Cost-effectiveness of an Intensive Upper Limb Rehabilitation Therapy for Children With Unilateral Cerebral Palsy: an Economic Evaluation of a Randomized Controlled Trial

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Research Article

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Abstract

Background

Unilateral cerebral palsy (UCP) is a major cause of childhood disability and a substantial economic burden. Intensive group-based therapy of either hybrid constraint-induced movement therapy (mCIMT) or bimanual therapy has been shown to be effective in improving specific domains of the Quality of Life (QoL) in children with this disability. However, there is a paucity of economic evaluation on its role as an adjunct to other therapies currently in use. This study aimed to address this paucity by evaluating whether an intensive group-based therapy model is cost-effective compared to individualized distributed standard care occupational therapy (SC).

Methods

An open-label parallel randomized controlled trial (RCT) and an embedded economic evaluation of intensive group-based hybrid-CIMT (combined mCIMT and bimanual therapy) were conducted. A total of 47 children were randomized to the hybrid-CIMT group (n=27) or the SC (n=20) group. Effectiveness was assessed using the Cerebral Palsy Quality of Life (Child) questionnaire across seven domains: 1) Social well-being and acceptance; 2) Functioning; 3) Participation and physical health; 4) Emotional well-being; 5) Access to services; 6) Pain; and 7) Impact of disability and family health. Using trial data, costs in Australian dollars (AUD) were assessed from a societal perspective. Non-parametric bootstrap analysis was used to quantify uncertainty intervals (UIs; around point estimates) accompanying incremental cost-effectiveness ratio estimates, the cost per unit of beneficial change in the quality of life.

Results

Only for the domains of Pain (Incremental cost-effectiveness ratio: $273; 95% Uncertainty interval: $107 - $945) and to a lesser extent, Access to services ($1732; -$6448 - $8775) and the Impact of disability and family health ($1071; -$5718 - $4606), was hybrid-CIMT therapy found to be cost-effective when compared to SC. The probability that hybrid-CIMT was cost-effective for the Pain domain was estimated to be 0.50.

Conclusions

Hybrid-CIMT was not found to be cost-effective when compared to SC over a 13-week time horizon. In order to assess benefits and costs more fully, we recommend that future research utilize time horizons that extend sufficiently into the future. Irrespective of study duration, therapy comparisons should also consider acceptance, equity and feasibility.

Trial registration

ACTRN12609000912280. 21/10/2009, https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12609000912280

Background

Cerebral palsy (CP) is a neurological condition caused by a lesion of the immature brain, leading to movement and posture disorders. It is the leading cause of childhood disability, with an estimated incidence rate ranging from 1.5 to 3.0 per 1000 live births [1–4]. Unilateral cerebral palsy (UCP), is the most common type of CP in children born preterm, with an incidence of 1 in 1300 live births [5, 6]. Among children with UCP, there are impairments in muscle tone, strength, sensation, and coordination of the impaired extremity that compromise unimanual and bimanual functionality. As a result, children with UCP have functional difficulties with grasping, reaching, releasing, and manipulating objects with the impaired upper limb [7, 8]. All of which contributes to reduced self-care, school and household activities [9]. Therapy to address and improve upper limb activity is paramount in improving quality of life (QoL) among children with UCP, as it relates to a person's individual perception of feelings of well-being across a number of domains, such as physical, social, and emotional [10].

A range of targeted upper limb therapy approaches has been developed for children with UCP over the last decade, based on principles of motor learning. In their meta-analysis of non-surgical upper limb therapies for children with UCP, Sakzewski et al. reported moderate to strong evidence supporting intensive models of modified constraint-induced movement therapy (mCIMT), bimanual therapy, or hybrid-CIMT combining both approaches to improve upper limb motor outcomes [9]. These intensive models contrast with traditionally delivered individualised and distributed standard occupational therapy (SC). While little evidence supports this traditional approach, the use of goal directed home programs may offer the opportunity to increase the dose of therapy leading to improved upper limb motor outcomes 11–13].

The health care system is very much impacted by therapy interventions for UCP, due to their costings. Treatments to increase QoL for the individual can, therefore, can add increase the burden to society by way of higher healthcare costs, therapy charges and professional cooperation and consultation. It has been estimated that the medical costs for children with CP to be ten-fold lifetime costs for children without CP [14].

As a result, there is a need to conduct economic evaluations of existing therapies compared to new intensive models (hybrid-CIMT) such that optimum benefit can be achieved from the available resources. Economic evaluations should take a societal perspective so that all relevant costs and effects contribute to the evaluation, regardless of who pays the costs or receives the benefits [15, 16, 17]. New or additional therapies should be effective and cost-effective [18].

While many studies have investigated relative comparative therapy effectiveness [9] few have utilized QoL as an outcome of interest [19], and none has incorporated a full economic evaluation. To address this paucity of evidence, an economic evaluation was conducted alongside a randomized controlled trial with the objective of comparing the cost-effectiveness of a hybrid model of rehabilitation to a model of SC.

Methods

Participants

Children with UCP were recruited from across Queensland, Australia from January 2012 to June 2013.7 Potential study participants were identified through a population-based research database of more than 1300 children with CP at the Queensland Cerebral Palsy and Rehabilitation Research Centre, the Queensland Paediatric Rehabilitation Service and the Cerebral Palsy Register. The recruitment process targeted both publicly funded services and private practitioners with the expectation that the sample would be representative of children with UCP.

Children were eligible to be included if they: 1) had a confirmed diagnosis of UCP; and 2) had reduced upper limb function due to predominant spasticity rather than dystonia; and 3) were aged 5 to 16 years; and 4) had sufficient co-operation and cognitive understanding to participate in the therapy activities. Children were ineligible if they: 1) had fixed contracture or severe muscle spasticity in the designated muscle groups; or 2) had previously undergone upper limb surgery; or 3) had received intramuscular Botulinum toxin A injections within six weeks before baseline assessments.

Full ethical approval for the study [20] was obtained from the Medical Ethics Committee of The University of Queensland (2011000553), The Royal Children's Hospital Brisbane (HREC/11/QRCH/37) and The Cerebral Palsy League Ethics Committee (CPL-2012-004). Trial registration was obtained with the Australian and New Zealand Clinical Trials Registry (ACTRN12609000912280). Before entering the trial, informed, written consent was obtained from all parents or guardians and assent from children (if 12 years of age or older). Full details of the study methods are reported in the published study protocol [20]. No subgroup analyses were predefined in the trial protocol.

Design

The present economic evaluation was embedded in an open-label parallel randomized controlled trial which compared the effectiveness of an intensive block group model of upper limb therapy delivered using a day camp model (hybrid-CIMT) [20] to an equal dose of a distributed model of individualized occupational therapy provided in the community (SC). The economic evaluation was performed from a societal perspective over a 13-week time horizon which was consistent with the trial period, including all costs (direct or indirect) and effects of each therapy. Due to a short follow-up period, no discount rate was applied to costs or effect measures.

Following baseline assessments, children were randomized within matched pairs to either hybrid-CIMT or standard occupational therapy care (SC). To maximize the homogeneity of the sample and minimize group differences at baseline, children were matched according to age (12-month bands), sex, and Manual Ability Classification System (MACS) level I-II [21–22]. The MACS is a simple five-level, ordinal grading system, created to classify the fine motor ability of children with CP in the range of 4–18 years, meeting international criteria. It describes what a child can do in their daily life, e.g., grasp and handle

objects using their hands (performance), and not what children can do at their best (capacity). The MACS is recognized as having high psychometric properties [23].

Therapy allocation was recorded on folded paper inside a concealed envelope. The randomization process was then achieved by allocating a number “1” or “2” to each member of the pair and the envelope was opened by non-study personnel. Study personnel was informed of group allocation.

Sample size

An appropriate sample size determination for this study was based on having sufficient power to compare the functional effects of hybrid-CIMT and SC therapies at 13 weeks. Based on data from a previous study [24], a mean difference of 7 units (10% of the control group mean at baseline on the Melbourne Assessment of Unilateral Upper Limb Function (MUUL) was postulated as the minimum difference likely to have clinical implications. We assumed a standard deviation of 30. With an alpha of 0.05 and a power of 0.80, it was calculated that a sample size of 25 subjects in each group (n = 50) was required.

Intervention and standard care

Participants received either hybrid-CIMT or a SC rehabilitation approach. While both groups received a dosage of 45 hours upper limb training, they differed by 1) delivery method (group versus individualized); 2) intensity (high intensity over 2 weeks versus low intensity over 12 weeks); and 3) environment (community-based camp versus community centre/rehabilitation unit or home).

For the hybrid-CIMT group, participation was by attendance at one of two camps. The first camp was held in January 2012, while the second camp was held in mid-2012. Therapy consisted of intensive direct upper limb training spread over two weeks using a novel circus theme to enhance children’s motivation for engagement and participation. Children in this group attended a community facility, ‘Flipside Circus’ in Brisbane, Australia, for six hours a day coordinated by a team consisting of occupational therapists and physiotherapists. In the first week, the intense tasks were given to the children to utilize their impaired arm through the constraint of their unimpaired arm with an individually made glove. The glove was constructed from breathable fabric with a volar plastic insert to prevent grasp and was removed for no more than 15 minutes per day. In the second week, the glove was removed, and adopting the strategy used by Gordon et al. [25], encouraged the use of both hands to implement bimanual tasks. All tasks were analyzed and selected to target specific movement components required for goal achievement and were novel, fun and motivating, and fostered self-generating voluntary repetition of bimanual tasks.

Children in the SC group received individualized occupational therapy (focused on improving upper limb function) of equal dosage to those in the hybrid-CIMT group. This dosage consisted of six weekly sessions of 1.5 hours of individual direct therapy in a hospital or community setting combined with other therapy in their own homes. As part of the latter component, families were provided with a 36-hour home program to practice goal areas from the commencement of the individual therapy sessions (30 minutes daily for six days/week for 12 weeks).

Cost measures

The economic evaluation aimed to determine and compare the total costs associated with either hybrid-CIMT or SC and relate these costs to effects. Firstly, relevant categories of resource utilization were identified; they being: 1) Direct medical costs; 2) Direct non-medical costs; and 3) Indirect costs Secondly, the volume of each category for each child was measured, and resource costs measured these volumes. Direct medical costs consisted of 1) Healthcare staff salaries; and 2) Flipside Circus registration fees; the latter being particular to the hybrid-CIMT group. Direct non-medical costs consisted of 1) Flipside Circus consumables (e.g. restraint gloves); and 2) Accommodation and Travel costs. The latter relates to the reimbursement of costs incurred by families of children participating in the trial. Indirect costs consisted of 1) Flipside Circus catering, and 2) Productivity costs; the latter being costs associated with primary caregivers' days off work. Self-reported data on primary caregivers' missed employment days were prospectively collected throughout the trial via phone calls. Productivity costs were then retrospectively assigned to any missed employment days by applying Australian median earnings data stratified by age, sex and level of highest educational qualification [26]. An estimate of the monthly productivity cost per participant was derived based on participants' last contact date. While all costs emanating from SC were individualized, costs that occurred from hybrid-CIMT consisted of both individual and aggregate data. All costs were valued in 2020 Australian dollars (AUD).

Effectiveness measures

The primary caregiver completed the Cerebral Palsy Quality of Life Child Questionnaire (CPQoL-Child) to assess the child's QoL from parents' perspectives [24]. The questionnaire contains 66 items across seven domains: 1) Access to services, 2) Emotional well-being, 3) Family health, 4) Feelings about functioning, 5) Participation and physical health, 6) Pain and impact of disability, and 7) Social well-being and acceptance. Access to services refers to access *to* community *services* or facilities, such as service provisions or accessibility, that support parents and children with CP. Emotional well-being refers to being happy, enjoying/being satisfied with achievements, and having a good emotional state. Family health refers to parents and primary caregivers' physical and emotional well-being and includes parental happiness. Feelings about functioning refer to communicating with other people in the family and community and performing daily living activities such as feeding, dressing, and toileting. Participation and physical health refer to involvement in school activities, sports and community activities; the possession of adequate motor skills; the capacity to use aids/equipment; and bodily health and wellness. Pain and impact of disability refer to physical pain or discomfort and pain related to therapy. Social well-being and acceptance refer to interactions with peers, family members and other people in the community. Social participation is a component of this domain and refers to social connectedness and relationships, the capacity for involvement in social activities, and social acceptance.

Each question on this form is worded in a way such as "How do you think your child feels about…" and requires an answer from 1 to 9 where 1 = Very unhappy, 3 = Unhappy, 5 = Neither happy nor unhappy, 7 = Happy, and 9 = Very happy. The scoring procedure included two steps. First, raw scores for each item were

transformed to a scale with a possible range of 0–100 points. Afterwards, the domain scores were calculated by averaging the scores of all items. Except for the domain of Pain, higher scores indicate better QoL. The CPQoL-Child has excellent psychometric properties [27] and high test–retest reliability ranging from 0.76 to 0.89 across all seven domains [28]. Furthermore, as QoL is defined as 'well-being across broad domains', scores are reported by domain rather than an aggregated score [29].

Statistical analysis

The analyses reported here were all planned *a priori*. There were no interim analyses or stopping rules. The primary analysis was intention-to-treat, with children analyzed in their randomized group, irrespective of whether they completed the trial. We used multiple imputation with chained equations (MICE) approach to compensate for data missingness to create ten imputed data sets and combined these results with Rubin's rules [30]. As multiple imputation has consistently been shown to be a valid approach in handing missing data, only estimates obtained by multiple imputation are reported [31]. All imputed data were assumed missing at random. Baseline characteristics of participants are reported as counts (percentages) and compared by use of Fisher's exact test. Due to non-normality, therapy costs per child are reported as medians (interquartile ranges (IQRs)) and compared using the Mann-Whitney U test. A difference-in-difference analysis was used to test the change in each CPQoL-Child domain within the hybrid-CIMT group, by accounting for any trend not attributable to the intervention by controlling for the measured change in the SC group. These changes between baseline and 13-week follow-up were assessed using the paired t-test with Satterthwaite's correction for unequal variances.

To assess hybrid-CIMIT cost-effectiveness, incremental cost-effectiveness ratios (ICERs) were calculated. ICERs were calculated for each CPQoL-Child domain by dividing the difference in the mean costs (between the two therapies) by the differences in the mean domain scores. Excepting the Pain domain, domain ICERs were interpreted as the incremental cost per unit of additional domain score [32]. For Pain, it is the converse, as a lower QoL score indicates less pain. The non-parametric bootstrap resampling method with 10,000 iterations was used to quantify uncertainty in estimating differences between COMBiT and SC groups for mean costs, mean effects, and ICERs by way of 95% uncertainty intervals (UIs).. Cost-effectiveness acceptability curves were produced to determine the relative likelihood that hybrid-CIMIT was cost-effective at varying willingness to pay thresholds.

All tests of significance were two-sided, and a P-value of less than 0.05 was considered significant. Analyses were conducted using version 17.0 of the STATA software package (StataCorp, College Station, Texas).

Results

Participants

One hundred and sixty-seven children were assessed for eligibility, and 114 (68%) were excluded, either due to refusal (n = 53; 32%), being not contactable (n = 44; 26%) or not satisfying eligibility criteria (n = 17;

10%), as shown in Fig. 1. A total of 53 children were randomized to either the hybrid-CIMT group (n = 28) or the SC group (n = 25). Our final sample consisted of 47 children; 27 in the hybrid-CIMT group and 20 in the SC group. This was due to the caregivers of six children withdrawing consent, after allocation but before receiving a therapy. No serious adverse events were recorded during the trial.

Socio-demographic characteristics of the children allocated to each group are reported in Table 1. Complete data were obtained for the characteristics of age, Hemiplegia (left or right-sided), sex, and Statistics Socio-Economic Indexes for Areas (SEIFA), and UCP, while family income had three cases of missing data. Overall, participating children were more likely to be male (70%), have parents with combined annual family income less than $50,000 (80%), and come from low/middle SEIFA locations (81%). The sample prevalence of right-sided and left-sided UCP was comparable. No major differences in baseline characteristics between the two therapy groups were seen to exist.

Table 1
Baseline characteristics of children and their families by therapy group

	Total	Hybrid-CIMT	Standard Care
	N = 47	N = 27	N = 20
Characteristic	**n (%)**	**n (%)**	**n (%)**
Age (years)			
4–8	28 (60)	15 (57)	13 (65)
9–13	19 (40)	12 (44)	7 (35)
Family income[a]			
<$25000	22 (50)	11 (44)	11 (58)
$25000 - $49999	13 (30)	8 (32)	5 (26)
$ 50000 - $74999	8 (18)	5 (20)	3 (16)
≥$75000	1 (2)	1 (4)	0 (0)
SEIFA[b]			
Low	19 (40)	10 (37)	9 (45)
Medium	19 (40)	11 (41)	8 (40)
High	9 (19)	6 (22)	3 (15)
Sex			
Female	14 (30)	8 (30)	6 30)
Male	33 (70)	19 (70)	14 (70)
Unilateral Cerebral Palsy			
Left-sided	22 (47)	12 (44)	10 (50)
Right-sided	25 (53)	15 (56)	10 (50)

Hybrid-CIMT: Group-based therapy combining modified constraint induced movement therapy and bimanual therapy.

[a] Three missing values; [b] Socio-economic Index for Area.

Costs

Table 2 presents the median costs per child for administering hybrid-CIMT and SC therapies. The median cost per child was $5733 (IQR: $2344 - $7494) for those in the hybrid-CIMT group, while the median cost

per child was $2970 (IQR: $2970 – $3855) for those in the SC group. This difference was found to be statistically significant (p = 0.016). Of the three cost types, indirect costs were the most comparable across therapy groups, with a median cost per child being $2964 (IQR: $272 - $2964) and $2288 ($1615 - $2961) for hybrid-CIMT and SC, respectively. Whilst this comparison between therapies was found to be non-significant ($2,964 vs $2,288; p = 0.117), this was not the case for direct medical costs ($2,056 vs $690; p < 0.001) or direct non-medical costs ($713 vs $0; p = 0.002). With the exception of direct medical costs, there is a relatively large amount of uncertainty in these results as indicated by the wide interquartile ranges for accommodation & travel and productivity cost.

Table 2
Comparison of costs between Hybrid-CIMT and Standard Care groups costs.

	Therapy Costs (AUD)				
Costs	**Hybrid-CIMT**		**SC**		
	N = 27		**N = 20**		
	Median	**IQR**	**Median**	**IQR**	**P-value[b]**
Direct medical costs					
Flipside Camp registration	425	425–425	0	0–0	n.a.
Healthcare staff salaries	1631	1631–1631	690	392–761	< 0.001
Sub-total	2056	2056–2056	690	392–761	< 0.001
Direct non-medical costs					
Accommodation & Travel	697	0–2458	0	0–534	0.078
Flipside Camp consumables	16	16–16	0	0–0	n.a.
Sub-total	713	16–2474	0	0–534	0.002
Indirect costs					
Flipside Camp catering	272	272–272	0	0–0	n.a.
Productivity cost	2692	0–2692	2288	1615–2961	0.025
Sub-total	2964	272–2964	2288	1615–2961	0.117
Total cost	5733	2344–7494	2970	2376– 3855	0.016

AUD: Australian dollars (2020); Hybrid-CIMT: Group-based therapy combining modified constraint induced movement therapy and bimanual therapy; IQR: Interquartile range; n.a.: Not applicable; SC: Standard Care therapy.

[a] Mann-Whitney U for difference in change scores between therapy groups.

Effectiveness

With the inclusion of imputed data, scores for the seven CPQoL-Child primary domains are presented in Table 3 for both groups, at baseline and 13-week follow-up. Besides Emotional well-being, QoL scores improved across all domains within the hybrid-CIMT group, with the largest improvement being for Participation and physical health (Baseline: 70.94 vs Follow-up: 66.33). Similarly, the largest improvement within the SC group was also seen on the same domain (Baseline: 71.48; Follow-up: 71.48). The difference-in-difference estimate for Pain was the only intervention effect that was statistically significant ($p = 0.024$) when adjusted for change within the SC group, with scores improving by 0.31 units in the hybrid-CIMT group and worsening by 8.81 units in the SC group.

Table 3
Difference-in-difference analyses between hybrid-CIMT and Standard Care groups for intervention effect during 13-week follow-up.

	Therapy						
CPQoL-Child Domain	**Hybrid-CIMT N = 27**			**SC N = 20**			
	Baseline Mean (SD)	**Follow-up Mean (SD)**	**Change Mean[a] (SD)**	**Baseline Mean (SD)**	**Follow-up Mean (SD)**	**Mean Change[b] (SD)**	**Difference-in-difference P-value[c]**
1.Functioning	68.71 (10.03)	70.49 (12.51)	1.78 (9.45)	74.95 (14.09)	78.29 (11.12)	3.34 (14.74)	0.681
2.Participation and physical heath	66.33 (14.57)	70.94 (11.59)	4.61 (13.64)	71.48 (15.49)	79.04 (10.13)	7.56 (14.32)	0.481
3.Access to services	63.40 (18.37)	65.06 (14.45)	1.66 (14.48)	64.70 (15.01)	64.95 (18.73)	0.25 (19.58)	0.789
4.Emotional well-being	79.63 (11.18)	79.52 (11.21)	-0.11 (10.71)	83.44 (15.09)	85.96 (9.23)	2.52 (14.72)	0.503
5.Impact of disability and family health	65.97 (17.54)	66.28 (16.74)	0.31 (11.45)	76.41 (15.56)	74.36 (10.54)	-2.05 (12.54)	0.513
6.Pain[d]	27.72 (16.05)	27.41 (17.45)	-0.31 (16.09)	27.05 (16.34)	35.86 (12.56)	8.81 (10.63)	0.024
7.Social well-being and acceptance	79.16 (11.43)	81.10 (10.73)	1.94 (12.20)	83.42 (11.01)	86.99 (8.70)	3.56 (11.51)	0.643

CPQoL-Child: Cerebral Palsy Quality of Life Child Questionnaire; CI: Confidence interval; Hybrid-CIMT: Combined bimanual training and modified constraint induced

movement therapies; SC: Standard Care therapy; SD: Standard deviation.

[a] The mean change in quality of life scores under hybrid-CIMT therapy between baseline and follow-up.

[b] The mean change in quality of life scores under Standard Care therapy between baseline and follow-up.

[c] Paired t-test for difference in change scores between therapy groups.

[d] Unlike other CPQoL-Child Domains, higher scores on Pain indicates a reduction in quality of life, while lower scores indicate an improvement in quality of life.

Cost-effectiveness

Point and interval estimates of domain ICERs are reported in Table 4. For all domains, the incremental cost was $2527 per child. For four domains, they being Emotional well-being, Functioning, Participation and physical health and Social well-being and acceptance, hybrid-CIMT was dominated by SC, being less effective and more costly. Of the three remaining domains, a base-case analysis indicated hybrid-CIMT to be more cost-effective in reducing Pain than improvements relating to the Impact of disability and family health or Access to services. For the domain of Pain, the cost to reduce Pain by one QoL unit was estimated to be $273 (95% Uncertainty Interval: $107 - $945).

Table 4
Incremental cost-effectiveness for an additional unit of quality of life gained during 13-week follow-up.

CPQoL-Child Domain	Incremental cost per child (AUD)		Incremental effect per child		ICER (AUD)
	Mean	UI	Mean	UI	Mean (UI)[a]
1. Access to services	2528	1373–3638	1.46	-8.43–11.90	1732 (-6448–8775)
2. Emotional well-being	2527	1325–3729	-2.63	-10.18–4.25	Dominated
3. Functioning	2527	1325–3729	-1.56	-8.91–5.30	Dominated
4. Impact of disability and family health	2527	1325–3729	2.36	-1.99–11.20	1071 (-5718–4606)
5. Pain[b]	2527	1325–3729	-9.24[b]	-16.72 – -2.14	273 (107 – 945)[c]
6. Participation and physical health	2527	1325–3729	-2.95	-10.89–4.75	Dominated
7. Social well-being and acceptance	2527	1325–3729	-1.62	-8.12–4.88	Dominated

AUD: Australian dollars; ICER: Incremental cost-effectiveness ratio; UI: 95% uncertainty interval.

[a] UI obtained from 10,000 non-parametric bootstrapping iterations.

[b] unlike other CPQoL - Child Domains, higher scores on Pain indicates a reduction in quality of life.

[c] ICER estimate indicates the cost of adverting or reducing Pain score by one unit on 0–100 QoL scale.

In cases where the hybrid-CIMT intervention resulted in higher costs and higher QoL scores than SC, cost-effectiveness can be assessed based on a decision maker's willingness to pay (WTP) for a beneficial change of one QoL unit. If this cost falls below the WTP value, then the intervention can be considered cost-effective. For each of the three domains in which SC did not dominate hybrid-CIMT, the results of a probabilistic sensitivity analysis in the form of cost-effectiveness acceptability curve, whereby the likelihood of the program being cost-effective is plotted against varying levels of WTP, are shown in Fig. 2. For Pain, the probability of cost-effectiveness was greater than 0.50 when the WTP threshold of $370, whilst the equivalent thresholds for Access to services and Impact of disability and family health were $636 and $822, respectively.

Discussion

This study reports an economic evaluation of hybrid-CIMT compared to SC in improving the QoL in children with congenital UCP. Besides the domain Emotional well-being, QoL scores improved under hybrid-CIMT therapy. However, hybrid-CIMT was found to be substantially more costly than SC in the base-case analysis, driven by staffing salaries. Consequently, hybrid-CIMT, when compared to SC, was cost-effective only for Access to services, the Impact of disability and family health, and Pain, domains in which difference-in-difference analyses indicated greater QoL improvement among children in the hybrid-CIMT group. For all other domains, hybrid-CIMT was dominated by SC. This is consistent with findings reported in other studies comparing hybrid-CIMT with SC [33–36].

Our study has several strengths, not the least being its originality. To our knowledge, it is the first formal economic evaluation to compare an intensive group-based model of therapy embedded in a community leisure facility (hybrid-CIMT) with individualized SC in children with UCP from a societal perspective. An important strength of the current study was that it was conducted alongside a randomized controlled trial of the two therapies, comparing equal doses in a matched pairs design to minimize subject differences. The data is thus less prone to sources of bias and confounding than data generated by non-randomized study designs [37, 38]. A further strength is that this was a pragmatic study, thereby reflecting a situation close to clinical practice [39].

This study also presents some caveats that need to be discussed. First, no algorithm was available for aggregating domain QoL scores into a single index, as per the SF-36 or the Euroqol questionnaire (EQ-5D) [40]. Instead, using the WHO definition of QoL as 'broad domains of well-being', the CPQoL-Child questionnaire was developed to be condition-specific. Consequently, aggregating domain QoL scores were considered inappropriate [41], and therefore our cost-effectiveness analysis of hybrid-CIMT therapy is domain-specific. Secondly, it is also possible that the occurrence of QoL missingness at the 13-week follow-up could compromise our finding's validity [42]. However, the inference drawn from the non-reported complete-case analysis did not differ from the inference drawn from the results of our analysis using multiple imputation, suggesting the results are robust to the influence of missing data [43, 44]. Thirdly, caregiver productivity costs were based on primary caregiver data and did not extend to secondary caregivers or other family members who may have also required time off work due to caring

responsibilities. The cost assigned to missing caregiver employment days was based on national survey data, as individual-level data on earnings was not collected as part of the trial. These limitations may have resulted in underestimating the total costs incurred by patients within both groups.

Whilst the use of self-report is the gold standard of QoL assessment [45], hybrid-CIMT may have a broader set of benefits than can be represented in a single QoL domain measure, including non-health outcomes such as patient and family experience and satisfaction with care, as well as provider satisfaction [46]. These potential benefits of the hybrid-CIMT model were not captured in this study.

Implications and recommendations for future research

The lack of notable benefit in terms of QoL from hybrid-CIMT drives the main conclusion of this analysis. Only for the domain of Pain, reported to be experienced by three in four children with CP [47], did hybrid-CIMT appear to be substantially more cost-effective than SC. As such, this economic evaluation does not support the use of hybrid-CIMT in place of SC as appropriate use of resources. Intensive group-based models of therapy hybrid-CIMT may be a cost-effective therapy option under varying circumstances that differ from this study, one possibility being a longer follow-up period.

Our results are limited to a certain extent by our inability to interpret cost-effectiveness associated with changes on a generic QoL scale. While we agree that condition-specific QoL measures are developed across broad domains of well-being based on the WHO definition of QoL, cost-utility outcomes may need to be considered in future economic analyses. As participants needed to be aged between 5 and 16 years of age, generalisability to children aged 4 years or younger was not possible. Also, it is recommended future research incorporates ‘willingness to pay’ measures in their analyses to ascertain what stakeholders are prepared to fund. This is highly relevant given current international funding priorities for disability schemes such as Australia’s National Disability Insurance Scheme (NDIS) [48, 49]. Ongoing research should examine the long term effectiveness of hybrid-CIMT and strategies to improve the cost-effectiveness of hybrid-CIMT.

Conclusions

This economic evaluation found that an intensive group model delivered in a community leisure facility such as hybrid-CIMT compared to an individualized distributed model such as SC is not a cost-effective option for children with UCP. The results of this study should be used to improve the quality of care for children with this UCP. Nevertheless, it also needs to be realized that decisions relating to health service delivery are not based solely on cost-effectiveness analysis, and any final recommendation for or against intensive group delivered models will also be influenced by issues such as acceptance, equity, and feasibility [16, 32].

Abbreviations

CIMT: Constraint induced movement therapy

CP: Cerebral palsy

CPoL-Child: Cerebral Palsy Quality of Life Child Questionnaire

ICER: Incremental cost-effectiveness ratio

IQR: Interquartile range

MACS: Manual Ability Classification System

mCIMT: Modified constraint induced movement therapy

NDIS: National Disability Insurance Scheme

QoL: Quality of life

SC: Standard care

SEIFA: Statistics Socio-Economic Indexes for Areas

UC: Uncertainty interval

UCP: Unilateral cerebral palsy

WHO: World Health Organization

Declarations

Availability of data and materials

The datasets analysed during the current study are not publicly available as the authors do not have the authority to disseminate the data. To access the data please contact r.boyd@uq.edu.au.

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Contributions

HH and were involved in the conception of the study. MD drafted the first version of the manuscript. HH and MD read and approved the final manuscript.

Ethics declarations

Ethics approval and consent to participate

Ethics approval to conduct the study and experimental protocols was approved by Medical Ethics Committee of The University of Queensland (2011000553), The Royal Children's Hospital Brisbane (HREC/11/QRCH/37) and The Cerebral Palsy League Ethics Committee (CPL-2012-004). Consequently all methods utilised in the study were carried out in accordance with relevant guidelines and regulations. The participants in the study were provided written and verbal information about the study. They were also informed that their participation was voluntary. Written informed consent was obtained from parents and guardians of each study participant. All the requirements of the Helsinki Declaration were fulfilled.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

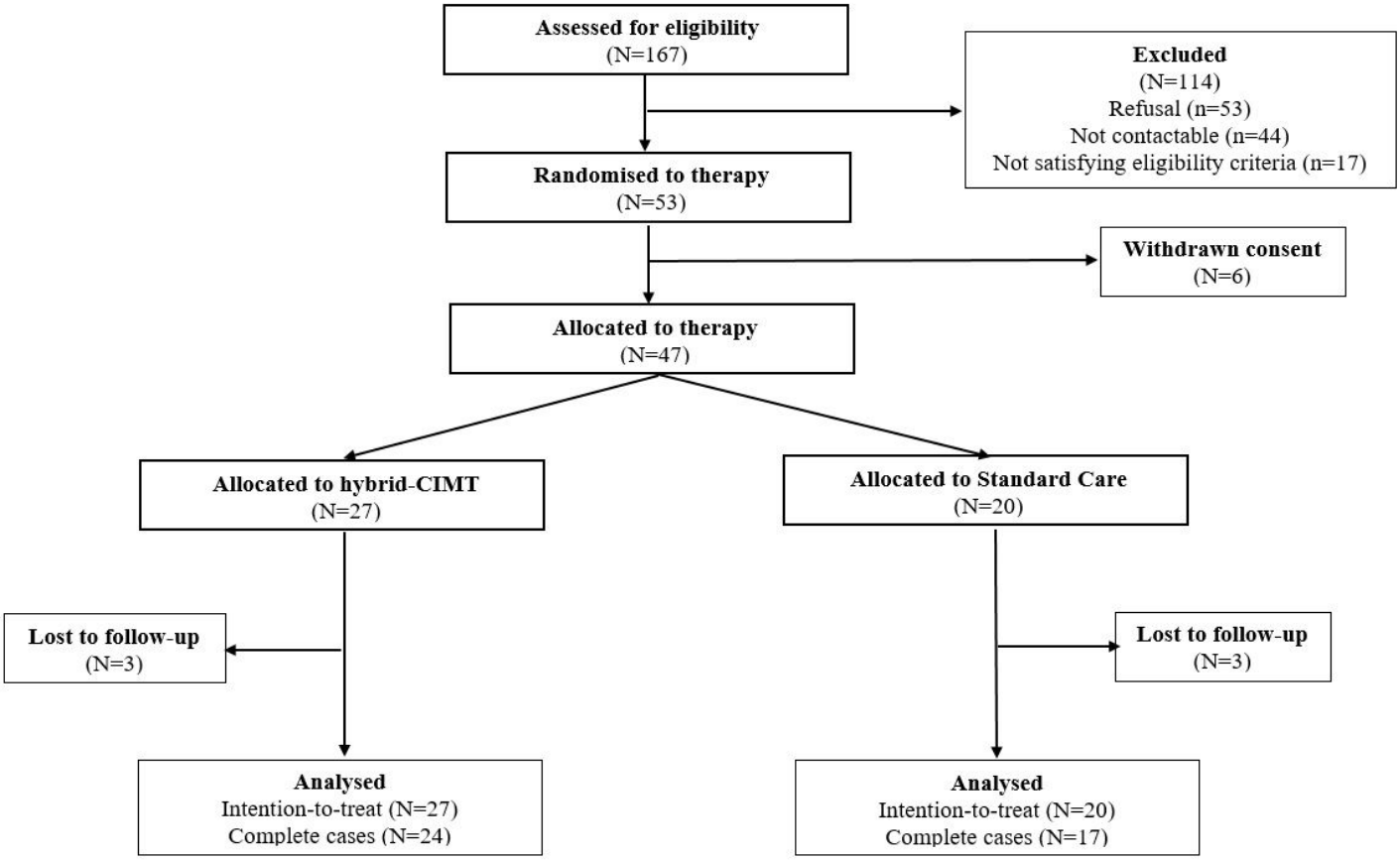

Figure 1

Participation flowchart for COMBiT study

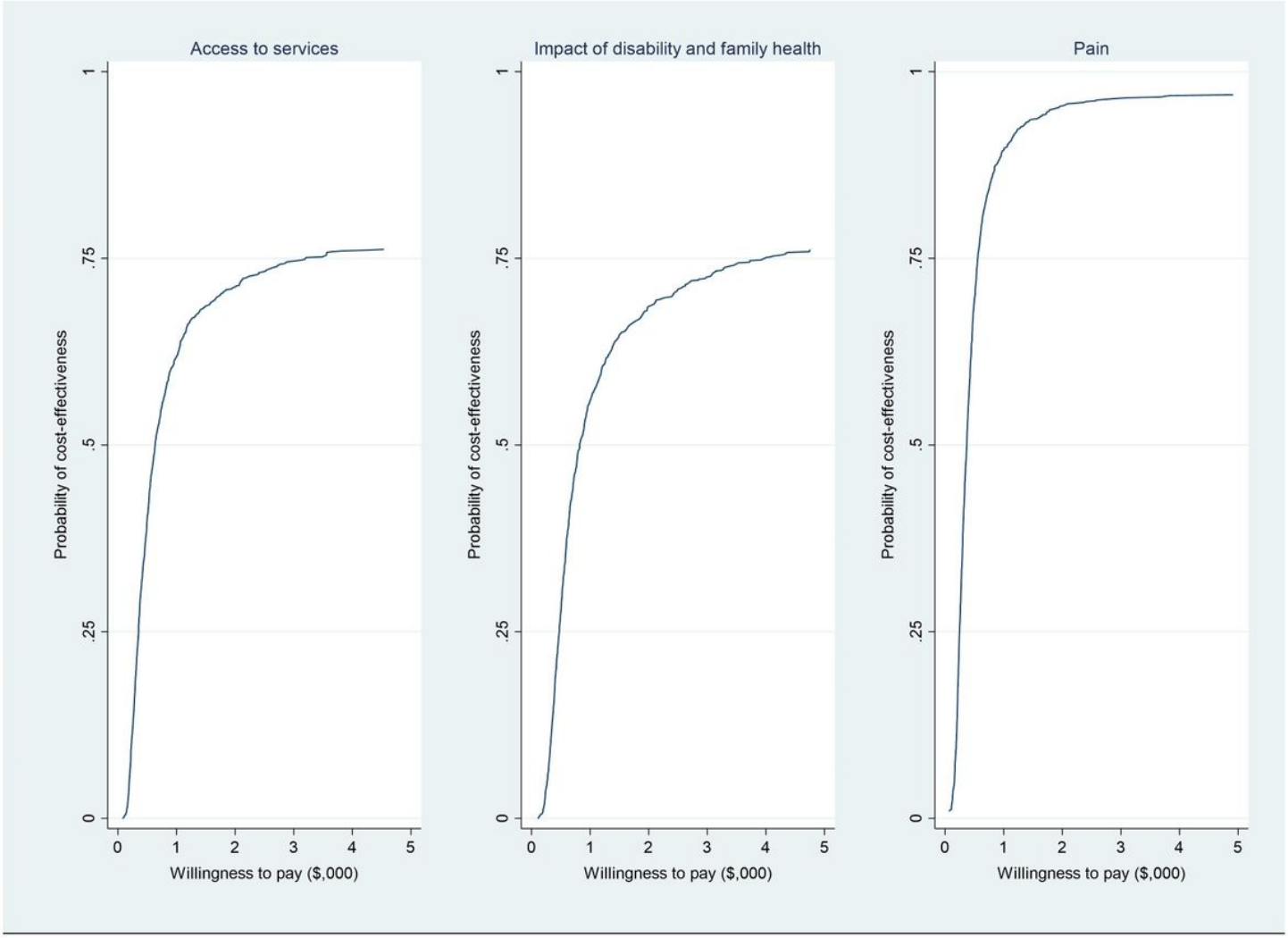

Figure 2

Cost-effectiveness acceptability curves for the CPQoL-Child domains of Access to services, Impact of disability and family health and Pain.