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Text S1. PRISMA-IPD Checklist of items to include when reporting a systematic review and meta-analysis of individual participant data (IPD)

PRISMA-IPD Section/topic	Item No	Checklist item	Reported on page
Title			
Title	1	Identify the report as a systematic review and meta-analysis of individual participant data.	Title page
Abstract			
Structured summary	2	Provide a structured summary including as applicable:	Abstract, Title page
		Background: state research question and main objectives, with information on participants, interventions, comparators and outcomes.	
		Methods: report eligibility criteria; data sources including dates of last bibliographic search or elicitation, noting that IPD were sought; methods of assessing risk of bias.	
		Results: provide number and type of studies and participants identified and number (%) obtained; summary effect estimates for main outcomes (benefits and harms) with confidence intervals and measures of statistical heterogeneity. Describe the direction and size of summary effects in terms meaningful to those who would put findings into practice.	
		Discussion: state main strengths and limitations of the evidence, general interpretation of the results and any important implications.	
		Other: report primary funding source, registration number and registry name for the systematic review and IPD meta-analysis.	
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction: paragraph 1-2
Objectives	4	Provide an explicit statement of the questions being addressed with reference, as applicable, to participants, interventions, comparisons, outcomes and study design (PICOS). Include any hypotheses that relate to particular types of participant-level subgroups.	Introduction: paragraph 3
Methods			
Protocol and registration	5	Indicate if a protocol exists and where it can be accessed. If available, provide registration information including registration number and registry name. Provide publication details, if applicable.	Methods: paragraph 1
Eligibility criteria	6	Specify inclusion and exclusion criteria including those relating to participants, interventions, comparisons, outcomes, study design and characteristics (e.g. years when conducted, required minimum follow-up). Note whether these were applied at the study or individual level i.e. whether eligible participants were included (and ineligible participants excluded) from a study that included a wider population than specified by the review inclusion criteria. The rationale for criteria should be stated.	Methods: 2.2
Identifying studies - information sources	7	Describe all methods of identifying published and unpublished studies including, as applicable: which bibliographic databases were searched with dates of coverage; details of any hand searching including of conference proceedings; use of study registers and agency	Methods: 2.1

		or company databases; contact with the original research team and experts in the field; open adverts and surveys. Give the date of last search or elicitation.	
Identifying studies - search	8	Present the full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S9
Study selection processes	9	State the process for determining which studies were eligible for inclusion.	Methods: 2.2
Data collection processes	10	Describe how IPD were requested, collected and managed, including any processes for querying and confirming data with investigators. If IPD were not sought from any eligible study, the reason for this should be stated (for each such study).	Methods: 2.2, 2.4, 2.5
		If applicable, describe how any studies for which IPD were not available were dealt with. This should include whether, how and what aggregate data were sought or extracted from study reports and publications (such as extracting data independently in duplicate) and any processes for obtaining and confirming these data with investigators.	
Data items	11	Describe how the information and variables to be collected were chosen. List and define all study level and participant level data that were sought, including baseline and follow-up information. If applicable, describe methods of standardising or translating variables within the IPD datasets to ensure common scales or measurements across studies.	Methods: 2.2, 2.4, 2.5
IPD integrity	A1	Describe what aspects of IPD were subject to data checking (such as sequence generation, data consistency and completeness, baseline imbalance) and how this was done.	Methods: 2.3
Risk of bias assessment in individual studies.	12	Describe methods used to assess risk of bias in the individual studies and whether this was applied separately for each outcome. If applicable, describe how findings of IPD checking were used to inform the assessment. Report if and how risk of bias assessment was used in any data synthesis.	Methods: 2.3
Specification of outcomes and effect measures	13	State all treatment comparisons of interests. State all outcomes addressed and define them in detail. State whether they were pre-specified for the review and, if applicable, whether they were primary/main or secondary/additional outcomes. Give the principal measures of effect (such as risk ratio, hazard ratio, difference in means) used for each outcome.	Methods: 2.2, 2.4, 2.5
Synthesis methods	14	Describe the meta-analysis methods used to synthesise IPD. Specify any statistical methods and models used. Issues should include (but are not restricted to): • Use of a one-stage or two-stage approach. • How effect estimates were generated separately within each study and combined across studies (where applicable). • Specification of one-stage models (where applicable) including how clustering of patients within studies was accounted for. • Use of fixed or random effects models and any other model assumptions, such as proportional hazards. • How (summary) survival curves were generated (where applicable). • Methods for quantifying statistical heterogeneity (such as I^2 and τ^2). • How studies providing IPD and not providing IPD were analysed together (where applicable). • How missing data within the IPD were dealt with (where applicable).	Methods: 2.4, 2.5
Exploration of variation in effects	A2	If applicable, describe any methods used to explore variation in effects by study or participant level characteristics (such as estimation of interactions between effect and covariates). State all participant-level characteristics that were analysed as potential effect modifiers, and whether these were pre-specified.	Methods: 2.4, 2.5
Risk of bias across studies	15	Specify any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to not obtaining IPD for particular studies, outcomes or other variables.	Methods: 2.3

Additional analyses	16	Describe methods of any additional analyses, including sensitivity analyses. State which of these were pre-specified.	Methods: 2.4, 2.5
Results			
Study selection and IPD obtained	17	Give numbers of studies screened, assessed for eligibility, and included in the systematic review with reasons for exclusions at each stage. Indicate the number of studies and participants for which IPD were sought and for which IPD were obtained. For those studies where IPD were not available, give the numbers of studies and participants for which aggregate data were available. Report reasons for non-availability of IPD. Include a flow diagram.	Results: 3.1, Figure 1
Study characteristics	18	For each study, present information on key study and participant characteristics (such as description of interventions, numbers of participants, demographic data, unavailability of outcomes, funding source, and if applicable duration of follow-up). Provide (main) citations for each study. Where applicable, also report similar study characteristics for any studies not providing IPD.	Table 1
IPD integrity	A3	Report any important issues identified in checking IPD or state that there were none.	Results: 3.1
Risk of bias within studies	19	Present data on risk of bias assessments. If applicable, describe whether data checking led to the up-weighting or down-weighting of these assessments. Consider how any potential bias impacts on the robustness of meta-analysis conclusions.	Results: 3.2 Table S1
Results of individual studies	20	For each comparison and for each main outcome (benefit or harm), for each individual study report the number of eligible participants for which data were obtained and show simple summary data for each intervention group (including, where applicable, the number of events), effect estimates and confidence intervals. These may be tabulated or included on a forest plot.	Results: 3.3-3.6, Figure 2, Figure 3, Figure S1-S15
Results of syntheses	21	Present summary effects for each meta-analysis undertaken, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified, and report the numbers of studies and participants and, where applicable, the number of events on which it is based.	Results: 3.3-3.7, Figure 2, Figure 3, Figure S1-S15
		When exploring variation in effects due to patient or study characteristics, present summary interaction estimates for each characteristic examined, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified. State whether any interaction is consistent across trials.	
		Provide a description of the direction and size of effect in terms meaningful to those who would put findings into practice.	
Risk of bias across studies	22	Present results of any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to the availability and representativeness of available studies, outcomes or other variables.	Results: 3.2 Table S1
Additional analyses	23	Give results of any additional analyses (e.g. sensitivity analyses). If applicable, this should also include any analyses that incorporate aggregate data for studies that do not have IPD. If applicable, summarise the main meta-analysis results following the inclusion or exclusion of studies for which IPD were not available.	Results: 3.3-3.7, Figure 2, Figure 3, Figure S1-S20, Table S2-S8
Discussion			

Summary of evidence	24	Summarise the main findings, including the strength of evidence for each main outcome.	Discussion: paragraph 1-2, Figure 5-6
Strengths and limitations	25	Discuss any important strengths and limitations of the evidence including the benefits of access to IPD and any limitations arising from IPD that were not available.	Discussion: paragraph 12-13
Conclusions	26	Provide a general interpretation of the findings in the context of other evidence.	Discussion: paragraph 14
Implications	A4	Consider relevance to key groups (such as policy makers, service providers and service users). Consider implications for future research.	Discussion: paragraph 14
Funding			
Funding	27	Describe sources of funding and other support (such as supply of IPD), and the role in the systematic review of those providing such support.	Funding, acknowledge, author contribution

A1 – A3 denote new items that are additional to standard PRISMA items. A4 has been created as a result of re-arranging content of the standard PRISMA statement to suit the way that systematic review IPD meta-analyses are reported.

Text S2. Comparison of macronutrient intake

a. Macronutrient intakes between trials using formula as primary feed and breast milk as primary feed.

To explore whether the differences in effects of supplements between infants receiving breast milk or formula as their primary feed were due to different baseline macronutrient intakes or quantity of supplements, we compared the mean macronutrient intakes in the unsupplemented groups receiving breast milk or formula as their primary feed, and the mean difference in intakes between supplemented and unsupplemented groups. Infants in the unsupplemented group who received breastmilk as their primary feed had similar protein, fat, carbohydrate and energy intakes to those whose primary feed was formula. However, amongst infants who received breastmilk as their primary feed, those in the supplemented group received more protein, energy and carbohydrate than those in unsupplemented group, whereas amongst infants who received formula as their primary feed, the supplemented formula group received much smaller increases in protein, energy and carbohydrate than the unsupplemented group.

	Breast milk		**Formula**		
	Mean	**SD**	**Mean**	**SD**	**P Value**
Mean intakes in the unsupplemented groups					
Protein (g/100 ml)	1·43	0·24	1·64	0·33	0·26
Fat (g/100 ml)	4	0·49	3·94	0·39	0·84
Carbohydrate (g/100 ml)	6·53	2·33	7·26	0·45	0·49
Energy (g/100 ml)	68	5·29	70·17	4·92	0·48
Mean differences intakes between supplemented and unsupplemented groups					
Protein (g/100 ml)	0·92	0·49	0·46	0·15	0·07
Fat (g/100 ml)	0·06	0·73	0·14	0·21	0·84
Carbohydrate (g/100 ml)	2·15	0·46	0·24	0·17	0·0001
Energy (g/100 ml)	11·5	6·89	5·17	3·37	0·07
The composition information for formulae were from IPD or extracted from the publications, and the composition of breastmilk was from IPD or estimated according to the recent guideline[1].					

b. Macronutrient intakes between trials conducted up to 2000 and those conducted after 2000.

To explore whether the differences in effects of supplements between trials conducted before and during 2000 or after 2000 were due to gradual increases in baseline macronutrient intakes over time, we compared the mean macronutrient intakes in the unsupplemented groups in trials conducted before or after 2000, and the mean differences in intakes between supplemented and unsupplemented groups. This showed that there were no differences between the two epochs in mean baseline intakes or in mean differences in intake between supplemented and unsupplemented groups for protein, fat, carbohydrate or energy.

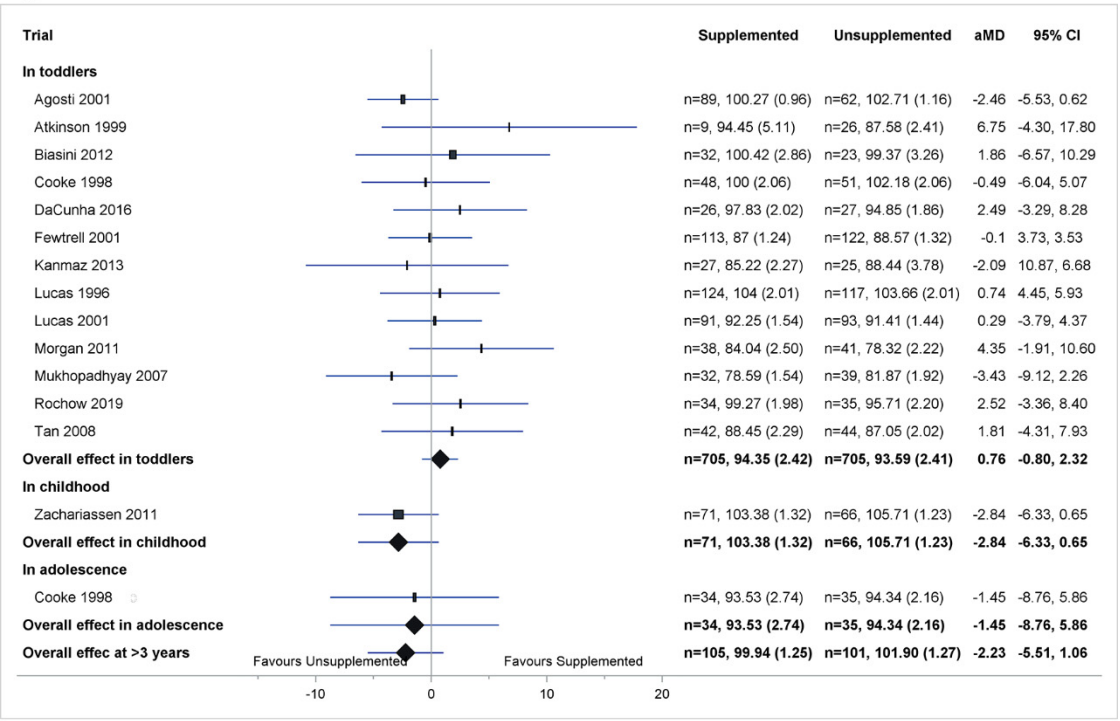
	Before and during 2000		**After 2000**		
	Mean	**SD**	**Mean**	**SD**	**P Value**
Mean intakes in the unsupplemented groups					
Protein (g/100 ml)	1·46	0·15	1·58	0·38	0·52
Fat (g/100 ml)	3·87	0·25	4·05	0·53	0·54
Carbohydrate (g/100 ml)	7·03	0·12	6·68	2·39	0·78
Energy (g/100 ml)	68	1·1	70·17	7·14	0·48
Mean differences intakes between supplemented and unsupplemented groups					
Protein (g/100 ml)	0·54	0·15	0·86	0·55	0·23
Fat (g/100 ml)	0·18	0·15	0·03	0·73	0·69

Carbohydrate (g/100 ml)	0·92	1·21	1·6	0·95	0·39
Energy (g/100 ml)	7·5	3·89	9·17	8·13	0·66
The composition information for formulae were from IPD or extracted from the publications, and the composition of breastmilk was from IPD or estimated according to the recent guideline[1].					

References

1. National Health & Medical Research Council (NHMRC). Dietary guidelines for children and adolescents in Australia - incorporating the infant feeding guidelines for health workers. Australia: The National Health and Medical Research Council; 2003 [updated 10 April 2003; cited 2019 17 June]. Available from: http://childaustralia.mrooms.net/pluginfile.php/4134/mod_page/content/38/diet-guidelines.pdf

a.



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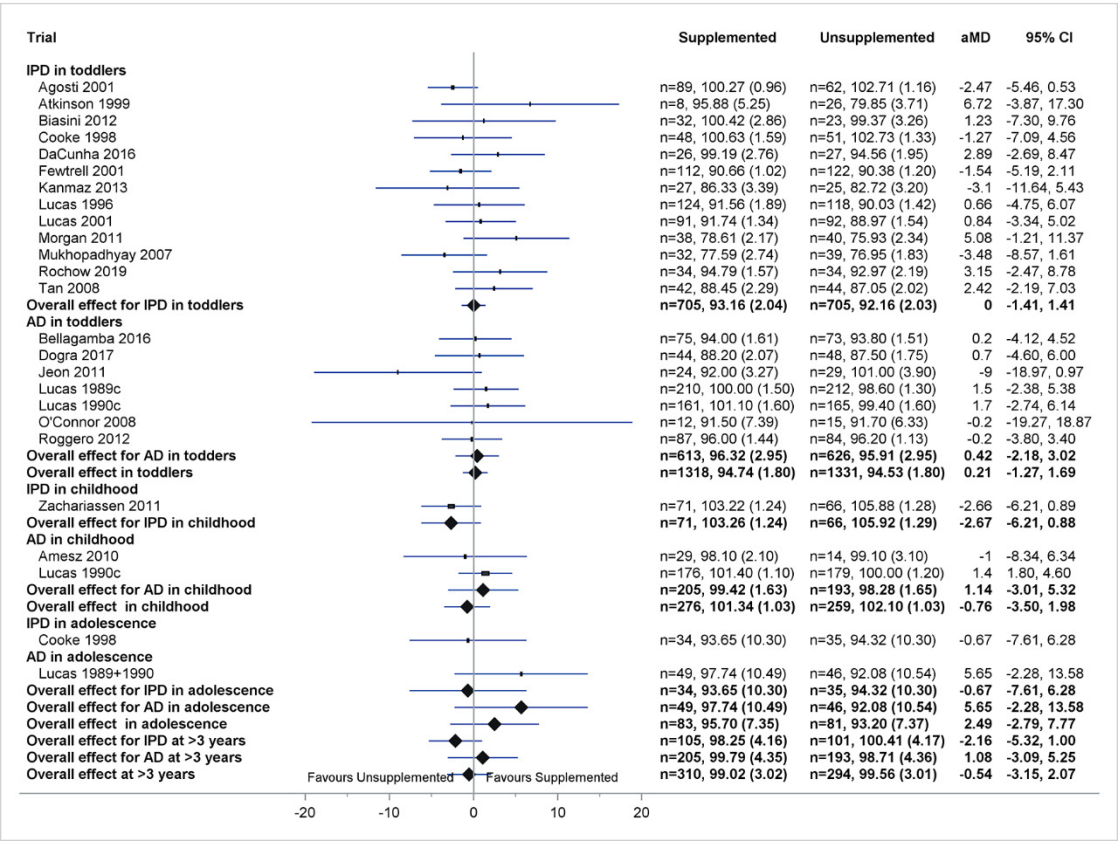
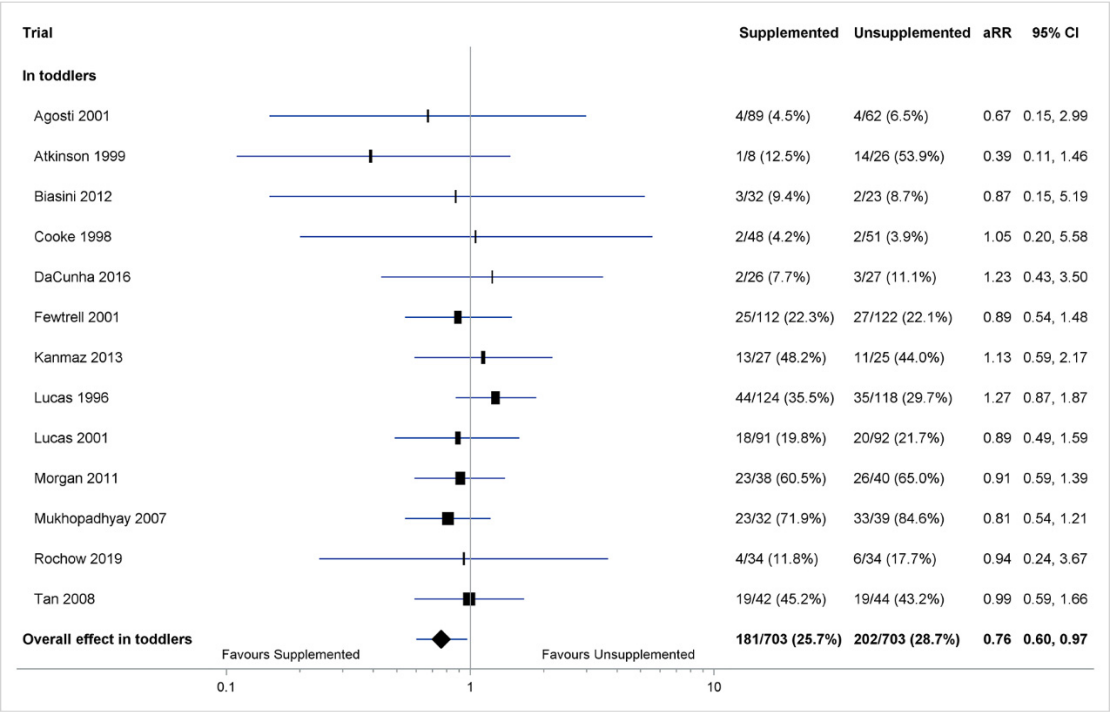


Figure S1. Forest plot of effect of macronutrient supplementation on cognitive scores. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusting for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in toddlers p=0.77, tau^2=0.63; at >3 years p=0.69, tau^2=2.66. Heterogeneity of combined IPD and AD analysis in toddlers tau^2=0.52, in childhood tau^2=1.74, in adolescence tau^2=6.97, at >3 years tau^2=2.66. IPD, individual participant data; AD, aggregated data.

a.



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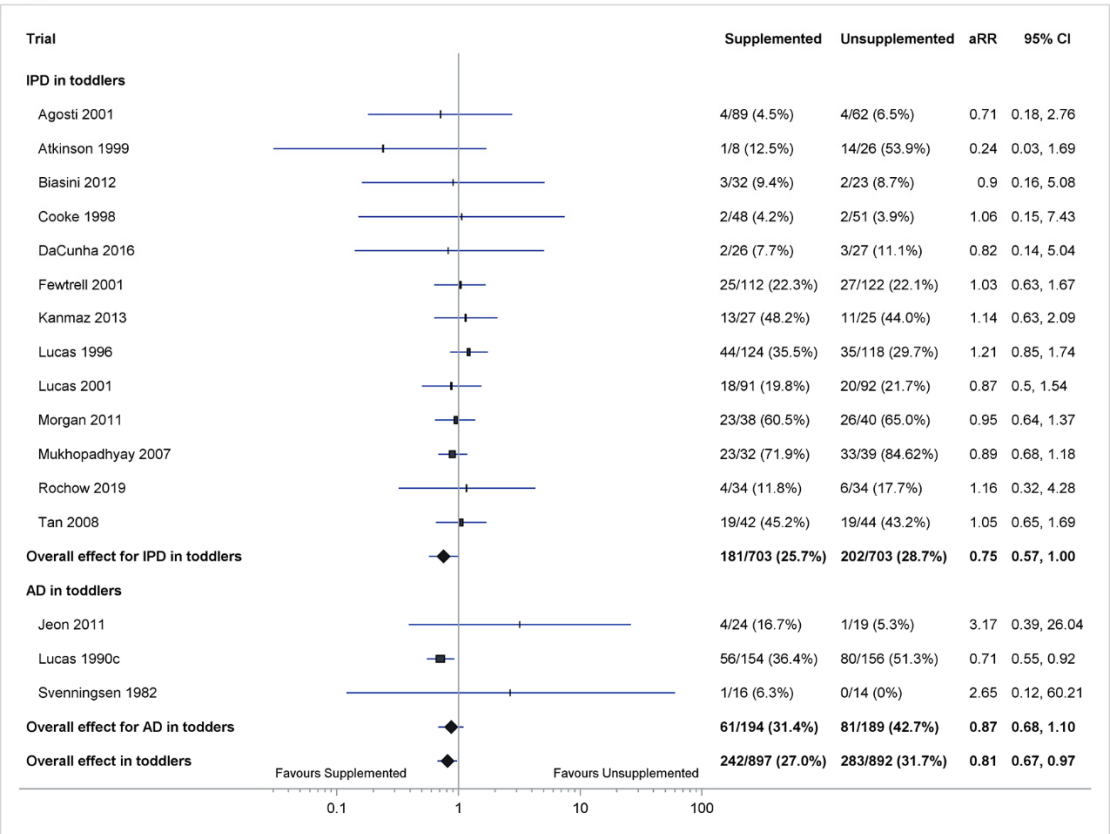
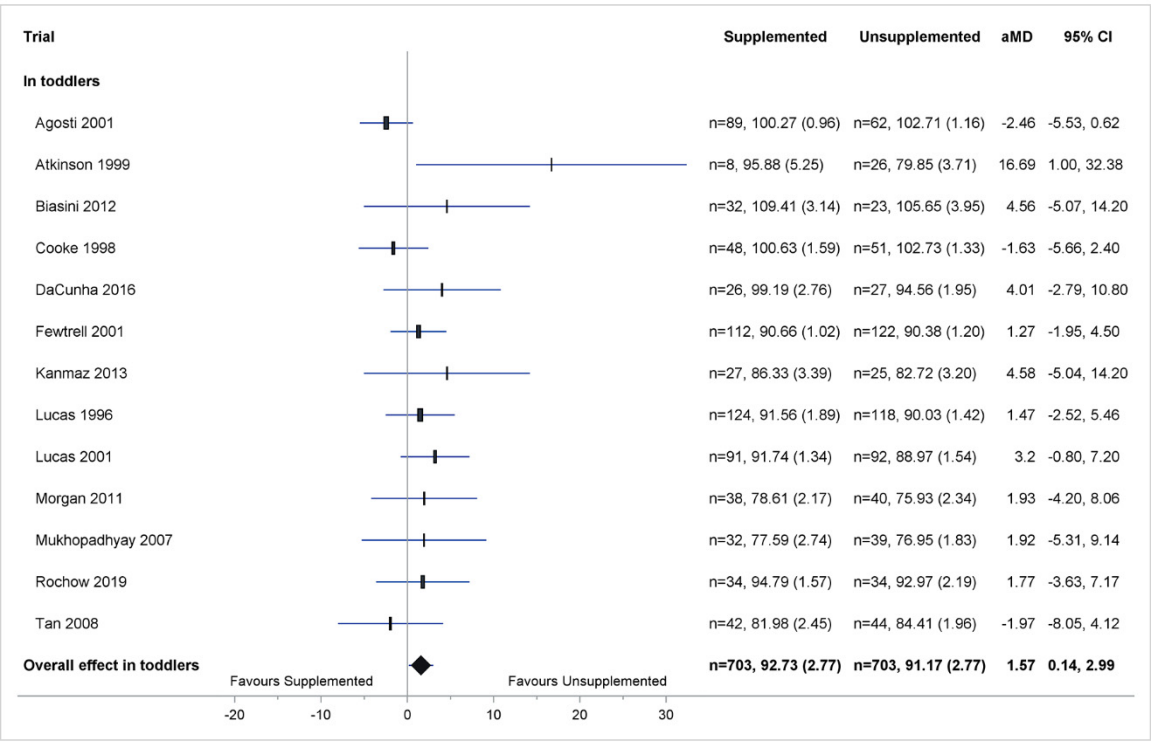


Figure S2. Forest plot of effect of macronutrient supplementation on motor impairment. a. IPD analysis, b. Combined IPD and AD analysis. Data are numbers (percentages) with adjusted relative risk (aRR) and 95% confidence intervals (CIs) for treatment effect adjusting for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity: IPD analysis in toddlers p=0.87, tau^2=0.02; Combined IPD and AD analysis in toddlers tau^2=0.01. IPD, individual participant data; AD, aggregated data.

a.



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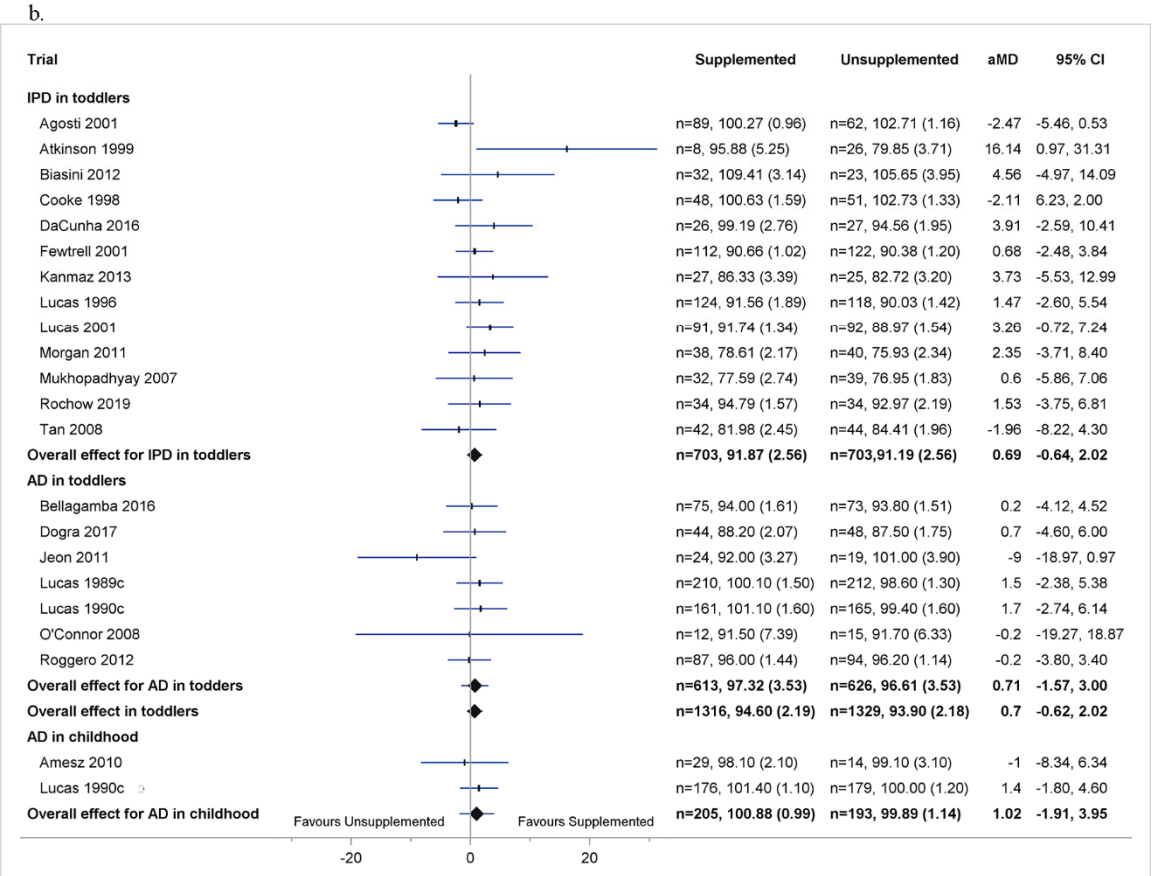


Figure S3. Forest plot of effect of macronutrient supplementation on motor scores. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusting for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity: IPD analysis in toddlers p=0.25, tau^2=0.53; Combined IPD and AD analysis tau^2=0.45. IPD, individual participant data; AD, aggregated data.

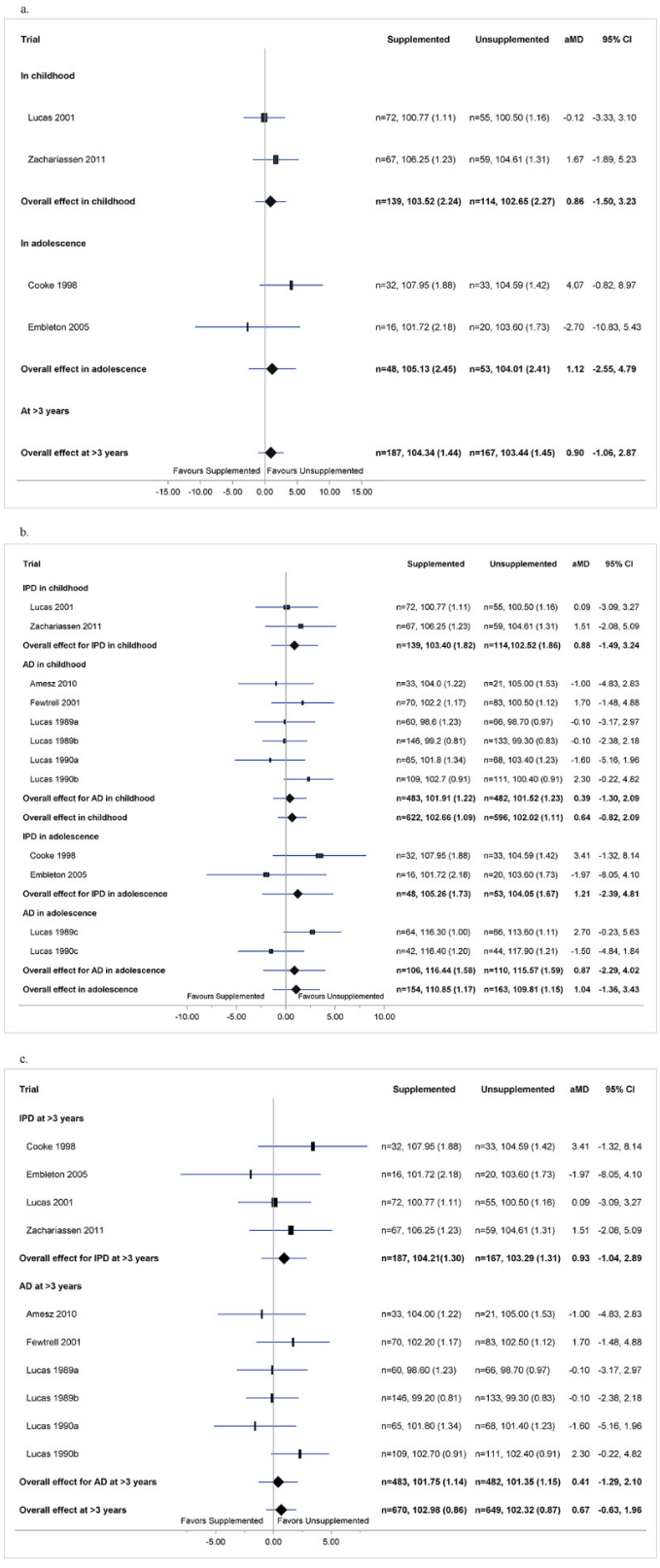


Figure S4. Forest plot of effect of macronutrient supplementation on SBP. a. IPD analysis, b. Combined IPD and AD analysis in childhood and in adolescence. C. Combined IPD and AD analysis at >3 years. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in childhood p=0.44, tau^2=1.44; in adolescence p=0.10, tau^2=3.39; at >3 years p=0.46, tau^2=0.98. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.55; in adolescence tau^2=1.44; at >3 years tau^2=0.44. SBP, systolic blood pressure; IPD, individual participant data; AD, aggregated data.

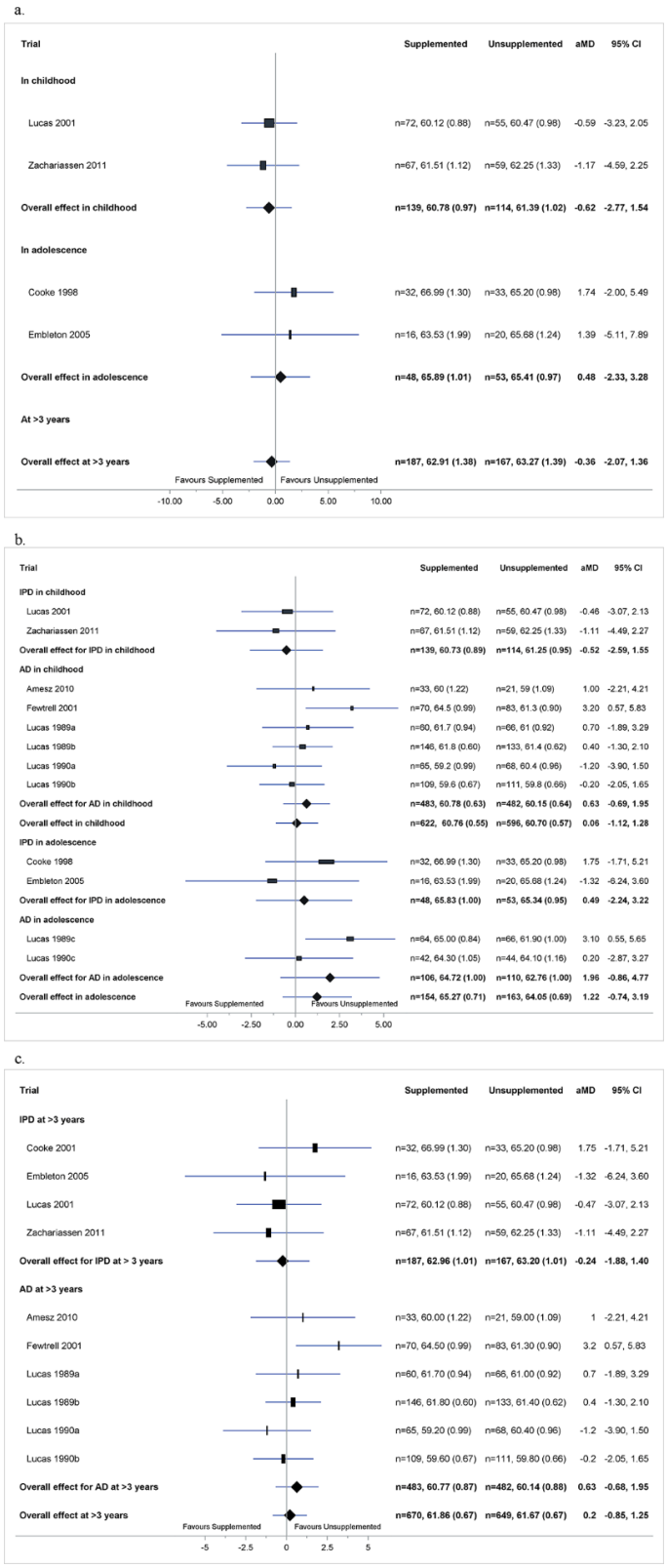
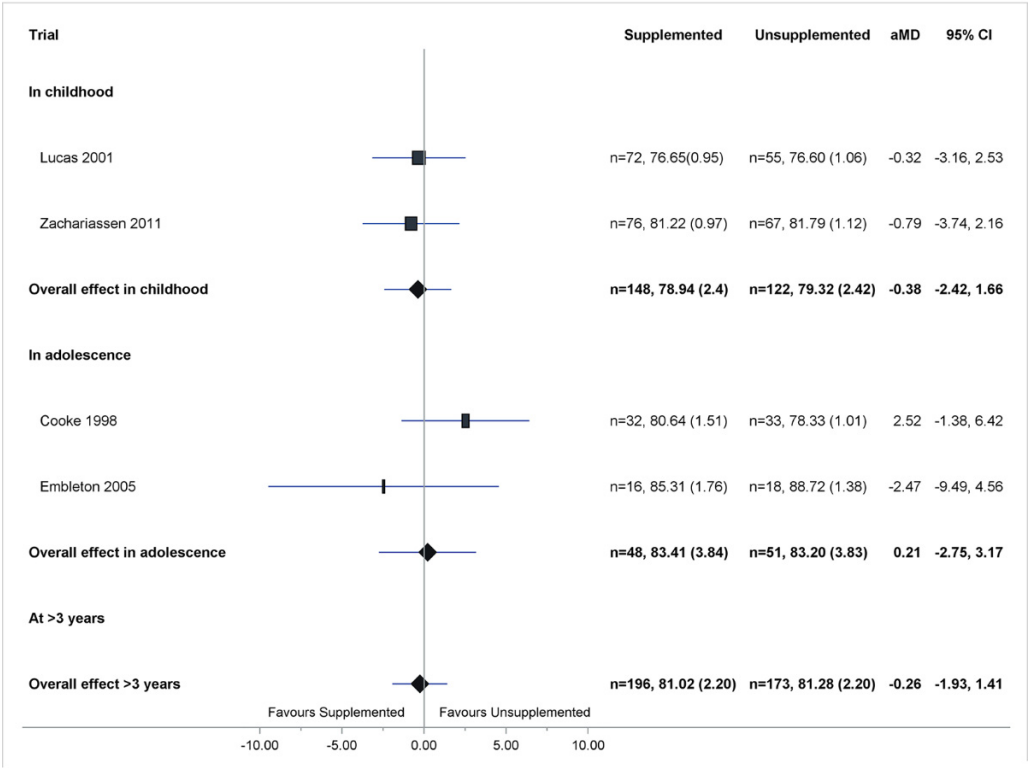


Figure S5. Forest plot of effect of macronutrient supplementation on DBP. a. IPD analysis, b. Combined IPD and AD analysis in childhood and in adolescence. C. Combined IPD and AD analysis at >3 years. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in childhood p=0.83, tau^2=1.19, in adolescence p=0.32, tau^2=1.99; at >3 years p=0.73, tau^2=0.76. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.36; in adolescence tau^2=0.98; at >3 years tau^2=0.25. DBP, diastolic blood pressure; IPD, individual participant data; AD, aggregated data.

a,



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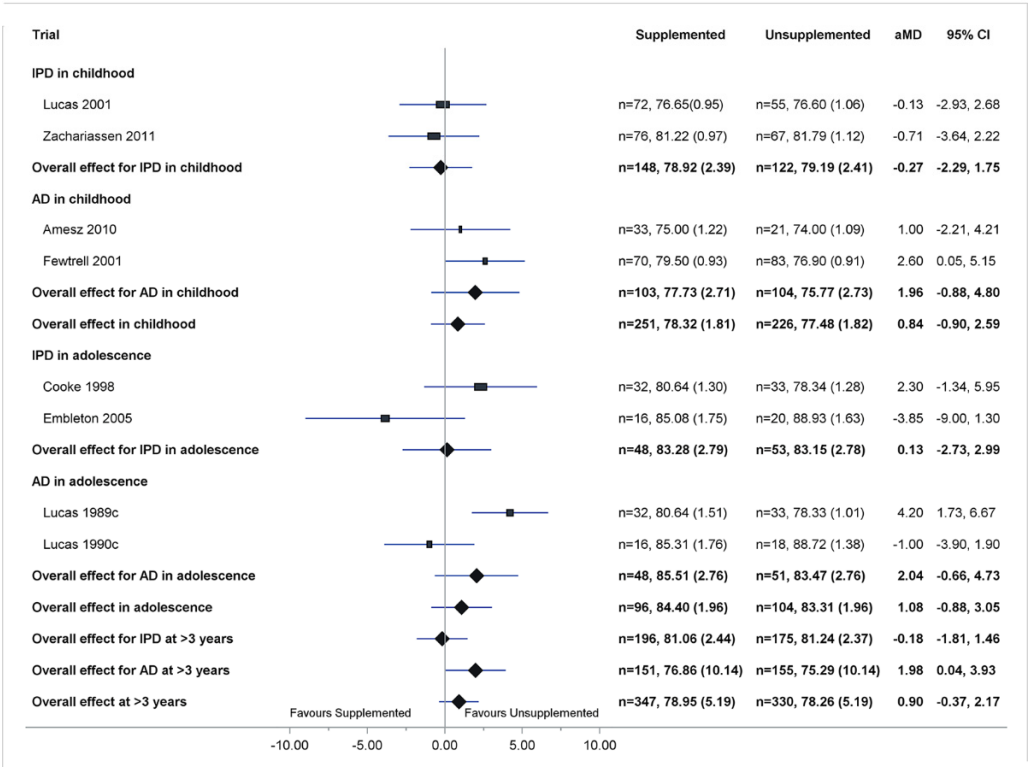
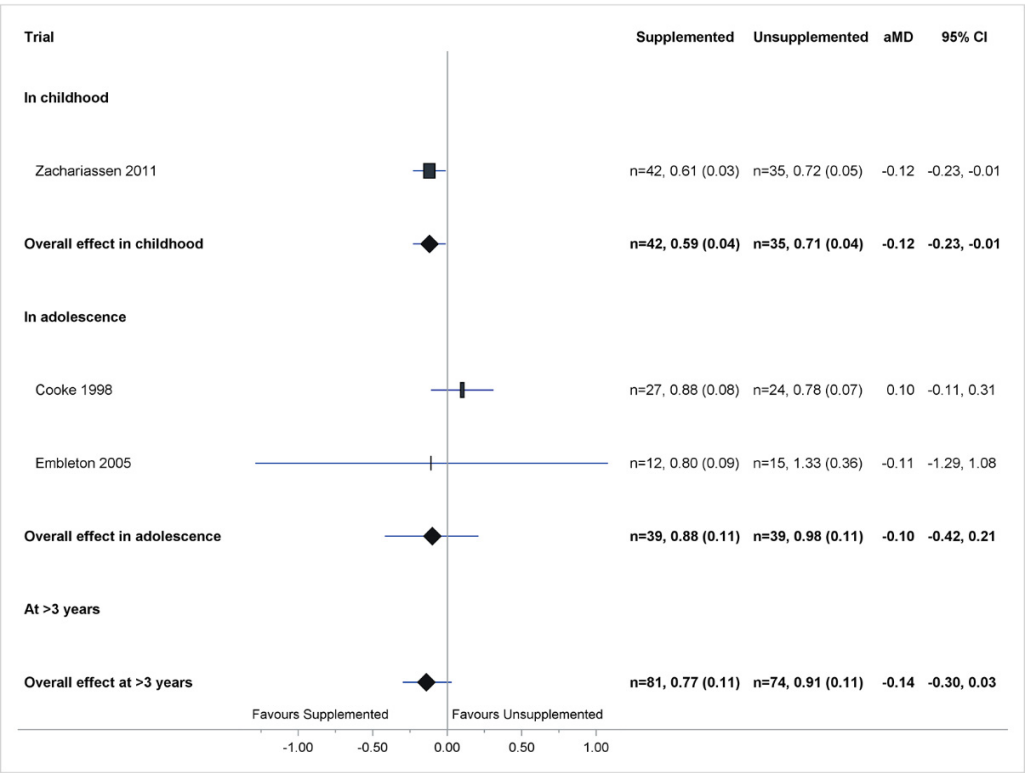


Figure S6. Forest plot of effect of macronutrient supplementation on MAP. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in childhood p=0.84, tau^2=1.06; in adolescence p= 0.07, tau^2=2.22; at >3 years p=0.42, tau^2=0.72. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.77; in adolescence tau^2=0.98; at >3 years tau^2=0.42. MAP, mean arterial pressure; IPD, individual participant data; AD, aggregated data.

a.



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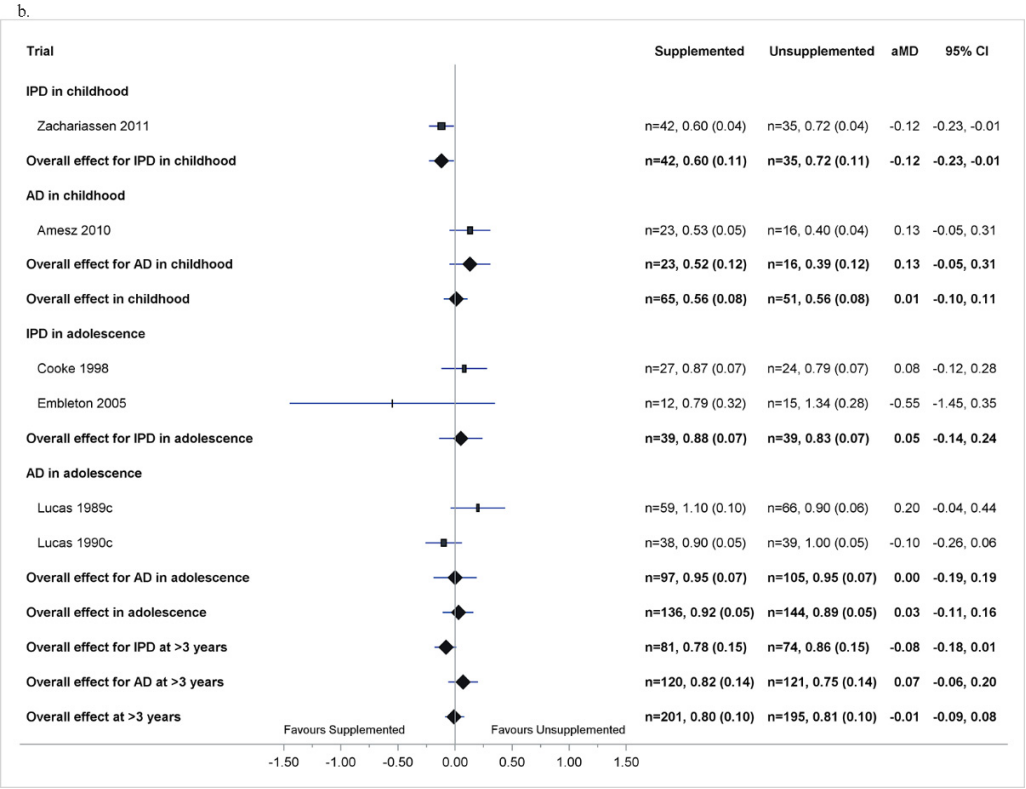


Figure S7. Forest plot of effect of macronutrient supplementation on triglyceride concentrations. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis: in adolescence = 0.17, tau^2=0.03; at >3 years =0.11, tau^2=0.01. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.002; in adolescence tau^2=0.004; at >3 years tau^2=0.002. IPD, individual participant data; AD, aggregated data.

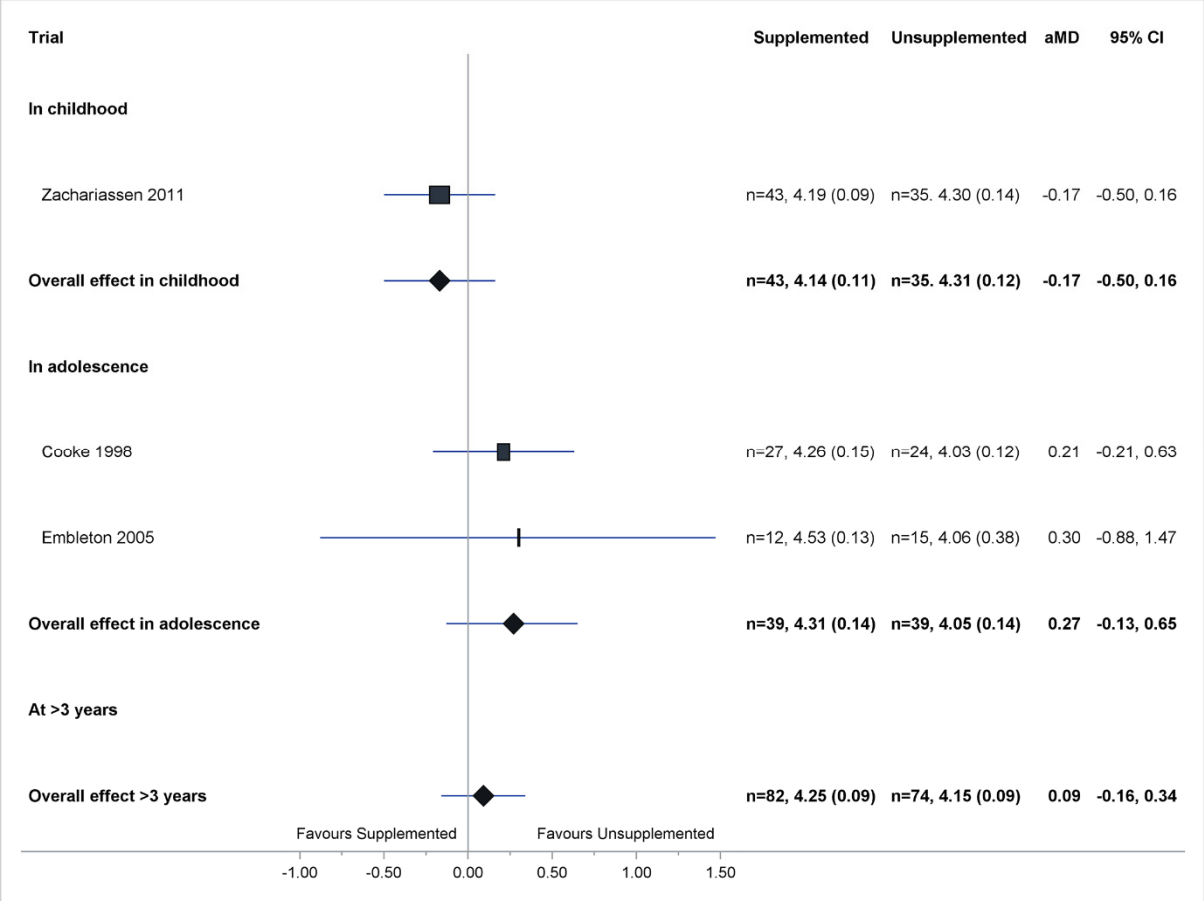
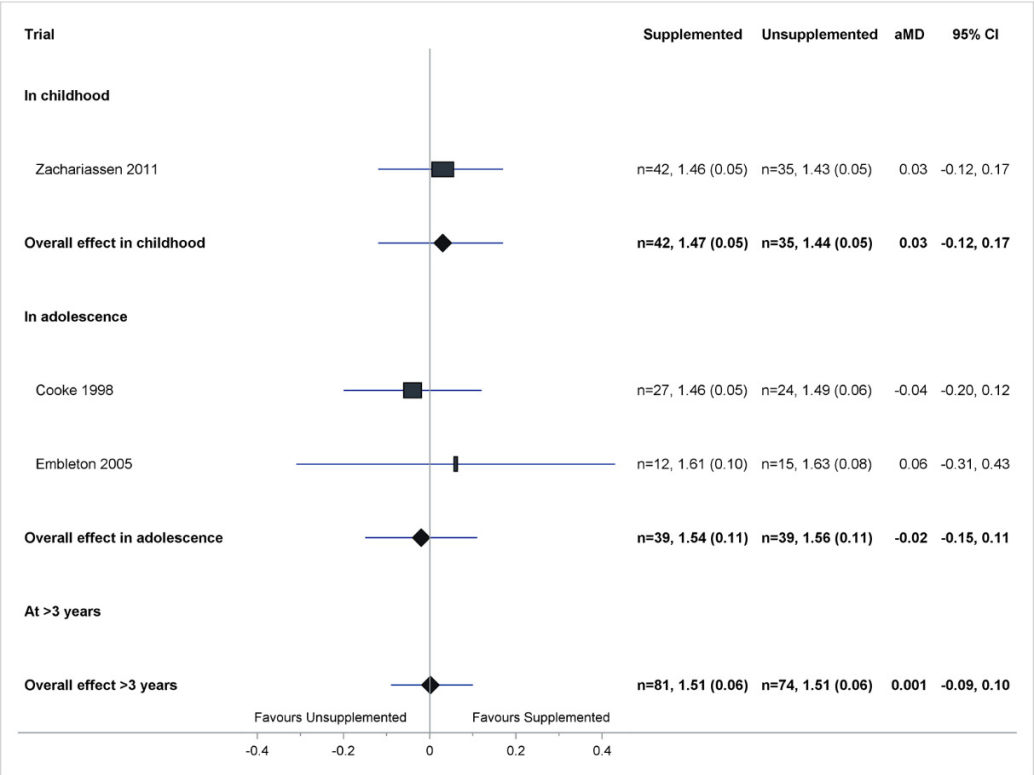


Figure S8. Forest plot of effect of macronutrient supplementation on cholesterol concentration (IPD analysis). Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. for Heterogeneity in adolescence p=0.73, tau^2=0.03; at >3 years p=0.20, tau^2=0.032.

a.



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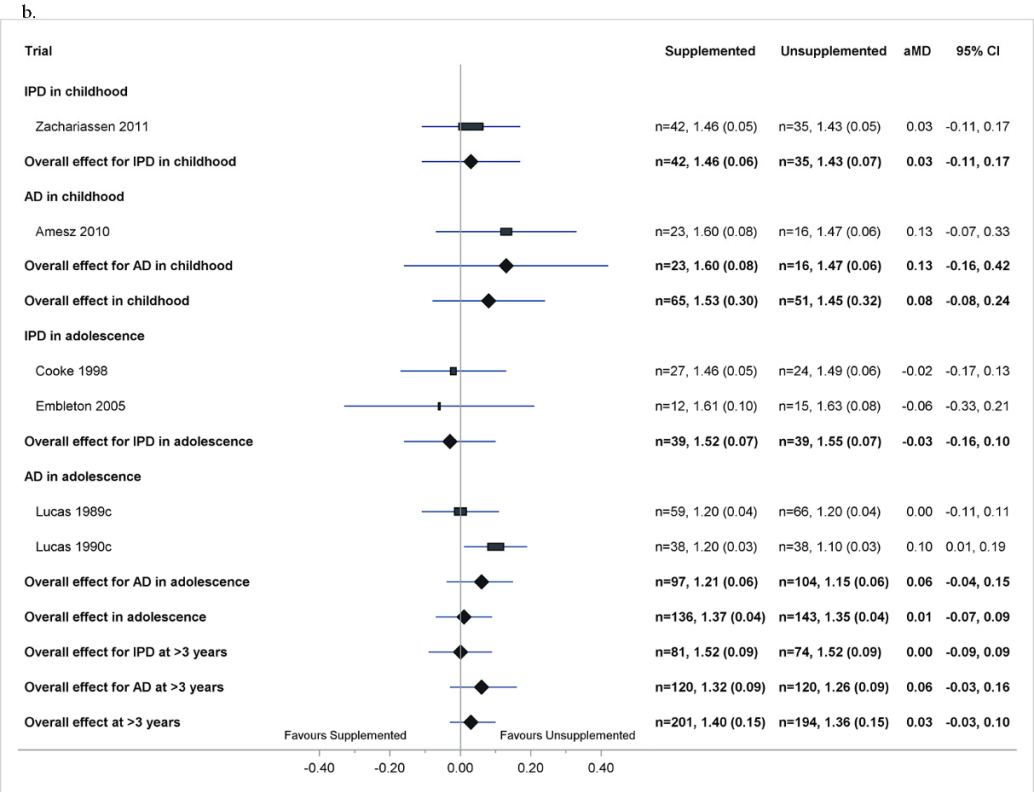

Figure S9. Forest plot of effect of macronutrient supplementation on HDL. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in adolescence = 0.77, tau^2=0.01; at >3 years p=0.90, tau^2=0.003. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.01; in adolescence tau^2=0.002; at >3 years tau^2=0.001. IPD, individual participant data; AD, aggregated data.

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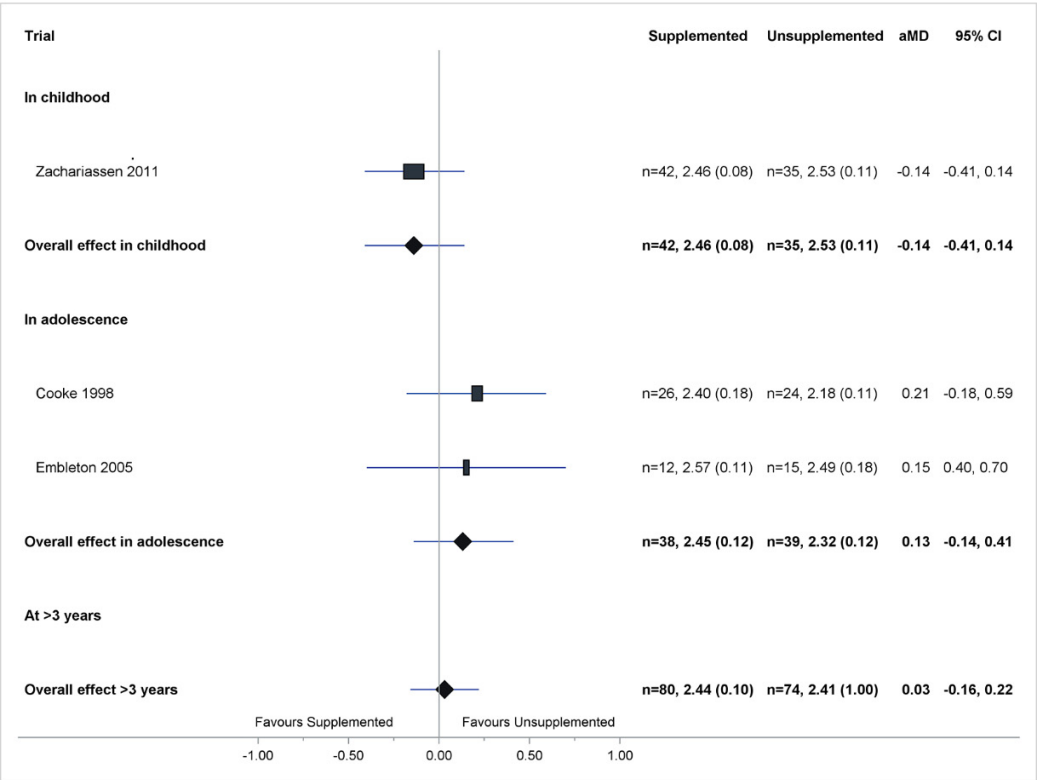

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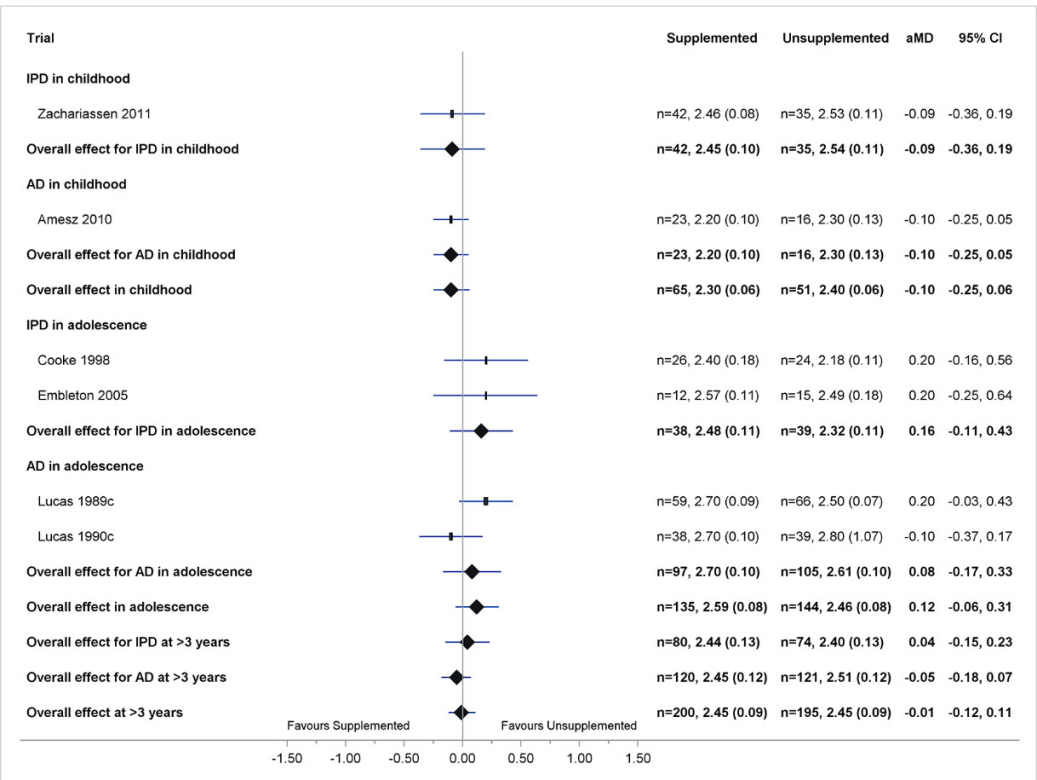
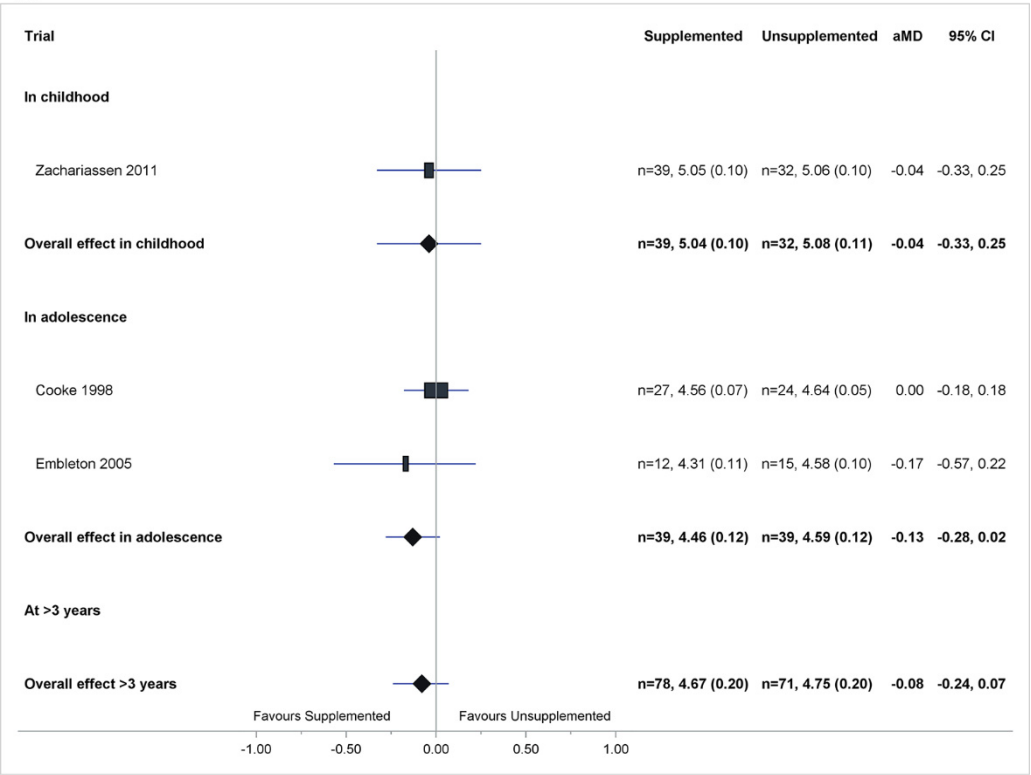


Figure S10. Forest plot of effect of macronutrient supplementation on LDL. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in adolescence p=0.47, tau^2=0.02; at >3 years p=0.49, tau^2=0.01. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.01; in adolescence tau^2=0.01; at >3 years tau^2=0.003. IPD, individual participant data; AD, aggregated data.

a.



b.

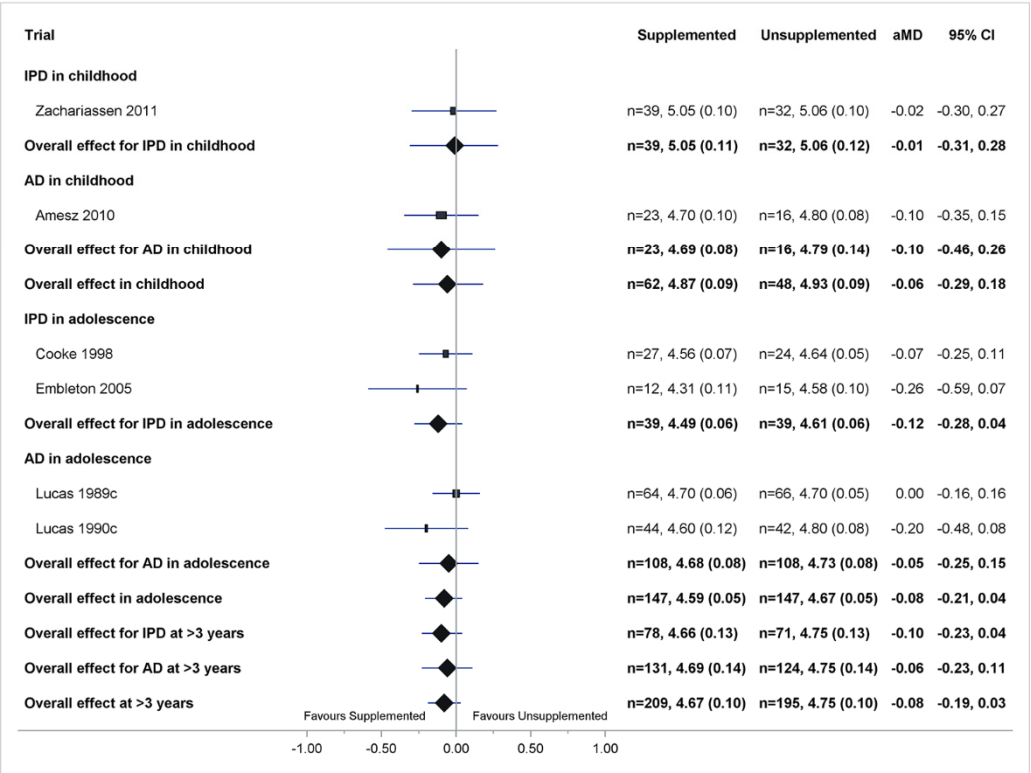
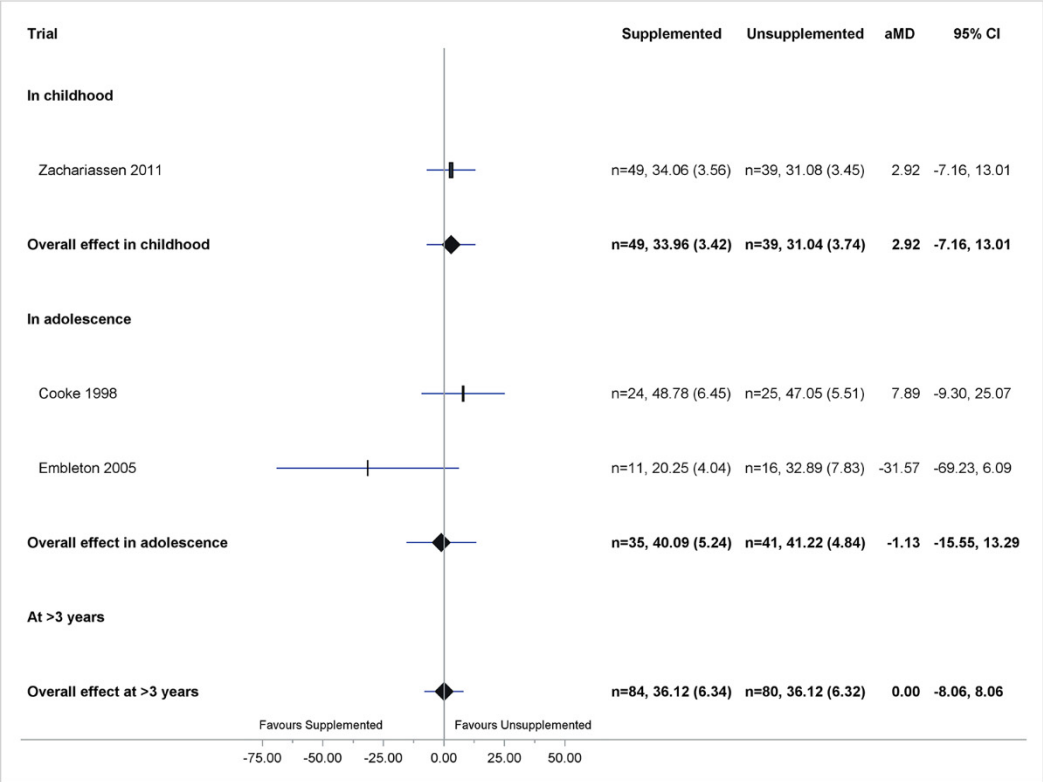


Figure S11. Forest plot of effect of macronutrient supplementation on fasting blood glucose concentration. a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in adolescence p=0.13, tau^2=0.01; at >3 years p=0.62, tau^2=0.01. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.01; in adolescence tau^2=0.004; at >3 years tau^2=0.003. IPD, individual participant data; AD, aggregated data.

a.



b.

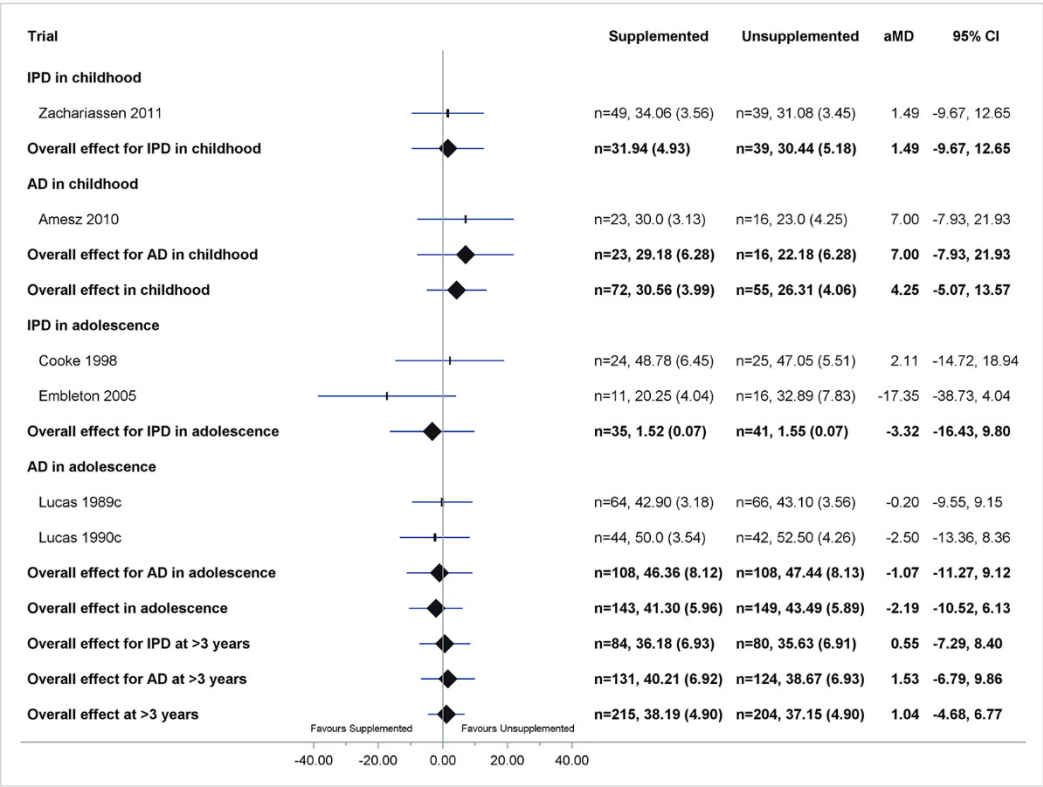


Figure S12. Forest plot of effect of macronutrient supplementation on fasting insulin concentration.
a. IPD analysis, b. Combined IPD and AD analysis. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis heterogeneity in adolescence p=0.29, tau^2=46.24, at >3 years p=0.32; tau^2=16.13. Heterogeneity of combined IPD and AD analysis in childhood tau^2=21.72; in adolescence tau^2=17.43; at >3 years tau^2=8.41. IPD, individual participant data; AD, aggregated data.

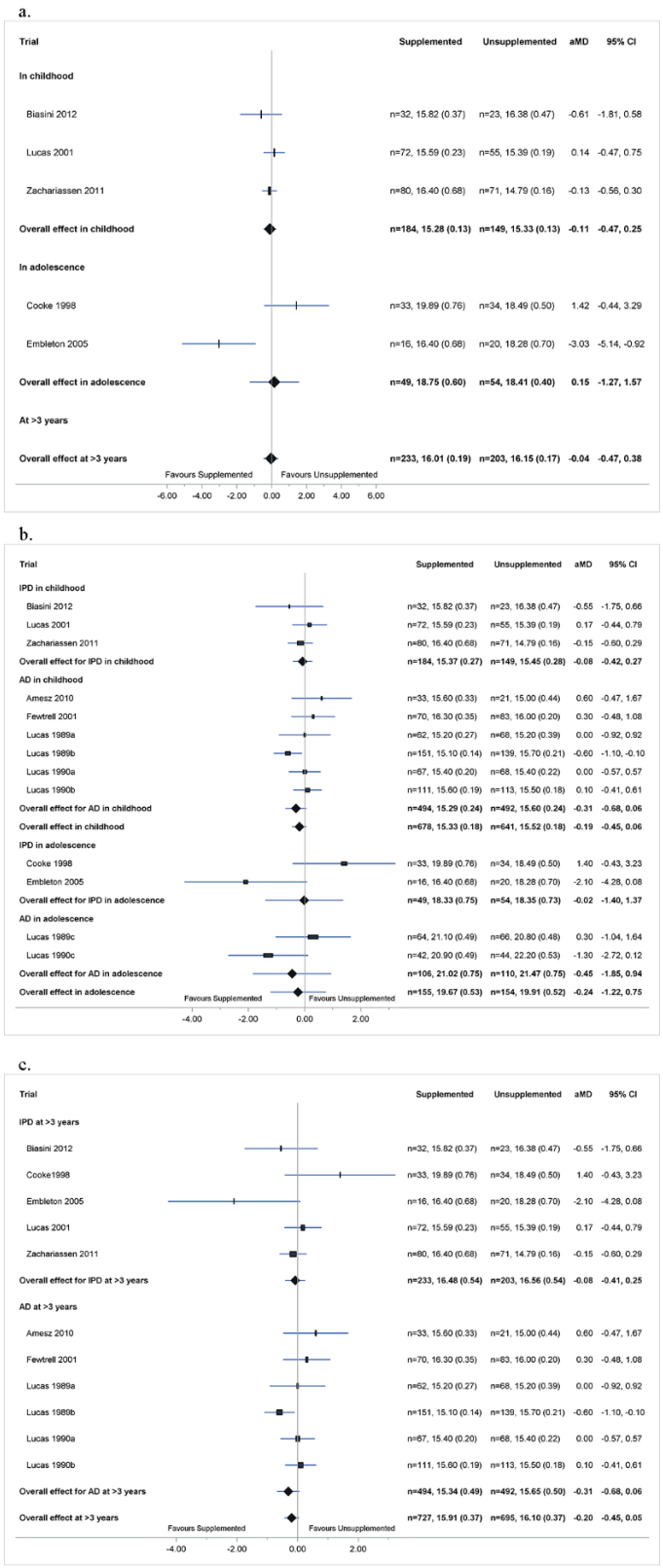


Figure S13. Forest plot of effect of macronutrient supplementation on BMI. a. IPD analysis, b. Combined IPD and AD analysis in childhood and in adolescence. C. Combined IPD and AD analysis at >3 years. Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity of IPD analysis in childhood p=0.39, tau^2=0.03; in adolescence p=0.01, tau^2=0.51; at >3 years p=0.006, tau^2=0.04. Heterogeneity of combined IPD and AD analysis in childhood tau^2=0.02, in adolescence tau^2=0.25; at >3 years tau^2=0.02. IPD, individual participant data; AD, aggregated data.

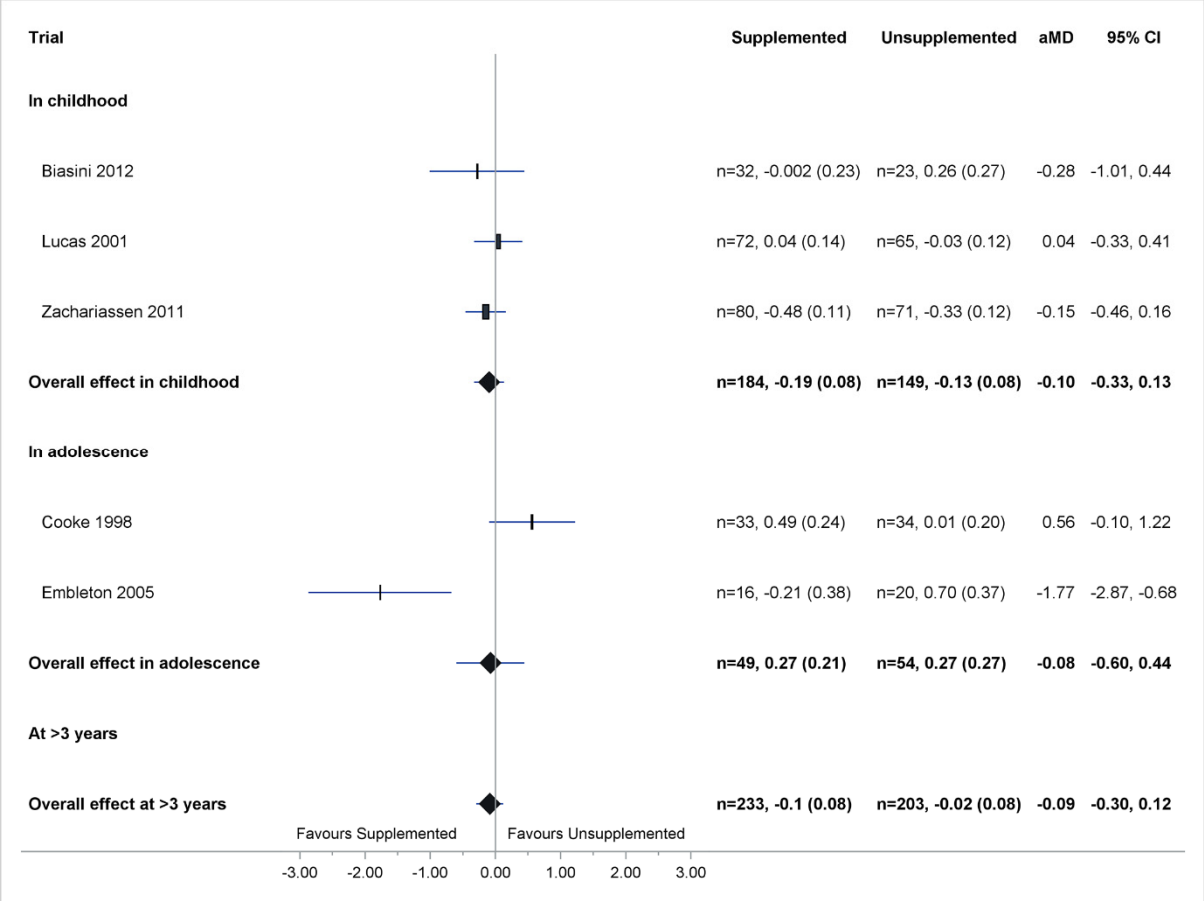


Figure S14. Forest plot of effect of macronutrient supplementation on BMI z-scores (IPD analysis).
Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity in childhood p=0.64, tau^2=0.01; in adolescence p=0.005, tau^2=0.07; at >3 years p=0.04, tau^2=0.01.

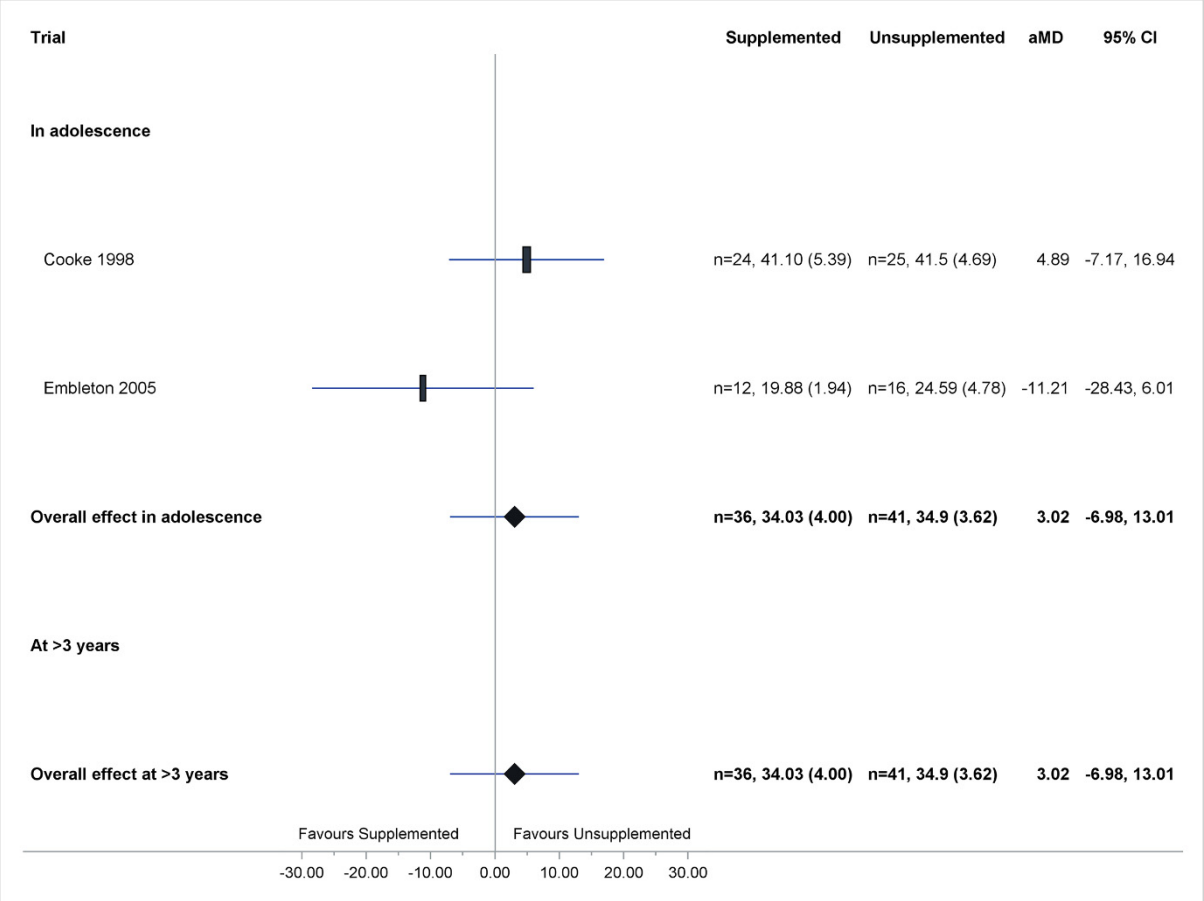
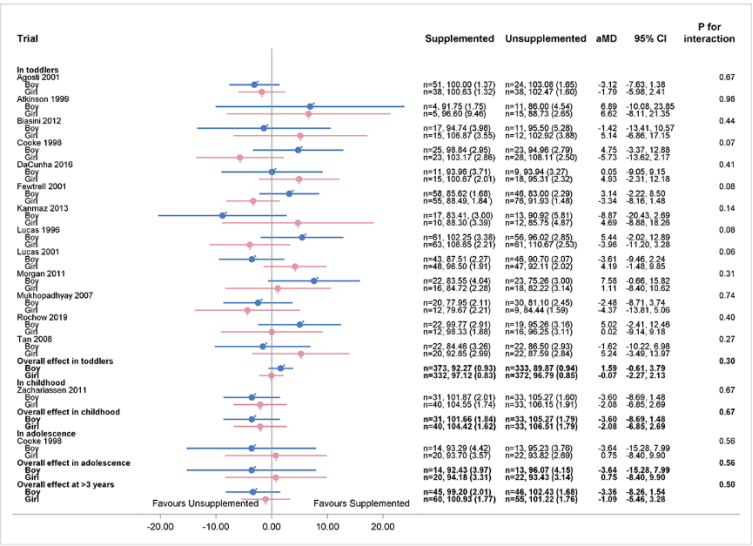
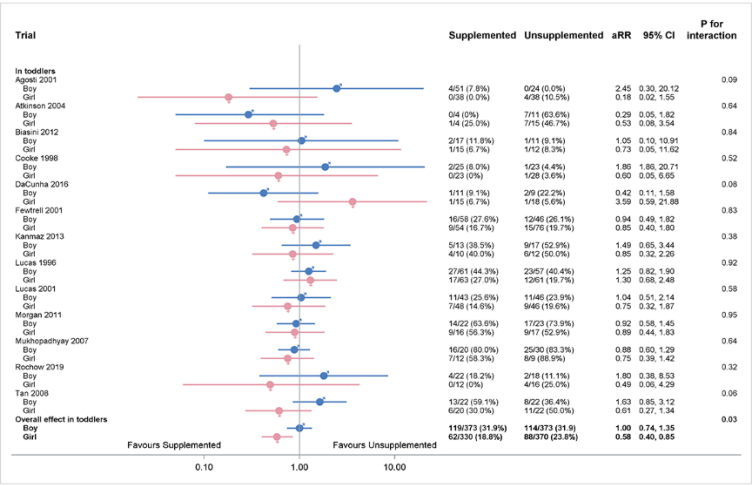


Figure S15. Forest plot of effect of macronutrient supplementation on IGF-I concentration (IPD analysis). Data are mean and standard error, with adjusted mean difference (aMD) for treatment effect and 95% confidence intervals (CIs) adjusted for sex, gestational age and birthweight z-scores. The box size of point estimate is proportional to inverse variance. Heterogeneity in adolescence p=0.80, tau^2=22.66.

a.



b.



c.

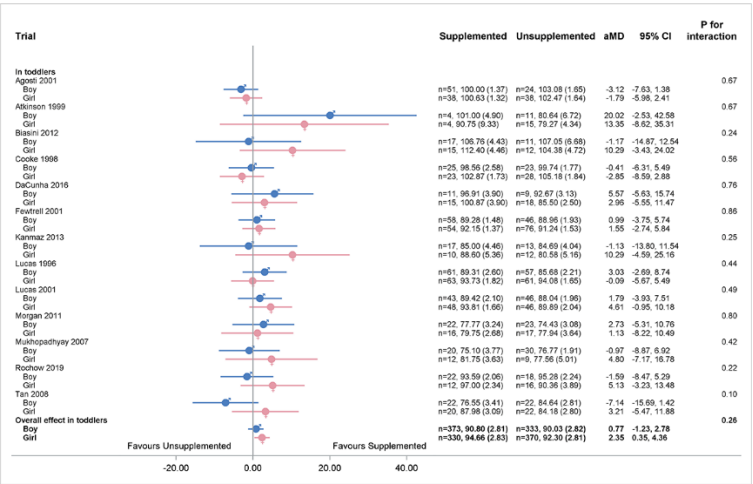
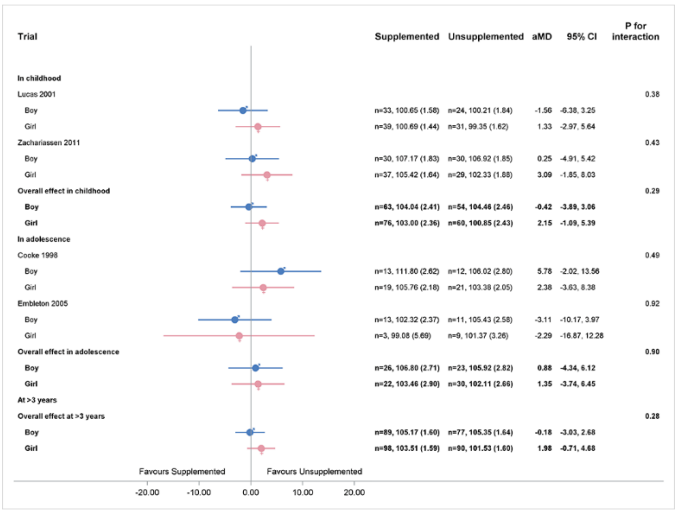
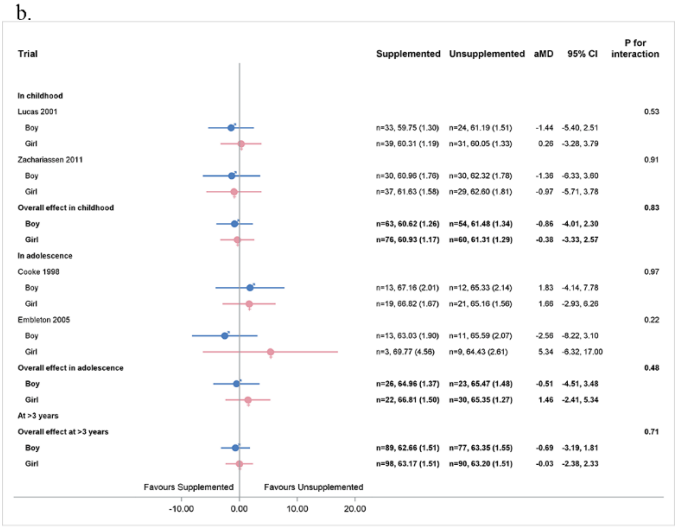


Figure S16. IPD analysis of secondary developmental outcomes separated for boys and girls. a. cognitive scores, b. motor impairment, c. motor scores. Data are mean and standard error, with adjusted mean difference (aMD) or data are numbers (percentages) with adjusted relative risk (aRR) and 95% confidence intervals (CIs) adjusted for gestational age and birthweight z-scores. Heterogeneity for a.cognitive scores, boys in toddlers p=0.34, tau^2=1.25; at >3 years p=0.91, tau^2=6.15; girls in toddlers p=0.27, tau^2=1.25; at >3 years p=0.53, tau^2=4.93. Heterogeneity for b. motor impairment, boys in toddlers p=0.98, tau^2=0.03; girls in toddlers p=0.95, tau^2=0.04. Heterogeneity for c. motor scores, boys in toddlers p=0.35, tau^2=0.03; girls in toddlers p=0.42, tau^2=0.04.

a.



b.



c.

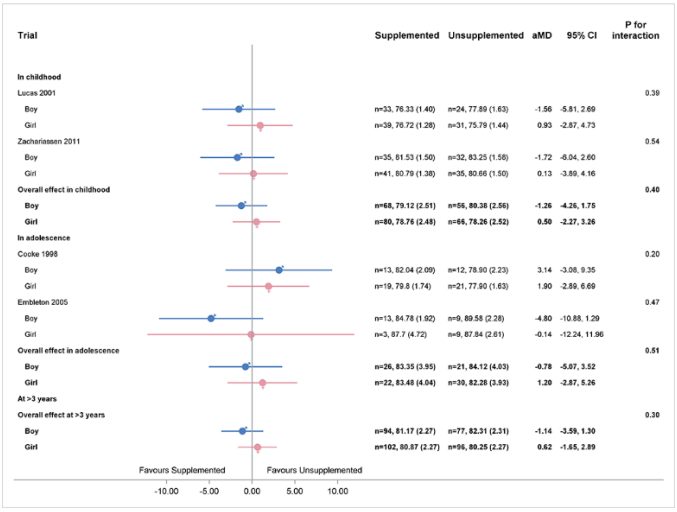


Figure S17. IPD analysis of blood pressure separated for boys and girls. a. SBP, b. DBP, c. MAP. Data are mean and standard error, with adjusted mean difference (aMD) and 95% confidence intervals (CIs) adjusted for gestational age and birthweight z-scores. Heterogeneity for a. SBP, boys in childhood p=0.63, tau^2=3.10; in adolescence p=0.19, tau^2=6.92; at >3 years p=0.64, tau^2=2.10. Girls in childhood p=0.54, tau^2=2.72; in adolescence p=0.19, tau^2=6.66; at >3 years p=0.74, tau^2=1.88. Heterogeneity for b. DBP, boys in childhood p=0.87, tau^2=2.56; in adolescence p= 0.25, tau^2=4.04; at >3 years p= 0.86, tau^2=1.61. Girls in childhood p=0.68, tau^2=2.25; in adolescence p=0.42, tau^2=3.80; at >3 years p=0.87, tau^2=1.44. Heterogeneity for c. MAP, boys in childhood p=0.87, tau^2=2.31; in adolescence p=0.11, tau^2=4.67; at >3 years p= 0.53, tau^2=1.56. Girls in childhood p=0.75, tau^2=1.99; in adolescence p=0.29, tau^2=4.20, at >3 years p= 0.94, tau^2=1.32.

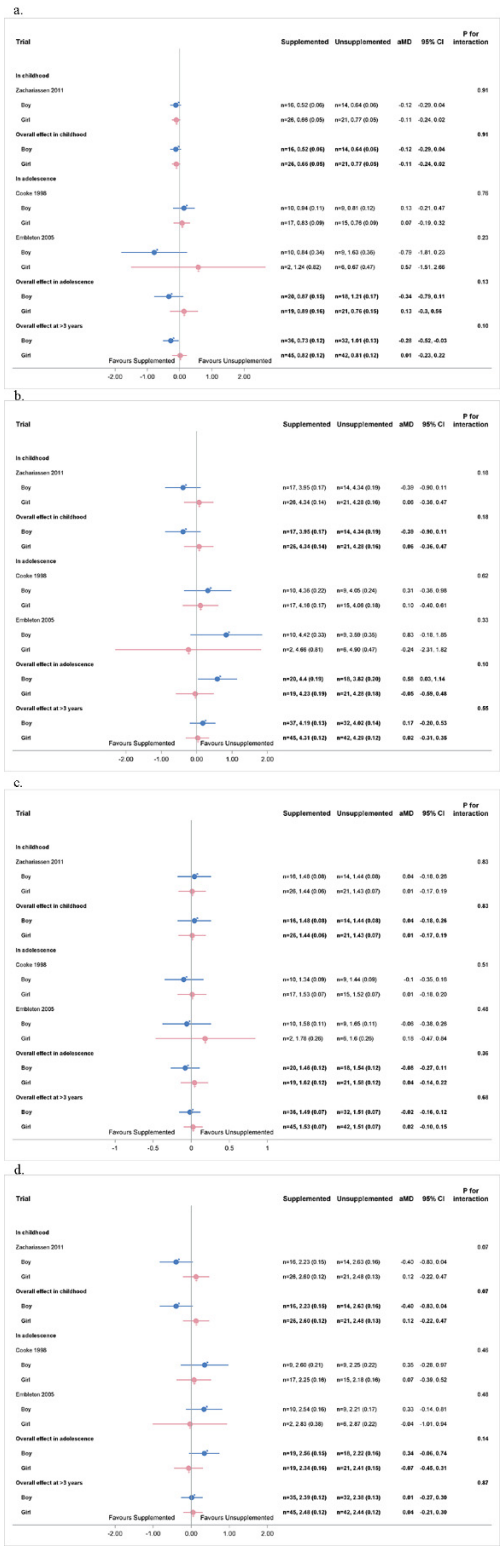
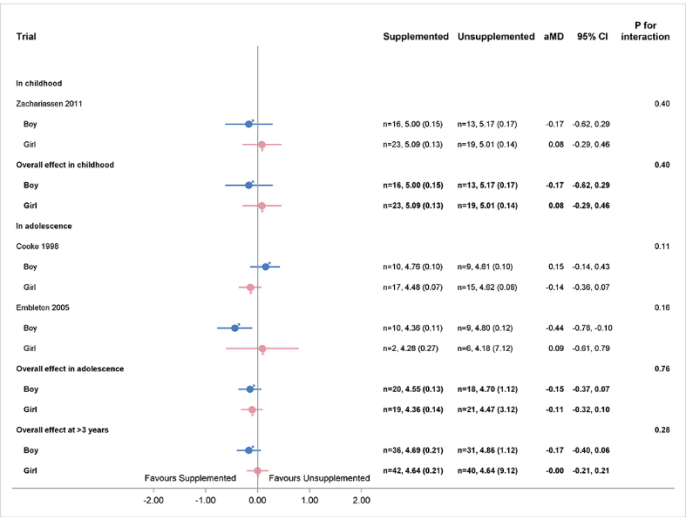
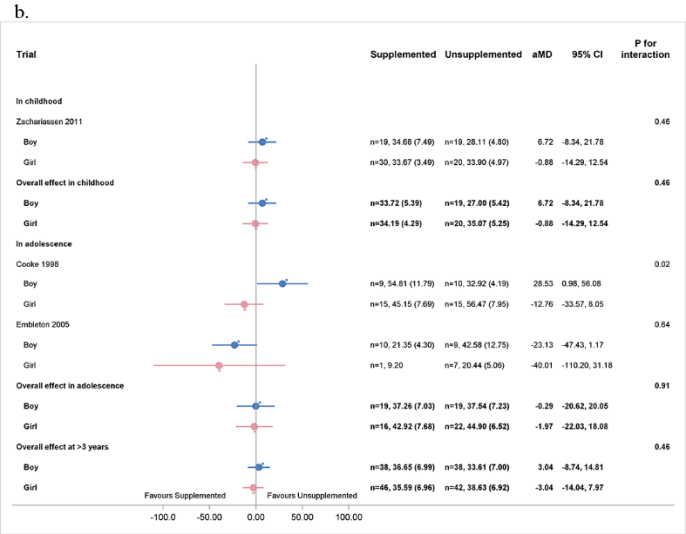


Figure S18. IPD analysis of metabolic outcomes separated for boys and girls. a. Triglyceride concentrations, b. Cholesterol concentrations, c. HDL concentrations, d. LDL concentrations. Data are mean and standard error, with adjusted mean difference (aMD) and 95% confidence intervals (CIs) adjusted for gestational age and birthweight z-scores. For triglyceride concentrations, heterogeneity for boys in adolescence p=0.08, tau²=0.05; at >3 years p=0.07, tau²=0.02. Heterogeneity for girls in adolescence p=0.39, tau²=0.05; at >3 years p=0.13, tau²=0.01. For cholesterol concentrations, heterogeneity for boys in adolescence p=0.49, tau²=0.34; at >3 years p=0.34, tau²=0.04. Heterogeneity for girls in adolescence p=0.04, tau²=0.07; at >3 years p=0.01, tau²=0.03. For HDL concentrations, heterogeneity for boys in adolescence p=0.77, tau²=0.01; at >3 years p=0.89, tau²=0.01. Heterogeneity for girls in adolescence p=0.93, tau²=0.01; at >3 years p=0.98, tau²=0.004. For LDL concentrations, heterogeneity for boys in adolescence p=0.98, tau²=0.04; at >3 years p=0.11, tau²=0.02. Heterogeneity for girls in adolescence p=0.59, tau²=0.04; at >3 years p=0.84, tau²=0.02.

a.



b.



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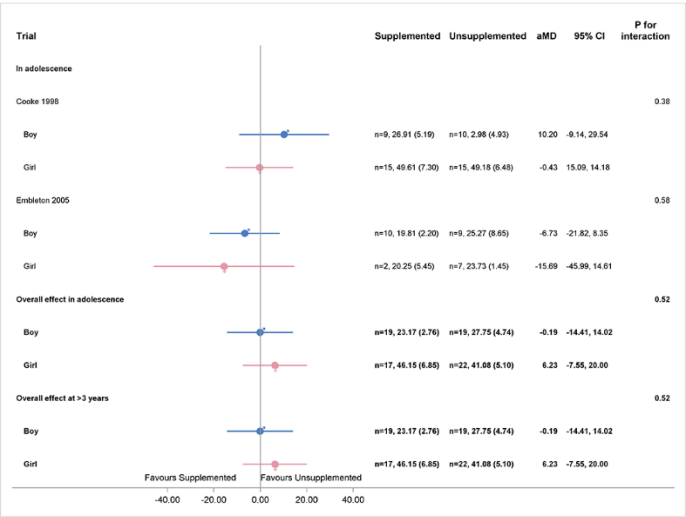
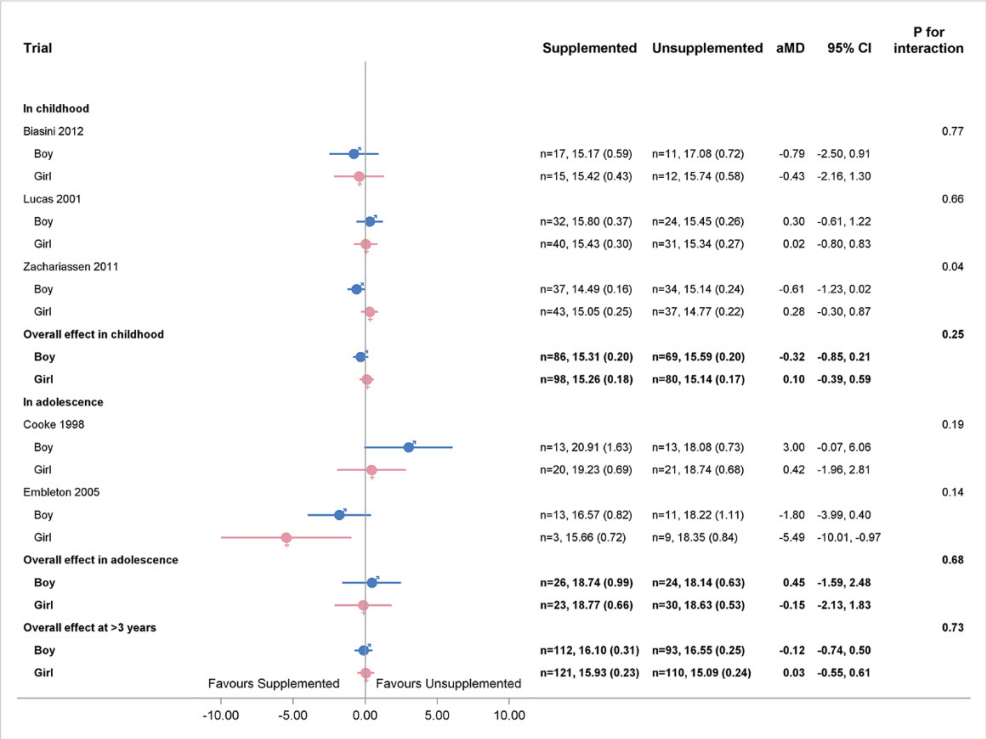


Figure S19. IPD analysis of metabolic outcomes separated for boys and girls. a. Blood glucose concentrations, b. Fasting insulin concentrations, c. IGF-I. Data are mean and standard error, with adjusted mean difference (aMD) and 95% confidence intervals (CIs) adjusted for gestational age and birthweight z-scores. For blood glucose concentrations, heterogeneity for boys in adolescence p=0.01, tau^2=0.01; at >3 years p=0.27, tau^2=0.11. Heterogeneity for girls in adolescence p=0.84, tau^2=0.01; at >3 years p=0.54, tau^2=0.11. For fasting insulin concentrations, heterogeneity for boys in adolescence p=0.03, tau^2=103.84; at >3 years p=0.06, tau^2=35.52. Heterogeneity for girls in adolescence p=0.41, tau^2=101.20; at >3 years p=0.52, tau^2=31.03. For IGF-I, heterogeneity for boys in adolescence p=0.85, tau^2=45.83; heterogeneity for girls in adolescence p=0.29, tau^2=43.69.

a.



b.

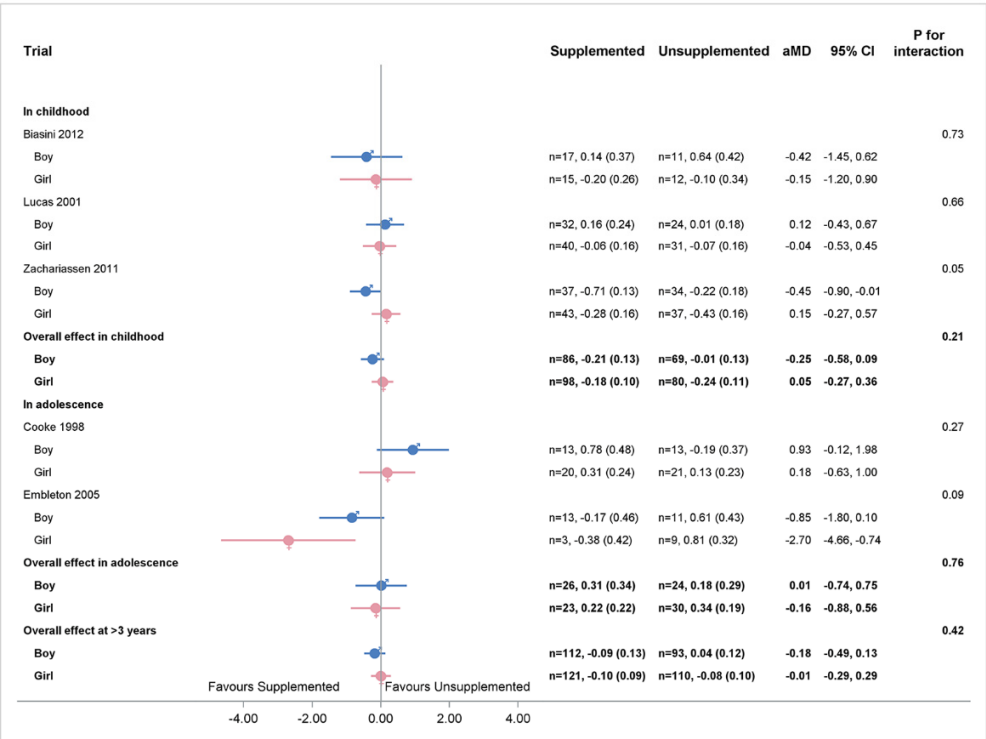


Figure S20. IPD analysis of metabolic outcomes separated for boys and girls. a. BMI, b. BMI z-scores. Data are mean and standard error, with adjusted mean difference (aMD) and 95% confidence intervals (CIs) adjusted for gestational age and birthweight z-scores. For BMI, heterogeneity for boys in childhood p= 0.17, tau²=0.07; in adolescence for boys p=0.08, tau²=1.04; at >3 years p=0.01, tau²=0.10. Heterogeneity for girls in childhood p=0.74, tau²=0.06; in adolescence p=0.06, p=1.00; at >3 years p=0·15, tau²=0.09. For BMI z-scores, heterogeneity for boys in childhood p= 0.28, tau²=0.03; in adolescence p=0.10, tau²=0.14; at >3 years p=0.09, tau²=0.03. Heterogeneity for girls in childhood p=0·82, tau²=0.02; in adolescence p=0.02, tau²=0.13; at >3 years p=0·24, tau²=0.02.

Table S1. Risk of bias within studies

Study	Randomisation[1]	Concealment[2]	Performance[3]	Detection[4]	Attrition[5]	Reporting[6]
Studies with IPD						
Agosti 2003	Unclear	Unclear	Low	Low	High	Low
Atkinson 1999	Low	Low	Low	Low	Low	Low
Biasini 2012	High	High	High	Low	Low	Low
Cooke 1998	Low	Low	Low	Low	Low	Low
Embleton 2005	Low	Low	Low	Low	High	Low
da Cunha 2016	Low	Low	High	Low	Low	Low
Fewtrell 2001	Low	Low	Low	Low	Low	Low
Kanmaz 2013	Low	Low	High	Low	Low	Low
Lucas 1996	Low	Low	High	Low	Low	Low
Lucas 2001	Low	Low	Low	Low	Low	Low
Morgan 2011	Low	Low	Low	Low	Low	Low
Mukhopadhyay 2007	Low	Low	Unclear	Unclear	Low	Low
Rochow 2019	Low	Low	Low	Low	Low	Low
Tan 2008	Low	Low	High	High	Low	Low
Zachariassen 2011	Low	Low	High	High	Low	Low
Studies with AD						
Amesz 2010	Low	Low	Low	Unclear	High	Low
Bellagamba 2016	Low	Unclear	Low	Low	Unclear	Low
Dorga 2017	Low	Low	Low	Low	High	Low
Goldman 1969	Unclear	Unclear	High	Low	High	Low
Jeon 2011	Unclear	Unclear	Unclear	Unclear	High	Unclear
Lucas 1989	Low	Low	High	Low	High	Low
Lucas 1990	Low	Low	High	Low	High	Low

O'Connor 2008	Low	Low	Unclear	Unclear	High	Low
Roggero 2012	Low	Unclear	Unclear	Low	Low	High
Svenningsen 1982	Unclear	Unclear	Unclear	Unclear	Low	High

[1]Random sequence generation. [2]Allocation concealment. [3]Blinding of participants and personnel. [4]Blinding of outcome assessment. [5]Incomplete outcome data. [6]Selective reporting.
We used IPD not the published data for studies with IPD, so the risk of reporting bias is low for all the studies with IPD.
IPD: individual participant data; AD: aggregated data.

Table S2. Subgroup analyses of size for gestation of the infants

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Cognitive impairment in toddlers	AGA	13 trials	990	1.05 (0.77, 1.41)	0.76	0.91	0.02	0.21
	SGA	13 trials	420	0.77 (0.54, 1.11)	0.16	0.14	0.03	
Cognitive impairment in childhood	AGA	1 trial	187	1.01 (0.62, 1.63)	0.98	N/A	N/A	1.00
	SGA	1 trial	20	1.00 (0.30, 3.31)	0.99	N/A	N/A	
Cognitive impairment in adolescence	AGA	1 trial	57	1.23 (0.54, 2.74)	0.63	N/A	N/A	0.80
	SGA	1 trial	12	1.64 (0.19, 14.31)	0.65	N/A	N/A	
Cognitive impairment at >3 years	AGA	2 trials	244	1.16 (0.50, 2.73)	0.73	0.81	0.05	0.78
	SGA	2 trials	32	1.02 (0.73, 1.44)	0.91	0.59	0.29	
Metabolic risk in childhood	AGA	3 trials	280	1.07 (0.78, 1.45)	0.68	0.29	0.03	0.32
	SGA	3 trials	54	0.72 (0.35, 1.48)	0.37	0.34	0.14	
Metabolic risk in adolescence	AGA	2 trials	84	0.89 (0.67, 1.18)	0.42	0.09	0.27	0.77
	SGA	2 trials	20	0.80 (0.41, 1.55)	0.51	0.25	1.02	
Metabolic risk at >3 years	AGA	5 trials	364	0.98 (0.78, 1.23)	0.86	0.19	0.01	0.21
	SGA	5 trials	74	0.68 (0.40, 1.16)	0.15	0.33	0.07	
Cognitive scores in toddlers	AGA	13 trials	990	0.27 (-1.58, 2.11)	0.78	0.62	0.88	0.29
	SGA	13 trials	420	2.11 (-0.76, 4.97)	0.15	0.69	2.13	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cognitive scores in childhood	AGA	1 trial	187	-2.01 (-5.66, 1.64)	0.28	N/A	N/A	0.10
	SGA	1 trial	20	-12.92 (-25.36, -0.48)	0.04	N/A	N/A	
Cognitive scores in adolescence	AGA	1 trial	57	-1.51 (-9.33, 6.31)	0.70	N/A	N/A	0.63
	SGA	1 trial	12	3.08 (-14.13, 20.28)	0.72	N/A	N/A	
Cognitive scores at >3 years	AGA	2 trials	244	-1.68 (-5.16, 1.80)	0.34	0.89	3.10	0.53
	SGA	2 trials	32	-5.02 (-14.89, 4.85)	0.32	0.21	25	
Motor impairment in toddlers	AGA	13 trials	987	0.91 (0.69, 1.23)	0.56	0.97	0.02	0.09
	SGA	13 trials	419	0.59 (0.38, 0.90)	0.02	0.95	0.05	
Motor scores in toddlers	AGA	13 trials	987	0.79 (-0.86, 2.45)	0.35	0.34	0.74	0.06
	SGA	13 trials	419	3.79 (1.17, 6.42)	0.005	0.36	1.77	
SBP in childhood (mmHg)	AGA	2 trials	219	1.55 (-1.01, 4.11)	0.23	0.79	1.69	0.25
	SGA	2 trials	34	-2.58 (-9.11, 3.95)	0.44	0.41	10.96	
SBP in adolescence (mmHg)	AGA	2 trials	81	1.22 (-2.83, 5.27)	0.55	0.36	4.17	0.93
	SGA	2 trials	20	0.81 (-7.69, 9.31)	0.85	0.03	18.32	
SBP at >3 years (mmHg)	AGA	4 trials	300	1.50 (-0.63, 3.63)	0.17	0.79	1.17	0.24
	SGA	4 trials	54	-1.76 (-6.82. 3.30)	0.50	0.42	6.61	
DBP in childhood (mmHg)	AGA	2 trials	219	-0.37 (-2.69, 1.95)	0.75	0.41	1.39	0.59
	SGA	2 trials	34	-2.11 (-8.02, 3.80)	0.48	0.27	9.00	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
DBP in adolescence (mmHg)	AGA	2 trials	81	1.71 (-1.36, 4.78)	0.27	0.89	2.40	0.11
	SGA	2 trials	20	-4.08 (-10.50, 2.33)	0.21	0.01	10.43	
DBP at >3 years (mmHg)	AGA	4 trials	300	0.15 (-1.70, 2.01)	0.87	0.66	0.88	0.18
	SGA	4 trials	54	-3.13 (-7.54, 1.28)	0.16	0.22	5.02	
MAP in childhood (mmHg)	AGA	2 trials	235	-0.08 (-2.26, 2.11)	0.95	0.46	1.23	0.56
	SGA	2 trials	35	-1.87 (-7.58, 3.83)	0.52	0.42	8.41	
MAP in adolescence (mmHg)	AGA	2 trials	79	-0.07 (-3.36, 3.22)	0.97	0.07	2.76	0.65
	SGA	2 trials	20	1.67 (-5.13, 8.46)	0.63	0.48	11.70	
MAP at >3 years (mmHg)	AGA	4 trials	314	-0.09 (-1.90, 1.72)	0.92	0.28	0.85	0.74
	SGA	4 trials	55	-0.89 (-5.23, 3.46)	0.69	0.68	4.88	
Triglyceride concentrations in childhood (mmol/L)	AGA	1 trial	68	-0.11 (-0.22, 0.003)	0.06	N/A	N/A	0.53
	SGA	1 trial	9	-0.22 (-0.56, 0.12)	0.19	N/A	N/A	
Triglyceride concentrations in adolescence (mmol/L)	AGA	2 trials	21	0.02 (-0.31, 0.35)	0.89	0.64	0.03	0.10
	SGA	2 trials	6	-0.70 (-1.50, 0.10)	0.09	0.20	0.16	
Triglyceride concentrations at >3 years (mmol/L)	AGA	3 trials	133	-0.03 (-0.21, 0.14)	0.71	0.46	0.01	0.008
	SGA	3 trials	22	-0.66 (-1.09, -0.23)	0.03	0.26	0.05	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Cholesterol concentrations in childhood (mmol/L)	AGA	1 trial	69	-0.19 (-0.53, 0.15)	0.27	N/A	N/A	0.30
	SGA	1 trial	9	0.39 (-0.65, 1.42)	0.46	N/A	N/A	
Cholesterol concentrations in adolescence (mmol/L)	AGA	2 trials	65	0.17 (-0.24, 0.57)	0.42	0.21	0.04	0.38
	SGA	2 trials	13	0.63 (-0.35, 1.61)	0.20	0.40	0.05	
Cholesterol concentrations at >3 years (mmol/L)	AGA	3 trials	134	-0.02 (-0.28, 0.24)	0.88	0.19	0.05	0.03
	SGA	3 trials	22	0.74 (0.09, 1.39)	0.03	0.18	0.11	
HDL concentrations in childhood (mmol/L)	AGA	1 trial	68	0.003 (-0.15, 0.15)	0.97	N/A	N/A	0.37
	SGA	1 trial	9	0.21 (-0.23, 0.65)	0.34	N/A	N/A	
HDL concentrations in adolescence (mmol/L)	AGA	2 trials	65	-0.04 (-0.18, 0.10)	0.58	0.41	0.01	0.43
	SGA	2 trials	13	0.11 (-0.24, 0.45)	0.53	0.02	0.03	
HDL concentrations at >3 years (mmol/L)	AGA	3 trials	133	-0.02 (-0.12, 0.08)	0.69	0.67	0.003	0.21
	SGA	3 trials	22	0.15 (-0.10, 0.40)	0.24	0.05	0.02	
LDL concentrations in childhood (mmol/L)	AGA	1 trial	68	-0.13 (-0.43, 016)	0.38	N/A	N/A	0.39
	SGA	1 trial	9	0.27 (-0.61, 1.15)	0.54	N/A	N/A	
LDL concentrations in adolescence (mmol/L)	AGA	2 trials	64	0.17 (-0.12, 0.47)	0.25	0.49	0.02	0.40
	SGA	2 trials	13	-0.16 (-0.87, 0.56)	0.66	0.37	0.13	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
LDL concentrations at >3 years (mmol/L)	AGA	3 trials	132	0.02 (-0.19, 0.23)	0.84	0.27	0.01	0.72
	SGA	3 trials	22	0.12 (-0.39, 0.63)	0.64	0.22	0.07	
Blood glucose concentrations in childhood (mmol/L)	AGA	1 trial	62	0.03 (-0.28, 0.33)	0.86	N/A	N/A	0.36
	SGA	1 trial	9	-0.40 (-1.28, 0.48)	0.36	N/A	N/A	
Blood glucose concentrations in adolescence (mmol/L)	AGA	2 trials	65	-0.13 (-0.29, 0.04)	0.13	0.38	0.01	0.77
	SGA	2 trials	13	-0.19 (-0.59, 0.21)	0.34	0.01	0.04	
Blood glucose concentrations at >3 years (mmol/L)	AGA	3 trials	127	-0.05 (-0.21, 0.12)	0.60	0.60	0.01	0.29
	SGA	3 trials	22	-0.28 (-0.69, 0.13)	0.17	0.20	0.04	
Fasting insulin in childhood (pmol/L)	AGA	1 trial	81	3.97 (-6.68, 14.62)	0.46	N/A	N/A	0.40
	SGA	1 trial	7	-14.20 (-54.96, 26.55)	0.49	N/A	N/A	
Fasting insulin in adolescence (pmol/L)	AGA	2 trials	62	-8.91 (-23.30, 5.47)	0.22	0.31	51.98	0.04
	SGA	2 trials	14	29.67 (-3.65, 62.98)	0.08	0.30	27.89	
Fasting insulin at >3 years (pmol/L)	AGA	3 trials	143	-1.56 (-10.13, 7.00)	0.72	0.18	27.25	0.25
	SGA	3 trials	21	12.86 (-9.95, 35.66)	0.27	0.53	133.17	
IGF-I in adolescence (nmol/L)	AGA	2 trials	63	-2.45 (-12.95, 8.05)	0.64	0.83	27.67	0.15
	SGA	2 trials	14	17.32 (-7.26, 41.90)	0.16	0.19	151.78	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
BMI in childhood (kg/m^2)	AGA	3 trials	280	0.02 (-0.38, 0.41)	0.93	0.63	0.04	0.21
	SGA	3 trials	53	-0.63 (-1.55, 0.29)	0.18	0.17	0.25	
BMI in adolescence (kg/m^2)	AGA	2 trials	83	0.04 (-1.54, 1.61)	0.96	0.03	0.64	0.68
	SGA	2 trials	20	0.82 (-2.54, 4.18)	0.63	0.01	2.89	
BMI at >3 years (kg/m^2)	AGA	5 trials	363	0.01 (-0.46, 0.48)	0.97	0.01	0.06	0.79
	SGA	5 trials	73	-0.15 (-1.20, 0.90)	0.78	0.01	0.28	
BMI z-score in childhood	AGA	3 trials	280	-0.03 (-0.28, 0.23)	0.85	0.72	0.02	0.29
	SGA	3 trials	53	-0.37 (-0.96, 0.22)	0.21	0.25	0.09	
BMI z-score in adolescence	AGA	2 trials	83	-0.05 (-0.63, 0.53)	0.87	0.02	0.08	1.00
	SGA	2 trials	20	-0.05 (-1.29, 1.18)	0.93	0.004	0.38	
BMI z-score at >3 years	AGA	5 trials	363	-0.04 (-0.28, 0.19)	0.73	0.06	0.01	0.55
	SGA	5 trials	73	-0.22 (-0.74, 0.31)	0.42	0.01	0.07	

Abbreviation: AGA: appropriate for gestational age; SGA: small for gestational age; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; N/A: not applicable

Relative risk and mean difference were adjusted for sex and gestational age.

Table S3. Subgroup analyses of size of infant at birth

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Cognitive impairment in toddlers	≤1 kg	12 trials	335	0.85 (0.63, 1.14)	0.28	0.99	0.02	0.47
	>1 kg	13 trials	1075	0.92 (0.76, 1.11)	0.39	0.99	0.01	
Cognitive impairment in childhood	≤1 kg	1 trial	41	0.96 (0.42, 2.19)	0.93	N/A	N/A	0.89
	>1 kg	1 trial	166	1.03 (0.68, 1.55)	0.90	N/A	N/A	
Cognitive impairment in adolescence	≤1 kg	1 trial	9	1.17 (0.08, 17.86)	0.89	N/A	N/A	0.74
	>1 kg	1 trial	60	1.36 (0.66, 2.79)	0.40	N/A	N/A	
Cognitive impairment at >3 years	≤1 kg	2 trials	50	0.98 (0.48, 2.02)	0.97	0.84	0.13	0.86
	>1 kg	2 trials	226	1.06 (0.75, 1.52)	0.73	0.72	0.03	
Metabolic risk in childhood	≤1 kg	3 trials	77	1.43 (0.66, 3.08)	0.36	0.21	0.14	0.06
	>1 kg	3 trials	257	0.93 (0.69, 1.26)	0.63	0.38	0.02	
Metabolic risk in adolescence	≤1 kg	2 trials	10	1.32 (0.39, 4.50)	0.61	0.84	0.27	0.39
	>1 kg	2 trials	94	0.85 (0.65, 1.11)	0.24	0.39	0.02	
Metabolic risk at >3 years	≤1 kg	5 trials	87	1.43 (0.74, 2.79)	0.29	0.36	0.11	0.09
	>1 kg	5 trials	351	0.87 (0.70, 1.09)	0.22	0.62	0.01	
Cognitive scores in toddlers	≤1 kg	12 trials	335	1.56 (-1.76, 4.89)	0.35	0.55	2.86	0.49
	>1 kg	13 trials	1075	0.41 (-1.37, 2.19)	0.65	0.96	0.83	
	≤1 kg	1 trial	41	-6.89 (-18.01, 4.24)	0.21	N/A	N/A	0.29

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cognitive scores in childhood	>1 kg	1 trial	166	-2.19 (-5.72. 1.34)	0.22	N/A	N/A	
Cognitive scores in adolescence	≤1 kg	1 trial	9	10.72 (-17.08, 38.51)	0.38	N/A	N/A	0.19
	>1 kg	1 trial	60	-2.54 (-10.04, 4.37)	0.50	N/A	N/A	
Cognitive scores at >3 years	≤1 kg	2 trials	50	-2.36 (-12.23, 7.51)	0.63	0.12	23.52	0.84
	>1 kg	2 trials	226	-2.15 (-5.59, 1.29)	0.22	0.94	3.03	
Motor impairment in toddlers	≤1 kg	12 trials	334	0.92 (0.69, 1.23)	0.58	0.99	0.06	0.85
	>1 kg	13 trials	1072	0.82 (0.60, 1.12)	0.21	0.97	0.03	
Motor scores in toddlers	≤1 kg	12 trials	334	0.74 (-2.20, 3.69)	0.62	0.69	2.82	0.61
	>1 kg	13 trials	1072	1.61 (-0.04, 3.25)	0.06	0.48	0.66	
SBP in childhood (mmHg)	≤1 kg	2 trials	43	-1.58 (-8.34, 5.18)	0.64	0.44	11.16	0.38
	>1 kg	2 trials	210	1.34 (-1.22, 3.91)	0.30	0.78	1.69	
SBP in adolescence (mmHg)	≤1 kg	2 trials	9	-13.42 (-27.54, 0.71)	0.06	0.12	30.25	0.07
	>1 kg	2 trials	92	2.19 (-1.60, 5.97)	0.25	0.18	3.61	
SBP at >3 years (mmHg)	≤1 kg	4 trials	52	-3.42 (-9.30, 2.47)	0.25	0.70	8.53	0.12
	>1 kg	4 trials	302	1.61 (-0.49, 3.71)	0.13	0.60	1.12	
DBP in childhood (mmHg)	≤1 kg	2 trials	43	-1.02 (-7.73, 5.70)	0.76	0.93	11.02	0.90
	>1 kg	2 trials	210	-0.72 (-2.96, 1.53)	0.53	0.81	1.30	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
DBP in adolescence (mmHg)	≤1 kg	2 trials	9	-0.11 (-5.91, 5.68)	0.96	0.63	5.06	0.06
	>1 kg	2 trials	92	1.27 (-1.56, 4.11)	0.37	0.008	2.05	
DBP at >3 years (mmHg)	≤1 kg	4 trials	52	-2.48 (-8.22, 3.25)	0.39	0.94	8.12	0.49
	>1 kg	4 trials	302	-0.18 (-1.95, 1.59)	0.84	0.75	0.81	
MAP in childhood (mmHg)	≤1 kg	2 trials	46	-2.68 (-8.60, 3.24)	0.37	0.85	8.58	0.33
	>1 kg	2 trials	224	0.05 (-2.12, 2.22)	0.97	0.93	1.21	
MAP in adolescence (mmHg)	≤1 kg	2 trials	9	-0.95 (-10.46, 8.56)	0.81	0.15	13.69	0.94
	>1 kg	2 trials	90	0.24 (-2.91, 3.39)	0.88	0.05	2.53	
MAP at >3 years (mmHg)	≤1 kg	4 trials	55	-1.99 (-7.18, 3.21)	0.45	0.96	6.66	0.36
	>1 kg	4 trials	314	0.06 (-1.72, 1.83)	0.95	0.31	0.81	
Triglyceride concentrations in childhood (mmol/L)	≤1 kg	1 trial	13	-0.03 (-0.28, 0.22)	0.78	N/A	N/A	0.31
	>1 kg	1 trial	64	-0.14 (-0.26, -0.02)	0.03	N/A	N/A	
Triglyceride concentrations in adolescence (mmol/L)	≤1 kg	2 trials	9	-0.22 (-0.56, 0.13)	0.17	0.35	0.02	0.87
	>1 kg	2 trials	69	-0.16 (-0.51, 0.19)	0.38	0.10	0.03	
Triglyceride concentrations at >3 years (mmol/L)	≤1 kg	3 trials	22	-0.13 (-0.33, 0.07)	0.18	0.76	0.01	0.78
	>1 kg	3 trials	133	-0.12 (-0.31, 0.07)	0.22	0.17	0.01	
	≤1 kg	1 trial	14	0.34 (-0.20, 0.87)	0.20	N/A	N/A	0.25

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cholesterol concentrations in childhood (mmol/L)	>1 kg	1 trial	64	-0.23 (-0.61, 0.15)	0.24	N/A	N/A	
Cholesterol concentrations in adolescence (mmol/L)	≤1 kg	2 trials	9	-0.23 (-1.07, 0.61)	0.52	0.20	0.11	0.63
	>1 kg	2 trials	69	0.34 (-0.09, 0.78)	0.12	0.67	0.05	
Cholesterol concentrations at >3 years (mmol/L)	≤1 kg	3 trials	23	0.18 (-0.22, 0.58)	0.36	0.12	0.04	0.74
	>1 kg	3 trials	133	0.08 (-0.21, 0.36)	0.60	0.11	0.02	
HDL concentrations in childhood (mmol/L)	≤1 kg	1 trial	13	0.20 (-0.13, 0.52)	0.20	N/A	N/A	0.20
	>1 kg	1 trial	64	-0.01 (-0.17, 0.15)	0.92	N/A	N/A	
HDL concentrations in adolescence (mmol/L)	≤1 kg	2 trials	9	-0.04 (-0.82, 0.73)	0.89	0.15	0.09	0.30
	>1 kg	2 trials	69	-0.05 (-0.18, 0.08)	0.45	0.46	0.004	
HDL concentrations at >3 years (mmol/L)	≤1 kg	3 trials	22	0.23 (-0.08, 0.55)	0.14	0.27	0.02	0.06
	>1 kg	3 trials	133	-0.04 (-0.14, 0.06)	0.47	0.72	0.003	
LDL concentrations in childhood (mmol/L)	≤1 kg	1 trial	13	0.18 (-0.44, 0.81)	0.53	N/A	N/A	0.50
	>1 kg	1 trial	64	-0.15 (-0.46, 0.17)	0.36	N/A	N/A	
LDL concentrations in adolescence (mmol/L)	≤1 kg	2 trials	8	-0.23 (-0.78, 0.32)	0.31	0.37	0.04	0.38
	>1 kg	2 trials	69	0.21 (-0.11, 0.52)	0.19	0.71	0.02	
	≤1 kg	3 trials	21	0.04 (-0.18, 0.26)	0.73	0.24	0.03	0.88

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
LDL concentrations at >3 years (mmol/L)	>1 kg	3 trials	133	0.05 (-0.32, 0.42)	0.76	0.28	0.01	
Blood glucose concentrations in childhood (mmol/L)	≤1 kg	1 trial	13	0.00 (-0.81, 0.81)	1.00	N/A	N/A	0.96
	>1 kg	1 trial	58	-0.02 (-0.34, 0.30)	0.88	N/A	N/A	
Blood glucose concentrations in adolescence (mmol/L)	≤1 kg	2 trials	9	-0.30 (-0.91, 0.31)	0.26	0.08	0.06	0.17
	>1 kg	2 trials	69	-0.12 (-0.28, 0.04)	0.14	0.22	0.01	
Blood glucose concentrations at >3 years (mmol/L)	≤1 kg	3 trials	22	-0.15 (-0.65, 0.35)	0.54	0.69	0.06	0.57
	>1 kg	3 trials	127	-0.07 (-0.23, 0.10)	0.44	0.64	0.01	
BMI in childhood (kg/m^2)	≤1 kg	3 trials	76	0.47 (-0.37, 1.31)	0.27	0.13	0.18	0.12
	>1 kg	3 trials	257	-0.25 (-0.66, 0.15)	0.22	0.26	0.04	
BMI in adolescence (kg/m^2)	≤1 kg	2 trials	10	-3.05 (-6.59, 0.50)	0.08	0.20	2.07	0.22
	>1 kg	2 trials	93	0.57 (-0.95, 2.08)	0.46	0.04	0.58	
BMI at >3 years (kg/m^2)	≤1 kg	5 trials	86	0.13 (-0.70, 0.96)	0.75	0.08	0.02	0.76
	>1 kg	5 trials	350	-0.05 (-0.54, 0.45)	0.86	0.01	0.06	
BMI z-score in childhood	≤1 kg	3 trials	76	0.33 (-0.20, 0.86)	0.22	0.11	0.08	0.07
	>1 kg	3 trials	257	-0.21 (-0.46, 0.05)	0.12	0.45	0.02	
	≤1 kg	2 trials	10	-1.19 (-3.01, 0.63)	0.16	0.38	0.56	0.13

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
BMI z-score in adolescence	>1 kg	2 trials	93	0.13 (-0.41, 0.68)	0.63	0.03	0.07	
BMI z-score at >3 years	≤1 kg	5 trials	86	0.16 (-0.35, 0.66)	0.54	0.11	0.06	0.36
	>1 kg	5 trials	350	-0.12 (-0.36, 0.12)	0.33	0.04	0.01	
Fasting insulin in childhood (pmol/L)	≤1 kg	1 trial	16	3.49 (-28.34, 35.31)	0.82	N/A	N/A	0.67
	>1 kg	1 trial	72	0.93 (-10.03, 11.89)	0.87	N/A	N/A	
Fasting insulin in adolescence (pmol/L)	≤1 kg	2 trials	9	-3.78 (-18.64, 11.09)	0.61	0.41	190.72	0.80
	>1 kg	2 trials	67	-3.97 (-39.47, 31.52)	0.79	0.49	55.35	
Fasting insulin at >3 years (pmol/L)	≤1 kg	3 trials	25	-0.93 (-9.83, 7.96)	0.84	0.58	20.25	0.61
	>1 kg	3 trials	139	-0.03 (-21.47, 21.41)	0.99	0.99	10.68	
IGF-I in adolescence (nmol/L)	≤1 kg	2 trials	9	-14.31 (-47.77, 19.15)	0.32	0.60	169.52	0.49
	>1 kg	2 trials	68	0.53 (-10.01, 11.07)	0.92	0.89	27.88	

Abbreviation: SBP: systolic blood pressure; DBP diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; N/A: not applicable
Relative risk and mean difference were adjusted for sex.

Table S4. Subgroup analyses of gestational age of infant at birth

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cognitive impairment in toddlers	≤28 weeks	12 trials	469	0.94 (0.71, 1.23)	0.64	0.93	0.46	0.95
	29 to 32 weeks	10 trials	544	0.81 (0.61, 1.08)	0.15	0.99	0.02	
	33 to 36 weeks	7 trials	157	0.81 (0.48, 1.35)	0.42	0.91	0.07	
Cognitive impairment in childhood	≤28 weeks	1 trial	51	1.04 (0.48, 2.22)	0.92	N/A	N/A	0.99
	29 to 32 weeks	1 trial	86	1.02 (0.58, 1.80)	0.94	N/A	N/A	
Cognitive impairment in adolescence	≤28 weeks	1 trial	14	0.63 (0.12, 3.34)	0.55	N/A	N/A	0.68
	29 to 32 weeks	1 trial	47	1.64 (0.57, 4.72)	0.35	N/A	N/A	
	33 to 36 weeks	1 trial	8	0.67 (0.04, 13.09)	0.72	N/A	N/A	
Cognitive impairment at >3 years	≤28 weeks	2 trials	65	0.97 (0.56, 1.69)	0.93	0.69		0.87
	29 to 32 weeks	2 trials	133	1.12 (0.74, 1.70)	0.60	0.50		
	33 to 36 weeks	1 trial	8	0.67 (0.04, 13.09)	0.72	N/A	N/A	
Metabolic risk in childhood	≤28 weeks	3 trials	121	1.40 (0.83, 2.36)	0.20	0.36	0.07	0.22
	29 to 32 weeks	3 trials	188	0.84 (0.59, 1.21)	0.35	0.99	0.03	
	33 to 36 weeks	2 trials	25	1.07 (0.24, 4.82)	0.93	0.93	0.52	
Metabolic risk in adolescence	≤28 weeks	2 trials	18	1.07 (0.37, 3.14)	0.89	0.87	0.18	0.56
	29 to 32 weeks	2 trials	70	0.83 (0.61, 1.13)	0.24	0.13	0.03	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
	33 to 36 weeks	2 trials	16	0.58 (0.16, 2.11)	0.38	0.77	0.18	
Metabolic risk at >3 years	≤28 weeks	5 trials	139	1.37 (0.88, 2.13)	0.16	0.65	0.24	0.10
	29 to 32 weeks	5 trials	258	0.79 (0.61, 1.02)	0.07	0.69	0.02	
	33 to 36 weeks	4 trials	41	0.73 (0.31, 1.67)	0.44	0.54	0.17	
Cognitive scores in toddlers	≤28 weeks	12 trials	469	0.51 (-2.27, 3.28)	0.72	0.66	1.99	0.53
	29 to 32 weeks	10 trials	544	0.62 (-1.83, 3.06)	0.62	0.57	0.38	
	33 to 36 weeks	7 trials	157	3.28 (-1.95, 8.50)	0.22	0.87	6.97	
Cognitive scores in childhood	≤28 weeks	1 trial	51	-2.48 (-9.80, 4.84)	0.50	N/A	N/A	0.94
	29 to 32 weeks	1 trial	86	-2.96 (-6.93, 1.01)	0.14	N/A	N/A	
Cognitive scores in adolescence	≤28 weeks	1 trial	14	1.00 (-18.86, 20.87)	0.91	N/A	N/A	0.94
	29 to 32 weeks	1 trial	47	0.23 (-7.35, 7.79)	0.95	N/A	N/A	
	33 to 36 weeks	1 trial	8	3.41 (-37.48, 44.30)	0.83	N/A	N/A	
Cognitive scores at >3 years	≤28 weeks	2 trials	65	-2.59 (-9.49, 4.30)	0.45	0.82	0.08	0.87
	29 to 32 weeks	2 trials	133	-1.80 (-5.46, 1.85)	0.33	0.61	0.04	
	33 to 36 weeks	1 trial	8	3.41 (-37.48, 44.30)	0.83	N/A	1.14	
Motor impairment in toddlers	≤28 weeks	12 trials	467	0.96 (0.75, 1.22)	0.73	0.41	0.01	0.87
	29 to 32 weeks	10 trials	543	0.80 (0.60, 1.05)	0.11	0.13	0.02	
	33 to 36 weeks	7 trials	156	0.67 (0.39, 1.17)	0.16	0.96	0.08	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Motor scores in toddlers	≤28 weeks	12 trials	467	0.57 (-2.09, 3.23)	0.67	0.99	0.32	0.37
	29 to 32 weeks	10 trials	543	1.78 (-0.46, 4.01)	0.12	0.02	1.30	
	33 to 36 weeks	7 trials	156	4.35 (0.14, 8.56)	0.04	0.72	4.54	
SBP in childhood (mmHg)	≤28 weeks	2 trials	77	0.31 (-4.55, 5.16)	0.90	0.41	5.96	0.88
	29 to 32 weeks	2 trials	152	1.43 (-1.66, 4.53)	0.36	0.14	2.47	
	33 to 36 weeks	1 trial	24	-0.26 (-6.36, 5.84)	0.93	N/A	N/A	
SBP in adolescence (mmHg)	≤28 weeks	2 trials	16	4.21 (-8.27, 16.68)	0.47	0.56	32.15	0.43
	29 to 32 weeks	2 trials	69	-0.27 (-4.55, 4.01)	0.90	0.14	4.58	
	33 to 36 weeks	2 trials	16	9.59 (-0.59, 19.77)	0.06	0.18	21.34	
SBP at >3 years (mmHg)	≤28 weeks	4 trials	93	0.16 (-4.17, 4.50)	0.60	0.79	4.75	0.92
	29 to 32 weeks	4 trials	221	0.92 (-1.56, 3.41)	0.46	0.26	1.59	
	33 to 36 weeks	3 trials	40	2.58 (-2.79, 7.96)	0.34	0.15	6.97	
DBP in childhood (mmHg)	≤28 weeks	2 trials	77	-1.65 (-6.19, 2.89)	0.47	0.02	5.20	0.75
	29 to 32 weeks	2 trials	152	-0.59 (-3.27, 2.09)	0.67	0.06	1.85	
	33 to 36 weeks	1 trial	24	0.71 (-0.54, 6.77)	0.81	N/A	N/A	
DBP in adolescence (mmHg)	≤28 weeks	2 trials	16	1.18 (-4.11, 7.66)	0.52	0.67	29.27	0.98
	29 to 32 weeks	2 trials	69	0.13 (-2.98, 3.24)	0.93	0.19	2.43	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
	33 to 36 weeks	2 trials	16	1.18 (-4.11, 7.66)	0.52	0.56	7.13	
DBP at >3 years (mmHg)	≤28 weeks	4 trials	93	-1.23 (-5.39, 2.94)	0.56	0.07	4.37	0.88
	29 to 32 weeks	4 trials	221	-0.35 (-2.41, 1.72)	0.74	0.14	1.10	
	33 to 36 weeks	3 trials	40	1.15 (-3.34, 5.65)	0.61	0.86	4.88	
MAP in childhood (mmHg)	≤28 weeks	2 trials	81	-0.56 (-4.69, 3.57)	0.75	0.08	4.29	0.66
	29 to 32 weeks	2 trials	165	-0.60 (-3.22, 2.02)	0.59	0.13	1.77	
	33 to 36 weeks	1 trial	24	2.11 (-2.99, 7.22)	0.40	N/A	N/A	
MAP in adolescence (mmHg)	≤28 weeks	2 trials	15	8.23 (-3.68, 20.15)	0.25	0.16	28.62	0.66
	29 to 32 weeks	2 trials	68	-0.81 (-4.34, 2.72)	0.60	0.003	3.13	
	33 to 36 weeks	2 trials	16	3.99 (-4.42, 12.39)	0.32	0.07	14.59	
MAP at >3 years (mmHg)	≤28 weeks	4 trials	96	0.07 (-3.74, 3.89)	0.97	0.16	3.67	0.60
	29 to 32 weeks	4 trials	233	-0.63 (-2.43, 1.46)	0.54	0.14	1.15	
	33 to 36 weeks	3 trials	40	2.59 (-1.52, 6.70)	0.21	0.73	4.08	
Triglyceride concentrations in childhood (mmol/L)	≤28 weeks	1 trial	24	-0.004 (-0.17, 0.16)	0.96	N/A	N/A	0.22
	29 to 32 weeks	1 trial	53	-0.15 (-0.29, -0.008)	0.04	N/A	N/A	
Triglyceride concentrations in adolescence (mmol/L)	≤28 weeks	3 trials	15	-0.05 (-0.34, 0.23)	0.68	0.53	0.02	0.49
	29 to 32 weeks	3 trials	52	-0.18 (-0.62, 0.27)	0.43	0.04	0.05	
	33 to 36 weeks	2 trials	11	0.37 (-0.50, 1.23)	0.34	0.64	0.02	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Triglyceride concentrations at >3 years (mmol/L)	≤28 weeks	3 trials	39	-0.02 (-0.15, 0.11)	0.76	0.72	0.004	0.17
	29 to 32 weeks	3 trials	105	-0.19 (-0.42, 0.04)	0.11	0.05	0.11	
	33 to 36 weeks	2 trials	11	0.37 (-0.50, 1.23)	0.34	0.64	0.12	
Cholesterol concentrations in childhood (mmol/L)	≤28 weeks	1 trial	25	0.37 (-0.09, 0.84)	0.11	N/A	N/A	0.06
	29 to 32 weeks	1 trial	53	-0.29 (-0.70, 0.13)	0.17	N/A	N/A	
Cholesterol concentrations in adolescence	≤28 weeks	3 trials	15	0.13 (-0.39, 0.66)	0.58	0.07	0.06	0.82
	29 to 32 weeks	3 trials	52	0.36 (-0.17, 0.90)	0.18	0.42	0.07	
	33 to 36 weeks	2 trials	11	0.18 (-1.19, 1.54)	0.56	0.94	0.30	
Cholesterol concentrations at >3 years (mmol/L)	≤28 weeks	3 trials	40	0.29 (-0.04, 0.62)	0.08	0.29	0.03	0.85
	29 to 32 weeks	3 trials	105	0.07 (-0.26, 0.40)	0.69	0.12	0.03	
	33 to 36 weeks	2 trials	11	0.18 (-1.19, 1.54)	0.76	0.83	0.31	
HDL concentrations in childhood (mmol/L)	≤28 weeks	1 trial	24	0.12 (-0.10, 0.34)	0.28	N/A	N/A	0.30
	29 to 32 weeks	1 trial	53	-0.03 (-0.22, 0.15)	0.70	N/A	N/A	
HDL concentrations in adolescence (mmol/L)	≤28 weeks	3 trials	15	0.17 (-0.16, 0.49)	0.28	0.68	0.02	0.20
	29 to 32 weeks	3 trials	52	-0.01 (-0.17, 0.15)	0.91	0.17	0.06	
	33 to 36 weeks	2 trials	11	-0.47 (-0.80, -0.13)	0.01	0.05	0.02	
	≤28 weeks	3 trials	39	0.13 (-0.04, 0.30)	0.12	0.98	0.06	0.08

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
HDL concentrations at >3 years (mmol/L)	29 to 32 weeks	3 trials	105	-0.03 (-0.15, 0.08)	0.58	0.75	0.004	
	33 to 36 weeks	2 trials	11	-0.47 (-0.80, -0.13)	0.01	0.05	0.02	
LDL concentrations in childhood (mmol/L)	≤28 weeks	1 trial	24	0.27 (-0.21, 0.75)	0.25	N/A	N/A	0.13
	29 to 32 weeks	1 trial	53	-0.17 (-0.52, 0.17)	0.31	N/A	N/A	
LDL concentrations in adolescence (mmol/L)	≤28 weeks	3 trials	14	-0.15 (-0.59, 0.29)	0.47	0.28	0.04	0.39
	29 to 32 weeks	3 trials	52	0.19 (-0.16, 0.54)	0.27	0.91	0.03	
	33 to 36 weeks	2 trials	11	0.46 (-0.84, 1.76)	0.42	0.62	0.28	
LDL concentrations at >3 years (mmol/L)	≤28 weeks	3 trials	38	0.12 (-0.21, 0.46)	0.47	0.34	0.03	0.56
	29 to 32 weeks	3 trials	105	0.01 (-0.23, 0.25)	0.93	0.31	0.01	
	33 to 36 weeks	2 trials	11	0.46 (-0.84, 1.76)	0.42	0.62	0.28	
Blood glucose concentrations in childhood (mmol/L)	≤28 weeks	1 trial	24	0.18 (-0.42, 0.79)	0.53	N/A	N/A	0.36
	29 to 32 weeks	1 trial	47	-0.09 (-0.43, 0.24)	0.58	N/A	N/A	
Blood glucose concentrations in adolescence (mmol/L)	≤28 weeks	3 trials	15	-0.08 (-0.40, 0.23)	0.57	0.04	0.02	0.19
	29 to 32 weeks	3 trials	52	-0.21 (-0.41, -0.01)	0.04	0.05	0.01	
	33 to 36 weeks	2 trials	11	0.35 (0.01, 0.68)	0.04	0.09	0.02	
	≤28 weeks	3 trials	39	0.07 (-0.30, 0.45)	0.70	0.61	0.03	0.25
	29 to 32 weeks	3 trials	99	-0.17 (-0.35, 0.02)	0.07	0.81	0.01	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Blood glucose concentrations at >3 years (mmol/L)	33 to 36 weeks	2 trials	11	0.35 (0.01, 0.68)	0.04	0.09	0.02	
BMI in childhood (kg/m²)	≤28 weeks	3 trials	121	0.62 (-0.03, 1.26)	0.06	0.15	0.11	0.01
	29 to 32 weeks	3 trials	187	-0.46 (-0.93, 0.01)	0.06	<.0001	0.06	
	33 to 36 weeks	2 trials	25	-0.84 (-1.91, 0.23)	0.51	0.13	0.03	
BMI in adolescence (kg/m²)	≤28 weeks	2 trials	17	-2.07 (-5.44, 1.30)	0.21	0.62	2.40	0.25
	29 to 32 weeks	2 trials	70	0.27 (-1.52, 2.06)	0.76	0.006	0.81	
	33 to 36 weeks	2 trials	16	2.81 (-1.16, 6.78)	0.15	0.36	3.24	
BMI at >3 years (kg/m²)	≤28 weeks	5 trials	138	0.33 (-0.35, 1.01)	0.34	0.04	0.11	0.44
	29 to 32 weeks	5 trials	257	-0.26 (-0.85, 0.32)	0.30	<.0001	0.09	
	33 to 36 weeks	4 trials	41	0.12 (-1.46, 1.70)	0.78	0.04	0.01	
BMI z-score in childhood	≤28 weeks	3 trials	121	0.38 (-0.03, 0.79)	0.06	0.01	0.04	0.01
	29 to 32 weeks	3 trials	187	-0.33 (-0.62, -0.03)	0.03	<.0001	0.02	
	33 to 36 weeks	2 trials	25	-0.63 (-1.34, 0.09)	0.08	0.09	0.12	
BMI z-score in adolescence	≤28 weeks	2 trials	17	0.83 (-1.00, 2.67)	0.34	0.34	0.40	0.56
	29 to 32 weeks	2 trials	70	-0.08 (-0.71, 0.55)	0.80	0.002	0.10	
	33 to 36 weeks	2 trials	16	-0.51 (-1.89, 0.87)	0.44	0.51	0.69	
	≤28 weeks	5 trials	138	0.27 (-0.11, 0.66)	0.27	0.13	0.04	0.10

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
BMI z-score at >3 years	29 to 32 weeks	5 trials	257	-0.26 (-0.54, 0.01)	0.06	<.0001	0.02	
	33 to 36 weeks	4 trials	41	0.34 (-0.82, 0.55)	0.69	0.05	0.04	
Fasting insulin in childhood (pmol/L)	≤28 weeks	1 trial	34	0.65 (-16.01, 17.31)	0.94	N/A	N/A	0.42
	29 to 32 weeks	1 trial	54	6.46 (-6.61, 19.53)	0.33	N/A	N/A	
Fasting insulin in adolescence (pmol/L)	≤28 weeks	3 trials	15	-13.25 (-35.27, 8.76)	0.21	0.25	97.61	0.18
	29 to 32 weeks	3 trials	48	-5.88 (-24.64, 12.88)	0.53	0.41	86.49	
	33 to 36 weeks	2 trials	13	30.03 (-15.88, 75.94)	0.17	0.18	396.01	
Fasting insulin at >3 years (pmol/L)	≤28 weeks	3 trials	49	-4.06 (16.59, 8.47)	0.52	0.37	38.56	0.17
	29 to 32 weeks	3 trials	102	-0.60 (-11.54, 10.35)	0.91	0.39	30.36	
	33 to 36 weeks	2 trials	13	30.03 (-15.88, 75.94)	0.17	0.18	396.41	
IGF-I in adolescence (nmol/L)	≤28 weeks	2 trials	15	-10.57 (-34.05, 13.67)	0.34	0.0002	111.73	0.26
	29 to 32 weeks	2 trials	49	1.47 (-9.12, 12.07)	0.78	0.55	27.67	
	33 to 36 weeks	2 trials	13	12.27 (-22.91, 47.44)	0.45	0.10	232.56	

Abbreviation: SBP: systolic blood pressure; DBP diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; N/A: not applicable
Relative risk and mean difference were adjusted for sex and birthweight z-scores.

Table S5. Subgroup analyses of timing of supplements

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Cognitive impairment in toddlers	In hospital	7 trials	653	0.91 (0.69, 1.20)	0.50	0.83	0.02	0.89
	Post discharge	6 trials	757	1.02 (0.75, 1.38)	0.89	0.69	0.02	
Metabolic risk in childhood	In hospital	1 trial	55	0.40 (0.14, 1.10)	0.07	N/A	N/A	0.04
	Post discharge	2 trials	279	1.16 (0.86, 1.56)	0.32	0.53	0.02	
Metabolic risk in adolescence	In hospital	1 trial	36	0.59 (0.38, 0.92)	0.02	N/A	N/A	0.04
	Post discharge	1 trial	68	1.11 (0.77, 1.59)	0.58	N/A	N/A	
Metabolic risk at >3 years	In hospital	2 trials	91	0.55 (0.34, 0.89)	0.02	0.43	0.06	0.003
	Post discharge	3 trials	347	1.12 (0.88, 1.42)	0.37	0.80	0.01	
Cognitive scores in toddlers	In hospital	7 trials	653	1.31 (-1.25, 3.86)	0.32	0.73	1.69	0.58
	Post discharge	6 trials	757	0.02 (-1.83, 1.87)	0.99	0.58	0.88	
Motor impairment in toddlers	In hospital	7 trials	652	0.95 (0.78, 1.17)	0.65	0.97	0.01	0.31
	Post discharge	6 trials	754	0.82 (0.56, 1.21)	0.32	0.84	0.04	
Motor scores in toddlers	In hospital	7 trials	652	1.16 (-0.63, 3.94)	0.16	0.92	1.35	0.97

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
	Post discharge	6 trials	754	1.32 (-0.44, 3.08)	0.14	0.008	0.80	
SBP in childhood (mmHg)	In hospital	None	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	2 trials	253	0.95 (-1.41, 3.32)	0.43	0.46	1.42	
SBP in adolescence (mmHg)	In hospital	1 trial	36	-2.95 (-9.22, 3.32)	0.34	N/A	N/A	0.11
	Post discharge	1 trial	65	3.64 (-1.06, 8.35)	0.54	N/A	N/A	
SBP at >3 years (mmHg)	In hospital	1 trial	36	-2.95 (-9.22, 3.32)	0.34	N/A	N/A	0.19
	Post discharge	3 trials	318	1.41 (-0.68, 3.51)	0.19	0.55	1.14	
DBP in childhood (mmHg)	In hospital	None	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	2 trials	253	-0.60 (-2.75, 1.54)	0.58	0.83	1.19	
DBP in adolescence (mmHg)	In hospital	1 trial	36	-1.07 (-6.22, 4.08)	0.67	N/A	N/A	0.26
	Post discharge	1 trial	65	1.72 (-1.87, 5.31)	0.34	N/A	N/A	
DBP at >3 years (mmHg)	In hospital	1 trial	36	-1.07 (-6.22, 4.08)	0.67	N/A	N/A	0.55
	Post discharge	3 trials	318	-0.14 (-1.98, 1.71)	0.89	0.61	0.88	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
MAP in childhood (mmHg)	In hospital	None	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	2 trials	270	-0.31 (-2.34, 1.72)	0.76	0.82	1.06	
MAP in adolescence (mmHg)	In hospital	1 trial	34	-3.97 (-9.55, 1.61)	0.16	N/A	N/A	0.06
	Post discharge	1 trial	65	2.36 (-1.38, 6.11)	0.21	N/A	N/A	
MAP at >3 years (mmHg)	In hospital	1 trial	34	-3.97 (-9.55, 1.61)	0.16	N/A	N/A	0.16
	Post discharge	3 trials	335	0.18 (-1.59, 1.96)	0.84	0.52	0.81	
Triglyceride concentrations in childhood (mmol/L)	In hospital	none	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	1 trial	77	-0.12 (-0.22, -0.01)	0.03	N/A	N/A	
Triglyceride concentrations in adolescence (mmol/L)	In hospital	1 trial	27	-0.54 (-1.49, 0.40)	0.25	N/A	N/A	0.07
	Post discharge	1 trial	51	0.09 (-0.11, 0.29)	0.37	N/A	N/A	
Triglyceride concentrations at >3 years (mmol/L)	In hospital	1 trial	27	-0.50 (-0.90, -0.10)	0.01	N/A	N/A	0.04
	Post discharge	2 trials	128	-0.04 (-0.22, 0.14)	0.67	0.05	0.003	
	In hospital	none	N/A	N/A	N/A	N/A	N/A	N/A

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Cholesterol concentrations in childhood (mmol/L)	Post discharge	1 trial	78	-0.12 (-0.45, 0.20)	0.45	N/A	N/A	
Cholesterol concentrations in adolescence (mmol/L)	In hospital	1 trial	27	0.64 (-0.29, 1.56)	0.17	N/A	N/A	0.42
	Post discharge	1 trial	51	0.18 (-0.22, 0.58)	0.38	N/A	N/A	
Cholesterol concentrations at >3 years	In hospital	1 trial	27	0.64 (-0.29, 1.56)	0.17	N/A	N/A	0.13
	Post discharge	2 trials	129	0.01 (-0.24, 0.26)	0.94	0.21	0.01	
HDL concentrations in childhood (mmol/L)	In hospital	none	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	1 trial	77	0.02 (-0.12, 0.16)	0.74	N/A	N/A	
HDL concentrations in adolescence (mmol/L)	In hospital	1 trial	27	-0.02 (-0.31, 0.27)	0.89	N/A	N/A	0.97
	Post discharge	1 trial	51	-0.03 (-0.18, 0.12)	0.70	N/A	N/A	
HDL concentrations at >3 years (mmol/L)	In hospital	1 trial	27	-0.02 (-0.31, 0.27)	0.89	N/A	N/A	0.82
	Post discharge	2 trials	128	0.01 (-0.09, 0.11)	0.86	0.64	0.03	
LDL concentrations in childhood (mmol/L)	In hospital	none	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	1 trial	77	-0.08 (-0.36, 0.19)	0.56	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
LDL concentrations in adolescence (mmol/L)	In hospital	1 trial	27	0.27 (-0.16, 0.70)	0.21	N/A	N/A	0.85
	Post discharge	1 trial	50	0.16 (-0.21, 0.53)	0.38	N/A	N/A	
LDL concentrations at >3 years (mmol/L)	In hospital	1 trial	27	0.27 (-0.16, 0.70)	0.21	N/A	N/A	0.72
	Post discharge	2 trials	127	0.02 (-0.19, 0.24)	0.82	0.25	0.01	
Blood glucose concentrations in childhood (mmol/L)	In hospital	none	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	1 trial	71	-0.02 (-0.30, 0.27)	0.91	N/A	N/A	
Blood glucose concentrations in adolescence (mmol/L)	In hospital	1 trial	27	-0.34 (-0.66, -0.02)	0.04	N/A	N/A	0.13
	Post discharge	1 trial	51	-0.03 (-0.21, 0.14)	0.67	N/A	N/A	
Blood glucose concentrations at >3 years (mmol/L)	In hospital	1 trial	27	-0.34 (-0.66, -0.02)	0.04	N/A	N/A	0.24
	Post discharge	2 trials	122	-0.04 (-0.21, 0.14)	0.70	0.79	0.01	
BMI in childhood (kg/m^2)	In hospital	1 trial	55	-0.61 (-1.80, 0.57)	0.30	N/A	N/A	0.23
	Post discharge	2 trials	278	-0.01 (-0.37, 0.35)	0.97	0.46	0.03	
	In hospital	1 trial	36	-2.49 (-4.51, -0.48)	0.02	N/A	N/A	0.02

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
BMI in adolescence (kg/m^2)	Post discharge	1 trial	67	1.40 (-0.48, 3.27)	0.14	N/A	N/A	
BMI at >3 years (kg/m^2)	In hospital	2 trials	91	-1.17 (-2.25, -0.10)	0.03	0.18	0.29	0.01
	Post discharge	3 trials	345	0.26 (-0.20, 0.71)	0.27	0.06	0.05	
BMI z-score in childhood	In hospital	1 trial	55	-0.29 (-1.01, 0.43)	0.43	N/A	N/A	0.48
	Post discharge	2 trials	278	-0.06 (-0.29, 0.18)	0.63	0.51	0.01	
BMI z-score in adolescence	In hospital	1 trial	36	-1.20 (-2.08, -0.31)	0.01	N/A	N/A	0.01
	Post discharge	1 trial	67	0.47 (-0.17, 1.11)	0.15	N/A	N/A	
BMI z-score at >3 years	In hospital	2 trials	91	-0.55 (-1.11, 0.02)	0.06	0.22	0.08	0.02
	Post discharge	3 trials	345	0.04 (-0.18, 0.26)	0.73	0.18	0.01	
Fasting insulin in childhood (pmol/L)	In hospital	none	N/A	N/A	N/A	N/A	N/A	N/A
	Post discharge	1 trial	88	2.48 (-7.51, 12.47)	0.62	N/A	N/A	
Fasting insulin in adolescence (pmol/L)	In hospital	1 trial	27	-27.74 (-47.54, -1.94)	0.03	N/A	N/A	0.34
	Post discharge	1 trial	49	2.29 (-15.09, 19.68)	0.79	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Fasting insulin at >3 years (pmol/L)	In hospital	1 trial	27	-27.74 (-47.54, -1.94)	0.03	N/A	N/A	0.21
	Post discharge	2 trials	137	1.68 (-7.04, 10.39)	0.70	0.87	19.36	
IGF-I in adolescence (nmol/L)	In hospital	1 trial	28	-8.41 (-21.91, 5.09)	0.21	N/A	N/A	0.87
	Post discharge	1 trial	49	3.45 (-8.11, 15.01)	0.55	N/A	N/A	
Abbreviation: SBP: systolic blood pressure; DBP diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; N/A: not applicable. Relative risk and mean difference were adjusted for sex, gestational age and birthweight z-scores.								

Table S6. Subgroup analyses of type of supplement

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Cognitive impairment in toddlers	Protein	1 trial	55	1.58 (0.28, 8.81)	0.59	N/A	N/A	0.37
	Multicomponent	12 trials	1355	0.92 (0.73, 1.17)	0.51	0.90	0.01	
Metabolic risk in childhood	Protein	1 trial	55	0.40 (0.14, 1.10)	0.07	N/A	N/A	0.04
	Multicomponent	2 trials	279	1.16 (0.86, 1.56)	0.32	0.53	0.02	
Metabolic risk in adolescence	Protein	1 trial	36	0.59 (0.38, 0.92)	0.02	N/A	N/A	0.04
	Multicomponent	1 trial	68	1.11 (0.77, 1.59)	0.58	N/A	N/A	
Metabolic risk at >3 years	Protein	2 trials	91	0.55 (0.34, 0.89)	0.02	0.43	0.06	0.003
	Multicomponent	3 trials	347	1.12 (0.88, 1.42)	0.37	0.80	0.01	
Cognitive scores in toddlers	Protein	1 trial	55	1.86 (-6.53, 10.25)	0.66	N/A	N/A	0.86
	Multicomponent	12 trials	1355	0.71 (-0.88, 2.30)	0.38	0.71	0.64	
Motor impairment in toddlers	Protein	1 trial	55	0.82 (0.12, 5.75)	0.84	N/A	N/A	0.78
	Multicomponent	12 trials	1351	0.82 (0.65, 1.04)	0.10	0.98	0.01	
	Protein	1 trial	55	4.56 (-5.11, 14.22)	0.35	N/A	N/A	0.46

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Motor scores in toddlers	Multicomponent	12 trials	1351	0.73 (0.02, 2.87)	0.05	0.19	0.53	
SBP in childhood (mmHg)	Protein	None	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	2 trials	253	0.95 (-1.41, 3.32)	0.43	0.46	1.42	
SBP in adolescence (mmHg)	Protein	1 trial	36	-2.95 (-9.22, 3.32)	0.34	N/A	N/A	0.11
	Multicomponent	1 trial	65	3.64 (-1.06, 8.35)	0.54	N/A	N/A	
SBP at >3 years (mmHg)	Protein	1 trial	36	-2.95 (-9.22, 3.32)	0.34	N/A	N/A	0.19
	Multicomponent	3 trials	318	1.41 (-0.68, 3.51)	0.19	0.55	1.14	
DBP in childhood (mmHg)	Protein	None	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	2 trials	253	-0.60 (-2.75, 1.54)	0.58	0.83	1.19	
DBP in adolescence (mmHg)	Protein	1 trial	36	-1.07 (-6.22, 4.08)	0.67	N/A	N/A	0.26
	Multicomponent	1 trial	65	1.72 (-1.87, 5.31)	0.34	N/A	N/A	
DBP at >3 years (mmHg)	Protein	1 trial	36	-1.07 (-6.22, 4.08)	0.67	N/A	N/A	0.55
	Multicomponent	3 trials	318	-0.14 (-1.98, 1.71)	0.89	0.61	0.88	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
MAP in childhood (mmHg)	Protein	None	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	2 trials	270	-0.31 (-2.34, 1.72)	0.76	0.82	1.06	
MAP in adolescence (mmHg)	Protein	1 trial	34	-3.97 (-9.55, 1.61)	0.16	N/A	N/A	0.06
	Multicomponent	1 trial	65	2.36 (-1.38, 6.11)	0.21	N/A	N/A	
MAP at >3 years (mmHg)	Protein	1 trial	34	-3.97 (-9.55, 1.61)	0.16	N/A	N/A	0.16
	Multicomponent	3 trials	335	0.18 (-1.59, 1.96)	0.84	0.52	0.81	
Triglyceride concentrations in childhood (mmol/L)	Protein	none	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	1 trial	77	-0.12 (-0.22, -0.01)	0.03	N/A	N/A	
Triglyceride concentrations in adolescence (mmol/L)	Protein	1 trial	27	-0.54 (-1.49, 0.40)	0.25	N/A	N/A	0.07
	Multicomponent	1 trial	51	0.09 (-0.11, 0.29)	0.37	N/A	N/A	
Triglyceride concentrations at >3 years (mmol/L)	Protein	1 trial	27	-0.54 (-1.49, 0.40)	0.25	N/A	N/A	0.04
	Multicomponent	2 trials	128	-0.04 (-0.15, 0.06)	0.41	0.05	0.003	
	Protein	none	N/A	N/A	N/A	N/A	N/A	N/A

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cholesterol concentrations in childhood (mmol/L)	Multicomponent	1 trial	78	-0.12 (-0.45, 0.20)	0.45	N/A	N/A	
Cholesterol concentrations in adolescence (mmol/L)	Protein	1 trial	27	0.64 (-0.29, 1.56)	0.17	N/A	N/A	0.42
	Multicomponent	1 trial	51	0.18 (-0.22, 0.58)	0.38	N/A	N/A	
Cholesterol concentrations at >3 years (mmol/L)	Protein	1 trial	27	0.64 (-0.29, 1.56)	0.17	N/A	N/A	0.13
	Multicomponent	2 trials	129	0.01 (-0.24, 0.26)	0.94	0.21	0.01	
HDL concentrations in childhood (mmol/L)	Protein	none	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	1 trial	77	0.02 (-0.12, 0.16)	0.74	N/A	N/A	
HDL concentrations in adolescence (mmol/L)	Protein	1 trial	27	-0.02 (-0.31, 0.27)	0.89	N/A	N/A	0.97
	Multicomponent	1 trial	51	-0.03 (-0.18, 0.12)	0.70	N/A	N/A	
HDL concentrations at >3 years (mmol/L)	Protein	1 trial	27	-0.02 (-0.31, 0.27)	0.89	N/A	N/A	0.82
	Multicomponent	2 trials	128	0.01 (-0.09, 0.11)	0.86	0.64	0.03	
LDL concentrations in childhood (mmol/L)	Protein	none	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	1 trial	77	-0.08 (-0.36, 0.19)	0.56	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
LDL concentrations in adolescence (mmol/L)	Protein	1 trial	27	0.27 (-0.16, 0.70)	0.21	N/A	N/A	0.85
	Multicomponent	1 trial	50	0.16 (-0.21, 0.53)	0.38	N/A	N/A	
LDL concentrations at >3 years (mmol/L)	Protein	1 trial	27	0.27 (-0.16, 0.70)	0.21	N/A	N/A	0.72
	Multicomponent	2 trials	127	0.02 (-0.19, 0.24)	0.82	0.25	0.01	
Blood glucose concentrations in childhood (mmol/L)	Protein	none	N/A	N/A	N/A	N/A	N/A	N/A
	Multicomponent	1 trial	71	-0.02 (-0.30, 0.27)	0.91	N/A	N/A	
Blood glucose concentrations in adolescence (mmol/L)	Protein	1 trial	27	-0.34 (-0.66, -0.02)	0.04	N/A	N/A	0.13
	Multicomponent	1 trial	51	-0.03 (-0.21, 0.14)	0.67	N/A	N/A	
Blood glucose concentrations at >3 years (mmol/L)	Protein	1 trial	27	-0.34 (-0.66, -0.02)	0.04	N/A	N/A	0.24
	Multicomponent	2 trials	122	-0.04 (-0.21, 0.14)	0.70	0.79	0.01	
BMI in childhood (kg/m^2)	Protein	1 trial	55	-0.61 (-1.80, 0.57)	0.30	N/A	N/A	0.23
	Multicomponent	2 trials	278	-0.01 (-0.37, 0.35)	0.97	0.46	0.03	
	Protein	1 trial	36	-2.49 (-4.51, -0.48)	0.02	N/A	N/A	0.02

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
BMI in adolescence (kg/m^2)	Multicomponent	1 trial	67	1.40 (-0.48, 3.27)	0.14	N/A	N/A	
BMI at >3 years (kg/m^2)	Protein	2 trials	91	-1.17 (-2.25, -0.10)	0.03	0.18	0.29	0.01
	Multicomponent	3 trials	345	0.26 (-0.20, 0.71)	0.27	0.06	0.05	
BMI z-score in childhood	Protein	1 trial	55	-0.29 (-1.01, 0.43)	0.43	N/A	N/A	0.48
	Multicomponent	2 trials	278	-0.06 (-0.29, 0.18)	0.63	0.51	0.01	
BMI z-score in adolescence	Protein	1 trial	36	-1.20 (-2.08, -0.31)	0.01	N/A	N/A	0.01
	Multicomponent	1 trial	67	0.47 (-0.17, 1.11)	0.15	N/A	N/A	
BMI z-score at >3 years	Protein	2 trials	91	-0.55 (-1.11, 0.02)	0.06	0.22	0.08	0.02
	Multicomponent	3 trials	345	0.04 (-0.18, 0.26)	0.73	0.18	0.01	
Fasting insulin in childhood (pmol/L)	Protein	none					N/A	N/A
	Multicomponent	1 trial	88	2.48 (-7.51, 12.47)	0.62	N/A	N/A	
Fasting insulin in adolescence (pmol/L)	Protein	1 trial	27	-27.74 (-47.54, -1.94)	0.03	N/A	N/A	0.34
	Multicomponent	1 trial	49	2.29 (-15.09, 19.68)	0.79	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Fasting insulin at >3 years (pmol/L)	Protein	1 trial	27	-27.74 (-47.54, -1.94)	0.03	N/A	N/A	0.21
	Multicomponent	2 trials	137	1.68 (-7.04, 10.39)	0.70	0.87	19.36	
IGF-I in adolescence (nmol/L)	Protein	1 trial	28	-8.41 (-21.91, 5.09)	0.21	N/A	N/A	0.87
	Multicomponent	1 trial	49	3.45 (-8.11, 15.01)	0.55	N/A	N/A	
Abbreviation: SBP: systolic blood pressure; DBP diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; N/A: not applicable Relative risk and mean difference were adjusted for sex, gestational age and birthweight z-scores.								

Table S7. Subgroup analyses of primary milk feed

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cognitive impairment in toddlers	BM	6 trials	541	1.03 (0.72, 1.48)	0.87	0.84	0.03	0.54
	Formula	5 trials	704	1.02 (0.74, 1.39)	0.92	0.56	0.02	
	PN+EN	2 trials	165	0.76 (0.54, 1.07)	0.12	0.77	0.03	
Cognitive impairment at >3 years	BM	1 trial	137	1.01 (0.63, 1.60)	0.98	N/A	N/A	0.63
	Formula	1 trial	69	1.15 (0.50, 2.64)	0.73	N/A	N/A	
Metabolic risk in childhood	BM	2 trials	206	0.85 (0.59, 1.22)	0.38	0.12	0.03	0.12
	Formula	1 trial	128	1.34 (0.83, 2.18)	0.23	N/A	N/A	
Metabolic risk in adolescence	BM	none	N/A	N/A	N/A	N/A	N/A	N/A
	Formula	2 trials	104	0.86 (0.66, 1.11)	0.24	0.27	0.02	
Metabolic risk at >3 years	BM	2 trials	206	0.85 (0.59, 1.22)	0.38	0.12	0.03	0.51
	Formula	3 trials	232	0.98 (0.76, 1.26)	0.87	0.30	0.17	
Cognitive scores in toddlers	BM	6 trials	541	0.68 (-2.17, 3.53)	0.64	0.82	2.10	0.40
	Formula	5 trials	704	-0.25 (-2.20, 1.70)	0.80	0.60	0.98	
	PN+EN	2 trials	165	3.75 (-0.58, 8.08)	0.09	0.49	4.84	
Cognitive scores at >3 years	BM	1 trial	137	-2.84 (-6.33, 0.65)	0.11	N/A	N/A	0.69
	Formula	1 trial	69	-1.45 (-8.76, 5.86)	0.69	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Motor impairment in toddlers	BM	6 trials	541	0.94 (0.69, 1.27)	0.67	0.89	0.02	0.64
	Formula	5 trials	701	0.83 (0.56, 1.24)	0.37	0.74	0.04	
	PN+EN	2 trials	264	0.98 (0.73, 1.32)	0.90	0.87	0.02	
Motor scores in toddlers	BM	6 trials	541	2.32 (0.05, 5.06)	0.046	0.87	23.14	0.64
	Formula	5 trials	701	1.02 (-0.82, 2.85)	0.28	0.006	0.86	
	PN+EN	2 trials	264	0.28 (-4.00, 4.55)	0.90	0.38	4.67	
SBP in childhood (mmHg)	BM	1 trial	126	1.74 (-1.82, 5.29)	0.34	N/A	N/A	0.47
	Formula	1 trial	127	0.05 (-3.15, 3.24)	0.98	N/A	N/A	
SBP in adolescence (mmHg)	BM	None	N/A	N/A	N/A	N/A	N/A	N/A
	Formula	2 trials	101	1.13 (-2.52, 4.77)	0.54	0.11	3.24	
SBP at >3 years (mmHg)	BM	1 trial	126	1.74 (-1.82, 5.29)	0.34	N/A	N/A	0.51
	Formula	3 trials	228	0.52 (-1.86, 2.89)	0.52	0.22	1.44	
DBP in childhood (mmHg)	BM	1 trial	126	-1.16 (-4.57, 2.24)	0.50	N/A	N/A	0.83
	Formula	1 trial	127	-0.50 (-3.12, 2.12)	0.71	N/A	N/A	
	BM	None	N/A	N/A	N/A	N/A	N/A	N/A

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
DBP in adolescence (mmHg)	Formula	2 trials	101	0.51 (-2.29, 3.30)	0.72	0.26	1.99	
DBP at >3 years (mmHg)	BM	1 trial	126	-1.16 (-4.57, 2.24)	0.50	N/A	N/A	0.66
	Formula	3 trials	228	-0.14 (-2.04, 1.75)	0.88	0.38	0.92	
MAP in childhood (mmHg)	BM	1 trial	143	-0.73 (-3.66, 2.21)	0.62	N/A	N/A	0.82
	Formula	1 trial	127	-0.18 (-3.00, 2.64)	0.90	N/A	N/A	
MAP in adolescence (mmHg)	BM	None	N/A	N/A	N/A	N/A	N/A	N/A
	Formula	2 trials	99	0.27 (-2.68, 3.21)	0.86	0.06	2.22	
MAP at >3 years (mmHg)	BM	1 trial	143	-0.73 (-3.66, 2.21)	0.62	N/A	N/A	0.74
	Formula	3 trials	226	-0.05 (-2.07, 1.97)	0.96	0.14	1.04	
Triglyceride concentrations at >3 years (mmol/L)	BM	1 trial	77	-0.12 (-0.22, -0.01)	0.03	N/A	N/A	0.88
	Formula	2 trials	78	-0.09 (-0.41, 0.23)	0.57	0.06	0.03	
Cholesterol concentrations at >3 years (mmol/L)	BM	1 trial	78	-0.12 (-0.45, 0.20)	0.45	N/A	N/A	0.11
	Formula	2 trials	78	0.25 (-0.14, 0.64)	0.21	0.52	0.04	
	BM	1 trial	77	0.02 (-0.12, 0.16)	0.74	N/A	N/A	0.61

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
HDL concentrations at >3 years (mmol/L)	Formula	2 trials	78	-0.02 (-0.15, 0.11)	0.78	0.92	0.004	
LDL concentrations at >3 years (mmol/L)	BM	1 trial	77	-0.08 (-0.36, 0.19)	0.56	N/A	N/A	0.25
	Formula	2 trials	77	0.12 (-0.16, 0.40)	0.38	0.65	0.02	
Blood glucose concentrations at >3 years (mmol/L)	BM	1 trial	71	-0.02 (-0.30, 0.27)	0.91	N/A	N/A	0.46
	Formula	2 trials	78	-0.13 (-0.28, 0.02)	0.10	0.14	0.01	
BMI in childhood (kg/m²)	BM	2 trials	206	-0.26 (-0.71, 0.19)	0.25	0.42	0.05	0.26
	Formula	1 trial	127	0.14 (-0.47, 0.75)	0.65	N/A	N/A	
BMI in adolescence (kg/m²)	BM	none	N/A	N/A	N/A	N/A	N/A	N/A
	Formula	2 trials	103	0.14 (-1.27, 1.56)	0.84	0.02	0.50	
BMI at >3 years (kg/m²)	BM	2 trials	206	-0.26 (-0.71, 0.19)	0.25	0.42	0.05	0.32
	Formula	3 trials	230	0.14 (-0.56, 0.84)	0.70	0.01	0.13	
BMI z-score in childhood	BM	2 trials	206	-0.17 (-0.47, 0.12)	0.25	0.72	0.02	0.37
	Formula	1 trial	127	0.03 (-0.34, 0.39)	0.88	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
BMI z-score in adolescence	BM	none	N/A	N/A	N/A	N/A	N/A	N/A
	Formula	2 trials	103	-0.08 (-0.60, 0.44)	0.76	0.01	0.07	
BMI z-score at >3 years	BM	2 trials	206	-0.17 (-0.47, 0.12)	0.25	0.72	0.02	0.44
	Formula	3 trials	230	-0.03 (-0.33, 0.27)	0.84	0.01	0.02	
Fasting insulin at >3 years (pmol/L)	BM	1 trial	88	2.48 (-7.51, 12.47)	0.62	N/A	N/A	0.46
	Formula	2 trials	76	-2.57 (-16.24, 11.11)	0.71	0.32	47.06	

Abbreviation: BM: breast milk; SBP: systolic blood pressure; DBP diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; NA, not applicable; BM: breast milk; PN: parenteral nutrition; EN: enteral nutrition

Relative risk and mean difference were adjusted for sex, gestational age and birthweight z-scores.

Table S8. Subgroup analyse of different epochs

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
Cognitive impairment in toddlers	Before or in 2000	6 trials	945	1.00 (0.75, 1.33)	0.99	0.79		0.70
	After 2000	7 trials	465	0.87 (0.65, 1.16)	0.35	0.80		
Cognitive impairment at >3 years	Before or in 2000	1 trial	69	1.15 (0.50, 2.64)	0.73	N/A	N/A	0.63
	After 2000	1 trial	137	1.01 (0.63, 1.60)	0.98	N/A	N/A	
Metabolic risk in childhood	Before or in 2000	1 trial	128	1.34 (0.83, 2.18)	0.23	N/A	N/A	0.12
	After 2000	2 trials	206	0.85 (0.59, 1.22)	0.38	0.12	0.03	
Metabolic risk in adolescence	Before or in 2000	1 trial	68	1.11 (0.73, 1.68)	0.63	N/A	N/A	0.04
	After 2000	1 trial	36	0.59 (0.36, 0.97)	0.04	N/A	N/A	
Metabolic risk at >3 years	Before or in 2000	2 trials	196	1.16 (0.85, 1.59)	0.34	0.62	0.02	0.06
	After 2000	3 trials	242	0.78 (0.58, 1.05)	0.09	0.25	0.02	
Cognitive scores in toddlers	Before or in 2000	6 trials	945	0.34 (-1.66, 2.34)	0.40	0.83		0.42
	After 2000	7 trials	465	1.62 (-0.80, 4.04)	0.19	0.44		
Cognitive scores at >3 years	Before or in 2000	1 trial	69	-1.45 (-8.76, 5.86)	0.69	N/A	N/A	0.69
	After 2000	1 trial	137	-2.84 (-6.33, 0.65)	0.11	N/A	N/A	
Motor impairment in toddlers	Before or in 2000	6 trials	943	0.87 (0.63, 1.21)	0.62	0.48		0.94
	After 2000	7 trials	463	0.84 (0.62, 1.14)	0.25	0.99		

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
Motor scores in toddlers	Before or in 2000	6 trials	943	1.34 (-0.37, 3.04)	0.13	0.03		0.69
	After 2000	7 trials	463	2.01 (-0.54, 4.57)	0.12	0.87		
SBP in childhood (mmHg)	Before or in 2000	1 trial	127	0.04 (-3.15, 3.24)	0.65	N/A	N/A	0.46
	After 2000	1 trial	126	1.74 (-1.82, 5.29)	0.34	N/A	N/A	
SBP in adolescence (mmHg)	Before or in 2000	1 trial	65	3.64 (-1.06, 8.35)	0.13	N/A	N/A	0.11
	After 2000	1 trial	36	-2.95 (-9.22, 3.32)	0.35	N/A	N/A	
SBP at >3 years (mmHg)	Before or in 2000	2 trials	192	1.23 (-1.40, 3.85)	0.36	0.23	2.25	0.89
	After 2000	2 trials	162	0.84 (-2.14. 3.82)	0.56	0.24	2.25	
DBP in childhood (mmHg)	Before or in 2000	1 trial	127	-0.50 (-3.12, 2.12)	0.71	N/A	N/A	0.83
	After 2000	1 trial	126	-1.16 (-4.57, 2.45)	0.50	N/A	N/A	
DBP in adolescence (mmHg)	Before or in 2000	1 trial	65	1.72 (-1.87, 5.31)	0.34	N/A	N/A	0.26
	After 2000	1 trial	36	-1.07 (-6.22, 4.08)	0.67	N/A	N/A	
DBP at >3 years (mmHg)	Before or in 2000	2 trials	192	0.28 (-1.80, 2.37)	0.79	0.33	1.12	0.42
	After 2000	2 trials	162	-1.07 (-3.86, 1.72)	0.45	0.89	1.99	
MAP in childhood (mmHg)	Before or in 2000	1 trial	127	-0.18 (-2.99, 2.64)	0.90	N/A	N/A	0.82
	After 2000	1 trial	143	-0.73 (-3.66, 2.21)	0.62	N/A	N/A	
MAP in adolescence (mmHg)	Before or in 2000	1 trial	65	2.36 (-1.38, 6.11)	0.21	N/A	N/A	0.05
	After 2000	1 trial	34	-3.97 (-9.55, 1.61)	0.16	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
MAP at >3 years (mmHg)	Before or in 2000	2 trials	192	0.66 (-1.57, 2.88)	0.56	0.32	0.44	0.26
	After 2000	2 trials	177	-1.15 (-3.67, 1.36)	0.37	0.47	1.61	
Triglyceride concentration in childhood (mmol/L)	Before or in 2000	none	N/A	N/A	N/A	N/A	N/A	N/A
	After 2000	1 trial	77	-0.12 (-0.22, -0.01)	0.03	N/A	N/A	
Triglyceride concentration in adolescence (mmol/L)	Before or in 2000	1 trial	51	0.09 (-0.11, 0.29)	0.37	N/A	N/A	0.07
	After 2000	1 trial	27	-0.54 (-1.49, 0.10)	0.25	N/A	N/A	
Triglyceride concentration at >3 years (mmol/L)	Before or in 2000	1 trial	51	0.09 (-0.11, 0.29)	0.37	N/A	N/A	0.06
	After 2000	2 trials	104	-0.23 (-0.45, -0.00)	0.05	0.12	0.03	
Cholesterol concentration in childhood (mmol/L)	Before or in 2000	none	N/A	N/A	N/A	N/A	N/A	N/A
	After 2000	1 trial	78	-0.12 (00.45, 0.20)	0.45	N/A	N/A	
Cholesterol concentration in adolescence (mmol/L)	Before or in 2000	1 trial	51	0.18 (-0.22, 0.58)	0.37	N/A	N/A	0.42
	After 2000	1 trial	27	0.64 (-0.29, 1.56)	0.17	N/A	N/A	
Cholesterol concentration at >3 years (mmol/L)	Before or in 2000	1 trial	51	0.18 (-0.22, 0.58)	0.37	N/A	N/A	0.61
	After 2000	2 trials	105	0.05 (-0.27, 0.36)	0.77	0.12	0.04	
HDL concentration in childhood (mmol/L)	Before or in 2000	none	N/A	N/A	N/A	N/A	N/A	N/A
	After 2000	1 trial	77	0.02 (-0.12, 0.16)	0.74	N/A	N/A	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau²	P for subgroup interaction
HDL concentration in adolescence (mmol/L)	Before or in 2000	1 trial	51	-0.03 (-0.18, 0.12)	0.70	N/A	N/A	0.97
	After 2000	1 trial	27	-0.02 (-0.31, 0.27)	0.90	N/A	N/A	
HDL concentration at >3 years (mmol/L)	Before or in 2000	1 trial	51	-0.03 (-0.18, 0.12)	0.70	N/A	N/A	0.76
	After 2000	2 trials	104	0.01 (-0.11, 0.13)	0.83	0.86	0.004	
LDL concentration in childhood (mmol/L)	Before or in 2000	none	N/A	N/A	N/A	N/A	N/A	N/A
	After 2000	1 trial	77	-0.08 (-0.36, 0.20)	0.56	N/A	N/A	
LDL concentration in adolescence (mmol/L)	Before or in 2000	1 trial	50	0.16 (-0.21, 0.53)	0.38	N/A	N/A	0.85
	After 2000	1 trial	27	0.27 (-0.16, 0.69)	0.21	N/A	N/A	
LDL concentration at >3 years (mmol/L)	Before or in 2000	1 trial	50	0.16 (-0.21, 0.53)	0.38	N/A	N/A	0.35
	After 2000	2 trials	104	-0.03 (-0.25, 0.20)	0.82	0.58	0.02	
Blood glucose concentration in childhood (mmol/L)	Before or in 2000	none	N/A	N/A	N/A	N/A	N/A	N/A
	After 2000	1 trial	71	-0.02 (-0.30, 0.27)	0.91	N/A	N/A	
Blood glucose concentration in adolescence (mmol/L)	Before or in 2000	1 trial	51	-0.04 (-0.21, 0.14)	0.67	N/A	N/A	0.13
	After 2000	1 trial	27	-0.34 (-0.67, -0.02)	0.04	N/A	N/A	
Blood glucose concentration at >3 years (mmol/L)	Before or in 2000	1 trial	51	-0.04 (-0.21, 0.14)	0.67	N/A	N/A	0.89
	After 2000	2 trials	98	-0.09 (-0.31, 0.14)	0.45	0.28	0.05	
	Before or in 2000	1 trial	127	0.14 (-0.47, 0.75)	0.65	N/A	N/A	0.26

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
BMI in childhood (kg/m^2)	After 2000	2 trials	206	-0.26 (-0.71, 0.19)	0.25	0.42	0.05	
BMI in adolescence (kg/m^2)	Before or in 2000	1 trial	67	1.40 (-0.48, 3.27)	0.14	N/A	N/A	0.02
	After 2000	1 trial	36	-2.49 (-4.51, -0.48)	0.02	N/A	N/A	
BMI at >3 years (kg/m^2)	Before or in 2000	2 trials	194	0.57 (-0.17, 1.32)	0.13	0.13	0.14	0.01
	After 2000	3 trials	242	-0.52 (-1.00, -0.04)	0.03	0.03	0.06	
BMI z-score in childhood	Before or in 2000	1 trial	127	0.03 (-0.34, 0.39)	0.88	N/A	N/A	0.37
	After 2000	2 trials	206	-0.17 (-0.47, 0.12)	0.25	0.72	0.03	
BMI z-score in adolescence	Before or in 2000	1 trial	67	0.47 (-0.17, 1.11)	0.15	N/A	N/A	0.006
	After 2000	1 trial	36	-1.20 (-2.08, -0.31)	0.01	N/A	N/A	
BMI z-score at >3 years	Before or in 2000	2 trials	194	0.17 (-0.15, 0.49)	0.30	0.23	0.03	0.03
	After 2000	3 trials	242	-0.29 (-0.57, -0.01)	0.04	0.14	0.02	
Fasting insulin in childhood (pmol/L)	Before or in 2000	none	N/A	N/A	N/A	N/A	N/A	N/A
	After 2000	1 trial	88	2.48 (-7.51, 12.47)	0.62	N/A	N/A	
Fasting insulin in adolescence (pmol/L)	Before or in 2000	1 trial	49	2.29 (-15.09, 19.68)	0.79	N/A	N/A	0.34
	After 2000	1 trial	27	-24.74 (-47.54, -1.94)	0.03	N/A	N/A	
Fasting insulin at >3 years (pmol/L)	Before or in 2000	1 trial	49	2.29 (-15.09, 19.68)	0.79	N/A	N/A	0.90
	After 2000	2 trials	115	-0.87 (-9.79, 8.06)	0.85	0.09	47.06	

Outcome	Subgroup	No. of trials	No. of participants	aRR or aMD (95% CI)	P for overall effect	P for heterogeneity	Tau^2	P for subgroup interaction
IGF-I in adolescence (nmol/L)	Before or in 2000	1 trail	49	3.45 (-8.11, 15.01)	0.55	N/A	N/A	0.87
	After 2000	1 trial	28	-8.41 (-21.91, 5.09)	0.21	N/A	N/A	
Abbreviation: SBP: systolic blood pressure; DBP diastolic blood pressure; MAP: mean arterial pressure; HDL: high-density lipoproteins; LDL: low-density lipoproteins; BMI: body mass index; aRR: adjusted relative risk; aMD: adjusted mean difference; NA, not applicable								

Table S9. Search strategies

Embase from 1980 to 2019 April 01	
#	Search strategies
1	exp prematurity/
2	exp low birth weight/
3	exp small for date infant/
4	exp very low birth weight/
5	(prematur* adj2 infant*).tw.
6	(prematur* adj2 newborn*).tw.
7	(prematur* adj2 neonate*).tw.
8	preterm.tw.
9	low birth weight.tw.
10	low birthweight.tw.
11	VLBW.tw.
12	LBW.tw.
13	ELBW.tw.
14	small for gestation*.tw.
15	SGA.tw.
16	(less than adj6 g).tw.
17	(less than adj3 32 weeks).tw.
18	birth weight below.tw.
19	(gestation* adj2 less than).tw.
20	or/1-19
21	exp breast feeding/
22	exp infant nutrition/
23	exp protein intake/
24	exp dietary supplement/
25	exp omega 3 fatty acid/ct, ad, dt, ig, pa [Clinical Trial, Drug Administration, Drug Therapy, Intragastric Drug Administration, Parenteral Drug Administration]
26	exp arachidonic acid/ae, ct, ad, dt, ig, pa, th [Adverse Drug Reaction, Clinical Trial, Drug Administration, Drug Therapy, Intragastric Drug Administration, Parenteral Drug Administration, Therapy]
27	exp unsaturated fatty acid/ct, dt, pa, th [Clinical Trial, Drug Therapy, Parenteral Drug Administration, Therapy]
28	exp fat intake/ae, ad, dt [Adverse Drug Reaction, Drug Administration, Drug Therapy]
29	exp enteric feeding/
30	exp parenteral nutrition/
31	exp artificial milk/
32	exp breast milk/
33	exp fortified food/
34	exp elemental diet/
35	exp baby food/
36	(breast milk or human milk).tw.
37	formula.tw.
38	PUFA supplement*.tw.
39	feed* regimen*.tw.
40	(protein* adj2 concentration*).tw.
41	probiotic$.tw.
42	parenteral*.tw.
43	enteral*.tw.
44	maternal milk.tw.
45	multinutrient supplement*.tw.

46	(breast fed or breastfed).tw.
47	prebiotic*.tw.
48	diet* supplement*.tw.
49	nutrient enriched.tw.
50	Docosahexaenoic Acid*.tw.
51	arachidonic acid*.tw.
52	(glutamine adj2 supplement*).tw.
53	(taurine adj2 supplement*).tw.
54	(calcium adj2 supplement*).tw.
55	palm olein.tw.
56	palmitic acid.tw.
57	(fortification or fortified).tw.
58	fatty acids.tw.
59	supplement* feed*.tw.
60	complementary feed*.tw.
61	nutrition*.tw.
62	Hydrolysed liquid.tw.
63	Hydrolyzed liquid.tw.
64	gamma-linoleic acid.tw.
65	(diet* adj3 protein*).tw.
66	or/21-65
67	20 and 66
68	Clinical Trial/
69	Randomized Controlled Trial/
70	exp randomization/
71	Single Blind Procedure/
72	Double Blind Procedure/
73	Crossover Procedure/
74	Placebo/
75	Randomi?ed controlled trial$.tw.
76	Rct.tw.
77	random allocation.tw.
78	randomly.tw.
79	randomly allocated.tw.
80	allocated randomly.tw.
81	(allocated adj2 random).tw.
82	Single blind$.tw.
83	Double blind$.tw.
84	((treble or triple) adj blind$).tw.
85	placebo$.tw.
86	prospective study/
87	or/68-86
88	case study/
89	case report.tw.
90	abstract report/ or letter/
91	or/88-90
92	87 not 91
93	67 and 92

Table S10. Definitions for primary outcome of metabolic risk.

Measurement	Guideline/ Equipment	Age	Abnormal	Notes
Size for gestation at birth	INTERGROWTH 21 Charts [1]	≤6 months	≤10th centile vs >10th centile	INTERGROWTH 21 charts for babies younger than 6 months [1]
Overweight/obese	WHO Growth Charts [2, 3]	<5 years [2]	Overweight: weight-for-height greater than 2 SD above WHO Child Growth Standards median; Obesity: weight-for-height greater than 3 SD above the WHO Child Growth Standards median.	Charts and tables: WHO child growth standards for children aged under 5 years [2]
		5-19 years [3]	Overweight: BMI-for-age greater than 1 SD above the WHO Growth Reference median; Obesity: greater than 2 SD above the WHO Growth Reference median.	Charts and tables: WHO growth reference for children aged between 5-19 years [2]
Waist Circumference	NHANES 2011-2014 [4]	2- 60 years	≥90th percentile [5]	
Fat mass (FM)	DXA-NHANES [6]	≥8 years	Fat Mass Index (kg/m^2) classification ranges for sex	
	BIA [7]	5-18 years	≥85th percentile (%FM)	
	ADP- BodPod [7]	5-18 years	≥85th percentile (%FM)	
	ADP- PedPod [8]	0·5-24 months	%FM greater than 1 SD above the reference mean	
	Skinfolds- NHES II, NHES III, NHANES I, NHANES II and NHANES III [9]	1·5-19 years	≥85th percentile [9]	
	Multicomponent model	0·5-24 month [8]	%FM greater than 1 SD above the reference mean	
		5-20 years [10]	FM greater than 1 SD above the reference mean	Fat mass reference data for males and females by z-score or percentile [10]

Measurement	Guideline/ Equipment	Age	Abnormal	Notes
Blood pressure	NHBPEP [11]	1 to 17 years	≥90th percentile [5] (age, sex and height specific) Charts and tables: WHO Child growth standards for length/height	Compared with Jackson LV 2007 [12], although the NHBPEP is older, it contains the appropriate age range and reported the actual numbers at each cut point.
Triglycerides	NHANES III, NHANES 1999–2004, Bogalusa, Muscatine, Fels, and Princeton [13]	4-18 years	≥90th percentile [14]	Compared to NHANES III, NCEP, and NGHS, this includes a wider age range.
	NHANES	>18 years	≥150 mg/dL (8·3 mmol/L) [13]	
HDL-C	NHANES III, NHANES 1999–2004, Bogalusa, Muscatine, Fels, and Princeton [13]	4-18 years	≤10th percentile [14]	Compared to NHANES III, NCEP, and NGHS, this includes a wider age range.
	NHANES [13]	>18 years	<40 mg/dL (2·2 mmol/L) [13] for male	
			<50 mg/dL (2·8 mmol/L) [13] for female	
LDL-C	NHANES III, NHANES 1999–2004, Bogalusa, Muscatine, Fels, and Princeton [13]	4-18 years	≥90th percentile [13]	Compared to NHANES III, this includes a wider age range.
	NCEP ATP III	>18 years	>130 mg/dL (7·2 mmol/L) [13]	
Fasting plasma glucose concentration	ADA criterion [15] (increased risk for diabetes or prediabetes)		FPG ≥100 mg/dL (5·6 mmol/L)	
Impaired glucose tolerance	ADA criterion [15] (increased risk for diabetes or prediabetes)		2 hours post meal glucose ≥140mg/dL (7·8 mmol/L) during a 75g oral glucose tolerance test	

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Table S11. Definitions for secondary outcomes.

Term	Classification	Definition	Note
Cerebral palsy		1. Cerebral palsy is a physical disability that affects movement and posture. Any definition that includes the following five key elements: (1) is an umbrella term for a group of disorders (2) is a condition that is permanent but not unchanging (3) involves a disorder of movement and/or posture and of motor function (4) is due to a non-progressive interference, lesion or abnormality, and (5) the interference, lesion or abnormality originates in the immature brain 2. As defined by investigators	Australian cerebral palsy register report - CP Register.[1]
Severity of cerebral palsy	GMFCS Level I	Children walk at home, school, outdoors and in the community. They can climb stairs without the use of a railing. Children perform gross motor skills such as running and jumping, but speed, balance and coordination are limited.	Gross Motor Function Classification System (GMFCS).[2]
	GMFCS Level II	Children walk in most settings and climb stairs holding onto a railing. They may experience difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. Children may walk with physical assistance, a handheld mobility device or used wheeled mobility over long distances. Children have only minimal ability to perform gross motor skills such as running and jumping.	
	GMFCS Level III	Children walk using a hand-held mobility device in most indoor settings. They may climb stairs holding onto a railing with supervision or assistance. Children use wheeled mobility when traveling long distances and may self-propel for shorter distances.	
	GMFCS Level IV	Children use methods of mobility that require physical assistance or powered mobility in most settings. They may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community children are transported in a manual wheelchair or use powered mobility.	
	GMFCS Level V	Children are transported in a manual wheelchair in all settings. Children are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements.	
Developmental delay or intellectual impairment	Mild	A score on scale from 2 SD to <1 SD below test mean.	Scores were obtained relative to the mean and SD for the normal birthweight population.[3]
	Moderate	A score on scale from 3 SD to <2 SD below test mean.	
	Severe	A score on scale 3 SD below test mean.	
Visual impairment	None	Presenting visual acuity 6/18 or better in the better eye.	WHO Definition of visual impairment.[4]
	Moderate/ low vision	Can see a toy and able to follow a toy. Presenting visual acuity worse than 6/18, equal to or better than 6/60 in the better eye in the better eye.	

Term	Classification	Definition	Note
	Severe/ no useful vision	Able to see light or gross movement up close (within 40cm). Presenting visual acuity worse than 6/60, equal to or better than 1/60 in the better eye.	Visual Standards- Aspects and Ranges of Vision Loss.[5]
	Blindness/ no light perception	No useful vision. Presenting visual acuity worse than 1/60 in the better eye or no light perception.	
	Legal blindness	Medically diagnosed central visual acuity of 20/200 (6/60) or less in the better eye with the best possible correction, and/or a visual field of 20 degrees or less.	American Foundation for the Blind.[6]
Hearing impairment (Classification 1)	None	None diagnosed.	WHO Grades of hearing impairment- Prevention of blindness and deafness.[7]
	Mild	Hearing level in decibels: 26-40dB A child with this level of hearing loss will have trouble hearing and understanding soft speech, speech from a distance or speech against a background of noise.	
	Moderate	Hearing level in decibels: 41-60db A child with this level of hearing loss will have difficulty hearing regular speech, even at close distance.	
	Severe	Hearing level in decibels: 61-80dB A child with this level of hearing loss may only hear very loud speech or loud sounds in the environment, such as a fire truck siren or a door slamming. Most conversational speech is not heard.	
	Profound	Hearing level in decibels: over 81dB A child with this level of hearing loss may perceive loud sounds as vibrations.	
Motor dysfunction	mild impairment	Test score between 5th and 15th centile on the Movement ABC / A score from 2 SD to <1 SD below the population mean on the BOTMP.	Movement Assessment Battery for Children (Movement ABC) Bruininks–Oseretsky Test of Motor Proficiency (BOTMP)[8]
	moderate to severe impairment	Test score less than 5th centile on the Movement ABC / more than 2 SD below the population mean on the BOTMP.	
School performance	Defined by teachers based on their observation and academic scores; at or above vs below expected performance/level for age.		Poor school performance[9]
Growth Z-scores	WHO Growth Charts.		Charts and tables: WHO child growth standards for children[10]

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