Motor Development Interventions for Preterm Infants: A Systematic Review and Meta-analysis

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abstract

CONTEXTS: Preterm infants are at an increased risk of neurodevelopmental delay. Some studies report positive intervention effects on motor outcomes, but it is currently unclear which motor activities are most effective in the short and longer term.

OBJECTIVE: The aim of the study was to identify interventions that improve the motor development of preterm infants.

DATA SOURCES: An a priori protocol was agreed upon. Seventeen electronic databases from 1980 to April 2015 and gray literature sources were searched.

STUDY SELECTION: Three reviewers screened the articles.

DATA EXTRACTION: The outcome of interest was motor skills assessment scores. All data collection and risk of bias assessments were agreed upon by the 3 reviewers.

RESULTS: Forty-two publications, which reported results from 36 trials (25 randomized controlled trials and 11 nonrandomized studies) with a total of 3484 infants, met the inclusion criteria. A meta-analysis was conducted by using standardized mean differences on 21 studies, with positive effects found at 3 months (mean 1.37; confidence interval 0.48–2.27), 6 months (0.34; 0.11–0.57), 12 months (0.73; 0.20–1.26), and 24 months (0.28; 0.07–0.49). At 3 months, there was a large and significant effect size for motor-specific interventions (2.00; 0.28–3.72) but not generic interventions (0.33; −0.03 to −0.69). Studies were not excluded on the basis of quality; therefore, heterogeneity was significant and the random-effects model was used.

LIMITATIONS: Incomplete or inconsistent reporting of outcome measures limited the data available for meta-analysis beyond 24 months.

CONCLUSIONS: A positive intervention effect on motor skills appears to be present up to 24 months' corrected age. There is some evidence at 3 months that interventions with specific motor components are most effective.

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Dr Hughes identified the studies, carried out the analysis, and drafted the initial manuscript; Profs Redsell and Glazebrook assessed the studies for inclusion and reviewed and revised the initial manuscript; and all authors approved the final manuscript as submitted.

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BACKGROUND

Preterm birth is categorized as extremely preterm (<28 weeks' gestation), very preterm (28 to <32 weeks' gestation), and moderate to late preterm (32 to <37 weeks' gestation), with decreasing gestational age at birth associated with increased risk of mortality and disability and greater intensity of care.[1,2] Platt[3] highlighted that preterm birth is a common worldwide issue, with an estimated 10% of all births being preterm, although the majority of these births (85%) occur after 31 weeks' gestation. Extremely and very preterm infants (<32 weeks' gestation) are at high risk of developmental delay,[4,5] but even infants who are free of major neurodevelopmental delays are still at a higher risk of poor motor outcomes, such as subtle deficits in eye-hand coordination, sensory-motor integration, manual dexterity, and gross motor skills.[6,7] If these difficulties persist, integration and performance at school can be affected, leading to lower self-esteem.[8,9] In addition, a higher risk of attention-deficit/hyperactivity disorder has been identified not only in extremely/very preterm infants or those with a very low birth weight but also in late preterm infants and those with a weight of only 1 SD below the mean.[8] This finding has additional implications for motor development, because children with attention-deficit/hyperactivity disorder symptoms were found to be overrepresented in a community sample of children with low levels of confidence in relation to physical exercise and other barriers to physical activity.[10]

Interventions for Preterm Infants

A number of interventions have aimed to enhance the neurodevelopment of preterm infants and although these are predominantly focused on improving cognitive skills, the relationship between motor and cognitive development is well established.[11–13] The majority of studies initiate recruitment while the infant is in the NICU, and a number of these focus the intervention so that it is conducted solely in the NICU setting. An example of such a program is the Newborn Individualized Developmental Care and Assessment Program (NIDCAP). The NIDCAP intervention involves trained health professionals observing the infant's behavior and adapting the care provided, such as positioning the infant and/or altering the environment of the neonatal unit, such as lighting levels. Initial results from the NIDCAP program were promising, but the longer term impact is unclear.[14–18] A systematic review on NIDCAP interventions[19] concluded that the evidence for long-term positive neurodevelopmental effects or short-term medical effects is limited. This finding may reflect restricted opportunities to develop motor skills in the neonatal unit and the importance of the timing and length of intervention, given the complexity and rapidity of developmental changes that occur in the first 3 years.[20] Evidence suggests that interventions that continue beyond discharge from the neonatal unit, and those that involve parents,[21] are more likely to show benefits.[22]

Parent-Infant Interactions

There is a good rationale for involving parents in intervention delivery because mothers experience difficulties interacting with their extremely or very preterm infants.[21] Mothers may perceive their preterm infants as being too sleepy or fragile for play in the early months after discharge and are reluctant to rouse sleeping infants,[23] with the result that infants spend long periods asleep in the supine position, restricting opportunities for motor activity. Providing opportunities for time and play in the prone position is associated with better motor outcomes,[24] and guided play may also increase the confidence of the mother in handling and interacting with her preterm infant.

A recent Cochrane review[25] of early developmental intervention programs to prevent motor and cognitive impairment highlighted the impact that even a minor motor impairment can have on a child and concluded that effective activities to enhance the motor skills of preterm infants need to be identified. This review adds to the Spittle et al[25] review by identifying activities that can improve infants' motor skills, tested via randomized controlled trials (RCTs) and nonrandomized trials that commenced in the neonatal unit or on discharge from hospital. In addition, the analyses are separated according to the age of the infant at the assessment, thus enhancing the review by Spittle et al.

Objectives

The objective was to determine whether early interventions with preterm infants that are commenced in or after discharge from the neonatal unit within the first year of life improve the development of fine and gross motor skills. A further objective was to identify the components of effective interventions to inform the development of clinical guidelines for early intervention and the delivery of care programs to reduce motor delay.

Questions

To meet the objectives the following questions were divised:

1. What interventions are effective in improving the motor development of preterm infants?

2. What activities are most effective in the short/medium term?

METHODS

Inclusion and Exclusion Criteria

A protocol for the selection of studies was agreed upon by using Cochrane

TABLE 1 Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria
Participant	Premature infants born at <37 weeks' gestation	Full-term infants only
Intervention	Intervention that aims to enhance infants' development	No intervention
	Interventions that continue or start once the infant has been discharged from hospital	Intervention conducted only in the neonatal unit before initial hospital discharge
Comparison	Control group from premature population	Comparison group only full-term infants
Outcome	Measure of motor development at ≤5 years	No measure of motor development preschool (≤5 years)
Study design	RCTs	Review papers; no new data
	Controlled trials	Case studies or case reports
	Cohort/comparison studies	Protocol or development publications

guidance[26] criteria for health condition/population, intervention, and study design. The elements of comparison and outcome were also incorporated into the inclusion and exclusion criteria (Table 1).

All studies that included preterm infants were eligible for inclusion. Studies reporting outcomes in children >5 years of age were not included in this review. An earlier scoping search revealed limited work in the school-aged population.

Search Strategy

A combination of approaches were incorporated to minimize bias in the review process.[27] These included a systematic search of 17 electronic databases, including "gray literature" (Table 2).

In addition, hand searches of relevant journals and conference proceedings, reviewing reference lists, and conducting author and citation searches were also done. Myers and Ment[28] suggested that when looking at outcomes for preterm infants, advances in neonatal intensive care should be taken into account, and the available treatments for preterm infants born before the 1980s need to be considered as confounding variables. The search parameters were therefore from 1980 up to and including April 2015. No other limitations were set to the search strategy, and translations were sought when the full text was not originally published in English. Search terms are shown in Supplemental Tables 8 and 9. Supplemental Table 8 uses the Lefebrve et al[29] criteria, and an example of the search strategy is shown in Supplemental Table 9.

TABLE 2 Databases Used

Electronic Databases
AMED
CINAHL
Cochrane Central Registry
Embase
ERIC
Maternity and Infant Care
Medline
PEDro
ProQuest
PsycInfo
PubMed
Science Direct
SCOPUS
Web of Knowledge
Web of Science
EThoS
OpenGrey

The articles from the initial searches (N = 1399) were screened by the first author (A.J.H.) using title and abstract. For the second round, the full texts of the 143 remaining articles were screened independently by the authors with the use of the inclusion and exclusion criteria. One hundred articles were excluded for reasons relating to 1 of the 5 Participant Intervention Comparison Outcome Study design (PICOS) elements, as shown in Fig 1, with the use of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement.[30]

Data Extraction

The data extraction sheet for this review was adapted from the Centre for Review and Dissemination[27] and The Cochrane Collaboration Handbook.[26] Data were checked for appropriateness and quality by the first author and then assessed by the remaining authors. Studies were not excluded on the basis of quality and non-RCTs were included, resulting in higher heterogeneity. Therefore, a random-effects model was used for the meta-analysis.

FINDINGS

Types of Studies

The 42 remaining publications consisted of 36 trials, 5 follow-up studies[31–35] from 3 of the primary studies, and 1 study that reported different elements over 2 publications[36,37] Of the 36 trials, 25 were RCTs[36,38–61] and 11 were nonrandomized comparison trials.[62–72] Studies with follow-up data were all RCTs that reported outcome measures at different time points (6 months' to 5.5 years' corrected age [CA][31]). Duplicated data were excluded, and only the new data were included in the relevant age-based analyses. For the meta-analysis, the data were subdivided by CA of the infant, which enabled only 1 set of data for each time point to be included. In cases in which at least 2 studies reported outcome measure data at a set age, meta-analysis was conducted within RevMan 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark).[73] The data extracted were continuous: means and SDs or medians and ranges, with higher scores denoting better motor skills.

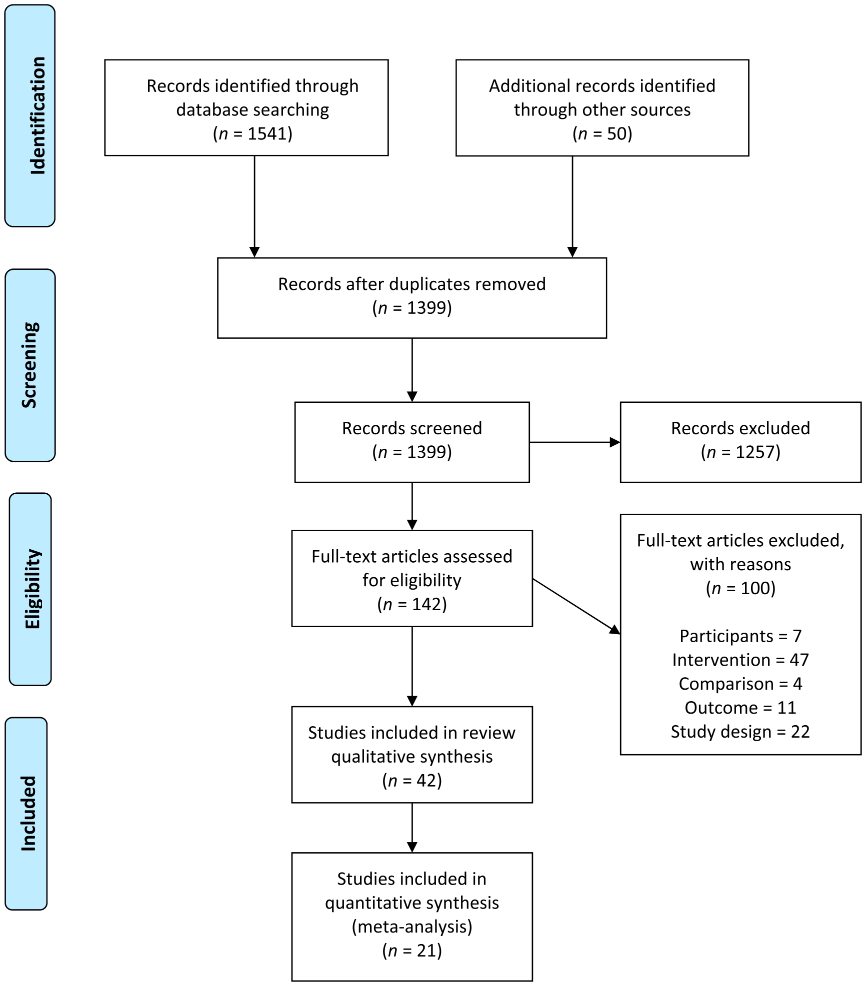

FIGURE 1
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flowchart of study selection process.

Moreover the scales used to measure motor outcomes varied; therefore, standardized mean differences and random effects were used.[74] When medians and ranges were provided, the means and SDs were calculated by the first author. Heterogeneity was measured by using the I^2 test available via the Cochrane Collaboration.

Risk of bias is shown in Table 3, and the characteristics of nonrandomized studies are shown in Table 4. Both tables are displayed in the order of age at assessment.

Participants

A total of 3484 preterm infants were enrolled in the 36 studies, with *n* = 2750 participants in the 25 RCTs and an additional 734 participants included in the 11 nonrandomized studies. The sample sizes for the included studies varied from 10[64] to 285[50] participants.

The majority of RCTs recruited infants with a gestational age of <34 weeks, although the birth weight and gestational age of participants at the time of intervention varied within the studies. Almost all studies (34 of 36) recruited samples of exclusively preterm infants, with only 2 of 34 studies[41,55] including both preterm and term infants. Two studies[59,72] included an additional control group of infants born exclusively at term, but data from these groups were excluded from the review.

Those with a wide range of gestational ages and/or birth weights tended to stratify the results into early/late preterm and/or very low/low birth weight.[31–33,35,40,46–48,50,75] This method is appropriate because there is evidence that the lower the gestational age or birth weight, the higher the risk of developmental problems. However, stratification criteria were not consistently identified within the included studies.

Aim and Focus of the Interventions

The majority of the studies included interventions aimed at improving both the cognitive and motor development of the preterm infant. Of those 13 studies that aimed specifically at enhancing motor development, 9 were RCTs [36,38,41,42,49,50,52,55,58] and an additional 4 were nonrandomized studies.[63,64,67,68] The type of intervention varied because the focus for some of the studies was to enhance the parent-infant relationship as a means to improving infant development, whereas others provided additional support or sessions with either a physiotherapist or occupational therapist. This situation resulted in the theoretical components and implementation of the intervention activities also varying. For all studies, the intervention was in addition to usual care. When categorizing by type of intervention, 8 of 13 (61.5%) studies that specifically targeted motor skills showed a significant benefit for motor skills compared with 9 of 22 (40.9%) generic interventions.

Initiation and Implementation of Intervention

Studies varied in the age that an intervention started, although the majority commenced while the infant was still in the neonatal unit.[32,45–47,51,55,58,61,66,69–72] Some interventions did not commence until the infant was 3[41,60,64] or 6 months' CA.[68] The intervention programs within the majority of the studies comprised activities that involved both

TABLE 3 Characteristics of Included RCTs

First Author, Year	Participants, n	Intervention	Outcome Measure	Age at Assessment Term
Lekskulchai, 2001[49]	111 (43 int, 41 con)	Motor development	BSID	1, 2, 3, and 4 months
Chen, 2014[43]	117 (63 int, 54 con)	Multidisciplinary	BSID	2, 3, 6, 12, 18, and 24 months
Blauw-Hospers, 2011[41]	46 (21 int, 25 con)	Family-centered physiotherapy	AIMS	3, 6, and 18 months
Tan, 2004[54]	60 (30 int, 30 con)	Early-stage upbringing plan	GSID	3, 6, 9, and 12 months
Barrera, 1986[40]	59 (40 int, 19 con)	Development or Interaction	BSID	4 and 16 months
Barrera, 1990[35]	—[ab]	—[ab]	MSCA and MCDI	54 months
Cameron 2005[42]	72 (34 int, 38 con)	Physiotherapy	AIMS	4 months
Heathcock, 2008[36]	26 (13 int, 13 con)	Motor training	AIMS	4 months
Heathcock, 2009[37]	—[ab]	—[ab]	No set scale	—[ab]
Resnick, 1988[51]	41 (21 int, 20 con)	Multidisciplinary	BSID	6 and 12 months
Koldewijn, 2009[47]	176 (86 int, 90 con)	IBAIP	BSID	6 months
Jeukens-Visser, 2014[31]	—[cd]	—[cd]	BSID	12 and 18 months
Koldewijn, 2010[32]	—[cd]	—[cd]	BSID	24 months
Verkerk, 2012[33]	—[cd]	—[cd]	BSID	44 months
Nurcombe, 1984[59]	74 (34 int, 40 con)	Mother-infant transaction	BSID	6 months
Ohgi, 2004[61]	23 (12 int, 11 con)	Early intervention	BSID	6 months
Widmayer, 1981[56]	30	Brazelton mother and neonatal	BSID	12 months
Bao, 1999[39]	103 (52 int, 51 con)	Early intervention	BSID	18 and 24 months
Johnson, 2009[45]	243 (112 int, 121 con)	Parenting	BSID	24 months
Kaaresen, 2008[46]	136 (69 int, 67 con)	Mother-infant transaction	BSID	24 months
Spittle, 2010[53]	120 (61 int, 59 con)	Preventive care program	BSID	24 months
Spencer-Smith, 2012[34]	—[ab]	—[ab]	Movement ABC	48 months
Weindling, 1996[55]	105 (51 int, 54 con)	Early physiotherapy	MAI, LbL, and GSID	24 months
Wu, 2014[57]	178 (120 int, 58 con)	Clinic or home based	BSID	24 months
Kynø, 2012[48]	118 (62 int, 57 con)	Mother-infant transaction	ASQ and MSEL	36 months
Gianní, 2006[60]	38 (18 int, 18 con)	Mother-child intervention	GSID	36 months
Johnson, 2005[44]	284 (68 dev int, 84 soc int, 63 con)	Developmental or social support	Movement ABC	60 months
Angulo-Barroso, 2013[38]	28 (15 int, 13 con)	Treadmill training	No set scale	No set age
Ma, 2015[50]	285	Multidisciplinary	No set scale	No set age
Soares, 2013[52]	36 (24 int, 12 con)	Practice reaching	No set scale	No set age
Yiğit, 2002[58]	160 (80 int, 80 con)	Early intervention	No set scale	No set age

Several scales were used. Outcomes were measured by using the following scales: AIMS, ASQ, BSID, GSID, LbL, Movement ABC, MAI, MCDI, MSCA, MSEL, and TIMP. AIMS, Alberta Infant Motor Scale; ASQ, Ages and Stages Questionnaire; con, control; dev, developmental; GSID, Griffiths Scales of Infant Development; IBAIP, infant behavioral assessment and intervention program; int, intervention; LbL, Limb-by-Limb; MAI, Movement Assessment of Infant; MCDI, Minnesota Child Development Inventory; Movement ABC, Movement Assessment Battery for Children; MSCA, McCarthy Scales of Children's Abilities; MSEL, Mullen Scales of Early Learning; soc, social.

[a] As above.

[b] As above.

[c] Follow-up of Koldewijn 2009.

[d] Follow-up of Koldewijn 2009.

health care professionals and parents/caregivers. In these interventions, the activities were demonstrated by the health care professionals for parents to engage in with their infant in the home environment.

Intervention Activities

The majority of studies included activities such as interacting with the infant and some form of handling and positioning in the initial 2 months after birth. The positioning was adapted according to age and ability, with the amount of support decreasing as the infant's development progressed. The studies that provided the most detail about intervention activities were commenced from term to 4–6 months' CA.[41,42,49] Activities and suggested appropriate age are shown in Table 5.

Many of the studies in which the intervention activities were for ≤12 months tended to include a basic description of the type of activity included, and discriminated between fine and gross motor exercises. However, most of the studies that delivered longer term interventions provided very little detail of the activities undertaken.[39,54,58,64,72] To identify effective activities, data were extracted and the studies that reported interventions with a significant effect size ($P < .05$) were scrutinized to determine any recurring stage-appropriate activities.

Duration of Intervention

Information regarding the duration and frequency of the intervention was described in the majority of studies and varied from 10 minutes[36,37] to sessions that lasted up to 120 minutes.[76] The number of sessions varied from 6[45] to 120.[64] The duration of the intervention program also varied: for example, lasting from birth up to term[66] as well as an intervention that commenced at 3 months' CA and lasted until the infant was 39 months' CA.[64] The majority of included studies continued the intervention beyond 3 months' CA. Most common were interventions that lasted until the infant was 6

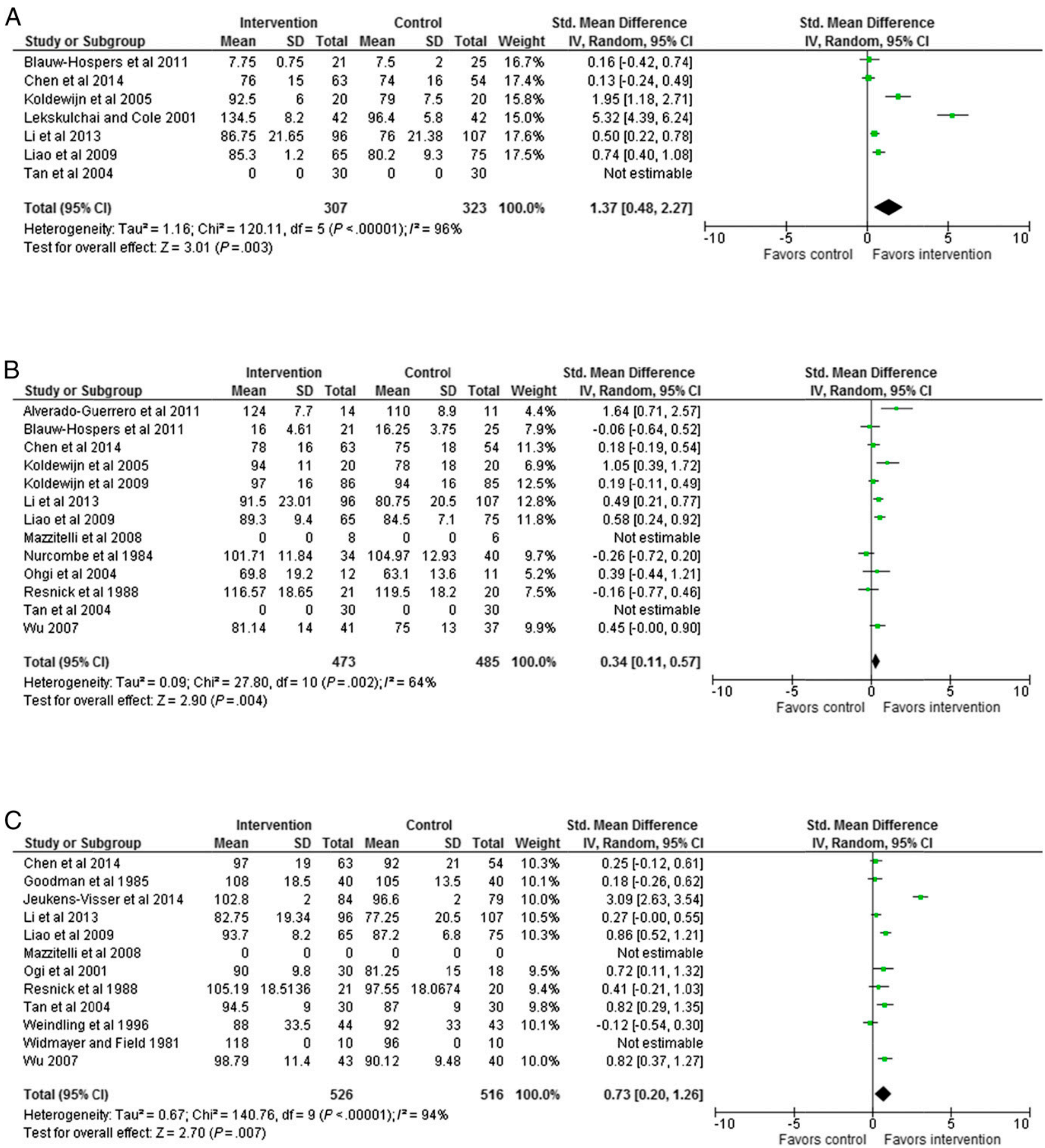

FIGURE 2
Forest plots for motor assessments at 3 (A), 6 (B), and 12 (C) months' CA. CI, confidence interval; IV, inverse variance.

months' CA[41,42,46,47,49,50,61,62,67,69,71] or 12 months' CA.[51,55,60,63,65,70,72,76]

Outcome Measures

A range of assessment tools were used to measure motor function, with some studies using >1 scale[41,55,70] and others assessing motor behaviors rather than using a standardized test.[37,58,64] Nineteen studies used the Bayley Scales of Infant and Toddler Development (BSID), either the first or second edition (see Tables 3 and 4). The age at assessment also varied, although the most frequently used CA for studies that used the BSID was 6 or 24 months, followed by 12 months.

Meta-analysis

In cases in which motor assessment scores were provided at specific ages

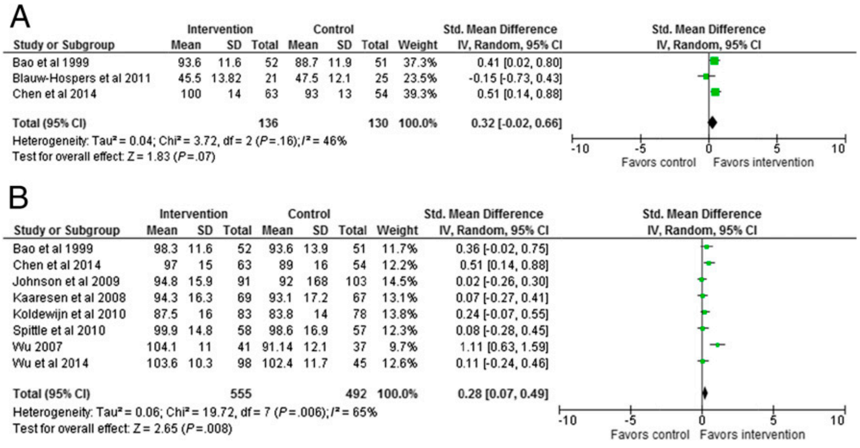

FIGURE 3
Forest plots for assessments at 18 (A) and 24 (B) months' CA. CI, confidence interval; IV, inverse variance.

by >2 studies, meta-analysis was undertaken. Studies that measured motor function at a time point from term (40–42 weeks' gestation) to 5 years' CA were included, although most studies assessed infants up to 24 months. When sufficient intervention and control group data were provided, the effectiveness of interventions was assessed. Therefore, a meta-analysis was conducted on data at 8 different ages: term, 2 months, 3 months, 4 months, 6 months, 12 months, 18 months, and 24 months. Table 6 shows the outcome for each of the age ranges. Figures 2 and 3 show forest plots for the age ranges that contained data from at least 3 studies (Fig 2: ages 3, 6, and 12 months; Fig 3: ages 18 and 24 months).

The meta-analysis revealed that interventions can enhance the motor development of preterm infants, although the effect varies over time. Significant differences were found at 3 months' CA (1.37 mean; 95% confidence interval 0.48–2.27), 6 months' CA (0.34; 0.11–0.57), 12 months' CA (0.73; 0.20–1.26), and at 24 months' CA (0.28; 0.07–0.49), although the effect diminished over time. These time points had a range of sample sizes from 630 (3 months) to 1047 (24 months). There was no significant effect at term or at the 2-month, 4-month, and 18-month time points, but this finding may relate to the limited amount of data at those time points, because there were ≤3 studies in these analyses (n = 117–266). Data to compare motor-specific interventions with generic early intervention were limited. However, when looking at interventions with 3-month follow-up data, motor-specific interventions (N = 4)[41,49,69,70] showed a large and significant effect size at 3 months' adjusted age (2.00; 0.28–3.72), but generic interventions (N = 3)[43,54,65] showed no significant benefit for motors skills (0.33; –0.03 to 0.69). The heterogeneity of the pooled data ranged from low to high (I^2 = 36%, 99%, 96%, 99%, 64%, 94%, 46%, and 65% for term, 2 months, 3 months, 4 months, 6 months, 12 months, 18 months, and 24 months, respectively).

Data Synthesis

Meta-analysis was not conducted for assessments beyond 24 months due to the limited amount of data at time points beyond this age. Seven studies (N = 704) assessed preterm infants' motor development beyond 2 years (3–5 years), 5 of which found no significant effect of the intervention on motor outcomes (N = 517).[34,35,44,48,68] Gianní et al[60] found no significant difference for the locomotor subscale of the Griffiths development assessment but found a significant difference on an eye-hand coordination subscale. Verkerk et al[33] found a significant difference at 44 months' CA on the domains of mobility of the Pediatric Evaluation of Disability Inventory–Dutch version (PEDI-NL). Of those who did not find a significant difference, Johnson et al[44] stated that there was no difference between groups at 5 years of age, but highlighted that the intervention stopped when the child was 2 years of age.

The remaining 5 studies[38,50,52,58,64] were unsuitable for meta-analysis due to either not having details of the outcome measure or age of assessment. However, 3 studies[38,50,64] found a significant difference between the intervention and control groups, in favor of the intervention.

Risk of Bias

Two different assessment tools developed by the Cochrane Collaboration were used to assess risk of bias: Higgins et al's[77] criteria for risk of bias assessment was conducted on the included RCTs (Table 7) and Reeves et al's[78] guidance was used for the nonrandomized studies, where there is an increased risk of selection bias.

The highest risk of bias in the RCTs was lack of blinding of participants and researchers. There was also a risk in relation to incomplete outcome data, which may reflect the duration of intervention or the stratification of participants by weight and gestational age. The potential for performance bias is known to be problematic for these types of studies; therefore, detection bias is key, which for the majority of studies (RCTs and nonrandomized studies) were of low risk for detection bias, which enhances the quality of the data.

A main concern with nonrandomized studies is the risk of selection bias.

TABLE 4 Characteristics of Nonrandomized Studies

First Author, Year	Participants, n	Intervention	Outcome Measure	Age at Assessment
Mathai, 2001[66]	48 (25 int, 23 con)	Tactile-kinesthetic	BNBAS	Term
Koldewijn, 2005[69]	40 (20 int, 20 con)	IBAIP	BSID	3 and 6 months
Li, 2013[65]	203 (96 int, 107 con)	Neurodevelopmental training	BSID	3, 6, 9, and 12 months
Liao, 2009[70]	140 (65 int, 75 con)	Early intervention	BSID	3, 6, and 12 months
Wu, 2007[72]	83 (43 int, 40 con)	Early intervention	BSID	6, 12, and 24 months
Mazzitelli, 2008[67]	14 (8 int, 6 con)	Visuomotor stimulation	GSID	4, 6, 8, 10, and 12 months
Alvarado-Guerrero, 2011[62]	25 (14 int, 11 con)	Multidisciplinary	BSID	6 months
Goodman, 1985[63]	80 (40 int, 40 con)	Home exercise	GSID	12 months
Ogi, 2001[71]	48 (30 int, 18 con)	Early intervention	BSID	12 months
Salokorpi, 2002[68]	126 (63 int, 63 con)	Home-based occupational therapy	MAP	48 months
Kanda, 2004[64]	10 (5 int, 5 con)	Vojte method	No set scale	N/A

BNBAS, Brazelton Neonatal Behavioral Assessment Scale; con, control; GSID, Griffiths Scales of Infant Development; IBAIP, infant behavioral assessment and intervention program; int, intervention; MAP, Miller Assessment for Preschoolers.

TABLE 5 Examples of Activities: Term to 4 Months

CA	Activity
Term to 4 months	Midline activities in supine and alternate side-lying positions
	Promotion of symmetrical head turning, eye and head movement (eg, support the infant and use visual/auditory stimulation to encourage eye and head movement)
	Facilitate upper limb reaching and midline activities in supine position
	Facilitate hands to midline, hands to mouth, hands to feet in supine position, and supported sitting position in a seat
	Play in supine, prone, sitting, side-lying positions
	Assisted kicking (eg, stroking the infant's legs)
1 to 4 months	Facilitate symmetrical reaching in supine positions
2 to 4 months	Facilitate upper limb reaching and midline activities
	Facilitate rolling from supine to side-lying to prone positions
3 to 4 months	Facilitate symmetrical reaching in prone position
	Facilitate reaching

Adapted from Lekskulchai and Cole (2001)[49] and Cameron et al (2005)[42].

For the 11 studies that were not randomized, selection onto the trial was through parent choice or systematically allocated or, in the case of the pilot study by Koldewijn et al,[69] compared with a cohort from the previous year.

Dealing With Missing Data

The majority of studies provided clear detail on the sample at recruitment or follow-up. There were instances where insufficient data were available in the publication to include in the meta-analysis and attempts were made to obtain any relevant data from the authors.

DISCUSSION

This review set out to determine whether intervention can enhance the motor development of preterm infants and to identify the most effective activities to include in a future intervention. The overall findings suggest that focused early intervention is of benefit to preterm infants, because there is a positive impact on motor skills in infants up to 24 months' CA, although the strength of the effect was reduced over time. Beyond 2 years' CA the evidence is inconclusive due to the limited amount of outcome data on motor development skills from studies. This disparity may reflect the focus, because the majority of studies with longer follow-up tended to be general rather than motor specific, incorporating early intervention principles of being multidisciplinary and involving parenting skills and cognitive and motor skills. This lack of longer term data together with limited detail regarding the intervention activities result in challenges to developing an intervention for preterm infants that incorporates activities appropriate from birth to school age.

The RCTs and nonrandomized studies included within the review were assessed as being of acceptable quality for the main aspects of comparison group and assessment of outcome. All studies had a comparison/control group of preterm infants, and the majority had an assessment of the infants conducted by researchers who were unaware of group allocation. The outcome measure for this review was motor activity, and most studies used a validated development scale, of which the most frequently used was an edition of the BSID (Tables 4 and 5). Several of the studies did not use a validated scale and instead looked at age when the infant either lost or

TABLE 6 Outcomes and Effect Sizes

Outcome, Subgroup	Number of Studies	Participants, n	Method	Effect, mean (95% CI)
Motor score, term	2	117	Standardized mean difference (IV, random, 95% CI)	0.19 (−0.43 to 0.67)
Motor score, 2 months	2	201	Standardized mean difference (IV, random, 95% CI)	2.22 (−1.93 to 6.37)
Motor score, 3 months	7[a]	630	Standardized mean difference (IV, random, 95% CI)	1.37 (0.48–2.27)
Motor score, 4 months	3[a]	114	Standardized mean difference (IV, random, 95% CI)	2.25 (−2.71 to 7.20)
Motor score, 6 months	13[a]	958	Standardized mean difference (IV, random, 95% CI)	0.34 (0.11–0.57)
Motor score, 12 months	12[a]	1042	Standardized mean difference (IV, random, 95% CI)	0.73 (0.20–1.26)
Motor score, 18 months	3	266	Standardized mean difference (IV, random, 95% CI)	0.32 (−0.02 to 0.66)
Motor score, 24 months	8	1047	Standardized mean difference (IV, random, 95% CI)	0.28 (0.07–0.49)

CI, confidence interval; IV, inverse variance.
[a]Includes studies with incomplete data.

TABLE 7 Risk of Bias Assessment of Included RCTs

First Author, Year(s)	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting
Angulo-Barroso, 2013[38]	Low	Low	High	Low	Low	Low
Bao, 1999[39]	Unclear	Unclear	High	Unclear	Unclear	Low
Barrera, 1986[40], 1990[35]	Unclear	Unclear	High	Low	Unclear	Unclear
Blauw-Hospers, 2011[41]	Unclear	Unclear	High	Low	Low	Unclear
Cameron, 2005[42]	Low	High	High	Low	Unclear	Unclear
Chen, 2014[43]	Low	Unclear	High	Unclear	Unclear	Unclear
Gianní, 2006[60]	Unclear	Unclear	High	Low	Low	Unclear
Heathcock, 2008[36], 2009[37]	Unclear	Unclear	High	Low	Unclear	Unclear
Johnson, 2005[44]	Low	Low	Unclear	Low	Low	Unclear
Johnson, 2009[45]	Unclear	Low	Unclear	Low	Unclear	Low
Kaaresen, 2008[46]	Low	Low	High	Low	Low	Unclear
Koldewijn, 2009[47], 2010[32], 2012[33], 2014[31]	Low	Low	High	Low	Low	Unclear
Kynø, 2012[48]	Low	Unclear	High	Unclear	Low	Unclear
Lekskulchai, 2001[49]	Low	Unclear	High	Low	Low	Unclear
Ma, 2015[50]	Low	Low	High	Low	Unclear	Unclear
Nurcombe, 1984[59]	Low	Low	High	Low	Unclear	Unclear
Ohgi, 2004[61]	Low	Unclear	High	Unclear	Unclear	Unclear
Resnick, 1988[51]	Unclear	Unclear	High	Low	Unclear	Unclear
Soares, 2013[52]	Low	Unclear	Unclear	Low	High	Unclear
Spittle, 2010[53], 2012[34]	Low	Low	Unclear	Low	Low	Unclear
Tan, 2004[54]	Unclear	Unclear	High	Low	Unclear	Unclear
Weindling, 1996[55]	Low	Low	High	Low	Unclear	Unclear
Widmayer, 1981[56]	Unclear	Unclear	Unclear	Low	High	Unclear
Wu, 2014[57]	Low	Low	Unclear	Low	Low	Unclear
Yiğit, 2002[58]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

gained a particular motor behavior, such as walking.

This review focused particularly on motor development interventions as a means of ascertaining the types of activities that are most effective and to obtain information on any longer term effects. To date, there has been a stronger focus on interventions aimed at improving cognitive function, because subsequent education performance was deemed reliant on mental processing.[13] However, the interrelatedness of motor and cognitive development is clearly established,[12,79] and motor skills are a proven indicator of future math and reading success.[13]

This review attempted to add to the available data by analyzing findings at a specific CA, rather than combine them as in previous reviews,[25,80] thus allowing for potential continual effectiveness to be explored. The main trend was for a positive effect up to 24 months' CA. The time points of <24 months that were analyzed but showed no significant differences were most likely due to limited data being available. Studies that conducted assessments at several time points were included, but duplicate data were removed. Koldewijn and colleagues[31–33,47] consistently found a significant difference with their intervention group up to 42 months' CA. However, not enough data were available from the studies assessing beyond 24 months to conduct meta-analysis.

Identifying Activities

Orton et al[23] found that significant levels of heterogeneity when pooling outcomes made it problematic to assess the intervention activities that were most beneficial. Despite a similar issue for this review, the number of studies included and the inclusion of nonrandomized studies ensured that some general activities and movements that were common between studies could be identified, and their effectiveness assessed, especially from birth to 6 months' CA. These included providing opportunities for movement in supine, prone, and side-lying positions with appropriate support, and facilitating hands to midline in a variety of supported positions. This is important because the most recent update of the Cochrane review on intervention programs in preterm infants[25] emphasized the need to identify effective early development interventions.

Conducting the Activities

The findings suggest that parenting interventions implemented by health care professionals have positive effects on motor skills. Providing mothers with advice and ideas of ways of interacting with their infant may help reduce the perception of preterm infants as too fragile for play in the early months after discharge.[23] Parents may have more confidence to, for example, provide opportunities for play in the prone position, which is associated with better motor outcomes. There is evidence that interventions that specifically target the infant's motor development produce substantial benefits for motor skills, at least in the short term. Nearly two-thirds of studies of motor-specific inventions produced significant effects compared with 40% of generic interventions.

Strengths and Limitations

There were limitations in relation to obtaining complete data to include in the meta-analysis, because despite attempts to obtain data, only published data were available. However, wherever possible, data were incorporated into the review via qualitative data synthesis. The strengths of the process include citation searches for authors of dissertations and theses and translation of studies not published in English. In addition, the number of duplications during the search indicates that an exhaustive search of the databases was conducted. Despite issues of potential bias, especially with including nonrandomized studies, the included trials were all of an acceptable quality for inclusion in the review. This addition is mainly because the majority of motor skill assessments were conducted by trained professionals, who were unaware of the group allocation of the infant being assessed.

CONCLUSIONS

The findings of the review suggest that interventions that are continued beyond the period of neonatal care can have an impact on the motor development of preterm infants, with strongest effects noted before 6 months of age, particularly where interventions specifically targeted motor skills. Stage-appropriate activities for the first 6 months and some additional activities at ~6 to 12 months' CA were identified. However, it is important that future studies provide clearer details of intervention activities to enable replication, which would help in identifying effective activities that could be used to prevent poor motor skills and developmental coordination disorder. Data on the length of interventions and long-term impact are also needed to assess if positive outcomes can be maintained beyond 24 months.

ABBREVIATIONS

BSID: Bayley Scales of Infant and Toddler Development
CA: corrected age
NIDCAP: Newborn Individualized Developmental Care and Assessment Program
RCT: randomized controlled trial

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