School-Age Outcomes of Early Intervention for Preterm Infants and Their Parents: A Randomized Trial

Alicia J. Spittle, PhD, MPhysio, BPhysio,[a,b,c] Sarah Barton, DPsych,[a] Karli Treyvaud, DPsych,[a,c,d,e] Carly S. Molloy, PhD,[a] Lex W. Doyle, MD,[a,c,d,f] Peter J. Anderson, PhD[a,d]

abstract

OBJECTIVE: To examine the child and parental outcomes at school age of a randomized controlled trial of a home-based early preventative care program for infants born very preterm and their caregivers.

METHODS: At term-equivalent age, 120 infants born at a gestational age of <30 weeks were randomly allocated to intervention (n = 61) or standard care (n = 59) groups. The intervention included 9 home visits over the first year of life focusing on infant development, parental mental health, and the parent–infant relationship. At 8 years' corrected age, children's cognitive, behavioral, and motor functioning and parental mental health were assessed. Analysis was by intention to treat.

RESULTS: One hundred children, including 13 sets of twins, attended follow-up (85% follow-up of survivors). Children in the intervention group were less likely to have mathematics difficulties (odds ratio, 0.42; 95% confidence interval [CI], 0.18 to 0.98; P = .045) than children in the standard care group, but there was no evidence of an effect on other developmental outcomes. Parents in the intervention group reported fewer symptoms of depression (mean difference, –2.7; 95% CI, –4.0 to –1.4; P < .001) and had reduced odds for mild to severe depression (odds ratio, 0.14; 95% CI, 0.03 to 0.68; P = .0152) than parents in the standard care group.

CONCLUSIONS: An early preventive care program for very preterm infants and their parents had minimal long-term effects on child neurodevelopmental outcomes at the 8-year follow-up, whereas primary caregivers in the intervention group reported less depression.

[a]*Victorian Infant Brain Study, Murdoch Childrens Research Institute, The Royal Children's Hospital, Parkville, Victoria, Australia; Departments of* [b]*Physiotherapy,* [d]*Paediatrics, and* [f]*Obstetrics and Gynaecology, University of Melbourne, Parkville, Victoria, Australia;* [c]*Women's Newborn Research Centre, The Royal Women's Hospital, Victoria, Australia; and* [e]*Department of Psychology and Counselling, La Trobe University, Bundoora, Victoria, Australia*

Dr Spittle conceptualized and designed the study, drafted the initial manuscript, and carried out the initial analyses; Drs Barton, Treyvaud, Doyle, and Anderson coordinated and supervised data collection and critically reviewed the manuscript; Dr Molloy coordinated the initial ethics submission and study coordination and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

This trial has been registered with the Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au/) (identifier ACTRN12606000252516).

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WHAT'S KNOWN ON THIS SUBJECT: Early developmental interventions for preterm infants are known to have short-term benefits on cognitive and motor outcomes. However, long-term benefits of these interventions on neurodevelopmental outcomes for children and on the well-being of parents remain unclear.

WHAT THIS STUDY ADDS: Our early developmental intervention supporting parental well-being had long-term benefits for parents of very preterm children. However, the program, which supported child development, was not associated with neurobehavioral improvements at school age for preterm infants, except for mathematics performance.

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Long-term quality of life is the major concern for families of very preterm children who survive the neonatal period.[1] Approximately 50% of very preterm children display persisting neurobehavioral deficits, including attention difficulties,[2] impaired memory,[3] delayed language skills,[4] executive dysfunction,[5] academic difficulties,[6] social-emotional and psychiatric difficulties,[7] and developmental coordination disorder.[8] In addition, parents of very preterm children report increased anxiety, depression, stress, and an increased negative impact on family functioning compared with parents of term-born children.[9–11]

Neurobehavioral impairments in very preterm children are associated with medical risk factors (eg, gestational age, white matter brain injury), although these constitute only a portion of the variance in outcomes.[12] Nonmedical factors, such as primary caregiver education and mental health, parenting style, family functioning, and home environment, are also important for early and later development.[10,13,14] The important role of social and environmental factors on development in this high-risk group of children justifies the development and implementation of early intervention programs designed to strengthen the home and parenting environment for the child.

Studies examining the effectiveness of early developmental intervention programs for preterm children report short-term benefits for infants and their parents.[15,16] However, the longer-term benefits of these programs remain unclear, with some studies showing improved cognitive outcomes at school age, and others showing no sustained effects.[17,18] Limited studies examining long-term outcomes have typically focused on child outcomes by using omnibus cognitive and/or motor measures. Less is known about outcomes in specific cognitive domains (eg, attention, working memory, academic skills), or child social and emotional functioning after early developmental intervention.[15] In addition, there have been no follow-up studies on long-term parental mental health after early intervention for preterm infants and their caregivers into school age.

We have previously demonstrated in a randomized controlled trial (RCT) that an early developmental intervention program improved behavioral outcomes for very preterm children and the psychological wellbeing of their parents at 2 and 4 years' corrected age.[19–21] However, there were no significant differences in cognitive and motor outcomes. Because parental mental health is associated with child development,[13] later benefits related to this early developmental intervention program are possible. Thus, it is vital to determine the long-term benefits of our early developmental intervention program.

The aim of this study was to determine the long-term neurodevelopmental outcomes for very preterm children after a preventative care program conducted within the home during the first year of life. The aim was to assess a range of areas at 8 years of age, including cognitive (IQ, processing speed, attention, memory, executive function, academic performance), behavior, and motor outcomes for the child, as well as the long-term mental health status of the primary caregiver. We hypothesized that children who were randomized to the preventative care group would have better cognitive and behavioral outcomes at the 8-year follow-up, and their primary caregivers would have less anxiety and depression compared with the standard care group.

METHODS

Study Design

This follow-up study involved 118 surviving very preterm infants who participated in a previously reported RCT,[21] where infants were randomized, after consent, by computer-generated random sequences (allocation concealed by using opaque envelopes), stratified for white matter injury (normal to mild vs moderate to severe)[12] on MRI (to ensure equal rates of brain injury between groups), and multiple births (because multiples had to be allocated to the same group given the nature of the intervention).

Participants

Eligible infants were recruited between January 2005 and December 2007 from the Royal Women's Hospital and/or Royal Children's Hospital (Parkville, Victoria, Australia). Inclusion criteria were being born at <30 weeks of gestation, living within 100 km of the hospital (because of home visits), and parents who could speak English (because no funding was available for interpreters). Exclusion criteria were infants with congenital anomalies likely to affect neurodevelopment. At the 4-year follow-up, a term-born group, comprised of 41 children born at >36 weeks of gestation with no significant congenital anomalies or developmental problems, were recruited from Melbourne metropolitan kindergartens as a comparison group. Parents provided informed consent for themselves and their children to participate in the 8-year follow-up, which occurred between July 2012 and March 2015. The initial study was approved by the Royal Women's Hospital human research ethics committee and the 8-year follow-up by the Royal Children's Hospital human research ethics committee.

Intervention

The intervention consisted of 9 home visits at 2 weeks, 4 weeks and at 3, 4, 6, 8, 9, and 11 months'

corrected age. A physiotherapist and psychologist together delivered the preventative care program at home with the infant and the primary caregiver, with sessions lasting 1.5 to 2 hours. The primary aim of the program was to improve infant development (cognitive, motor, and language) by working with the family to understand their infant's behavioral cues, enriching the environment by encouraging positive play and interactions, positioning and handling, problem solving difficult tasks (eg, sleeping and feeding), providing information on milestones specific to preterm infants, and optimizing parent mental health. Additional details of the interventions have been reported in the study protocol.[21] Because of the nature of the intervention, the therapists administering the intervention were not blind to group assignment.

Outcome Measures

Children and their families attended a 4-hour outpatient assessment conducted by an assessor blinded to the study group. If the family was not able to attend at the hospital, a home or school visit was conducted. All outcome measures were chosen because they have good psychometrics in children, including reliability. Scores of >1 SD below the mean for the term-born children on relevant tests were classified as impaired. The term comparison group was used to classify impairment because of previous reports of underestimation of impairment when using test norms.[22] Children who were unable to complete specific tests because of significant impairment in that domain were assigned a score of 4 SD below the mean or scores of 0 for raw scores. Age was corrected for prematurity to avoid a known bias in cognitive test scores, even at school age.[23,24]

Cognitive Assessment

General Cognitive Ability

The General Conceptual Ability score from the Differential Ability Scale, Second Edition,[25] assesses general cognitive ability. The Differential Ability Scale, Second Edition has 6 subtests in the core school-aged battery (Recall of Designs, Word Definition, Pattern Construction, Matrices, Verbal Similarities, Sequential and Quantitative Reasoning) ,which provide indices for verbal, nonverbal, and spatial reasoning abilities. All scales have a normative mean of 100 (SD = 15).

Attention

Attention was assessed by using subtests from the Test of Everyday Attention for Children.[26] Sky Search is a measure of selective attention; children search for and circle target spaceships while ignoring distractor stimuli. Score! is a measure of sustained attention; children listen to an audio recording and count target tones that are presented at intermittent intervals (10 trials). Creature Counting is a measure of shifting attention; children count the number of targets (creatures) displayed on a sheet but alternate between counting forward and backward according to the direction of arrows. Sky Search Dual Task is a measure of divided attention; children simultaneously count the number of target tones on an audio recording while searching for and circling all the visual targets on a sheet. Subtests have a normative mean of 10 (SD = 3).

Working Memory

Working memory was assessed by using subtests from the Working Memory Test Battery for Children.[27] Digit Recall assessed immediate verbal memory; children recalled sequences of digits presented verbally. Block Recall assessed immediate visual memory; children recalled the spatial location of blocks tapped in specific sequences. Backward Digit Recall assessed verbal working memory; children recalled sequences of digits presented verbally in the reverse order. These subtests all have a normative mean of 100 (SD = 15).

Executive Functioning

The Tower of London (TOL)[28] assessed spatial planning and behavioral inhibition; children moved 3 balls across 3 pegs of different heights to achieve a specific pattern while adhering to prescribed rules. There are 12 items that increase in difficulty. The number of items correctly solved (within a 60-second time limit) and the number of items correctly solved in the first attempt (ie, with no errors) were used as measures.

Academic Skills

The Wide Range Achievement Test, Fourth Edition[29] was used to assess word reading, spelling, and mathematical computation. These scales have a normative mean of 100 (SD = 15).

Social-Emotional Functioning

Social-emotional functioning was assessed by using 2 parent-reported questionnaires, the Problem Behavior Index from the Social Skills Improvement System Rating Scales[30] and the Total Problem Score from the Strengths and Difficulties Questionnaire.[31] Using the raw scores for both scales (Problem Behavior on the Social Skills Improvement System Rating Scales and Total Problems on the Strengths and Difficulties Questionnaire), children were classified as having a "social-emotional impairment" if raw scores on either measure were >1 SD above the mean raw scores for the control group.

Motor

The Movement Assessment Battery for Children, Second Edition[32] was used to assess manual dexterity, aiming and catching, and balance.

The total standard score (mean = 10; SD = 3) was used to assess motor competence and a cut-off of ≤15th percentile was used to categorize children at risk for motor impairments. The Movement Assessment Battery for Children, Second Edition is a valid and reliable tool for assessing motor competence and motor impairment in children and can be used from ages 3 to 16 years.

Parental Wellbeing

The Hospital Anxiety Depression Scale (HADS)[33] was used to assess parental symptoms of anxiety and depression. For both the anxiety and the depression scales, a score of ≥8 was used to categorize elevated (mild to severe) symptoms.

Data Analysis

Analysis was by intention to treat by using Stata version 14 (Stata Corp, College Station, TX). Perinatal risk factors and social risk were compared between those who did and did not participate in the 8-year follow-up by using *t* tests and χ^2 tests. For continuous and categorical variables, outcomes between groups were analyzed by using linear and logistic regression, respectively, adjusted for the stratification factors of multiple birth and moderate to severe white matter abnormality. Models were fitted by using generalized estimating equations with an exchangeable correlations structure and robust SEs to allow for correlations between twins/triplets in the study for child outcomes. For parental outcomes of mental health, standard linear and logistic regression was used because there was only 1 set of primary caregiver results regardless of multiple births. Results are presented as mean differences between the groups and 95% confidence intervals (CIs) for each continuous child and parent outcome measure, and odds ratios (OR) and 95% CIs for categorical data, along with *P* values, which represent the strength of evidence against the null hypothesis, consistent with modern statistical practice.[34] Analyses were adjusted for age at assessment on outcomes based on raw scores (rather than age standardized scores). All analyses were repeated by using nonimputed results for children who were unable to complete test items because of significant impairments.

Power Calculations

At the 8-year follow-up, we anticipated a follow-up rate of 85%, similar to our previous study at 4 years of follow-up,[19] which would be a sample of 100 children. A sample size of 50 in preterm intervention and control groups provided 81% power to detect a difference of 0.57 SD in means between groups (based on a 2-sided test with an α-level of 0.05). The primary outcome measure was cognitive outcome, with all other child and parent measures considered secondary outcome measures.

RESULTS

At school age, 85% of surviving very preterm children attended follow-up, including 53 of 60 (88%) children in the intervention group and 47 of 58 (81%) children in the standard care group (Fig 1). In addition to the very preterm children, 33 of 41 (80%) full-term controls participated in the follow-up. There was no difference in perinatal characteristics between those who did and did not participate in the 8-year follow-up (data not shown). There were no adverse side effects reported as a result of the standard care or the preventative care program. There were no adverse side effects as a result of the preventative care program. The mean age (corrected for prematurity) at follow-up for the very preterm children was 8.15 years for the treatment group, 7.78 years for the standard care group, and 8.12 years for the term group (Table 1). There were no differences in mean age between groups (ie, preterm versus term control or intervention versus standard care).

There were no significant differences between intervention and standard care groups for the child outcomes for the continuous scores, with both preterm groups performing below their term-born peers (Table 2). With respect to impairment rates, there were no differences between the intervention and standard care groups (Table 3), except children in the intervention group (38%) were less likely to have a mathematics impairment compared with the standard care group (53%) (OR, 0.42; 95% CI, 0.18 to 0.98; *P* = .045). Results remained similar when analysis was repeated by using nonimputed data.

There were 41 primary caregivers in each of the treatment and control groups who reported anxiety and depression outcomes using the HADS, including caregivers of 8 sets of twins. At the 8-year follow-up, the parents in the intervention group reported fewer symptoms of anxiety and depression (Table 4), with intervention parents having lower rates of mild to severe depression (5%) than the standard care parents (27%) (OR, 0.14; 95% CI 0.03 to 0.68; *P* = .015).

DISCUSSION

This study has demonstrated that an early developmental intervention program for preterm infants and their caregivers in the first year of life has an important long-term positive effect on parental mental health for primary caregivers at the 8-year follow-up. Specifically, parents in the intervention group had 54% lower odds of mild to severe symptoms of anxiety, and 85% lower odds of mild to severe symptoms of depression than the preterm control group. Importantly, rates of anxiety and depression in the preterm intervention group were similar to those in the parents of term-born children (20% to 22% for

anxiety and 5% to 7% for depression), whereas in the preterm control group, almost half (42%) of parents reported elevated anxiety and over one-quarter (27%) reported elevated depression symptoms. These high rates in the preterm control group are alarming, although consistent with the evidence that parents of preterm children report higher rates of anxiety and depression across early childhood.[10,11,35] Parental mental health problems can have a negative effect on preterm children's development and mental health,[36,37] and thus the results from the current study demonstrating improvement in parental mental health after the intervention are clinically important and have the potential to also improve children's outcomes in the longer term.

Our study found no long-term benefits of the early developmental intervention on child outcomes, consistent with other RCTs in this area.[15] Our finding of no difference in general cognitive ability is similar to those of the modified-Mother Infant Transaction Program (MITP) from Norway, which found no long-term effects on overall cognitive outcome at 7 and 9 years of age, and the Infant Behavioural Assessment and Intervention Program (IBAIP) from the Netherlands at 5.5 years.[17,18] Although all 3 trials reported higher scores (although not significant) for the intervention groups compared with the control groups for general cognition, they were most likely underpowered to detect subtle differences between groups. Importantly, all 3 trials reported improvements for the intervention groups in specific neurodevelopmental domains, with the IBAIP reporting less performance IQ impairment, and the modified-MITP reporting that the intervention group had higher verbal comprehension index scores. Consistent with this pattern of improvement in specific, isolated areas of development, our study found fewer mathematics difficulties for the intervention group. However, given that this was an isolated finding and that there was no difference in the continuous data for mathematics, this is likely a chance finding. These improvements in specific domains warrant additional exploration and highlight the importance of

TABLE 1 Characteristics of Participants at School-Age Follow-up

	Preterm Intervention	Preterm Control	Term Control
No. of school-age children assessed	47	53	33
Gestational age (wk), mean (SD)	27.4 (1.3)	27.5 (1.6)	39.6 (1.2)
Birth weight (g), mean (SD)	1062 (230)	1018 (286)	3527 (476)
Boys, *n* (%)	31 (58.5)	23 (48.9)	16 (48)
Cerebral palsy, *n* (%)	3 (5.6)	4 (8.5)	0 (0)
Maternal antenatal corticosteroids, *n* (%)	48 (90.6)	39 (83.0)	N/A
Postnatal corticosteroids, *n* (%)	2 (3.8)	2 (4.3)	N/A
Oxygen dependent at 36 wk, *n* (%)	16 (30.2)	14 (29.8)	N/A
Proven/suspected necrotizing enterocolitis, *n* (%)	7 (13.2)	5 (10.6)	N/A
Grade III/IV intraventricular hemorrhage, *n* (%)	2 (3.7)	5 (10.6)	N/A
Cystic periventricular leucomalacia, *n* (%)	1 (1.9)	3 (4.3)	N/A
Moderate to severe white matter brain injury, *n* (%)	4 (7.6)	4 (8.5)	N/A
Higher social risk, *n* (%)	17 (32.1)	18 (38.3)	11 (33)[a]
Primary caregiver with tertiary education at baseline, *n* (%)	24 (46.2)	24 (57.4)	27 (87)[a]
Age at 8-y assessment (y), mean (SD)	8.2 (0.7); range, 7.0–9.7	7.8 (0.6); range, 7.0–9.3	8.1 (0.5); range, 6.8–8.9

[a] Data missing for 2 subjects.

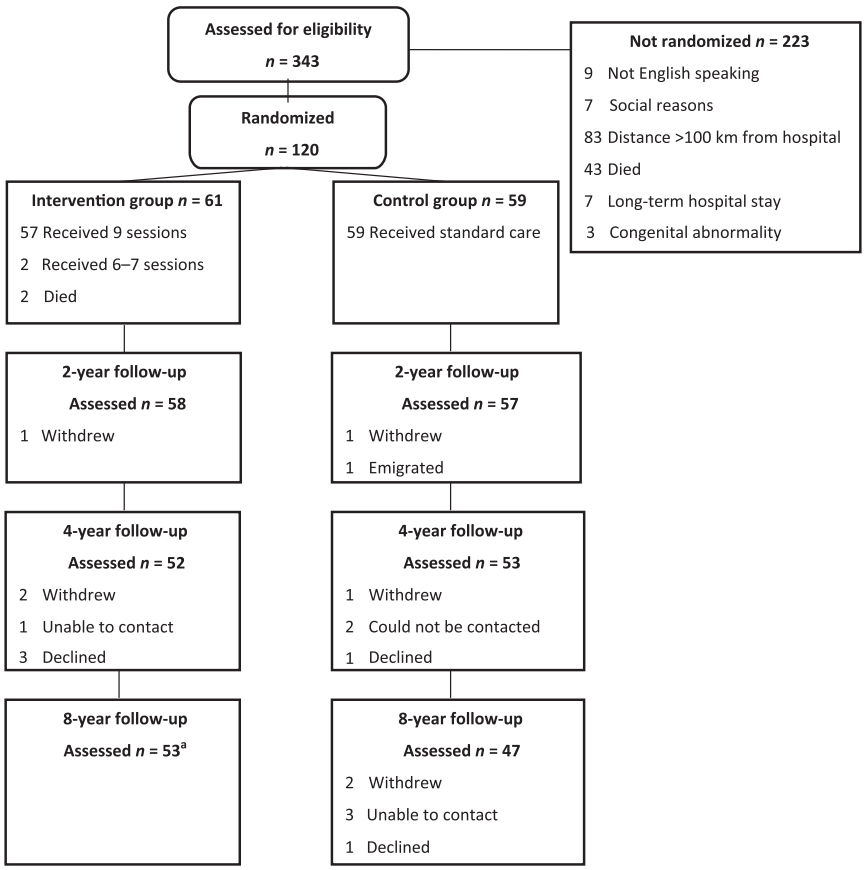

FIGURE 1
Flow diagram of participants included in the RCT. [a]One patient who declined at the 4-year follow-up participated in the 8-year follow-up.

TABLE 2 School-Age Child Outcomes Between Preterm Intervention and Control Groups, Including Reference Values for Health Term Controls

Child	Term		Preterm				Preterm Comparison	
			Intervention		Control			
Score	*n*	Mean ± SD	*n*	Mean ± SD	*n*	Mean ± SD	Adjusted Mean (95% CI)	*P*
General cognition								
General conceptual ability	32	110.5 ± 10.6	51	101.6 ± 12.6	43	99.8 ± 12.4	0.9 (–4.5 to 6.4)	.74
Verbal composite	32	111.7 ± 12.9	51	101.4 ± 11.4	43	100.4 ± 13.7	1.2 (–4.7 to 7.1)	.70
Nonverbal reasoning composite	33	104.3 ± 12.9	51	97.9 ± 12.8	44	95.1 ± 12.9	2.0 (–3.4 to 7.3)	.47
Spatial reasoning composite	33	111.0 ± 12.9	51	105.1 ± 14.3	44	102.4 ± 15.8	2.7 (–3.5 to 8.8)	.40
Attention								
Selective attention	33	9.9 ± 2,8	53	9.0 ± 3.8	47	8.1 ± 3.5	0.6 (–1.0 to 2.2)	.47
Shifting attention	32	10.8 ± 3.2	53	7.3 ± 4.2	47	7.1 ± 4.5	−0.3 (–2.0 to 1.3)	.69
Sustained attention	32	9.3 ± 3.1	53	7.1 ± 3.5	47	7.9 ± 4.0	−1.1 (–2.5 to 0.4)	.16
Divided attention	31	7.7 ± 4.1	52	5.2 ± 4.7	47	5.1 ± 4.3	0.0 (1.8 to 1.8)	.99
Working memory								
Digit recall	33	107.2 ± 14.8	51	101.4 ± 20.6	46	100.4 ± 16.2	4.8 (–3.0 to 12.6)	.23
Block recall	33	101.7 ± 20.2	47	86.7 ± 19.0	43	87.6 ± 18.7	−1.7 (9.8 to 6.4)	.68
Backward digit recall	33	104.6 ± 19.6	49	95.3 ± 16.0	46	90.7 ± 16.3	5.4 (–2.3 to 13.2)	.17
Executive function								
TOL (*N* correct in 60 s)	32	10.3 ± 2.1	48	9.0 ± 2.9	45	9.2 ± 2.3	−0.5 (–1.6 to 0.6)[a]	.36
TOL (*N* correct on first attempt)	31	7.1 ± 1.6	48	5.7 ± 2.2	45	6.1 ± 2.0	−0.8 (–1.7 to 0.7)[a]	.07
Academic achievement								
Word reading	32	112.7 ± 14.5	51	104.2 ± 16.3	47	105.9 ± 16.4	−0.2 (–7.1 to 6.8)	.96
Spelling	32	110.4 ± 15.5	51	100.8 ± 17.9	46	103.9 ± 17.3	−0.8 (–8.2 to 6.6)	.83
Mathematical computation	32	106.3 ± 14.1	51	94.2 ± 13.6	47	93.8 ± 17.8	1.9 (–4.4 to 8.1)	.56
Motor								
Total standard score	32	11.5 ± 3.2	53	8.3 ± 3.7	47	7.9 ± 4.1	0.2 (–1.5 to 1.9)	.82

Adjusted analysis for stratification factors of multiple birth and white matter abnormality grade 3/4.
[a] Adjusted for age at assessment.

longitudinal follow-up to explore developmental trajectories of higher-level cognitive and academic skills. Neither our study nor the study from the IBAIP found differences in cognitive outcomes earlier in childhood, whereas the modified-MITP reported a diminished effect on cognitive outcomes over time, with improvements at 5 years not sustained at 7 and 9 years.

One of the strengths of our study was the comprehensive assessment of many functional neurodevelopmental domains, including cognitive, academic, motor, and behavioral outcomes. Although we were able to assess a wide range of outcomes, a small loss to follow-up and the resultant decrease in sample size reduced the power to detect differences between groups. Nonetheless, our follow-up rate of 85% of survivors at 8 years was very high for a study of long-term outcomes of an early intervention program that occurred within the first year of life. An additional strength of the study was the inclusion of a healthy-term control reference group. Although this group was relatively small, they were an important inclusion because many of the scores on the developmental assessments for the term controls were higher than the expected published norms. For the majority of the assessments, the preterm children scored 0.5 to 1.0 SDs below their term-born peers, whereas, in comparison with test norms, the performance of the preterm children would be in the average range. A limitation was that we did not have the sample size necessary to perform subgroup analyses to determine if the intervention was more effective for specific families, such as those who were more socially disadvantaged

Early developmental intervention programs in the first year of life are not enough to mitigate the adverse start to life of being born preterm long-term and additional research needs to focus on interventions that are sustained for longer periods.[16,38] There is increasing evidence that intervention needs to be targeted to infants' and parents' needs. Although there was flexibility in our program to focus on the family's specific goals, our intervention was designed as a preventative care program rather than a treatment program.[39] Although preterm infants are at risk for a range of neurodevelopmental impairments, it is important to assess the infants' and families' needs and target interventions appropriately, rather than implement a "one-size-fits-all" approach. Additional research is needed not only to help preterm infants have the best start to life in their important first year but also across the longer term as they transition to school and beyond.

CONCLUSIONS

Our preventative care program for preterm infants and their caregivers

TABLE 3 School-Age Child Outcomes Between Preterm Intervention and Control Groups, Including Reference Values for Healthy Term Controls

Child	Term		Preterm				Comparison Within Preterm Groups	
			Intervention		Control			
Impairment	*n*	*N* (%)	*n*	*N* (%)	*n*	*N* (%)	Adjusted OR (95% CI)	*P*
General cognition								
General conceptual ability	32	5 (16)	51	41 (41)	43	18 (42)	1.21 (0.47 to 3.09)	.69
Verbal composite	32	3 (9)	51	20 (39)	43	18 (42)	0.92 (0.36 to 2.33)	.86
Nonverbal reasoning composite	33	7 (21)	51	17 (33)	44	15 (34)	1.07 (–0.41 to 2.87)	.88
Spatial reasoning composite	33	5 (15)	51	13 (25)	44	13 (30)	0.97 (0.34 to 2.79)	.96
				Attention				
Selective attention	33	8 (24)	53	15 (28)	47	24 (51)	0.45 (0.18 to 1.09)	.08
Shifting attention	32	6 (18)	53	26 (49)	47	20 (43)	0.99 (0.41 to 2.37)	.98
Sustained attention	32	6 (18)	53	27 (51)	47	21 (45)	1.23 (0.59 to 2.77)	.53
Divided attention	31	8 (25)	52	26 (50)	47	21 (45)	1.21 (0.51 to 2.88)	.66
				Working memory				
Digit recall	33	4 (12)	51	16 (31)	46	14 (30)	0.97 (0.38 to 2.49)	.88
Block recall	33	4 (14)	47	16 (34)	43	15 (35)	0.96 (0.35 to 2.64)	.94
Backward digit recall	33	4 (12)	50	13 (26)	46	17 (37)	0.75 (0.29 to 1.95)	.56
				Executive function				
TOL (*N* correct in 60 s)	32	2 (6)	48	12 (25)	45	13 (29)	0.93 (0.35 to 2.47)[a]	.89
TOL (*N* correct on first attempt)	32	6 (19)	48	19 (40)	45	17 (38)	1.37 (0.52 to 3.62)[a]	.52
				Academic achievement				
Word reading	33	4 (12)	53	18 (34)	47	15 (32)	0.84 (0.34 to 2.09)	.72
Spelling	33	2 (6)	53	13 (25)	47	8 (17)	1.10 (0.44 to 2.73)	.84
Mathematical computation	33	4 (12)	53	20 (38)	47	25 (53)	0.42 (0.18 to 0.98)	.045
Motor								
<15th percentile	33	2 (6)	53	19 (36)	47	13 (28)	1.42 (0.52 to 3.86)	.49
Behavior								
Any social-emotional impairment	31	7 (23)	48	16 (33)	46	15 (33)	0.93 (0.35 to 2.45)	.88

Adjusted analysis for stratification factors of multiple birth and white matter abnormality grade 3/4.
[a] Adjusted for age at assessment.

TABLE 4 Primary Caregiver Outcomes Between Preterm Intervention and Control Groups, Including Reference Values for Healthy Term Control Group

Primary Caregiver	Term Control		Preterm Intervention		Preterm Control		Preterm Comparison	
				HADS				
Score	*n*	Mean ± SD	*n*	Mean ± SD	*n*	Mean ± SD	Adjusted Mean (95% CI)	*P*
Anxiety	30	5.3 ± 3.7	41	5.1 ± 3.6	41	6.5 ± 4.1	−1.4 (–3.1 to 0.3)	.09
Depression	30	2.2 ± 2.5	41	2.9 ± 2.4	41	5.6 ± 3.4	–2.7 (–4.0 to –1.4)	<.001
Clinical range	*n*	*N* (%)	*n*	*N* (%)	*n*	*N* (%)	Adjusted OR	*P*
Anxiety	30	6 (20)	41	9 (22)	41	17 (42)	0.46 (0.19 to 1.11)	.08
Depression	30	2 (7)	41	2 (5)	41	11 (27)	0.14 (0.03 to 0.68)	.015

in the first year of life mostly had no long-term benefits on child outcomes, with the exception of reduced mathematical computation difficulties. However, parents did report sustained benefits on their mental health, with primary caregivers in the intervention group reporting lower rates of depression at the 8-year follow-up of age, which is a clinically important result that has the potential to support child and parent quality of life and functioning over time.

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ABBREVIATIONS

CI: confidence interval
HADS: Hospital Anxiety and Depression Scale
IBAIP: Infant Behavioural Assessment and Intervention Program
MITP: Mother Infant Transaction Program
OR: odds ratio
RCT: randomized controlled trial
TOL: Tower of London

Address correspondence to Alicia Spittle, PhD, MPhysio, BPhysio, Department of Physiotherapy, University of Melbourne, Level 7, Alan Gilbert Building, 161 Barry St, Carlton, VIC, Australia, 3053. E-mail: aspittle@unimelb.edu.au

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