Title Effect of early childhood development interventions delivered by healthcare providers to improve cognitive outcomes in children at 0-36 months: A systematic review and meta-analysis

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Abstract

Objective: To determine the effect of early childhood development interventions delivered by healthcare providers (HCP-ECD) on child cognition and maternal mental health.

Design: Systematic review, meta-analysis.

Setting: Healthcare setting or home.

Participants: Infants under 1 month of age.

Interventions: HCP-ECD interventions that supported responsive caregiving, early learning, and motor stimulation. MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Health Technology Assessment Database, Database of Abstracts of Reviews of Effects, and Cochrane Database of Systematic Reviews were searched until 15 November 2021. Studies reporting prespecified outcomes were pooled using standard meta-analytic methods. (PROSPERO: CRD42019122021)

Main outcome measures: Cognitive development in children aged 0-36 months.

Results: Forty-two randomised controlled trials with 15,557 infants were included in the narrative synthesis. Twenty-seven trials were included in the meta-analyses. Pooled data from 13 trials suggest that HCP-ECD interventions may improve cognitive outcomes in children between 0-36 months (Bayley scales of infant development version IIII [BSID-III] mean difference [MD] 2·65; 95% confidence interval (95% CI) 0·61 to 4.70;2482 participants; low certainty evidence). Pooled data from nine trials suggest improvements in motor development (BSID-III MD 4·01 95% CI 1·54 to 6·48; 1437 participants; low certainty evidence). There was no evidence of improvement in maternal mental health (standardised mean difference [SMD] -0·13; 95% CI -0·28 to 0·03; 2806 participants; 11 trials; low certainty evidence).

Conclusions: We report evidence, particularly for cognitive and motor outcomes, of the effect of HCP-ECD interventions. However, effect sizes were small, and the certainty of the evidence ranged from very low to moderate. Additional high quality research is required.

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Introduction

Globally, more than 40% of disadvantaged children under five years have neurodevelopmental problems resulting in social, emotional, and educational functioning deficits into adulthood.[1-3] The World Health Organisation (WHO) defines early childhood development (ECD) interventions as physical, socio-emotional, cognitive, and motor development interventions implemented between birth and eight years of age.[4-10] The importance of the family and social environment in influencing children's neurodevelopment is well known. However, the impact of health services on the neurodevelopment of children, particularly primary care (the first level of the health system), is less well understood.[11,12] Healthcare providers working in primary care, including community health workers, generalist nurses, health visitors, midwives, child health nurses, and general practitioners, are uniquely positioned to augment early child development. However, many lack skills and confidence in neurodevelopmental care and few receive appropriate training, education, and resources.[13,14] Healthcare provider delivered ECD interventions include: WHO's Care for Child Development package (CCD), family partnership working, and motivational interviewing.[15-20]

Four systematic reviews have examined the effectiveness of ECD interventions to improve early child development.[21-24] Most recently, a systematic review of 102 studies, reported that parenting interventions improved a range of ECD outcomes at three years.[24] However, these reviews had various individuals delivering the ECD interventions such as peer counsellors, family support workers, healthcare providers, and researchers. To our knowledge, there have been no systematic reviews that have examined the effect of ECD interventions delivered solely by a healthcare provider (HCP-ECD) to families in high income country (HIC) and low and middle income country (LMIC) settings.

There is a growing body of evidence that babies develop important communication and social behaviours within the first days and weeks of life, especially eye contact, visual locking, auditory responses, responsiveness, and self-quietening behaviour. [4,25-29] Systematic reviews have assessed the effect of interventions delivered in the antenatal period.[23,24] However, to our knowledge there have been no reviews of the effects of ECD interventions in a subgroup of babies who received ECD interventions in the neonatal period from 0- 28 days ('neonatal ECD').[23,24] The optimal number of visits or contacts ('dose') and types of ECD interventions delivered in the neonatal and infant periods is also not known.

The primary objective of this review was to assess effects of HCP-ECD on cognitive outcomes in children aged 0–36 months. Secondary objectives were to assess effects on (i)

childhood neurodevelopmental domains (speech, language, fine motor, gross motor, social emotional, behaviour) at 0–36 months; (ii) maternal mental health at 0-36 months; and (iii) in prespecified subgroups (number and timing of infant and neonatal contacts, type of intervention, income level of country).

Methods

The protocol was registered in PROSPERO: CRD42019122021, and the detailed protocol is published separately.[30] Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Protocol (PRISMA-P) guidance was followed.[31] Modifications made from the original protocol are provided in Appendix 1.

Search strategy

We searched the following databases with no restrictions to time periods and language: Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Cochrane Database of Systematic Reviews, Health Technology Assessment (HTA) Database and the Database of Abstracts of Reviews of Effects (DARE). We also searched clinical trial registries. Reference lists from included studies and relevant systematic reviews were inspected for additional citations. The search was completed on 15 November 2021. The search strategy is presented in Appendix 2.

Eligibility criteria

The HCP-ECD interventions had to be delivered by primary level healthcare providers (e.g. generalist nurses, health visitors, midwives, child health nurses, general practitioners, primary care doctors, community health workers). The interventions could commence in the hospital but had to include community based post discharge follow up.[32] Interventions were required to be face to face in nature, e.g. delivered through home visiting, mobile health team visits, clinic visits, child health checks or group programs. The comparator group was 'no HCP-ECD interventions', i.e., any other care, standard care that did not include ECD, or no care. Only individual, cluster and quasi RCTs were eligible for inclusion.

Interventions

We used WHO definitions and classified the ECD interventions into three categories: responsive caregiving, early learning support, and motor stimulation.[10] We also classified interventions as: any responsive caregiving, no responsive caregiving; and ECD predominant and ECD non-predominant. ECD predominance was defined as ECD implemented for more than 50% of the contact time (Table 1).

Outcomes

The primary outcome measure was cognitive development in children at 0-36 months follow up. Secondary outcomes were: (i) speech, language, fine motor, gross motor, social, emotional, behaviour, executive functioning, and adaptive functioning; and (ii) maternal mental health. Studies were included in the systematic review regardless of the type of outcomes. However, only standardised measures, for example the Bayley Scales of Infant and Toddler Development or the Griffiths Mental Development Scales for cognitive development, were used in the meta-analyses.

Our apriori primary analysis was the period between 0-36 months where an infant received assessment for outcomes ‘’at latest follow up’’ . We did this to ensure that the maximum amount of data could contribute to the primary outcome ie that all studies with follow up could be included regardless of the duration of follow up. We expected that the duration of follow up would vary across studies so we reported the mean (sd) and median (iqr) duration of follow up for each outcome and presented this in each forest plot. For completeness we also assessed effects at 12, 24 and 36 months of follow up. However these time points were not prespecified as primary or secondary outcomes. Apriori we expected that these results would be underpowered and imprecise with wide confidence intervals.***Subgroups***

We assessed effects on cognitive development in children aged 0-36 months in seven prespecified subgroups: (i) number of contacts in the neonatal period (one contact, two contacts, three or more contacts); (ii) timing of contact (first week, second week or later); (iii) antenatal period exposure (intervention delivered in the antenatal period, intervention not delivered in the antenatal period); (iv) type of intervention (responsive caregiving, early learning support, and motor stimulation) (any responsive caregiving, no responsive caregiving) (intervention predominantly ECD, intervention not predominantly ECD); (v) type of health care provider (child health workers, nurse [including general nurse and child health nurse], child health workers and others); (vi) income level of the country (HIC, LMIC); and (vi) risk of bias (high risk of bias, some concerns of bias).

Study selection and data collection process

All titles, abstracts and full-text articles were reviewed and extracted independently by two review authors. Discussions with a third author were used to resolve any disagreement. Standardised pretested data collection forms were used. Data collected were: study design, study setting, intervention components, participant demographics, and outcomes.

Risk of bias assessment

Two independent review authors used the Cochrane risk-of-bias assessment tool (ROB 2) to assess the risk of bias.[33] We also assessed meta-biases, including publication bias and selective reporting. No studies were excluded based on risk of bias assessment.

Data management and statistical analysis

We searched for both continuous and dichotomous data for all outcomes (Appendix 3,4). In the meta-analyses, we reported mean differences (MD) for continuous data if they were measured on the same scales and standardised mean differences (SMD) for outcomes that were reported on different scales. Relative risks (RR) were reported for dichotomous data. We contacted authors where possible to request data.

Random effects models were used with restricted maximum likelihood estimates and Knapp-Hartung standard errors. Where possible, we imputed data using standard methods. We used the I^2 statistic to measure heterogeneity among the primary and secondary outcomes of all included trials. An I^2 value >50% was considered to represent substantial heterogeneity. For outcomes with at least 10 studies, funnel plots and Egger's test were used to assess publication bias and small study effects, respectively. We completed an unadjusted random effects meta-regression with Knapp-Hartung standard errors on the primary outcome for the number of expected visits (''doses''). Statistical analyses were performed using STATA 16.1 statistical software (Stata, College Station, TX, USA).

Grading of evidence

We used the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the body of evidence associated with specific outcomes which included assessment of risk of bias, consistency of effect, imprecision, indirectness, and publication bias.[34]

Role of funding source

No funding.

Results

Study characteristics

After the removal of duplicates, 9401 papers were eligible for inclusion (PRISMA flow diagram, Appendix 5). After assessing inclusion and exclusion criteria, 97 papers reporting on 42 trials were included in the narrative synthesis, of which 27 trials were included in the

meta-analyses (Appendix 5).[15,35-130] Appendix 3 displays the outcomes and scales reported by each study and those included in the meta-analyses. Appendix 6 shows the ongoing studies.

Of the 42 trials, 38 were individual RCTs[37,38,44-49,54-77,79-122,124-129], and four were cluster RCTs[15,35,36,39,40,123,130 41-43,50-53,78] (Table 2). Thirty-three trials were conducted in HICs[44-49,54-67,69-77,79-97,100,103,105-108,111-119,121,122,125,126,128] and nine were conducted in LMICs (Pakistan, Bangladesh, South Africa, Columbia, Jamaica, Brazil, India and Zambia).[15,35-38,41-43,50-53,68,78,96,98,99,101,102,104,109,110,120,123,124,127,129,130]

A total of 15,661 infants participated in the 41 trials; 7857 intervention and 7804 comparison. There were 12,118 infants from HIC, 3136 from MIC and 407 from LMIC. All infants were from families experiencing some level of adversity such as low socioeconomic status, maternal drug abuse, adolescent mothers, or were premature (Table 2).

Thirty-six trials used a single healthcare provider to implement the intervention (four trials used child health nurses; 17 used generalist nurses; four used health visitors; 17 used community health workers; and six used multidisciplinary health care teams including child health nurses, general practitioners, generalist nurses) (Appendix 4). Forty trials used home visits and two used community clinics to implement their ECD intervention. The number of contacts in the trials varied from six to 312 (Median 25, Interquartile range 9, 52), with the interventions lasting between 6 weeks to 36 months (M 19.7, SD 3.21). The number of contacts in the neonatal period ranged from one to four. Twelve trials included contact in the antenatal period. Most interventions were classified as responsive caregiving only (15 trials) or early learning support only (18 trials). Nineteen trials provided responsive caregiving along with other interventions and 19 were classified as predominantly ECD (Appendix 4).

Risk of bias

For assessor reported outcomes, five trials[15,74,113,119,121] had moderate risk of bias and the remaining 20 trials had high risk of bias (Appendix 7). For patient reported outcomes, two trials[15,119] had moderate risk of bias and 27 had high risk of bias (Appendix 7). There was no evidence of publication bias or small study effects shown for any outcome including the cognitive development outcome (Egger's test p=0.17) and maternal mental health outcome (Egger's test p=0.10) (Funnel plots, Appendix 7).

Primary analysis

Data for the primary analysis are presented in Table 3, Figure 1. The GRADE summary of findings are presented in Appendix 8. Pooled data from 13 trials suggest that HCP-ECD compared to usual care improved cognitive outcomes in infants at 0-36 months follow up (Bayley scales of infant development version IIII [BSID-III] MD 2·65; 95% CI 0·61 to 4·70; 2482 participants; low certainty evidence). We downgraded one level for heterogeneity (I^2 = 63%) and one level for risk of bias (six trials had a high risk of bias in the selection of the reported result and two trials had a high risk of bias in outcome measurement). No publication bias was reported. There was little to no evidence of an effect of HCP-ECD interventions at 12 months, 24 months, and 36 months follow-up (Table 3 and Appendix 9). However, these analyses had small sample sizes and wide confidence intervals and were downgraded for imprecision and risk of bias.

Secondary analyses

Data from the secondary analyses are presented in Table 3, Appendix 10. Pooled data from nine trials suggest that HCP-ECD improves motor outcomes in infants aged 0-36 months (BSID-III MD 4·01; 95% CI 1·54 to 6·48; 1437 participants; moderate certainty evidence). Pooled data from eight trials suggest that HCP-ECD improves home environments for children at 0-36 months (HOME inventory scales[131] MD 1·37; 95% CI 0·29 to 2·45; 1534 participants; low certainty evidence).

There was little to no effect on maternal health (SMD -0·13; 95% CI -0·29 to 0·03; 2806 participants; 11 trials; low certainty evidence); speech and language (SMD 0·30; 95% CI -0·53 to 1·13; 1551 participants; 3 trials; very low certainty evidence), socio-emotional (Ages and Stages Questionnaire-Social Emotional scales [ASQ-SE] MD -0·91; 95% CI -27·72 to 25·89; 369 participants; 2 trials; very low certainty evidence) or infant behaviour outcomes (SMD 8·34; 95% CI -31·20 to 47·88; 1769 participants; 3 trials; very low certainty evidence). No studies reported on executive or adaptive functioning.

Subgroup analyses

There was no evidence of differences in the effect of HCP-ECD on the primary outcome (cognitive development) in any subgroup (number of contacts, timing, type of intervention, type of health care provider, income level of country, risk of bias) except for ECD predominance (i.e., ECD implemented for more than 50% of the contact time between healthcare provider and family (Table 3, Appendix 11). The effect of ECD predominant interventions (BSID-III MD 3·31; 95% CI 0·74 to 5·88; 1672 participants; 10 trials) was greater than the effect of interventions that were not ECD predominant (BSID-III MD 0·27;

95% CI -1·62 to 2·16; 810 participants; 3 trials) (chi squared statistic 4.16, p value = 0.04). No other differentials in effect were found for any other subgroup analysis. In particular, there was no evidence of a 'dose response' ie an effect of HCP-ECD by number of expected HCP visits (β coefficient 0.018; 95% CI -0.07 to 0.11, 1811 participants; 12 trials; Table 3).

Few studies reported dichotomous outcomes. These analyses had wide confidence intervals and were limited by imprecision. Results are presented in Appendices 9 and 10.

Discussion

Our systematic review of 15,557 infants aged 0-36 months in 42 trials showed that healthcare provider delivered ECD interventions may improve cognitive and motor outcomes and the quality of the home environment for infants aged 0-36 months across HIC and LMICs. No effect was seen on speech, language, social-emotional, behaviour, or maternal mental health outcomes.

Our effects on cognitive outcomes (MD 2·65; 95% CI 0·61 to 4·70) at 36 months appeared greater than the four recent parenting reviews which reported SMD scores ranging from 0.25 to 0.42. [23,24,132,133] We prespecified the combined 0-36 months period of follow up as our primary outcome to ensure that the maximum amount of data could contribute to the primary outcome ie all studies could be included regardless of the duration of follow up. The other analyses at 12 months, 24 months and 36 months were downgraded for imprecision due to small sample sizes and wide confidence intervals and showed little to no evidence of an effect of HCP-ECD interventions at 12 months, 24 months, and 36 months follow-up.

Effects on motor development were similar to other reviews.[22,23] No effects were seen on language, behaviour, and socio-emotional development domains. However few trials assessed these outcomes (speech [2 trials, 354 infants], language [2 trials, 369 infants] and social and emotional development [3 trials, 1769 infants]). The trials also had wide confidence intervals and we downgraded the certainty of the evidence two levels for imprecision. We found no impact of HCP-ECD on maternal mental health. This is similar to most other reviews of ECD interventions,[22-24,134] and could be because ECD interventions do not include techniques that directly address parental mental health, such as behavioural activation and cognitive behavioural therapy. However, we did show that HCP-ECD interventions improved home environment scores. Forty of the 42 studies used home visits

as the main delivery channel which may be an important mechanism, though further research is needed.

Trials that fulfilled the definition of 'ECD predominance' (ECD implemented for more than 50% of contact time) had a greater effect on child neurodevelopment than trials with ECD implemented for less than 50% contact time. However, caution is needed in interpreting these results due to unexplained heterogeneity, especially in the ECD predominant group (I^2 = 68%). There was no differential effect by type of intervention (responsive caregiving, learning support, or other), antenatal contact or timing of neonatal interventions. However, these subgroup analyses had small sample sizes and limited power to detect effects.

There were a number of methodological limitations in the trials included in our meta-analysis. Using the GRADE system,[34] we judged that the evidence for our primary outcome was low certainty due to risk of bias and heterogeneity. Many different scales were also used for measurement of child neurodevelopment and maternal mental health. However, we found sufficient data for pooling using SMDs or mean differences for the follow up period of 0-36 months. We also did not find publication bias or small study effects for our primary and secondary outcomes. All the ECD interventions in our systematic review were delivered to infants facing adversity including: poverty, maternal drug abuse, and preterm birth. However, these situations are unfortunately not uncommon, and children facing these types of adversities are most in need of ECD interventions. Our study also had a number of other strengths. We included 12,013 infants and 27 trials in our meta-analyses. Our search was intentionally broad to capture all relevant studies, and we did not limit our search geographically, by language or by intervention approach. The interventions were delivered by a range of healthcare workers, including community health workers, generalist nurses, general practitioners and health visitors, making the findings relevant across many settings.

To our knowledge, this is the first systematic review and meta-analysis that has examined the impact of HCP-ECD interventions across HIC and LMICs. We report evidence of impacts on child neurodevelopment. Importantly, our review shows 'what the health system can do' to improve neurodevelopmental outcomes in the first three years of a child's life. This is especially important as healthcare providers (such as midwives and child health nurses) have multiple contacts with the mother and child in the first three years of life and are well placed to integrate and support maternal health as well as ECD.

We believe a sustained long term commitment to ECD from governments and donors that focuses on three core ECD interventions (responsive caregiving, early learning support and

motor stimulation) could quickly accelerate the gains we reported in our meta-analysis. More investment is also needed to train and build the skills and confidence of healthcare providers in neurodevelopmental care.[13,14] Many countries have committed to reaching the 2030 United Nations Sustainable Development Goal for ECD.[5] Our findings suggest that the health system has a potentially important role to play in achieving this goal, especially in the early years.

Contributions

KE conceived the idea for the review. NS designed and undertook the search. RH, NS, CA, CK, DN, LH completed the review of abstracts, full text and data extraction. RH, NS, CA, CK, LH completed the risk of bias on all studies. RH completed the statistical analysis, figures and appendix with support from NS and KE. RH wrote the first draft of the manuscript with input from NS and KE. LH and KE provided content expertise. All authors reviewed and revised subsequent drafts.

Declaration of interests

We declare no competing interests.

Data sharing

All data collected for this article, including data extraction tables and the statistical analysis, will be available from the publication date. Requests to access these data should be made to the corresponding author.

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TABLES AND FIGURES

Table 1 Intervention definitions used in included studies

Interventions	Definitions*	Example ECD programs delivered by health care providers
Responsive caregiving	Interventions that promote responsive caregiving and interactions, and strengthen the parent-child relationship. These interventions aim to support and encourage sensitivity and responsiveness or secure attachment	WHO UNICEF Care for child development program,[15] Philani Plus (+)[51]
Early learning support	Interventions that enhance parent and/or caregivers' access, attitudes, knowledge, skills or practices to support early learning and development of children. This could be through providing direct support to parents and/or caregivers which enable them to provide new early learning opportunities to their children. Other interventions may include providing education, information or guidance of early child development	Healthy steps[70], Family Nurse Partnership[59]
Motor stimulation	Interventions that target fine and gross motor development of children including interventions such as GAME (Goals-activity-motor enrichment) or CIMT (constraint-induced movement therapy)	BRAIN-HIT progam[37]
Any responsive caregiving	Any trial with an intervention that includes responsive caregiving (even in low dose) regardless of the provision of other ECD or non ECD interventions	WHO UNICEF Care for child development program,[15] Philani Plus (+)[51]
ECD predominant intervention	Any trial where ECD interventions (responsive caregiving, early learning support or motor stimulation as defined above) were implemented for more than 50% of contact time between healthcare provider and family	WHO UNICEF Care for child development program,[15] Philani Plus (+),[51] Healthy steps[70], Family Nurse Partnership[59], BRAIN-HIT progam[37]

ECD = early childhood development

*Definitions from: World Health Organization. Early childhood development https://www.who.int/maternal_child_adolescent/topics/child/development/en/[10]

Table 2 Participant characteristics in included studies of early childhood development interventions delivered by healthcare providers (HCP-ECD)

Study title; year	Country	No. infant[1]	Description of caregiver/infant	Sex of child (male (%))	Primary caregiver	Age of mother
Ara 2019	Bangladesh *LMIC*	378	Married pregnant women aged 16-49 years	Not recorded	All mothers	Mean age in years (SD) intervention: 23.38 (4.0) control: 23.54 (4.32)
Aracena 2009	Chile *HIC*	90	Primiparous adolescent mothers living in an extremely poor neighbourhood	Intervention 61%, control 45%	All mothers	Mean age in years (SD) intervention: 17.3 (0.23) control: 17.15 (0.22)
Armstrong 1999	Australia *HIC*	181	High-risk mothers with at least one liveborn infant	Not recorded	All mothers	Mean age in years (SD) intervention: 25.72 (5.61) control: 26.67 (6.08)
Barlow 2003	England *HIC*	131	Vulnerable/high-risk women	Intervention 52%, control 48%	All mothers	<17 years n (%) intervention: 12 (17.9) control: 14 (22.2)
Barnes 2013	England *HIC*	166	Expectant mothers with low educational qualifications and/or less than 20 years of age	Intervention 54%, control 63%	All mothers	Mean age in years (SD) intervention: 21.7 (1.9) control: 21.9 (1.6)
Black 1994	USA *HIC*	60	Low income, inner-city, multiparous, polydrug abusers	Intervention 45%, control 59%	All mothers	Mean age in years (SE) intervention: 26.4 (0.9) control: 27.9 (0.7)
Brooten 1986	USA *HIC*	79	Infants with birth weights of 1500 g or less	Not recorded	All mothers	Mean age in years (SD) intervention: 24 (7) control: 23 (6)
Butz 2001	USA *HIC*	117	Mothers who used cocaine and/or opiates	Intervention 41%, control 59%	Mother 69%, other 31%	Mean age in years at infant birth (SD) intervention: 28.9 (4.5) control: 28.0 (4.6)
Cooper 2009	South Africa *LMIC*	449	Women in their last trimester of their pregnancy	Intervention 48% control 48%	All mothers	Mean age in years (SD) intervention: 25.5 (5.23) control: 26.2 (5.84)
Cooper 2015	England *HIC*	301	Primiparous women at risk of postnatal depression	Intervention: 38%, control 46%	All mothers	Mean age in years (SD) intervention: 27.94 (5.4) control: 28.66 (6.0)
Cremer 1977	Colombia *LMIC*	148	Mothers in the first/second trimester of pregnancy with at least 50% of their other children classified as malnourished	Not recorded	Not recorded	Not recorded
El-Mohandes 2003	USA *HIC*	286	Mothers receiving no or inadequate prenatal care	Not recorded	All mothers	Mean age in years intervention: 24.8 control: 25.2
Fatori 2019	Brazil *LMIC*	80	Low-income pregnant youth aged 14-19 years	Not recorded	All mothers	Mean age in years (SD) intervention: 16.9 (1.3) control: 17.3(1.2)
Gardner 2003	Jamaica *LMIC*	140	Low-income women with infants with birth weight < 2500 g	Intervention 41%, control 46%	All mothers	Mean age in years (SD) intervention: 23.0 (6.6) control: 24.6 (7.3)
Goldfeld 2017	Australia *HIC*	722	Pregnant mothers <37 weeks gestation with 2 or more of 10 risk factors	Intervention 46%, control 44%	All mothers	Mean age in years (SD) intervention: 27.5 (6.1) control: 27.8 (6.4)
Gray 1979	USA *HIC*	100	Women who had their first or second child at the Colorado general hospital	Not recorded	Not recorded	Not recorded
Gutelius 1977	USA *HIC*	95	Primiparous mothers who were black, unmarried and between 15 and 18 years of age	Not recorded	Mothers or grand mothers	Not recorded
Infante - Rivard 1989	Canada *HIC*	47	Mothers from low socioeconomic background	Not recorded	All mothers	Mean age in years (SD) intervention: 25.3 (5.7) CON: 23.5 (3.8)
Jack 2015	Canada *HIC*	739	Primiparous pregnant women (<24 years) with <28 weeks gestation experiencing socioeconomic disadvantage	Not recorded	All mothers	Mean age in years for total sample (SD) 19.76 (2.36)
Jungmann 2010	Germany *HIC*	755	Primiparous low-income mothers between their 12th and 28th week of pregnancy	Not recorded	All mothers	Mean age in years (SD) intervention: 21.27 (4.2) control: 21.53 (4.4)

Kemp 2008	Australia *HIC*	208	At-risk mothers from a disadvantaged community	Not recorded	All mothers	Mean age in years (SD) intervention: 27.6 (6.7) control: 27.7 (5.9)
Kitzman 1997	USA *HIC*	1139	Primiparous women less than 29 weeks pregnant with sociodemographic risks	Not recorded	All mothers	Mean age in years (SD) intervention: 18.1 (3.2) control: 18.1 (3.3)
Kormacher 1999 RCT 1	USA *HIC*	490	Primiparous women	Not recorded	All mothers	Mean age in years (SD) intervention: 20.24 (4.17) control: 19.70 (4.13)
Kormacher 1999 RCT 2	USA *HIC*	500	Primiparous women	Not recorded	All mothers	Mean age in years (SD) intervention: 19.44 (3.69) control: 19.70 (4.13)
Letourneau 2001a	Canada *HIC*	24	Primiparous inexperienced adolescent mothers aged between 13 and 19 years	Not recorded	All mothers	Mean age in years at time of infant birth (SD) for total sample 18.06 (1.01)
Mejdoubi 2011	Netherland *HIC*	460	High risk primiparous women	Not recorded	All mothers	Mean age in years (SD) intervention: 19.5 (2.8) control: 19.2 (2.6)
Minkovitz 2001	USA *HIC*	2235	Not recorded	Not recorded	All mothers	<20 years (%) intervention: 15.2 control: 14.9 20-29 years (%) intervention: 53.0 control: 51.5 => 30 years (%) intervention: 31.8 control: 33.5
Norr 2003	USA *HIC*	477	Low-income, inner-city women in neighbourhoods with high infant mortality	Not recorded	All mothers	Under the age of 20 (%) intervention: 105 (40.7) control 85 (38.8)
Olds 1986	USA *HIC*	400	Primiparous women	Not recorded	All mothers	Mean age in years intervention: 19.53 control: 19.57
Owen-Jones 2013	England *HIC*	1645	Nulliparous pregnant women aged 19 or under	Not recorded	All mothers	Mean age in years (range) intervention: 17.9 (17.0 - 18.8) control: 17.9 (16.9 - 18.8)
Resnick 1988	USA *HIC*	41	Premature infants weighing <1800 g at birth	Intervention 52%, control 40%	Not recorded	Mean age in years (SD) intervention: 24.0 (5.8) CON: 24.9 (7.8)
Rotheram Borus 2014	South Africa *LMIC*	1190	Pregnant women at least 18 years old	Not recorded	All mothers	Mean age in years (SD) intervention: 26.5 (5.5) control: 26.3 (5.6)
Sadler 2013	USA *HIC*	105	Primiparous women aged 14-25	Intervention 51% control 52%	All mothers	Mean age in years (SD) intervention: 19.5 (2.6) control: 19.7 (2.8)
Salo 2019	Finland *HIC*	45	Mothers with depressive symptoms	Not recorded	All mothers	Not recorded
Siegel 1980 - RCT 1	USA *HIC*	99	Low- income women in their third trimester	Not recorded	All mothers	Mean age in years intervention: 21.3 control: 19.8
Siegel 1980 - RCT 2	USA *HIC*	105	Low- income women in their third trimester	Not recorded	All mothers	Mean age in years intervention: 20.6 control: 19.8
Siegel 1980 - RCT 3	USA *HIC*	112	Low- income women in their third trimester	Not recorded	All mothers	Mean age in years intervention: 20.7 control: 21.0
Slade 2020	USA *HIC*	164	Primiparous mothers aged between 14 and 25 years	Intervention 52%, control 53%	All mothers	Mean age in years (SD) intervention: 20.1 (2.8) control: 20.0 (2.5)
Tsiantis 1996	Cyprus, Greece, Yugoslavia, Portugal *HIC*	Not recorded	Not recorded	Not recorded	All mothers	Not recorded
Wallander 2010 RCT 1	India, Pakistan, Zambia *LMIC*	164	Infants with birth asphyxia who were unresponsive to bag and mask ventilation	Intervention 59%, control 61%	All mothers	Mean age in years (SD) intervention: 24.6 (5.5) control: 24.2 (4.0)
Wallander 2010 RCT 2	India, Pakistan, Zambia *LMIC*	243	Infants without birth asphyxia who did not require any resuscitation	Intervention 54%, control 58%	All mothers	Mean age in years (SD) intervention: 25.5 (5.1); control: 25.6 (5.7)
Yousafzai 2014	Pakistan *LMIC*	751	Mothers from a predominantly rural and impoverished community	Intervention 55%, control 55%	All mothers	Not recorded

[1]Number of infants randomised; HIC: High Income country; LMIC: Low- and middle- income country; NR: Not recorded

Table 3 Meta-analyses of effects of early childhood development interventions delivered by healthcare providers (HCP-ECD) on primary and secondary outcomes and in subgroups at 0-36 months

	No of studies	No of participants	Pooled effect (95% CI)
Primary analyses			
Cognitive development at 0-36 months	13	2482	2.65 (0.61 to 4.70)
Cognitive development at 12 months	7	1192	
Cognitive development at 24 months	2	873	5.14 (-59.57 to 69.84)
Cognitive development at 36 months	2	293	3.15 (-10.09 to 16.38)
Expected number of visits (dose)	12	1811	0.02 (-0.07 to 0.11)^
Secondary analyses at 0-36 months			
Maternal mental health	11	2806	-0.13 (-0.28 to 0.03)*
Motor development	9	1437	4.01 (1.54 to 6.48)
Speech and language development	2	354	-0.31 (-12.65 to 12.02)*
Social emotional development	2	369	-0.91 (-27.72 to 25.89)
Behavioural development	3	1769	8.34 (-31.20 to 47.88)*
Child's home environment	8	1534	1.37 (0.29 to 2.45)
Subgroup analyses at 0-36 months for primary outcome			
Number of contacts			
At least one contact in the neonatal period	4	1391	4.63 (-4.68 to 13.94)
Two contacts in the neonatal period	4	383	1.92 (-1.10 to 4.94)
Three or more contacts in the neonatal period	5	708	2.28 (0.33 to 4.23)
Timing of contact			
First week	6	755	1.94 (0.30 to 3.58)
Second week or later	7	1727	3.48 (-0.70 to 7.66)
Antenatal contact			
Intervention delivered in the antenatal period	3	353	1.55 (-1.17 to 4.26)
Intervention not delivered in the antenatal period	8	1248	4.03 (0.51 to 7.56)
Type of intervention			
Responsive caregiving alone	3	321	2.29 (-2.45 to 7.03)
Early learning support alone	6	1625	0.77 (-0.40 to 1.94)
Motor stimulation alone	0	0	-
Any responsive caregiving	4	523	5.02 (-3.23 to 13.28)
No responsive care giving	9	1959	1.36 (-0.08 to 2.79)
ECD predominant	10	1672	3.31 (0.74 to 5.88)
Non ECD predominant	3	810	0.27 (-1.62 to 2.16)
Type of health care provider			
Community health worker (CHW) only	5	801	4.03 (-1.00 to 9.06
Mixed (CHW or nurse or other health worker)	4	852	1.68 (-2.91 to 6.26)
Nurse only	4	829	0.78 (-2.11, 3.67)
Income level of country			
High income	9	1724	1.06 (-0.53 to 2.64)
Low and middle income	4	758	4.61 (-1.40 to 10.63)
Risk of bias			
High risk of bias	10	2141	1.64 (0.32 to 2.96)
Some concerns of bias	3	341	4.21 (-11.54 to 19.96)

^Beta coefficient for meta-regression; *Standardised mean difference (SMD)

Figure 1 Effect of ECD interventions delivered by healthcare providers on cognitive development at 0-36 months*:* mean (SD) 18 +/- 10 months; median (IQR) 18 (12, 25)

N = Number of children in study, SD = Standard deviation, 95% CI = 95% confidence interval