Early intervention to improve neurodevelopmental outcomes for high-risk infants☆

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Abstract

Many babies cared for on a neonatal unit are at risk of adverse neurodevelopmental outcomes. The aim of early intervention (EI), therefore, is to support a child and their family to achieve the best outcome possible. Notably, EI is not one specific thing. The term encompasses a wide range of approaches and interventions that can vary in a number of ways, including who undertakes them, where they happen and when they start. There is debate as to the most effective approach, but the evidence supports the implementation of EI from soon after birth, continuing post-discharge. Furthermore, involving the parents in EI is critical, not only to ensure sustained effects throughout childhood, but also because of the beneficial impact on parental wellbeing. All in all, the evidence shows improved neurodevelopmental outcomes for children exposed to EI, particularly in the short-term. This review will explore what EI means in practice, considering the variations in application, as well as the evidence of benefit. It will also consider the limitations of current research.

Keywords Developmental care; early intervention; family integrated care; neurodevelopment

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Introduction

The old adage is that 'prevention is better than cure', i.e. it's better to intervene pre-emptively rather than waiting for problems to arise; by which point it may be harder, if not impossible, to resolve them. This is where the philosophy of Early Intervention (EI) arises. Given that many of the babies cared for on neonatal units are at risk of adverse neurodevelopmental outcomes, rather than waiting for potential issues to be picked up by routine screening methods, it is logical to implement EI with enhanced follow-up, to support the baby and family to achieve their optimal neurodevelopmental outcome.

This is important for many reasons, not least because of the improving survival rates of extreme preterm infants, a population of patients who are at high-risk of long-term sequalae. We know from experimental research that the in-utero and early years development of the brain is its most important period. This is when complex processes of cell proliferation, migration and myelination occur. Indeed, the first thousand days of a child's life are considered critical for their development, with early experiences affecting lifelong health generally, not just in matters related to learning and behaviour.

Notably, beyond direct injury to the brain, research shows that the environment and parenting that a child is exposed to plays a central role in their early development. The quality of the parent-infant relationship has an impact on brain growth and maturation and parent-child synchrony has a strong positive influence on cognitive and social-emotional competence. Importantly, the young brain demonstrates plasticity, so positive interventions during this early critical period are likely to pay greater dividends. This is perhaps why some studies report that babies born at lower gestations seemingly gain the most from intensive EI.[1]

The risk of an adverse outcome is variable for any one baby, even those born at the same gestation, as there may be many factors that increase the likelihood of complications for any individual baby, e.g. the presence of growth restriction, periventricular leukomalacia, intraventricular haemorrhage, necrotising enterocolitis or chronic lung disease of prematurity. However, even in the absence of macroscopic pathology, preterm infants are vulnerable to an array of more subtle delays and neurobehavioural disorders. Furthermore, some term babies may also face early difficulties that warrant extra support. For instance, babies who have suffered from a neonatal encephalopathy; those with congenital or acquired brain malformations or insults, such as a neonatal stroke; and those with congenital or acquired infections affecting the central nervous system. Although some elements of EI can be considered universal and applied to all babies on a neonatal unit, for example developmentally supportive care (DC), some babies can benefit from more specialised input which is targeted and tailored to their needs.

This review will clarify some terminology and discuss what EI means in practice, considering the variations in implementation. It will explore the evidence for EI and will consider the limitations of current research.

Terminology

EI is a broad term which will mean different things to different people, not least because it's used across health and social care with variable definitions. In the context of child development, a common definition stems from a book by Shonkoff et al. at the turn of the millennium, which states that EI aims to, "'promote child health and wellbeing, enhance emerging competencies, minimise developmental delays, remediate existing or emerging disabilities, prevent functional deterioration, and promote adaptive parenting and overall family function".[2]

EI can take many forms, but at its most distilled, it relates to the implementation of specific interventions and/or targeted training, which is offered to a baby and their family. This is usually achieved with a multi-disciplinary approach. However, there remains a large variation in how this translates to practice and debate as to which approach is the most effective. There is a need for greater specificity of what will work for any individual baby.

Figure 1 outlines some of the many considerations. It's this heterogeneity which, in part, is why it can be a difficult area to study. Relatedly, a browse of the literature surrounding EI will present a large number of acronyms, frameworks and assessment tools which all have subtle differences in intention and application. Although a thorough exploration of the advantages and disadvantages of all these specific approaches is beyond the scope of this article, Table 1 outlines some of the major organisations, approaches and terms that are associated with EI in the UK.

EI has to be coupled with enhanced neurodevelopmental follow-up, to facilitate the early detection of specific needs in individual patients, allowing for further targeted intervention as necessary. A detailed review of neurodevelopmental follow-up is provided in the Further Reading section at the end of this article. Follow-up led by the neonatal team typically extends to 2 years corrected gestational age, although some units are extending this to 4 years, with onward referral as required.

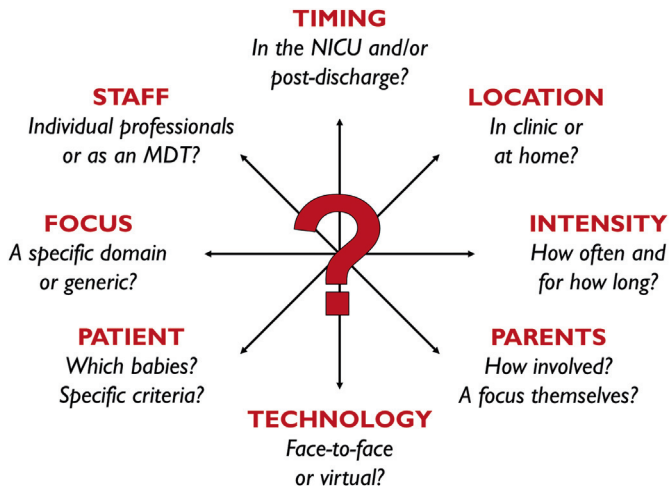

Figure 1 Variations in approach to early intervention.

There are also arguments for a more integrated approach from the start, i.e. involving community paediatric colleagues in neonatal neurodevelopmental assessment. Figure 2 outlines a theoretical pathway that a baby may follow, highlighting some investigations, interventions and health professionals that they may encounter. It is important to remember though that it is the responsibility of all health professionals that have interaction with children to be vigilant for early signs of difficulties or concerns that might benefit from further assessment and intervention. Furthermore, by increasing awareness of EI, healthcare professionals can be supportive to parents, encouraging them to remain engaged with EI interventions and follow-up appointments.

How early is early?

One key discussion related to EI is when to start the planned interventions. There are some approaches that can be started in the neonatal unit, indeed some well-established approaches only deal with babies whilst they're on the unit, e.g. NIDCAP (see Table 1). Other approaches only start after discharge and yet others exist that bridge the gap between the two. There is evidence to support intervention at all stages, although the longer-term impact of inpatient-only intervention does wane. As such, it's important that interventions don't stop once the baby is discharged from the neonatal unit.

When it comes to EI on the neonatal unit, beyond specific plans developed by the medical or therapy teams, there are some overarching philosophies and approaches to care that are beneficial, such as units who adopt a Family-Integrated Care approach and who are advocates for DC, discussed further below. Such approaches are supported by numerous organisations, including being a component of the Bliss Baby Charter accreditation, which is conferred by the neonatal charity, Bliss.

Before exploring elements of EI in more detail, it's important to remember that there are many other aspects of perinatal care that can have a profound impact on neurodevelopmental outcomes. Although not often considered in the context of EI, there are numerous important factors that all perinatal healthcare professionals need to be aware of and champion, e.g. the administration of antenatal corticosteroids and magnesium sulphate; service development, training and care bundles surrounding extreme preterm birth; encouraging the provision of maternal breast milk; highly attentive care when using intensive interventions, such as ventilation and inotropes. These factors are of critical importance and are inextricably linked to the aims of EI, because for example, even a short period of overzealous ventilation leading to hypocarbia and subsequent brain injury will have a profound impact on that baby's prognosis, applying a limit to the best-case outcome which EI would be hoping to achieve.

Developmentally supportive care on the neonatal unit

The dark, warm, protected atmosphere of the uterus is in stark contrast to the bright, loud and stimulating environment of a neonatal unit. For preterm infants, exposure to such an environment at a critical time of brain development is well known to lead to negative consequences, both in the short and long-term. Even for term infants, there can be a degree of parental separation, altered feeding patterns and exposure to noxious stimuli, compared to what they would have experienced if not admitted to a neonatal unit.

Example organisations, approaches and terms associated with early intervention

Term	Meaning	Comments
BAPM	British Association of Perinatal Medicine	A UK-based charity with an MDT membership, which aims to improve standards of perinatal care Produces a number of resources and frameworks for practice, with a number of specialist interest groups, including the British Association of Neonatal Neurodevelopmental Follow-up (BANNFU)
BSID	Bayley Scales of Infant and Toddler Development	A comprehensive, validated, development assessment tool, which requires trained staff to administer It has evolved through different versions, with the 4th edition now released Provides scores across five scales; cognitive, language, motor, social-emotional and adaptive behaviour Generally regarded as the 'gold standard' and is often used as an outcome measure in research
Ei SMART	Early Intervention — Sensory, Motor, Attention and Regulation, Relationships, Together	A UK-based charity providing a clinical reasoning framework derived from consensus clinical expertise in partnership with parents and supported by current evidence Encourages health professionals to work collaboratively with parents, with the aim of optimising outcomes and making EI manageable for infants and their families Provides training and resources for both health professionals and families
eTIPS	Early Therapy in Perinatal Stroke	A home based, parent delivered intervention for babies affected by perinatal stroke Focussed on lateralised interventions in the first 6 months of life to promote movement on the affected side
FI-Care	Family Integrated Care	A model of neonatal care which supports the parents to become confident and independent caregivers, in partnership with staff. It is not one single intervention or change. There is a wealth of supportive evidence and a number of organisations that promote its use, including a 'Framework for Practice' document, published by BAPM
FINE	Family and Infant Neurodevelopmental Education	A multi-level education programme to develop healthcare professionals to put family-centered, developmentally supportive care into practice Endorsed in the UK by the neonatal charity, Bliss
GMA	General Movements Assessment	Eponymously referred to as the Prechtl's assessment. It has good predictive validity for cerebral palsy and delayed motor development. It can be performed from birth and the video recordings can be done at home by parents and then assessed by trained staff
Griffiths III	Griffiths Scales of Child Development	A comprehensive, validated, developmental assessment tool, which requires trained staff to administer Provides a profile across five areas: foundations of learning; language and communication; eye and hand coordination; personal-social-emotional; gross motor.
HNNE/HINE	Hammersmith Neonatal or Infant Neurological Examination	Standardised assessments of neurology, behaviour and aspects of development, which can be used up to 24 months of age No formal certification is required and they have good sensitivity and specificity in predicting neuromotor outcomes up to 11 years of age
NIDCAP	Newborn Individualised Developmental Care and Assessment Program	One of the original proponents of EI that has a strong evidence base Focusses on an approach whilst the baby is an inpatient, that is individualised and responsive to a baby's cues and behaviours, assessing these prior to any intervention Embeds parents as a core part of caregiving and supports them to gain independence
PRISM	Premature Infants' Skills in Mathematics	The PRISM study team developed the 'Preterm Birth Information for Education Professionals' programme, which provides learning modules and resources to improve knowledge and confidence of supporting preterm infants at school Linked with the 'Prem Aware' school scheme led by The Smallest Things charity

Table 1

Accordingly, there is a move towards DC on neonatal units. Such care aims to support a baby's neurodevelopment by minimising stress, pain and noxious stimuli; safeguarding sleep; ensuring appropriate positioning; and supporting the development of a strong attachment with the parents. Some of the approaches of DC are outlined in Table 2. The impact on late preterm and term infants can also be minimised by the use of transitional care facilities where appropriate, where the postnatal care of the mother and baby occurs in the same place. Indeed, in some countries, single family rooms are utilised on the neonatal unit for all patients.

Unpicking the benefits of specific interventions is difficult, given the complex, dynamic nature of neonatal units. However, data does exist to support DC practices. This includes a meta-analysis of 13 studies, reported by Soleimani et al. (2020), which showed improved outcomes at 12 months of age, as

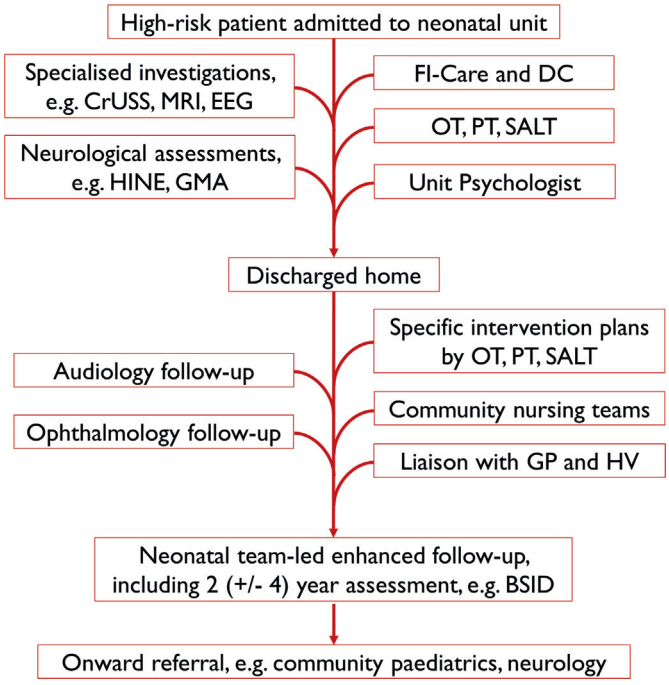

Figure 2 A theoretical pathway that a high-risk infant may follow. BSID, Bayley Scales of Infant and Toddler Development; CrUSS, cranial ultrasound; DC, developmental supportive care; EEG, electroencephalogram; FI-care, family-integrated care; GMA, General Movements Assessment; GP, general practitioner; HINE, Hammersmith Infant Neurological Examination; HV, health visitor; MRI, magnetic resonance imaging; OT, occupational therapist; PT, physiotherapist; SALT, speech and language therapist.

assessed by the Bayley Scale of Infant and Toddler Development, for babies exposed to DC practices. Another review specifically explored differences in neurodevelopmental indices soon after discharge before other confounding factors could take effect. For example, a meta-analysis by Aita et al. in 2021, evidenced improved outcomes across various domains at 2 weeks corrected gestational age, for babies who had received the NIDCAP intervention. Beyond neurodevelopmental outcomes, there is also evidence for improvement in other medical outcomes for babies exposed to EI on the neonatal unit, such as the length of respiratory support, gastric tube feeding and hospital stay.

Areas of focus for EI

Neurodevelopment is complex and has traditionally been considered in different domains. Some aspects of EI may be focussed on improving outcomes in one particular domain, e.g. focussed exercises to improve motor outcomes, with others providing more generic interventions, e.g. parental training for a baby's cues. The following sections explore different areas of EI and the evidence for them. However, in practice, rather than focussing on one or two specific areas, it is pragmatic to provide an integrated collaborative approach to EI, such as that promoted by the EiSMART framework (Table 1).

Parental involvement

One factor that is clear from the research is the importance of supporting and involving parents in any interventions. It is well established that having a baby admitted on a neonatal unit is a stressful period for parents and this effect on their wellbeing and mental health does not stop at the point of discharge. Many studies have reported increased rates of mental health problems in parents of babies on the neonatal unit, including depression, anxiety, and post-traumatic stress disorder. Furthermore, beyond the impact such conditions have on the parents themselves, is the indirect impact on the child, as it is known that the outcomes for children are worse when the parents have mental health problems. The social and physical environment the baby is exposed to is also important, i.e. factors such as parental education, socio-economic status, family structure and function, all have additive effects on developmental outcomes. These factors may also pose barriers to EI, such as the time commitment and financial costs of attending frequent appointments. It is important parents are aware of the purpose and benefits of the follow-up appointments and interventions, as decreased rates of attendance are associated with increased rates of disability.[3]

It is vital that parents are supported throughout this whole process. Ideally, this would include easy access to psychological support on the neonatal unit itself, with follow-up sessions as required. Connection with the parents' GP and perinatal mental health services may also be required. Taking a holistic approach to ensuring they have access to all relevant benefits and allowances, social support and appropriate housing, is also important to enrich the baby's developmental environment.

When it comes to EI approaches themselves, incorporating parents into the interventions is of proven benefit, facilitating the development of a strong parent-infant relationship. Often, this involves specific assessment and training of the parents using validated tools, helping them to become responsive to their baby's individual cues and behaviours. This supports the establishment of a strong attachment at a young age which is crucial for many aspects of development, allowing the baby to develop self-regulatory behaviours. One tool is the Infant Behavioural Assessment and Intervention Program (IBAIP) which was shown to improve performance IQ, visuomotor skills and some gross motor skills in very low birthweight infants at 5.5 years, compared to standard care. Other similar tools include the Brazelton Newborn Behavioural Observation (NBO) which is a specific relationship building tool designed to support and promote the parent-infant relationship; it is used widely in the UK by early intervention therapists and health visiting teams.

The benefits of parental involvement and training to become responsive parents, with a focus on child development, extend well beyond early infancy. Rates of behavioural problems in children were lower when their parents had been involved in parenting-based programs, compared with controls. One study by Guralnick et al. concluded that, of preventative EI programmes that were initiated within the first 12 months of birth in preterm infants, those programmes focussing on sensitive and responsive parenting along with infant development had the greatest impact on improvement in developmental outcomes.

Motor

Motor development can be drastically impacted by damage to the developing brain and ultimately lead to conditions such as cerebral palsy (CP). There are various tools available that allow for

Considerations for developmentally supportive care on the neonatal unit

Area	Comments
Kangaroo care	Skin-to-skin with a parent is known to have a myriad of benefits for both the baby and parent, this includes short-term benefits, e.g. improved haemodynamic stability and weight gain, but also longer-term benefits, such as increased breastfeeding rates, earlier discharge and improved parental mental health There are only a few contraindications to Kangaroo Care and with appropriate support can be undertaken with babies receiving invasive ventilation
Positioning	In-utero, the foetus maintains a flexed posture and moves against their boundaries to develop tone and strength. They also self-soothe by bringing their hands to their face. In the neonatal unit, a baby's position is dependent on staff and can be restricted by medical equipment and medication Inadequate positioning leads to short-term instability as well as longer-term issues, such as joint contractures Specific scoring systems exist to assess a baby's position and various aids can also be used, including nests and gel pillows, but they should be used correctly Variation in position (supine, prone, side-lying) can also be beneficial, although when approaching discharge, the importance of safe sleeping advice should be taught and modelled to the parents
Pain and comfort	Some procedures are unavoidable, but increased awareness of a baby's cues and signs of distress can be gained, allowing for proactive and reactive adaptations to be made Babies should be treated with the dignity and respect that any other patient would expect. Both pharmacological and non-pharmacological methods can be employed to aid comfort, e.g. sucrose, analgesia, containment holding. Validated pain and comfort scoring systems exist that can be integrated into routine care Procedures and cares should ideally be clustered to facilitate prolonged periods of sleep
Light exposure	Preterm babies are particularly vulnerable to bright light due to immaturity of their eyelids and pupillary function, exacerbated by certain interventions such as retinopathy of prematurity screening medications Bright lighting can increase desaturations and bradycardias and interrupt sleep. Although there is a role for introducing diurnal variation once more mature to aid the development of circadian rhythms, babies should be protected from noxious levels of light at all times. As such, the use of dimmable nursery lights, window blinds, task specific downlighting, incubator covers, as well as eye covers when indicated, is encouraged.
Noise exposure	Excessive noise can lead to haemodynamic instability and disrupt sleep, impacting on the development of sensory pathways Babies who have been cared for on a neonatal unit are at a significantly increased risk of hearing impairment Bliss recommends that the noise in nurseries does not exceed 50 decibels, which is equivalent to quiet conversational speech Visual decibel monitors can be installed Thought should be given to appropriate alarm limits and volumes for monitors and equipment, with prompt attention given to alarms Incubators can accentuate certain sounds, so caution is needed with incubator drawers and portholes Parents should be encouraged to speak to their baby with an open incubator porthole to avoid distortion of the sound The implementation of 'quiet time', where there is a concerted effort to minimise noise and disruptions to the baby can help facilitate sleep
Taste and smell	Babies can be exposed to a number of negative oral experiences, e.g. suctioning, oro-gastric tubes, medication administration, which can lead to long term consequences, such as feeding difficulties and oral aversion Approaches to minimise these experiences and promote positive ones, e.g. using EBM for mouthcares, is encouraged Implementation of non-nutritive sucking can facilitate the development of oro-motor skills Strong smells, e.g. perfumes and cleaning agents, should be avoided as much as possible, although familiarisation of parental smells with bonding squares is encouraged

Table 2

the assessment of the highest-risk infants to help prognostication. This may include data obtained from radiological investigations, such as MRI, but also structured clinical assessments such as the General Movement Assessment (GMA) and the Hammersmith Neonatal or Infant Neurological Examination (HNNE/HINE), see Table 1.[4] By highlighting which children will be at higher risk for adverse motor outcomes, targeted interventions can be employed. Traditionally, physical therapies such as physiotherapy and occupational therapy have tended to focus on achievement of motor milestones. However, in recent years, research has indicated the importance of motor learning theories, supporting cognition, problem solving, meaningful activities and active participation. Repetition into everyday activities is emphasised alongside postural supports, and facilitation of exploration of their environments, which are ideally enriched to facilitate development. Overall, these features form the concept of scaffolding, which refers to an adult's structuring of the task, providing verbal or physical support to enable the child's active participation and then weaning that support as the child develops self-initiated movements.

Currently there are many different approaches to remediating motor difficulties, which unfortunately can sometimes lead to conflicting advice being given to parents and resultant stress and guilt if the programme is not followed.

A summary of findings from a Cochrane Review (2015) exploring EI in preterm infants[3]

	Number of studies (patients)	Standard mean difference[a]	Confidence interval (p-value)
Cognitive outcome — early developmental intervention versus standard follow-up			
At infancy	16 (2372)	**0.32**	**0.16, 0.47 (p <0.0001)**
At preschool age	8 (1436)	**0.43**	**0.32, 0.54 (p <0.0001)**
At school age	5 (1372)	0.18	-0.08, 0.43 (p = 0.17)
Motor outcome — early developmental intervention versus standard follow-up			
At infancy	12 (1895)	**0.10**	**0.01, 0.19 (p = 0.03)**
At preschool age	3 (264)	0.08	−0.16, 0.32 (p = 0.53)
At school age	2 (185)	−0.18	−0.47, 0.11 (p = 0.22)
Rates of cerebral palsy — early developmental intervention versus standard follow-up			
	7 (985)	0.82	0.52, 1.27 (p = 0.37)

[a] A standard mean difference greater than 0.00 supports the intervention, compared with standard care. Statistically significant findings (p <0.05) are highlighted in bold.

Table 3

A Cochrane Review in 2015 exploring the impact of EI on both motor and cognitive outcomes showed a small, but positive effect, on motor development, see Table 3. This was not sustained into school years but the number of included studies at this age group was small. Potential reasons for this are discussed later.

Cognitive and sensory

There are various interventions that can be employed which aim to improve cognitive and sensory outcomes. Many have already been mentioned in this article, e.g. DC practices on neonatal units, responsive parenting training and enriching the developmental environment. Other specific interventions may also be employed to improve individual domains, e.g. visual stimulation exercises using age-appropriate patterns, images, and toys.

Aspects of cognition can be difficult, but not impossible, to assess in young babies. Table 3 summarises the main results from a Cochrane Review from 2015, which identified statistically significant improvements in cognitive outcomes in infancy and preschool age, for babies exposed to EI.[3] Differences in cognition and behaviour do become less clear when follow-up is extended to school age, but there may be various confounding factors for this, discussed further below.

Limitations of research

As has been alluded to, research into this area can be difficult. Some of the interventions are non-specific, with many factors becoming standards of care nowadays. Other interventions are labour and cost intensive, requiring a number of sessions with experienced specialist staff, which can limit study size. Also, given the nature of the interventions, it's difficult to enact blinding, although blinding of outcome assessment could be improved. What is considered a clinically significant outcome can also vary depending on opinion.

Furthermore, it can be difficult to discern longer-term differences between intervention and control groups due to the fact that children in the control groups who start to exhibit delays or specific concerns will, quite rightly, be referred for intervention. It would be unethical to withhold such intervention from these children. However, such support is likely to minimise the differences between groups by the time children reach school age. It has been demonstrated, however, that the interventions that do have the greatest long-term impact are those that involve a developmentally supportive culture in the family, where the environment and parenting promotes the child's development and is attuned to their needs.

Ultimately though, despite all these difficulties, evidence does exist to support the benefits of EI.

Conclusion

As has been explored, there are varying approaches to EI, which is itself not one specific thing, but various interventions that are offered to a child and their family to optimise the child's neurodevelopmental outcome. It is broadly considered that commencing interventions early, including whilst on the neonatal unit, with transition to ongoing input post-discharge is of most benefit. Importantly, there needs to be strong parental involvement, not just as bystanders, but as active participants in the interventions, acknowledging the central role that relationships have in optimising a child's development, wellbeing and overall outcome. Specific focus on the parents' wellbeing is of importance too, due to the indirect impact this can have on the child.

There is a multitude of tailored and specific interventions available, for which there are many published papers not touched upon in this article. As discussed though, the conclusions drawn from meta-analyses and systematic reviews are supportive for EI as a whole. By creating cultures that are supportive of EI and tailoring specific interventions for each child, under the guidance of an expert MDT, it allows for the benefit from the aggregation of marginal gains that ultimately provides the child and their family with the best outcome possible. ◆

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Practice points

- Early Intervention refers to a broad range of multidisciplinary approaches to care and therapeutic programmes that aim to optimise a baby's neurodevelopmental outcome
- Early Intervention can start on the neonatal unit, including the adoption of family-integrated and developmentally supportive care, but for sustained benefit, interventions should continue post-discharge
- Involvement of the parents is critical and longer-term benefits on the child into school age are most apparent when parents have been focussed on development and are responsive to their child's behaviours and needs