ORIGINAL ARTICLE

Randomised trial of parental support for families with very preterm children: outcome at 5 years

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Aims: To test the effectiveness of a home based developmental education intervention in improving outcome at 5 years for very preterm infants.

Methods: The Avon Premature Infant Project (APIP) is a randomised controlled trial in which the parents of 284 babies born <33 weeks gestational age received a developmental education programme, a social support intervention, or standard care. A term reference population was also recruited. This study reports outcomes at 5 years (mean age 58 months 15 days) for 187 (66%) of these children without disability. Outcomes were assessed using the British Ability Scales II for cognitive development, the Movement ABC for motor impairment, and the Child Behavior Checklist for behavioural problems.

Results: Preterm infants showed poorer cognitive performance than their term peers. Mean (SD) general conceptual ability (GCA) scores were: Portage 99.2 (15.7); parent adviser 100.3 (14.8); preterm control 101.1 (15.0); term reference 107.2 (13.4). There were no significant differences between preterm groups in GCA scores indicating no effect of either intervention. Similarly, there was no significant effect of intervention on behavioural or motor outcomes. Further analyses, in which outcome data were adjusted for social factors, did not reveal any differences between the three preterm groups or by subgroups classified by a range of perinatal variables.

Conclusion: The small advantage shown at 2 years of age is no longer detectable at 5 years. These results question the effectiveness of early intervention in enhancing cognitive, behavioural, and motor function at 5 years.

Preterm birth and events that occur in the perinatal period may have adverse effects on a child's future development.^{1–2} Preterm children have well documented poorer cognitive, motor, and behavioural outcomes than their term peers, and these effects persist into adolescence and adulthood.^{3–13} Not all preterm babies will have poor outcomes: the impact of prematurity and perinatal insult leads to an increased developmental vulnerability that may be mediated in part by environmental experience.^{14–17}

There has been increasing interest in a range of early intervention programmes of developmental care and education for preterm children and their families. Studies of the efficacy of these interventions have shown modest improvements in short term cognitive and behavioural outcomes.^{18–20} However, such studies have generally lacked methodological rigour, being small single site studies or having focused on subsets of the population,²¹ and have rarely assessed outcomes long after the period of intervention has finished.

Other studies have investigated effects of interventions on both short and long term outcomes for more heterogeneous samples. In the Infant Health and Development Program (IHDP)²²—a multicentre randomised trial of early intervention from discharge to 3 years—children in the intervention group showed significantly better cognitive development scores than the control group at 2 and 3 years, with a larger effect size for the heavier infants (2001–2500 g); small differences were also noted in behavioural outcomes. However, these effects were not sustained after the period of intervention. At both 5 and 8 years there were no differences between intervention and control groups for cognitive or behavioural outcomes, although the heavier infants alone continued to show modest improvements in cognition.^{22–28} In contrast, other studies have found increasing beneficial effects several years after the intervention

period.^{29–30} The results to date with regards the long term efficacy of such interventions are thus inconclusive.

These studies recruited relatively mature preterm infants and the IHDP combined early developmental education with family support services; it is thus difficult to disentangle the effects of developmental education alone from the effects of enhanced parental support on the gains observed in short term outcomes.

We investigated the effect of a two year home based developmental education programme for parents of very preterm babies, the Avon Premature Infant Project (APIP).³¹ At two years of age corrected for prematurity there were only small positive effects on cognitive outcome for those children whose families had received the intervention. However, after planned secondary analysis significant effects were seen among children without severe disability after correction for social confounders. Although early interventions are costly to apply, sustained effects would attenuate the need for remedial intervention at school age. Furthermore, the poor predictive value of infant developmental assessment for school age performance means that it is important to investigate whether these effects have persisted. In this study, we aimed to show the presence of persisting effects on cognitive, behavioural, and motor outcomes at 5 years for the children in the APIP study.

METHODS

Participants

A total of 284 babies born <33 weeks gestational age were recruited to the Avon Premature Infant Project (APIP) at birth and were randomised to one of three groups: a Portage group whose parents received a developmental education programme, a parent adviser group who received a parental support intervention, or a preterm control group who

Figure 1 Patient flow and long term follow up at 5 years.

received standard care. Detailed descriptions of participant characteristics have been published previously.³¹ Children who survived to 5 years of age formed the sample for the present study. All were invited to participate, including families who had initially rejected the intervention following randomisation and who had defaulted on outcome assessments at 2 years. Children with known disabilities were examined (NM) and excluded if they were unable to complete the cognitive and motor tests because the study was not designed to determine benefit among these children. Analysis was on an intention to treat basis.

Of the 240 children without disability who were invited to participate, 179 (75%) were evaluated for this study, together with a further eight children who had not been assessed at 2 years. Thus a total of 187 children without disability (66% of those initially recruited) were assessed at 5 years (fig 1). These children did not differ from those without serious disability who were not assessed in terms of gestation at birth, birth weight, sex distribution, or distribution of intervention group (table 1). There was evidence of response bias, however, in that the children evaluated at 5 years had higher Griffiths' scores at 2 years and more advantageous social and demographic markers than those not assessed.

An additional 109 singleton babies were recruited at birth to a term reference group; of these, 87 children were evaluated at 2 years, 66 were reassessed at 5 years. Children were assessed at a mean age of 58 months 15 days (range 51–76 months).

Interventions³¹

The two intervention groups (Portage and parent adviser) were structured to be as similar as possible in number of intervention workers, visiting frequency, and supervision by a clinical psychologist. All interventions were mediated by nurses with either nursery nurse (n = 6) or state enrolled

nurse (n = 2) qualifications and experience of the hospital care of small babies. All received basic training in child protection issues and in non-directive counselling skills.

Developmental intervention: the Portage group

Portage (London: NFER Nelson) is a widely available package that has been adapted for use in the UK. We used Portage for its original target population—children with developmental delay. The package has not been the subject of a previous randomised trial. The research team developed a programme of activities to introduce the parent to aspects of their child's development, which facilitated the introduction of Portage earlier. The detailed precision teaching, which involves a task analysis approach, was generalised for many of the children who were developing normally, within the Portage model. Throughout the course of the project, care was taken to maintain consistency of intervention. The four nurses received weekly structured supervision by a clinical psychologist and regular contact with the National Portage Association.

Non-developmental intervention: the parent adviser group

The primary focus of Portage is the developmental progress of the child, although parental support is provided as part of the delivery. We developed a second intervention with parental support as the main focus, based on the parent adviser scheme.³² Training comprised a series of seminars and individual and group work, using a supportive counselling model. To isolate the effect of the developmental intervention further, the research nurses from the Portage group were also trained in this intervention. Ongoing supervision for the four parent adviser nurses was also supplied on a weekly basis by a clinical psychologist.

Table 1 Comparison of responders to non-responders for children without disability at 5 years

	Not seen at 5 years		Seen at 5 years		p value
	n		n		
Gestation at birth (med; IQR)	86	30 (29–31)	187	30 (29–32)	0.66
Birth weight (g; med; IQR)	86	1480 (1090–1745)	187	1440 (1140–1700)	0.48
Male sex (n (%))	86	46 (54%)	187	112 (60%)	0.32
Portage group (n (%))	86	33 (38%)	187	65 (35%)	0.56
Parent adviser group (n (%))	86	31 (36%)	187	61 (33%)	0.58
GQ at 2 years (mean (SD))	61	92 (8.3)	179	101 (10.1)	<0.001
Maternal age (y; mean (SD))	73	25 (5.1)	179	26.9 (4.8)	0.004
Only child (n (%))	78	31 (40%)	185	92 (50%)	0.005
Non-manual SES (n (%))	77	13 (17%)	185	85 (45%)	<0.001
Car use by mother (n (%))	73	32 (44%)	177	121 (68%)	<0.001
Single parent (n (%))	78	19 (22%)	183	16 (9%)	0.004

GQ, general quotient; IQR, interquartile range.

Intervention delivery

Both interventions began on discharge from the intensive care nurseries. Visiting was weekly for the first few months, reduced to 2–4 weekly for the next year, and then to monthly by the time disengagement occurred at 2 years, or earlier if requested by the parent. To a limited extent the frequency of visiting was tailored to suit the family. The visiting frequency and duration of each visit was similar for each group. The research nurse endeavoured to coordinate care with each family's health visitor. Following a referral to the community disability service, the research nurse liaised with the disability team to facilitate management. Regular outpatient visits occurred as part of the normal neonatal service. Both term and preterm children were examined by independent observers at 2 years who were blinded to study group. Disability and impairment were coded by one observer (NM) using standardised definitions.

Procedure

At 4½–5 years of age parents of surviving APIP children were contacted and asked to attend an appointment at a clinic in one of two local neonatal units. Prior to the appointment children with disability at 2 years were re-evaluated by a neonatal consultant to assess their ability to complete the outcome assessments at 5 years. At the study appointment children were assessed by a psychologist who was blind to the randomised group allocation of participants.

Measures

Cognitive development was assessed using the British Ability Scales 2nd Edition (BAS-II);³³ motor impairment was assessed using the Movement ABC (M-ABC);³⁴ and behavioural outcome was assessed using the Child Behavior Checklist (CBCL/4–18).³⁵ Children were randomly assigned to commence testing with cognitive or motor tests.

Approval for the present follow up was granted by the local research ethics committee at United Bristol Healthcare NHS Trust and at Southmead Hospital NHS Trust. Data were encoded for computer analysis using SPSS for Windows (version 11.1). Statistical tests are described in the results section.

RESULTS

The original sample size was calculated to detect a 5–6 point difference in scores on the primary outcome measure of cognitive development. The present data were analysed using SPSS v11.0 on an intention to treat basis.

Cognitive development

The BAS-II is designed to produce three subscale scores and an overall general conceptual ability (GCA) score; these are norm referenced scores with a mean of 100 (SD 15). The scores are shown in table 2 by study group.

Mean differences from the term control group are shown in fig 2. Although the Portage group achieved significantly lower GCA scores than their term peers (one way ANOVA, $F(3,240) = 3.44$; $p < 0.05$), there were no significant differences between the three preterm groups. Thus children whose families received either the Portage or parent adviser programme did not show improved overall cognitive scores at 5 years. The direction of effect with the lowest scores in the Portage group is the reverse of the effect at 2 years.

One way ANOVAs computed for differences in subscale scores indicated significant differences after Bonferroni correction for multiple comparisons ($p < 0.0125$). However, although children in the parent adviser and preterm control groups performed significantly worse than those in the term reference group in spatial ability ($p = 0.009$) and verbal

Figure 2 Mean differences (95% CI) in GCA scores for the Portage, parent adviser, and preterm control groups from the term reference group.**Table 2** Cognitive development at 5 years; mean (SEM) BAS-II subscale and GCA scores

BAS-II scores	Portage			Parent adviser			Preterm control			Term reference		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Verbal reasoning	67	101.8	13.2	64	102.0	13.5	67	99.3	18.0	63	107.7	12.8
Spatial ability	62	99.8	16.9	61	96.4	16.0	63	99.1	14.1	57	105.8	13.9
Pictorial representation	65	97.7	13.7	61	101.5	17.2	64	101.3	15.2	59	103.3	13.7
GCA	63	99.2	15.7	61	100.3	14.8	63	101.1	15.0	57	107.2	13.4

Table 3 Multiple regression analysis: independent effects of social and demographic factors at recruitment on BAS-II GCA scores at 5 years (preterm groups only)

Variable	Size of effect (B)*	95% CI	p value
Both parents at home	+5.55	(-2.2 to 13.3)	0.157
Non-manual SES	+8.42	(3.9 to 13.0)	0.000
Maternal age (years)	+0.28	(-0.2 to 0.8)	0.242
Number of siblings	-1.76	(-4.3 to 0.8)	0.171
Maternal use of a car	+5.18	(0.4 to 10.0)	0.035

*GCA points.

reasoning ($p = 0.010$) respectively, there were no significant differences in performance between the three preterm groups. Thus the use of either the Portage or parent adviser programme did not improve performance on any subscale.

Effect of social and demographic factors

At 2 years, despite randomisation, there were differences between the preterm groups in the distribution of social and demographic factors, and five were independently associated with developmental scores: maternal age, non-manual parental occupations, use of a car, living with both parents, and number of siblings at recruitment. Using linear regression on the 2 year data, and after correction for these five variables, independent effects of both interventions compared to the control group were identified. Linear regression analyses were similarly conducted on the present data to determine whether these effects had persisted (table 3).

These factors accounted for 16% of the variance in GCA scores at 5 years, but only the mother's use of a car and

employment in a non-manual occupation were independently associated with GCA scores in the preterm population. The direction of effect was the same as at 2 years. Within this regression model neither the Portage nor the parent adviser interventions were associated with enhanced GCA scores (fig 3).

Cognitive development: effect of perinatal variables

Further planned secondary analysis at 2 years indicated significant associations between perinatal factors and developmental scores. These analyses were repeated using GCA scores, after adjustment for the effect of sociodemographic factors, in order to identify any subgroup effects (table 4).

The present analyses did not indicate advantage in GCA scores after adjustment for social factors for children in the Portage or parent adviser groups when categorised by any perinatal variable. Figure 4 shows the mean (95% CI) differences from the preterm control group for each intervention group for the perinatal data items in table 4. In contrast to the advantage shown by intervention at 2 years, there were non-significant trends for intervention to have had negative effects in these analyses and for children with birth weight >1250 g GCA scores were 2.8 points (95% CI 0.2 to 5.5) lower than preterm control children, reflecting a raw scores difference of 6.8 points (95% CI 0.2 to 12.7).

Motor impairment

The Movement ABC (M-ABC) is a standardised assessment of motor impairment yielding three subscale scores and a total motor impairment (TMI) score; median (IQR) subscale and TMI scores are shown in table 5.

A Kruskal-Wallis test indicated significant differences between the study groups ($\chi^2 (3) = 18.16$, $p = 0.000$). Post

Figure 3 Effect size (95% CI) of social variables and interventions on BAS-II GCA scores at 5 years.**Table 4** GCA scores adjusted for effect of sociodemographic factors grouped by perinatal variables (preterm groups only)

Variable	Portage		Parent adviser		Preterm control	
	n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)
Male	39	99.7 (1.0)	34	99.3 (1.2)	33	103.0 (1.0)
Birth weight						
≤ 1250 g	16	99.5 (2.0)	26	98.6 (1.2)	21	99.4 (1.6)
> 1250 g	44	99.9 (0.9)*	34	100.3 (1.2)	36	102.7 (1.0)
Gestation						
≤ 28 weeks	8	96.1 (2.6)	13	101.5 (1.9)	13	100.6 (1.9)
> 28 weeks	52	100.3 (0.9)	47	99.1 (0.9)	44	101.8 (1.0)
Appropriate size for gestational age	58	99.8 (0.9)	60	99.6 (0.9)	56	101.5 (0.9)
Normal ultrasound	58	99.8 (0.9)	58	99.5 (0.9)	53	101.2 (0.9)
Any haemorrhage (PVH)	8	103.0 (2.7)	4	96.9 (4.6)	5	99.3 (3.7)
Any periventricular leucomalacia	6	98.5 (3.9)	4	94.0 (1.5)	5	98.4 (4.4)
Not ventilated	18	100.4 (1.3)	18	98.6 (1.6)	19	100.2 (1.5)
Ventilated ≤ 7 days	49	100.0 (0.9)	41	99.6 (1.2)	41	101.7 (1.1)
Ventilated > 7 days	11	98.5 (2.6)	19	99.7 (1.6)	16	100.9 (1.6)

PVH, periventricular haemorrhage.

* $p < 0.05$ for difference from preterm control group.

Figure 4 Mean differences (95% CI) in GCA scores from preterm controls for the Portage (P) and parent adviser (PA) groups categorised by perinatal variables.

hoc Mann-Whitney U tests revealed that although preterm children had higher scores than the term reference group ($p < 0.01$), there were no significant differences between the three preterm groups. Thus neither intervention improved motor development in comparison to standard care.

A cut off equivalent to the upper quartile of the term reference group scores defined motor impairment. In the preterm control group, 51% were classified as impaired compared to 52% of children in the Portage group (relative risk (RR) 1.03, 95% CI 0.52 to 2.04) and 55% of children in the parent adviser group (RR 1.14, 95% CI 0.57 to 2.26).

Behavioural outcome

The Child Behavior Checklist (CBCL) is a parent report questionnaire designed to assess problem behaviours from which are derived two main subscale scores and a total raw score. Table 6 details the median scores for each group.

A Kruskal-Wallis test indicated significant differences between the study groups ($\chi^2 (3) = 7.98$, $p < 0.05$). Post hoc Mann-Whitney U tests revealed that although the two intervention groups had significantly higher scores than the term reference group ($p < 0.05$), there were no differences between the three preterm groups. Thus the delivery of either intervention did not improve behavioural outcomes at 5 years.

CBCL subscale and total raw scores are converted to T scores for comparison with a normative sample. Using published cut offs, 11% of the preterm control group were considered to have problem behaviours within the clinical

range (>98 th centile), compared to 12% in the parent adviser group (RR 1.39, 95% CI 0.60 to 3.19) and 17% of children in the Portage group (RR 1.48, 95% CI 0.64 to 3.9); these differences were not significant.

DISCUSSION

The APIP Study was designed to determine the effectiveness of the Portage developmental education programme in enhancing the outcome of very preterm children. Predictably, at 5 years, performance of preterm children was poorer than that of their term peers on all outcomes assessed.²⁻¹³ In keeping with outcomes at 2 years, primary analyses again revealed no beneficial effects of either intervention on the cognitive, motor, or behavioural function of preterm infants at 5 years. After planned secondary analyses at 2 years the authors identified improved cognition for children with birth weights <1250 g and those with ultrasound abnormalities; by 5 years of age these effects were no longer detectable.

We were disappointed in the response rate for the current study. Analysis of the children seen identified no differences in important study or baseline perinatal variables with those not evaluated. However, there was significant response bias in that the children seen came from families with more markers of social advantage. Given the observation that interventions such as these may be more effective in the presence of social disadvantage,²² it is possible that we may have missed some advantage persisting in these groups. The results of Griffiths' scores at two years for the group not seen

Table 5 Motor impairment at 5 years; median (IQR) Movement ABC subscale and total motor impairment scores

Movement ABC scores	Portage			Parent adviser			Preterm control			Term reference		
	n	Median	IQR	n	Median	IQR	n	Median	IQR	n	Median	IQR
Manual dexterity	66	0.25	0.0–2.1	64	1.75	0.0–3.0	68	0.75	0.0–3.9	61	0.0	0.0–0.0
Ball skills	66	0.0	0.0–2.0	64	0.0	0.0–1.0	68	0.0	0.0–2.0	61	0.0	0.0–0.3
Static and dynamic balance	65	2.5	0.0–7.3	64	2.0	0.5–5.0	68	2.5	0.0–6.5	61	0.5	0.0–3.5
Total motor impairment	65	4.5	1.0–10.8	64	5.0	2.0–9.9	68	4.5	1.1–9.4	61	2.0	0.0–4.3

Table 6 Behaviour at 5 years; median (IQR) CBCL subscale and total raw scores

CBCL scores	Portage			Parent adviser			Preterm control			term reference		
	n	Median	IQR	n	Median	IQR	N	Median	IQR	n	Median	IQR
Internalising subscale	70	4	3–7	63	4	2–8	69	4	2–7	66	3	2–5
Externalising subscale	70	10	5–13	64	9	5–12	69	7	4–14	66	8	5–10
Total score	70	24	15–38	65	23	15–36	69	25	13–34	66	18	13–28

What is already known on this topic

- While developmental interventions have shown modest improvements in preterm outcomes, particularly for heavier and more mature infants, the evidence regarding longer term sustained effects is inconclusive
- In the authors' randomised trial, developmental education (Portage) and enhanced parental support (parent adviser) for parents of very preterm (<33 weeks) children both showed small positive effects on cognitive development at 2 years

at 5 years were slightly lower than for those evaluated, but there were no significant differences on raw or adjusted general quotient values when analysed by treatment group. This response bias we believe is also responsible for the slightly higher term comparison group scores than expected and apparently normal mean preterm scores.

Although developmental outcome did not appear to have improved by the end of the intervention, it is important to assess outcome later in childhood to identify any potentially later occurring or longer term effects on development, particularly given the poor predictive validity of infant assessments. We did not find any continued or new beneficial effect of either intervention 3 years after the period of delivery. This is consistent with previous studies of developmental interventions.^{29–30} Results of such studies, together with the present findings, question the efficacy of early home based developmental interventions in improving the outcomes of preterm children beyond the period of support. It may thus be the case that the period of delivery of interventions tested to date needs to be sustained throughout early childhood and up to school entry for any effects of early developmental education to be maintained in later childhood and evidenced in early scholastic attainment.

The success of previous studies showing beneficial effects of intervention up to 3 years have been attributed to a combined programme of enhanced social support and targeted developmental education. The present study, in which we distinguished between these aspects of home based parental support, did not provide evidence that developmental education is any more beneficial than the provision of parental support alone. In future studies it might therefore be profitable to combine these elements in global individualised family intervention programmes, although careful economic evaluation, not undertaken here, will be required.

In addition, previous studies have enrolled heavier or more mature infants; IHDP investigators found the greatest effect of intervention for infants of heavier birth weights (2001–2500 g).^{24–28} Thus the efficacy of developmental interventions with very preterm infants has not been directly investigated. The utility of such interventions with very low birth weight infants is suggested by IHDP investigators who, in comparison with our secondary analyses at 2 years, found a significant reduction in behaviour problems and a trend to improved cognition at 3 years for extremely low birth weight babies after adjustment for infant and social characteristics, and after excluding those with severe disability.³⁶ However, these effects were not maintained past the period of intervention delivery in either study. The present results, indicating no benefit of intervention targeted directly at such a sample, thus suggest that more refined programmes may be required to adequately fulfil the longer term needs of these families.

What this study adds

- Developmental advantages found at 2 years are lost by 5 years
- The subgroup effects found at 2 years are no longer present at 5 years

The administration of both intervention programmes in the present study commenced on discharge from the neonatal unit; for some families this may have been some 2–3 months after birth, with even greater periods of admission for babies born extremely preterm and those with a more complicated neonatal course. It is possible that intervention programmes for very preterm infants, commenced as soon as possible after birth while the baby is in the care of the neonatal unit, may have a greater impact on early development and be more effective in enhancing both short and longer term outcomes. Indeed, feedback provided by the research nurses delivering the interventions in the APIP study, and subsequent pilot work carried out to further develop the Portage programme for families with young very preterm babies,³⁷ indicated that the parenting patterns they encountered had already been established by the time the intervention commenced; parents also expressed the opinion that the interventions were provided too late for real benefits to ensue. Developmental intervention programmes commenced during admission, and thus before anxiety and uncertainty regarding their parental role and inappropriate patterns of parental behaviour have become established,^{38–39} but none have been evaluated in a prospective trial to date.

Effective developmental interventions with persisting long term effects are thus still required. Prevention of the cognitive disadvantage associated with very preterm birth remains one of the more elusive goals of modern perinatal care.

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