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Multilevel surgery for children with cerebral palsy: A meta-analysis

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3 Multilevel surgery for children with cerebral palsy: A meta-analysis
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19

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33

34 **Abbreviations:** CP: Cerebral palsy; ICF: International Classification of Functioning, Disability
35 and Health; ICIDH: International Classification of Impairments, Disabilities, and Handicaps,
36 MLS: multi-level surgery; RCT: randomised controlled trial
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38
39 **Table of Contents Summary:** This review summarises the literature on multilevel surgery for
40 children with cerebral palsy, including the effects of and satisfaction with outcomes following
41 multilevel surgery.
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6 **Contributors' Statement page:** Noor Amirah Amirmudin designed the search strategy, selected
7 the articles, extracted the data, assessed the quality of the evidence, performed the data analysis,
8 and drafted the initial manuscript. Jennifer M. Ryan conceptualised and designed the review, co-
9 ordinated and supervised the review, designed the search strategy, selected the articles, extracted
10 the data, assessed the quality of the evidence, performed the data analysis, interpreted the data
11 analysis, drafted the initial manuscript, reviewed and revised the manuscript. Grace Lavelle
12 conceptualised and designed the review, co-ordinated and supervised the review, designed the
13 search strategy, interpreted the data, reviewed and revised the manuscript. Tim Theologis and
14 Nicky Thompson conceptualised and designed the review, interpreted the data, reviewed and
15 revised the manuscript. All authors approved the final manuscript as submitted and agree to be
16 accountable for all aspects of the work.
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Review Copy

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3 **Abstract**

4 **Context:** Multilevel surgery (MLS) is standard care for reducing musculoskeletal disorders among
5 children with spastic cerebral palsy (CP).

6 **Objective:** To summarise the literature on MLS for children with CP, including the effects of MLS
7 and satisfaction with outcomes following MLS.

8 **Data Sources:** MEDLINE, Embase, CINAHL and Cochrane Central Register of Controlled Trials
9 were searched.

10 **Study Selection:** Studies reporting effects of or satisfaction with MLS in children with CP.

11 **Data Extraction:** Two authors screened and extracted data on gross motor function, gait speed,
12 summary statistics of gait (e.g. Gait Profile Score [GPS]), range of motion, strength, spasticity,
13 participation, quality of life, satisfaction, and adverse events.

14 **Results:** 74 studies (3551 participants) were identified; one was a randomised controlled trial
15 (RCT; n=19) and the remainder were cohort studies. Pooled analysis of cohort studies showed that
16 MLS did not have a long-term effect on gross motor function (SMD: 0.38, 95% CI -0.25 to 1.01,
17 p=0.24), or gait speed (SMD: 0.12, 95% CI -0.01 to 0.25, p=0.08), but did improve gait (SMD: -
18 0.80, 95% CI -0.95 to -0.65, p<0.001). The RCT also found no effect of MLS on gross motor
19 function but improvements in the Gait Profile Score at 1 year. Only five studies reported
20 participation and quality of life and seventeen adequately reported adverse events.

21 **Limitations:** Data were largely from cohort studies. There was moderate heterogeneity in meta-
22 analyses.

23 **Conclusions:** Findings suggest that gait but not gross motor function improves following MLS.
24 RCTs and improved reporting of studies of MLS are required.
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1 Cerebral palsy (CP) is characterised by abnormal fine and gross motor functioning.¹ The incidence
2 of CP is approximately 2-3 per 1000 live births worldwide.^{2,3} Musculoskeletal disorders, including
3 contractures of muscle tendon units and bony deformities, are a secondary impairment of CP,
4 which contribute to restricted mobility.¹ Multilevel surgery (MLS) followed by intensive
5 rehabilitation is considered standard care for reducing musculoskeletal disorders among children
6 with spastic CP.⁴

7
8 To date, two systematic reviews have examined the literature on MLS for children with CP. The
9 first, conducted in 2010, included 31 studies and concluded that there was a trend towards
10 improvements in passive range of motion, gait kinematics and kinetics, and gait efficiency, but
11 little evidence for improvements in gross motor function or quality of life (QoL).⁵ However, study
12 quality was variable and a meta-analysis of data was not performed. The authors also identified
13 variability in the quality of reporting of surgical procedures, rehabilitation, and adverse events.
14 The second review examined the effect of MLS specifically on gait parameters.⁶ Authors
15 concluded from a narrative synthesis that there was a trend towards improvements in gait
16 parameters, but reported variability in study quality.

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18 The World Health Organisation's International Classification of Functioning, Disability and
19 Health (ICF) framework is useful for considering the impact of CP on the individual.⁷ Developed
20 in 2001, the ICF classifies health-related domains using the terms "body functions and structure",
21 "activity" and "participation". The ICF replaced the International Classification of Impairments,
22 Disabilities, and Handicaps (ICIDH), which conceptualised a health condition leading to
23 impairment, disability and handicap in a linear manner. The ICF places greater emphasis on the

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3 1 role of the social and physical environment on functioning, and conceptualises that functioning
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5 2 results from a complex interaction between the person with the health condition and their context
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8 3 (consisting of personal and environmental factors). When developed, it was envisaged that one use
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10 4 of the ICF would be the evaluation of interventions. However, the review in 2010 found that few
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12 5 studies evaluate the effect of MLS across multiple domains of the ICF.
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17 7 Given the impact of MLS on children with CP and their families,⁸ a summary of the current
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19 8 literature on MLS and systematic evaluation of the effects of MLS is required. Thus, the aim of
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21 9 this review was to summarise the current literature on MLS for children with CP, including the
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23 10 effects of MLS and satisfaction with outcomes following MLS. We also aimed to examine the use
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25 11 of the ICF and ICIDH by authors when reporting outcomes of MLS.
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31 Method

32 33 Study selection criteria 34

35 15 We included studies meeting the following criteria: 1. included children with CP. We chose to
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37 16 define a child as a person aged 0-20 yr, in order to be inclusive of all studies evaluating MLS in
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39 17 children as we expected variation in the age range across studies; 2. reported outcomes before and
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41 18 after MLS or reported satisfaction with MLS; 3. additional interventions, such as Botulinum toxin
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43 19 injections, were not performed simultaneously to surgery. We defined MLS as "two or more soft-
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45 20 tissue or bony surgical procedures at two or more anatomical levels".⁹ Original peer-reviewed
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47 21 articles published in English were included. To provide a comprehensive overview of the current
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49 22 literature we did not limit studies to randomised controlled trials (RCTs). However, qualitative
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51 23 studies, reviews, commentaries, conference abstracts, and case reports were excluded.
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45 2 Search strategy
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8 3 We searched Ovid MEDLINE, Embase Ovid, CINAHL and Cochrane Central Register of
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10 4 Controlled Trials (CENTRAL) from January 2000 to June 2018. Search terms relating to children,
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12 5 CP and surgery were combined. Each search was adapted for the respective database (see
13
14 6 Appendix). Additionally, reference lists of previous reviews were searched.
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19 8 Two investigators screened titles and abstracts independently against eligibility criteria. Where
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21 9 articles met eligibility criteria or there was doubt over inclusion, full texts were obtained. Any
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23 10 disagreement regarding the inclusion of an article was resolved through discussion.
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26 11
2728 12 Data extraction
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31 13 Two authors (NAA, JMR) extracted data independently using a standardised piloted data
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33 14 extraction form. Data on study design, study population (e.g. Gross Motor Function Classification
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35 15 System [GMFCS] level), intervention (e.g. procedures performed), rehabilitation received,
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37 16 duration of follow-up, adverse events, and outcomes were extracted. We noted if studies reported
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39 17 outcomes according to ICIDH or ICF frameworks.
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45 19 We extracted data on gross motor function as measured by the Gross Motor Function Measure
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47 20 (GMFM-66 or GMFM-88), the Functional Mobility Scale (FMS), and the Gillette Functional
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49 21 Assessment Questionnaire (FAQ). Although some studies assessed gross motor function using the
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51 22 GMFCS we did not consider the GMFCS a measure of gross motor function as it is primarily a
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53 23 classification system. We extracted data on gait speed and summary statistics of gait i.e., the Gait
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3 1 Deviation Index (GDI), Gait Profile Score (GPS), or Gillette Gait Index (GGI).¹⁰⁻¹² Where studies
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5 2 reported more than one summary score we extracted data on the GPS. We chose to extract data on
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7 3 gait summary scores rather than individual kinematic or kinetic variables as many studies reported
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9 4 a large number of variables obtained from three-dimensional gait analysis. Further, we extracted
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11 5 data on participation, QoL and satisfaction with surgery. Since the publication of the ICF there has
12
13 6 been lack of consensus regarding measurement tools to assess participation. For the purpose of
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15 7 this review, we extracted data on measures that mapped to the recently developed family of
16
17 8 participation-related constructs.¹³ Finally, we extracted data on passive range of motion, muscle
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19 9 strength, and spasticity, as these are commonly evaluated before and after MLS as part of a clinical
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21 10 examination and inform clinical decision making on surgery. We extracted data on passive knee
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23 11 extension and passive dorsiflexion only as these were the most commonly reported joints. As
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25 12 authors typically reported muscle strength and spasticity for more than one muscle group, we
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27 13 ranked muscle groups in order of frequency of reporting across all included studies. For each study,
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29 14 we then extracted data for strength and spasticity, respectively, for the most frequently reported
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31 15 muscle group. If data were not reported for the most frequently reported muscle group we extracted
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33 16 data for the next most frequently reported muscle group, and so on. If data were reported on both
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35 17 limbs, data on the most affected limb or the right limb were extracted.
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45 19 Data on short-term (≤ 6 months post-surgery), intermediate-term (6 months to 1 year post-surgery),
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47 20 and long-term (> 1 year post-surgery) effects were extracted. If more than one assessment was
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49 21 performed during any of these time-periods, the last measurement taken during that period was
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51 22 extracted. Where studies compared two groups that received MLS, we extracted pre- and post-
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53 23 surgery data for the whole sample, if available, or pre- and post-surgery data for the two groups
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1 separately. In these cases, we report results according to number of groups included in meta-
2 analysis.
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10 Quality assessment

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12 The Methodological Index for Non-Randomised Studies (MINORS) checklist was used to assess
13 the quality of studies based on 8 or 12 items.¹⁴ Items related to the description of the aim, selection,
14 prospective data collection and sample size calculation, appropriateness of follow-up period, and
15 loss to follow-up. In addition, the adequacy of reporting of surgical procedures, previous surgery,
16 adverse events, and rehabilitation was rated as 0 (not reported), 1 (reported but inadequate), or 2
17 (reported adequately).
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30 Data analysis

31 Where sufficient data were obtained, we conducted separate meta-analyses for each outcome at
32 each time-point.
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38 Weighted effect sizes were calculated using the inverse-variance method. A random effects model
39 was used as there was large variation between studies in terms of procedures, populations, and
40 context.¹⁵ Effect sizes were calculated as Hedges' g^* to correct for bias associated with small
41 sample size.¹⁶ The standard deviation for the change score (i.e. mean difference [MD] between
42 baseline and follow-up values) (SD_{change}) was used to calculate g^* . Where this was not provided
43 SD_{change} was estimated using statistics provided (e.g. t values, confidence intervals [CI], standard
44 errors, p values) or standard deviations for the baseline and follow-up score (SD_{baseline} and SD_{fu} ,
45 respectively), and the correlation between baseline and follow-up scores (r). Where r was not
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1 provided, we estimated r using either individual data or using SD_{baseline} , SD_{fu} and SD_{change} . If this
2 was not possible we imputed r as 0.7 for the analysis of short-term effect on gross motor function
3 and imputed r as 0.3 for all other analyses, based on the strength of correlations observed in studies
4 with similar samples, outcome measures, and follow-up periods.¹⁷ However, sensitivity analyses
5 were performed by imputing r as 0.1, 0.3 and 0.7 to examine the robustness of the findings to this
6 assumption.¹⁷ Finally, the standard error of g^* was calculated using the provided, estimated or
7 imputed r . We conducted a subgroup analysis of studies that included children with bilateral CP
8 only. We assessed statistical heterogeneity and its impact using the Chi^2 test and the I^2 statistic.¹⁸
9 To aid interpretation we proposed an effect size of 0.2, 0.5 and 0.8 represents a small, moderate,
10 and large effect, respectively,¹⁹ although this was used cautiously.

11 12 Results

13 Database searches identified 2364 articles; 2 articles were obtained from reviewing reference lists
14 (Figure 1). After removal of duplicates, 1,823 titles and abstracts were screened. 164 full text
15 articles were obtained. Of these, 75 articles reporting findings from 74 studies were included. A
16 description of each study is presented in Table 1. MINORS score ranged from 4²⁰ to 21⁹
17 (supplemental table).

18 19 Study Design

20 We identified one RCT comparing MLS to progressive resistance training at 1-year.⁹ This study
21 also reported outcomes for the MLS group at 2-years. Fifty-two studies were retrospective cohort
22 studies. Where these studies included a comparison group they compared results between males
23 and females,²¹ participants with diplegia and hemiplegia,²² participants with more or less than a

1 5° increase in anterior pelvic tilt,²³ or between patients who received different surgical procedures
2 as part of MLS.^{20,24-31} Seventeen studies were prospective cohort studies, of which one used a
3 single-subject AB design³² and two compared two surgical procedures as part of MLS.^{33,34} Four
4 studies were RCTs comparing two surgical procedures as part of MLS^{35,36} or comparing two types
5 of rehabilitation following MLS.³⁷⁻³⁹ We treated these as cohort studies in pooled analyses as they
6 were not comparisons of MLS to control.

8 Participants

9 In total, 3551 participants were included in 74 studies. Sample sizes ranged from 7⁴⁰ to 314.⁴¹ We
10 considered 58 studies (78%) were small (n<50), 8 medium sized (n=50-100), and 8 large (n>100).
11 Participants were 3 to 20 years at time of surgery (mean age 6.0yr⁴² to 14.0yr²⁶). Where sex was
12 reported, the percentage of males ranged from 20%⁴³ to 100%;⁴⁴ overall 62% were male.

14 Where type was reported (76% of included studies), all participants had spastic CP. Eighty-six
15 percent of studies reported anatomical distribution. Two studies included children with unilateral
16 CP only.^{45,46} Twelve studies included children with unilateral and bilateral CP. The remaining
17 studies included children with bilateral CP only.

19 Forty-seven studies included children in GMFCS levels I-III. One included children in level IV
20 only⁴⁶ and the remainder included participants in levels I-IV, I-V or II-IV.^{28,30,42-44,47-50} Seventeen
21 studies did not report GMFCS level; all children were described as ambulatory with or without a
22 walking aid except for Khan,⁵¹ who reported all participants were non-ambulatory.

1 Description of surgery and rehabilitation

2 Description of surgery was rated adequate in 48 studies (65%). Soft tissue procedures only were
3 performed in seven studies.^{42,50,52-56} Bony and soft tissue procedures were performed in 64 studies.
4 Three studies did not state the type of procedures performed.⁵⁷⁻⁵⁹ Where reported, the number of
5 procedures conducted per participant ranged from 2⁵⁴ to 18;⁶⁰ the mean per patient was 2.2²⁵ to
6 12.9.³⁴ Provision of previous surgery was adequately reported in thirty-three studies.

7
8 Nineteen studies (26%) did not report any information regarding rehabilitation provided following
9 surgery. Twenty-five studies (34%) provided inadequate description of rehabilitation. Thirty
10 studies (40%) reported the frequency and/or duration of rehabilitation provided. Where reported,
11 the content of rehabilitation included active and passive movements, strengthening exercises,
12 stretching, balance, and gait training.

14 Outcome assessment

15 The duration of follow-up varied widely between studies. Where described, the mean duration of
16 follow-up was 1.0 years³⁰ to 21.3 years.⁶¹ We extracted data on short-term outcomes from three
17 studies,^{39,40,50} on intermediate-term outcomes from 26 studies, and on long-term outcomes from
18 45 studies. No study described outcomes in terms of the ICIDH framework. Seven studies
19 described outcomes in terms of the ICF framework but there was inconsistency in the measures
20 used to assess each domain.^{9,32,40,59,62-64} Authors reported assessing the collective domain of
21 “activity and participation” using the FMS,^{59,63} GMFM-66,^{9,64} Pediatric Evaluation of Disability
22 Inventory (PEDI),⁴⁰ time spent in upright positions measured with an activity logger,⁹ and self-
23 reported walking ability.³²

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2 Fifteen studies assessed gross motor function; ten studies used the GMFM-66 or GMFM-
3 88,^{9,25,28,32,33,38-40,50,64} three studies used the FAQ,^{30,52,65} and two studies used the FMS.^{59,63} Twenty-
4 nine studies assessed gait speed and thirty-five assessed gait using a summary score. Four studies
5 assessed participation,^{40,52,58,65} three assessed QoL,^{9,32,52} and four reported satisfaction with
6 surgery.^{32,65-67} Twenty-two studies assessed passive range of motion (knee extension [n=15] and
7 ankle dorsiflexion [n=17]), fourteen assessed muscle strength, and six assessed
8 spasticity.^{23,35,38,50,68,69}

9
10 Seventeen studies (23%) adequately reported adverse events. These included intra-operative
11 haemorrhage, poor post-operative pain management, hardware removal for pain, superficial
12 wound infection, nerve palsy, avascular necrosis, permanent reflex sympathetic dystrophy
13 syndrome, and occurrence of genu recurvatum. Three studies reported adverse events according to
14 the Clavien-Dindo classification.^{35,45,70} In these studies, 68 Grade I, 52 Grade II, nine Grade III,
15 and one Grade IV complication were reported among 265 children.

17 Effects of multilevel surgery

18 Data from 54 studies were included in meta-analysis; data from one RCT are reported separately.⁶⁴
19 Results from a further 8 studies are reported descriptively as insufficient information was provided
20 to include them in meta-analysis.^{52,59,63,65-67,71,72} Data on 12 studies are not reported as eight studies
21 assessed individual gait variables or GMFCS level,^{20,29,42,47,49,55,73,74} and four studies did not report
22 results from statistical analyses to allow interpretation of findings.^{32,51,58,60}

1 *Gross motor function*

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1 One RCT of 19 children, found that gross motor function as measured by the GMFM-66 did not
2 differ between children receiving MLS and children receiving resistance training at 1-year post-
3 surgery (MD between groups: 0.3, 95% CI -4.5 to 5.0). However, at 2-years post-surgery the
4 children receiving MLS demonstrated an improvement in GMFM-66 from baseline (MD: 4.9, 95%
5 CI 0.98 to 8.7). Pooled analysis indicated that gross motor function did not improve in the short-
6 term (standardised mean difference [SMD]: 0.01, 95% CI -0.48 to 0.50, $p=0.97$, $I^2=92%$, $p<0.001$,
7 $n=52$), intermediate-term (SMD: 0.51, 95% CI -0.56 to 1.58, $p=0.35$, $I^2=97%$, $p<0.001$, $n=104$),
8 or long-term (SMD: 0.38, 95% CI -0.25 to 1.01, $p=0.24$, $n=103$; Figure 2). Two studies ($n=118$)
9 reported that FAQ improved by a mean of 1.06 (<0.001) and 0.5 ($p=0.002$), respectively,^{52,65} and
10 one study ($n=75$) reported no change in FAQ ($p>0.05$),³⁰ in the intermediate-term.

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12
13 One study ($n=156$) reported that 5 years after MLS, 23%, 18% and 19% of participants required
14 less assistance at 5m, 50m and 500m, respectively.⁶³ A second study ($n=66$) found evidence of a
15 poorer rating on the FMS at 6 months compared to pre-surgery at all distances.⁵⁹ This study found
16 no evidence of change in FMS at 12 months, but evidence of an improvement in rating at 24
17 months at all distances.

18 19 *Gait speed*

20 One study assessed the short-term change in normalised walking speed following surgery and
21 found it declined (MD: -0.04, $p=0.002$, $n=20$).³⁹ There was no evidence that walking speed
22 changed in the intermediate-term (SMD: -0.08, 95% CI -0.22 to 0.07, $p=0.30$, $I^2=43%$, $p=0.02$,
23 $n=481$) or long-term (SMD: 0.12, 95% CI -0.01 to 0.25, $p=0.08$; Figure 3).

1

2 *Gait*

3 GPS improved in children who received MLS compared to those who received resistance training
4 at 1-year (MD between groups: -5.5, 95% CI -7.8 to -3.4, n=19). Pooled analysis indicated that
5 gait improved at 1-year following MLS (SMD: -0.78, 95% CI -0.98 to -0.57, p<0.001, I²=70%,
6 p<0.001, n=497). There was also improvement in gait in the long-term (SMD: -0.80, 95% CI -0.95
7 to -0.65, p<0.001; Figure 4). One study, not included in pooled analysis, reported improvements
8 in GDI in the intermediate-term (MD: 12.1, p<0.001, n=39) and long-term (MD: 10.3, p<0.001,
9 n=39).⁷²

10

11 *Passive range of motion*

12 Passive ankle dorsiflexion was greater among children who received MLS compared to those who
13 received resistance training at 1-year (MD between groups=7, 95% CI 3 to 12, p<0.001, n=19).
14 Knee extension declined in both groups (MD: -1 degrees for MLS group and MD: -3 degrees for
15 control group) but a comparison between groups was not conducted.

16

17 There was evidence of intermediate-term improvements in knee extension (SMD: 0.60, 95% CI
18 0.43 to 0.77, p<0.001, I²=0%, p=0.58, n=228) and dorsiflexion (SMD: 0.48, 95% CI 0.10 to 0.86,
19 p=0.01, I²=49%, p=0.12, n=96) following MLS. Long-term improvements in knee extension
20 (SMD: 0.43, 95% CI 0.24 to 0.61, p<0.001; Figure 5) and dorsiflexion (SMD: 0.47, 95% CI 0.17
21 to 0.76, p=0.002, I²=76%, p<0.001, n=324) were also observed. One study, not included in pooled
22 analysis, reported an improvement in dorsiflexion in the intermediate-term (p<0.001, n=19).⁷¹

23

1 *Strength*

2 Plantar flexor strength improved by a larger amount in children following MLS compared to
3 resistance training at 1-year (MD between groups: 1.9 kg, 95% CI 0.01 kg to 3.9 kg; n=19).⁹
4 Although quadriceps strength, hip extensor strength, and hip abductor strength were also measured
5 in the RCT, comparisons between groups were not conducted.

6
7 One study (n=20) found evidence of a decline in strength of the hip flexors (MD: -0.2 Nm/kg,
8 p<0.001), hip extensors (MD: -0.5 Nm/kg, p<0.001), hip abductors (MD: -0.1 Nm/kg, p=0.002),
9 knee flexors (MD: -0.6 Nm/kg, p<0.001), and knee extensors (MD: -0.5 Nm/kg, p<0.001) at 6
10 months post-surgery.³⁹ The second study reported an increase in general muscle strength at 6
11 months post-surgery (median 2 vs 3 on a scale of 0-4, p=0.020; n=25).⁵⁰ Pooled analysis found no
12 evidence for change in muscle strength in the intermediate-term (SMD:-0.22, 95% CI -0.50 to
13 0.06, p=0.12, I²=51%, p=0.08, n=117). We were unable to pool data from two studies; one reported
14 no change⁷⁵ and the second reported a decline in muscle strength.⁶⁹

15
16 Pooled analysis found no evidence of change in muscle strength in the long-term (SMD: -0.39,
17 95% CI -0.79 to 0, p=0.05, I²=74%, p<0.001, n=165). We were unable to include three studies in
18 pooled analysis; two found no change^{75,76} and one reported an improvement (p<0.05).⁶⁹

19 *Spasticity*

20 All studies that assessed short-term (n=25)⁵⁰ and intermediate-term (n=145)^{35,38,68,69} changes in
21 spasticity reported reduced spasticity (p<0.05). Two studies reported reductions and one reported
22 no change in spasticity in the long-term (n=118).^{23,68,69}

1

2 *Participation and quality of life*

3 Evidence for improvement in participation was observed at 6-months,⁴⁰ 1-year,^{40,52,65} and 2-years⁴⁰
4 following MLS (Table 2). Intermediate and long-term improvements in QoL were also observed
5 (Table 2).

6

7 *Satisfaction*

8 Satisfaction with the outcome of surgery was rated as mean (SD) 7.9 (2.0) on a scale of 0-10 (with
9 10 being completely satisfied) by 279 parents.⁶⁶ Sixty-one parents rated satisfaction with
10 functional and cosmetic outcomes as mean (SD) 6.8 (2.0) and 6.6 (2.0) out of 10, respectively.⁶⁵
11 Of 11 parents, 91% reported that they were satisfied with surgical outcomes.⁶⁷ When 11 children
12 were asked if the “results from SEMLS and rehabilitation were worth the effect” 9 and 10,
13 respectively, said yes at 1- and 2-years post-MLS.³²

14

15 Sensitivity analyses

16 Imputing the correlation co-efficient as 0.7 instead of 0.3 resulted in a change in conclusions for
17 the change in gait speed in the long-term (SMD: 0.17, 95% CI 0.04 to 0.30, p=0.01, I²=78%,
18 p<0.001), and strength in the long-term (SMD: -0.58, 95% CI -1.0 to -0.15, p=0.008, I²=91%,
19 p<0.001).

20

21 Subgroup analysis

22 When children with bilateral CP only were included in pooled analyses, there was evidence that
23 muscle strength declined in the intermediate-term (SMD: -0.35, 95% CI -0.64 to -0.07, p=0.02,

1 I²=9%, p=0.33, n=40) and long-term (SMD: -0.49, 95% CI -0.96 to -0.02, p=0.04, I²=75%,
2 p<0.001, n=134). All other analyses of children with bilateral CP only produced similar effect
3 sizes and identical inference to that obtained from the primary analysis.

4 5 **Discussion**

6 In summary, we found no evidence from a meta-analysis that gross motor function improved
7 following MLS, but some evidence of improvements in gait and passive range of motion. It should
8 be noted however, that there was significant heterogeneity associated with pooled analysis of gross
9 motor function and inconsistent findings across studies; while many studies found no evidence of
10 change in gross motor function following MLS some found evidence of improvement. Conversely,
11 there was some evidence that muscle strength declined in the 6 months following MLS and was
12 not different to pre-surgery levels at 1-year following MLS. Although only three and two studies
13 assessed participation and QoL, respectively, there was some evidence that participation and QoL
14 improved following MLS. Overall, parents reported being satisfied with outcomes of MLS,
15 although there was considerable variation in satisfaction ratings. Adverse events following MLS
16 appear relatively rare; only one adverse event that resulted in a “life-threatening complication
17 (including CNS complications) requiring IC/ICU management” (Grade IV complication according
18 to the Clavien-Dindo classification⁷⁷) was reported. However, adverse event reporting was
19 incomplete, with only 23% of studies adequately reporting adverse events.

20
21 Our findings support two previous reviews of MLS for CP.^{5,6} Both concluded that gait kinematics
22 improved following MLS, although neither conducted a quantitative synthesis of data. With a
23 similar search strategy to that used in the current review, McGinley identified 31 studies that

1 examined the effect of MLS for children with CP.⁵ Despite including twice as many studies in the
2 current review, we identified similar issues with the evidence base to those identified in 2010.
3 There was consistently inadequate reporting of participant characteristics, surgical interventions,
4 previous surgery, and rehabilitation. MLS is a complex intervention, consisting of interacting
5 components, which are particularly difficult to evaluate. For example there are difficulties
6 standardising the design and delivery of MLS and rehabilitation, and the causal association linking
7 the intervention and outcome is lengthy, complex and likely context dependent.⁷⁸ The results of
8 this review suggest that a pattern of initial deterioration in gross motor function occurs in the year
9 after MLS, followed by a return to baseline at 1-2 years post-MLS, and potentially further
10 improvements in the longer-term. However, it is difficult to comment on the long-term impact of
11 MLS on gross motor function given the relatively small number of patients who were assessed
12 beyond 1 year after surgery. This complex and lengthy interaction between the intervention and
13 outcome indicate that the content of MLS and rehabilitation are likely crucial to explaining
14 effectiveness or otherwise. Improved reporting of these factors is therefore essential to improving
15 the evidence base for MLS. Future studies should use reporting guidelines such as the CONSORT
16 statement⁷⁹ and the TIDiER checklist⁸⁰ to ensure that the study and the intervention are described
17 in sufficient detail to appraise and replicate.

18
19 A lack of RCTs is a significant limitation to the evidence base. We identified just one RCT of 19
20 children. All other evidence was from cohort studies, with many being retrospective reviews of
21 clinical records. As a result, studies often excluded patients without routine follow-up assessments
22 suggesting that the findings are subject to significant selection bias. While effect estimates may be
23 biased as a result of excluding participants from the analysis,⁸¹ the extent of attrition bias is

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3 1 unknown as the majority of studies did not report the proportion of eligible participants included
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5 2 in analyses. Further, few prospective cohort studies reported loss to follow-up. In addition,
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7 3 establishing causality is difficult without a comparison group to control for the potential impact of
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9 4 known and unknown confounding variables on the outcome. It should be noted however, that
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11 5 findings from the RCT largely align with pooled analyses of data from cohort studies. In particular,
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13 6 the mean difference of -5.5 in GPS score, observed between the intervention and control group at
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15 7 1-year,⁹ was very similar to the improvement in GPS observed in cohort studies (-3.7 to -
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17 8 7.1).^{35,45,57,64}
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24 10 The pilot RCT demonstrates that it is feasible to conduct RCTs of MLS. However, researchers still
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26 11 face several barriers to conducting well-designed RCTs. These include ethical concerns regarding
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28 12 allowing people to experience progression of musculoskeletal deformities without intervening,
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30 13 difficulty recruiting patients given the relatively small number of children that undergo MLS
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32 14 annually, and difficulties obtaining funding to conduct a multi-centre trial with sufficient duration
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34 15 of follow-up to evaluate the impact of MLS. Further, when designing future studies, careful
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36 16 consideration should be given to the comparator in order to overcome ethical concerns and provide
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38 17 clinically meaningful results. Although the current review suggests that MLS improves gait, it
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40 18 does not establish if MLS is the most appropriate approach to improving gait.
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47 20 We found very few studies that assessed outcomes according to ICF domains, despite all but three
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49 21 studies being published after the introduction of the ICF in 2001. The lack of prospective studies
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51 22 may explain why so few studies assessed outcomes across ICF domains. Lack of consensus
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53 23 regarding how to assess each ICF domain is also a barrier to using this framework. Regardless of
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1 whether or not a framework was used to evaluate MLS, it is concerning that only 10 studies
2 assessed activity using the GMFM, which is considered the criterion measure of gross motor
3 function. Additionally only four studies assessed participation and three studies assessed QoL.
4 More studies assessed passive range of motion, strength and spasticity, even though these are
5 arguably less meaningful outcomes to participants. Indeed, passive range of motion and spasticity
6 are associated with no change or very small changes in gross motor function.⁸² In order to provide
7 comprehensive information on the effects of MLS to families and professionals, future studies
8 need to prospectively plan to collect data on a range of outcomes. While the ICF provides a
9 standardised framework for the evaluation of interventions, it may be unrealistic to expect MLS to
10 improve activity and participation, given that activity and participation result from a complex
11 interaction between the individual and the environment. However, even if MLS does not improve
12 activity or participation, it may prevent further activity limitations and participation restrictions by
13 preventing deterioration in musculoskeletal deformities.

14
15 The lack of prospective data collection may explain why approximately 70% of studies did not
16 report information on adverse events. This review can therefore not make conclusions regarding
17 the safety of MLS. Standardised recording and reporting of adverse events should be implemented
18 in future studies to ensure consistent and deliberative reporting of safety. Additional limitations of
19 the evidence base are that all included studies are at high risk of bias for blinding of outcome
20 assessment and the majority had small sample sizes. Lack of blinding may exaggerate the effect
21 of MLS, particularly when outcomes are assessed using self-report measures, such as participation
22 and QoL.⁸³ Sample sizes may have impacted results by either inflating effect sizes or resulting in
23 statistically non-significant findings.^{84,85}

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5 2 There are also limitations to this review. We did not include grey literature or studies published in
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8 3 any language other than English. We included studies that reported outcomes before and after MLS
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10 4 even if the primary aim of the study was not to assess the effect of MLS. In order to include some
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12 5 data in meta-analyses we imputed correlation coefficients. However, sensitivity analyses,
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14 6 demonstrated that our findings were generally robust for different imputed values. There was
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17 7 evidence of at least moderate heterogeneity in all models, which may be explained by the large
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19 8 amount of clinical and methodological diversity in included studies.
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23 24 10 **Conclusions**

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26 11 This review represents the most comprehensive summary of the evidence on MLS for children
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28 12 with CP to date. Findings suggest that MLS is associated with changes in gait but not gross motor
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30 13 function in children with CP. However, the review identified considerable limitations to the
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32 14 evidence base that need to be addressed in future trials. Specifically, there is a need for RCTs and
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34 15 improvements in reporting of trials.
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Table 1. Description of included studies

Author	Design ^a	Participants				Surgery Type ^b	Procedure per patient, mean±SD (range)	Duration of follow-up, yr
		n (M,F)	Age, yr mean±SD (range)	Distribution (%)	GMFCS level (%)			
Adolfson 2007	Retro	31 (NS)	8.5±2 (5-15)	D (65), H (32), Q (3)	NS	Soft tissue	4.4	<i>Mean (range)</i> 1.9 (0.7- 6.4)
Akerstedt 2010	Prosp single-subject	11 (10,1)	13.8 (9-18)	Uni (9), Bi (91)	I (27), II (55), III (8)	Mixed	NS	2
Ancillao 2017	Unclear	9 (7,2)	11.1±2.4	Bi (100)	II-III	Mixed	NS	<i>Mean±SD</i> 1.2±0.4
Bernthal 2010	Prosp	23 (NS)	9.2 (6-14)	NS	NS	Soft tissue	4.2 (2-8)	1
Blumetti 2015	Retro (RFT, non-RFT)	216 (NS)	DRFT: 12.6±5.8 Non DRFT: 10.3±5.6	D (100)	I-III	Mixed	NS	<i>Mean±SD</i> DRFT: 3.38±3.19; Non- DRFT: 3.4±2.74
Bohm 2017	Retro (PT, PN)	32 (NS)	PT: 13.5±1.9 PN: 13.7±2.3 (8-18)	Bi (100)	I (16), II (84)	Mixed	NS	<i>Mean±SD</i> 2.0±0.2
Braatz 2013	Prosp	30 (18,12)	11.6±2.9	Bi (100)	I-III	Mixed	6.4	<i>Mean±SD</i> 1.1±0.2
Buckon 2004	Prosp	7 (4,3)	6.6 (4.3-11)	D (100)	I (29), II(14), III (57)	Mixed	NS	2
Chang 2017	Prosp	25 (20,5)	8.6 (4-12)	Bi (52), Q (48)	II (36), III (48), IV (16)	Soft tissue	NS	0.5
Cuomo 2007	Prosp	57 (NS)	9.5 (5-15)	NS	NS	Soft tissue	NS	<i>Mean (range)</i> 1.3 (0.8 -2.5)
Desailly 2017	Retro (PTS, no-PTS)	41 (NS)	PT: 10.8±1.6 No PTS: 10.8±1.9	NS	I-III	Mixed	NS	<i>Mean±SD</i> 2.3±0.8
Dreher 2007	Prosp	30 (22,8)	10.0± 2.9 (6-16)	D (100)	I (10), II (67), III (3),	Mixed	10.5	<i>Mean±SD</i> 11.3±0.7

					IV (20)			
Dreher 2012a	Prosp (DRFT, non-DRFT)	32 (19,13)	10.9±2.8 (6-16)	D (100)	I (9), II (53), III (38)	Mixed	7.1	<i>Mean±SD</i> DRFT: 1.0±0.6; Non-DRFT: 1.2±0.2
Dreher 2012b	Retro	39 (26,13)	10.2±3.5 (6-16)	D (100)	I (15), II (54), III (31)	Mixed	10.1	<i>Mean±SD</i> 8.1±1.8
Dreher 2012c	Retro (C-DRFT, P-DRFT) ^c	53 (36,17)	11.0±3.4	D (100)	I-III	Mixed	NS	<i>Mean±SD</i> 8.8±2.3
Dreher 2012d	Retro	44 (26,18)	9.8±3.4	D (100)	I (16), II (64), III (20)	Mixed	NS	<i>Mean±SD</i> 8.6 ±2
Dreher 2013a	Prosp (CBM, MTL)	42 (28,14)	CBM: 11.3±3.1 MTL: 11.1±5.4 (6-16)	D (100)	I (14), II (57), III (29)	Mixed	12.9	<i>Mean±SD</i> CBM: 9.2±2.5 MTL: 9.1±2.6
Dreher 2013b	Retro	42 (27,15)	9.8±2.8 (6-16)	D (100)	I (14), II (67), III (19)	Mixed	NS	<i>Mean±SD</i> 3.2±1.1
Dreher 2018	Retro	231 (142,89)	10.6±2.9 (5-16)	Bi (100)	I (8), II (62), III (29)	Mixed	8±3	<i>Mean±SD</i> 9.1±3.0
Feger 2015	Retro (O, MTL) ^d	48 (27,21)	O: 9.9±3.6 MTL: 9.0±3.6	D (65), H (29), Other (6)	I (29), II (35), III (35)	Mixed	O: 3.0±1.5 (1-5) MTS: 2.2±1.3 (1-4)	<i>Mean±SD (range)</i> O: 1.7±0.6 (1.0-2.9) MT: 1.9±0.6 (1.0-3.0)
Firth 2013	Retro	40 (25,15)	9.3 (4.8-15.1)	D (100)	II (68), III (32)	Mixed	9.1 (5-18)	<i>Mean (range)</i> 7.5 (4.4-14.6)
Gannotti 2007	Retro	20 (19,1)	9.5±3.0 (4.9-16.0)	D (100)	II (80), III (20)	Mixed	3.6	<i>Minimum</i> 4
Gannotti 2010	Retro	11 (5,6)	9.9 (7-13)	D (73), Q (27)	II (55), III (45)	Mixed	NS	<i>Mean (range)</i> 13 (11-15)
Godwin 2009	Retro	84 (35,49)	5.99±2.59 (3.25-16.33)	D (51), H (21), Q (27)	I (15), II (18), III (20), IV (33),	Soft tissue	5.45	5

					V (13)			
Gough 2004	Retro	12 (8,4)	9.8±3.3 (5.5-15.3)	D (100)	NS	Mixed	NS	<i>Mean (range)</i> 1.5 (0.8-2.4)
Gough 2008	Retro	13 (13,0)	6.4 (5.5-8.9)	Bi (100)	II (54), III (38), IV (8)	Mixed	5.1	<i>Mean</i> 4.2
Dobson 2005	Prosp	17 (14,3)	12.1 (7.1-17.1)	H (100)	IV (100)	Mixed	4.2 (2-7)	<i>Mean±SD</i> 2.9±0.9
Harvey 2007	Retro	66 (34,32)	10±2.5 (6-16)	D (100)	I (27), II (36), III (36)	NS	8 (4-12)	2
Harvey 2012	Retro	156 (99,57)	11.1±2.47 (6-19)	NS	I/II (62), III (38)	Mixed	7.6±2.1	5
Khan 2007	Prosp	85 (53,32)	8.5 (5-12)	D (100)	-	Mixed	NS	<i>Mean (range)</i> 3.5 (2-5)
Khouri 2013	Retro	25 (NS)	12±3	NS	I (27), II (42), III (23), IV (4)	Mixed	NS	<i>Mean±SD</i> 2.1±0.8
Klotz 2013	Retro	19 (13,6)	9.4±4.9 (4-23)	Bi (100)	II (100)	Mixed	NS	<i>Mean±SD (range)</i> 1.1±0.5 (0.8-2.8)
Klotz 2017	Retro	22 (14,8)	12.1±3.1 (6-16)	Bi (100)	I (9), II (41), III (50)	Mixed	NS	<i>Mean±SD (range)</i> 1.3±0.3 (1.0-1.9)
Klotz 2018	Prosp (PTS, no-PTS)	20 (NS)	10.4±2.6 (6-18)	Bi (100)	II (55), III (45)	Mixed	NS	<i>Mean±SD</i> 1.1±0.1
Kwon 2013	Retro (FDO, no-FDO)	53 (38,15)	FDO: 6.8±1.5 no FDO: 7.4±2.4	D (100)	I (68), II (32)	Mixed	NS	<i>Mean±SD</i> 1.1±0.4
Laracca 2014	Retro ^e	30 (17,13)	Group 1: 14.0 (11-17); Group 2: 12.6 (10-14)	D (100)	NS	Mixed	G1: 7.7 G2: 6.8	<i>Mean (range)</i> G1: 2.3 (1.1-4.3) G2: 1.8 (0.7-3.2)
Lee 2010	Prosp	61 (40,21)	10.2±3.8 (5.1-18)	D (13), H (87)	I (46), II (30), III (24)	Mixed	NS	<i>Mean±SD (range)</i> 2.2±0.5 (1.1-2.8)
Lee 2009	Retro	279 (191,88)	NS	D (58),	I (69),	Mixed	5.4±3.0	<i>Mean±SD</i>

				H (42)	II (26), III (5)			6.0±3.7
Lehtonen 2015	Retro	10 (2,8)	NS	D (100)	II (30), III (60), IV (10)	Mixed	4.2 (2–7)	5
Lofterød 2010	Retro	28 (16,12)	12 (7–19)	D (100)	I (21), II (50), III (29)	Soft tissue	6	<i>Mean (range)</i> 1.2 (1.0-2.1)
Mallet 2016	Retro (IMPL, no-IMPL)	34 (26,8)	13±2.8 (6.8–18.5)	D (100)	II (88), III (12)	Mixed	NS	<i>Mean±SD (range)</i> 2.4±2.0 (1.0–8.7)
Metaxiotis 2004	Prosp	20 (13,7)	11.5 (5.6-17.0)	D (100)	NS	Mixed	12.05	<i>Mean (range)</i> 3.1 (2.0-4.5)
Ng 2018	Retro	20 (14, 6)	12.7±3.1 (5.6-18.2)	D (100)	I (23), II (9), III (36), IV (27), V (5)	Mixed	NS	<i>Mean±SD (range)</i> 5.45±3.06 (1.48-13.11)
Õunpuu 2002	Prosp	20 (NS)	8.1±2.9 (5–15)	NS	NS	Mixed	NS	5
Õunpuu 2015	Retro	22 (11,11)	8.0±2.7	D (64), T (5), H (18), Q(14)	I (22.5), II (55), III (22.5)	Mixed	NS	<i>Mean±SD</i> 11±2
Patikas 2006	Prosp (EG, CG)	39 (27,12)	ST: 10.6±3.2 C: 8.9±1.9 (6-16)	D (100)	I (31), II (46), III (23)	Mixed	NS	2
Patikas 2007	Prosp	34 (22,12)	10.1±3.0 (6-16)	D (53), H (47)	NS	Mixed	NS	<i>Mean±SD (range)</i> 2.53±1.23 (1–5)
Rodda 2006	Retro	10 (7,3)	12.0 (7.9-16.2)	D (100)	II (30), III (70)	Mixed	7 (5-8)	<i>Minimum</i> 5
Rutz 2012	Retro	107 (61,46)	10.6±2.7 (6–17)	Bi (100)	II (69), III (31)	Mixed	8 (4–14)	<i>Mean±SD (range)</i> 5.0±2.7 (2–12)
Rutz 2013a	Retro	121 (73,48)	10.7±2.7	Bi (100)	II (66), III (34)	Mixed	7.6±2.1	<i>Mean±SD</i> 1.3±1.0
Rutz 2013b	Retro	14 (10,4)	13 (7–18)	D (100)	I (7), II (71), III (21)	NS	7.4±2.8 (4-15)	<i>Mean (range)</i> 1.8 (1-3)

Saraph 2000	Retro	22 (NS)	12.6 (7.4-16.6)	D (100)	NS	Mixed	8.2 (3-8)	<i>Mean (range)</i> 2 (2.1-4.0)
Saraph 2001	Retro	12 (NS)	12.7±3.3	D (100)	NS	Mixed	6.2	<i>Mean±SD</i> 3.2±0.6
Saraph 2002a	Retro (D, H)	22 (NS)	11.9 (9.2-15.5)	D (36), H (64)	NS	Mixed	7.4	<i>Mean (range)</i> 3.1 (3.0-3.9)
Saraph 2002b	Retro	25 (NS)	13.6 (6.0-15.5)	D (100)	NS	Mixed	8.2	<i>Mean (range)</i> 3.3 (3.0-3.9)
Saraph 2005	Retro	32 (NS)	11.1 (8.7-13.5)	D (100)	NS	Mixed	8.1	<i>Mean±SD</i> 4.4±1.1
Saraph 2006	Retro	11 (NS)	12.4 (9.5-17.2)	D (27), H (73)	NS	Mixed	7.5	<i>Mean (range)</i> 3.2 (2.3-4.0)
Schranz 2017	Retro	14 (9,5)	12.1±3.3 (6-17)	Uni (100)	I (43), II (57)	Mixed	5.1	<i>Mean±SD (range)</i> 9.4±2.2 (6-13)
Schwartz 2016	Retro	176 (99,77)	10.0±3.4	NS	I (14), II (48), III (38)	NS	NS	<i>Mean±SD</i> 1.4±0.4
Seniorou 2007	Prosp (EG, CG)	20 (10,10)	12.5±2.5 (7-16)	D (100)	I (15), II (65), III (20)	Mixed	9.1	1
Steinwender 2000	Retro	16 (NS)	10.2 (6-14)	D (100)	NS	Soft tissue	5.69	<i>Mean (range)</i> 3.4 (2.0-5.7)
Stephan-Carlier 2014	Retro	12 (10,2)	14.0±2.5 (11-18)	D (83), H (17)	I (25), II (25), III (50)	Mixed	8 (3-16)	<i>Mean (range)</i> 2.5 (1.0-4.8)
Sung 2013	Retro	29 (18,11)	8.3±2.6 (5.4-16.3)	D (100)	I (24), II (66), III(10)	Mixed	7.3	<i>Mean (range)</i> 11.8 (10.0-13.3)
Sung 2017	Retro	314 (198,116)	7.9 ± 3.7 (3.4-20.0)	D (100)	I-III	Mixed	6.2	<i>Mean±SD (range)</i> 2.7±2.9 (1.0-14.7)
Svehlík 2011	Retro	32 (17,15)	10.3±3.1 (5.7-15.5)	Bi (100)	II (38), III (62)	Mixed	NS	<i>Mean±SD</i> 21.3±3.3
Svehlík 2016	Retro	39 (22,17)	10.3±3.1 (5.7-15.5)	Bi (100)	II (51), III (49)	Mixed	7.5	<i>Minimum</i> 10
Taylor 2016	Retro (DFEO, PKC)	31 (NS)	13 (7-18)	D (87), H (3), Q (10)	I (6), II (32), III (58), IV (3)	Mixed	NS	<i>Mean (range)</i> PKC: 2 (0.8-4); DFEO: 1 (1-2)

Thomason 2011	RCT	19 (12,7)	9.7 (6-12)	D (100)	II-III	Mixed	8±4	2
Thomason 2013	Prosp	18 (11,7)	10.2±1.7 (7-17)	Bi (100)	II (72), III (28)	Mixed	8±3	5
Thompson 2010	Prosp (MI-SEMLS, SEMLS)	20 (12,8)	11.0±1.9 (7.8-14.3)	D (100)	I (15), II (65), III (20)	Mixed	NS	1
Truong 2011	Retro (Control, Psoas) ^f	87 (NS)	NS (3-8)	NS	I/II (66), III/IV (34)	Mixed	NS	<i>Mean±SD</i> 1.0±0.3
Van Drongelen 2013	Retro	14 (8,6)	9.3±2.0 (6.6-12.0)	D (100)	I (14), II (64), III (21)	Mixed	NS	<i>Mean (range)</i> 2.0 (1.3-3.2)
Zwick 2001	Retro	17 (NS)	11.2 (5.7-16.4)	D (100)	NS	Mixed	NS	<i>Mean (range)</i> 3.8 (2.6-5.7)
Zwick 2012	Retro (M, F)	34 (19,15)	M: 9.9±3.2, F: 11.3±2.8	D (100)	II-III	Mixed	M: 4.09±2.85 F: 3.92±2.36	<i>Minimum</i> 10

^aComparison groups in parentheses if applicable; ^bmixed: soft tissue and bony surgery; ^ccompared group that had distal rectus femoris transfer to correct decreased peak knee flexion in swing phase (C-DRFT) and group that had prophylactic distal rectus femoris transfer (P-DRFT); ^dcompared group that had osteotomy with or without muscle-tendon procedure (O) to group that had muscle-tendon procedure only (MTL); ^ecompared patients treated prior to year 2000 (group 1) and patients treated after 2000 (group 2); ^fcompared patients who had psoas lengthening as part of multilevel surgery (psoas) and patients who did not have psoas lengthening as part of multilevel surgery (control)

Bi: Bilateral; CBM: conversion of biarticular muscles; CG: control group; D: Diplegia; Dist: Distribution; DFEO: distal femoral extension osteotomy; DRFT: distal rectus femoris transfer; EG: exercise group; F: female; FDO: femoral derotation osteotomy; GMFCS: Gross motor function classification system; H: Hemiplegia; IMPL: intramuscular psoas lengthening; M: male; MI-SEMLS: minimally; MTL: muscle tendon lengthening; invasive single event multilevel surgery; NS: not stated; PKC: posterior knee capsulotomy; PN: no anterior pelvic tilt group; Prosp: prospective; PT: anterior pelvic tilt group; PTS: patellar tendon shortening; Q: Quadriplegia; Retro: retrospective; RCT: randomised controlled trial; RFT: rectus femoris transfer; SD: standard deviation; SEMLS: single event multilevel surgery; Uni: Unilateral.

Table 2. Changes in participation and quality of life following multilevel surgery.

Study	Sample size	Outcome	Outcome measure	Domain	Result
Intermediate-term results					
Buckon 2004	7	Participation	PEDI	Social skills	MD: 7.41, 95% CI 2.56 to 12.26
Buckon 2004	7	Participation	PEDI	Self-care	MD: 5.5, 95% CI 0.63 to 10.37
Cuomo 2007	57	Participation	PODCI	Global function	MD: 8.25, p<0.001
Lee 2010	61	Participation	PODCI	Global function	MD: 2.6, p=0.02
Cuomo 2007	57	Quality of life	PedsQL		MD: 10.03, p<0.001
Long-term results					
Buckon 2004	7	Participation	PEDI	Self-care	MD: 8.17, 95% CI 2.35 to 13.99
Buckon 2004	7	Participation	PEDI	Mobility	MD: 7.34, 95% CI 0.39 to 14.2
Buckon 2004	7	Participation	PEDI	Social skills	MD: 7.67, 95% CI 3.10 to 12.24
Thomason 2011	11	Quality of life	CHQ		MD: 22, 95% CI 4 to 39

PEDI: Pediatric Evaluation of Disability Inventory; MD: mean difference; CI: confidence interval; PODCI: Pediatric Outcomes Data Collection Instrument; PedsQL: Pediatric Quality of Life instrument; Child Health Questionnaire.

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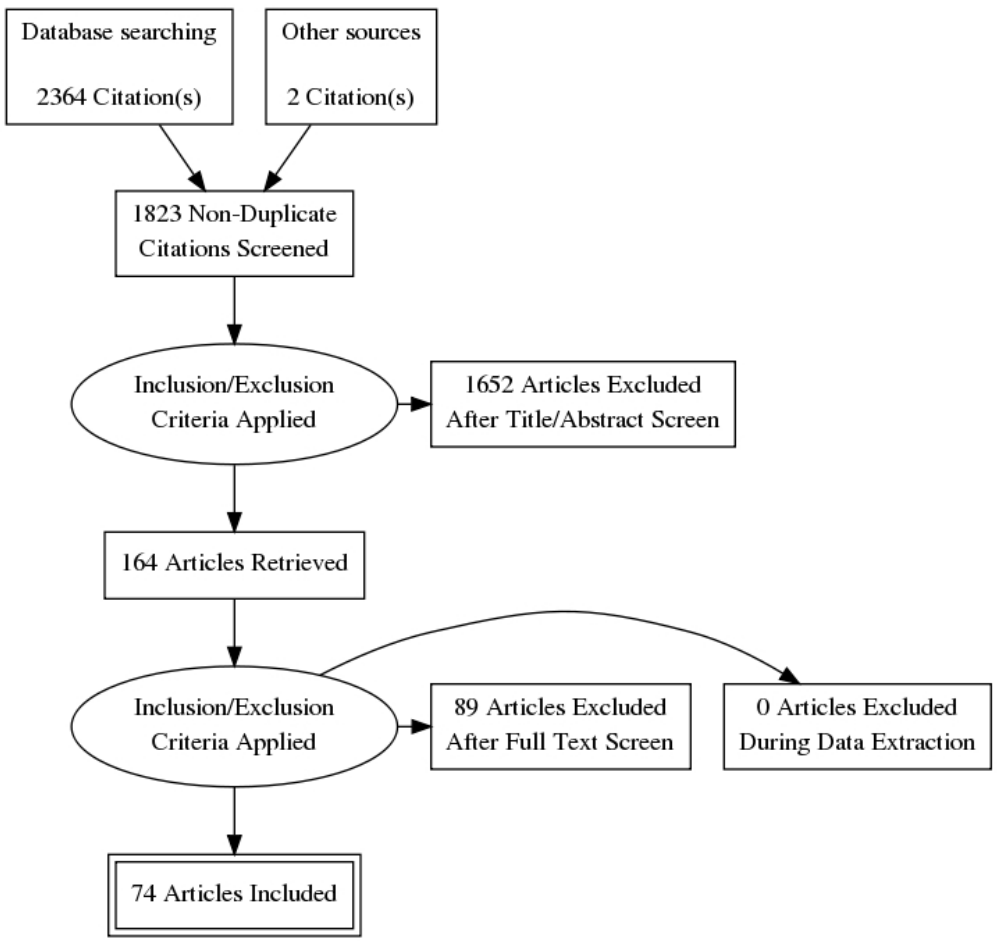


Figure 1. Study flow diagram
253x238mm (72 x 72 DPI)

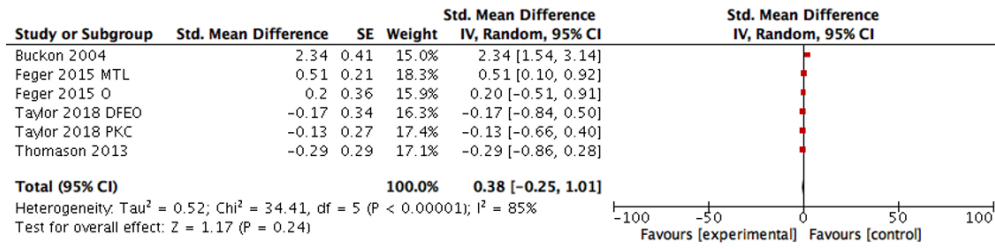


Figure 2. Long-term effect of multilevel surgery on gross motor function

298x72mm (96 x 96 DPI)

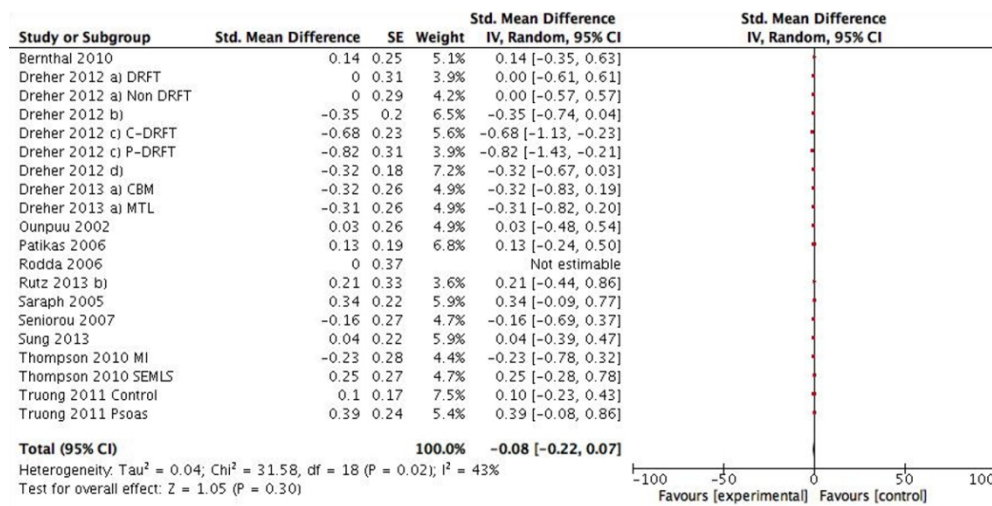


Figure 3. Long-term effect of multilevel surgery on gait speed

316x158mm (96 x 96 DPI)

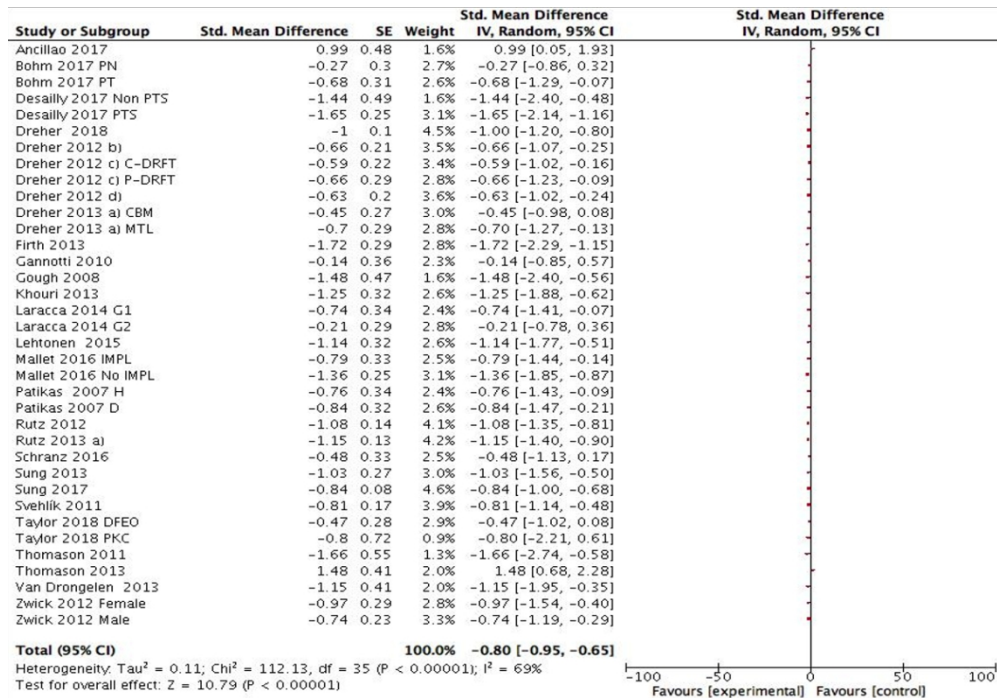


Figure 4. Long-term effect of multilevel surgery on gait

317x221mm (96 x 96 DPI)

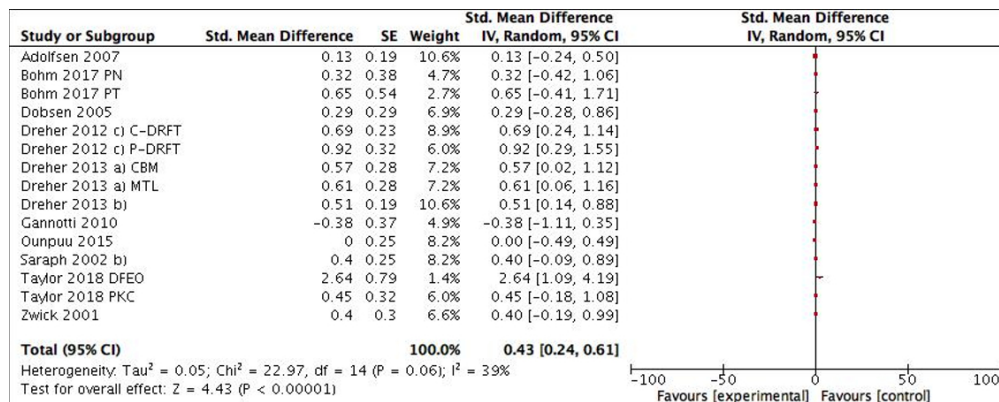


Figure 5. Long-term effect of multilevel surgery on knee extension range of motion.

299x120mm (96 x 96 DPI)

Supplemental table. Quality assessment of included studies

Author	Quality of reporting ^a				MINORS ^b
	Surgery	Previous surgery	Adverse events	Rehabilitation	
Adolfson 2007	2	1	0	0	7
Akerstedt 2010	1	0	2	2	12
Ancillao 2017	1	1	0	0	6
Bernthal 2010	2	0	0	2	12
Blumetti 2015	1	0	0	0	4
Bohm 2017	1	0	0	0	5
Braatz 2013	1	2	0	1	10
Buckon 2004	2	0	0	2	10
Chang 2017	2	2	0	2	10
Cuomo 2007	1	0	0	1	11
Desailly 2017	1	0	0	1	5
Dreher 2007	2	2	0	1	8
Dreher 2012a	2	2	0	1	13
Dreher 2012b	2	0	2	1	5
Dreher 2012c	2	0	0	1	7
Dreher 2012d	2	0	1	1	7
Dreher 2013a	2	2	2	1	7
Dreher 2013b	1	2	0	0	7
Dreher 2018	1	2	2	0	6
Feger 2015	2	2	0	2	8
Firth 2013	2	1	0	1	7
Gannotti 2007	2	1	0	0	7
Gannotti 2010	1	0	0	0	9
Godwin 2009	2	0	0	0	9

Gough 2004	1	0	0	1	6
Gough 2008	2	0	1	1	6
Dobson 2005	2	1	2	2	9
Harvey 2007	0	0	0	0	10
Harvey 2012	1	0	0	1	10
Khan 2007	2	0	2	2	6
Khoury 2013	2	0	0	0	4
Klotz 2013	2	2	0	1	9
Klotz 2017	2	2	0	1	8
Klotz 2018	2	2	2	1	12
Kwon 2013	2	2	0	1	8
Laracca 2014	2	1	0	1	5
Lee 2010	1	2	0	1	12
Lee 2009	2	2	0	0	9
Lehtonen 2015	1	0	0	2	9
Lofterød 2010	2	2	0	0	7
Mallet 2016	1	1	0	0	7
Metaxiotis 2004	2	2	2	2	8
Ng 2018	1	0	0	0	7
Õunpuu 2002	2	2	2	1	7
Õunpuu 2015	2	0	0	1	8
Patikas 2006	2	2	1	2	9
Patikas 2007	2	2	0	0	6
Rodda 2006	2	2	0	2	10
Rutz 2012	1	0	0	1	7
Rutz 2013a	1	1	1	1	7
Rutz 2013b	2	1	2	2	9
Saraph 2000	2	0	2	2	4
Saraph 2001	2	0	0	2	6
Saraph 2002a	2	2	0	2	6
Saraph 2002b	2	2	0	2	5

Saraph 2005	2	2	0	2	6
Saraph 2006	2	2	0	2	4
Schranz 2017	2	2	2	2	8
Schwartz 2016	0	0	0	0	7
Seniorou 2007	2	1	0	2	11
Steinwender 2000	2	2	0	2	7
Stephan-Carlier 2014	1	0	0	1	7
Sung 2013	2	0	0	2	8
Sung 2017	2	0	0	1	8
Svehlík 2011	1	2	0	2	5
Svehlík 2016	1	2	0	2	5
Taylor 2016	2	0	2	2	8
Thomason 2011	2	2	2	2	21
Thomason 2013	2	2	2	2	13
Thompson 2010	2	1	2	2	8
Truong 2011	1	2	2	0	5
Van Drongelen 2013	1	0	0	0	8
Zwick 2001	2	2	0	2	9
Zwick 2012	1	2	0	2	5

^aassessed as 0 (not reported), 1 (reported but inadequate), 2 (reported and adequate); ^btotal possible score is 16 for all studies except for Thomason 2011;

Appendix 1 Search strategy**CINAHL**

1. AB Cerebral palsy
2. Orthopaedic surgery OR
3. Orthopedic surgery OR
4. Orthopaedics OR
5. Orthopedics OR
6. Surgery OR
7. SEMLS OR
8. Single event multilevel surgery OR
9. Single event multi level surgery OR
10. Multilevel OR
11. Multi level OR
12. AB (2 to11)
13. 1 AND 12

Ovid MEDLINE

1. Keyword: Cerebral palsy
2. Orthopaedic surgery OR
3. Orthopedic surgery OR
4. Orthopaedics OR
5. Orthopedics OR
6. Surgery OR
7. SEMLS OR
8. Single event multilevel surgery OR
9. Single event multi level surgery OR
10. Multilevel OR
11. Multi level OR
12. Keyword (2 to 11)
13. Map term to subheading 12
14. 1 AND 13

EMBASE

1. Title, abstract, keywords: Cerebral palsy
2. Orthopaedic surgery OR
3. Orthopedic surgery OR
4. Orthopaedics OR
5. Orthopedics OR
6. Surgery OR
7. SEMLS OR
8. Single event multilevel surgery OR
9. Single event multi level surgery OR
10. Multilevel OR
11. Multi level OR
12. Title, abstract, keywords (2 to 11)
13. 1 AND 12

Cochrane Central Register of Controlled Trials (CENTRAL)

1. Title, abstract, keywords:Cerebral palsy
2. Orthopaedic surgery OR
3. Orthopedic surgery OR
4. Orthopaedics OR
5. Orthopedics OR
6. Surgery OR
7. SEMLS OR
8. Single event multilevel surgery OR
9. Single event multi level surgery OR
10. Multilevel OR
11. Multi level OR
12. Title, abstract, keywords (2 to 11)
13. 1 AND 12

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