## **Supplemental Online Content**

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Assessments and Secondary Outcomes in the CHYLD Mid-Childhood Outcome Study

Domain	Test	Subtest	Skill or function		Prespecified outcome	Values and interpretation	Minimum clinically important difference (continuous data)
Executive function	Cambridge Neuropsychological Test Automated Battery	Attention Switching Task	Attention	1. 2.	Switching median response latency (ms) Congruent median response latency (ms)	Shorter latency indicates better attention	0.3 SD
	(CANTAB)**	One-touch Stockings of Cambridge	Working memory and planning	3. 4.	Number of problems solved on first choice Median latency to first choice (ms)	Greater number of problems solved (maximum 20) and shorter latency indicate better working memory and planning	Count ratio 0.8 or 1.20 (problems) 0.3 SD (latency)
		Spatial Working Memory			Between search errors (number of times the subject revisited a box in which a token had previously been found, sum of trials of four, six and eight tokens) Strategy score	Fewer search errors and higher strategy score indicate better special working memory	Count ratio 0.8 or 1.20 (errors) 0.3 SD (strategy score)
		Paired Associate Learning	Visual memory	<ul><li>7.</li><li>8.</li></ul>	First attempt memory score (number of correct choices made on the first attempt during assessment problems) Total errors (adjusted)	Higher memory score and fewer errors indicate better visual memory	0.3 SD (memory score) Count ratio 0.8 or 1.20 (errors)
		Stop Signal Task	Inhibition (impulse control)	9.	Mean reaction time (length of time between the go stimulus and the stop stimulus at which the child was able to successfully inhibit their response on 50% of the trials, ms)	Shorter reaction time indicates better impulse control; typical mean (SD) reaction time in 9-year-old children 301 (96) ms <sup>1</sup>	0.3 SD (reaction time) Risk ratio 0.8 or 1.20 (reaction time less than go/increases)

	Behavior Rating Inventory of Executive Function (BRIEF)	Parent questionnaire	Behavioural manifestations of executive function in the home environment	<ul> <li>10. Proportion with failed stop reaction time less than go reaction time</li> <li>11. Failed stop reaction time increases</li> <li>12. T-scores for Behavioral Regulation</li> <li>13. T-scores for Metacognition</li> <li>14. T-scores for Global Executive Composite</li> </ul>	Higher T-scores indicate a higher level of dysfunction; normative mean (SD) 50 (10), 95% range 30 to 70	3 (T-score)
		Teacher questionnaire	Behavioural manifestations of executive function in the school environment	15. T-scores for Behavioral Regulation 16. T-scores for Metacognition 17. T-scores for Global Executive Composite 18. Proportion of children with Global Executive Composite in the clinical range (>65) on either parent or teacher report	Higher T-scores indicate a higher level of dysfunction; normative mean (SD) 50 (10), 95% range 30 to 70	3 (T-score)
Motor	Movement Assessment Battery for Children, 2 <sup>nd</sup> edition (MABC-2)		Fine motor skills	<ul> <li>19. Fine motor scale score</li> <li>20. Proportion of children at risk (≤15<sup>th</sup> percentile)</li> <li>21. Proportion of children with significant (≤5<sup>th</sup> percentile) motor difficulty</li> </ul>	Lower motor scale score indicates worse fine motor control; normative mean (SD) 10 (3), 95% range 4 to 16	1 (scale score)
Motor and visual perception and processing	Beery-Buktenica Developmental Test of Visual Motor Integration, 6 <sup>th</sup> edition (BBVMI-6)		Integration of visual and motor skills, visual perception and coordination	<ul> <li>22. Motor coordination standard score</li> <li>23. Visual perception standard score</li> <li>24. Visual motor integration standard scores</li> <li>25. Proportion of children with visual motor integration impairment (&lt;85)</li> </ul>	Lower standard scores indicate worse visual motor function; normative mean (SD) 100 (15), 95% range 70 to 130	5 (standard score)

	Laptop based tests of motion coherence and form coherence	Function of the dorsal visual cortical stream	27. 28.	Motion coherence threshold Form coherence threshold Difference between form and motion coherence thresholds	Lower coherence threshold indicates better visual perception; coherence threshold is a percentage with potential range 1 to 100 (mean threshold in normal adults is 6) <sup>2</sup>	0.3 SD
Academic achievement	Computer based school achievement tests (e-asTTle)	Reading Comprehension and Mathematics (English Curriculum); Pānui and Pāngarau (Māori medium)	30.	e-asTTle z-score for year and term of school in Reading Comprehension/Pānui e-asTTle z-score for year and term of school in Mathematics/Pāngarau Low reading achievement: e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui Low mathematics achievement: e-asTTle score below or well below the normative curriculum level in Mathematics/Pāngarau	Lower z-score indicates worse educational achievement; normative mean (SD) 0.0 (1.0), 95% range - 2.0 to 2.0	0.3 (z-score)
	Teacher questionnaire	Teacher report of academic performance		Teacher report (global judgement) of low academic achievement in reading, relative to peers (much worse or worse than peers) and expected curriculum level (well below or below expected level)  Teacher report (global judgement) of low academic achievement in mathematics relative to peers (much worse or worse		

				than peers) and expected curriculum level (well below or below expected level)  35. Teacher report (global judgement) of low academic achievement in writing		
				relative to peers (much worse or worse than peers) and expected curriculum level (well below or below expected level)  36. Need for additional learning support or older than		
				expected for year level 37. Need for additional learning support or older than expected for year level or low educational achievement, defined as an e-asTTle score below or		
				well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau		
Social- emotional and adaptive	Strengths and Difficulties Questionnaire (SDQ)	Parent questionnaire (SDQ-P)	Emotional symptoms, conduct problems, hyperactivity/inattention, peer relationships, pro-	38. SDQ-P Total Difficulties Score 39. SDQ_P Prosocial Behaviour Score	Higher Total Difficulties Score indicates worse emotional and	0.3 SD
behaviour		Teacher questionnaire (SDQ-T)	social behaviour	<ul> <li>40. SDQ-T Total Difficulties     Score</li> <li>41. SDQ_T Prosocial Behaviour     Score</li> <li>42. Proportion of children with     borderline or abnormal     Total Difficulties Scores on     either SDQ questionnaire     (SDQ-P ≥14 or SDQ-T ≥12)</li> </ul>	behavioral regulation; boys have an expected mean (SD) of 8.3 (7.1) and girls of 5.3 (5.7), possible range 0 to 40 <sup>3</sup> Lower Prosocial Behavior Score indicates greater social difficulties; boys have	0.3 SD (scores)
				43. Proportion of children with	an expected mean (SD)	

	Autistic Spectrum Quotient (AQ)	Parent questionnaire	Autistic spectrum disorder traits	borderline or abnormal Prosocial Behaviour Scores on either SDQ questionnaire (SDQ-P or SDQ-T subscale ≤5)  44. AQ Total Score 45. Proportion of children in clinical range (>75)	of 7.4 (2.5) and girls of 8.5 (2.0), possible range 0 to 10 <sup>3</sup> Higher Total Score indicates greater autistic traits; test range 0 to 150; typical mean	0.3 SD
					(SD) in 4- to 11-year- old children 41.7 (18.6), possible range 0 to 150 <sup>4</sup>	
General health	Child Health Questionnaire (CHQ)	Parent questionnaire	General health, behaviour, limitation in everyday and school activities	<ul><li>46. Physical functioning scaled score</li><li>47. Psychosocial scaled score</li></ul>	Higher scaled score indicates better functioning; normative mean (SD) 50 (10), 95% range 30 to 70	3

<sup>\*</sup> Prespecified in Statistical Analysis Plan, version 1.5, 22 June 2020. SD, standard deviation. \*\*Normative data were not available for children; typical mean (SD) are provided where available.

eTable 2. Characteristics of Children Who Did and Did Not Participate in the CHYLD Mid-Childhood Outcome Study

	Assessed	N	Not Assessed	N
Maternal characteristics				
Age at entry—y	30.3 (6.3)	466	29.0 (6.6)	100
BMI in early pregnancy—kg/m <sup>2</sup>	28.8 (7.3)	466	27.5 (6.1)	100
Diabetes in pregnancy None Gestational Pre-gestational	274 (61%) 138 (31%) 34 (7%)	466	58 (58%) 33 (33%) 9 (9%)	100
Smoking in pregnancy	130 (31%)	418	14 (27%)	51
Alcohol use in pregnancy	58 (14%)	413	7 (13%)	53
Highest education level Schooling incomplete High school ≥3 y Technical or trade University	32 (9%) 83 (22%) 132 (36%) 124 (33%)	371	7 (17%) 5 (12%) 16 (39%) 13 (32%)	41
Neonatal characteristics	, , ,		· /	
Primary risk factor for hypoglycemia IDM Preterm Small Large Other	175 (36%) 170 (35%) 71 (15%) 47 (10%) 17 (4%)	480	42 (39%) 40 (37%) 14 (13%) 6 (6%) 5 (5%)	107
Sex—female	230 (48%)	480	49 (46%)	107
Twins	67 (14%)	480	16 (15%)	107
Gestational length—week	37.3 (2.1)	480	37.4 (1.9)	107
Birthweight—g	3005 (878)	480	3023 (852)	107
Birth weight z-score	0.09 (1.65)	480	0.07 (1.7)	107
Apgar <7 at 5 minutes	10 (2%)	480	1 (1%)	107
Admitted to NICU	239 (50%)	480	42 (39%)*	107
Prioritized ethnicity Māori Pacific	149 (32%) 9 (2%)	472	* 25 (25%) 4 (4%)	101

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Other	22 (5%)		14 (14%)	
NZ European	292 (61%)		58 (57%)	
Socio-economic status		479		107
Most deprived <sup>b</sup>	192 (40%)		51 (48%)	
Less deprived	287 (60%)		56 (52%)	
Neonatal glycemia		480		107
BGC—mmol/L [range]				
<12 h	3.3 (0.7) [0.0, 8.5]		3.4 (90.7) [0.0, 7.4]	
12 to <24 h	3.7 (0.7) [0.8, 9.8]		3.7 (0.7) [2.0, 7.5]	
24 to <48 h	3.8 (0.8) [0.6, 9.4]		3.7 (0.6) [2.0, 7.3]	
≥48 h	4.2 (0.8) [1.1, 11.5]		4.3 (0.9) [1.6, 8.8]	
Percentage of BGC outside central band of 3 to 4	53 (23)	480	51 (25)	107
mmol/L in first 48 h				
CGM	377 (79%)	480	75 (70%)	72
SGC—mmol/L [range]				
<12 h	3.6 (0.8) [0.0, 9.9]	340	3.7 (0.9) [0.9, 9.6]	67
12 to <24 h	3.7 (0.7) [1.4, 9.8]	357	3.7 (0.7) [1.8, 8.8]	72
24 to <48 h	3.9 (0.8) [0.9, 13.2]	337	3.8 (0.7) [1.0, 9.1]	66
≥48 h	4.3 (0.9) [1.1, 13.9]	195	4.4 (0.9) [1.1, 9.0]	36
Percentage of SGC outside central band of 3 to 4 mmol/L in first 48 h	49 (26)	372	52 (28)	74
Feeding in the first week		480		107
No enteral feeds	8 (2%)	100	1 (1%)	107
Breast milk only	165 (34%)		42 (39%)	
Formula milk only	31 (6%)		3 (3%)	
Breast and formula milk	276 (58%)		61 (57%)	
Intravenous dextrose <48 h	91 (19%)		21 (20%)	107

Data are mean (standard deviation) or number (percent), unless otherwise indicated. Abbreviations: BGC, blood glucose concentration; BMI, body mass index; CHYLD, Children with HYpoglycaemia and their Later Development; CGM, continuous glucose monitoring; IDM, infant of diabetic mother; SGC, sensor glucose concentration; NICU, neonatal intensive care unit; NZ, New Zealand. To convert BGC from mmol/L (SI units) to mg/dL, divide by 0.0555. <sup>a</sup>Hypoglycemia defined as ≥1 hypoglycemic event, representing the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as ≥1 consecutive BGC <2.6 mmol/L (<47 mg/dL) and an interstitial episode as SGC <2.6 mmol/L (<47 mg/dL) for ≥10 minutes. <sup>b</sup> Most deprived is defined as New Zealand Deprivation Index 8-10. <sup>c</sup> Inadequate family resources is defined as a total score <32 on the New Zealand Family Resource Scale, questions 1, 2, 5, 6, 7, 9, 11, 12 (maximum score 40; scores of 32 or above indicate that resources are usually adequate for all items). \* P <0.05 for comparison between participants and non-participants.

eTable 3. Neonatal Hypoglycaemic Episodes vs. No Hypoglycemic Episodes and Primary and Critical Secondary Outcomes at Mid-Childhood

	Hypoglycemic episodes	N	No hypoglycemic episodes	N	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	123 (46%)	268	97 (49%)	200	0.94 (0.78, 1.12)	0.47
Achievement z-score in Reading Comprehension/Pānui <sup>c</sup>	-0.23 (1.13)	268	-0.29 (1.21)	200	0.06 (-0.15, 0.26)	0.60
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.13 (0.85)	267	-0.20 (0.78)	199	0.08 (-0.06, 0.23)	0.27
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	189 (69%)	274	143 (70%)	203	1.00 (0.89, 1.12)	0.97
One-touch Stockings of Cambridge (Planning/Working Memory)						
Number of problems solved on first choice	8 (5, 10)	271	8 (5, 10)	201	1.01 (0.95, 1.08)	0.72
Median latency to first choice—ms	12653 (6600)	271	13259 (7482)	201	-567 (-1850, 716)	0.39
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	115 (42%)	271	90 (45%)	199	0.96 (0.79, 1.15)	0.63
Beery-Buktenica visual-motor integration score <85	98 (36%)	271	82 (41%)	201	0.91 (0.72, 1.14)	0.40
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	110 (41%)	266	80 (40%)	202	1.09 (0.87, 1.35)	0.45
Autism Spectrum Quotient Total Score	54.5 (17.6)	215	54.2 (15.5)	149	0.9 (-2.5, 4.3)	0.62

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemic episode defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL). <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 4. Undetected vs. Detected Neonatal Hypoglycemia And primary and Critical Secondary Outcomes at Mid-Childhooda

			Hypoglycen	nia			Undetected vs. non	e	Detected vs. none	
	None	N	Undetected	N	Detected	N	Adjusted RR or MD or CR (95% CI)	P	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	59 (48%)	124	15 (54%)	28	123 (46%)	268	1.04 (0.69, 1.57)	0.97	0.93 (0.73, 1.19)	0.75
Achievement z-score in Reading Comprehension/Pānui <sup>c</sup>	-0.37 (1.33)	124	-0.06 (0.90)	28	-0.23 (1.13)	286	0.34 (-0.18, 0.86)	0.26	0.14 (-0.13, 0.42)	0.42
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.22 (0.80)	124	-0.18 (0.78)	28	-0.13 (0.85)	267	0.05 (-0.32, 0.42)	0.93	0.10 (-0.10, 0.29)	0.44
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	84 (67%)	125	23 (79%)	29	189 (69%)	274	1.05 (0.82, 1.35)	0.86	1.03 (0.87, 1.22)	0.89
One-touch Stockings of Cambridge (Planning/Working Memory)										
Number of problems solved on first choice	8 (5, 10)	125	8 (5, 9)	28	8 (5, 10)	271	0.95 (0.80, 1.13)	0.76	1.02 (0.93, 1.11)	0.88
Median latency to first choice—ms	13862 (8023)	125	11127 (6170)	28	12653 (6600)	271	-2636 (-5878, 607)	0.13	-1097 (-2790, 595)	0.27
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	53 (43%)	123	15 (54%)	28	115 (42%)	271	1.24 (0.82, 1.86)	0.41	1.02 (0.79, 1.31)	0.99
Beery-Buktenica visual-motor integration score <85	52 (42%)	124	11 (39%)	28	98 (36%)	271	0.87 (0.50, 1.54)	0.83	0.88 (0.66, 1.19)	0.56
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	50 (40%)	126	12 (41%)	29	110 (41%)	266	1.11 (0.75, 1.64)	0.79	0.95 (0.79, 1.15)	0.81
Autism Spectrum Quotient Total Score	54.4 (16.0)	94	52.3 (13.5)	21	54.5 (17.6)	215	-2.6 (-11.3, 6.0)	0.74	0.4 (-4.1, 4.8)	0.98

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Detected hypoglycemia defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL); undetected hypoglycaemia defined as ≥1 interstitial episode, representing sensor glucose concentration <2.6 mmol/L (<47 mg/dL) for ≥10 minutes, without hypoglycemia by blood glucose. <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 5. Different Degrees of Neonatal Hypoglycemia and Primary and Critical Secondary Outcomes in Mid-Childhood<sup>a</sup>

			Hypoglycemic	events			Mild vs. none		Severe vs. none	
	None	N	Mild	N	Severe	N	Adjusted RR or MD or CR (95% CI)	P	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	82 (48%)	172	75 (44%)	172	63 (51%)	124	0.93 (0.73, 1.20)	0.77	0.97 (0.75, 1.25)	0.95
Achievement z-score in Reading Comprehension/Pānui <sup>c</sup>	-0.32 (1.26)	172	-0.12 (1.14)	172	-0.33 (1.07)	124	0.19 (-0.07, 0.46)	0.19	0.02 (-0.27, 0.31)	0.99
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.21 (0.78)	171	-0.11 (0.82)	171	-0.16 (0.87)	124	0.09 (-0.10, 0.28)	0.47	0.08 (-0.13, 0.29)	0.60
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	120 (69%)	174	127 (72%)	176	85 (67%)	127	1.03 (0.89, 1.20)	0.85	0.97 (0.81, 1.16)	0.91
One-touch Stockings of Cambridge (Planning/Working Memory)										
Number of problems solved on first choice	8 (5, 10)	173	8 (6, 10)	174	7 (5, 10)	125	1.02 (0.93, 1.11)	0.86	0.97 (0.88, 1.07)	0.69
Median latency to first choice—ms	13604 (7632)	173	12771 (6324)	174	12147 (6900)	125	-844 (-2502, 814)	0.43	-1365 (-3179, 449)	0.17
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	75 (44%)	171	70 (40%)	174	60 (48%)	125	0.96 (0.75, 1.24)	0.92	1.05 (0.82, 1.35)	0.85
Beery-Buktenica visual-motor integration score <85	71 (41%)	173	57 (33%)	174	52 (42%)	125	0.81 (0.59, 1.10)	0.22	0.98 (0.72, 1.34)	0.99
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	68 (39%)	173	65 (38%)	171	57 (46%)	124	1.05 (0.78, 1.42)	0.90	1.14 (0.85, 1.54)	0.53
Autism Spectrum Quotient Total Score	54.5 (15.9)	128	53.2 (17.1)	133	55.8 (17.5)	103	-0.6 (-5.0, 3.8)	0.94	1.2 (-3.5, 5.9)	0.79

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemic event defined as the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL) and an interstitial episode as sensor glucose concentration <2.6 mmol/L (<47 mg/dL) for ≥10 minutes; a severe event represents a blood or sensor glucose concentration <2.0 mmol/L; <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 6A. Sensitivity Analysis of Primary and Critical Secondary Outcomes in Mid-Childhood, Excluding Children Who Experienced a Postnatal Neurological Insult

	Hypoglycemic events	N	No hypoglycemic events	N	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	135 (46%)	292	81 (48%)	168	0.94 (0.78, 1.14)	0.53
Achievement z-score in Reading Comprehension/Pānui <sup>c</sup>	-0.20 (1.11)	292	-0.33 (1.26)	168	0.10 (-0.05, 0.25)	0.21
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.13 (0.84)	291	-0.22 (0.79)	167	0.21 (-0.05, 0.25)	0.21
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	208 (70%)	299	116 (68%)	170	1.01 (0.89, 1.15)	0.86
One-touch Stockings of Cambridge (Planning/Working Memory)						
Number of problems solved on first choice	8 (5, 10)	295	8 (5, 10)	169	1.00 (0.93, 1.07)	0.99
Median latency to first choice—ms	12569 (6559)	195	13756 (7647)	169	-1168 (-2488, 151)	0.08
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	127 (43%)	295	73 (44%)	167	1.00 (0.82, 1.21)	0.97
Beery-Buktenica visual-motor integration score <85	107 (36%)	295	69 (41%)	169	-0.88 (0.70, 1.12)	0.32
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	119 (41%)	291	65 (38%)	169	1.11 (0.88, 1.40)	0.38
Autism Spectrum Quotient Total Score	54.2 (17.0)	233	54.3 (15.7)	125	0.2 (-3.2, 3.7)	0.90

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemic event defined as the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL) and an interstitial episode as sensor glucose concentration <2.6 mmol/L; <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 6B. Sensitivity Analysis of Primary and Critical Secondary Outcomes in Mid-Childhood, Excluding Children Who Were Educated Outside of New Zealand

	Hypoglycemic events	N	No hypoglycemic events	N	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	138 (47%)	296	82 (48%)	172	0.95 (0.78, 1.15)	0.60
Achievement z-score in Reading Comprehension/Pānui <sup>c</sup>	-0.21 (1.11)	296	-0.32 (1.26)	172	0.12 (-0.09, 0.33)	0.26
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.13 (0.84)	295	-0.21 (0.78)	171	0.09 (-0.06, 0.24)	0.26
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	208 (70%)	296	119 (69%)	172	1.00 (0.89, 1.14)	0.95
One-touch Stockings of Cambridge (Planning/Working Memory)						
Number of problems solved on first choice	8 (5, 10)	295	8 (5, 10)	172	1.00 (0.93, 1.07)	0.99
Median latency to first choice—ms	12540 (6532)	295	13673 (7600)	172	-1099 (664)	0.10
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	127 (43%)	295	74 (43%)	170	1.00 (0.82, 1.22)	0.99
Beery-Buktenica visual-motor integration score <85	107 (36%)	295	71 (41%)	170	0.88 (0.70, 1.11)	0.28
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	118 (41%)	288	67 (40%)	169	1.07 (0.85, 1.34)	0.56
Autism Spectrum Quotient Total Score	54.6 (17.2)	231	54.5 (15.9)	127	0.3 (-3.2, 3.8)	0.88

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemic event defined as the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL) and an interstitial episode as sensor glucose concentration <2.6 mmol/L; <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 6C. Sensitivity Analysis of Primary and Critical Secondary Outcomes in Mid-Childhood, Excluding Children Who Were Classified as Normoglycemic But Did Not Have Neonatal Continuous Glucose Monitoring to Potentially Detect Low Sensor Glucose Concentrations

	Hypoglycemic events	N	No hypoglycemic events	N	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	138 (47%)	296	59 (48%)	124	0.94 (0.76, 1.17)	0.60
Achievement z-score in Reading Comprehension/Pānui <sup>c</sup>	-0.21 (1.11)	296	-0.37 (1.33)	124	0.16 (-0.07, 0.40)	0.18
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.13 (0.84)	295	-0.22 (0.80)	123	0.09 (-0.08, 0.26)	0.28
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	212 (70%)	303	84 (67%)	125	1.03 (0.89, 1.19)	0.71
One-touch Stockings of Cambridge (Planning/Working Memory)						
Number of problems solved on first choice	8 (5, 10)	299	8 (5, 10)	125	1.01 (0.95, 1.09)	0.80
Median latency to first choice—ms	12511 (6566)	299	13862 (8023)	1215	-1269 (-2734, 196)	0.09
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	130 (43%)	299	53 (43%)	123	1.04 (0.83, 1.29)	0.75
Beery-Buktenica visual-motor integration score <85	109 (36%)	299	52 (42%)	124	0.88 (0.68, 1.14)	0.34
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	173 (59%)	295	76 (60%)	126	1.10 (0.86, 1.41)	0.46
Autism Spectrum Quotient Total Score	54.3 (17.3)	236	54.4 (16.0)	94	0.1 (-3.7, 4.0)	0.95

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemic event defined as the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as  $\geq 1$  consecutive blood glucose concentration < 2.6 mmol/L (< 47 mg/dL) and an interstitial episode as sensor glucose concentration < 2.6 mmol/L; <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 6D. Sensitivity Analysis of Primary And Critical Secondary Outcomes in Mid-Childhood, Excluding Children Who Were Born at <35 Weeks' Gestation

	Hypoglycemic events	N	No hypoglycemic events	N	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	126 (47%)	268	77 (48%)	162	0.97 (0.80, 1.18)	0.76
Achievement z-score in Reading Comprehension/Pānui°	-0.18 (1.14)	268	-0.32 (1.26)	162	0.1 (-0.1, 0.4)	0.21
Achievement z-score in Mathematics/Pāngarau <sup>c</sup>	-0.12 (0.83)	267	-0.19 (0.75)	162	0.1 (-0.1, 0.2)	0.29
Received additional learning support or older than expected for year level or low educational achievement <sup>d</sup>	197 (72%)	275	114 (70%)	164	1.02 (0.90, 1.16)	0.73
One-touch Stockings of Cambridge (Planning/Working Memory)						
Number of problems solved on first choice	8 (5, 10)	271	8 (5, 10)	163	1.02 (0.95, 1.09)	0.61
Median latency to first choice—ms	12591 (6401)	271	13271 (7370)	163	-664 (-1976, 648)	0.32
Movement Assessment Battery for Children fine motor scale score <15 <sup>th</sup> percentile	116 (43%)	271	68 (42%)	161	1.03 (0.84, 1.27)	0.77
Beery-Buktenica visual-motor integration score <85	97 (36%)	271	66 (40%)	163	0.88 (0.69, 1.12)	0.30
Proportion of children with borderline or abnormal Total Difficulties Score on parent or teacher Strengths and Difficulties Questionnaire	159 (59%)	269	96 (59%)	163	1.03 (0.82, 1.30)	0.77
Autism Spectrum Quotient Total Score	54.1 (17.2)	212	54.4 (15.8)	121	0.2 (-3.4, 3.8)	0.91

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemic event defined as the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL) and an interstitial episode as sensor glucose concentration <2.6 mmol/L; <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. <sup>c</sup>Achievement z-score is the standardized e-asTTle score for current term of schooling. <sup>d</sup>Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

eTable 7. Neonatal Hypoglycemia and Primary Outcome, Executive Function and Visual-Motor Integration at Mid-Childhood, Adjusted for Neurocognitive Function at 4.5 Years (Exploratory Post Hoc Analysis)

	Hypoglycemia <sup>a</sup>	N	No hypoglycemia	N	Adjusted RR or MD or CR (95% CI)	P
Low educational achievement (primary outcome) <sup>b</sup>	121 (45%)	269	68 (48%)	143	0.99 (0.94, 1.06)	0.86
Attention Switching Task <sup>c</sup>						
Switching median response latency—ms	840 (182)	268	836 (168)	140	6 (-29, 42)	0.73
Congruent median response latency—ms	721 (127)	268	715 (119)	140	7 (-19, 32)	0.61
One-touch Stockings of Cambridge <sup>c</sup>						
Number of problems solved on first choice	8 (6, 10)	269	8 (5, 10)	140	1.02 (0.95, 1.10)	0.61
Median latency to first choice—ms	12641 (6622)	269	13563 (7598)	140	-946 (-2368, 475)	0.19
Spatial Working Memory <sup>c</sup>						
Between search errors	19 (12, 22)	269	19 (12, 22)	140	1.06 (0.98, 1.15)	0.11
Strategy score	9.0 (1.5)	269	9.1 (1.7)	140	-0.1 (-0.4, 0.2)	0.63
Paired Associate Learning <sup>c</sup>						
First attempt memory score	13.4 (3.7)	139	13.7 (3.9)	139	-0.1 (-0.9, 0.6)	0.76
Total errors (adjusted)	9 (5, 14)	139	8 (4, 14)	139	0.99 (0.94, 1.06)	0.84
Stop Signal Task <sup>c</sup>						
Stop signal reaction time—ms	339 (78)	269	333 (86)	139	7 (-9, 23)	0.37
Failed stop reaction time less than go reaction time	260 (98%)	265	136 (98%)	139	1.00 (0.61, 1.63)	0.99
Mean failed stop reaction time increases	240 (91%)	265	122 (88%)	139	1.01 (0.94, 1.10)	0.71
Beery-Buktenica visual-motor integration score <85 <sup>d</sup>	96 (35%)	271	59 (41%)	144	0.98 (0.91, 1.05)	0.50

Data are number (percent), mean (standard deviation) or median (interquartile range). <sup>a</sup>Hypoglycemia defined as ≥1 hypoglycemic event, representing the sum of non-concurrent hypoglycemic and interstitial episodes more than 20 minutes apart; a hypoglycemic episode is defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL) and an interstitial episode as sensor glucose concentration <2.6 mmol/L (<47 mg/dL) for ≥10 minutes. <sup>b</sup>Low educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau; adjusted for full-scale intelligence quotient at 4.5 years. <sup>5</sup> cAdjusted for executive function score at 4.5 years. <sup>5</sup> dAdjusted for visual-motor integration score at 4.5 years.

aHypoglycemic episode defined as ≥1 consecutive blood glucose concentration <2.6 mmol/L (<47 mg/dL). bLow educational achievement is defined as an e-asTTle score below or well below the normative curriculum level in Reading Comprehension/Pānui or Mathematics/Pāngarau. Achievement z-score is the standardized e-asTTle score for current term of schooling. Older than expected for year level was defined as the child being one or more years older than 95% of children in their year level on 1 July of the year in which they were assessed, i.e., being 9 years or older in Year 4, 10 years or older in Year 5, or 11 years or older in Year 6. Adjusted for potential confounding by sex, primary risk factor for hypoglycemia and New Zealand Deprivation Index at study entry. See manuscript text for statistical methods.

## **eReferences**

- 1. Green R, Till C, Al-Hakeem H, Cribbie R, Téllez-Rojo MM, Osorio E, et al. Assessment of neuropsychological performance in Mexico City youth using the Cambridge Neuropsychological Test Automated Battery (CANTAB). J Clin Exp Neuropsychol. 2019;41(3):246-56.
- 2. Yu TY, Jacobs RJ, Anstice NS, Paudel N, Harding JE, Thompson B, et al. Global motion perception in 2-year-old children: a method for psychophysical assessment and relationships with clinical measures of visual function. Invest Ophthalmol Vis Sci. 2013;54(13):8408-19.
- 3. Hayes L. Problem behaviours in early primary school children: Australian normative data using the Strengths and Difficulties Questionnaire. Aust N Z J Psychiatry. 2007;41(3):231-8.
- 4. Auyeung B, Baron-Cohen S, Wheelwright S, Allison C. The Autism Spectrum Quotient: Children's Version (AQ-Child). J Autism Dev Disord. 2008;38(7):1230-40.
- 5. McKinlay CJ, Alsweiler J, Anstice N, Burakevych N, Chakraborty A, Chase JG, et al. Association of neonatal glycemia with neurodevelopmental outcomes at 4.5 years. JAMA Pediatr. 2017;171(10):1-12.