LIST OF PUBLICATIONS

1) **Keeratisiroj O**, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M. Prognostic predictors for ambulation in Thai children with cerebral palsy aged 2 to 18 years. J Child Neurol. 2015;30:1812-8.

2) **Keeratisiroj O**, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M., Pratoomsoot C. Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational study. Disabil Rehabil. 2016;1-9. [Epub ahead of print]

3) **Keeratisiroj O**, Thawinchai N, Buntragulpoontawee M, Siritaratiwat W, Derivation of an ambulatory score chart for Thai children with cerebral palsy aged 2–18. J Med Assoc Thai. 2016;99:1298-305.

Appendices

Appendix A

Philosophical context of
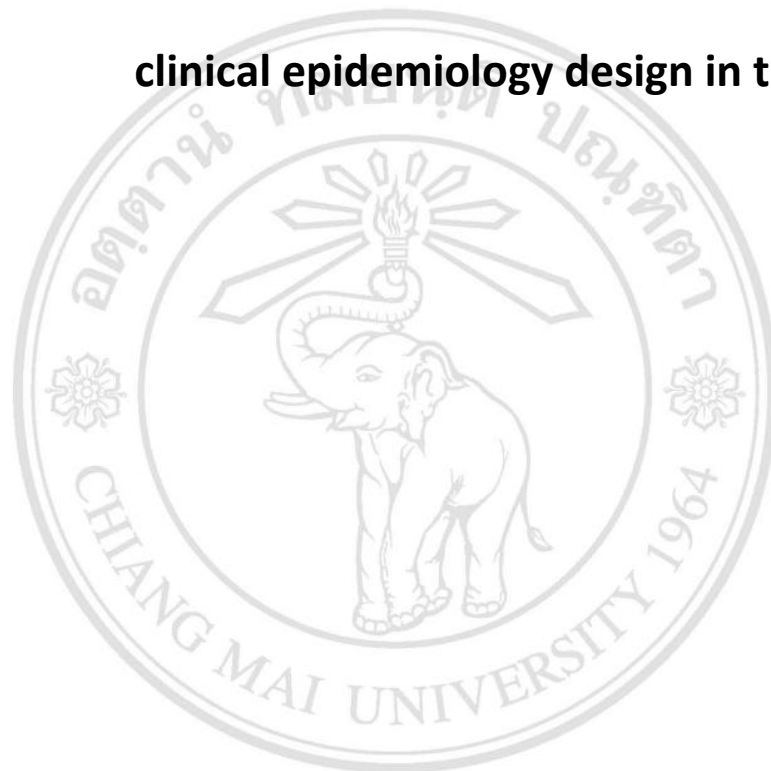
clinical epidemiology design in this thesis

Philosophical context of clinical epidemiology design in this thesis

1. Research questions included in this thesis

1. What are prognostic predictors for ambulation in Thai children with CP?

2. What are prognostic predictors that predict walking ability in children with CP when using a systematic review?

3. Is it possible to develop a prognostic scoring scheme for predicting ambulatory status in Thai children with CP from those prognostic predictors?

2. Research titles

<u>Study I</u>

Prognostic predictors for ambulation in Thai children with cerebral palsy aged 2 to 18 years

<u>Study II</u>

Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational study

<u>Study III</u>

Derivation of an ambulatory score chart for Thai children with cerebral palsy aged 2–18

3. Theoretical design

All three studies are clinical epidemiology research under prognostic both causal and prediction theoretical design predicting event from determinants. There are three main areas of prognostic research. Occurrence relation can be written as

Causal research

Outcome (y) $= f(x_1 + x_2 + x_3 \ldots x_n \mid$ confounders) or

Outcome (y) $= f($prognostic predictors x's $\mid$ confounders)

Example: Ambulatory status $= f($gender + antibiotics + hyperbilirubinemia + gestational age + birth weight + type of CP + epilepsy + gross motor skills + intellectual disability + visual impairment + hearing impairment + hand use + eating + speech $\mid$ age + surgical intervention)

Prediction research

Outcome (y)   =   f ($x_1 + x_2 + x_3 \dots x_n$) or

Outcome (y)   =   f (prognostic predictors x's)

Example: Ambulatory status =   f (age + gender + caregiver + BMI + antibiotics + hyperbilirubinemia + gestational age + birth weight + type of CP + epilepsy + gross motor skills + intellectual disability + visual impairment + hearing impairment + hand use + eating + speech)

3.1   Prognostic causal research

This type of research explains or evaluates prognostic characteristic from routine data. In this thesis, study I and study II are under this topic. There are two abilities that can be measured; prognostic causal research and systematic review of observational study. In study I, prognostic predictors for ambulation in Thai children with cerebral palsy were investigated from prognostic causal research.

Occurrence relation:

Pr (prognostic outcome) = f (prognostic predictors x's | confounders)

Pr (ambulatory status)   =   f (type of CP + sitting independently at age 2 years

+ eating independently | age + surgical intervention)

In study II, prognostic predictors for ambulation in Thai children with cerebral palsy were investigated from systematic review and meta-analysis for observational study (cross-sectional, case control, and cohort study) according to Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group.[1]

3.2   Prognostic prediction research (Clinical prediction rule)

A clinical prediction rule is a set of model with a combination of prognostic predictors that have statistically significance from study I. Study III in this thesis aimed to develop an ambulatory score chart for Thai children with cerebral palsy.

Occurrence relation:

Pr (prognostic outcome)   = f (prognostic predictors x's)

Pr (ambulatory status)   = f (age + type of cp + sitting independently at age 2

+ eating independently)

4. Data collection design

4.1 Study design

Two studies in this thesis are an extended retrospective cohort study. One study is systematic review and meta-analysis for observational study.

4.2 Data collection process

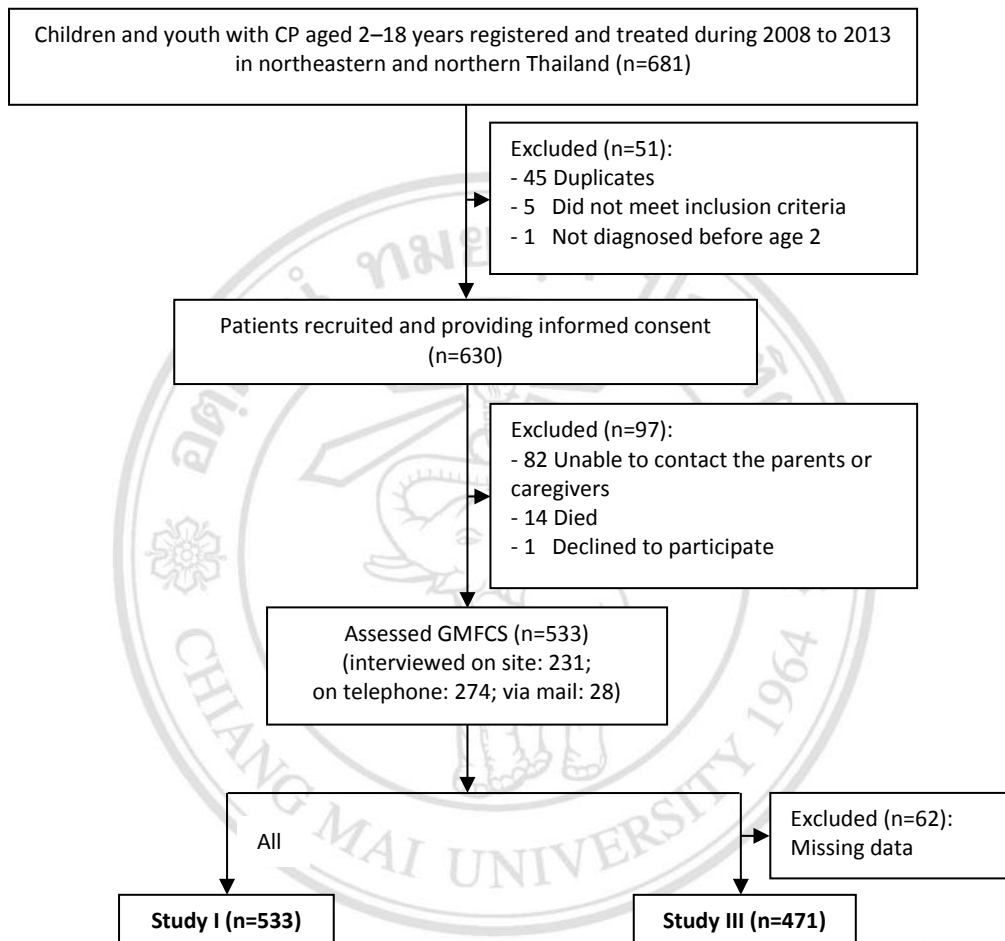**Study I and study III: Retrospective cohort study**

The medical and physical therapy records of children with CP were retrospectively reviewed from 2008 to 2013. They were registered and treated at six special schools or hospitals for children with physical disability in northeastern and northern Thailand. They were recruited if aged 2 to 18 and have been diagnosed by physicians or physiotherapists. The following were the reasons for the children to be excluded from the study: the children being duplicated between settings, not meeting the inclusion criteria, not being diagnosed during the early years of life (>2 years), unable to contact the parents or caregivers, death, and declining to participate.

Study II: Systematic review and meta-analysis for observational study

This study followed the meta-analysis of observational studies in epidemiology (MOOSE)[1] and preferred reporting items for systematic review and meta-analysis protocol (PRISMA-P) guidelines.[2] A systematic literature search was performed in PubMed, SCOPUS, CINAHL, ProQuest, Ovid, Wiley InterScience, and ScienceDirect databases. These databases were searched from their start dates to December 2015. A search strategy was developed and adapted for each database with a combination of free text and controlled vocabulary terms. This search employed the Medical Subject Headings (MeSH) "cerebral palsy", "predict*", and "ambula*", and explored these keywords with slight modifications based on the source.
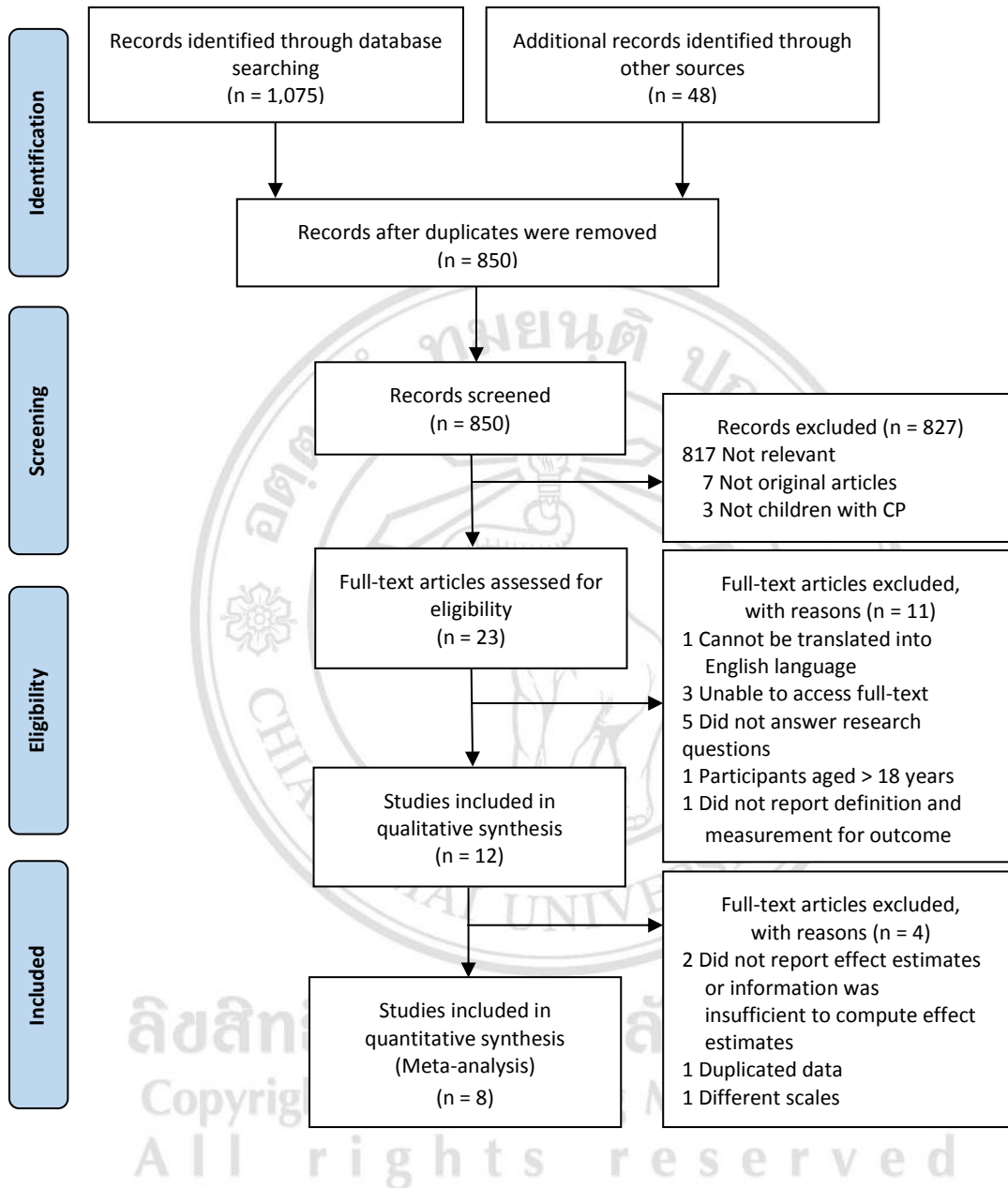
4.3 Study flow

Flow chart of retrospective cohort study

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┌─────────────────────────────────────────────────────────────────────┐
│ Children and youth with CP aged 2–18 years registered and treated     │
│ during 2008 to 2013 in northeastern and northern Thailand (n=681)     │
└─────────────────────────────────────────────────────────────────────┘
                            │
                            │        ┌──────────────────────────────────┐
                            ├───────►│ Excluded (n=51):                  │
                            │        │ - 45 Duplicates                   │
                            │        │ - 5  Did not meet inclusion       │
                            │        │      criteria                     │
                            │        │ - 1  Not diagnosed before age 2   │
                            │        └──────────────────────────────────┘
                            ▼
┌─────────────────────────────────────────────┐
│ Patients recruited and providing informed     │
│ consent (n=630)                               │
└─────────────────────────────────────────────┘
                            │
                            │        ┌──────────────────────────────────┐
                            ├───────►│ Excluded (n=97):                  │
                            │        │ - 82 Unable to contact the        │
                            │        │      parents or caregivers        │
                            │        │ - 14 Died                         │
                            │        │ - 1  Declined to participate      │
                            │        └──────────────────────────────────┘
                            ▼
┌─────────────────────────────────────────────┐
│ Assessed GMFCS (n=533)                        │
│ (interviewed on site: 231;                    │
│ on telephone: 274; via mail: 28)              │
└─────────────────────────────────────────────┘
                            │
          ┌─────────────────┴──────────────────┐
          │ All                                 │        ┌──────────────────────┐
          ▼                                     ▼───────►│ Excluded (n=62):      │
┌──────────────────────┐          ┌──────────────────────┐ Missing data         │
│ Study I (n=533)       │          │ Study III (n=471)     │                      │
└──────────────────────┘          └──────────────────────┘
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Flow chart of systematic review and meta-analysis for observational study

Identification	Records identified through database searching (n = 1,075) — Additional records identified through other sources (n = 48) → Records after duplicates were removed (n = 850)

```
Identification:
  Records identified through database          Additional records identified through
  searching (n = 1,075)                        other sources (n = 48)
                          ↓                ↓
              Records after duplicates were removed (n = 850)

Screening:
  Records screened (n = 850)  →  Records excluded (n = 827)
                                 817 Not relevant
                                   7 Not original articles
                                   3 Not children with CP

Eligibility:
  Full-text articles assessed for  →  Full-text articles excluded,
  eligibility (n = 23)                with reasons (n = 11)
                                      1 Cannot be translated into
                                        English language
                                      3 Unable to access full-text
                                      5 Did not answer research
                                        questions
                                      1 Participants aged > 18 years
                                      1 Did not report definition and
                                        measurement for outcome

  Studies included in  →  Full-text articles excluded,
  qualitative synthesis    with reasons (n = 4)
  (n = 12)                 2 Did not report effect estimates
                             or information was
                             insufficient to compute effect
                             estimates
                           1 Duplicated data
                           1 Different scales

Included:
  Studies included in
  quantitative synthesis
  (Meta-analysis)
  (n = 8)
```

5. Data analysis design

5.1 Prognostic causal research

Statistical analysis will be performed using STATA Statistical software Release 11.0 (Stata Corporation, College Station, TX) as follows:

1) Baseline Characteristics and clinical history data of participants were described by descriptive statistics: frequencies, percentages, mean, and standard deviation according to the

3 ambulatory statuses. Nonparametric tests for trend across ordered groups were applied to the different distributions.

2) Ambulatory status of children with CP were estimated using descriptive and inferential statistics: frequencies, percentages, and 95% confident interval.

3) The univariable analysis was used to identify the association between independent factors and ambulatory status by univariable ordinal continuation ratio logistic regression analysis.

4) Candidate predictors with the *p*-value <0.2 were selected to multivariable ordinal logistic regression analysis using backward elimination method with adjusting for covariate factors.

5) The proportional odds assumption for the ordinal logistic regression models were tested using the Brant test of parallel regression[3], with a violation considered when *p*-value <0.05.

6) The possible interactions were considered.

7) Cumulative odds ratios (cumulative OR) with 95% Confidence interval were presented for the results and the level of significance were set at *p*-value 0.05.

5.2 systematic review and meta-analysis for observational study

Meta-analysis is performed using an ambulatory status as binary outcome (ambulation and non-ambulation). The pooled relative risk (RR) with 95% CIs for predicting of ambulatory status were calculated using random-effects model.[4] The presence of heterogeneity was assessed using the Cochran's Q-test when *p*-value <0.10 is considered evidence of heterogeneity. And I^2 is used to describe which quantifies the effect of heterogeneity, which describes the percentage of total variation across studies of heterogeneity rather than chance. Value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity.[5, 6] Thresholds for the interpretation of I^2 depend on several factors. In this study, the criteria according to Cochrane Handbook[7], this is described as follows:

0% to 40%: might not be important;

30% to 60%: may represent moderate heterogeneity;

50% to 90%: may represent substantial heterogeneity;

75% to 100%: considerable heterogeneity.

If heterogeneity existed, attempts to explore the sources of heterogeneity were made. Publication bias was assessed using Egger's test of asymmetry tests with a visual inspection of the funnel plot. The shape of asymmetry, which indicates the existence of bias and *p*-value <0.05 in publication bias tests, was suggestive of publication bias. Forest plots were generated to show RRs with corresponding CIs for each study and the overall random effects pooled estimate. Potential sources of heterogeneity were further explored by visual inspection of the data and forest plot, and subgroup analyses. Finally, sensitivity analyses were used to investigate the robustness of the pooled results. All analysis will be conducted using STATA Statistical software Release 11.0 (Stata Corporation, College Station, TX).

5.3   Prognostic prediction research (Clinical prediction rule)

Statistical analyses were performed using STATA Statistical software Release 11.0 (Stata Corporation, College Station, TX) as follows:

1) Regression coefficients of potential predictors (from study I) were converted into scores, which are added to the total score for each subject.

2) The total scores were used to represent the summary measure of predicting ambulatory children with cerebral palsy.

3) The receiver operating characteristic (ROC) was used to assess the probability of the total score showed ambulatory status.

4) The Hosmer and Lemeshow chi-square goodness of fit test[8], are available that compare how well the predicted probabilities fit with the actual probabilities.

5) Score-classified ambulatory statuses were compared to criterion-classified ambulatory statuses to indicate the estimation validity by percentage of agreement.

6) The level of significance were set at *p*-value 0.05.

6. Power of analysis

The number of examinable events per variable was 23 (186/8), which should be at least 10, according to the rule of thumb. These results show that this thesis had sufficient statistical power and performance to determine predictors. The power analysis test is shown by G*Power program as follows.[9]

For multivariable model with independent eating is the least effect size with odds ratio 2.59
(see Table 4.2)

Options: Large sample z-Test, Demidenko (2007) with var corr

Analysis: Post hoc: Compute achieved power

Input: Tail(s) = Two

Odds ratio = 2.59

Pr(Y=1|X=1) H0 = 0.1

α err prob = 0.05

Total sample size = 533

R^2 other X = 0.417

X distribution = Binomial

X parm π = 0.61

Output: Critical z = 1.9599640

Power (1-β err prob) = 0.8031834

REFERENCES

1. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. J Am Med Assoc. 2000;283:2008-12.

2. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1-9.

3. Brant R. Assessing proportionality in the proportional odds model for ordinal logistic regression. Biometrics. 1990;46:1171-8.

4. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7:177-88.

5. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21:1539-58.

6. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557-60.

7. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions version 5.1.0: The Cochrane Collaboration; 2011 [cited 2012 Sep 9]. Available from: http://www.cochrane-handbook.org/.

8. Hosmer DW, Lemeshow S. Applied logistic regression. second ed. New York: John Wiley & Sons Inc.; 2000.

9. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods. 2007;39:175-91.

Appendix B

Keeratisiroj O, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M. Prognostic predictors for ambulation in Thai children with cerebral palsy aged 2 to 18 years. J Child Neurol. 2015;30:1812-8.

Prognostic Predictors for Ambulation in Thai Children With Cerebral Palsy Aged 2 to 18 Years

Orawan Keeratisiroj, MPH[1,2], Nuanlaor Thawinchai, PhD[3],
Wantana Siritaratiwat, PhD[4], and Montana Buntragulpoontawee, MD[5]

Abstract

The objectives of this study were to determine prognostic predictors for ambulation among Thai children with cerebral palsy and identify their ambulatory status. A retrospective cohort study was performed at 6 special schools or hospitals for children with physical disabilities. The prognostic predictors for ambulation were analyzed by multivariable ordinal continuation ratio logistic regression. The 533 participants aged 2 to 18 years were divided into 3 groups: 186 with independent ambulation (Gross Motor Function Classification System [GMFCS I-II]), 71 with assisted ambulation (Gross Motor Function Classification System III), and 276 with nonambulation (Gross Motor Function Classification System IV-V). The significant positive predictors for ambulation were type of cerebral palsy (spastic diplegia, spastic hemiplegia, dyskinesia, ataxia, hypotonia, and mixed type), sitting independently at age 2 years, and eating independently. These predictors were used to develop clinical scoring for predicting the future ability to walk among Thai children with cerebral palsy.

Cerebral palsy is a range of nonprogressive disorders of posture and motor impairment.[1] The prevalence of cerebral palsy is about 1 to 3 per 1000 live births in Europe.[2,3] This prevalence increases to 40 to 100 per 1000 live births among infants born prematurely or of low birth weight; this rate is likely to increase.[4,5] However, cerebral palsy prevalence has been observed to be lower in Asians than among Europeans, although the cause has yet to be explained.[6-8]

Several conceptual models of disability—most prominently and recently, the World Health Organization's International Classification of Functioning, Disability, and Health[9]—have shifted the primary focus of treatment for cerebral palsy to the level of activity and participation of the individual patient. One of the treatment goals is to ensure that patients can ambulate and take care of themselves independently.[10] Most parents of children with cerebral palsy want to know its severity and whether their children will walk independently. However, predicting ambulatory outcome in these children is difficult because several factors can influence ambulatory status during a child's growth.

The factors to predict ambulation in children with cerebral palsy have been informed for decades by Sala and Grant.[11] The factors are divided into 3 main groups: (1) primitive reflexes and postural reactions, (2) gross motor skills, and (3) type of cerebral palsy. In addition to these factors, other factors (eg, epilepsy, intellectual disability, visual impairment, and hearing impairment) have been considered in several studies,[12-22] although with no consensus to date on their contribution. Some previous studies about predictors of ambulation in children with cerebral palsy had a relatively small number of patients recruited from a single clinic,[12,13,18,20,21,23] studied only a subgroup of cerebral palsy,[12,15,20,23] and/or used only univariable analysis,[12,19-22] with sometimes conflicting results.

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Previous studies differing on the definition of "ambulation" made comparisons difficult. In addition, important operational definitions did not provide enough information to determine whether the term "ambulation" can be used to achieve the function. The Gross Motor Function Classification System is the functional assessment that has been widely accepted.[24] However, only 2 recent studies used this to classify ambulatory status.[12,22]

The objectives of the present study were to determine prognostic predictors for ambulation after 2 years of age in Thai children with cerebral palsy and to identify ambulatory status according to the Gross Motor Function Classification System.

Methods

Recruitment

A retrospective cohort study was carried out at 6 special schools or hospitals for children with physical disabilities in northeastern and northern Thailand, including Rajanagarindra Institute of Child Development, Chiang Mai Province, Srisangwanchiangmai School, Srisangwankhonkaen School, Special Education Center Region 7, Special Education Center Region 8, and Special Education Center Region 9. All children with cerebral palsy registered at the 6 selected hospitals or special educational schools and centers during the period from 2008 to 2013 were recruited (681 children). To be included in the study, the children had to be 2 to 18 years old and diagnosed with cerebral palsy by a physician or a physiotherapist, with the cerebral palsy first appearing before age 2. After eliminating duplicates and those not meeting the inclusion criteria, 630 participants were enrolled, and they provided informed consent. This number was subsequently reduced to 533 participants because some participants could not be evaluated using the Gross Motor Function Classification System (Figure 1).

Measures

The Gross Motor Function Classification System–expanded and revised version[25,26] was used to classify the ambulatory status. The Gross Motor Function Classification System–expanded and revised version family and self-report questionnaires (Thai version) have been licensed for translation into Thai by Siriratatiwat and Thomas.[27,28] This tool has 5 locomotor scales for each age group: I, walks without limitations; II, walks with limitations; III, walks using a hand-held mobility device; IV, self-mobility with limitations, or may use powered mobility; and V, transported in a manual wheelchair. The ambulatory status was classified as 3 ordinal groups: (1) independent ambulation (Gross Motor Function Classification System I-II), (2) assisted ambulation (Gross Motor Function Classification System III), and (3) nonambulation (Gross Motor Function Classification System IV-V).

The baseline characteristics (age, gender, weight, height, and caregiver) and clinical data (type of cerebral palsy, gestational age, birth weight, hyperbilirubinemia, epilepsy or seizure, sitting independently at age 2 years, intellectual disability, visual impairment, hearing impairment, hand function, eating, speech, medication, history of orthopedic surgery, and orthotics use) were reviewed from the medical and physical therapy records. These were confirmed by interview on site, on telephone, or via mail. Accompanying impairments were obtained through interview with the child's caregivers or observation of the child when possible, just to make sure whether the child has disability. Some baseline and clinical data, including gender, body mass
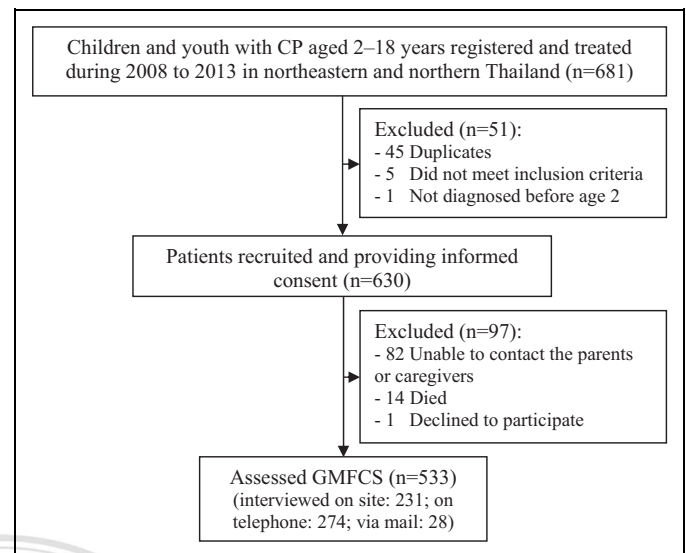

Figure 1. The flow chart of patients included in the study.

index, type of cerebral palsy, gestational age, birth weight, hyperbilirubinemia, epilepsy or seizure, sitting independently at age 2 years, intellectual disability, visual impairment, hearing impairment, hand function, eating, and speech, were analyzed as factors predicting ambulation. Age and history of orthopedic surgery were treated as confounding factors.

Data Analysis

Statistical analyses were performed using Stata statistical software, release 11.0 (Stata Corporation, College Station, TX). In our data, some independent variables were missing values. We assumed that the missing data were missing completely at random, and tested this by comparing whether the means or proportions of each variable between groups were missing or not.[29,30] As no significant differences between groups were evident, the data were missing completely at random, allowing us to use complete-case analysis in data analysis.[31] Descriptive statistics were used to characterize participants according to the 3 ambulatory statuses. Nonparametric tests for trend across ordered groups were applied to the different distributions. The outcomes were estimated using descriptive and inferential statistics: frequencies, percentages, and 95% confidence interval. Univariable ordinal continuation ratio logistic regression analysis was used to identify the association between each independent factor and ambulatory status. Variables that had P values $\leq.20$ were selected as candidate predictors for the multivariable ordinal continuation ratio logistic regression analysis using backward elimination and adjusting for covariate factors. We considered possible interactions and presented the crude and adjusted odds ratios with 95% confidence interval for the results. All levels of significance were set at $P = .05$.

Results

A total of 533 children with cerebral palsy were included, and their levels of Gross Motor Function Classification System were classified into 3 groups: (1) independent ambulation (n = 186), (2) assisted ambulation (n = 71), and (3) nonambulation (n = 286). Table 1 shows a comparison of the baseline characteristics

Table 1. Baseline Characteristics and Clinical History Comparison Between Groups.

Variables	Nonambulation[a] (n = 276)	Assisted ambulation[a] (n = 71)	Independent ambulation[a] (n = 186)	P value[b]
Age (y)	8.7 ± 4.2	10.7 ± 4.2	11.1 ± 4.0	<.001
Male gender	153 (55.4)	40 (56.3)	112 (60.2)	.316
Body mass index (n = 456)	15.0 ± 3.4	16.1 ± 4.2	16.3 ± 3.3	<.001
Caregiver				.643
Other (foundation, orphanage)	7 (2.5)	4 (5.6)	9 (4.8)	
Grandparents	69 (25.0)	16 (22.6)	37 (19.9)	
Parents	200 (72.5)	51 (71.8)	140 (75.3)	
Type of cerebral palsy[c] (n = 503)				<.001
Spastic quadriplegia	131 (48.9)	7 (10.8)	3 (1.8)	
Spastic diplegia	61 (22.8)	34 (52.3)	48 (28.2)	
Spastic hemiplegia	15 (5.6)	13 (20.0)	88 (51.7)	
Dyskinesia	33 (12.3)	4 (6.2)	18 (10.6)	
Ataxia	0 (0)	3 (4.6)	10 (5.9)	
Hypotonia	7 (2.6)	1 (1.5)	1 (0.6)	
Mixed	21 (7.8)	3 (4.6)	2 (1.2)	
Gestational age (wk) (n = 511)	35.6 ± 4.3	34.9 ± 4.6	35.8 ± 3.8	.904
Extremely preterm (<28)	13 (4.9)	7 (10.3)	7 (3.9)	
Very preterm (28 to <32)	50 (18.9)	13 (19.1)	30 (16.8)	
Moderate to late preterm (32 to <37)	34 (12.9)	4 (5.9)	21 (11.7)	
Normal (≥37)	167 (63.3)	44 (64.7)	121 (67.6)	
Birth weight (g) (n = 506)	2520.6 ± 800.1	2447.4 ± 798.1	2595.1 ± 802.5	.436
No hyperbilirubinemia (n = 511)	203 (76.0)	57 (82.6)	128 (73.1)	.560
No epilepsy/seizure (n = 527)	129 (46.9)	50 (71.4)	102 (56.0)	.031
Maximal motor milestone achieved at present				<.001
Does not roll	63 (22.8)	0 (0)	0 (0)	
Rolls	84 (30.4)	3 (4.2)	2 (1.1)	
Sits without support	110 (39.9)	38 (53.5)	15 (8.1)	
Pulls to stand	19 (6.9)	30 (42.3)	169 (90.8)	
Sitting independently at age 2 (n = 500)	29 (10.7)	37 (58.7)	138 (83.1)	<.001
No intellectual disability	227 (82.2)	59 (83.1)	139 (74.7)	.056
No visual impairment	224 (81.2)	65 (91.5)	172 (92.5)	<.001
No hearing impairment	264 (95.6)	67 (94.4)	180 (96.8)	.587
Have functional use of hands	188 (68.2)	70 (98.6)	184 (98.9)	<.001
Eating independently	101 (36.6)	61 (85.9)	165 (88.7)	<.001
Speech (can say single words, sentences)	116 (42.0)	57 (80.3)	147 (79.0)	<.001
Medication (oral/focal) (n = 527)	219 (80.2)	43 (60.6)	119 (65.0)	<.001
History of orthopedic surgery (n = 522)	20 (7.3)	17 (23.9)	28 (15.6)	.004
Orthotics use (n = 519)	97 (35.3)	30 (42.9)	52 (29.9)	.302

[a]The data shows n (%) for categorical data and mean ± standard deviation for continuous data.
[b]Trend test across ordered groups.
[c]Spastic quadriplegia included spastic triplegia; spastic diplegia included spastic paraplegia; spastic hemiplegia included spastic monoplegia and spastic double hemiplegia; and mixed type included spastic athetosis and spastic ataxia.

and the clinical history between the groups of participants. The most common type of cerebral palsy in the independent ambulatory group was spastic hemiplegia (51.7%); in the assisted ambulatory group, the most common type was diplegia (52.3%); and in the nonambulatory group, the most common type of cerebral palsy was quadriplegia (48.9%). There were no statistically significant differences in gender, caregiver, gestational age, birth weight, hyperbilirubinemia, intellectual disability, hearing impairment, and orthotics use between the groups.

Table 2 lists the 5 levels of ambulatory status from Gross Motor Function Classification System. Of the children with cerebral palsy, the Gross Motor Function Classification System IV group presented 27.8% (95% confidence interval = 24.0-31.8) and the Gross Motor Function Classification System V

Table 2. Ambulatory Status of Children With Cerebral Palsy (n = 533).

GMFCS level	Ambulatory status	n (%)	95% CI	%
I	Independent ambulation (I-II)	108 (20.3)	16.9-23.9	34.9 (I-II)
II		78 (14.6)	11.7-17.9	
III	Assisted ambulation (III)	71 (13.3)	10.6-16.5	13.3 (III)
IV		148 (27.8)	24.0-31.8	
V	Nonambulation (IV-V)	128 (24.0)	20.4-27.9	51.8 (IV-V)

Abbreviations: CI, confidence interval; GMFCS, Gross Motor Function Classification System.

Table 3. Univariable and Multivariable Analysis of Predictors for Ambulatory Status.

Predictors	OR$_{crude}$ (95% CI)[a]	P value	OR$_{adjusted}$ (95% CI)[b,c]	P value
Type of cerebral palsy[d]				
Spastic quadriplegia	1.00		1.00	
Spastic diplegia	13.10 (6.94-24.76)	<.001	8.96 (3.47-23.16)	<.001
Spastic hemiplegia	62.89 (31.08-127.25)	<.001	44.44 (16.19-121.97)	<.001
Dyskinesia	10.64 (5.13-22.04)	<.001	12.28 (4.39-34.36)	<.001
Ataxia	70.57 (18.49-269.37)	<.001	101.81 (16.87-614.47)	<.001
Hypotonia	3.81 (0.90-16.21)	.070	10.56 (1.99-55.95)	.006
Mixed	2.99 (1.08-8.27)	.035	4.59 (1.24-16.99)	.023
Sitting independently at age 2	13.96 (9.60-20.31)	<.001	7.74 (4.83-12.40)	<.001
Eating independently	7.47 (5.19-10.77)	<.001	2.59 (1.44-4.64)	.001
Male gender	1.17 (0.87-1.56)	.302	Not selected	
Body mass index	1.09 (1.04-1.14)	.001	Not selected	
Gestational age	1.01 (0.98-1.05)	.484	Not selected	
Birth weight	1.00 (1.00-1.00)	.285	Not selected	
No hyperbilirubinemia	0.86 (0.61-1.21)	.384	Not selected	
No epilepsy/seizure	1.25 (0.93-1.67)	.141	Not selected	
No intellectual disability	0.69 (0.48-0.99)	.043	Not selected	
No visual impairment	2.22 (1.40-3.52)	.001	Not selected	
No hearing impairment	1.29 (0.62-2.67)	.492	Not selected	
Have functional use of hands	24.42 (9.74-61.22)	<.001	Not selected	
Can say single words, sentences	3.41 (2.48-4.69)	<.001	Not selected	

Abbreviations: CI, confidence interval; OR, odds ratio.
[a]Univariable ordinal continuation ratio logistic regression.
[b]Multivariable ordinal continuation ratio logistic regression.
[c]Adjusted for covariate (current age and history of orthopedic surgery).
[d]Spastic quadriplegia included spastic triplegia; spastic diplegia included spastic paraplegia; spastic hemiplegia included spastic monoplegia and spastic double hemiplegia; and mixed type included spastic athetosis and spastic ataxia.

group presented 24.0% (95% confidence interval = 20.4-27.9) of severe mobility restrictions in the entire sample. The results of univariable and multivariable ordinal continuation ratio logistic regression are shown in Table 3. Only the 3 strongest positive predictors of ambulatory status were selected for use in the last multivariable model, after adjusting for confounders (current age and history of orthopedic surgery). These 3 predictors were the following: (1) type of cerebral palsy, including spastic diplegia, spastic hemiplegia, dyskinesia, ataxia, hypotonia, and mixed type; (2) sitting independently at age 2 years; and (3) eating independently.

Discussion

In this retrospective cohort study of Thai children with cerebral palsy, we found that the prognostic predictors for ambulation were types of cerebral palsy (spastic diplegia, spastic hemiplegia, dyskinesia, ataxia, hypotonia, and mixed type compared to spastic quadriplegia), sitting independently at age 2 years, and eating independently. In addition, our study also found that of the Thai children with cerebral palsy aged 2 to 18 years in our sample, 34.9% were capable of independent ambulation, 13.3% were dependent on assisted ambulation, and 51.8% were affected with nonambulation.

These predictors in our study confirmed the findings of previous studies. The type of cerebral palsy has been considered as a predictor of ambulation since Sala and Grant,[11] in 1995. In addition, Montgomery[14] concluded that spastic hemiplegia was

the best predictor of ambulation in children, whereas children with spastic diplegia were most likely to require an assistive device, and those with spastic quadriplegia had the worst prognosis for ambulation. This conclusion is consistent with the findings of our study: most of the cerebral palsy children in the independent ambulatory group had spastic hemiplegia; in the assisted ambulatory group, most of the cerebral palsy children had spastic diplegia; and in the nonambulatory group, most of the cerebral palsy children had spastic quadriplegia. Therefore, spastic quadriplegia was selected as the reference group to compare with others in our study. Other types of cerebral palsy, including dyskinesia, ataxia, hypotonia, and mixed, were smaller and they rarely got discussed. We found that ataxia has a better prognosis than the others; all 13 ataxic children in our study walked with assistance or independently. This concurs with the findings of Wu et al,[16] who found that ataxic cerebral palsy has a better prognosis for ambulation than spastic and dyskinetic cerebral palsy.

The ability to sit independently by age 2, in this study, was a strong predictor for ambulation, as with previous studies.[13,16,20,22] Montgomery[14] reviewed the literature to identify predictors of ambulation in children with cerebral palsy, in the years 1970 to 1995; he concluded that the best gross motor skills to predicting ambulation was sitting. Later studies confirmed that the ability to sit without support at 2 years of age was a good prognosis for ambulation.[15,16,22] Previous studies also examined different ages (1 year and 3 years) for sitting independently.[21,32]

Finally, this study found that eating independently (functional use of the hands with no oromotor dysfunction) was a significant predictor for ambulation. More recent studies have looked at accompanying impairments. In one large study of children with cerebral palsy who were not yet walking at 2 years of age,[16] the ability to feed themselves was a univariable predictor for ambulation, but not a multivariable predictor. Kulak et al[19] found that more than half of the nonambulatory group were eating with assistance. It is well known that children with cerebral palsy are associated with poor growth, the main reason being feeding problems.[18,33] The ability to eat, therefore, affects the gait of these children.

This study found other variables (body mass index, intellectual disability, visual impairment, hand function, and speech) that are associated with ambulatory status in univariable analysis. However, these variables were not statistically significant predictors for the multivariable model. Some previous research studies have found that these variables are related to walking ability. It has long been known that intellectual disability is a factor determining lack of independent walking of children with cerebral palsy.[13,15,17,21,22] Several studies have shown an association between visual acuity and ambulation in children with cerebral palsy.[15-17] As with our results, Wu et al[16] found that increasing hand function was associated with achieving ambulation in univariable analysis but not in multivariable analysis. It is likely that hand function is connected with other covariates, such as the ability to eat independently, so we did not find this correlation. Additionally, Kulak et al[19] reported that lack of speech development was a predictor for independent ambulation. Some variables, such as seizure or epilepsy, for which we found no association with ambulation, were predictors in other studies.[12,16,17,22,23] This may be due to our classifying the data into those with a history of seizures or not, rather than specifying the severity and frequency of seizures.

The distribution of ambulatory status in this study is not consistent with reports from several European countries. A large project of the collaboration "Surveillance of Cerebral Palsy in Europe: A Collaboration of Cerebral Palsy Surveys and Registers"[17] showed that among children with cerebral palsy at age 5 years, 54% were independently ambulatory, 16% walked with assistance, and 30% could not walk at all. This is similar to the findings of 2 previous studies which reported that more than half of children with cerebral palsy could walk without an assistive device.[34,35] In contrast, our study showed that Thailand had a burden of disability from nonambulatory children with cerebral palsy. However, our study was conducted at special schools or hospitals for children with physical disabilities. It is possible that most Thai children with cerebral palsy who can walk independently are not enrolled or admitted in these institutions.

Routine data were used in this study, so other variables related to ambulation of children with cerebral palsy, such as primitive reflexes and postural reactions, were not analyzed. Additionally, our data seem to be missing completely at random. So we are confident that there is no bias because of the missing data, but its ineffectiveness is important enough to be taken into consideration.[30,36] All the same, we selected an ordinal continuation ratio logistic regression model, with the last model missing 11.63% (62/533) of values, so the complete-case analysis is a good estimation of predictive performance with the missing completely at random assumption. The number of examinable events per variable was 23 (186/8), which should be at least 10, according to the rule of thumb.[37] These results show that our study had sufficient statistical power and performance to determine predictors. Differences in measurements are also potential limitations. The type of cerebral palsy is a subjective measurement, so perhaps assessments vary; for example, children classified as quadriplegic by one physician might be classified as diplegic by another.

The above limitations are offset by the strengths. First, the ambulatory status was determined by Gross Motor Function Classification System, which has been examined for interrater reliability and stability, as well as content, construct, discriminative, and predictive validity.[26] In addition, Gross Motor Function Classification System has been widely used worldwide and has been translated into more than 20 languages.[28] Second, multivariable analysis was used for the predictors, with covariate factors adjusted. Finally, our samples were diverse—derived from several locations in northeastern and northern Thailand and across children with all types of cerebral palsy—allowing for widely generalized results.

In conclusion, our findings indicate that good predictors for ambulation among children with cerebral palsy include the type of cerebral palsy (spastic diplegia, spastic hemiplegia, dyskinesia, ataxia, hypotonia, and mixed type), sitting independently at age 2 years, and eating independently. The children were classified as follows: capable of independent ambulation (Gross Motor Function Classification System I-II, 34.9%), dependent on assisted ambulation (Gross Motor Function Classification System III, 13.3%), and affected with nonambulation (Gross Motor Function Classification System IV-V, 51.8%). These predictors were used to develop the clinical scoring scale for predicting the ability to walk in future among Thai children with cerebral palsy. Our results are potentially beneficial in the long-term treatment and rehabilitation of children with cerebral palsy in Thailand.

Author Contributions

OK drafted manuscript and contributed to conception, design, acquisition, analysis, and interpretation. NT, WS, and MB critically revised manuscript and also contributed to conception, design, acquisition and interpretation.

Declaration of Conflicting Interests

The authors declare no potential conflicts of interests with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by the ethics committee of the Faculty of Medicine, Chiang Mai University (The IRB approval number 188/2013), and Rajanagarindra Institute of Child Development, Chiang Mai Province. The participants were informed of the research purpose and procedures of this study. Additionally, all the participants or their parents signed a written informed consent to participate in the study.

References

1. Koman LA, Smith BP, Shilt JS. Cerebral palsy. *Lancet*. 2004;363: 1619-1631.
2. Clark SL, Hankins GDV. Temporal and demographic trends in cerebral palsy—fact and fiction. *Am J Obstet Gynecol*. 2003; 188:628-633.
3. Nelson KB. The epidemiology of cerebral palsy in term infants. *Ment Retard Dev Disabil Res Rev*. 2002;8:146-150.
4. Krägeloh-Mann I, Cans C. Cerebral palsy update. *Brain Dev*. 2009;31:537-544.
5. SCPE working group. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. *Dev Med Child Neurol*. 2000;42:816-824.
6. Wu YW, Croen LA, Shah SJ, et al. Cerebral palsy in a term population: risk factors and neuroimaging findings. *Pediatrics*. 2006; 118:690-697.
7. Wu YW, Xing G, Fuentes-Afflick E, et al. Racial, ethnic, and socioeconomic disparities in the prevalence of cerebral palsy. *Pediatrics*. 2011;127:e674-e681.
8. Lang TC, Fuentes-Afflick E, Gilbert WM, et al. Cerebral palsy among Asian ethnic subgroups. *Pediatrics*. 2012;129: e992-e998.
9. World Health Organization. International classification of functioning, disability and health (ICF). Available at: http://www.who.int/classifications/icf/en/. Accessed February 6, 2011.
10. Rosenbaum P. Cerebral palsy: what parents and doctors want to know. *BMJ*. 2003;326:970-974.
11. Sala DA, Grant AD. Prognosis for ambulation in cerebral palsy. *Dev Med Child Neurol*. 1995;37:1020-1026.
12. Simard-Tremblay E, Shevell M, Dagenais L. Determinants of ambulation in children with spastic quadriplegic cerebral palsy: a population-based study. *J Child Neurol*. 2010;25: 669-673.
13. Watt JM, Robertson CMT, Grace MGA. Early prognosis for ambulation of neonatal intensive care survivors with cerebral palsy. *Dev Med Child Neurol*. 1989;31:766-773.
14. Montgomery PC. Predicting potential for ambulation in children with cerebral palsy. *Pediatr Phys Ther*. 1998;10:148-155.
15. Fedrizzi E, Facchin P, Marzaroli M, et al. Predictors of independent walking in children with spastic diplegia. *J Child Neurol*. 2000;15:228-234.
16. Wu YW, Day SM, Strauss DJ, et al. Prognosis for ambulation in cerebral palsy: a population-based study. *Pediatrics*. 2004;114: 1264-1271.
17. Beckung E, Hagberg G, Uldall P, et al. Probability of walking in children with cerebral palsy in Europe. *Pediatrics*. 2008;121: e187-e192.
18. Gokkaya NKO, Caliksan A, Karakus D, et al. Relation between objectively measured growth determinants and ambulation in children with cerebral palsy. *Turk J Med Sci*. 2009; 39:85-90.
19. Kuak W, Okurowska-Zawada B, Sienkiewicz D, et al. The clinical signs and risk factors of non-ambulatory children with cerebral palsy. *J Pediatr Neurol*. 2011;9:447-454.
20. Campos da Paz AJ, Burnett SM, Braga LW. Walking prognosis in cerebral palsy: a 22-year retrospective analysis. *Dev Med Child Neurol*. 1994;36:130-134.
21. Souza A, Ferraretto I. Clinical signs for the prognosis of walking in cerebral palsy. *Arquivos de Neuro-Psiquiatria*. 1992;50: 80-81.
22. Kułak W, Sendrowski K, Okurowska-Zawada B, et al. Prognostic factors of the independent walking in children with cerebral palsy. *Neurologia*. 2011;20:29-34.
23. Trahan J, Marcoux S. Factors associated with the inability of children with cerebral palsy to walk at six years: a retrospective study. *Dev Med Child Neurol*. 1994;36:787-795.
24. Palisano R, Rosenbaum P, Walter S, et al. Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Dev Med Child Neurol*. 1997;39: 214-223.
25. CanChild Centre for Childhood Disability Research. Distribution and translation of the GMFCS E&R. Available at: http://motorgrowth.canchild.ca/en/GMFCS/expandedandrevised.asp. Accessed January 9, 2013.
26. Palisano RJ, Rosenbaum P, Bartlett D, et al. Content validity of the expanded and revised Gross Motor Function Classification System. *Dev Med Child Neurol*. 2008;50:744-750.
27. Siritaratiwat W, Thomas I. Gross Motor Function Classification System–Expanded and Revised (2007 Thai version). Available at: http://motorgrowth.canchild.ca/en/GMFCS/resources/20071112 FINALGMFCS-ERnov1207thaiversionFINALforposting.pdf. Accessed September 11, 2012.
28. CanChild Centre for Childhood Disability Research. GMFCS Family and Self Report Questionnaire. Available at: http://motorgrowth.canchild.ca/en/GMFCS/familyreportquestionnaire.asp. Accessed January 10, 2013.
29. Little RJA. A test of missing completely at random for multivariate data with missing values. *J Am Stat Assoc*. 1988;83: 1198-1202.
30. van der Heijden GJ, Donders AR, Stijnen T, et al. Imputation of missing values is superior to complete case analysis and the missing-indicator method in multivariable diagnostic

research: a clinical example. *J Clin Epidemiol*. 2006;59: 1102-1109.

31. Haukoos JS, Newgard CD. Advanced statistics: missing data in clinical research—part 1: an introduction and conceptual framework. *Acad Emerg Med*. 2007;14:662-668.

32. Pallás Alonso CR, de la Cruz Bértolo J, Medina López MC, et al. Cerebral palsy and age of sitting and walking in very low birth weight infants. *Anales de Pediatría*. 2000; 53:48-52.

33. Jan MM. Cerebral palsy: comprehensive review and update. *Ann Saudi Med*. 2006;26:123-132.

34. Himmelmann K, Beckung E, Hagberg G, et al. Gross and fine motor function and accompanying impairments in cerebral palsy. *Dev Med Child Neurol*. 2006;48:417-423.

35. Shevell MI, Dagenais L, Hall N, et al. The relationship of cerebral palsy subtype and functional motor impairment: a population-based study. *Dev Med Child Neurol*. 2009;51:872-877.

36. Little RJA. Regression with missing X's: a review. *J Am Stat Assoc*. 1992;87:1227-1237.

37. Steyerberg EW. *Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating*. New York: Springer Science and Business Media, LLC; 2009.

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Appendix C

Keeratisiroj O, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M., Pratoomsoot C. Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational study. Disabil Rehabil. 2016. 1-9. [Epub ahead of print]

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REVIEW ARTICLE

Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational studies

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ABSTRACT

Purpose: The purpose of this study is to investigate the prognostic predictors for ambulation in children with cerebral palsy using meta-analysis of observational studies.
Method: Electronic searches were conducted in PubMed, SCOPUS, CINAHL, ProQuest, Ovid, Wiley InterScience, and ScienceDirect databases from their start dates to December 2015.
Results: Of the 1123 identified articles, 12 met the inclusion criteria for qualitative synthesis, eight of which were deemed appropriate for meta-analysis. Qualitative synthesis found that the type of cerebral palsy, early motor milestones, primitive reflexes and postural reactions, absence of visual impairment, absence of intellectual disability, absence of epilepsy or seizure, and ability to feed self were indicated as potential predictors for ambulation. Meta-analysis detected four significant prognostic predictors for ambulation: sitting independently at 2 years, absence of visual impairment, absence of intellectual disability, and absence of epilepsy or seizure.
Conclusion: These prognostic predictors should be taken into consideration in therapeutic plans and rehabilitation goals, especially sitting independently before the age of 2 years.

> ➤ **IMPLICATIONS FOR REHABILITATION**
> - The meta-analysis supports strong evidence that sitting independently at 2 years of age, absence of visual impairment, absence of intellectual disability, and absence of epilepsy or seizure are positive predictors for ambulation in children with cerebral palsy.
> - The therapeutic plans and rehabilitation goals should be considered cautiously for these predictors, especially sitting independently before the age of two years.

Introduction

Cerebral palsy is the most common physical disability in childhood.[1,2] Recent data show that the overall prevalence of cerebral palsy declined both in the European [3] and Australian [4] Registers. In addition, the survival rate of at-risk preterm infants has increased. The prevalence of cerebral palsy was about 2.0 per 1000 live births, as obtained from two systematic reviews.[5,6]

At present, cerebral palsy cannot yet be cured. The main treatment goals as recommended by the World Health Organization (WHO) [7] take patient level of activity into account, where therapists consider the participation of the individual patient as important. When the child is diagnosed with cerebral palsy, many parents wish to know whether their child would be able to walk. The Gross Motor Function Classification System (GMFCS) [8,9] has been widely used internationally to classify level of functional mobility or activity limitation. However, the prognosis of walking (ambulation) in children with cerebral palsy is difficult because there are many factors (such as type of cerebral palsy, age, and impairments) as well as treatments that affect the child's development.[10,11]

The predictive factors for ambulation in children with cerebral palsy have been suggested for decades by Sala and Grant.[12] These were divided into three main groups: primitive reflexes and postural reactions, gross motor skills, and the type of cerebral palsy. In addition, accompanying impairments including epilepsy, intellectual disability, visual impairment, and hearing impairment have been mentioned in several studies.[13–20] However, there was no consensus that these factors may have contributed to the success of walking independently.

The amount of research for predicting ambulation in children with cerebral palsy has increased.[14–16,18–26] Yet, no quantitative synthesis of the evidence could be found. There was only a literature review by Montgomery [13] which concluded from seven studies that the persistence of primitive reflexes at 18–24 months was poor prognostic predictors for ambulation, while early motor milestones were the best prognostic predictors. Therefore, the objective of this study was to identify prognostic predictors for ambulation in children with cerebral palsy by a systematic review and meta-analysis of observational studies. Evidence resulting from this systematic review will be valuable in supporting appropriate therapeutic plans and rehabilitation goals.

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Methods

Search strategies

We followed the meta-analysis of observational studies in epidemiology (MOOSE) [27] and preferred reporting items for systematic review and meta-analysis protocol (PRISMA-P) guidelines.[28] A systematic literature search was performed in PubMed, SCOPUS, CINAHL, ProQuest, Ovid, Wiley InterScience, and ScienceDirect databases. These databases were searched from their start dates to December 2015. A search strategy was developed and adapted for each database with a combination of free text and controlled vocabulary terms. This search employed the Medical Subject Headings (MeSH) "cerebral palsy," "predict,*" and "ambula,*" and explored these keywords with slight modifications based on the source.

The additional strategies were hand searching of journals not indexed in the electronic sources, web-based searches, and screening of reference lists of retrieved studies for further potentially relevant articles, with no limitations to the study design and language. The first reviewer (O.K.) retrieved and performed the primary screening of the titles and abstracts; a second reviewer (N.T.) checked for accuracy. If there were disagreements regarding eligibility, the article was judged by a third reviewer (W.S.). Then, the full-text articles were assessed for eligibility by the same method.

Selection criteria

The inclusion criteria for the current study were as follows: studies using cross-sectional, case–control, or cohort (including longitudinal studies) designs; the participants consisted of children or youth from 0 to 18 years of age who were diagnosed with cerebral palsy by physicians; definitions and measurements of outcomes were reported; and either relative risks (RRs) or raw data were reported to enable their calculation. The exclusion criteria consisted of the following: articles other than original articles such as comments, letters, reviews, meta-analyses, case reports, surveys, or editorials; and articles not reporting effect estimates or with information that is insufficient to compute effect estimates.

Data extraction, quality assessment, and qualitative synthesis

All the included studies were independently assessed by two investigators (O.K. and N.T.) using the Newcastle–Ottawa Scale [29] for assessing the quality of non-randomized studies in meta-analyses. The score was calculated based on three main components: selection (0–4 points), comparability (0–3 points), and outcome (0–2 points). A higher score represented high methodological quality. Any disparities between two investigators were resolved by discussion and consensus.

The first reviewer (O.K.) extracted data for the study setting, study design, number and characteristics of participants, outcomes, predictors, and results; a second reviewer (N.T.) checked for accuracy. Potential predictors were subsequently extracted, and qualitatively synthesized. From which, the selected potential predictors were used in quantitative synthesis.

Quantitative synthesis (meta-analysis)

The meta-analysis was performed using ambulatory status as the binary outcome (ambulation and non-ambulation). The pooled RRs with 95% CI for predicting ambulatory status were calculated using random-effects models, which were most suitable for both random variations within the study and between different studies.[30] The presence of heterogeneity was assessed using Cochran's Q-test: when $p < 0.10$, it was considered as evidence of heterogeneity. Furthermore, the effect of heterogeneity was quantified by I^2 which describes the percentage of total variation across the studies of heterogeneity rather than by chance. A value of 0% indicates no observed heterogeneity, with $I^2 \geq 50\%$ represent substantial heterogeneity.[31,32]

Publication bias was assessed using Egger's test for asymmetry with a visual inspection of the funnel plot.[33] The shape of asymmetry indicates the existence of bias, and the accompanying $p < 0.05$ was suggestive of publication bias. Forest plots were generated to show RR with corresponding CI for each study and the overall random-effects pooled estimates. Potential sources of heterogeneity were further explored by visual inspection of the data, forest plots, and subgroup analyses. Finally, sensitivity analyses were used to investigate the robustness of the pooled results. All the analyses were conducted using STATA Statistical Software Release 11.0 (Stata Corporation, College Station, TX).

Results

Study selection and characteristics

A total of 1123 potentially relevant articles were retrieved. Of these, 273 were excluded as they were duplicates. After reviewing the titles and abstracts of the 850 records, 827 studies were excluded due to the fact that they were not relevant, not original articles, or not regarding children with cerebral palsy, thus 23 were retrieved for full-text review. Among the full texts, 11 articles were excluded for the following reasons: it was not possible to translate into English language, it was not possible to access the full texts, they did not answer the research question, the participants were aged over 18 years, or they did not report the definitions and measurements for outcomes. Consequently, 12 studies were deemed suitable for qualitative synthesis.[14–16,18–26] Finally, eight studies were selected for meta-analysis, which consisted of four prospective cohort studies,[14,16,18,22] three retrospective cohort studies,[20,23,24] and one case–control study.[19] Two studies were excluded from the meta-analysis because they did not report effect estimates or there was insufficient information to compute effect estimates,[15,21] the other two were excluded because of data duplication,[25] and different scales were used to report outcomes [26] (Figure 1).

The characteristics of the 12 eligible studies in the qualitative synthesis are shown in Table 1. The studies were conducted in 13 countries (two in Asia, two in North America, and nine in Europe). The sample size of these studies ranged widely from 31 to 9012 participants. Nine studies included all types of cerebral palsy [15,16,19–22,24–26] and three studies [14,18,23] were of some particular types of cerebral palsy. The median length of follow-up period was 5 years (a range of 0–8 years). Ambulatory statuses were assessed by different methods; only four studies [18–20,25] used the same method as defined by the GMFCS.[9] Children were assessed for ambulatory status at the age range of 5–8 years. The total Newcastle–Ottawa Scale scores of the 12 observational studies ranged from 6 to 9.

Qualitative synthesis

There were 12 studies included in the qualitative synthesis. The potential predictors for ambulation in these studies were synthesized from multivariable analysis and were shown to be statistically significant (Table 2). The type of cerebral palsy, early motor milestones, primitive reflexes and postural reactions, visual
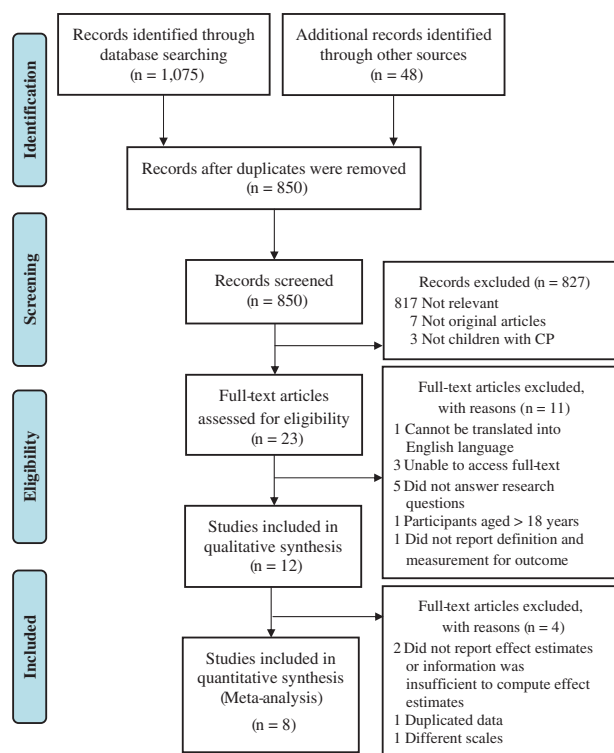
Figure 1. The PRISMA flow Chart of the study selection process.

impairment, intellectual disability, epilepsy or seizure, and ability to self-feed were detected as robust prognostic predictors by several studies.[14–16,18–26] Some studies also found other prognostic predictors, these were gestational age,[16,18,19,23,24] birth weight,[16,18,19,24] gender,[15,19] maternal ethnicity,[15,18] antibiotic use,[18] APGAR score,[19] hyperbilirubinemia,[18] hearing impairment,[16] hand function,[15,20] expressive language,[15,20] body mass index,[20] postural control,[26] reciprocal lower limb movement,[26] microcephaly,[23] and magnetic resonance imaging abnormality.[19]

Quantitative synthesis (meta-analysis)

Pooled RRs and 95% CIs from eight studies were analyzed to determine the significant predictors for ambulation in children with cerebral palsy. Table 3 summarizes the pooled results, heterogeneity statistics, subgroup analyses, and publication bias. Forest plots displaying the meta-analysis of each prognostic predictor are shown in Figure 2.

The data from four studies (983 participants) [14,19,20,22] were used to analyze the prediction of ambulation based on sitting at 2 years of age, because of the completeness of these data. This finding indicated that sitting independently at 2 years of age was good prognosis for ambulation (RR =4.82; 95% CI =3.20–7.24) with non-significant heterogeneity between these studies ($I^2 = 43.8$; $p = 0.148$). The results of sensitivity analyses demonstrated that the association was similar when one study was omitted. Publication bias was not present in this meta-analysis ($p = 0.877$).

Five studies (9914 participants) [14,16,20,22,23] reported an association between visual impairment and ambulation. The results found that the absence of visual impairment was a positive predictor for ambulation (RR =2.62; 95% CI =1.70–4.03) with significant heterogeneity between these studies ($I^2 = 68.0$; $p = 0.014$).

The subgroup analyses showed that the source of heterogeneity was study design (RR$_1$ (hospital based) = 2.01, 95% CI =1.45–2.77; RR$_2$ (population based) = 3.63, 95% CI =3.22–4.09, respectively). The result of publication bias ($p = 0.061$) was not statistically significant. The pooled RRs were not observed to have changed in the sensitivity analysis.

The impact of intellectual disability on ambulation from four studies (9 773 participants) was analyzed.[14,16,19,24] The findings indicated that absence of intellectual disability was a significant predictor for ambulation (RR =2.12; 95% CI =1.35–3.34). Strong heterogeneity was present between these studies ($I^2 = 97.4$; $p = 0.001$). Study design was detected as a confounding factor that led to heterogeneity. The subgroup analysis was stratified by study design gave the following results: RR$_1$ (hospital based) = 1.75, 95% CI =1.59–1.93; RR$_2$ (population based) = 3.08, 95% CI =2.88–3.29, respectively. The sensitivity analysis showed the robustness of pooled RR. Egger's test indicated no significant publication bias ($p = 0.496$).

Meta-analysis of seven studies (10 698 participants) [16,18–20,22–24] suggested a positive association between the absence of epilepsy or seizure and ambulation (RR =1.68; 95% CI =1.41–2.01). Statistically significant heterogeneity was detected by subject ($I^2 = 74.8$; $p = 0.001$). The subgroup analysis showed a difference in the pooled estimates between groups (RR$_1$ (all type of CP) = 1.59, 95% CI =1.32–1.91; RR$_2$ (some type of CP) = 2.69, 95% CI =1.27–5.70). The sensitivity analysis reported no variation in the pooled RRs upon excluding any of the studies. There was no evidence of publication bias ($p = 0.235$).

Discussion

To our current knowledge, this is the first systematic review and meta-analysis of prognostic predictors for ambulation in children with cerebral palsy. The results from meta-analysis confirmed that sitting independently at the age of 2 years, absence of visual impairment, absence of intellectual disability, and absence of epilepsy or seizure are positive predictors for ambulation. Although it provides new strong quantitative evidence about these prognostic predictors, this seems to be expected. As children with more severe cerebral palsy would likely have more concomitant impairments and less likelihood of independent ambulation, these impairments may reflect severity as much as they are predictors for non-ambulation. Hence, it is recommended to always assess for the presence of the aforementioned impairments. These should be detected or resolved as early as possible to prevent or impede the development of physical disability.[34,35]

Furthermore, while some other studies pointed out a few other prognostic predictors including type of cerebral palsy,[15,16,19,20,22–25] primitive reflexes and postural reactions,[21–23] gestational age,[16,18,19,23,24] birth weight,[16,18,19,24] gender,[15,19] ability to feed self,[15,20] hand function,[15,20] expressive language,[15,20] maternal ethnicity,[15,18] antibiotic use,[18] APGAR score,[19] hyperbilirubinemia,[18] hearing impairment,[16] body mass index,[20] postural control,[26] reciprocal lower limb movement,[26] microcephaly,[23] and magnetic resonance imaging abnormality,[19] these prognostic predictors were not statistically significant or were not pooled estimates in our study.

The prognostic predictors were considered eligible for both qualitative and quantitative syntheses of supporting evidence regarding strong ambulatory predictors in children with cerebral palsy. The potential predictors of each study were included in the qualitative synthesis. The studies which did not report the estimated effects or reported insufficient data for the calculation of the estimated effects were excluded from the quantitative

Table 1. Characteristics of studies included in qualitative synthesis.

First author (year)	Study design	Study based on	Country	Participants(n)	Enrollment and follow-up period (year)	% Event	Outcome	Adjustment for covariates	Quality (NOS score)
Beck (1975)[a]	Pro. cohort	Hospital based	USA	Children with all types of CP (73)	1–5	74.0 (54/73)	*Ambulatory status:* "ambulation" (The ability to walk at least 15 m independently on a level surface [i.e., a carpeted or uncarpeted floor, a clipped lawn, or an outdoor smooth surface] without falling.)	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 2
Watt (1989)	Pro. cohort	Hospital based	Canada	Children with all types of CP (74)	1–6	63.5 (47/74)	*Ambulatory status:* "ambulation" (community ambulators). If they are able to walk independently for 15 m on a level surface, with or without ankle-foot orthoses and/or upper extremity aids (Bleck, 1975). Crutches, rollator walkers, and ankle-foot orthoses were allowed. All others, including household and exercise "ambulators," were regarded as non-ambulators, along with those confined to wheelchairs	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 3
Trahan (1994)	Retro. cohort	Hospital based	Canada	Children with quadriplegia or diplegia CP (264)	<2 to >8	53.0 (140/264)	*Ambulatory status* (the childat locomotion level at age six describes the way the child usually moves about at home or at school): - "Able to walk," if he or she could walk (with or without crutches or walkers) when performing all his or her daily activities (community ambulator) - "Unable to walk," if he or she depended on a wheelchair (self-propelled or motorized) for all or some activities	- Age - Therapy - Type of CP	Selection: 4 Comparability: 2 Outcome: 3
Fedrizzi (2000)	Pro.cohort	Hospital based	Italy	Children with spastic diplegia or triplegia (31)	2–6	58.1 (18/31)	*Ambulatory status* (as determined at the most recent follow-up examination): - Independent ambulation - Ambulation only with assistance (sticks, crutches, or walkers) - Ambulation not achieved	- Age - Therapy - Type of CP	Selection: 4 Comparability: 2 Outcome: 3
Wu (2004)[a]	Retro.cohort	Population based	USA	Children with all types of CP who were not yet walking at 2–3 ½ years of age (2295)	<3 to 7	31.2 (716/2295)	*Ambulatory status:* - "Full ambulation," as the child has the ability to walk well alone at least 20 feet without assistive devices, on the basis of the CDER definition for ambulation at level 4; also, the child balances well. Clients who have an unusual or awkward gait but who are not in danger of stumbling or falling should also be rated at this level - "No ambulation," if a client typically uses a wheelchair; rate at level 1	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 2
Lee (2006)	Retro.cohort	Hospital based	Korea	Children with all types of CP (385)	0–5	58.2 (224/385)	*Ambulatory status:* "independent" (walking aids or independently walking, regardless of the distance.)	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 2
Beckung (2008)	Pro.cohort	Population based	14 European centers in 8 countries	Children with all types of CP (9,012)	2 to N/A	69.9 (6301/9012)	*Ambulatory status* (walking at 5 years of age): - Unaided walking - Walking with aids - Unable to walk	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 3
Shevell (2009)[a]	Pro.cohort	Population based	Canada	Children with all types CP (243)	2 to N/A	66.3 (161/243)	*Ambulatory status:* - Ambulant group (GMFCS ≤ III) - Non-ambulant group (GMFCS ≥ IV)	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 2

(continued)

synthesis. The first strong predictor was "sitting independently at 2 years of age". In the meta-analysis, we found that children who had the ability to sit independently before the age of two were more likely to walk unaided, by about 5-folds, than children who had the ability to sit independently only after 2 years of age. Each study [14,19,20,22] concluded that sitting independently at 2 years can be used to predict walking ability in children with cerebral palsy which is in agreeance with the predictive factors of the GMFCS levels.[36] It is clear that early gross motor milestones, especially sitting, are important for predicting walking since anti-gravity muscles for the trunk or postural control during sitting is fundamental for the upright position development.[37,38]

As for the absence of visual impairment, we pooled RRs from five studies.[14,16,20,22,23] which supported the notion that children without visual impairment have the ability to walk unaided more than about 2- to 3-folds compared with children with visual impairment. Additionally, a large population-based study in the United States [15] also found that the absence of blindness was associated with walking independently at the age of 6, by a multi-variable analysis. Children with visual impairment may have more difficulties in developing head and trunk control in exploring their environment because vision is a very important sensorimotor for the development of balance and movement in the first 3 years of life, including walking.[39] In addition, the development of motor milestones in childhood, and the development of cognitive and visual skills are linked to each other and act upon each other.[14]

Furthermore, the absence of intellectual disability is a positive predictor of ambulation. Children with learning disabilities are less able to learn how to walk independently compared with children without any intellectual disability, because intellect or cognition is needed for movement learning.[40] In addition, children with intellectual disability are also observed to have delayed motor milestones and impaired sensorimotor function, which affects ambulation in children.[41,42] The present meta-analysis concluded that children without intellectual disability can walk independently better than children with such condition, by about 2-folds.[14,16,19,24]

Finally, the absence of epilepsy or seizure represented a good predictor of ambulation in children with cerebral palsy. Seizures are abnormal electrical activity of the brain resulting in brain development problem which causes gross motor development failure.[43] The seven studies were combined and the same conclusion was reached: approximately 1–2-folds of the number of children without epilepsy or seizure were able to walk compared with the number of children with these symptoms.[16,18–20,22–24] There was a study by Simard-Tremblay et al. [18] which reported a higher RR because in this study, the specific participants were children with spastic quadriplegia. Quadriplegic children demonstrate more frequent onset of seizures than other types of cerebral palsy.[40]

The high quality of 12 observational studies included in the qualitative synthesis was assessed using the Newcastle–Ottawa Scale (scores obtained; 6–9). Only one case–control study [19] was found to have very low quality. The RRs were used for pooled effect estimates in this meta-analysis because most studies were cohort studies, with only one case-control study. In addition, the prevalence of ambulatory outcome was more than 10% (Table 2). Therefore, the use of RR is more appropriate than the use of OR.[44] We explored the possible sources of heterogeneity by sub-group analyses. The heterogeneity in this study was caused by study designs which included both hospital-based and population-based studies and types of cerebral palsy, which differed from study to study. However, there was a possibility of occurrence of bias because we were unable to exclude some studies,

Table 1. Continued

First author (year)	Study design	Study based on	Country	Participants (n)	Enrollment and follow-up period (year)	% Event	Outcome	Adjustment for covariates	Quality (NOS score)
Simard-Tremblay (2010)	Pro.cohort	Population based	Canada	Children with spastic quadriplegia (85)	Age of outcome =6	23.5 (20/85)	Ambulatory status: - Ambulant group (GMFCS ≤III) - Non-ambulant group (GMFCS ≥ IV)	- Age - Therapy - Type of CP	Selection: 4 Comparability: 2 Outcome: 2
Kutco (2011)	Case control	Hospital based	Poland	Children with all types of CP aged 6ged years (345)	2–8	61.4 (212/345)	Ambulatory status: - Ambulant group (GMFCS ≤III) - Non-ambulant group (GMFCS ≥ IV)	Age, therapy	Selection: 3 Comparability: 2 Outcome: 1
First author (year)	Study design	Study based on	Country	Participants (n)	Enrollment and follow-up period (year)	% Event	Outcome	Adjustment for covariates	Quality (NOS score)
Keeratisi-roj (2015)	Retro.cohort	Hospital based	Thailand	Children with all types of CP aged 2–18 years (533)	NA	48.2 (257/533)	Ambulatory status: - Ambulant group (GMFCS I–II) - Assisted ambulation (GMFCS III) - Non-ambulant group (GMFCS IV–V)	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 2
Begnoche (2015)[a]	Retro.cohort	Population based	USAand Canada	Children with all types of CP in GMFCS II–III aged 2–6 years (80)	NA	26.3 (21/80)	Ambulatory status: "Independent walking ability" The ability to walk ≥3 steps independently, was measured using item 69 on the Gross Motor Function Measure (GMFM-66)	- Age - Therapy	Selection: 4 Comparability: 2 Outcome: 2

CP: cerebral palsy; GMFCS: Gross Motor Function Classification System; NOS: Newcastle–Ottawa Scale; Pro. : prospective; Retro.: retrospective.
[a]Studies were excluded from the meta-analysis.

Table 2 Prognostic predictors of studies included in qualitative synthesis.

Prognostic predictor	Bleck (1975)[a]	Watt (1989)	Trahan (1994)	Fedrizzi (2000)	Wu (2004)[a]	Lee (2006)	Beckung (2008)	Shevell (2009)[a]	Simard-Tremblay (2010)	Kulak (2011)	Keeratisiroj (2015)	Begnoche (2015)[a]
Type of cerebral palsy	*	*	**		**	#	*	*		#	*, **	
Early motor milestones (1le years)												
Prone weight on hands				**								
Rolling			*	*	**							
Crawling			*		*							
Sitting independently		*	**	*	**					*	*, **	
Pull to stand					**					*		**
Primitive reflexes and postural reactions												
Tonic labyrinthine reflex	*	*	*									
Asymmetrical tonic neck reflex	*	*	**									
Symmetrical tonic neck reflex	*	*	*									
Moro reflex	*	*	**									
Extensor thrust	*											
Foot placement reaction	*	*										
Parachute reaction	*	*										
Visual impairment		#		**	**		**			*	*	
Intellectual disability		#		*	*		**			*	*	
Epilepsy/seizure		#			*	*	*		*			
Ability to feed self					*	*				*	*, **	
Gestational age			*		*	#	*		*	*	*	
Birth weight					*	#	*		*	*	*	
Gender					*					#		
Hand function							*					
Expressive language/say simple words												
Maternal ethnicity									*			
Antibiotic use									*			
APGAR score									*	*		
Hyperbilirubinemia												
Hearing impairment												
Body mass index											*	
Postural control (GMFM, 53)												*
Reciprocal lower limb movement (GMFM, 45)												*
Microcephaly			*									
Magnetic resonance imaging abnormality										*		

[a]Studies were excluded from the meta-analysis. GMFM: Gross Motor Function Measurement.
*Significance for univariable analysis.
**Significance for multivariable analysis.
#Influence.
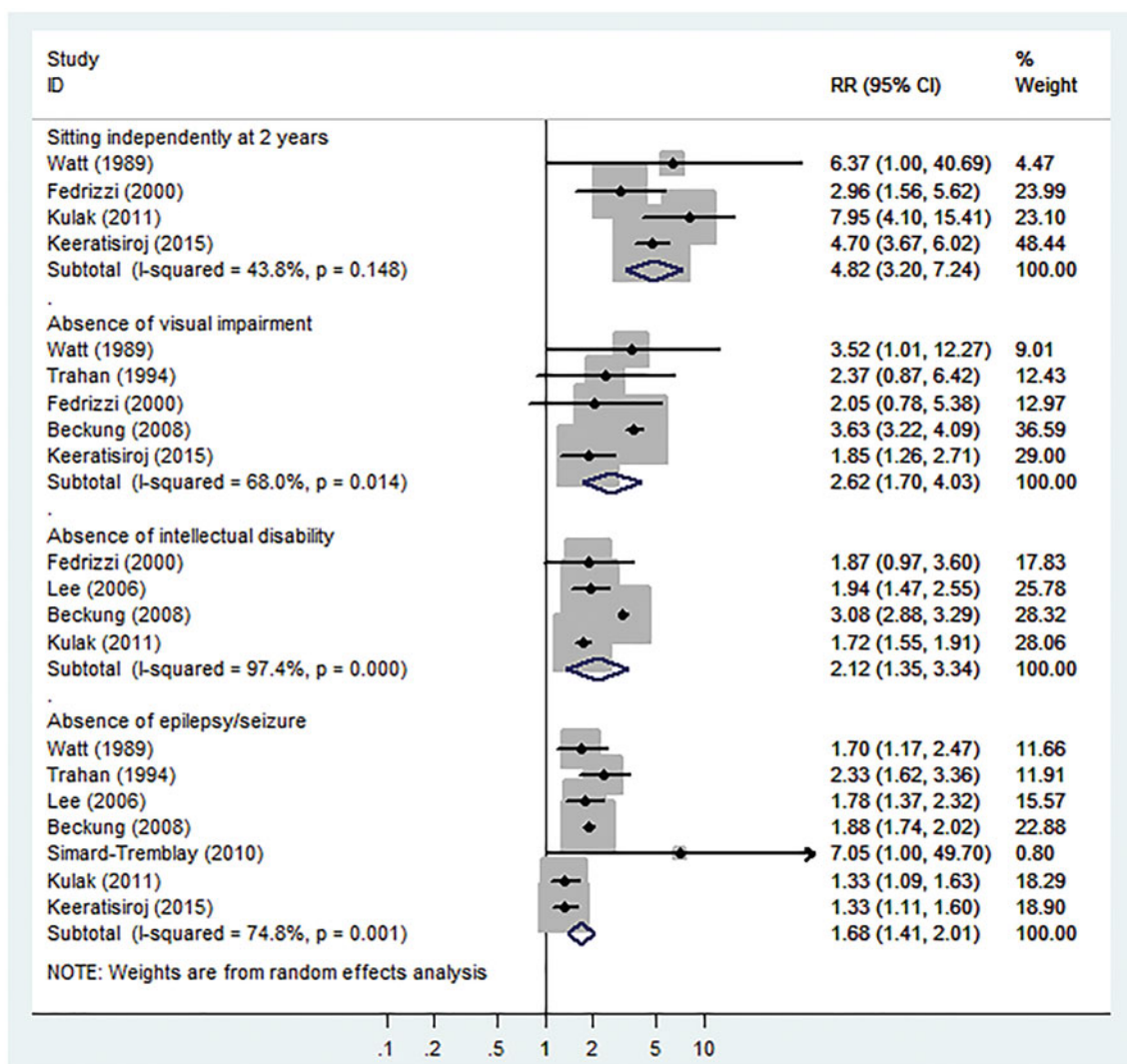
Figure 2. Forest plots displaying the meta-analysis of significant predictors for ambulation in children with cerebral palsy.

since the number of studies was limited. In addition, the interpretation of the Q-test and I^2 should be performed with care since the meta-analysis of a few studies can pose a problem of reducing the power of the test.[31] Furthermore, although the RRs of each study were different, they were of the same direction. Plus, subgroup analyses were used to identify source of heterogeneity were found not to affect the overall findings.

The systematic review of prognostic predictors for ambulation in children with cerebral palsy was concluded from 12 studies conducted worldwide with 13 420 children with cerebral palsy. However, there were some limitations that must be considered. First, the RRs were pooled from univariable meta-analysis of prognostic predictors. Multivariable meta-analysis could not be performed because there were only one to three studies per predictor with the adjusted covariates.[14–16,20,23] These studies could not be pooled together because of the difference in the effect estimates. Therefore, univariable meta-analysis was the most appropriate method for pooled RRs in the present study. Second, there were not sufficient numbers of studies to enable the use of meta-regression. However, the influences of some confounding factors (age, therapy, and type of cerebral palsy) in the various studies were controlled by a study design. Finally, the ambulatory status outcomes were defined by various operational definitions.

There were four studies which defined the ambulant group and the non-ambulant group with the GMFCS,[18–20,25] and other studies defined the meaning of walking independently slightly differently with regards to distance, environment, or age of children. For instance, ambulant group was defined as that of children with cerebral palsy who walk well alone at least 15 m in two studies [21,22] and 20 m in one study.[15] Nevertheless, all definitions clearly identified the ability to walk.

Conclusion

In summary, the present meta-analysis confirmed that sitting independently at 2 years of age, absence of visual impairment, absence of intellectual disability, and absence of epilepsy or seizure are good predictors for ambulation in children with cerebral palsy. Therefore, in determining therapeutic plans and rehabilitation goals for children with cerebral palsy, these factors should be taken into consideration in order to encourage children with cerebral palsy to walk with their full potential. Although evidence suggests that the likelihood of walking independently in children with independent sitting after 2 years is less than children who are able to sit independently at 2 years, children in the former

Table 3. Meta-analysis and subgroups analysis of significant predictors for ambulation.

		Heterogeneity		Meta-analysis,subgroup analysis		
Total or subgroup	Study (n)	I^2 (%)	Q-test p values	Pooled RR (95% CI)	p values	Egger's test p values
Sitting independently at 2 years	4	43.8	0.148	4.82 (3.20–7.24)	<0.001	0.877
Absence of visual impairment	5	68.0	0.014	2.62 (1.70–4.03)	<0.001	0.061
Study design						
Hospital based	4	0	0.785	2.01 (1.45–2.77)	<0.001	
Population based	1	–	–	3.63 (3.22–4.09)	<0.001	
Absence of intellectual disability	4	97.4	0.001	2.12 (1.35–3.34)	<0.001	0.496
Study design						
Hospital based	3	0	0.541	1.75 (1.59–1.93)	<0.001	
Population based	1	–	–	3.08 (2.88–3.29)	<0.001	
Absence of epilepsy/seizure	7	74.8	0.001	1.68 (1.41–2.01)	<0.001	0.235
Subject						
All type of CP	5	79.2	0.001	1.59 (1.32–1.91)	<0.001	
Some type of CP	2	20.7	0.262	2.69 (1.27–5.70)	0.010	

RR: relative risk; CI: confidence interval; CP: cerebral palsy.

group are still able to practice walking independently, since there are other prognostic predictors for ambulation.

Disclosure statement

References

[1] Cans C, De-la-Cruz J, Mermet M-A. Epidemiology of cerebral palsy. Paediatr Child Health. 2008;18:393–398.

[2] Krägeloh-Mann I, Cans C. Cerebral palsy update. Brain Dev. 2009;31:537–544.

[3] Sellier E, Platt MJ, Andersen GL, et al. Decreasing prevalence in cerebral palsy: a multi-site European population-based study, 1980 to 2003. Dev Med Child Neurol. 2016;58:85–92.

[4] Reid SM, Meehan E, McIntyre S, et al. Temporal trends in cerebral palsy by impairment severity and birth gestation. Dev Med Child Neurol. 2016;58 Suppl 2:25–35.

[5] Oskoui M, Coutinho F, Dykeman J, et al. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. Dev Med Child Neurol. 2013;55:509–519.

[6] Odding E, Roebroeck ME, Stam HJ. The epidemiology of cerebral palsy: incidence, impairments and risk factors. Disabil Rehabil. 2006;28:183–191.

[7] World Health Organization. International classification of functioning, disability, and health. Geneva: World Health Organization; 2001 [cited 2011 6 February]. Available from: http://www.who.int/classifications/icf/en/.

[8] Palisano R, Rosenbaum P, Walter S, et al. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol. 1997;39:214–223.

[9] Rosenbaum PL, Palisano RJ, Bartlett DJ, et al. Development of the Gross Motor Function Classification System for cerebral palsy. Dev Med Child Neurol. 2008;50:249–253.

[10] Molnar GE. Cerebral palsy: prognosis and how to judge it. Pediatr Ann. 1979;8:596–605.

[11] Morgan P, McGinley J. Gait function and decline in adults with cerebral palsy: a systematic review. Disabil Rehabil. 2013;36:1–9.

[12] Sala DA, Grant AD. Prognosis for ambulation in cerebral palsy. Dev Med Child Neurol. 1995;37:1020–1026.

[13] Montgomery PC. Predicting potential for ambulation in children with cerebral palsy. Pediatr Phys Ther. 1998;10:148–155.

[14] Fedrizzi E, Facchin P, Marzaroli M, et al. Predictors of independent walking in children with spastic diplegia. J Child Neurol. 2000;15:228–234.

[15] Wu YW, Day SM, Strauss DJ, et al. Prognosis for ambulation in cerebral palsy: a population-based study. Pediatrics. 2004;114:1264–1271.

[16] Beckung E, Hagberg G, Uldall P, et al. Probability of walking in children with cerebral palsy in Europe. Pediatrics. 2008;121:e187–e192.

[17] Gokkaya NKO, Caliksan A, Karakus D, et al. Relation between objectively measured growth determinants and ambulation in children with cerebral palsy. Turk J Med Sci. 2009;39:85–90.

[18] Simard-Tremblay E, Shevell M, Dagenais L. Determinants of ambulation in children with spastic quadriplegic cerebral palsy: a population-based study. J Child Neurol. 2010;25:669–673.

[19] Kułak W, Sendrowski K, Okurowska-Zawada B, et al. Prognostic factors of the independent walking in children with cerebral palsy. Neurologia Dziecięca. 2011;20:29–34.

[20] Keeratisiroj O, Thawinchai N, Siriratiwat W, et al. Prognostic predictors for ambulation in Thai children with cerebral palsy aged 2 to 18 years. J Child Neurol. 2015;30:1812–1818.

[21] Bleck EE. Locomotor prognosis in cerebral palsy. Dev Med Child Neurol. 1975;17:18–25.

[22] Watt JM, Robertson CMT, Grace MGA. Early prognosis for ambulation of neonatal intensive care survivors with cerebral palsy. Dev Med Child Neurol. 1989;31:766–773.

[23] Trahan J, Marcoux S. Factors associated with the inability of children with cerebral palsy to walk at six years: a retrospective study. Dev Med Child Neurol. 1994;36:787–795.

[24] Lee JH, Koo JH, Jang DH, et al. The functional prognosis of ambulation in each type of cerebral palsy. J Korean Acad Rehabil Med. 2006;30:315–321.

[25] Shevell MI, Dagenais L, Hall N. The relationship of cerebral palsy subtype and functional motor impairment: a population-based study. Dev Med Child Neurol. 2009;51:872–877.

[26] Begnoche DM, Chiarello LA, Palisano RJ, et al. Predictors of independent walking in young children with cerebral palsy. Phys Ther. 2016;96:183–192.

[27] Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. J Am Med Assoc. 2000;283: 2008–2012.

[28] Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015; 4:1–9.

[29] Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa (ON): Ottawa Hospital Research Institute; 2010 [cited 2012 Sep 6]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.

[30] Der Simonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7:177–188.

[31] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21:1539–1558.

[32] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–560.

[33] Harbord RM, Egger M, Sterne JA. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. Stat Med. 2006;25:3443–3457.

[34] Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol. 2007;49:8–14.

[35] Scherzer AL. Early diagnosis and interventional therapy in cerebral palsy: an interdisciplinary age-focused approach. New York: M. Dekker; 2001.

[36] Rosenbaum PL, Walter SD, Hanna SE, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. JAMA. 2002;288:1357–1363.

[37] Kimura-Ohba S, Sawada A, Shiotani Y, et al. Variations in early gross motor milestones and in the age of walking in Japanese children. Pediatr Int. 2011;53:950–955.

[38] de Graaf-Peters VB, Blauw-Hospers CH, Dirks T, et al. Development of postural control in typically developing children and children with cerebral palsy: possibilities for intervention? Neurosci Biobehav Rev. 2007;31:1191–1200.

[39] Stiers P, Vanderkelen R, Vanneste G, et al. Visual-perceptual impairment in a random sample of children with cerebral palsy. Dev Med Child Neurol. 2002;44:370–382.

[40] Martin SC, Kessler M. Cerebral Palsy. Neurologic interventions for physical therapy. St. Louis: Elsevier Saunders; 2006. p. 124–152.

[41] Hogan DP, Rogers ML, Msall ME. Functional limitations and key indicators of well-being in children with disability. Arch Pediatr Adolesc Med. 2000;154:1042–1048.

[42] Wuang YP, Wang CC, Huang MH, et al. Profiles and cognitive predictors of motor functions among early school-age children with mild intellectual disabilities. J Intellect Disabil Res. 2008;52:1048–1060.

[43] Carlsson M, Hagberg G, Olsson I. Clinical and aetiological aspects of epilepsy in children with cerebral palsy. Dev Med Child Neurol. 2003;45:371–376.

[44] Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998;280:1690–1691.

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Title: Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational studies

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Appendix D

Keeratisiroj O, Thawinchai N, Buntragulpoontawee M, Siritaratiwat W, Derivation of an ambulatory score chart for Thai children with cerebral palsy aged 2–18. J Med Assoc Thai. 2016;99: 1298-305.

Derivation of an Ambulatory Prognostic Score Chart for Thai Children with Cerebral Palsy Aged 2 to 18

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Background: Most parents want to know that their children with cerebral palsy will be able to walk. A simple tool to predict ambulatory status and one uses The Gross Motor Function Classification System is still lacking.

Objective: To develop a simple prognostic score chart for predicting ambulatory status in Thai children with cerebral palsy.

Material and Method: Four hundred seventy one children with cerebral palsy aged 2 to 18 registered and treated at six special schools or hospitals for children with physical disability between 2008 and 2013 were recruited. Baseline characteristics and clinical histories of children with cerebral palsy were collected from medical and physical therapy records. Ambulatory status was classified as three ordinal scales by The Gross Motor Function Classification System - Expanded and Revised version.

Results: Multivariable ordinal continuation ratio logistic regression analysis identified age, type of cerebral palsy, sitting independently at the age of two, and eating independently as significant predictors of ambulation. These items were combined into a clinical prediction score: non-ambulation (scores <7), assisted ambulation (scores 7 to 8), and independent ambulation (scores >8).

Conclusion: The prognostic tool has high discriminative values of ambulatory status among children with cerebral palsy. However, the validation of this tool needs to be tested in other subjects before clinical practice application.

Keywords: Cerebral palsy, Clinical prediction rule, Decision support techniques, Prognosis, Walking

Cerebral palsy (CP) is a disorder of motor control as a result of damage to the developing brain[1]. In developed countries, over the last three decades, the probability of survival has increased even in children with severe disabilities. In contrast, the prevalence of CP has not decreased but remained constant as about 2 to 3 per 1,000 live births[2]. Thailand has never had a true study on the prevalence of CP because there is no database or Cerebral Palsy Registry. There is only reported Disability Survey by the National Statistical Office, showed that among the 29,841 persons with CP, the most (12,019) were located in the northeastern part of the country, followed by the remaining (8,944) in northern Thailand[3].

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When children are first diagnosed as being CP, most parents ask the following questions: 'Will my child walk?' and 'When will he/she walk?'. The prognosis for their ambulation is very difficult because of several factors can influence the ambulatory status of a child during his/her growth. Nonetheless, the identification of predictors for ambulation is most important in order to assist in formulating an appropriate plan of intervention[4-6]. This is important for prognostic capacity regard to walking tends to be poor, an appropriate treatment planning is the most effective way to prevent the loss of ambulatory capacity[7].

The scoring method for the prognosis for walking in children with CP has been previously established by Bleck in 1975[8]. This scoring system has seven primitive reflexes and postural reactions as predictors, while there have also been other clinical predictors affecting walking prognosis[4,5,9-13]. This scoring method was discriminated into good prognosis, guarded prognosis, and poor prognosis. He stated that

it appeared simple, easy to understand, and easy to apply. It may be inappropriate to use in some context; however, a recent correlational study in Japan[14] showed that there was no difference in Bleck's scores between the ambulation group and the non-ambulation group. A large retrospective study conducted by Wu et al[5] created a simple tool for predicting the probability of ambulatory outcome from various levels in children with CP aged 2 to 14. This tool was divided into four ambulatory charts according to gross motor function achieved at the age of two, using Aalen-Johansen estimators of long-term transition probabilities. Additionally, there were also prognostic tools of gross motor function[15,16]. The gross motor function curves among the 5-level The Gross Motor Function Classification System (GMFCS) were constructed to inform regarding the prognosis of children with CP at each age.

Performing a comparison between the different studies is difficult because of the variations in the definitions of ambulatory operational[17]. In 1997, Palisano et al[18] created a five-level of GMFCS for children with CP and edited it in 2007[19]. Only the studies, recently, of Simard-Tremblay et al[12] and Kułak et al[13] used the GMFCS as a tool to classify ambulation. Many experts in clinical practice have developed their own specific criteria for predicting the ambulatory status in these children. These criteria may provide reasonable prognostic accuracy, but they are not necessarily transferable to and applicable in other contexts[4]. Although the prognostic tools for gross motor function of children with CP have been developed[5,8,15,16], a simple tool to predict ambulatory status and one that uses GMFCS is still lacking. Therefore, the study aims to develop a simple prognostic score chart for predicting the ambulatory status in Thai children with CP from the authors' prognostic predictors[20].

Material and Method
Ethics approval

The present study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University (The IRB approval number 188/2013), and Rajanagarindra Institute of Child Development, Chiang Mai. The participants were informed of the purpose and procedures of the present research. All the participants or their parents signed a written informed consent to participate in the study.

Study design and data collection

The medical and physical therapy records of children with CP were retrospectively reviewed between 2008 and 2013. They were registered and treated at six special schools or hospitals for children with physical disability in northeastern and northern Thailand. They were recruited if aged 2 to 18 and have been diagnosed by physicians or physiotherapists. The following criteria were the reasons for exclusion from the study: the children being duplicated between settings, not meeting the inclusion criteria, being diagnosed after two years old, unable to contact the parents or caregivers, death, and declining to participate.

Outcome variable

The GMFCS was used to describe walking ability. This tool had five ordinal levels: I) walks without limitations, II) walks with limitations, III) walks using a hand-held mobility device, IV) self-mobility with limitations or may use powered mobility, and V) transported in a manual wheelchair[19]. The subjects were assessed using the GMFCS - Expanded and Revised family and self-report questionnaires, which have been allowed to be translated into Thai language[21]. We classified the ambulatory status as three levels: independent ambulation (GMFCS I-II), assisted ambulation (GMFCS III), and non-ambulation (GMFCS IV-V).

Explanatory variable

The patient's data included for the present study were as follows: prognostic predictors (age, type of CP, sitting independently at age two, and eating independently)[20] and other variables (gender, body mass index, caregivers, gestational age, birth weight, hyperbilirubinemia, epilepsy or seizure, intellectual impairment, visual impairment, hearing impairment, hand function, speech, medication, history of orthopedic surgery, and orthotics use). These variables were confirmed and the GMFCS was assessed using interviews on site, telephone, or mail.

Statistical analysis

The authors selected 471 cases having complete significant predictors' values for analyses. An adequate sample size was considered that at least 10 to 15 subjects per predictor should be included in the study[22]. For this reason, the present study had an adequate sample with 471 subjects, and the final model contained 10 variables. Then, the subjects were categorized into three groups by their GMFCS: independent ambulation, assisted ambulation, and non-ambulation (criterion-classified ambulatory

status). Baseline characteristics and clinical histories data were described by descriptive statistics: frequencies and percentages for categorical data, mean, and standard deviation for continuous data. The different data between the three groups were tested using the nonparametric test for trends across the ordered groups.

Multivariable ordinal continuation ratio logistic regression was used to analyze after the candidate predictors (*p*-value ≤0.20) were selected through univariable analysis. Coefficients of the significant predictors from multivariable models were converted into scores by division of the lowest coefficient, and they were rounded off to the nearest integer or half. The items and the total scores for each subject were created and used to represent the summary measure for predicting the ambulatory status in children with CP, and these were categorized into three levels (score-classified ambulatory status).

The discriminative and predictive abilities of the ambulatory status scores were presented with probability curves. The receiver operating characteristic (ROC) curve which was used to assess the probability of the total score showed ambulation. The Hosmer and Lemeshow Chi-square goodness-of-fit test[23] was made use to compare how well the predicted probabilities fit with the actual probabilities. Score-classified ambulatory statuses were compared to criterion-classified ambulatory statuses to indicate the estimation validity by percentage of agreement. All the analyses were performed using STATA statistical software Release 11.0 (Stata Corporation, College Station, TX) and those values for which *p*-value <0.05 were considered significant.

Results

There were 533 children with CP who were included in the current study, but we found missing values for some significant predictors in 62 subjects (11.6%), the remaining 471 subjects were considered for the data analysis. These missing predictors were type of CP (5.6%), and sitting independently at age two (6.2%). The subjects were classified into three groups according to their GMFCS levels: non-ambulation (n = 264), assisted ambulation (n = 57), and independent ambulation (n = 150) as illustrated in Fig. 1. Baseline characteristics and clinical histories, as illustrated in Table 1, showed that there were similarities as regards gender, caregivers, gestational age, birth weight, hyperbilirubinemia, intellectual impairment, hearing impairment, and orthotics use between the three groups.

In multivariable analysis, the significant predictors were age, type of CP, sitting independently at age two, and eating independently. Item scores for the significant predictors of the ambulatory status were derived from the coefficients. They varied from 0 to 6, and the total scores ranged from 0 to 12, as illustrated in Table 2. Fig. 2 demonstrated a simple score chart for predicting the ambulatory status, in which the subjects were classified into three groups according to their total scores: non-ambulation (scores <7), assisted ambulation (scores 7 to 8), and independent ambulation (scores >8). The author's scores predicted the non-ambulation group correctly in 244 out of 264, assisted ambulation in 10 out of 57, and independent ambulation in 113 out of 150. The prognostic estimation validity of the subjects into their original levels had a correctness percentage of 77.9%, underestimation had a correctness percentage of 12.1%, and overestimation had a correctness percentage of 10%, as illustrated in Table 3.

The distributions of the ambulatory status were presented with mean total scores: 3.4±2.5 in non-ambulation, 7.5±2.0 in assisted ambulation, and 9.2±1.8 in independent ambulation, as shown in Table 3. Fig. 3 illustrated the probability curves of the ambulatory status scores, which discriminate the non-ambulation group from the other groups (area
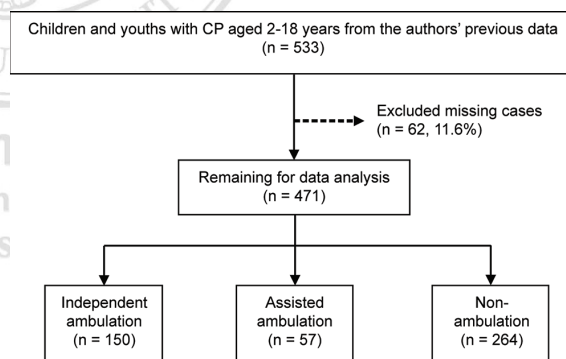

Fig. 1 Flow chart of data in the study.

Fig. 2 The ambulatory prognostic score chart for children with cerebral palsy.

Table 1. Baseline characteristics and clinical histories of children with cerebral palsy

Variable	All subjects* (n = 471)	Non-ambulation* (n = 264)	Assisted ambulation* (n = 57)	Independent ambulation* (n = 150)	*p*-value#
Age (year)	10.1±4.3	9.2±4.2	10.9±4.0	11.4±4.1	<0.001
Male gender	272 (57.8)	147 (55.7)	34 (59.7)	91 (60.7)	0.312
Body mass index (kg/m²) (n = 407)	15.6±3.5	15.0±3.4	16.3±4.4	16.2±3.1	<0.001
Parents caregiver	345 (73.3)	189 (71.6)	41 (71.9)	115 (76.7)	0.293
Type of CP					<0.001
Spastic quadriplegia	136 (28.9)	130 (49.2)	5 (8.8)	1 (0.7)	
Spastic diplegia	131 (27.8)	59 (22.3)	31 (54.4)	41 (27.3)	
Spastic hemiplegia	109 (23.2)	15 (5.7)	12 (21.0)	82 (54.7)	
Dyskinesia	50 (10.6)	32 (12.2)	3 (5.3)	15 (10.0)	
Ataxia	10 (2.1)	0 (0)	2 (3.4)	8 (5.3)	
Hypotonia	9 (1.9)	7 (2.7)	1 (1.8)	1 (0.7)	
Mixed	26 (5.5)	21 (7.9)	3 (5.3)	2 (1.3)	
Gestational age (week) (n = 453)	35.5±4.2	35.5±4.2	34.7±4.7	35.8±3.8	0.720
Birth weight (kg) (n = 451)	2.5±0.8	2.5±0.8	2.3±0.8	2.5±0.8	0.655
No Hyperbilirubinemia (n = 453)	347 (76.6)	195 (76.5)	46 (83.6)	106 (74.1)	0.694
No Epilepsy/seizure (n = 468)	250 (53.4)	124 (47.2)	42 (73.7)	84 (56.8)	0.028
Sitting independently at age 2	188 (39.9)	29 (11.0)	35 (61.4)	124 (82.7)	<0.001
No intellectual impairment	376 (79.8)	217 (82.2)	46 (80.7)	113 (75.3)	0.100
No visual impairment	406 (86.2)	214 (81.1)	52 (91.2)	140 (93.3)	<0.001
No hearing impairment	452 (96.0)	253 (95.8)	53 (93.0)	146 (97.3)	0.535
Have functional use of hands	385 (81.7)	181 (68.6)	56 (98.3)	148 (98.7)	<0.001
Eating independently	278 (59.0)	96 (36.4)	50 (87.7)	132 (88.0)	<0.001
Speech (says single words, sentences)	276 (58.6)	111 (42.1)	46 (80.7)	119 (79.3)	<0.001
Medication history (n = 466)	349 (74.9)	213 (81.6)	34 (59.7)	102 (68.9)	0.002
Orthopedic surgery (n = 460)	53 (11.5)	19 (7.3)	12 (21.1)	22 (15.4)	0.008
Orthotics use (n = 458)	167 (36.5)	94 (35.7)	27 (48.2)	46 (33.1)	0.763

CP = cerebral palsy; SD = standard deviation

* Values represent n (%) for categorical data and mean ± SD for continuous data

Trend test across the ordered groups

Table 2. Item score for significant predictors of ambulatory status (n = 471)

Predictors	OR (95% CI)*	*p*-value*	Coefficient*	Scores
Age (year)				
2 to less than 6	Reference		Reference	0
6 to less than 12	2.07 (1.07 to 3.98)	0.030	0.73	1
12 to 18	3.26 (1.59 to 6.72)	0.001	1.18	1.5
Type of CP				
Spastic quadriplegia	Reference		Reference	0
Mixed	3.94 (1.09 to 14.25)	0.037	1.37	2
Hypotonia	9.76 (1.89 to 50.39)	0.007	2.28	3
Spastic diplegia	8.07 (3.27 to 19.95)	<0.001	2.09	3
Dyskinesia	12.09 (4.42 to 33.04)	<0.001	2.49	3.5
Spastic hemiplegia	40.47 (15.37 to 106.56)	<0.001	3.70	5
Ataxia	91.49 (15.26 to 548.58)	<0.001	4.52	6
Sitting independently at age 2				
No	Reference		Reference	0
Yes	7.74 (4.85 to 12.34)	<0.001	2.05	3
Eating independently				
No	Reference		Reference	0
Yes	2.95 (1.65 to 5.24)	<0.001	1.08	1.5

CI = confidence interval; CP = cerebral palsy; OR = odds ratio

* Analysis using multivariable ordinal continuation ratio logistic regression

Table 3. Score-classified ambulatory status, criterion-classified ambulatory status, and prognostic estimation validity

Score-classified ambulatory status	Total score	Criterion-classified ambulatory status			Validity*		
		Non-ambulation	Assisted ambulation	Independent ambulation	% over	% correct	% under
Mean ± SD		3.4±2.5	7.5±2.0	9.2±1.8			
IQR		1 to 5.5	6 to 9	8.5 to 10.5			
Non-ambulation (n = 284)	<7	244	20	20	-	51.8	8.5
Assisted ambulation (n = 34)	7 to 8	7	10	17	1.5	2.1	3.6
Independent ambulation (n = 153)	>8	13	27	113	8.5	24.0	-
Total (n = 471)	0 to 12	264	57	150	10.0	77.9	12.1

IQR = interquartile range; SD = standard deviation
* Percentage of total subjects

None vs. others (AuROC = 0.9391, 95% CI = 0.9193 to 0.9589, graph not shown)
Independent vs. others (AuROC = 0.9205, 95% CI = 0.8969 to 0.9440, graph not shown)
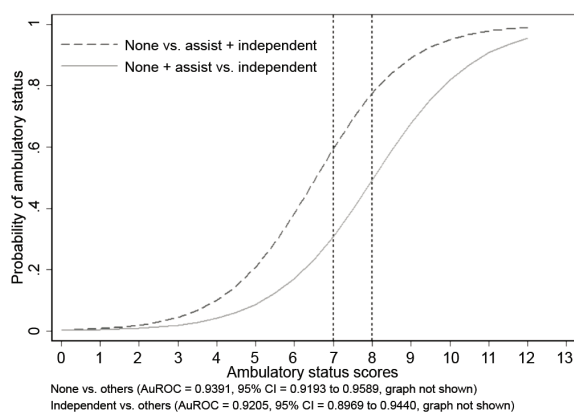
Fig. 3 The discrimination of the ambulatory status scores.

under the receiver operating characteristic curve; AuROC = 0.9391, graph not shown), and discriminate the independent ambulation group from the other groups (AuROC = 0.9205, graph not shown).

Discussion

This is the first development of a simple ambulatory score chart of Thai children with CP based on the operational definition outcome from GMFCS. It was constructed using routine data including age, type of CP, sitting independently at the age of two, and eating independently. The ambulatory status was classified into three levels according to their GMFCS and total score: independent ambulation, assisted ambulation, and non-ambulation. The ability to predict ambulation in these children appeared accurate, with 77.9% of correctness and high discrimination with AuROC more than 0.9.

The authors' prognostic tool is different from the previous tools in both outcome and predictors, including techniques and applications. The significant predictors of this score chart have been mentioned in

the authors' previous study[20]. It is well known that age or maturation is associated with different aspects of child development including walking[17]. The type of CP and gross motor skills (sitting independently) were found to have a strong association with ambulation in several previous studies for a long time[4,5,9,10,13,17,24,25]. In addition, it had been recently found that eating independently was associated with ambulation in two previous studies[5,13]. Nevertheless, strong predictors such as primitive reflexes and postural reactions were excluded from the present study because the authors took into consideration of predictors from routine data to clinical usefulness.

The ambulatory prognostic score chart was developed for the simple use of clinicians and therapists. The ambulatory outcome was divided into three groups, which may be useful for clinical practice. The first group, of children scoring <7, was classified as the 'non-ambulation' group. The health care team should inform the parents that the children could not walk in the first age range, and the team should have a treatment plan chalked out with the parents to improve the walking ability of the children to bring it to its full potential. If the children were more likely to continue as having non-ambulation in the next age, their parents should plan to adjust the environmental context and the daily life of the children with assistive devices. The second group, with the children scoring from 7 to 8, was classified as the 'assisted ambulation' group. In the first stage, these children were assisted to walk with aids such as wheel walkers, but when they grow up, there might be a possibility that the children will walk independently. Thus, the health care team should plan for parents to emphasize the enhancement of the children's walking ability. The last group, of children scoring >8, was classified as the 'independent ambulation' group. These children could walk

independently before six years of age, so an appropriate treatment plan would be to maintain the walking ability and the cardiopulmonary fitness of the children or to encourage social participation. When children with CP grow into adolescence, they may effectively experience a decline in the walking ability. However, the present data show that adolescents with CP aged 12 to 18 succeeded in walking in comparison with children with CP aged 2 to 6 (OR = 3.26; 95% CI = 1.59 to 6.72). There are studies that support the possibility that some children with CP continue to maintain and develop the walking ability into adolescence[5,26-28]. On the other hand, Kerr et al[29] point out that the lowest effective walking ability is at about 12 years of age, and that deterioration of the gross motor skill takes over after the age of 13. This issue in adolescence remains unclear. However, in adults, it has been reported that when children with CP grow into adulthood (>20 years), they have the potential to experience walking decline due to fatigue, inefficiency of ambulation, or increased joint pains[27,30].

For instance, the sum scores for a child with spastic diplegia (score = 3) aged four (score = 0) who can sit independently before age two (score = 3) and eats independently now (score = 1.5) is 7.5 (0+3+3+1.5, see Fig. 1). This means that in the period of age ranging from 2 years to 6 years, he is able to walk with assistive devices. When he grows up (score = 1, for the age range 6 to 12), the sum scores will have one point added, as 8.5 (1+3+3+1.5, see Fig. 1), which means that he has a chance to walk independently. However, the present data still had 10% of overestimation (children were detected as over true ambulatory levels) and 12.1% of underestimation (children were detected as under true ambulatory levels) which can be the result of other predictors, such as primitive reflexes, not being taken into consideration for the analyses, but this is acceptable. So, this tool is reliable for the prediction of the ambulatory status in children with CP. Additionally, the discriminative and predictive abilities of the authors' tool showed that the performance of the model was good.

Some limitations of the present study need to be mentioned. First, the routine data had some of the predictors missing; however, the authors assumed that they were missing completely at random. Consequently, we confirm that the data collection was unbiased. Second, primitive reflex and postural reaction, which are associated with ambulatory status, were excluded from the present study since it is not routine data. Finally, this score chart may be restricted,

in generalization to other contexts, because it was constructed from routine clinical practice of the settings in northeastern and northern Thailand. These settings are in the form of hospitals or special schools for children with physical disability that the parents take their children to for treatment when they find their children encountering problems with regard to carrying out normal functions, routine functions which these children are unable to perform since birth. Some children with CP who walk independently, may not be discovered in the present study. Thus, this prognostic tool holds potential and should be externally validated in a different setting before utilization in clinics.

In conclusion, a simple ambulatory prognostic score chart was derived from age, type of CP, sitting independently at the age of two, and eating independently, which shows high discriminative values of ambulatory status in children with CP. However, the validation of this score chart should be tested in other subjects before clinical practice application.

What is already known on this topic?

Type of CP, sitting independently at age two, and eating independently are prognostic predictors for ambulation in children with CP. Age is associated with ambulation in children with CP.

What this study adds?

The ambulatory prognostic score chart is developed from age, type of CP, sitting independently at the age of two, and eating independently can predict ambulatory status in Thai children with CP aged 2 to 18 years.

Potential conflicts of interest

None.

References

1. Koman LA, Smith BP, Shilt JS. Cerebral palsy. Lancet 2004; 363: 1619-31.
2. Krageloh-Mann I, Cans C. Cerebral palsy update. Brain Dev 2009; 31: 537-44.
3. Social Statistics Group. The 2007 disability survey. Bangkok: National Statistical Office of Thailand; 2008.
4. Fedrizzi E, Facchin P, Marzaroli M, Pagliano E, Botteon G, Percivalle L, et al. Predictors of independent walking in children with spastic diplegia. J Child Neurol 2000; 15: 228-34.
5. Wu YW, Day SM, Strauss DJ, Shavelle RM. Prognosis for ambulation in cerebral palsy: a population-based study. Pediatrics 2004; 114: 1264-71.
6. Novak I, Hines M, Goldsmith S, Barclay R. Clinical prognostic messages from a systematic review on cerebral palsy. Pediatrics 2012; 130: e1285-e1312.
7. Bottos M, Gericke C. Ambulatory capacity in cerebral palsy: prognostic criteria and consequences for intervention. Dev Med Child Neurol 2003; 45: 786-90.
8. Bleck EE. Locomotor prognosis in cerebral palsy. Dev Med Child Neurol 1975; 17: 18-25.
9. Lee JH, Koo JH, Jang DH, Park EH, Sung IY. The functional prognosis of ambulation in each type of cerebral palsy. J Korean Acad Rehab Med 2006; 30: 315-21.
10. Beckung E, Hagberg G, Uldall P, Cans C. Probability of walking in children with cerebral palsy in Europe. Pediatrics 2008; 121: e187-e192.
11. Ordu Gökkaya NK, Çalışkan A, Karakuş D, Uçan H. Relation between objectively measured growth determinants and ambulation in children with cerebral palsy. Turk J Med Sci 2009; 39: 85-90.
12. Simard-Tremblay E, Shevell M, Dagenais L. Determinants of ambulation in children with spastic quadriplegic cerebral palsy: a population-based study. J Child Neurol 2010; 25: 669-73.
13. Kułak W, Sendrowski K, Okurowska-Zawada B, Sienkiewicz D, Paszko-Patej G. Prognostic factors of the independent walking in children with cerebral palsy. Neurologia 2011;20:29-34.
14. Kifune N, Hamazato S. Comparison on Bleck's scores for walking prognosis between walking children and non-walking children with spastic quadriplegia cerebral palsy. The Bulletin of the Center for Special Needs Education Research and Practice, Graduate School of Education, Hiroshima University; 2010:1-3.
15. Palisano RJ, Hanna SE, Rosenbaum PL, Russell DJ, Walter SD, Wood EP, et al. Validation of a model of gross motor function for children with cerebral palsy. Phys Ther 2000; 80: 974-85.
16. Rosenbaum PL, Walter SD, Hanna SE, Palisano RJ, Russell DJ, Raina P, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. J Am Med Assoc 2002; 288: 1357-63.
17. Montgomery PC. Predicting potential for ambulation in children with cerebral palsy. Pediatr Phys Ther 1998; 10: 148-55.
18. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997; 39: 214-23.
19. Palisano RJ, Rosenbaum P, Bartlett D, Livingston MH. Content validity of the expanded and revised Gross Motor Function Classification System. Dev Med Child Neurol 2008; 50: 744-50.
20. Keeratisiroj O, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M. Prognostic predictors for ambulation in Thai children with cerebral palsy aged 2 to 18 years. J Child Neurol 2015; 30: 1812-8.
21. Siritaratiwat W, Thomas I. Gross motor function classification system expanded and revised (Thai version). Hamilton, Ontario Canada: CanChild; 2007 [cited 2012 Sep 11]. Available from: https://www.canchild.ca/system/tenon/assets/attachments/000/000/081/original/GMFCS-ER_Translation-Thai.pdf
22. Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. Ann Intern Med 1993; 118: 201-10.
23. Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York: John Wiley & Sons; 2000.
24. Sala DA, Grant AD. Prognosis for ambulation in cerebral palsy. Dev Med Child Neurol 1995; 37: 1020-6.
25. Pallás Alonso CR, de La Cruz Bértolo J, Medina López MC, Orbea Gallardo C, Gómez Castillo E, Simón De Las Heras R. Cerebral palsy and age of sitting and walking in children weighing less than 1,500 g at birth. An Esp Pediatr 2000; 53: 48-52.
26. Day SM, Wu YW, Strauss DJ, Shavelle RM, Reynolds RJ. Change in ambulatory ability of

adolescents and young adults with cerebral palsy. Dev Med Child Neurol 2007; 49: 647-53.

27. Strauss D, Ojdana K, Shavelle R, Rosenbloom L. Decline in function and life expectancy of older persons with cerebral palsy. NeuroRehabilitation 2004; 19: 69-78.

28. Rodby-Bousquet E, Hägglund G. Better walking performance in older children with cerebral palsy. Clin Orthop Relat Res 2012; 470: 1286-93.

29. Kerr C, McDowell BC, Parkes J, Stevenson M, Cosgrove AP. Age-related changes in energy efficiency of gait, activity, and participation in children with cerebral palsy. Dev Med Child Neurol 2011; 53: 61-7.

30. Bottos M, Feliciangeli A, Sciuto L, Gericke C, Vianello A. Functional status of adults with cerebral palsy and implications for treatment of children. Dev Med Child Neurol 2001; 43: 516-28.

การสร้างแผนภูมิคะแนนทำนายการเดินสำหรับเด็กไทยสมองพิการ อายุ 2 ถึง 18 ปี

อรวรรณ กีรติสิโรจน์, นวลลออ ธวินชัย, มนธนา บุญตระกูลพูนทวี, วัฒนา ศิริธราธิวัตร

ภูมิหลัง: ผู้ปกครองส่วนใหญ่ต้องการทราบว่าบุตรของพวกเขาซึ่งมีภาวะสมองพิการจะเดินได้หรือไม่ ประเทศไทยยังขาดเครื่องมืออย่างง่ายที่ใช้ทำนายสถานะการเดินซึ่งใช้คำจำกัดความของการเดินด้วย Gross Motor Function Classification System

วัตถุประสงค์: เพื่อสร้างแผนภูมิคะแนนทำนายอย่างง่ายสำหรับทำนายสถานะการเดินในเด็กไทยสมองพิการ

วัสดุและวิธีการ: เด็กสมองพิการอายุ 2 ถึง 18 ปี จำนวนทั้งหมด 471 คน ซึ่งลงทะเบียนและรับการรักษาที่โรงเรียนการศึกษาพิเศษ หรือ โรงพยาบาลสำหรับเด็กที่บกพร่องทางการเคลื่อนไหว ระหว่าง พ.ศ. 2551 ถึง พ.ศ. 2556 จำนวน 6 แห่ง ได้รับการคัดเลือก ผู้นิพนธ์เก็บรวบรวมข้อมูลทั่วไปและประวัติทางคลินิกของเด็กสมองพิการจากเวชระเบียน สถานะการเดินถูกจำแนกเป็น 3 มาตราอันดับ โดย Gross Motor Function Classification System - Expanded and Revised version

ผลการศึกษา: การวิเคราะห์ ordinal continuation ratio logistic regression แบบหลายตัวแปรบ่งชี้ว่า อายุ ชนิดของสมองพิการ การนั่งได้เองเมื่ออายุ 2 ปี และการกินได้เอง คือ ปัจจัยทำนายสำคัญของการเดิน รายการเหล่านี้ถูกนำมารวมกันเป็นคะแนนการทำนายทางคลินิก ได้แก่ เดินไม่ได้ (น้อยกว่า 7 คะแนน) เดินโดยการช่วยเหลือ (7 ถึง 8 คะแนน) และเดินได้เองโดยอิสระ (มากกว่า 8 คะแนน)

สรุป: เครื่องมือทำนายมีค่าการจำแนกสถานะการเดินในกลุ่มเด็กสมองพิการสูง อย่างไรก็ตามการตรวจสอบความตรงของเครื่องมือนี้ต้องการการทดสอบในตัวอย่างกลุ่มอื่น ก่อนนำไปประยุกต์ใช้ในทางคลินิก

ที่ จพสท. 85/2560

วันที่ 22 พฤษภาคม 2560

เรื่อง   ขออนุญาตนำบทความไปอ้างอิง

เรียน   คุณอรวรรณ กีรติสิโรจน์

        ตามที่ท่านได้แจ้งให้บรรณาธิการออกหนังสืออนุญาตนำบทความที่ตีพิมพ์ในวารสาร จพสท. เรื่อง Rule เพื่อนำไปใช้ใน Derivation of an Ambulatory Prognostic Score Chart for Thai Children with Cerebral Palsy Aged 2 to 18 Vol.99 No.12 page 1298-1305 การไปอ้างอิงในเล่มวิทยานิพนธ์ การศึกษาในระดับปริญญาเอก สาขาระบาดวิทยาคลินิก คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ เรื่อง Ambulation in Children with Cerebral Palsy: Prognostic Predictors and Clinical Prediction Rule

        บรรณาธิการขอเรียนให้ทราบว่า จพสท. ได้อนุมัติให้ท่านใช้บทความดังกล่าวได้ โดยให้มีการอ้างอิงถึงวารสาร จพสท. ฉบับที่ตีพิมพ์ดังกล่าว ตามที่ท่านได้อ้างอิงในบทความในเล่มวิทยานิพนธ์ดังกล่าวแล้ว

        จึงเรียนมาเพื่อทราบ

ขอแสดงความนับถือ

(ศาสตราจารย์นายแพทย์อมร ลีลารัศมี)
หัวหน้าบรรณาธิการวารสารจดหมายเหตุทางแพทย์

Appendix E

Certificate of approval

No. 188/ /2013

Certificate of Approval

Name of Ethics Committee : Research Ethics Committee **4,** Faculty of Medicine, Chiang Mai University **Address of Ethics Committee :** 110 Intavaroros Rd., Amphoe Muang, Chiang Mai, Thailand 50200	

Principal Investigator: Orawan Saetan

Department of Community Medicine, Faculty of medicine, Chiang Mai University.

Protocol title: Ambulation in children with cerebral palsy: prognostic predictors and clinical prediction model.

STUDY CODE: COM–2556–01638 / Research ID :1638

Sponsor: –

Documents filed	Document reference
Research protocol	Version 1.0 date 21 February 2013
Patient Information Sheet	Version 1.0 date 21 February 2013
Case Record Form	Version date 4 June 2013
Principal Investigator Curriculum vitae	Version date 4 June 2013

DECISION : [✔ } By expedited review

[   ] By full committee meeting ....Date : ....

Opinion of the Ethics Committee/Institutional Review Board : PLS. CHECK ONE
_____✔____ Approval _____Conditional approval (Specify on space below)

....

Progress report submit every	☐ 3 months	☐ 6 months
	✓ 1 year	☐ Other............................

Date of Approval: 4 June 2013 Expiration Date: 3 June 2014

This Ethics Committee is organized and operates according to GCPs and relevant international ethical guidelines, the applicable laws and regulations.

Signed : ....*P. Kulapongs*..................

(Emeritus Professor Panja Kulapongs, M.D.)

Chairperson, Faculty of Medicine

GENERAL CONDITION OF APPROVAL:

- Please refer to www.med.cmu.ac.th/research/ethics/inv sop announce.pdf article 13.
- Please submit the progress report at least once a year except where required more frequent by the REC.
- In particular, approval of this study must be renewed at least three months before the expiration date if work is to continue.
- Prior Research Ethics Committee approval is required before implementing any changes in the consent documents or protocol unless those changes are required urgently for the safely of subjects.
- Any event or new information that may affect the benefit/risk ratio of the study must be reported to the REC promptly
- Any protocol deviation/violation must be reported to the REC

Appendix F

GMFCS – E & R Thai version

AMBULATION IN CHILDREN WITH CEREBRAL PALSY: PROGNOSTIC PREDICTORS AND CLINICAL PREDICTION MODEL.

<u>GMFCS</u>-แบบสอบถามการจำแนกระดับความสามารถในการเคลื่อนไหว รายงานโดยครอบครัว: สำหรับเด็กอายุ 2-4 ปี

กรุณาอ่านข้อความข้างล่างนี้ และทำเครื่องหมายในช่องสี่เหลี่ยมข้างข้อความ **เพียงช่องเดียว**ที่อธิบายความสามารถในการเคลื่อนไหวของ ลูกท่านได้ดีที่สุด

ลูกของฉัน/ เด็กในความดูแลของฉัน...

☐ มีความยากลำบากในการควบคุมศีรษะและลำตัวในเกือบทุกๆ ท่าทาง
<u>และ</u> ใช้อุปกรณ์ดัดแปลงพิเศษสำหรับการนั่งเพื่อให้นั่งได้อย่างสะดวกสบาย
<u>และ</u> ต้องมีคนช่วยยกในการเคลื่อนย้าย

☐ สามารถนั่งได้เองเมื่อถูกจับให้อยู่ในท่านั่งกับพื้น และสามารถเคลื่อนย้ายภายในห้องได้
<u>และ</u> ใช้มือค้ำเพื่อช่วยพยุงการทรงตัวในท่านั่ง
<u>และ</u> โดยทั่วไป มักใช้อุปกรณ์ดัดแปลงช่วยในการนั่งและยืน
<u>และ</u> เคลื่อนย้ายตัวโดยการกลิ้ง การคืบโดยท้องยังสัมผัสพื้น หรือการคลาน

☐ สามารถนั่งได้เอง และเดินได้ในระยะทางสั้นๆ โดยใช้เครื่องช่วยเดิน
(เช่น โครงหัดเดิน โครงหัดเดินล้อเลื่อน ไม้ค้ำยัน ไม้เท้า เป็นต้น)
<u>และ</u> อาจต้องการความช่วยเหลือจากผู้ใหญ่ในการเคลื่อน และกลับตัวขณะเดินโดยใช้เครื่องช่วยเดิน
<u>และ</u> โดยทั่วไปมักนั่งกับพื้นในท่าปลายเท้าชี้ออกด้านนอก (**w**) และอาจต้องการความช่วยเหลือจากผู้ใหญ่ในการจับให้อยู่ในท่านั่ง
<u>และ</u> อาจเกาะขึ้นมายืนและเกาะเดินไปได้ระยะทางสั้นๆ
<u>และ</u> ชอบที่จะเคลื่อนย้ายโดยการคืบและการคลานมากกว่า

☐ สามารถนั่งได้เอง และมักเคลื่อนย้ายโดยการเดินด้วยเครื่องช่วยเดิน
<u>และ</u> อาจมีความยากลำบากในการทรงตัวในท่านั่งเมื่อใช้มือทั้งสองเล่น
<u>และ</u> สามารถเปลี่ยนท่าทางมาอยู่ในท่านั่งและออกจากท่านั่งได้เอง
<u>และ</u> สามารถเกาะลุกขึ้นมายืนและเกาะเครื่องเฟอร์นิเจอร์เดินได้
<u>และ</u> สามารถคลานได้ แต่ชอบที่จะเคลื่อนย้ายโดยการเดินมากกว่า

☐ สามารถนั่งได้เอง และเคลื่อนย้ายโดยการเดินเอง ไม่ใช้เครื่องช่วยเดิน
<u>และ</u> สามารถทรงตัวในท่านั่งได้เมื่อใช้มือทั้งสองเล่น
<u>และ</u> สามารถเปลี่ยนท่าทางมาอยู่ในและออกจากท่านั่งและท่ายืนโดยไม่ต้องมีผู้ใหญ่ช่วยเหลือ
<u>และ</u> ชอบที่จะเคลื่อนย้ายโดยการเดินมากกว่า

ผู้ตอบแบบสอบถาม ชื่อ... เกี่ยวข้องเป็น......................

Site ID ☐☐　　　　　　　　　　Participant ID ☐☐☐

AMBULATION IN CHILDREN WITH CEREBRAL PALSY: PROGNOSTIC PREDICTORS AND CLINICAL PREDICTION MODEL.

GMFCS-แบบสอบถามการจำแนกระดับความสามารถในการเคลื่อนไหว รายงานโดยครอบครัว: สำหรับเด็กอายุ 4-6 ปี

กรุณาอ่านข้อความข้างล่างนี้ และทำเครื่องหมายในช่องสี่เหลี่ยมข้างข้อความ **เพียงช่องเดียว**ที่อธิบายความสามารถในการเคลื่อนไหวของ ลูกท่านได้ดีที่สุด

ลูกของฉัน/ เด็กในความดูแลของฉัน...

☐ มีความยากลำบากในการนั่งเอง และการควบคุมศีรษะและลำตัวในเกือบทุกๆ ท่าทาง
<u>และ</u> มีความยากลำบากในการเคลื่อนไหวด้วยตนเอง
<u>และ</u>ต้องการเก้าอี้ที่มีอุปกรณ์ดัดแปลงพิเศษช่วยพยุงเพื่อที่จะนั่งได้อย่างสะดวกสบาย
<u>และ</u> ต้องมีคนช่วยยกหรืออุปกรณ์ช่วยยกในการเคลื่อนย้ายตัว

☐ สามารถนั่งได้เอง แต่ไม่ยืนหรือเดินโดย ไม่มีผู้ใหญ่ช่วยพยุงและกำกับดูแล
<u>และ</u> อาจต้องการการพยุงเป็นพิเศษที่ลำตัวเพื่อให้แขนและมือทำงานได้ดีขึ้น
<u>และ</u> โดยทั่วไป มักต้องการความช่วยเหลือจากผู้ใหญ่เพื่อขึ้นมานั่งในเก้าอี้และออกจากเก้าอี้
<u>และ</u> อาจเคลื่อนที่ได้เองโดยใช้รถเข็นนั่งไฟฟ้า หรือเมื่อมีการเดินทางในชุมชน

☐ สามารถเดินได้เองโดยใช้เครื่องช่วยเดิน (เช่น โครงหัดเดิน โครงหัดเดินล้อเลื่อน ไม้ค้ำยัน ไม้เท้า เป็นต้น)
<u>และ</u> โดยปกติ สามารถมานั่งและลุกออกจากเก้าอี้โดยไม่ต้องมีผู้ใหญ่ช่วยเหลือ
<u>และ</u> อาจใช้รถเข็นนั่งเมื่อต้องเคลื่อนย้ายในระยะทางไกลๆ หรืออยู่นอกบ้าน
<u>และ</u> พบว่ามีความยากลำบากในการขึ้นบันได หรือเดินบนพื้นขรุขระหากไม่มีคนช่วยเหลืออย่างมาก

☐ สามารถเดินได้เองโดยไม่ใช้เครื่องช่วยเดิน แต่มีความยากลำบากในการเดินระยะทางไกลๆ หรือบนพื้นขรุขระ
<u>และ</u> สามารถนั่งบนเก้าอี้ปกติของผู้ใหญ่และใช้มืออย่างอิสระได้
<u>และ</u> สามารถลุกจากพื้นไปท่ายืนโดยไม่ต้องมีผู้ใหญ่ช่วยเหลือ
<u>และ</u> จำเป็นต้องจับราวบันไดเมื่อขึ้นหรือลงบันได
<u>และ</u> ยังไม่สามารถวิ่ง และกระโดดได้

☐ สามารถเดินได้เองโดยไม่ต้องใช้เครื่องช่วยเดิน รวมถึงการเดินในระยะทางไกล นอกบ้าน และบนพื้นขรุขระ
<u>และ</u> สามารถลุกจากพื้นหรือเก้าอี้ไปยืนได้โดยไม่ต้องใช้มือช่วยพยุง
<u>และ</u> สามารถขึ้นและลงบันไดได้โดยไม่จำเป็นต้องจับราวบันได
<u>และ</u> เริ่มที่จะวิ่งและกระโดดได้

ผู้ตอบแบบสอบถาม ชื่อ... เกี่ยวข้องเป็น...........................

Site ID [ ][ ]   Participant ID [ ][ ][ ]

GMFCS-แบบสอบถามการจำแนกระดับความสามารถในการเคลื่อนไหว รายงานโดยครอบครัว: สำหรับเด็กอายุ 6-12 ปี

กรุณาอ่านข้อความข้างล่างนี้ และทำเครื่องหมายในช่องสี่เหลี่ยมข้างข้อความ **เพียงช่องเดียว**ที่อธิบายความสามารถในการเคลื่อนไหวของ ลูกท่านได้ดีที่สุด

ลูกของฉัน/ เด็กในความดูแลของฉัน...

❑ มีความยากลำบากในการนั่งเอง และการควบคุมศีรษะและลำตัวในเกือบ ทุกๆ ท่าทาง
<u>และ</u> มีความยากลำบากในการเคลื่อนไหวด้วยตนเอง
<u>และ</u> ต้องการเก้าอี้ที่มีอุปกรณ์ดัดแปลงพิเศษช่วยพยุง เพื่อที่จะนั่งได้อย่าง สะดวกสบาย
<u>และ</u> ต้องมีคนช่วยยกหรืออุปกรณ์ช่วยยกในการเคลื่อนย้ายตัว

❑ สามารถนั่งได้เอง แต่ไม่ยืนหรือเดินโดยไม่มีผู้ใหญ่ช่วยพยุง
<u>และ</u> ดังนั้นจึงต้องพึ่งรถเข็นนั่งเป็นส่วนใหญ่เมื่ออยู่ที่บ้าน โรงเรียน และในชุมชน
<u>และ</u> บ่อยครั้งต้องการการพยุงเป็นพิเศษที่ลำตัวเพื่อปรับปรุงการทำงานของแขน และมือให้ดีขึ้น
<u>และ</u> อาจจะเคลื่อนรถเข็นได้เองโดยใช้รถเข็นไฟฟ้า

❑ สามารถยืนได้ด้วยตนเอง และจะเดินเมื่อใช้เครื่องช่วยเดินเท่านั้น (เช่น โครงหัดเดิน โครงหัดเดินล้อเลื่อน ไม้ค้ำยัน ไม้เท้า เป็นต้น)
<u>และ</u> พบว่ามันยากลำบากที่จะเดินขึ้นบันได หรือเดินบนพื้นขรุขระ
<u>และ</u> อาจใช้รถเข็นนั่งเมื่อเคลื่อนย้ายในระยะทางไกลๆ หรือท่ามกลางฝูงชน

❑ สามารถเดินได้เอง โดยไม่ต้องใช้เครื่องช่วยเดิน แต่จำเป็นต้องจับราว บันไดเมื่อเดินขึ้นหรือลงบันได
<u>และ</u> บ่อยครั้งที่พบว่ามันยากลำบากที่จะเดินบนพื้นขรุขระ ทางลาดชัน หรือเดิน ท่ามกลางฝูงชน

❑ สามารถเดินได้เองโดยไม่ต้องใช้เครื่องช่วยเดิน และสามารถขึ้นหรือลง บันไดโดยไม่จำเป็นต้องจับราวบันได
<u>และ</u> เดินในทุกที่ที่อยากไป(รวมถึงบนพื้นขรุขระ ทางลาดชัน หรือท่ามกลางฝูงชน)
<u>และ</u> สามารถวิ่งหรือกระโดดได้ แม้ว่าจะมีข้อจำกัดเล็กน้อยเกี่ยวกับความเร็ว การทรงตัว และการประสานสัมพันธ์ของการเคลื่อนไหว

ผู้ตอบแบบสอบถาม ชื่อ.. เกี่ยวข้องเป็น......................

AMBULATION IN CHILDREN WITH CEREBRAL PALSY: PROGNOSTIC PREDICTORS AND CLINICAL PREDICTION MODEL.

GMFCS-แบบสอบถามการจำแนกระดับความสามารถในการเคลื่อนไหว รายงานโดยครอบครัว: สำหรับวัยรุ่นอายุ 12-18 ปี

กรุณาอ่านข้อความข้างล่างนี้ และทำเครื่องหมายในช่องสี่เหลี่ยมข้างข้อความ **เพียงช่องเดียว**ที่อธิบายความสามารถในการเคลื่อนไหวของ ลูกท่านได้ดีที่สุด
ลูกของฉัน/ เด็กในความดูแลของฉัน...

☐ มีความยากลำบากในการนั่งเองและการควบคุมศีรษะและลำตัวในเกือบทุกๆ ท่าทาง
<u>และ</u> มีความยากลำบากในการเคลื่อนไหวด้วยตนเอง
<u>และ</u> ต้องการเก้าอี้ที่ดัดแปลงพิเศษ เพื่อที่จะนั่งได้อย่างสะดวกสบาย และได้รับการเคลื่อนย้ายโดยผู้อื่นไปในทุกๆ สถานที่
<u>และ</u> ต้องการคนช่วยยกหรือต้องการอุปกรณ์พิเศษช่วยยกในการเคลื่อนย้ายตัว

☐ สามารถนั่งได้โดยต้องมีการช่วยพยุงบ้างเล็กน้อยที่สะโพกทั้งสองข้างและลำตัวแต่จำเป็นต้องมีการช่วยพยุงอย่างมากจึงจะสามารถยืนหรือเดินได้
<u>และ</u> ดังนั้นจึงจำเป็นต้องพึ่งรถเข็นนั่งเมื่ออยู่นอกบ้าน
<u>และ</u> สามารถเคลื่อนที่ได้เองโดยใช้รถเข็นนั่งไฟฟ้า
<u>และ</u> สามารถคลานหรือกลิ้งไปได้ในระยะทางที่จำกัดเพื่อเคลื่อนที่ในห้อง

☐ สามารถยืนได้ด้วยตนเอง และจะเดินเมื่อใช้เครื่องช่วยเดินเท่านั้น (เช่น โครงหัดเดิน โครงหัดเดินล้อเลื่อน ไม้ค้ำยัน ไม้เท้า เป็นต้น)
<u>และ</u> พบว่ามันยากลำบากที่จะเดินขึ้นบันได หรือเดินบนพื้นขรุขระโดยไม่มีที่พยุง
<u>และ</u> ใช้วิธีการหลากหลายเพื่อเคลื่อนที่ไปรอบๆ ขึ้นอยู่กับสภาพแวดล้อม
<u>และ</u> ชอบที่จะใช้รถเข็นนั่งมากกว่าเพื่อที่จะเดินทางอย่างรวดเร็วหรือในระยะไกล

☐ สามารถเดินได้เอง โดยไม่ต้องใช้เครื่องช่วยเดิน แต่จำเป็นต้องจับราวบันไดเมื่อเดินขึ้นหรือลงบันได
<u>และ</u> ดังนั้นเดินไปในทุกๆ ที่เป็นส่วนใหญ่
<u>และ</u> บ่อยครั้งที่พบว่ามันยากลำบากที่จะเดินบนพื้นขรุขระ ทางลาดชัน หรือเดินในบริเวณที่มีคนหนาแน่น
<u>และ</u> บางครั้งที่ชอบใช้เครื่องช่วยเดินมากกว่า (เช่น ไม้เท้า หรือไม้ค้ำยัน) หรือใช้รถเข็นนั่งเพื่อที่จะเดินทางอย่างรวดเร็วหรือในระยะทางไกล

☐ สามารถเดินได้เองโดยไม่ต้องใช้เครื่องช่วยเดิน และสามารถขึ้นหรือลงบันไดโดยไม่จำเป็นต้องจับราวบันได
<u>และ</u> เดินไปในทุกที่ที่อยากไป (รวมถึงบนพื้นขรุขระ ทางลาดชัน หรือบริเวณที่มีคนหนาแน่น)
<u>และ</u> สามารถวิ่งหรือกระโดดได้ แม้ว่าจะมีข้อจำกัดบ้างเกี่ยวกับความเร็ว การทรงตัวและการประสานสัมพันธ์ของการเคลื่อนไหว

ผู้ตอบแบบสอบถาม ชื่อ.. เกี่ยวข้องเป็น........................

AMBULATION IN CHILDREN WITH CEREBRAL PALSY: PROGNOSTIC PREDICTORS AND CLINICAL PREDICTION MODEL.

<u>GMFCS-</u>แบบสอบถามการจำแนกระดับความสามารถในการเคลื่อนไหว รายงานด้วยตนเอง: สำหรับวัยรุ่นอายุ 12-18 ปี

กรุณาอ่านข้อความข้างล่างนี้ และทำเครื่องหมายในช่องสี่เหลี่ยมข้างข้อความ **เพียงช่องเดียว**ที่อธิบายความสามารถในการเคลื่อนไหวของท่านได้ดีที่สุด

ฉัน...

☐ มีความยากลำบากในการนั่งด้วยตัวฉันเอง และการควบคุมศีรษะและลำตัวของฉันในเกือบทุกๆ ท่าทาง
<u>และ</u> มีความยากลำบากในการเคลื่อนไหวด้วยตนเอง
<u>และ</u> ต้องการเก้าอี้ที่ดัดแปลงพิเศษ เพื่อที่จะนั่งได้อย่างสะดวกสบาย และได้รับการเคลื่อนย้ายโดยผู้อื่นไปในทุกๆ สถานที่
<u>และ</u> ต้องมีคนช่วยยกหรืออุปกรณ์พิเศษช่วยยกในการเคลื่อนย้ายตัว

☐ สามารถนั่งได้ด้วยตัวฉันเอง แต่ฉันจำเป็นต้องได้รับการช่วยพยุงอย่างมากฉันจึงจะสามารถยืนหรือเดินได้
<u>และ</u> ดังนั้นจึงจำเป็นต้องพึ่งรถเข็นนั่งเมื่อออกไปข้างนอก
<u>และ</u> สามารถเคลื่อนที่ได้เองโดยใช้รถเข็นนั่งไฟฟ้า
<u>และ</u> สามารถคลานหรือกลิ้งไปได้ในระยะทางที่จำกัดเพื่อเคลื่อนที่ในห้อง

☐ สามารถยืนได้ด้วยตัวฉันเอง และจะเดินเมื่อใช้เครื่องช่วยเดินเท่านั้น (เช่น โครงหัดเดิน โครงหัดเดินล้อเลื่อน ไม้ค้ำยัน ไม้เท้า เป็นต้น)
<u>และ</u> พบว่ามันยากลำบากที่จะเดินขึ้นบันได หรือเดินบนพื้นขรุขระโดยไม่มีที่พยุง
<u>และ</u> ใช้วิธีการหลากหลายเพื่อเคลื่อนที่ไปรอบๆ ขึ้นอยู่กับสภาพแวดล้อม
<u>และ</u> ชอบที่จะใช้รถเข็นนั่งมากกว่าเพื่อที่จะเดินทางอย่างรวดเร็วหรือในระยะไกล

☐ สามารถเดินได้ด้วยตัวฉันเอง โดยไม่ต้องใช้เครื่องช่วยเดิน แต่จำเป็นต้องจับราวบันไดเมื่อเดินขึ้นหรือลงบันได
<u>และ</u> ดังนั้นจึงเดินไปในทุกๆ ที่เป็นส่วนใหญ่
<u>และ</u> บ่อยครั้งที่พบว่ามันยากลำบากที่จะเดินบนพื้นขรุขระ ทางลาดชัน หรือเดินในบริเวณที่มีคนหนาแน่น
<u>และ</u> บางครั้งชอบใช้เครื่องช่วยเดินมากกว่า (เช่น ไม้เท้า หรือไม้ค้ำยัน) หรือใช้รถเข็นนั่งเพื่อที่จะเดินทางอย่างรวดเร็วหรือในระยะทางไกล

☐ สามารถเดินได้ด้วยตัวฉันเองโดยไม่ต้องใช้เครื่องช่วยเดิน และสามารถขึ้นหรือลงบันไดโดยไม่จำเป็นต้องจับราวบันได
<u>และ</u> เดินไปในทุกที่ที่ฉันอยากไป (รวมถึงบนพื้นขรุขระ ทางลาดชัน หรือบริเวณที่มีคนหนาแน่น)
<u>และ</u> สามารถวิ่งหรือกระโดดได้ แม้ว่าฉันมีข้อจำกัดเกี่ยวกับความเร็ว การทรงตัวและการประสานสัมพันธ์ของการเคลื่อนไหว

ผู้ตอบแบบสอบถาม ชื่อ... เกี่ยวข้องเป็น.......................

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2003-2005   Physical Therapist at Physical Therapy Clinic Bann-Sabai Health Center, Klaeng District, Rayong, Thailand

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Publications:

1. **Keeratisiroj O**, Thawinchai N, Buntragulpoontawee M, Siritaratiwat W, Derivation of an ambulatory score chart for Thai children with cerebral palsy aged 2–18. J Med Assoc Thai. 2016;99: 1298-305

2. **Keeratisiroj O**, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M., Pratoomsoot C. Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational study. Disabil Rehabil. 2016. 1-9. [Epub ahead of print]

3. **Keeratisiroj O**, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M. Prognostic predictors for ambulation in Thai children with cerebral palsy aged 2 to 18 years. J Child Neurol. 2015;30:1812-8.

4. **Keeratisiroj O**. Statistical knowledge tips: Systematic Review VS Literature Review differences in similarities. Thailand Journal of Health Promotion and Environmental Health. 2016;39:21-4. (in Thai)

5. Wanaratwichit C and **Keeratisiroj O**. Factors related to home and community based care for people with disabilities of primary care provider, lower Northern region. Journal of nursing and health sciences. 2016;10:176-88 (in Thai)

6. **Keeratisiroj O**. Statistical knowledge tips: Design effect with survey research. Thailand Journal of Health Promotion and Environmental Health. 2015;38: 20-3. (in Thai)

7. **Keeratisiroj O**. Statistical knowledge tips: Multiple imputation. Thailand Journal of Health Promotion and Environmental Health. 2015;38:21-4. (in Thai)

8. **Keeratisiroj O**. Statistical knowledge tips: Deal with missing data .Thailand Journal of Health Promotion and Environmental Health. 2015;38:27-30. (in Thai)

9. **Keeratisiroj O**. Statistical knowledge tips: Missing data. Thailand Journal of Health Promotion and Environmental Health. 2014;37(4):22-25. (in Thai)

10. **Keeratisiroj O**. Statistical knowledge tips: How to deal with confounder. Thailand Journal of Health Promotion and Environmental Health. 2014;37(3): 20-3. (in Thai)

11. **Keeratisiroj O**. Statistical knowledge tips: Third variable. Thailand journal of Health Promotion and Environmental Health. 2014;37:17-21. (in Thai)

12. Kitreerawutiwong N, **Saetan O**. Applying Research-Based Learning Model into the Course of Public Health Research. Journal of Public Health Learning. 2013;27:81-95. (in Thai)

13. **Saetan O**. To deal with multiple response data. Thailand of Health Promotion and Environmental Health. 2012;35:63-6. (in Thai)

14. Siritaratiwat W, **Saetan O**. Does a program of massage improve gross motor development in orphans aged between 1-12 months? A randomized controlled trial. Int J Child Adolesc Health. 2011;4:155-64.

15. Peongsuwan P, Kamolrat T, Siritaratiwat W, Arayauuchanon P, **Saetan O** .A Comparative Study of Heat Effect between Hot Pack and Thai Herbal Ball on Pain and Physiological Changes. J Med Tech Phy Ther. 2009;21:74-82. (in Thai)

16. Siritaratiwat W, Peongsuwan P, Phaphayon J, Chamnoe Y, Pongsanit A, **Saetan O**. Factors related to obesity in children aged 7-9 years old at Demonstration School Khon Kaen University. Arch Dis Child. 2008;93:A318.

17. **Saetan O**, Khiewyoo J, Jones C, Ayuwat D. Musculoskeletal Disorders among Northeastern Construction Workers with Temporary Migration. Srinagarind Med J. 2007;22:165-73. (in Thai)

18. **Saetan O**, Sarakarn P. Analysis of 2 x 2 crossover design with continuous data. DMBN Journal. 2006;2:27-36. (in Thai)

Presentations

1. Epidemiology of children with cerebral palsy in special school, Northern and Northeastern of Thailand. Oral presented at "the Northern Research 3" Northern College, Thailand. 26 May, 2017.

2. Factors Associated with Musculoskeletal Disorders among Construction Workers: A Multinomial Logistic Regression. Oral presented at "the Statistics and Applied Statistics Conference 2007" Faculty of Science Silpakorn University and Thailand statistician association, Thailand. 24-25 May, 2007.

3. Musculoskeletal Disorders among Northeastern Construction Workers with Temporary Migration. Oral presented at "The 6th National Symposium on Graduate Research" Graduate School, Chulalongkorn University, Bangkok, Thailand. 13-14 October, 2006.