australia Cerebral Palsy Register; Parkes et al., 2001). QoL was commonly measured using the Pediatric Quality of Life (PedsQL; $N_{studies}$= 4), followed by the CHQ ($N_{studies}$= 3). Both are generic instruments which are widely utilised to measure child and adolescent health. Calley et al (2011) adopted a CP-specific measure (CP-QoL). Three studies exclusively used child self-report, six included parental/proxy reports and five studies incorporated both child and parent perspectives in their QoL assessments.

3.2 Sample Characteristics

3.2.1 CP groups. The 14 independent studies examined a pooled sample of 2,042 individuals with CP with an overall mean age of 9.24 years (SD= 1.4; see Table 2). Differences in gender were observed with a higher proportion of males (9%) than females (6%); consistent with a known bias in CP diagnosis (Romeo et al., 2016).

The majority of studies ($N_{studies}$= 10) provided an index of disability severity, the GMFCS – as assessed by a physiotherapist. Accordingly, most children and adolescents were reported as having a Level I gross motor functional ability: indicative of a group that is not severely impaired physically but who may experience limitations in speed, balance and coordination (Reid, Carlin & Reddihough, 2011; Sankar & Mundkur, 2005). The majority also had mild intellectual impairment (52%), although this detail was not consistently reported by studies.

3.2.2 Control groups. A total pooled sample of 53, 180 peers was included in this review. Of this sample, 37, 396 (70%) were described as being sourced from the 'general population' ($N_{studies}$= 5), 2,551 (5%) were described as 'typically developing peers' ($N_{studies}$= 6), whereas three studies contributed 17,488 (33%) participants who were described as 'healthy controls'.

3.2.3 Group differences. Sample characteristics consistently reported by studies for both the CP and control groups were compared. Both groups were comparable in age (t (2) = 0.016, p = .989), possibly because studies typically controlled for this confound ($N_{studies}$ = 7). There was, however, a higher proportion of males in the control/comparison group than the CP group (χ^2 (1) = 30.811, p = 0.001). Sample size also differed across the two groups, likely due to the use of population norms ($N_{studies}$=7; t (2) = 26.197, p = <0.001).

3.3 Study Reporting Quality

The average *QualSyst* score was 20 (SD= 1.47, range 17-22) out of a possible 22, with most studies providing adequate detail relating to their statistical analyses

Table 2. Demographic Characteristics of Participants for Included Studies

	Total Sample		CP		Controls	
Variable	$N_{participants}$ (%)	$N_{studies}$	$N_{participants}$ (%)	$N_{studies}$	$N_{participants}$ (%)	$N_{studies}$
Sample size*	55222 (100)	14	2042 (4)	14	53180 (96)	14
Age (SD) in years	9.47 (1.27)	12	9.24 (1.4)	11	9.45 (1.02)	6
Gender*						
Female	9943 (19)	12	618 (6)	12	8825 (89)	7
Male	10305 (20)	12	892 (9)	12	9413 (91)	7
Intellectual ability						
Average or above (IQ >90)	51 (48)	1	47 (92)	1	4 (8)	1
None or mild impairment (IQ 70-89)	764 (2)	7	761 (52)	7	3 (0)	1
Moderate or severe impairment (IQ <70)	347(1)	7	338 (23)	7	9 (3)	1
GMFCS						
Level I	561 (33)	10	561 (33)	10	-	-
Level II	348 (21)	10	348 (21)	10	-	-
Level III	207 (12)	9	207 (12)	9	-	-
Level IV	152 (10)	7	152 (10)	7	-	-
Level V	119 (9)	6	119 (9)	6	-	-
Recruitment source						
Community-based	54303 (98)	11	1231 (2)	5	53069 (96)	11
Rehabilitation centre/hospital	679 (100)	7	679 (100)	7	-	-
Mixed	142 (11)	3	91 (63)	1	51 (37)	2

Abbreviations: $N_{participants}$= number of participants providing this data; $N_{studies}$= number of studies included; CP= cerebral palsy; GMFCS= Gross Motor Functioning Classification System; IQ= intelligence quotient; * significant group difference p <0.05

and procedure (see Figure 2 and Appendix C). Studies also consistently identified their study rationale and research objectives (*item 1*: 100%) with explicit reference to study design (*item 2*: 86%), method of subject selection (*item 3*: 79%) and reporting of key participant characteristics (e.g. age, disability, *item 4*: 93%); factors which help to determine the generalisability of a study's findings. The majority clearly defined and justified their selection of outcome measure (*item 5*: 93%), although priori or post hoc power analysis were omitted (*item 6:* 71%). Only 29% reported the management of missing data or response rates, hence the potential for attrition bias. Methods of statistical analyses (i.e. group comparisons; *item 7*: 79%;) were consistent with reported study aims. Some form of estimated variance (i.e. SDs, 95% CIs; *item 8*: 64%) was also usually reported. Potential sample confounds were controlled by recruiting (age and gender) matched controls or by reporting data from subgroup analyses (*item 9*: 71%). Results (both significant and non-significant) were described in adequate detail (*item 10:* 86%) and studies generally provided sufficient conclusions for their research, along with clinical implications, that were supported by their data analysis (*item 11:* 93%). In summary, most studies attempted to minimise potential sources of methodological bias in their design and implementation, resulting in good internal and external validity.

3.4 Group Differences in Total QoL

Effect sizes are rank ordered in size, from largest to smallest *g*, in Table 3. Four studies provided a single composite QoL score, as assessed by the PedsQL ($N_{studies}$ =2), Youth Quality of Life (YQOL; $N_{studies}$ = 1) and the Schedule for the Evaluation of Individual Quality of Life-Direct Weight (SEIQoL-DW; $N_{studies}$ = 1). Although the pooled effect estimate was large and negative, indicative of reduced

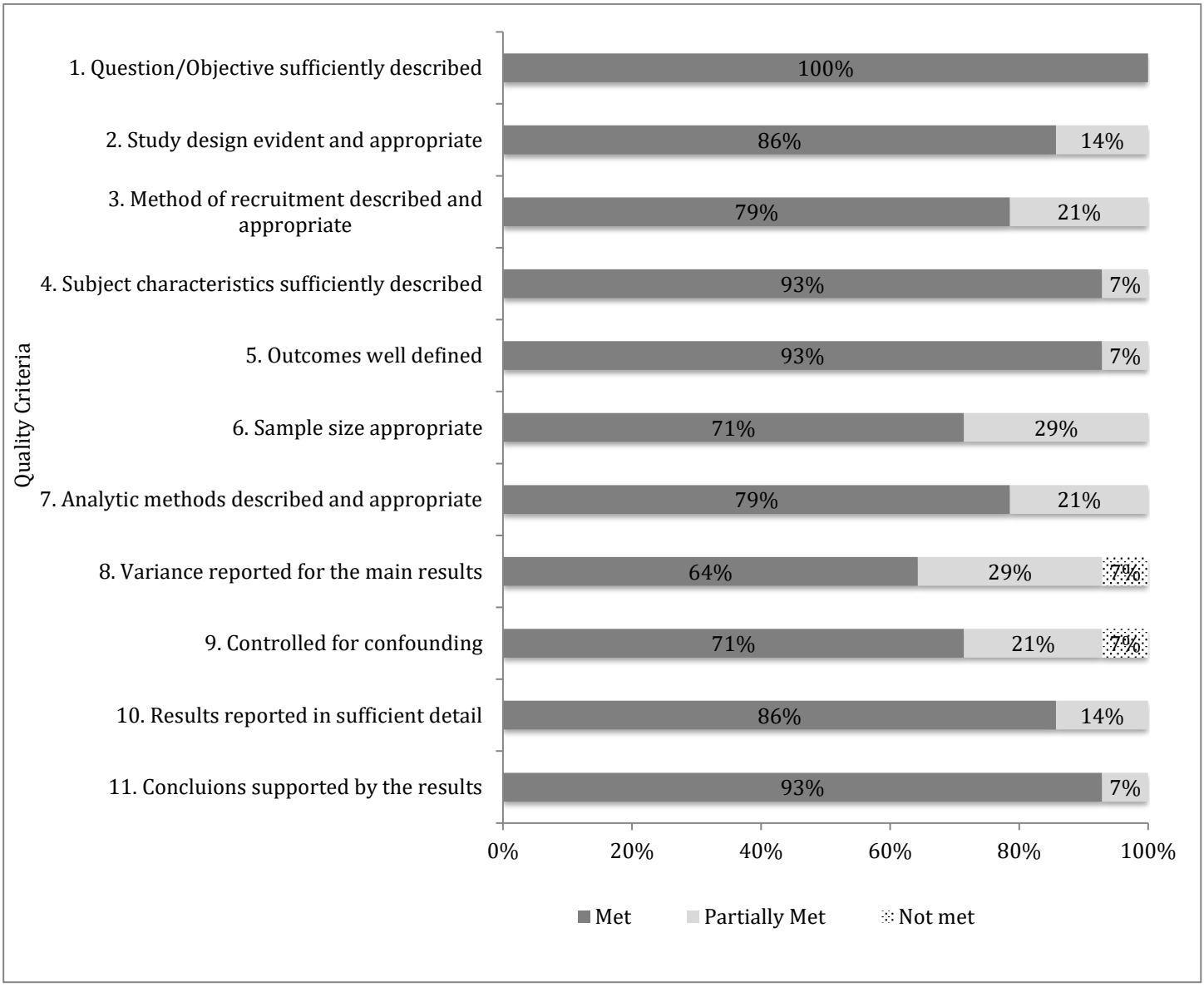

Figure 2. Percentage of included studies meeting each criterion on the *QualSyst*

Table 3. Standardised Mean Differences for Total QoL Scores

QoL measure	$N_{participants}$		g	g_w	95% CI		p	N_{fs}
	CP	Control			Lower	Upper		
PedsQL	143	1231		**-1.617**	-1.824	-1.410	< 0.001	18
YQOL	81	30	-0.337		-0.756	0.081	0.114	3
SEIQOL-DW	41	60	0.266		-0.169	0.622	0.262	2
Total	265	1321		-0.848	-1.752	0.057	0.066	21

Abbreviations. $N_{participants}$= number of participants providing data; 95% CI = confidence interval (with lower and upper limits); CP = cerebral palsy, g = Hedge's g effect estimate; g_w= pooled g (with inverse variance weighting); p = significance value associated with effect estimate; N_{fs} = fail safe N

Bold font denotes significant group difference ($g \geq 0.50$ p <0.05, CIs $\neq 0$, $N_{fs} > N_{studies}$)

QoL among children and adolescents with CP, this finding was not significant and was characterised by substantial between-study heterogeneity (Q (3) = 79.934, p = 0.066, I^2 = 96.247). Specifically, studies that utilised the PedsQL identified large and statistically significant group differences. This finding was relatively robust (N_{fs} > $N_{studies}$). In comparison, single studies that utilised the YQOL or SEIQOL-DW reported small to medium and non-significant effects.

3.5 Group Differences in Domain-Rated QoL

3.5.1 Physical domain. Nine studies, utilising five individual QoL measures and involving nine subscales, examined the relative impact of CP on physical functioning in comparison to controls (Table 4). Statistically significant group differences were observed across individual subscales. In particular, measures focusing one's ability to engage in physical activities (CHQ-PF50, PedsQL) yielded large and negative effects: children and adolescents with CP reported substantially impaired functioning in comparison to controls. This finding was corroborated by a large N_{fs} value. In comparison, CP and control groups did not significantly differ in their self-perceived health, including pain severity (CHQ-PF50) and overall number of somatic complaints (TACQOL). This finding was also robust, as suggested by the large N_{fs} value.

3.5.2 Psychological domain. Only one clinically significant finding was observed across the nine studies which contributed to this domain. A large positive mean difference was observed in relation to psychological well-being as measured by the KIDSCREEN (Table 5). However, this effect was associated with a fairly wide-

Table 4. Standardised Mean QoL Differences in Physical Domain

Measure	Subscale	$N_{studies}$	$N_{participants}$		g_w	95% CI		p	N_{fs}	Heterogeneity statistics			
			CP	Control		Lower	Upper			Q	p	I^2	T
CHQ-PF50	Physical functioning	3	309	10,892	**-2.727**	-3.434	-2.02	0.000	44	37.225	0.000	94.627	0.540
	Role physical	1	184	5414	**-1.564**	-2.749	-0.380	0.010	9	0.000	0.010	0.000	0.000
	Bodily pain	1	184	5414	-0.405	-1.589	0.779	0.503	3	0.000	0.503	0.000	0.000
CPQOL	Participation & physical health	1	21	21	-1.126	-2.470	0.217	0.100	7	0.000	0.100	0.000	0.000
	Functioning	1	21	21	-0.878	-2.212	0.457	0.198	5	0.000	0.198	0.000	0.000
KIDSCREEN	Physical well-being	2	898	25,514	0.410	-0.429	1.248	0.339	2	44.216	0.339	97.738	0.552
PedsQL	Physical functioning	1	148	12010	**-1.858**	-2.701	-1.014	0.000	10	0.144	0.000	0.000	0.000
TACQOL	Motor functioning	2	315	3,401	**-0.893**	-1.493	-0.293	0.004	11	225.173	0.004	98.668	1.026
	Physical complaints	2	315	3,401	0.333	-0.263	0.930	0.273	1	8.334	0.273	64.005	0.137
	Total	9	1,163	41,881	**-1.065**	-1.694	-0.435	0.001	39	2429.528	0.000	99.259	1.104

Abbreviations. $N_{studies}$ = number of studies included in analysis; $N_{participants}$= number of participants providing this data; 95% CI = confidence interval (with lower and upper limits); CP = Cerebral palsy, g_w = pooled Hedge's g with inverse variance weighting (note: weighting only applies to total effect sizes involving 2 or more studies); p = p value associated with effect estimate; N_{fs} = fail safe N; Q = Cochran's χ^2; I^2 = eta-squared; T = tau

Measures: CHQPF50 = Child Health Questionnaire Parent Form; CPQoL= Cerebral Palsy Quality of Life questionnaire; PedsQL = Pediatric Quality of Life; TNO AZL Children's Quality of Life

Bold font denotes significant group difference ($g \geq 0.50$ p <0.05, CIs ≠0, $N_{fs} > N_{studies}$)

Table 5. Standardised Mean QoL Differences in Psychological Domain

Measure	Subscale	$N_{studies}$	$N_{participants}$		g_w	95% CI		p	N_{fs}	Heterogeneity statistics			
			CP	Control		Lower	Upper			Q	p	I^2	T
CHQ-PF50	Role - emotional/behaviour	1	80	5414	-1.676	-4.023	0.671	0.162	9	0.000	0.000	0.000	0.000
	Parent impact - emotional	1	80	5414	-1.280	-3.627	1.067	0.285	7	0.000	0.000	0.000	0.000
	Role emotional	1	184	5414	-1.250	-3.592	1.091	0.295	7	0.000	0.000	0.000	0.000
	Mental health	2	234	10828	-0.709	-2.366	0.949	0.402	9	4.734	0.402	78.877	0.186
	Self-esteem	2	234	10828	-0.705	-2.362	0.953	0.405	9	0.027	0.405	0.000	0.000
CPQoL	Emotional well-being & self-esteem	1	21	21	-0.486	-2.902	1.930	0.693	3	0.000	0.000	0.000	0.000
KIDSCREEN	Psychological well-being	1	80	22295	**2.788**	0.441	5.135	0.020	13	0.000	0.000	0.000	0.000
	Moods & emotions	2	898	25514	1.555	-0.103	3.212	0.066	14	462.406	0.066	99.784	2.004
	Self-perception	2	898	25514	1.371	-0.286	3.028	0.105	12	423.968	0.020	99.764	1.914
PedsQL	Self-esteem	1	45	64	-0.787	-3.157	1.583	0.515	5	0.000	0.000	0.000	0.000
	Emotional functioning	1	142	6519	-1.590	-3.933	0.752	0.183	2	0.000	0.000	0.000	0.000
	Mental health	1	45	64	-0.425	-2.793	1.943	0.725	1	0.000	0.000	0.000	0.000
TACQOL	Negative moods	1	91	1054	-0.287	-1.947	1.372	0.734	2	4.829	0.000	79.293	0.217
	Psychological functioning	1	224	2347	-0.062	-1.720	1.596	0.942	1	2.710	0.000	63.096	0.130
	Total	9	1163	41881	-0.116	-0.665	0.433	0.678	17	3064.436	0.00	99.380	1.246

Abbreviations. $N_{studies}$ = number of studies included in analysis; $N_{participants}$= number of participants providing this data; 95% CI = confidence interval (with lower and upper limits); CP = Cerebral palsy, g_w = pooled Hedge's g with inverse variance weighting (note: weighting only applies to total effect sizes involving 2 or more studies); p = p value associated with effect estimate; N_{fs} = fail safe N; Q = Cochran's χ^2; I^2 = eta-squared; T = tau

Measures: CHQPF50 = Child Health Questionnaire Parent Form; CPQoL= Cerebral Palsy Quality of Life questionnaire; PedsQL = Pediatric Quality of Life; TNO AZL Children's Quality of Life

Bold font denotes significant group difference ($g \geq 0.50$ p <0.05, CIs ≠0, $N_{fs} > N_{studies}$)

ranging CI; suggesting that this particular effect size may represent an imprecise estimate. Substantial variability in effect sizes across subscales was also noted. This was confirmed by the heterogeneity index ($I^2 > 70$). However, the overall N_{fs} value exceeded the number of studies included in this analysis, suggesting that these results were not characterised by publication bias.

3.5.3 Social domain. Significant effects were observed across individual aspects of social functioning (see Table 6). This included a large, negative and statistically significant group difference in relation to family activities: children and adolescents with CP experienced significantly more interruptions in everyday family's activities (e.g. eating meals, watching TV; as measured by CHQ-PF50) due to the child's behaviour or health. In comparison, large and positive effects were noted in relation to social acceptance (CPQoL): those with CP did not feel rejected or bullied by their peers. Similarly, young persons with CP positively rated aspects of the school environment, including perceptions of their cognitive capacity, learning and concentration in school (KIDSCREEN). These results were not significantly affected by publication bias (i.e. all $N_{fs} > N_{studies}$). The overall, pooled effect for this domain was, however, not clinically significant ($g < 0.50$, CI $\neq 0$, $p > 0.05$). The heterogeneity ($I^2 > 70\%$) index also suggests that individual studies varied greatly in their effect estimates.

3.6 Moderator Analyses

3.6.1 Child vs parent perspectives on QoL. Within-group effect estimates based on studies which utilised child self-ratings or parent/proxy ratings of their child's QoL are reported in Table 7. Parents of children with CP identified significant impairment in their child's physical functioning and abilities in comparison to parents

of typically developing peers. However, between-group analyses revealed that parents tended to estimate their child's physical (Q_B (1) = 1116.709, p = <0.001), psychological (Q_B (1) = 3011.967, p = <0.001) and social (Q_B (1) = 170.738, p = <0.001) functioning significantly better than their child's own ratings. These findings were not characterised by publication bias.

3.6.2 Normative vs control data. Significant within and between-group differences were reported for the physical domain (Q_B (1) = 33.943, p = 0.004); those with CP experienced severe impairments, regardless of whether studies utilised normative data or consecutively recruited controls (Table 8). Similarly, studies which recruited their own controls identified reduced psychological QoL for children and adolescents with CP, although this difference was negligible for studies which utilised normative data based on the CHQ-PF50, KIDSCREEN-52, PedsQL 4.0 and TACQOL-CF/PF. Indeed, between-group analyses revealed comparable QoL ratings for the psychological (Q_B (1) = 0.127, p= 0.0.722) and social functioning domains (Q_B (1) = 1.345, p = 0.246). These analyses may, however, by underpowered given that only two studies recruited their own controls.

3.6.3 Matched vs unmatched controls. Table 9 lists the within-group effects for studies that matched their control/comparison group on age and gender and those that did not (see Table 9). Significant group differences were reported for the physical domain: children and adolescents with CP were rated as functionally impaired in comparison to peers. However, between-group analyses identified significant impairments across all three domains: those with CP performed poorly in relation to their physical (Q_B (1) = 134.299, p = <0.001), psychological (Q_B (1) = 23.852, p = <0.001) and social (Q_B (1) = 30.876, p = <0.001) wellbeing, even after controlling for sample confounds.

Table 6. Standardised Mean QoL Differences in Social Domain

Measure	Subscale	$N_{studies}$	$N_{participants}$		g_w	95% CI		p	N_{fs}	Heterogeneity statistics			
			CP	Control		Lower	Upper			Q	p	I^2	T
CHQ-PF50	Family activities	3	309	10892	**-1.467**	-2.577	-0.357	0.010	25	11.730	0.027	82.949	0.269
	Family cohesion	3	309	10892	-0.108	-1.216	0.999	0.848	5	1.612	0.870	0.000	0.000
CPQoL	Social well-being & acceptance	1	21	21	-0.330	-2.325	1.665	0.746	3	0.000	0.000	0.000	0.000
KIDSCREEN	Social acceptance	2	898	25514	**1.679**	0.330	3.029	0.015	15	561.521	0.037	99.822	2.210
	School environment	2	898	25514	**1.630**	0.280	2.979	0.018	14	411.18	0.043	99.757	1.887
	Social support & peers	2	898	25514	-0.096	-1.446	1.253	0.889	3	0.190	0.905	0.000	0.000
PedsQL	Social functioning	1	148	12010	-1.206	-2.557	0.145	0.080	7	0.000	0.000	0.000	0.000
	School functioning	1	148	12010	-1.151	-2.503	0.200	0.095	7	0.000	0.000	0.000	0.000
TACQOL	Social functioning	2	315	3401	-0.768	-1.070	0.188	0.115	10	21.155	0.178	85.819	0.256
	Total	9	1163	41881	-0.302	-0.793	0.189	0.228	23	2735.394	0.000	99.269	1.140

Abbreviations. $N_{studies}$ = number of studies included in analysis; $N_{participants}$= number of participants providing this data; 95% CI = confidence interval (with lower and upper limits); CP = Cerebral palsy, g_w = pooled Hedge's g with inverse variance weighting (note: weighting only applies to total effect sizes involving 2 or more studies); p = p value associated with effect estimate; N_{fs} = fail safe N; Q = Cochran's χ^2; I^2 = eta-squared; T = tau

Measures: CHQPF50 = Child Health Questionnaire Parent Form; CPQoL= Cerebral Palsy Quality of Life questionnaire; PedsQL = Pediatric Quality of Life; TNO AZL Children's Quality of Life

Bold font denotes significant group difference ($g \geq 0.50$ p <0.05, CIs ≠0, $N_{fs} > N_{studies}$)

Table 7. Within-group Effects as Reported by Child vs Parent

QoL domain	Subgroup	$N_{studies}$	$N_{participants}$		g_w	95% CI		p	N_{fs}	Heterogeneity statistics			
			CP	Control		Lower	Upper			Q	p	I^2	T
Physical	Parent	8	833	35660	**-1.163**	-1.839	-0.487	0.001	55	1116.709	0.000	99.373	1.164
	Child	4	560	9472	-0.625	-1.573	0.324	0.197	17	256.093	0.000	98.829	0.626
Psychological	Parent	8	833	35660	-0.187	-1.313	0.940	0.643	12	3011.967	0.000	99.768	1.451
	Child	4	560	35660	-0.259	-1.632	1.115	0.163	9	91.300	0.000	96.714	0.419
Social	Parent	8	833	35660	-0.382	-1.344	0.579	0.436	23	170.738	0.000	98.243	0.545
	Child	4	560	9472	-0.479	-1.834	0.876	0.489	14	2782.472	0.000	99.748	1.684

Abbreviations. $N_{studies}$ = number of studies providing this data; $N_{participants}$ = number of participants providing this data; 95% CI= confidence interval (with lower and upper limits); CP= cerebral palsy, g_w = pooled Hedge's g with inverse variance weighting (note: weighting only applied to total effect sizes involving 2 or more studies); p = significance value associated with effect estimate; N_{fs} = fail safe N; Q = Cochran's χ^2; I^2 = eta-squared; T = tau; Parent = parent/proxy reported QoL; Child= child or adolescent rated QoL

Bold font denotes significant group difference ($g \geq 0.50$ $p < 0.05$, CIs $\neq 0$, $N_{fs} > N_{studies}$)

Domain	Subgroup	$N_{studies}$	$N_{participants}$		g_w	95% CI		p	N_{fs}	Heterogeneity statistics			
			CP	Control		Lower	Upper			Q	p	I^2	T
Physical	Normative	7	1601	44388	**-0.806**	-1.509	-0.102	0.025	35	1509.264	0.000	99.602	0.940
	Control	2	66	85	**-2.010**	-3.367	-0.653	0.004	22	33.943	0.000	97.054	1.459
Psychological	Normative	7	1601	44388	-0.078	-1.007	0.850	0.869	8	3084.897	0.000	99.806	1.258
	Control	2	66	85	**-0.577**	-0.824	-0.330	0.000	8	0.127	0.000	0.000	0.000
Social	Normative	7	1601	44388	-0.189	-1.135	0.758	0.696	13	2935.399	0.000	99.796	1.282
	Control	2	66	85	-0.523	-2.322	1.275	0.568	7	1.345	0.000	25.661	0.140

Abbreviations. $N_{studies}$ = number of studies providing this data; $N_{participants}$ = number of participants providing this data; 95% CI= confidence interval (with lower and upper limits); CP= cerebral palsy, g_w = pooled Hedge's g with inverse variance weighting (note: weighting only applied to total effect sizes involving 2 or more studies); p = significance value associated with effect estimate; N_{fs} = fail safe N; Q = Cochran's χ^2; I^2 = eta-squared; T = tau; Normative = normative comparison group; Control = recruited own controls

Bold font denotes significant group difference ($g \geq 0.50$ $p < 0.05$, CIs $\neq 0$, $N_{fs} > N_{studies}$)

Table 9. Within-group Effects Based on Matched vs Unmatched Control Groups

Domain	Subgroup	$N_{studies}$	$N_{participants}$		g_w	95% CI		p	N_{fs}	Heterogeneity statistics			
			CP	Control		Lower	Upper			Q	p	I^2	T
Physical	Matched	3	884	3304	**-1.309**	-2.508	-0.110	0.032	23	134.299	0.000	98.511	1.443
	Unmatched	6	784	35755	-0.625	-1.573	0.324	0.197	25	1167.925	0.000	99.572	1.012
Psychological	Matched	3	884	3304	-0.328	-1.885	1.229	0.679	8	23.852	0.000	91.615	0.441
	Unmatched	6	784	35755	-0.104	-1.195	0.986	0.851	9	3020.374	0.000	99.834	1.406
Social	Matched	3	884	3304	-0.312	-1.980	1.356	0.714	8	30.876	0.000	93.522	0.515
	Unmatched	6	784	35755	-0.261	-1.407	0.934	0.692	14	2856.018	0.000	99.825	1.516

Abbreviations. $N_{studies}$ = number of studies providing this data; $N_{participants}$ = number of participants providing this data; 95% CI= confidence interval (with lower and upper limits); CP= cerebral palsy, g_w = pooled Hedge's g with inverse variance weighting (note: weighting only applied to total effect sizes involving 2 or more studies); p = significance value associated with effect estimate; N_{fs} = fail safe N; Q = Cochran's χ^2; I^2 = eta-squared; T = tau; Unmatched = comparison group not matched on age and gender; Matched = comparison group matched on age and gender

Bold font denotes significant group difference ($g \geq 0.50$ $p < 0.05$, CIs $\neq 0$, $N_{fs} > N_{studies}$)

CHAPTER 4

Discussion

4.1 Key Findings

Fourteen independent studies examining QoL ratings of 2,042 children and adolescents with CP relative to 55,180 typically developing peers were included in this review. Study quality, including internal and external validity was adequate. Despite individual variability between studies in QoL estimates, an examination of domain-specific measures identified physical and motor functioning as the primary area in which CP and comparison groups significantly differed. The present findings are critically evaluated in this chapter, with a discussion of practical and clinical implications along with methodological limitations provided.

4.1.1 Total QoL. Studies that utilised composite QoL scores, which are generally based upon a summary of all responded items, tended not to report significant group differences. This suggests that young persons with CP self-report comparable general QoL to typically developing peers. This is consistent with the disability paradox: despite potential impairments of varying severities, individuals with a disability do not necessarily perceive their QoL as compromised (Albrecht & Delieger, 1999; Olson & Schober, 1993). Instead, QoL may be rated from a holistic perspective whereby all aspects of an individual's life are taken into consideration when reporting on QoL (e.g. physical, psychological and social wellbeing). However, further research is needed to examine the contextual issues which may moderate or mediate the relationship between impairment and perceived QoL. This includes perceived quality of social supports, which have been shown to promote physical health and functioning, regardless of an individual's disability level (Fellinghauer, Reinhardt, Stucki & Bickenback, 2012). Interestingly, studies that utilised the

PedsQL identified large negative and significant group differences. This may reflect conceptual differences between QoL measures. The PedsQL specifically includes a module appropriate for children and adolescents with CP, assessing QoL on dimensions including daily and school activities, movement and balance, pain and hurt, fatigue, eating activities and speech and communication (Varni, 2003). As such, the PedsQL may be more sensitive in measuring QoL within CP populations in comparison to the CHQ and SEIQOL-DW, both of which do not include such case-specific modules.

4.1.2 Physical domain. The finding that children and adolescents with CP noted greater impairments in physical and motor abilities in comparison to peers, is somewhat expected given that functional impairments of varying severities are a direct consequence of CP (Sankar & Mundkur, 2005; Shevell, 2010). In particular, significant and large group differences were noted for subscales relating to objective physical functioning concepts, such as ability to get around, ability to take care of self, walking one block/climbing one stair (CHQ). Similarly, large group differences were noted in relation to specific physical roles and activities including problems with running, participating in sports activity or exercise, having hurts or aches (PedsQL; Asmussen et al., 2000; Varni, 2003). The suggestion is that children and adolescents with CP may perceive that their physical health status impedes their ability to interact to their full potential in a range of settings (Asmussen et al., 2000). This is a finding that has been consistently demonstrated in the CP literature (Colver, 2016; Sankar & Mundkur, 2005; Weber et al., 2016).

4.1.3 Psychological domain. For children and adolescents with CP, psychological wellbeing did not appear to be impaired in comparison to peers. This is somewhat surprising given that individual studies have reported impairments in

emotional functioning and psychological wellbeing across the lifespan in this population (Colver, 2016; Parkes & McCusker, 2008; Yamaguchi, Perry & Hines, 2014). Indeed, a large and significant positive effect estimate was associated with the psychological well-being subscale of the KIDSCREEN indicating that young persons with CP perceive themselves as having positive emotions and satisfaction with life (Dickinson et al., 2007). This finding was, however, based on a single study and therefore may not be representative of the entire CP population. Indeed, the majority of subscales within this QoL domain were utilised by single studies, which may help to explain why these findings conflict with previous literature.

4.1.4 Social domain. Overall, effect estimates within this domain were large, negative and non-significant. Taken at face value, this could indicate that children and adolescents with CP do not rate that their social ability and wellbeing as significantly compromised despite their disorder. However, a significant and negative effect was observed in relation to family activities (as measured by the CHQ), suggesting that children and adolescents perceive that their health negatively impedes on family activities or is a source of tension within the family (Wake et al., 2003). CP is a persistent and diverse disorder that often requires intensive input of medical and orthopedic care and behavioural and emotional therapy that may persist for a lifetime (Kent, 2013). The demanding nature of the disorder may, therefore, induce perceptions of familial stress for children and adolescents with CP. In contrast, ratings on subscales of social acceptance (CPQoL) and school environment (KIDSCREEN) were large and positive, suggesting that children and young people with CP generally report a feeling of acceptance by peers and are able to maintain a positive attitude and feelings towards learning, the school environment and their teachers (Dickinson et al., 2007). This is a promising finding given that individuals

with CP, especially during their childhood and adolescent years, may endure difficulties when socialising with peers (Janssen et al., 2010).

4.1.5 Subgroup analyses. Significant differences were observed across all QoL domains when comparing parent/proxy with child ratings of QoL. Parents reported that their children had worse QoL scores than what the children themselves reported. This is consistent with previous literature (Gates et al., 2010; Roy et al., 2010), which suggests that while parents are able to more easily identify the physical impairments that their child may experience, they are more limited in identifying the emotional and behavioural difficulties that their child distinguishes to be vital to their emotional health and wellbeing.

Further, significant differences on the physical domain were observed for studies that recruited controls in parallel to their CP group as opposed to studies which relied on normative data. There is the possibility that some of the population norms that were used are outdated. This includes the KIDSCREEN, TACQOL and CHQ, which provide norms sourced up to 13 years prior to the cited studies (e.g. Janssen et al., 2010; McCullough et al., 2013; Vles et al., 2015). As normative data cannot account for changes in population compositions over time on sociodemographic factors the findings that were originally observed my not be true for the current population (Kendall et al., 1999). Future CP research should therefore consider sourcing their comparison group in parallel to the CP group, whenever possible. Notably, the non-significant findings observed on the psychological and social domains may also reflect the limited amount of studies included in the subgroup analysis, hence true group differences may not have been able to be detected.

Lastly, in line with previous literature (Bjornson et al., 2008; Türkoglu et al., 2015), significant differences were observed across all domains in studies that matched their control/comparison groups on age and gender. This suggests that it is crucial to match control/comparison groups on important contextual variables, such as age and gender, in order to gain a more accurate representation of potential QoL differences between CP and their peers.

4.2 Clinical Implications and Future Research

The results of this meta-analysis have important clinical implications. The large and negative group differences provide direction for more specific, tailored treatment recommendations for individuals with CP. In particular, the physical domain warrants consideration. Systematic reviews have indicated that reducing sedentary time and increasing light to moderate physical activity in the form of aerobic, anaerobic and muscle-strengthening exercises is crucial for improving physical QoL of individuals with CP (Verschuren, Darrah, Novak, Ketelaar & Wiart, 2014; Verschuren, Ketelaar, Takken, Helders & Gorter, 2008). Such training is encouraged over a minimum of a six-week period in order to improve physical functioning and mobility. The health enhancing physical activities therefore can range from light (i.e. walking, knee extensions, turning) to moderate (i.e. swimming, squats, play (competitive) sports; Verschuren, Peterson, Balemans & Hurvitz, 2016). Such activities could involve a structured or unstructured exercise program integrated within a community or home setting, in order to promote the integration of physical activity into daily lifestyle and improving physical health and wellbeing (Maltais, Wiart, Fowler, Verschuren & Damiano, 2014; Vershcuren et al., 2008).

The use of virtual reality (VR) active video games presents another home-based physical activity. Traditionally, inpatient and outpatient rehabilitation programs have treated impairments associated with CP (i.e. motor function, aerobic capacity and posture control) separately, potentially limiting the overall effectiveness of rehabilitation (Ballaz, Robert, Prince & Lemay, 2011). VR, in the form of active video gaming consoles, is able to this simultaneously and in a more entertaining and interactive way (Ballaz et al., 2011). This could be in the form of clinician-developed gaming consoles or even in the form of the Nintendo Wii™ and Wii Fit™ consoles (Nintendo, Redmond, USA). Gaming consoles create opportunities for individuals with CP to conduct active and repetitive motor/sensory practices (Cifuentes-Zapien, Valdex-Aguilar, Rojas-Correa, Chong-Quero & Pineda-Olivares, 2011). A review of 17 available studies implementing VR technology in the treatment of children with CP reported promising, albeit preliminary, findings (Fehlings, Switzer, Findlay & Knights, 2013; Weiss, Tirosh & Fehlings, 2014). VR is becoming increasingly affordable and accessible and can be tailored to best suit the individual and their cognitive, motor and emotional abilities in the context of specific therapeutic goals (Weiss et al., 2014). This type of tailored intervention may promote the uptake of physical activity into daily routine. Indeed, children with CP have reported to be more engaged and motivated by VR in comparison to traditional rehabilitation methods (Weiss et al., 2014). Additionally, such consoles can be used by the entire family therefore promoting familial involvement also.

For clinicians and researchers, selecting the most appropriate and reliable QoL assessment tool can be a challenge, given the number and variety of generic and CP-specific measures, each with an individual focus on measuring QoL. While a specific instrument to measure QoL within the CP population (CP-QOL) has been developed,

generic measures are more widely utilised. This may threaten the validity of QoL estimates as the majority are rated primarily on self-report. This calls for the development of more inclusive measures of QoL which incorporate and psychological and social indexes that go beyond self-report, which for some individuals with CP may be extremely difficult. Even parent/proxy reported QoL can be problematic in that disparities exist between child and parent ratings on numerous psychosocial domains, thus introducing bias to the measurement of QoL (Piazza, Hennrikus, Schell, Armstrong & Fortuna, 2016). Developing more creative measures with a variety of response formats (e.g. visual analogue scales) would be more inclusive of children and adolescents with CP of varying severities and could potentially allow for more reliable and representative QoL estimates.

4.3 Limitations

The current findings must be considered in the context of several methodological limitations encountered during data collection and analysis. First, moderator analyses were limited in scope given that studies did not consistently report key sociodemographic characteristics that may be pertinent to QoL ratings, such as disability severity and intellectual ability (Fadwa, Suad & Mutaz, 2016; Türkoglu et al., 2015). Ideally, this data (i.e. GMFCS) should be available to allow for more extensive moderator analysis. Similarly, the subgroup analyses that were conducted may not have been sufficiently powered to detect true QoL differences in individuals with CP and controls. It is recommended that a combined minimum of approximately 6-10 studies is required for subgroup analyses (Fu, et al., 2011). Recent research has even suggested that a minimum of 20 studies (i.e. 10 per group) is required to reliably detect between-group differences (Rubio-Aparicio, Sànchez-Meca, López-López,

Botella & Marín-Martínez, 2017). Future research could go beyond aggregate data and conduct an individual patient data meta-analysis in order to address this limitation (Riley, Lambert & Abo-Zaid, 2010).

Second, heterogeneity estimates may have been biased due to the small number of studies included in this review. It has been identified that bias, associated with the I^2 statistic, is largest when the number of studies included is small (von Hippel, 2015). This leads to difficulties in detecting true heterogeneity estimates. Such a bias also extends to the *Q*-statistic. Importantly, tau (*T*) was also included in an attempt to address this bias (Borenstein et al., 2009)

The generalisability of the present findings to the broader CP population is also limited. A typical bias observed within the CP literature, and indeed within this review, is the exclusion of individuals with more severe physical impairments (Feldman, Battin, Shaw & Luckasson, 2013). Rather, there is a distinct focus upon a subgroup of children and adolescents with CP that experience mild to moderate physical disability. It is pivotal that future research be more inclusive of children and adolescents with more severe physical and intellectual impairments, which account for 10-15% of this population (Reid et al., 2011; Sankar & Mundkur, 2006), so that the results can be broadly generalised to the wider CP population.

Lastly, while the grouping of outcomes into three distinct QoL domains was more efficient for data analysis it was also problematic largely due to significant overlap between symptoms that were assessed. The interconnectedness of subscales within this review poses a challenge to categorising the measurement of QoL. For example, the role physical subscale of the CHQ-PF50 was conceptualised as impairment to physical health but could equally be considered as an impairment to social functioning, given that individuals are required to rate on the degree to which

their physical health and functioning impedes on their social activities and participation.

4.4. Conclusions

This meta-analysis is the first to collate and analyse existing data examining QoL among the young CP population. The combined findings are useful for health-care professionals who seek to understand the QoL of children and adolescents with CP in comparison to typically developing peers. Guidelines are provided for informing future research in addition to establishing priorities for treatments and interventions that can address the most significant and affected aspects of QoL. The pooled findings confirm that the repercussions of CP impact children and adolescents' physical functioning. This is not to say that mental and social functioning should be ignored. Rather, it is vital that a combination of all three domains be examined to ensure comprehensive assessment and care for individuals with CP.

REFERENCES

Albrecht, G. L. & Devlieger, P. J. (1999). The Disability Paradox: High Quality of Life Against all Odds. *Social Science & Medicine, 48*(8), 977-988. DOI: 10.1016/S0277-9536(98)00411-0

Arnaud, C., White-Koning, M., Michelsen, S. I., Parkes, J., Parkinson, K., Thyen, U., Beckung, E. Dickinson, H. O., Fauconnier, J., Marcelli, M., McManus, V. & Colver, A. (2008). Parent-Reported Quality of Life of Children with Cerebral Palsy in Europe. *Paediatrics, 121*, 54(11).

Asmussen, L., Olson, L. M., Grant, E. N., Landgraf, J. M., Fagan, J. & Weiss, K. B. (2000). Use of the Child Health Questionnaire in a Sample of Moderate and Low-Income Inner-City Children with Asthma. *American Journal of Respitory and Critical Care Medicine, 162*(4 Pt 1), 1215-21.

Ballaz, L., Robert, M., Prince, F. & Lemay, M. (2011). Active Video Games and Children with Cerebral Palsy: the Future of Rehabilitation? *International Conference on Virtual Rehabilitation,* 1-2. DOI: 10.1109/ICVR.2011.5971808

Balshem, H., Stevens, A., Ansari, M., Norris, S., Kansagara, D., Shamilyan, T., Chou, R., Chung, M., Moher, D. & Dickersin, K. (2013). *Finding Grey Literature Evidence and Assessing for Outcome and Analysis Reporting Biases When Comparing Medical Interventions: AHRQ and the Effective Health Care Program. Methods Guide for Comparative Effectiveness Reviews.* Retrieved

from: https://www.ncbi.nlm.nih.gov/books/NBK174882/pdf/Bookshelf_NBK174882.pdf

Beckung, E., White-Koning, M., Marcelli, M., McManus, V., Michelsen, S., Parkes, J., Parkinson, K., Thyen, U., Arnaud, C., Fauconnier, J. & Colver, A. (2008). Health Status of Children with Cerebral Palsy Living in Europe: A Multi-Centre Study. *Child: Care, Health and Development, 34*(6), 806-814. DOI: 10.1111/j.1365-2214.2008.00877.x

Bjornson, K. F., Belza, B. Kartin D., Logsdon, R. & McLaughlin, J. (2007). Amulatory Physical Activity Performance in Youth with Cerebral Palsy and Youth who are Developing Typically. *Physical Therapy, 87*(3), 248-257. DOI: http://dx.doi.org/10.2522/ptj.20060157

* Bjornson, K. F., Belza, B., Kartin, D., Logsdon, R. G. & McLaughlin, J. (2008). Self-Reported Health Status and Quality of Life in Youth with Cerebral Palsy and Typically Developing Youth. *Archives of Physical Medicine and Rehabilitation, 89*, 121-127. DOI: 10.1016/j.apmr.2007.09.016

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2009). *Introduction to Meta-Analysis.* Chichester: John Wiley & Sons, Ltd.

Browne, J., O'Boyle, C., McGee, H., McDonald, N. & Joyce, C. (1997). Development of a Direct Weighting Procedure for Quality of Life Domains. *Quality of Life Research, 6*(4), 301-309. DOI: 10.1023/A:1018423124390

* Calley, A., Williams S., Reid, S., Blair, E., Valentine, J., Girdler, A. & Elliot, C. (2011). A Comparison of Activity, Participation and Quality of Life in Children With and Without Spastic Diplegia Cerebral Palsy. *Disability and Rehabilitation, 34*(15), 1306-1310. DOI: https://doi.org/10.3109/09638288.2011.641662

Chen, K-L., Wang, H-Y., Tseng, M-H., Shieh, J-Y., Lu. L., Yao. K-P. G. & Huang, C-Y. (2013). The Cerebral Palsy Quality of Life for Children (CP QOL-Child): Evidence of Construct Validity. *Research in Developmental Disabilities, 34*(3), 994-1000. DOI: 10.1016/j.ridd.2012.11.025

Cifuentes-Zapien, J. E., Valdez-Aguilar, J. A., Rojas-Correa, F. J., Chong-Quero, J. E. & Pineda-Olivares, A. (2011). A Video Game for an Upper Limb Rehabilitation Robotic Sytem for Children with Cerebral Palsy. *Pan American Health Care Exchanges,* 189-193. DOI: 10.1109/PAHCE.2011.5871877

Cohen, J. (1988). *Statistical Power Analysis for the Behavioural Sciences* (2nd ed), Erlbaum, Hillsdale, NJ.

Cohen, J. (1968). Weighted Kappa: Nominal Scale Agreement with Provision for Scaled Disagreement or Partial Credit. *Psychological Bulletin, 70*(4), 213-220. DOI: 10.1037/h0026256

Colver, A. (2016). Outcomes for People with Cerebral Palsy: Life Expectancy and Quality of Life. *Paediatrics and Child Health, 26*(9), 383-386. DOI: 10.1016/j.paed.2016.04.014

Colver, A., Fairhurt, C. & Pharoah, P. O. D. (2013). Cerebral Palsy. *The Lancet, 383*(9924), 1240-1249. DOI: 10.1016/S0140-6736(13)61835-8

Colver, A., Rapp, M., Eisemann, N., Ehlinger, V., Thyen, U., O Dickinson, H., Parkes, J., Parkinson, K., Nystrand, M., Fauconnier, J., Marcelli, M., Michelsen, S. I. & Arnaud, C. (2015). Self-Reported Quality of Life of Adolescents with Cerebral Palsy: A Cross-Sectional and Longitudinal Analysis. *Lancet, 385,* 705-716. DOI: http://dx.doi.org/10.1016/S0140-6736(14)61229-0

Cumming, G. (2012) *Understanding the New Statistics: Effect Sizes, Confidence Intervals, and Meta-Analysis*. New York: Taylor & Francis.

Davis, E., Mackinnon, A., Davern, M., Boyd, R., Bohanna, I., Waters, E., Graham, H. K., Reid, S. & Reddihough, D. (2013). Description and Psychometric Properties oft he CP QOL-Teen: A Quality of Life Questionnaire for Adolescents with Cerebral Palsy. *Research in Developmental Disabilities, 34,* 344-352. DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1016/j.ridd.2012.08.018

Davis, E., Mackinnon, A. & Waters, E. (2011). Parent Proxy-Reported Quality of Life for Children with Cerebral Palsy: is it Related to Parental Psychosocial Distress?

Child: Care, Health and Development, 38(4), 553-560. DOI: 10.1111/j.1365-2214.2011.01267.x

* Dickinson, H. O., Parkinson, K. N., Ravens-Sieberer, U., Schirripa, G., Thyen, U., Arnaud, C., Beckung, E., Fauconnier, J., McManus, V., Michelsen, S. I., Parkes, J. & Colver, A. F. (2007). Self-Reported Quality of Life 8-12-Year-Old Children with Cerebral Palsy: A Cross-Sectional European Study. *The Lancet, 369*(9580), 2171-2178. DOI: 10.1016/S0140-6736(07)61013-7

* Du, R. Y., McGrath, C., Yiu, C. K. Y. & King, N. M. (2010). Health- and Oral Health-Related Quality of Life Among Preschool Children with Cerebral Palsy. *Quality of Life Research, 19*(9), 1367-1371. DOI: 10.1007/s11136-010-9693-6

Edwards, T. C., Huebner, C. E., Connell, F. A. & Patrick, D. L. (2002). Adolescent Quality of Life, Part I: Conceptual and Measurement Model. *Journal of Adolescence, 25*(3).

Eunson, P. (2016). Aetiology and Epidemiology of Cerebral Palsy. *Paediatrics and Child Health, 26*(9), 367-372. DOI: 10.1016/j.paed.2016.04.011

Ellis, P. D. (2010). *The Essential Guide to Effect Sizes: Statistical Power, Meta-Analysis, and the Interpretation of Research Results*, New York: Cambridge University Press.

Fadwa, M., Suad, A. & Mutaz, M. (2016). Quality of Life of Cerebral Palsy Patients and their Caregivers: A Cross Sectional Study in a Rehabilitation Center Khartoum-Sudan (2014-2015). *Journal of Neurosciences in Rural Practice, 7*(3), 355-361. DOI: 10.4103/0976-3147.182778

Fehlings, D., Switzer, L., Findlay, B. & Knights, S. (2013). Interactive Computer Play as "Motor Therapy" for Individuals with Cerebral Palsy. *Seminars in Pediatric Neurology*, *20*(2), 127-138. DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1016/j.spen.2013.06.003

Feldman, M. A., Battin, S. M., Shaw, O. A. & Luckasson, R. (2013). Inclusion of Children with Disabilities in Mainstream Child Development Research. *Disability & Society*, *28*(7), 997-1011. DOI: 10.1080/09687599.2012.748647

Fellinghauer, B., Reinhardt, J. D., Stucki, G. & Bickenbach, J. (2012). Explaining the Disability Paradox: A Cross-Sectional Analysis oft he Swiss General Population. *BMC Public Health,* 12, 655. DOI: 10.1186/1471-2458-12-655

Fu, R., Gartlehner, G., Grant, M., Shamilyan, T., Sedrakyan, A., Wilt, T. J., Griffith, L., Oremus, M., Raina, P., Ismaila, A., Satanguida, P., Lau, J. & Triklinos, T. A. (2011). Conducting Quantitative Syntehsis When Comparing Medical Interventions: AHRQ and the Effective Health Care Program. *Journal of Clinical Epidemiology*, *64*(11), 1187-1197. DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1016/j.jclinepi.2010.08.010

Gates, P., Otsuka, N., Sanders, J. & McGee-Brown, J. (2010). Functioning and Health-Related Quality of Life of Adolescents with Cerebral Palsy: Self Versus Parent Perspectives. *Developmental Medicine & Child Neurology, 52*(9), 843-849. DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1111/j.1469-8749.2010.03666.x

Gopalakrishnan, S. & Ganeshkumar, P. (2013). Systematic Reviews and Meta-Analysis: Understanding the Best Evidence in Primary Healthcare. *Journal of Family Medicine and Primary Care, 2*. DOI: 10.4103/2249-4863.109934

Hedges, L. V. & Olkin, I. (1985). *Statistical Methods for Meta-Analaysis*. Orlando: Academic Press.

Higgins, J. P. T & Green, S. *Cochrane Handbook for Systematic Reviews of Interventions.* Hoboken: John Wiley & Sons, Incorporated.

Horsman, M., Suto, M., Dudgeon, B. & Harris, S. R. (2010). Ageing with Cerebral Palsy: Psychosocial Issues. *Age and Ageing, 39*(3), 294-9. DOI: 10.1093/ageing/afq018

Hozo, S. P., Djulbegovic, B. & Hozo, I. (2005). Estimating the Mean and Variance from the Median, Range, and the Size of a Sample. *BMC Medical Research Methodology, 5*(13), 1-10. DOI: 10.1186/1471-2288-5-13

* Janssen, C. G. C., Voorman, J. M. Becher, J. G., Dallmeijer, A. J. & Schuengel, C. (2010). Course of Health-Related Quality of Life in 9-16-Year-Old Children with Cerebral Palsy: Associations with Gross Motor Abilities and Mental Health. *Disability & Rehabilitation, 32*(4), 344-351. DOI: 10.3109/09638280903166345

Jiang, B., Walstab, J., Reid, S. M., Davis, E. & Reddinhough, D. (2016). Quality of Life in Young Adults with Cerebral Palsy. *Disability and Health Journal, 9,* 673-681. DOI: http://dx.doi.org/10.1016/j.dhjo.2016.04.006

Juni, P., Holenstein, F., Sterne, J., Barlett, C. & Egger, M. (2002). Direction and Impact of Language Bias in Meta-Analyses of Controlled Trials: Empircal Study. *International Epidemiological Association,* 31, 115-123. DOI: http://dx.doi.org/10.1093/ije/31.1.115

Karimi, M. & Brazier, J. (2016). Health, Health-Related Quality of Life, and Quality of Life: Whats the Difference? *PharmacoEconomics*, *34,* 645-649. DOI: 10.1007/s40273-016-0389-9

Kendall, P. C., Marrs-Garcia, A., Nath, S. R. & Sheldrick, R. C. (1999). Normative Comparisons for the Evaluation of Clinical Significance. *Journal of Consulting and Clinical Psychology*, *67*(3), 285-299. DOI: 10.1037/0022-006X.67.3.285

Kent, R. M. (2013). Cerebral Palsy. *Handbook of Clinical Neurology, 110*, 443-59. DOI: 10.1016/B978-0-444-52901-5.00038-1

Kmet, L. M., Lee, R. C. & Cook, L. S. (2004). Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields. Alberta Heritage Foundation for Medical Research (AHFMR), Edmonton.

Landgraf, J. M., Abetz, L. & Ware, J. E. (1999). *Child Health Questionnaire (CHQ): a User's manual, 2nd Edition*. Boston: New England Medical Center.

Lipsey, M. W. & Wilson, D. B. (2001) *Practical Meta-Analysis.* Thousand Oaks, Calif: Sage Publications.

* Maher, C. A., Olds, T., Williams, M. T. & Lane, A. E. (2008). Self-Reported Quality of Life in Adolescents with Cerebral Palsy. *Physical & Occupational Therapy in Paediatrics, 28,* 41-57. DOI: 10.1300/J006v28n01_04

Maltais, D. B., Wiart, L., Fowler, E., Vershuren O. & Damiano, D. L. (2014). Health-Related Physical Fitness for Children with Cerebral Palsy. *Journal of Child Neurology, 29*(8), 1091-1100. DOI: 10.1177/0883073814533152

* McCullough, N., Parkes, J., Kerr, C. & McDowell, B. C. (2013). The Health of Children and Young People with Cerebral Palsy: A Longitudinal, Population-Based Study. *International Journal of Nursing Studies, 50,* 747-756. DOI: 10.1016/j.ijnurstu.2011.01.011

Mezgebe, M., Gileh-Gol, A-D., Streiner, D. L., Fayed, N., Rosenbaum, P. L. & Ronen, G. M. (2015). Quality of Life in Children with Epilepsy: How Does it

Compare with the Quality of Life in Typical Children and Children with Cerebral Palsy. *Epilepsy & Behaviour, 52,* 239-243. DOI: http://dx.doi.org/10.1016/j.yebeh.2015.09.009

Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Annals of Internal Medicine, 151*(4), 264-269

Mpundu-Kaambwa, C., Chen, G., Huynh, E., Russo, R. & Ratcliffe, J. (2018). A Review of Preference-Based Measures for the Assessment of Quality of Life in Children and Adolescents with Cerebral Palsy. *Quality of Life Research, 27,* 1781-1799. DOI: https://doi.org/10.1007/s11136-018-1837-0

Olson, G. & Schober, B. (1993). The Satisfied Poor. *Social Indicators Research, 28*(2), 173-193. DOI: 10.1007/BF01079657

Oskoui, M., Coutinho, F., Dykeman, J., Jetté, N. & Pringsheim, T. (2013). An Update on the Prevalence of Cerebral Palsy: A Systematic Review and Meta-Analysis. *Developmental Medicine & Child Neurology.* DOI: 10.1111/dmcn.12080

Paneth, N., Damiano, D., Rosenbaum, P., Leviton, A., Goldstein, M. & Bax, M. (2005). Proposed Definition and Classification of Cerebral Palsy, April 2005. *Developmental Medicine & Child Neurology,* 47(8), 571-576. DOI: 10.1111/j.1469-8749.2005.tb01195.x

Parkes, J., White-Koning, M., O Dickinson, H., Thyen, U., Arnaud, C., Beckung, E., Fauconnier, J., Marcelli, M., McManus, V., Michelsen, S. I., Parkinson, K. & Colver, A. (2009). Psychological Problems in Children with Cerebral Palsy: A Cross-Sectional European Study. *Child Psychology and Psychiatry, 49*(4), 405-413. DOI: 10.1111/j.1469-7610.2007.01845.x

Patrick, D. L., Edwards, T. C. & Topolski, T. D. (2002). Adolescent Quality of Life, Part II: Initial Validation of a New Instrument. *Journal of Adolescence*, *25*(3), 287-300. DOI: 10.1006/jado.2002.0471

Piazza, B., Hennrikus, W., Schell, R., Armstrong, D & Fortuna, K. (2016). The Factors Most Important for Quality of Life in Children and Adolescents with Cerebral Palsy. *Journal of Pediatric Neurology and Medicine, 1*, 1-4. DOI: 10.4172/2472-100x.1000102

Power, R., King, C., Muhit, M., Heanoy, E., Galea, C., Jones, C., Badawi, N. & Khandaker, G. (2018). Health-Related Quality of Life of Children and Adolescents with Cerebral Palsy in Low – and Middle – Income Countries: a Systematic Review. *Developmental Medicine & Child Neurology, 60*(5), 469-479. DOI: 10.1111/dmcn.13681

Rapp M., Eisemann, N., Arnaud, C., Ehlinger, V., Fauconnier, J., Marcelli, M., Michelsen, S. I., Nystrand, M., Colver, A. & Thyen, U. (2017). Predictors of Parent-Reported Quality of Life of Adolescents with Cerebral Palsy: A Longitudinal Study. *Research in Developmental Disabilities, 62*, 259-270. DOI: 10.1016/j.ridd.2016.12.005

Ravens-Sieberer, U., Gosh, A., Rajmil. L., Erhart, M., Bruil, J., Duer, W., Auqier, P., Power, M., Abel, T., Czemy, L., Mazur, J., Czimbalmos, A., Tountas, Y., Hagquist, C., Kilroe, J. & the European KIDSCREEN Group. (2005). KIDSCREEN-54 Quality-of-Life Measure for Children and Adolescents. *Expert Review. Pharmacoeconomics Outcomes Research, 5*(3), 353-364.

Reid, S. M., Carlin, J. B. & Reddihough, D. S. (2011). Using the Gross Motor Function Classification System to Describe Patterns of Motor Severity in Cerebral Palsy. *Developmental Medicine & Child Neurology*, *53*(11), 1007-1012. DOI: 10.1111/j.1469-8749.2011.04044.x

Riley, R. D., Lambert, P. C. & Abo-Zaid, G. (2010). Meta-Analysis of Individual Participant Data: Rationale, Conduct and Reporting. *BMJ, 340*. DOI: 10.1136/bmj.c221

Romeo, D. M., Sini, F., Brogna, C., Albamonte, E., Ricci, D. & Mercuri, E. (2016). Sex Differences in Cerebral Palsy on Neuromotor Outcome: A Critical Review. *Developmental Medicine & Child Neurology.* DOI: 10.1111/dmcn.13137

Rosenbaum, P. (2003). Cerebral Palsy: What Parent and Doctors Want to Know. (Clinical Review). *British Medical Journal, 326*(7396), 970(5). DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1136/bmj.326.7396.970

Rubio-Aparicio, M., Sánchez-Meca, J., López-López, J. A., Botella, J. & Marín-Martínez, F. (2017). Analysis of Categorical Moderators in Mixed-Effects Meta-

Analysis: Consequences of Using Pooled Versus Separate Estimates of the Residual Between-Studies Variances. *British Journal of mathematical and Statistical Psychology, 70*(3), 439-456. DOI: 10.1111/bmsp.12092

* Russo, R. N., Goodwin, E. J., Miller, M. D., Haan, E. A., Connell, T. M. & Crotty, M. (2008). Self-Esteem, Self-Concept, and Quality of Life in Children with Hemiplegic Cerebral Palsy. *The Journal of Pediatrics, 153*(4), 473-477. DOI: 10.1016/j.jpeds.2008.05.040

Sankar, C. & Mundkur, N. (2005). Cerebral Palsy-Definition, Classification, Etiology and Early Diagnosis. *Indian Journal of Pediatrics, 72*(10), 865-868. DOI: 10.1007/BF02731117

Salum, G. A., Patrick, D. L., Isolan, L. R., Manfro, G. G. & Fleck, M. P. A. (2012). Youth Quality of Life Instrument-Research Version (YQOL-R): Psychometric Properties in a Community Sample. *Journal De Pediatria, 88*(5), 443-8. DOI: doi:10.2223/JPED.2193

Shevell, M. I. (2010). Classifying Cerebral Palsy Subtypes. *Future Neurology, 5*(5), 765-775. DOI: http://dx.doi.org.proxy.library.adelaide.edu.au/10.2217/fnl.10.46

Suurmond, R., van Rhee, H. & Hak, T. (2017). Introdction, Comparison and Validation of Meta-Essentials: A Free and Simple Tool for Meta-Analysis. *Research Synthesis Methods, 8*(4), 537-553. DOI: 10.1002/jrsm.1260

* Tan, S. S., van Meeteren, J., Ketelaar, M., Schuengel, C., Reinders-Messelink, H. A., Raat, H., Dallmeijer, A. J. & Roebroek, M. E. (2014). Long-Term Trajectories of Health-Related Quality of Life in Individuals with Cerebral Palsy: A Multicenter Longitudinal Study. *Archives of Physical Medicine and Rehabilitation, 95*, 2029-39. DOI: http://dx.doi.org/10.1016/j.apmr.2014.04.031

Türkoglu, S., Bilgic, A., Türkoglu, G. & Yilmaz, S. (2015). Quality of Life and Related Factors in Child and Adolescent with Cerebral Palsy. *European Psychiatry, 30*, 28-31. DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1016/S0924-9338(15)31991-X

* Tuzun, E. H., Eker, L. & Daskapan, A. (2004). An Assessment of the Impact of Cerebral Palsy on Children's Quality of Life. *Fizyoterapi Rehabilitasyon, 15*, 3-8.

Van Roy, B., Groholt, B., Heyerdahl, S. & Clench-Aas, J. (2010). Understanding Discrepancies in Parent-Child Reporting of Emotional and Behavioural Problems: Effects of Relational and Socio-Demographic Factors. *BMC Psychiatry, 10*(56), 1-12. DOI: 10.1186/1471-244X-10-56

Vargus-Adams, J. (2006). Longitudinal use of the Child Health Questionnaire in Childhood Cerebral Palsy. *Developmental Medicine & Child Neurology, 48*(5), 343-347. DOI: 10.1017/S0012162206000752

* Varni, J. W., Burwinkle, T. M., Sherman, S. A., Hanna, K., Berrin, S. J., Malcarne, V. L. & Chambers, H. G. (2005). Health-Related Quality of Life of Children and

Adolescents with Cerebral Palsy: Hearing the Voices of Children. *Developmental Medicine Child Neurology, 47*(9), 592-597. DOI: 10.1017/S0012162205001179

Varni, J. W., Burwinkle, T. M., Seid, M. & Skarr, D. (2003). The PedsQL^{TM*} 4.0 as a Pediatric Population Health Measure: Feasibility, Reliability, and Validity. *Ambulatory Pediatrics, 3*(6), 329-341. DOI: 10.1367/1539-4409(2003)0032.0.CO;2

Varni, J. W., Seid, M. & Kurtin P. S. (2001). PedsQL 4.0: Reliability and Validity of the Pediatric Quality of Life Inventory Version 4.0 Generic Core Scales in Health and Patient Populations. *Medical Care, 39*(8), 800-812.

Verschuren, O., Darrah, J., Novak, I., Ketelaar, M. & Wiart, L. (2014). Health-Enhancing Physical Activity in Children with Cerebral Palsy: More of the Same is Not Enough. *Physical Therapy, 94*(2), 297-305. DOI: 10.2522/ptj.20130214

Verschuren, O., Ketelaar, M., Takken, T., Helders, P. J. M. & Gorter, J. W. (2008). Exercise Programs for Children with Cerebral Palsy: A Systematic Review of the Literature. *American Journal of Physical Medicine & Rehabilitation, 87*(5), 404-17. DOI: 10.1097/PHM.0b013e31815b2675

Verschuren, O., Peterson, M. D., Balemans, A. C. J. & Hurvitz, E. A. (2016). Excersise and Physical Activity Recommendations for People with Cerebral Palsy. *Developmental Medicine and Child Neurology, 58*(8), 798-808. DOI: https://dx.doi.org/10.1111%2Fdmcn.13053

* Vinson, J., Shank, L., Thomas, P. D. & Warschausky, S. (2010). Self-Generated Domains of Quality of Life in Children with and Without Cerebral Pasly. *Journal of Developmental Physical Disability, 22*, 497-508. DOI: 10.1007/s10882-010-9187-z

* Vles, G. F. Hendriksen, R. G. F., Hendrisken, J. G. M., van Raak, E. P. M., Soudant, D., Vles, J. S. H. & Gavilanes, A. W. D. (2015). Quality of Life of Children with Cerebral Palsy: A Cross-Sectional KIDSCREEN Study in the Southern part of the Netherlands. *CNS & Neurological Disorders-Drug Targets, 14*, 102-109.

Vogels, T., Verrips, G., Verloove-Vanhorick, S., Fekkes, M., Kamphius, R., Koopman, H. M., Theunissen N. & Wit, J. (1998). Measuring Health-Related Quality of Life in Children: the Development of the TACQOL Parent Form. *Quality of Life Research, 7*(5), 457-465. DOI: 10.1023/A:1008848218806

von Hippel, P. T. (2015). The Heteogeneity Statistic I^2 can be Biased in Small Meta-Analyses. *BMC Medical Research Methodology, 15*(35), 1-8. DOI: 10.1186/s12874-015-0024-z

* Wake, M., Salmon, B. L. & Reddinhough, D. (2003). Health Status of Australian Children with Mild to Severe Cerebral Palsy: Cross-Sectional Survey Using the Child Health Questionnaire. *Developmental Medicine & Child Neurology, 45*(3), 194-199. DOI: 10.1111/j.1469-8749.2003.tb00930.x

Waters, E., Maher, E., Salmon, L., Reddihough, D. & Boyd, R. (2005). Development of a Condition-Specific Measure of Quality of Life for Children with Cerebral Palsy: Empirical Thematic Data Reported by Parents and Children. *Child: Care, Health and Development, 31*(2), 127-35.

Weber, P., Bolli, P., Heimgartner, N., Merlo, P., Zehnder, T. & Kätterer, C. (2016). Behavioural and Emotional Problems in Children and Adults with Cerebral Palsy. *European Journal of Paediatric Neurology Society*, *20*(5), 270-274. DOI: http://dx.doi.org/10.1016/j.ejpn.2015.12.003

Weiss, P. L., Tirosh, E. & Fehlings, D. (2014). Role of Virtual Reality for Cerebral Palsy Management. *Journal of Child Neurology, 29*(8), 1119-1124. DOI: 10.1177/0883073814533007

World Health Organisation (1998). *Health Promotion Glossary. Retrieved from: http://www.who.int/healthpromotion/about/HPR%20Glossary%201998.pdf?ua=1*

World Health Organisation. (2002). *Towards a Common Language for Functioning, Disability and Health: ICF. International Classification of Functioning, Disability and Health.* Retrieved from http://www.who.int/classifications/icf/icfbeginnersguide.pdf?ua_1WHO

Yamaguchi, R., Perry, K. N. & Hines, M. (2014). Pain, Pain Anxiety and Emotional and Behavioural Problems in Children with Cerebral Palsy. *Disability and Rehabilitation, 36*(2), 125-130. DOI: 10.3109/09638288.2013.782356

Zakzanis, K. K. (2001). Statistics to Tell the Truth, the Whole Truth, and Nothing but the Truth: Formulae, Illustrative Numerical Examples, and Heuristic Interpretation of Effect Size Analyses for Neuropsychological Researchers. *Archives of Clinical Neuropsychology, 16*(7), 653-667. DOI: https://doi-org.proxy.library.adelaide.edu.au/10.1016/S0887-6177(00)00076-7

APPENDICES

Appendix A

Table A1. Logic grids per database informing overall search strategy

All searches conducted throughout May 2018. Additional results published/indexed from May onwards were sourced by bimonthly automatic alerts created within each database, forwarded to the lead researcher's email (T. M.). No further studies were identified.

Database	Quality of Life	Cerebral Palsy
PubMed (2, 115 studies)	"Quality of life"[mh] OR Quality of life[tw] OR Life quality[tw] OR QOL[tw] OR Quality of work life[tw] OR International classification of functioning, disability and health[tw] OR ICF[tw]	"Cerebral palsy" [mh] OR Cerebral pals*[tw] OR Neurodevelopmental disorder*[tw] OR Neurodevelopmentally disabled[tw] OR Physically disabled[tw] OR Physical disabilit*[tw]
PsycINFO (491 studies)	exp quality of life OR Quality of life.tw OR Life quality.tw OR Quality of work life.tw OR QOL.tw OR International classification of functioning, disability and health.tw OR ICF.tw	Cerebral palsy.sh OR Cerebral pals*.tw OR Neurodevelopmental disorder.sh OR Neurodevelopmental disorder.tw OR Neurodevelopmentally disabled.tw OR Physically disabled.tw OR Physical disabilit*.tw
Scopus (5, 502 studies)	"Quality of life" OR "Life quality" OR QOL OR "Quality of work life" OR "International classification of functioning, disability and health" OR ICF	"Cerebral pals*" OR "Neurodevelopmental disorder*" OR "Neurodevelopmentally disabled" OR "Physical disabilit*" OR "Physically disabled"
Embase (3, 578 studies)	'Quality of life'/de OR 'Quality of life':ti,ab OR 'Life quality':ti,ab OR 'Quality of work life':ti,ab OR QOL:ti,ab OR 'International classification of functioning, disability and health':ti,ab OR ICF:ti,ab	'Cerebral palsy'/de OR 'Cerebral pals*':ti,ab OR 'Neurodevelopmental disorder*':ti,ab OR 'Neurodevelopmentally disabled':ti,ab OR 'Physical disabilit*':ti,ab OR 'Physically disabled':ti,ab
Web of Science (2, 968 studies)	"quality of life" OR "life quality" OR "QOL" OR "quality of work life" OR "international classification of functioning, disability and health" OR "ICF"	"Cerebral pals*" OR "Neurodevelopmental disorder*" OR "Neurodevelopmentally disabled" OR "Physical disabilit*" OR "Physically disabled"

Appendix B

Table B2. Study characteristics of all studies included in meta-analytic review

Lead author	Country	Sample size		Age (SD)		QOL Measure	Recruitment	
		CP	Control	CP	Control		CP	Control
Bjornson (2008)	America	81	30	11.8 (1.3)	11.9 (1.2)	CHQ-CF87	Children's hospital/medical centre	Postal mailing
Calley (2011)	Australia	21	21	7.10 (1.11)	7.11 (1.10)	CP-QOL	Children's hospital	Convenience sample
Dickinson (2007)	Seven European countries	818	3219	N/A	N/A	KIDSCREEN	Population based registers	General population
Du (2007)	China	72	72	.56 (.12)	N/A	PedsQL	Government special child care centres	Mainstream preschools
Janssen (2010)	Netherlands	91	1054	11	N/A	TACQOL-PF, TACQOL-CF	Rehabilitation centres, special schools, outpatient clinics	Reference population
Maher	Australia	71	1159	N/A	N/A	PedsQL	Novita- community based therapy	Reference population
McCullough (2010)	Ireland	184	5414	10.8 (3.5)	11.58 (3.52)	CHQ-PF	Population based register (NICPR)	Normative sample
Russo (2008)	Australia	86	21	9.4 (3.7)	7.2	PedsQL	SA CP register	Emailing, advertisement, newsletter
Tan (2014)	Netherlands	224	2347	N/A	N/A	TACQOL-CF, TACQOL-PF	Rehabilitation centres	Reference population
Tuzun (2004)	Turkey	45	64	7.4 (2.3)	8.1 (2.1)	CHQ-PF50	Outpatient clinic	Community
Varni (2005)	America	148	12010	10 (3.9)	9.10 (3.2)	PedsQL	Children's hospital/therapy clinics	Reference population
Vinson (2010)	America	41	60	8.76 (1.81)	8.9 (1.7)	SEIQoL	N/A	N/A
Vles (2015)	Netherlands	80	22295	13.4 (2.98)	N/A	KIDSCREEN	Outpatient clinic	Reference population
Wake (2003)	Australia	80	5414	11.4 (3.6)	11.58 (3.52)	CHQ-PF50	Outpatient clinic	Normative sample

Appendix C

QualSyst evaluation for each study

Table C3. Evaluation of included studies using the *QualSyst* checklist

Lead author (date)	1: Question/objective sufficiently described	2: Study design evident and appropriate	3: Subject/comparison group selection or source of information/input variables described/appropriate	4: Subject (and comparison group, if applicable) characteristics sufficiently described	8: Outcome(s) well defined and robust to measurement/misclassification bias. Means of assessment reported.	9: Sample size appropriate	10: Analytic methods described/justified/ appropriate	11: Some estimate of variance reported	12: Controlled for confounding	13: Results reported in sufficient detail	14: Conclusions supported by results	Total (0-22)	Total (%)
Bjornson (2008)	●	●	●	●	◗	●	●	●	●	●	●	21	95%
Calley (2011)	●	●	●	●	●	●	●	●	●	●	●	22	100%
Dickinson (2007)	●	●	●	●	○	●	●	●	●	●	●	20	91%
Du (2007)	●	●	●	●	●	●	●	◗	●	●	●	21	95%
Janssen (2010)	●	●	◗	●	●	●	●	●	●	●	●	21	95%
Maher (2008)	●	◗	◗	●	●	◗	●	●	●	●	●	19	86%
McCullough (2010)	●	●	●	●	●	●	●	●	◗	●	●	21	95%
Russo (2008)	●	●	●	●	●	◗	●	●	●	◗	●	20	91%
Tan (2014)	●	●	●	●	●	●	◗	●	●	●	●	21	95%
Tuzun (2004)	●	●	●	●	●	◗	●	●	●	●	◗	20	91%
Varni (2005)	●	◗	●	◗	●	●	◗	◗	◗	●	●	17	77%
Vinson (2010)	●	●	●	●	●	◗	◗	●	●	●	●	20	91%
Vles (2015)	●	●	◗	●	◗	●	●	●	○	◗	●	17	77%
Wake (2003)	●	●	●	●	●	●	●	◗	◗	●	●	20	91%