



Centre for Clinical Effectiveness

Enhancing patient outcomes through clinical application of the best available evidence

**EVIDENCE CENTRE
CRITICAL APPRAISAL**
Series 2002: Therapy

Early intervention in premature infants

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SUMMARY STATEMENT

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REQUEST

Does early intervention or physiotherapy improve the motor developmental outcome of premature infants?

REQUESTED BY

Robyn Hudson, Physiotherapist, Paediatrics/Newborn Intensive Care Unit, Monash Medical Centre, Clayton.

METHODOLOGY

Search Strategy

The Centre for Clinical Effectiveness defines the 'best available evidence' as that research we can identify that is least susceptible to bias. We determine this according to pre-defined National Health and Medical Research Council (NHMRC, 2000) criteria (see Appendix 1).

First, we search for systematic reviews, evidence based clinical practice guidelines, health technology assessments and randomised controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalisable or have other methodological difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While we cite observational and case series studies, and narrative reviews and consensus statements, in our reports we do not critically appraise them. Such studies can produce accurate results but they are generally too prone to bias to allow determination of their validity beyond their immediate setting.

Details of Evidence Request

Patients (Subjects): prematurely-born infants, to school age

Intervention: early intervention, physiotherapy

Comparisons: standard care

Outcomes: motor development

Search terms

(see Appendix 2 for exact search strategy)

Patient (Subject): infant, premature; premature; preterm; pre-term

Intervention: early intervention; early childhood intervention

Resources Searched

We searched the following databases:

The Cochrane Library (CD-ROM) 2001 Issue 1

Medline (OVID)- 1966 to January Week 3 2002-02-07

PREMEDLINE (OVID)- February 4, 2002

CINAHL (OVID)- 1982 to December Week 2 2001

Current Contents (OVID)- 1993 Week 26 to 2002 Week 06

Cochrane Database of Systematic Reviews (OVID)- 1st Quarter 2002

Cochrane Controlled Trials Register (OVID)- 1st Quarter 2002

Australasian Medical Index- February 8, 2001

PEDro (The Physiotherapy Evidence Database) – searched 7 February 2002

Refinements, Searching & Reporting Constraints

We included items of evidence that were available to us on 2 May 2002. Only articles published in 1980 and later have been included. Critical appraisal was performed on the subset of studies published in English.

Articles concerning sensory therapy, chest or airway clearance, early discharge, interventions to enhance behaviour or intelligence, and tools for assessing the risk of neurodevelopmental problems have been excluded from consideration.

RESULTS

From our sources we identified 14 potentially relevant articles. We obtained the full text of these articles to determine their relevance.

After examination of the articles, the following were excluded as follows:

Reason for exclusion	Number
Early intervention to enhance outcomes other than motor development	2
Early intervention for children effected by poverty, not prematurity	1
Brief summary of other authors' report	1
Not obtained in timeframe of report	1
Total	5

8 articles then remained for appraisal. These studies are classified as follows:

Study Design	Number included
Randomised controlled trials	4
Psuedorandomised controlled trial	1
Controlled trials, cohort or case-control analytic studies	3
Comparative study with historical control	1
Total	9

Based on our refinements, searching and reporting constraints we are reasonably confident these articles represent the most relevant findings published to date.

Conflicting results have been reported and as there are serious methodological issues with several of the studies identified it is difficult to confidently state whether the early interventions described have had any beneficial effect on motor developmental outcomes.

EVIDENCE SUMMARIES

Format

Evidence summaries are presented as spreadsheets attached to this report. Each spreadsheet contains the article citation, details of the study design, patient description, scientific validity of the article, results, and pertinent remarks from the authors and Centre for Clinical Effectiveness reviewer.

REFERENCES

ARTICLES CRITICALLY APPRAISED FOR THIS REPORT

- Als H & Duffy FH (1989). Neurobehavioral assessment in the newborn period: opportunity for early detection of later learning disabilities and for early intervention. *Birth Defects: Original Article Series* **25**: 127-152.
- Girolami GL & Campbell SK (1994). Efficacy of a Neuro-Developmental Treatment program to improve motor control in infants born prematurely. *Pediatric Physical Therapy* **6**: 175-184.
- Kleberg A, Westrup B & Stjernqvist K (2000). Developmental outcome, child behaviour and mother-child interaction at 3 years of age following Newborn Individualized Developmental Care and Intervention Program (NIDCAP) intervention. *Early Human Development* **60**: 123-135.
- Lekskulchai R & Cole J (2001). Effect of a developmental program on motor performance in infants born preterm. *Aust J Physiother* **47**: 169-176.
- Matsuishi T, Ishibashi S, Kamiya Y, Shoji J, Yamashita Y, Fukuda S, Hashimoto T, Sato M, Inukai K, Miyao M, Nara T, Kawakami T, Morooka K, Yamaguchi K, Kuriya N & Maekawa K (1998). Early intervention for very-low-birth-weight infants. *Brain & Development* **20**: 18-21.
- Piper MC, Kunos VI, Willis DM, Mazer BL, Ramsay M & Silver KM (1986). Early physical therapy effects on the high-risk infant: a randomized controlled trial. *Pediatrics* **78**: 216-224.
- Rothberg AD, Goodman M, Jacklin LA & Cooper PA (1991). Six-year follow-up of early physiotherapy intervention in very low birth weight infants. *Pediatrics* **88**: 547-552.
- Salokorpi T, Sajaniemi N, Rajantie I, Hallback H, Hamalainen T, Rita H & Von Wendt L (1998). Neurodevelopment until the adjusted age of 2 years in extremely low birth weight infants after early intervention--a case-control study. *Pediatric Rehabilitation* **2**: 157-163.
- Saylor CF, Casto G & Huntington L (1996). Predictors of developmental outcomes for medically fragile early intervention participants. *Journal of Pediatric Psychology* **21**: 869-887.

ARTICLES NOT CRITICALLY APPRAISED

Early intervention to enhance outcomes other than motor development

- McCarton CM, Wallace IF & Bennett FC (1996). Early intervention for low-birth-weight premature infants: what can we achieve? *Annals of Medicine* **28**: 221-225.
- McCarton CM, Brooks-Gunn J, Wallace IF, Bauer CR, Bennett FC, Bernbaum JC, Broyles RS, Casey PH, McCormick MC, Scott DT, Tyson J, Tonascia J & Meinert CL (1997). Results at age 8 years of early intervention for low-birth-weight premature infants: the Infant Health and Development Program. *Jama: Journal of the American Medical Association* **277**: 126-132.

Early intervention for children effected by poverty, not prematurity

Berlin LJ, Brooks-Gunn J, McCarton C & McCormick MC (1998). The effectiveness of early intervention: examining risk factors and pathways to enhanced development. *Preventive Medicine* **27**: 238-245.

Brief summary of other authors' report

Flanders-Stepans MB (1999). Birthing briefs. Early intervention program for low birthweight premature infants gets results. *Journal of Perinatal Education* **8**: 43-44.

Not obtained in timeframe of report

O'Reilly KA, O'Reilly JP & Furuno S (1986). Predicting to 9-month performance of premature infants... early intervention project. *Physical Therapy* **66**: 508-515.

APPENDIX 1

Copyright

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Levels Of Evidence

Based on "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

Level I		Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials.
Level II		Evidence obtained from at least one randomised controlled trial.
Level III	-1	Evidence obtained from pseudo-randomised controlled trials (alternate allocation or some other method).
	-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.
	-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
Level IV		Evidence obtained from case series, either post-test or pretest/post-test.

APPENDIX 2

Search strategy

	Search terms for MEDLINE, CINAHL, PREMEDLINE, Current Contents
1	early intervention/ or early childhood intervention/
2	early intervention\$.tw
3	early childhood interventon\$.tw
4	or/1-3
5	infant, premature
6	prematu\$.mp
7	preterm.mp
8	pre-term.mp
9	(infant\$ or child\$).mp
10	or/6-8
11	9 and 10
12	5 or 11
13	4 and 12

<p>Evidence Summary Therapy/Intervention</p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p>Early intervention in children born prematurely</p> </div>	<p style="text-align: center;">Study 1</p>	<p style="text-align: center;">Study 2</p>	<p style="text-align: center;">Study 3</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p>Level II – Randomised controlled trial</p>	<p>Level II – Randomised controlled trial</p>	<p>Level II – Randomised controlled trial</p>
<p>DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients (subjects): Infants from special care nursery of North Carolina Memorial Hospital completed study. Intervention: 9 infants (PT). Program applied at 34 or 35 weeks of postconceptual age, 14 to 28 treatments during a period of 7 to 17 days, twice daily for 12 to 15 minutes. Comparisons: 10 preterm infants (PC), similar handling to intervention group but without treatment, and 8 fullterm infants (TC) completed study. Outcomes: Neonatal Behavioral Assessment Scale (NBAS) and a Supplemental Motor Test (SMT) for spontaneous and elicited movement patterns and motor control were employed. Incl & Excl Criteria: Infants were included if average for gestational age, born before 35th week of gestation and had at least 3 of: 5 minute Apgar score 5, intraventricular haemorrhage documented by ultrasound, seizures, respiratory distress syndrome, respiratory arrest, birth weight <1000g, central nervous system depression or irritability, asphyxia, need for mechanical ventilation, and thermal instability.</p>	<p>Patients (subjects): At-risk infants from special care nurseries of Siriraj Hospital, Thailand. Intervention: 43 infants. Home based, 12 activities for infants at 40 weeks postconceptual age, and at one, two and three months adjusted age, with three activities introduced each month. Comparisons: 41 at-risk premature infants (control group), 27 not-at-risk premature infants (comparison group). Outcomes: Motor performance assessment – Test of Infant Motor Performance (TIMP). Incl & Excl Criteria: Infants with gestational age <37 weeks, free of abnormalities and genetic disorders were eligible. Excluded if subsequently underwent surgery or developed serious illnesses including hydrocephalus, periventricular haemorrhage Grade III and above, ventricular dilatation or retinopathy of prematurity.</p>	<p>Patients (subjects): Infants at inborn neonatal care unit of Royal Victoria or Jewish General Hospital, Montreal. Intervention: 56 infants. Physical therapy program initiated at term. Seen by therapist one hour weekly for 3 months, every 2 weeks for the next 9 months. Comparisons: 59 infants. Outcomes: Wolanski Gross Motor Evaluation, Wilson Developmental reflex Profile, Milani-Comparetti Motor Development Screening test, Griffiths Mental Development Scale, Neurological Examination of the Collaborative Perinatal Project. Incl & Excl Criteria: Included infants weighing 1500g or less at birth, or who had experienced birth asphyxia, seizures or DNS dysfunction with abnormal EEG tracing during newborn period. Excluded infants with overt congenital abnormalities.</p>

<p>VALIDITY: Methodology, rigour, selection</p>	<p>Randomisation: Method not stated. Blinding: Examiners blinded to groups of premature infants but not to term infants. All patients accounted for: 42% attrition rate from 33 to 19, dropouts accounted for (transported to home hospitals) but not analysed on intention to treat basis. Patients treated equally: PC group handled in same way as PT group apart from the specific neurodevelopmental treatment protocol. Similar groups: PT group had an average of 4.3 medical complications, PC group had 3.7 complications. The PC group had a higher mean birth weight (1216.00g, PT group 1105.55g) The groups had different mix of ethnicities.</p>	<p>Randomisation: Randomisation according to letter code (C for control or I for intervention) on slips drawn blindly from a container. Blinding: Three appropriately trained physiotherapist research assistants who were blind to the infants' group assignments and additional identifying information scored the infants. All patients accounted for: Seven control and 5 intervention infants had incomplete followup due to inconvenience to parents of bringing infants to clinic. Data from these infants was not included on an intention to treat basis but comparison of baseline demographic data for infants with complete and incomplete followup did not reveal any statistically significant differences. Patients treated equally: Not stated. Similar groups: Mean birth weight, gestational age and 1 minute and 5 minute AGPAR scores did not differ significantly between groups.</p>	<p>Randomisation: "Balanced system of block randomisation", sealed envelopes. Blinding: Neonatologist from other hospital without prior knowledge of infant's medical condition assessed the neonates. Independent evaluators who were unaware of group assignment performed outcome evaluations. All patients accounted for: 19 dropouts, accounted for but not analysed on an intention to treat basis. Patients treated equally: All attended neonatal followup. Infants in control group could be referred for physical therapy. Similar groups: No significant differences in the 14 reported independent variables.</p>
<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>Posttest analysis of five NBAS clusters revealed a significant difference only on the Motor Performance and Autonomic Regulation clusters, TC group exhibiting superior performance on pull-to-sit item, and PC group having highest control over responses such as tremors, startles and jitteriness. Analysis of SMT scores indicated that the experimental group performed significantly better than either of the control groups in items such as antigravity movements, hands to midline, pelvic lifting, legs up and abducted, lifting and turning the head in prone, rotating head to midline.</p>	<p>Each infant's ability scores at term age, 1,2,3 and 4 months adjusted age were plotted against age. Mean TIMP scores were compared across groups. A group ANOVA on these scores revealed significant differences across ages and between groups. At 40 weeks postconceptual age the intervention (TIMP score 57.0 ± 3.7 SD) and control group (57.0 ± 3.7) both scored significantly lower than the comparative group (71.0 ± 3.1). The intervention group (152.3 ± 6.3) scored significantly higher than the control group (114.2 ± 9.2) at 4 months adjusted age, and no longer differed significantly from the comparative group (148.4 ± 9.9).</p>	<p>Infants in experimental group did not differ significantly from infants in control group on any of the measured outcomes at 12 months. Neurologically optimal children differed significantly from nonoptimal children only on height. Children who weighed <750 g at birth performed consistently more poorly at 12 months than their heavier counterparts. They exhibited slower motor development and lower locomotor developmental quotients than the higher birth weight groups.</p>
<p>AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research</p>	<p>The authors acknowledge that longterm outcome was not followed up and recommend further research in this area. They also note their small sample size and while suggesting that results would hold for a larger group, recommend replication of the study with a larger sample and revision of the treatment protocol.</p>	<p>The effectiveness of the program relied on the caregivers' understanding and cooperation. The motor development program was modified specially for the population of preterm born infants in Thailand, where child rearing style is quite different from that of Australia and other Western countries.</p>	<p>The authors suggest that more intensive, specialized treatment than offered in the trial (daily rather than weekly) might be required to effect developmental advances. Earlier initiation of the intervention, beginning in the neonatal intensive care unit, might be more effective. Longer followup, beyond 12 months, might detect significant effects associated with further maturation. Birth weight <750 g was associated with physical, motor and developmental delays regardless of intervention.</p>

<p>OUR COMMENTS: Opportunity for bias, weakness and strength</p>	<p>Potential for bias: Infants not all included in analysis, small sample size, duration differences in intervention. Weakness/es: Lack of longterm followup, no report of consideration of power required to detect significant differences between groups. Dropouts not included on intention-to-treat basis Strength/s: The SMT test was specifically designed to assess functional postural control in neonates and has since been expanded and renamed the Test of Infant Motor Performance.</p>	<p>Potential for bias: Infants who dropped out were not analysed on an intention to treat basis. Weakness/es: Lack of longterm followup. No report of consideration of power required to detect significant differences between groups.</p>	<p>Potential for bias: Comparison revealed that dropouts were more likely to have single parents and mothers and fathers with lower levels of education than the remaining children. Infants not all included in analysis. Strength/s: The ability to detect clinically important differences has been considered, although details of calculation are not provided. Baseline characteristics are provided for infants who did not complete program.</p>
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<p style="text-align: center;">Evidence Summary Therapy/Intervention</p> <div style="border: 1px solid black; padding: 5px; margin: 5px auto; width: fit-content;"> <p style="text-align: center;">Early intervention in children born prematurely</p> </div>	<p>Study 4</p>	<p>Study 5</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p>Level II – Randomised controlled trial</p>	<p>Level III-1 – Pseudorandomised controlled trial</p>
<p>DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients (subjects): 65 infants. Recruited from urban and rural areas within a 60 mile radius catchment area of a US Southwestern city. Intervention: Program beginning at 3 months adjusted age, number of infants not provided. Comparisons: Program beginning at 12 months adjusted age, number of infants not provided. Outcomes: Variety of tools including the Batelle Developmental Inventory for motor total functioning, nonverbal. Incl & Excl Criteria: Patients from the neonatal intensive care unit, if they had experienced intraventricular haemorrhage or had a birth weight of <1000g, and resided in catchment area.</p>	<p>Patients (subjects): At outset 80 infants, reducing to 49 at 6 years, who had been treated in the neonatal intensive care unit of a South African hospital. Intervention: During first year of life monthly treatments at hospital and home program of exercises daily. 13 normal and 15 at risk infants evaluated at 6 years. Comparisons: Nonintervention, no details provided. 12 normal and 9 at risk infants evaluated at 6 years. Outcomes: Neurodevelopmental Scores and locomotor subscale of Griffiths Mental Development Scale. Incl & Excl Criteria: Inclusion characteristics were birth weight <1700g and gestational age <34 weeks.</p>
<p>VALIDITY: Methodology, rigour, selection</p>	<p>Randomisation: Randomised by roll of four-sided die (sic). Blinding: Examiners were blinded to intervention. All patients accounted for: Loss to followup accounted for only for seventh (90 month) assessment, not included in analysis on intention to treat basis. Patients treated equally: Initial programs for the early intervention group were individualised. Individualised plans were also developed for all infants at 12 months. Infants in the delayed intervention group were referred to physical therapist if a motor delay was identified at 12 months. Similar groups: Of the 17 reported demographic characteristics the only significant difference was the higher proportion of males in the early intervention group. Medical data revealed significant differences favouring the delayed intervention group for gestational age and lower rate of retinopathy of prematurity. The early intervention group also had a higher number of days on ventilation and a higher percentage of cases with respiratory distress syndrome, both clinically but not statistically significant.</p>	<p>Allocation: Assessment at 3 months corrected age, then within normal and at-risk groups, alternative assignment to intervention or nonintervention subgroup. Blinding: Details not provided for NDS assessment, likely to be unblinded, as blinding stated for 1 year Griffiths Mental Development Scale assessment. All patients accounted for: Loss to follow up has been addressed, with no significant differences found between these children and children returning for 6 year followup, but dropouts not analysed on intention to treat basis. Patients treated equally: Not stated. Similar groups: Not reported in this paper, information may have been presented in a previous paper on development of these infants over the first year.</p>

<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>No measurable differences were observed between the two groups.</p>	<p>There were no significant differences detected between the intervention and control subgroups within either the normal or at risk groups. When intervention and control subgroups were combined, the at risk group had significantly lower scores than the normal group only on the locomotor subscale.</p>
<p>AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research</p>		<p>This paper claims to demonstrate that early physiotherapy intervention yields no longterm benefits after 6 years of followup, confirming findings of other shortterm followup studies. The authors suggest that other factors such as intraventricular haemorrhage, birth weight and socioeconomic status have more influence on longterm outcomes.</p>
<p>OUR COMMENTS: Opportunity for bias, weakness and strength</p>	<p>Potential for bias and weaknesses: The absence of information on exact numbers of infants in the two groups, the differences favouring the late intervention group and other methodological flaws make accurate interpretation of the results very difficult.</p>	<p>Potential for bias and weaknesses: The combination of the small numbers of infants within groups and the inability to control for other influences over six years make accurate interpretation of results difficult.</p>

<p style="text-align: center;">Evidence Summary Therapy/Intervention</p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p style="text-align: center;">Early intervention in children born prematurely</p> </div>	<p>Study 6</p>	<p>Study 7</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p>Level III-2 – Controlled trial</p>	<p>Level III-2 – Controlled trial</p>
<p>DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients (subjects): Infants cared for in neonatal intensive care unit in US (Boston?). Intervention: From day 10, individualised caregiving modifications implemented by primary nursing team, based on behavioural observations. Number not stated in article Comparisons: 8 control infants Outcomes: Assessment of Preterm Infants Behavior (APIB) , Bayley scales, Kangaroo-Box Paradigm and McCarthy Scales of Children’s Abilities, Kaufman Assessment Battery for Children and the Psychomotor Scale of the Bayley Scales. Incl & Excl Criteria: All infants initially respirator-dependent, birthweight <1250g, mechanical ventilation within 48 hours of delivery >24 hours in first 48 hours, at >.60 FiO₂ for >2 hours in first 48 hours, no chromosomal or other genetic anomalies, no major congenital infections, no major maternal illness including uterine infections, no twins.</p>	<p>Patients (subjects): Children from eight medical institutions in Japan. Intervention: 62 children. From 2 years of age, a centre based program of monthly meetings with team knowledgeable in motor, cognitive, self-help, language and socioemotional development and areas of family dynamics, physical health and nutrition. Comparisons: 48 children with normal development quotient (DQ) and neurological findings, not participating in early intervention program. Outcomes: Differences in DQ as determined by revised Kyoto Scale of Psychological Development Revised including postural-motor measures. Incl & Excl Criteria: Intervention group included children detected in routine screening as being at risk for some major disability. Children with static encephalopathies (cerebral palsy), mental retardation or other disabilities were excluded.</p>
<p>VALIDITY: Methodology, rigour, selection</p>	<p>Randomisation: Not stated in this paper Blinding: Not stated in this paper All patients accounted for: Not stated in this paper Patients treated equally: Not stated in this paper Similar groups: Not stated in this paper</p>	<p>Allocation: Details not provided apart from information above. Blinding: Not stated. All patients accounted for: Not stated Patients treated equally: Not stated Similar groups: Dissimilar, especially for neurological measures.</p>
<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>The intervention infants were better modulated as measured by the APIB scores, in terms of motor system and self regulation ability. They also showed a higher number of normal reflexes. The Psychomotor Developmental Index scores consistently showed the intervention infants significantly above the control infants. The initial advantage was well maintained in the intervention children while the control children deteriorated over time on many of the parameters. This advantage was also demonstrated on the Bayley Psychomotor Scale raw score at 3 years.</p>	<p>There was no significant difference reported in the DQ between the intervention and control groups measured after a year of the intervention program.</p>

<p>AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research</p>	<p>It appears that the programs ... must be geared to the infant's sensory thresholds. Careful environmental structure and caregiving manipulation in controlled studies with sensitive outcome measures will provide us with the answers. The complexity of the child's functioning requires complex assessments.</p>	<p>A limitation noted by the authors was the lack of investigation of socioeconomic status, parents' education, presence or absence of father and other potential risk factors during pregnancies.</p>
<p>OUR COMMENTS: Opportunity for bias, weakness and strength</p>	<p>Potential for bias: This article includes a summary of the trial reported elsewhere. We cannot comment on potential sources of bias beyond noting the small number of infants in the control group.</p>	<p>Potential for bias: Too few details have been provided for an accurate assessment of sources of bias, but the fact that the intervention group were identified as "at risk" and the control group had normal neurological findings is of primary concern. Weakness/es: Details of analysis of results have not been provided to allow accurate interpretation of the findings. Strength/s: The development of the whole child rather than a single deficit area has been taken into consideration and parental involvement has been encouraged.</p>

<p style="text-align: center;">Evidence Summary Therapy/Intervention</p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p style="text-align: center;">Early intervention in children born prematurely</p> </div>	<p style="text-align: center;">Study 8</p> <p style="text-align: center;">Salokorpi T, Sajaniemi N, Rajantie I, Hallback H, Hamalainen T, Rita H & Von Wendt L (1998). Neurodevelopment until the adjusted age of 2 years in extremely low birth weight infants after early intervention-- a case-control study. <i>Pediatric Rehabilitation</i> 2: 157-163.</p>	<p style="text-align: center;">Study 9</p> <p style="text-align: center;">Kleberg A, Westrup B & Stjernqvist K (2000). Developmental outcome, child behaviour and mother-child interaction at 3 years of age following Newborn Individualized Developmental Care and Intervention Program (NIDCAP) intervention. <i>Early Human Development</i> 60: 123-135.</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p>Level III-2 – Case-controlled trial</p>	<p>Level III-3 – Comparative study with historical control</p>
<p>DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients (subjects): 52 extremely low birth weight infants born between January 1991 and December 1994 and admitted to the NICU at a children’s hospital in Helsinki, Finland. Intervention: Weekly sessions at home of 60 minutes of occupational therapy from corrected age of 6 months up to 12 months. Comparisons: 52 infants with matching risk scores. Outcomes: Motor development was assessed at corrected age of 3,6, 9 and 12 months with Muenchener Funktionell Entwicklungs Diagnostik tool. At adjusted age of 18 and 24 months a neurodevelopmental test battery including evaluation of gross motor and fine motor skills was used. Incl & Excl Criteria: Infants with major neurological problems such as cerebral palsy or mental retardation were excluded from intervention but had an identical followup.</p>	<p>Patients (subjects): 15 infants born at Falu Hospital, Sweden between March 1992 and April 1993. Intervention: Care according to Newborn Individualised Developmental Care and Assessment Program (NIDCAP) starting within 3 days of birth. Comparisons: All 18 surviving very low birth weight infants born during 1990 who met inclusion criteria. Outcomes: Development assessed by Griffiths Developmental Scales II (includes locomotor and eye-hand coordination subscales) translated into Swedish and standardised for Swedish conditions. Incl & Excl Criteria: All surviving singleton infants with birthweight <1500g born consecutively without malformations to Swedish speaking parents.</p>
<p>VALIDITY: Methodology, rigour, selection</p>	<p>Allocation: Infants grouped as pairs on basis of risk score, every second infant randomly assigned to intervention group and every second to the control group. Blinding: As blinding has been mentioned for neoropsychological and verbal development, but not for the “neuropaediatric” assessments, it is unlikely that these assessors were blinded. All patients accounted for: Loss to followup addressed, but not analysed on intention to treat basis. Patients treated equally: Not stated. Similar groups: Groups similar in recorded characteristics.</p>	<p>Allocation: Children before or after implementation of administration of prenatal steroids and surfactant in clinical care. Blinding: Only for assessment of mother-child interaction. All patients accounted for: One child from each group excluded from analysis on basis of disability. Patients treated equally: Prenatal steroids were administered to 7/21 mothers in intervention group but none of the control group and surfactant was provided for 11/21 infants in intervention group but none of the control group. Similar groups: No statistical difference between groups on reported characteristics.</p>

<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>Cases and controls did not differ significantly as groups at 3, 6, 12, 18 or 24 months age.</p>	<p>The Griffiths test did not reveal any significant differences in the developmental quotients of the two groups.</p>
<p>AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research</p>	<p>The authors suggest that the most obvious reasons for the weak results were that the timing was too late, the intensity too low and the duration of the therapy too short. Another explanation may be the inability of the assessment methods to detect small differences in development. Intervention programmes of low intensity and low frequency are questionable investments... resources for implementing large scale intervention programmes are essential.</p>	<p>This 3 year followup does indicate positive longterm effects of NIDCAP on child behaviour and mother-child interaction which have not been reported previously. The authors acknowledge the methodological shortcomings of the study but hope that it will inspire larger randomised trials in order to confirm these findings.</p>
<p>OUR COMMENTS: Opportunity for bias, weakness and strength</p>	<p>Potential for bias: Infants lost to followup were not analysed on intention to treat basis. Weakness/es: There is no report that the power required to detect significant differences between groups has been considered.</p>	<p>Potential for bias: As noted by authors, different treatment of the groups and lack of blinding may have effected the results. Weakness/es: This was a pilot study in which there has not been consideration of the power required to detect differences. Strengths: A Swedish version of NIDCAP was developed for this study.</p>

EXPLANATION OF TERMINOLOGY USED IN SPREADSHEET

Level of evidence: A hierarchy of study evidence that indicates the degree to which bias has been eliminated in the study design.

Intervention: A therapeutic procedure such as treatment with a pharmaceutical agent, surgery, a dietary supplement, a dietary change or psychotherapy.

Randomisation: A process of allocating participants to treatment or control group within a controlled trial by using a random mechanism, such as coin toss, random number table or computer-generated random numbers. Study subjects have an equal chance of being allocated to an intervention or control group; thus, the two groups are comparable. Randomisation ensures that the results are not biased by the selection of particular types of patients to receive a specific therapy.

Blinding: Blinding or masking is a process used in epidemiological studies and clinical trials in which the observers and the subjects have no knowledge as to which treatment groups subjects are assigned. It is undertaken in order to minimise bias occurring in patient response and outcome measurement.

All patients accounted for: Once patients are randomly allocated to a specific group and withdraw before study conclusion, they have to be accounted for in order to ensure that patients withdrawing from the study are not significantly different from those continuing in the study. The final analysis should be conducted on an intention-to-treat basis, which includes the results of withdrawn patients in the analysis.

Patients treated equally: To be able to attribute any difference in the observed outcome to the intervention, study patients need to be treated equally in every way except for the intervention being evaluated.

Similar groups: Baseline characteristics of patients that are also likely to affect results should be evenly distributed between the intervention and control groups. Following proper randomisation, patients' attributes would be expected to be equally distributed between groups.

Validity:

Of measurement: an expression of the degree to which a measurement measures what it purports to measure; it includes construct and content validity.

Of study: the degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).

Potential for bias: Bias is a systematic deviation of a measurement from the 'true' value leading to either an over (or under) estimation of the treatment effect. Bias can originate from many different sources (including allocation of patients, measurement, interpretation, publication and review of data).