Early-life Nutrition and Cardiometabolic Health across the Life Course

Online Supplementary Material

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Supplementary Material S2.1.1. Details of the search strategy

	Before deduplication	After deduplication
Embase.com	3021	3013
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PubMed publisher	43	32
Google Scholar	200	152
Total	**6309**	**4377**

Embase.com

('carotenoid'/de OR 'xanthophyll'/de OR (carotenoid* OR xanthophyl* OR xanthofyl* OR xantophyl* OR xantofyl* OR lutein* OR epilutein*):ab,ti) AND (((((('cardiovascular disease'/exp NOT ('cardiovascular disease'/exp/dm_cn OR 'congenital disorder'/exp)) OR ((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital):ab,ti) OR 'non insulin dependent diabetes mellitus'/de OR ((diabetes NEAR/6 ('type 2' OR 'type ii' OR 'non insulin' OR noninsulin)) OR ((glucose OR insulin) NEAR/3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*))):ab,ti) OR (hypertension/exp OR (('blood pressure') OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) NEAR/3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*):ab,ti) OR (obesity/exp OR 'body mass'/de OR 'body fat'/de OR 'waist circumference'/de OR 'waist hip ratio'/de 'Metabolic Syndrome X'/de OR 'dual energy X ray absorptiometry'/de OR (obesity OR obese OR 'over weight' OR overweight OR adiposity OR dexa OR dxa OR 'dual energy X ray absorptiometry' OR 'dual x ray absorptiometry' OR 'metabolic syndrome' OR 'body mass index' OR BMI OR Quetelet OR (body NEXT/1 (composition* OR fat* OR weight*)) OR 'ponderal index' OR (weight NEXT/1 gain*) OR 'abdominal fat' OR (fat NEAR/3 (mass OR percentage*)) OR skinfold* OR (waist NEAR/3 (hip OR circumference*))):ab,ti) OR (autacoid/de OR chemokine/exp OR 'prostaglandin derivative'/de OR 'C reactive protein '/de OR (autacoid* OR chemokine* OR prostaglandin* OR ((inflammat*) NEAR/3 (marker* OR mediator*)) OR 'C reactive protein' OR 'creactive protein' OR crp OR 'c reaction protein'):ab,ti) OR ('anthropometric parameters'/de OR 'body height'/de OR 'body size'/de OR 'head circumference'/de OR (((body) NEAR/3 (height OR size)) OR 'head circumference' OR (height NEAR/3 age)):ab,ti)) OR ('respiratory tract disease'/exp OR 'respiratory function'/exp OR 'lung function test'/exp OR 'cystic fibrosis'/de OR (((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) NEAR/3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis):ab,ti) OR ('mental disease'/exp OR Epilepsy/exp OR cognition/exp OR 'mental function'/de OR 'brain function'/de OR memory/de OR (((cognit* OR learn* OR brain* OR neurolog* OR mental*) NEAR/3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention NEAR/3 Defic*) OR adhd OR epilep* OR cognit* OR dement*):ab,ti) OR ('nonalcoholic fatty liver'/de OR ((nonalcoholic OR 'non alcoholic') NEAR/3 ('fatty liver' OR steatohepatitis)):ab,ti)) AND (Epidemiology/exp OR 'cohort analysis'/de OR 'prospective study'/de OR 'follow up'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'case control study'/de OR 'intervention study'/de OR 'clinical study'/de OR 'clinical trial'/exp OR (((Hazard OR odds OR risk*) NEXT/1 Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect* OR intervent* OR clinical) NEXT/1 (stud* OR trial*)) OR (case* NEAR/3 control*) OR (Cross NEXT/1 section*)):ab,ti) NOT ([animals]/lim NOT [humans]/lim)

Medline (in OvidSP)

("carotenoids"/ OR "xanthophyll"/ OR "Lutein"/ OR (carotenoid* OR xanthophyl* OR xanthofyl* OR xantophyl* OR xantofyl* OR lutein* OR epilutein*).ab,ti.) AND ((((exp "cardiovascular diseases"/ NOT (exp cardiovascular diseases/cn OR exp "Congenital Abnormalities"/)) OR ((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital).ab,ti.) OR "Diabetes Mellitus, Type 1"/ OR ((diabetes ADJ6 ("type 2" OR "type ii" OR "non insulin" OR noninsulin)) OR ((glucose OR insulin) ADJ3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*))).ab,ti.) OR (exp hypertension/ OR (("blood pressure") OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*).ab,ti.) OR (exp obesity/ OR "Body Mass Index"/ OR exp "Body Fat Distribution"/ OR exp "Adipose Tissue"/ OR "waist circumference"/ OR "Waist-Hip Ratio"/ OR "Metabolic Syndrome X"/ OR "Absorptiometry, Photon"/ OR (obesity OR obese OR "over weight" OR overweight OR adiposity OR dexa OR dxa OR "dual energy X ray absorptiometry" OR "dual x ray absorptiometry" OR "metabolic syndrome" OR "body mass index" OR BMI OR Quetelet OR (body ADJ (composition* OR fat* OR weight*)) OR "ponderal index" OR (weight ADJ gain*) OR "abdominal fat" OR (fat ADJ3 (mass OR percentage*)) OR skinfold* OR (waist ADJ3 (hip OR circumference*))).ab,ti.) OR (exp autacoids/ OR exp chemokines/ OR "C-Reactive Protein"/ OR (autacoid* OR chemokine* OR prostaglandin* OR (inflammat* ADJ3 (marker* OR mediator*)) OR "C reactive protein" OR "creactive protein" OR crp OR "c reaction protein").ab,ti.) OR ("Body Weights and Measures"/ OR "Body Constitution"/ OR "Skinfold Thickness"/ OR exp "body size"/ OR (((body) ADJ3 (height OR size)) OR head circumference OR (height ADJ3 age)).ab,ti.) OR (exp "respiratory tract diseases"/ OR exp "Respiratory Physiological Phenomena"/ OR exp "Respiratory Function Tests"/ OR "cystic fibrosis"/ OR (((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) ADJ3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis).ab,ti.) OR (exp "Mental Disorders"/ OR exp Epilepsy/ OR exp cognition/ OR exp "Mental Processes"/ OR exp memory/ OR exp "Memory Disorders"/ OR (((cognit* OR learn* OR brain* OR neurolog* OR mental*) ADJ3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention ADJ3 Defic*) OR adhd OR epilep* OR cognit* OR dement*).ab,ti.) OR (((nonalcoholic OR 'non alcoholic') ADJ3 ('fatty liver' OR steatohepatitis)).ab,ti.)) AND (exp Epidemiologic Studies/ OR "Intervention Studies"/ OR "clinical trial".pt. OR (((Hazard OR odds OR risk*) ADJ Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect* OR intervent* OR clinical) ADJ (stud* trial*)) OR (case* ADJ3 control*) OR (Cross ADJ section*)).ab,ti.) NOT (exp animals/ NOT humans/)

Cochrane central

((carotenoid* OR xanthophyl* OR xanthofyl* OR xantophyl* OR xantofyl* OR lutein* OR epilutein*):ab,ti) AND ((((((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital):ab,ti) OR ((diabetes NEAR/6 ('type 2' OR 'type ii' OR 'non insulin' OR noninsulin)) OR ((glucose OR insulin) NEAR/3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*))):ab,ti) OR (('blood pressure' OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) NEAR/3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*):ab,ti) OR ((obesity OR obese OR 'over weight' OR overweight OR adiposity OR dexa OR dxa OR 'dual energy X ray absorptiometry' OR 'dual x ray absorptiometry' OR 'metabolic syndrome' OR 'body mass index' OR BMI OR Quetelet OR (body NEXT/1 (composition* OR fat* OR weight*)) OR 'ponderal index' OR (weight NEXT/1 gain*) OR 'abdominal fat' OR (fat NEAR/3 (mass OR percentage*)) OR skinfold* OR (waist NEAR/3 (hip OR circumference*))):ab,ti) OR ((autacoid* OR chemokine* OR prostaglandin* OR ((inflammat*) NEAR/3 (marker* OR mediator*)) OR 'C reactive protein' OR 'creactive protein' OR crp OR 'c reaction protein'):ab,ti) OR ((((body) NEAR/3 (height OR size)) OR 'head circumference' OR (height NEAR/3 age)):ab,ti)) OR ((((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) NEAR/3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis):ab,ti) OR ((((cognit* OR learn* OR brain* OR neurolog* OR mental*) NEAR/3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention NEAR/3 Defic*) OR adhd OR epilep* OR cognit* OR dement*):ab,ti) OR (((nonalcoholic OR 'non alcoholic') NEAR/3 ('fatty liver' OR steatohepatitis)):ab,ti)) AND ((((Hazard OR odds OR risk*) NEXT/1 Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect*) NEXT/1 stud*) OR (case* NEAR/3 control*) OR (Cross NEXT/1 section*)):ab,ti)

Web-of-Science

TS=(((carotenoid* OR xanthophyl* OR xanthofyl* OR xantophyl* OR xantofyl* OR lutein* OR epilutein*)) AND ((((((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital)) OR ((diabetes NEAR/6 ("type 2" OR "type ii" OR "non insulin" OR noninsulin)) OR ((glucose OR insulin) NEAR/3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR

homeosta*)))) OR (("blood pressure" OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) NEAR/3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*)) OR ((obesity OR obese OR "over weight" OR overweight OR adiposity OR dexa OR dxa OR "dual energy X ray absorptiometry" OR "dual x ray absorptiometry" OR "metabolic syndrome" OR "body mass index" OR BMI OR Quetelet OR (body composition* OR body fat* OR body weight*) OR "ponderal index" OR (weight gain*) OR "abdominal fat" OR (fat NEAR/3 (mass OR percentage*)) OR skinfold* OR (waist NEAR/3 (hip OR circumference*)))) OR ((autacoid* OR chemokine* OR prostaglandin* OR ((inflammat*) NEAR/3 (marker* OR mediator*)) OR "C reactive protein" OR "creactive protein" OR crp OR "c reaction protein")) OR ((((body) NEAR/3 (height OR size)) OR "head circumference" OR (height NEAR/3 age)))) OR ((((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) NEAR/3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis)) OR ((((cognit* OR learn* OR brain* OR neurolog* OR mental*) NEAR/3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention NEAR/3 Defic*) OR adhd OR epilep* OR cognit* OR dement*)) OR (((nonalcoholic OR "non alcoholic") NEAR/3 ("fatty liver" OR steatohepatitis)))) AND ((((Hazard OR odds OR risk*) NEAR/1 ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect*) NEAR/1 stud*) OR (case* NEAR/3 control*) OR (Cross section*))) NOT (Animal* NOT human*))

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((carotenoid*[tiab] OR xanthophyl*[tiab] OR xanthofyl*[tiab] OR xantophyl*[tiab] OR xantofyl*[tiab] OR lutein*[tiab] OR epilutein*[tiab])) AND (((((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital)) OR ((diabetes AND (type 2 OR type ii OR non insulin OR noninsulin)) OR ((glucose OR insulin) AND (level*[tiab] OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit*[tiab] OR insensitivity*[tiab] OR resistance OR homeosta*[tiab])))) OR (hypertension[mh] OR ((blood pressure) OR hypertensi*[tiab] OR ((cholesterol OR LDL*[tiab] OR HDL*[tiab] OR triglyceride*[tiab] OR lipoprotein*[tiab] OR lipid*[tiab]) AND (plasma OR blood OR serum OR level*[tiab] OR profile*[tiab])) OR hyperlip*[tiab] OR dyslip*[tiab])) OR (obesity[mh] OR Body Mass Index[mh] OR Body Fat Distribution[mh] OR Adipose Tissue[mh] OR waist circumference[mh] OR Waist-Hip Ratio[mh] OR Metabolic Syndrome X[mh] OR Absorptiometry, Photon[mh] OR (obesity OR obese OR over weight OR overweight OR adiposity OR dexa OR dxa OR dual energy X ray absorptiometry OR dual x ray absorptiometry OR metabolic syndrome OR body mass index OR BMI OR Quetelet OR body composition*[tiab] OR body fat*[tiab] OR body weight*[tiab] OR ponderal index OR weight gain*[tiab] OR abdominal fat OR (fat AND (mass OR percentage*[tiab])) OR skinfold*[tiab] OR (waist AND (hip OR circumference*[tiab])))) OR (autacoids[mh] OR chemokines[mh] OR C-Reactive Protein[mh] OR (autacoid*[tiab] OR chemokine*[tiab] OR prostaglandin*[tiab] OR (inflammat*[tiab] AND (marker*[tiab] OR mediator*[tiab])) OR C reactive protein OR creactive protein OR crp OR c reaction protein)) OR (Body Weights and Measures[mh] OR Body Constitution[mh] OR Skinfold Thickness[mh] OR body size[mh] OR (((body) AND (height OR size)) OR head circumference OR (height AND age))) OR (respiratory tract diseases[mh] OR Respiratory Physiological Phenomena[mh] OR Respiratory Function Tests[mh] OR cystic fibrosis[mh] OR (((respirat*[tiab] OR breath*[tiab] OR pulmonar*[tiab] OR lung*[tiab] OR airway*[tiab] OR bronchopulmon*[tiab]) AND (disease*[tiab] OR function*[tiab] OR disorder*[tiab] OR obstruct*[tiab])) OR COPD OR bronchitis)) OR (Mental Disorders[mh] OR Epilepsy[mh] OR cognition[mh] OR Mental Processes[mh] OR memory[mh] OR Memory Disorders[mh] OR (((cognit*[tiab] OR learn*[tiab] OR brain*[tiab] OR neurolog*[tiab] OR mental*[tiab]) AND (disorder*[tiab] OR disease*[tiab] OR function*[tiab] OR develop*[tiab] OR impair*[tiab])) OR memor*[tiab] OR dyslex*[tiab] OR Attention Defic*[tiab] OR adhd OR epilep*[tiab] OR cognit*[tiab] OR dement*[tiab])) OR non alcoholic fatty liver*[tiab]) AND ((Hazard Ratio*[tiab] OR odds Ratio*[tiab] OR risk Ratio*[tiab][tiab] OR Prospectiv*[tiab] OR Populat*[tiab] OR Observat*[tiab] OR Retrospect*[tiab] OR intervent*[tiab] OR clinical[tiab] OR case control*[tiab] OR Cross section*[tiab])) AND publisher[sb]

Google Scholar

carotenoid|xanthophyll|lutein cardiovascular|cardiac|diabetes|hypertension|cholesterol|obesity|bmi|overweight|C-reactive-protein|"body height|size"|respiratory|mental|cognition|adhd Epidemiology|cohort|prospective|follow-up|longitudinal|retrospective

Supplementary Material S2.1.2. Detailed results of reported associations between lutein and risk of cardiometabolic disease

First author (year)	Lutein measure	Statistical Analysis	Exposure	Outcome of interest	Measure of association	Effect estimate	LL 95%CI	UL 95%CI	p-value	Adjustment level[1]
Coronary heart disease										
Adults										
Ford (2000)	Blood level*	Logistic regression	Quartiles	Angina pectoris	OR	Q2: 1.01 Q3: 1.08 Q4: 0.79	Q2: 0.73 Q3: 0.81 Q4: 0.61	Q2: 1.40 Q3: 1.44 Q4: 1.02	0.13 (P trend)	+++
Gey (2010)	Blood level*	NM	Mean levels in cases vs. controls	Coronary heart disease cases					0.51	+++
Hak (2003)	Blood level	Logistic regression	Quintiles (based on controls)	Myocardial infarction	OR	Q2: 1.11 Q3: 1.64 Q4: 1.66 Q5: 1.25	Q2: 0.55 Q3: 0.82 Q4: 0.82 Q5: 0.64	Q2: 2.22 Q3: 3.26 Q4: 3.39 Q5: 2.46	0.43 (P trend)	+++
Ito (2006)	Blood level*	Cox regression	Per (log) micromol/L	Mortality from ischemic heart disease	HR	0.82	0.42	1.58	0.55	+++
Kabagambe (2005)	Dietary iintake*	Logistic regression	Quintiles	Myocardial infarction	OR	Q2: 0.88 Q3: 1.06 Q4: 0.99 Q5: 1.18	Q2: 0.67 Q3: 0.80 Q4: 0.74 Q5: 0.88	Q2: 1.15 Q3: 1.39 Q4: 1.33 Q5: 1.57	**0.02** (P trend)	+++
Knekt (2004)	Dietary intake	Cox regression	Quintiles	Coronary heart disease cases	HR	Q2: 1.07 Q3: 0.97 Q4: 0.92 Q5: 0.89	Q2: 0.94 Q3: 0.84 Q4: 0.79 Q5: 0.75	Q2: 1.23 Q3: 1.11 Q4: 1.07 Q5: 1.04	**0.03** (P trend)	+++
Koh (2011)	Blood level	Logistic regression	Quintiles	Myocardial infarction	OR	Q2: 0.63 Q3: 0.80 **Q4: 0.54** Q5: 0.62	Q2: 0.37 Q3: 0.48 **Q4: 0.30** Q5: 0.35	Q2: 1.06 Q3: 1.35 **Q4: 0.95** Q5: 1.10	0.09 (P trend)	+++
Murr (2009)	Blood level*	Welch's t- test	Mean levels in cases vs. controls	Coronary artery disease		↓			**<0.05**	-
Osganian (2003)	Dietary intake*	Pooled logistic regression	Quintiles	Coronary artery disease	RR	Q2: 0.90 Q3: 0.81 Q4: 0.78 Q5: 0.90	Q2: 0.74 Q3: 0.66 Q4: 0.63 Q5: 0.72	Q2: 1.10 Q3: 0.99 Q4: 0.97 Q5: 1.12	0.42 (P trend)	+++
Rerksuppaphol (2010)	Blood level	ANCOVA	Mean levels in cases vs. controls	Coronary heart disease					**NS**	+
Ruiz Rejon (2002)	Blood level*	NM	Mean levels in cases vs controls	Myocardial infarction		↓			**<0.05**	+
Street (1994)	Blood level	Logistic regression	Quintiles	Myocardial infarction	OR	Q1: 1.71 Q2: 1.06 Q3: 1.28 Q4: 0.72	NM	NM	0.09 (P trend)	+
Tavani (2006)	Dietary intake*	Logistic regression	Quartiles	Myocardial infarction	OR	Q2: 0.84 Q3: 0.92 Q4: 0.71	Q2: 0.61 Q3: 0.66 Q4: 0.50	Q2: 1.16 Q3: 1.28 Q4: 1.01	0.11 (P trend)	+++

Stroke										
Adults										
Ascherio (1999)	Dietary intake	Pooled logistic regression	Quintiles	Total stroke	RR	Q2: 0.89 Q3: 0.88 Q4: 0.87 Q5: 0.70	Q2: 0.64 Q3: 0.63 Q4: 0.69 Q5: 0.49	Q2: 1.24 Q3: 1.22 Q4: 1.21 Q5: 1.01	0.06 (P trend)	+++
				Ischemic stroke	RR	Q2: 0.82 Q3: 0.80 Q4: 0.93 Q5: 0.63	Q2: 0.55 Q3: 0.53 Q4: 0.62 Q5: 0.40	Q2: 1.25 Q3: 1.21 Q4: 1.39 Q5: 0.99	0.10 (P trend)	+++
				Hemorrhagic stroke	RR	Q2: 1.22 Q3: 1.22 Q4: 0.73 Q5: 0.88	Q2: 0.60 Q3: 0.60 Q4: 0.32 Q5: 0.40	Q2: 2.47 Q3: 2.49 Q4: 1.66 Q5: 1.92	0.41 (P trend)	+++
Hak (2004)	Blood level	Logistic regression	Quintiles (based on controls)	Ischemic stroke	OR	Q2: 0.75 Q3: 1.40 Q4: 1.08 Q5: 1.20	Q2: 0.33 Q3: 0.62 Q4: 0.48 Q5: 0.49	Q2: 1.71 Q3: 3.17 Q4: 2.40 Q5: 2.94	NM	+++
Hirvonen (2000)	Dietary intake*	Logistic regression	Quartiles	Cerebral infarction	RR	Q2: 0.92 Q3: 0.96 Q4: 0.81	Q2: 0.75 Q3: 0.79 Q4: 0.66	Q2: 1.12 Q3: 1.18 Q4: 1.00	0.10 (P trend)	+++
				Subarachnoid hemorrhage	RR	Q2: 0.84 Q3: 0.71 Q4: 0.47	Q2: 0.49 Q3: 0.40 Q4: 0.24	Q2: 1.47 Q3: 1.28 Q4: 0.93	**0.03** (P trend)	+++
				Intracerebral hemorrhage	RR	Q2: 0.59 Q3: 1.03 Q4: 0.81	Q2: 0.32 Q3: 0.60 Q4: 0.46	Q2: 1.09 Q3: 1.75 Q4: 1.43	0.86 (P trend)	+++
Ito (2006)	Blood level*	Cox regression	Per (log) micromol/L	Mortality from stroke	HR	0.72	0.37	1.37	0.32	+++
Combined cardiovascular events										
Adults										
Sesso (2004)	Blood level*	Logistic regression	Quartiles	Combined cardiovascular events (women only)	RR	Q2: 0.82 Q3: 0.89 Q4: 0.81	Q2:0.51 Q3:0.55 Q4:0.47	Q2: 1.33 Q3: 1.44 Q4: 1.41	0.58 (P trend)	+++
Sesso (2005)	Blood level	Logistic regression	Quartiles	Combined cardiovascular events (men only)	RR	Q2: 1.19 Q3: 1.21 Q4: 1.30	Q2: 0.76 Q3: 0.75 Q4: 0.79	Q2: 1.87 Q3: 1.94 Q4: 2.14	0.37 (P trend)	+++
Mortality from cardiovascular diseases										
Adults										
Bates (2011)	Blood level*	Cox regression	Z-scores	Vascular disease mortality	HR	0.90	0.75	1.08	0.3	+
Buijsse (2008)	Dietary intake	Cox regression	per SD	Cardiovascular mortality	RR	0.95	0.81	1.12	NS	+++
Ito (2006)	Blood level*	Cox regression	Per (ln) micromol/L	Cardiovascular mortality	HR	0.79	0.52	1.19	0.27	+++
Mayne (2004)	Blood level*	Cox regression	Above vs below median	Cardiovascular mortality	HR	0.74	0.28	1.96	NS	++
Shardell (2011)	Blood level*	Cox regression	Quartiles	Cardiovascular mortality	RR	Q1: 1.14 Q2: 0.92 Q3: 1.04	Q1: 0.89 Q2: 0.72 Q3: 0.84	Q1: 1.47 Q2: 1.18 Q3: 1.28	0.44 (P trend)	+++

Diabetes Mellitus type II										
Adults										
Hozawa (2006)	Blood level*	Cox PH	Per SD	Type 2 diabetes mellitus (current smokers)	HR	1.22	0.93	1.61	NS	+++
				(non-smokers)	HR	0.85	0.65	1.13	NS	+++
Kataja-Tuomola (2011)	Dietary intake*	Cox regression	Quintiles	Type 2 diabetes mellitus	RR	Q2: 0.77 Q3: 0.93 Q4: 0.92 Q5: 1.02	Q2: 0.59 Q3: 0.72 Q4: 0.72 Q5: 0.81	Q2: 1.00 Q3: 1.19 Q4: 1.19 Q5: 1.30	0.36 (P trend)	+++
Montonen (2004)	Dietary intake*	Cox regression	Quartiles	Type 2 diabetes mellitus	RR	Q2: 0.91 Q3: 0.95 Q4: 0.74	Q2: 0.69 Q3: 0.71 Q4: 0.55	Q2: 1.21 Q3: 1.26 Q4: 1.01	0.09 (P trend)	++
Wang (2006)	Blood level*	Logistic regression	Quartiles	Type 2 diabetes mellitus	OR	Q2: 1.13 Q3: 1.37 Q4: 1.35	Q2: 0.61 Q3: 0.73 Q4: 0.68	Q2: 2.11 Q3: 2.58 Q4: 2.69	0.32 (P trend)	+++
Metabolic syndrome										
Children										
Beydoun (2012)	Blood level*	Logistic regression	Per 0.09 micromol/L	MetS	OR	0.77	0.41	1.47	NS	+++
		ZIP regression	Per 0.09 micromol/L	MetS count score	beta	**-0.18**	**-0.30**	**-0.06**	**<0.05**	+++
Adults										
Beydoun (2011)	Blood level*	Logistic regression	Per 0.16 micromol/L	MetS	OR	**0.82**	**0.68**	**0.99**	**<0.05**	+++
		ZIP regression	Per 0.16 micromol/L	MetS count score	beta	**-0.08**	**-0.12**	**-0.04**	**<0.05**	+++
Coyne (2009)	Blood level*	Logistic regression	Quartiles	MetS	OR	Q2: 1.13 Q3: 1.12 Q4: 0.93	Q2: 0.55 Q3: 0.64 Q4: 0.56	Q2: 2.33 Q3: 1.95 Q4: 1.52	0.79 (P trend)	++
		ANOVA	Quartiles	MetS components	RR				0.39	-
Sluijs (2009)	Dietary intake*	Modified Poisson regression	Quartiles	MetS	RR	Q2: 0.72 Q3: 0.87 Q4: 0.82	Q2: 0.42 Q3: 0.52 Q4: 0.47	Q2: 1.21 Q3: 1.46 Q4: 1.42	0.57 (P trend)	+++
Sugiura (2008)	Blood level	Logistic regression	Tertiles	MetS	OR	T2: 1.09 T3: 0.85	T2: 0.58 T3: 0.41	T2: 2.07 T3: 1.78	0.70 (P trend)	++
Suzuki (2011)	Blood level	Logistic regression	Tertiles	MetS (men only)	OR	T2: 0.58 T3: 0.73	T2: 0.29 T3: 0.37	T2: 1.11 T3: 1.41	0.32 (P trend)	++
				MetS (women only)	OR	T2: 0.86 **T3: 0.37**	T2:0.41 **T3: 0.16**	T2: 1.81 **T3: 0.84**	**0.02** **(P trend)**	++
				MetS components (men only)	OR				0.51 (P trend)	++
				MetS components (women only)	OR				0.21 (P trend)	++

*Footnote: *measured together with zeaxanthin; ↓: Negative association ↑: Positive association*

[1]Adjustment level was categorized as followed; unadjusted –; 4 covariates or less +; 5 to 8 covariates ++, 9 or more covariates +++

ANCOVA: Analysis of covariance ANOVA: Analysis of variance, MetS: Metabolic Syndrome, PH: proportional hazards , OR: Odds Ratio, HR: Hazard Ratio, RR: Relative Risk, ZIP: zero-inflated Poisson regression , NM: not mentioned.

Supplementary Material S2.1.3. Detailed results of the reported associations between lutein and risk factors for cardiovascular diseases

First author (year)	Lutein measure	Statistical Analysis	Exposure	Outcome of interest	Sub-group	Measure of association	Effect estimate	LL 95%CI	UL 95%CI	p-value	Adjustment level[1]
Blood pressure Adults											
Coyne (2009)	Blood level*	Logistic regression	Quartiles	Hypertension		OR	Q2: 0.97 Q3: 0.88 Q4: 0.95	Q2: 0.61 Q3: 0.55 Q4: 0.74	Q2: 1.55 Q3: 1.41 Q4: 1.23	0.53 (P trend)	++
Hozawa (2009)	Blood level*	Linear regression	Continuous	Blood pressure categories (<119/<79; 120-129/80-84; 130-139/85-89; >140/>90)			↓			**0.03** **(P trend)**	++
		Cox regression	Per SD	Hypertension		HR	0.94	0.87	1.01	NS	++
Street (1994)	Blood level	T-test	Mean levels in cases vs controls	Hypertension			↑			**<0.01**	-
Sluijs (2009)	Dietary intake*	Linear regression	Quartiles	Systolic blood pressure		Beta	Q2:-0.35 Q3:-3.83 Q4:-0.09	Q2:-6.32 Q3:-9.90 Q4:-6.34	Q2: 5.62 Q3: 2.24 Q4: 6.16	0.51 (P trend)	+++
				Diastolic blood pressure		Beta	Q2: 0.95 Q3:-0.48 Q4:-0.56	Q2:-2.14 Q3:-3.62 Q4:-3.79	Q2: 4.04 Q3: 2.66 Q4: 2.68	0.36 (P trend)	+++
Sugiura (2008)	Blood level	Linear regression	Continuous	Systolic blood pressure		Beta	-0.048			0.12	++
				Diastolic blood pressure		Beta	**-0.079**			**0.01**	++
Suzuki (2011)	Blood level*	Partial correlation	Continuous	Systolic blood pressure	men	Correlation coefficient	-0.059			NS	++
					women	Correlation coefficient	-0.019			NS	++
				Diastolic blood pressure	men	Correlation coefficient	-0.108			NS	++
					women	Correlation coefficient	-0.062			NS	++
Atherosclerosis Adults											
D'Odorico (2000)	Blood level	Logistic regression	Continuous	Atherosclerosis (carotid and femoral)		OR				NS	+++
Dwyer (2001)	Blood level	Linear regression	Continuous	IMT progression (mm/18months)		Beta	**-0.07**	**-0.11**	**-0.03**[5]	**<0.01**	+++
Iribarren (1996)	Blood level*	Logistic regression	per 0.17 micromol/L	Asymptomatic atherosclerosis (carotids)		OR	0.77	0.57	1.03	NS	+++
Karppi (2011)	Blood level	ANCOVA	Continuous	Carotid IMT (quartiles)						0.18	+++

Klipstein-Grobusch (2000)	Blood level	Logistic regression	Quartiles	Atherosclerosis (abdominal aorta)		OR	Q2: 1.09 Q3: 1.30 Q4: 0.96	Q2: 0.50 Q3: 0.58 Q4: 0.42	Q2: 2.37 Q3: 2.91 Q4: 2.20	0.96 (P trend)	++
Nieto (2000)	Blood level*	ANCOVA	Mean levels in cases vs. controls	Carotid IMT						NS	+
Polidori (2007)	Blood level	ANOVA	Mean levels in cases vs. controls	Atherosclerosis (iliofemoral or carotid)			↓			**<0.01**	+++
Xu (2012)[A]	Blood level	ANOVA	Mean levels in cases vs. controls	Carotid IMT			↓			**<0.01**	-
Zou (2011)	Blood level	Pearson correlation	Continuous	Carotid IMT	left	Correlation coefficient	-0.112			NS	+
					right	Correlation coefficient	**-0.256**			**p<0.01**	+
Zou (2014)	Blood level	Linear regression	Continuous	Carotid IMT		Beta	**-0.340**			**0.03**	+
Other cardiovascular outcomes											
Adults											
Nakamura (2006)	Blood level	Logistic regression	Tertiles	Pulse wave velocity		OR	T2: 1.05 T3: 1.35	T2: 0.57 T3: 0.75	T2: 1.91 T3: 2.41	0.28 (P trend)	+++
Tornwall (2000)	Dietary intake	Cox regression	Quartiles	Intermittent claudication		RR	Q2:0.89 Q3:0.85 Q4:0.81	Q2:0.80 Q3:0.76 Q4:0.73	Q2:0.99 Q3:0.95 Q4:0.91	**<0.01** **(P trend)**	+++
Zou (2011)	Blood level	Pearson correlation	Continuous	Arterial stiffness[2]						NS	+
Inflammatory markers											
Adults											
Almushatat (2006)	Blood level	Spearman rank correlation	Continuous	C-reactive protein						NS	-
Ben Amara (2014)	Blood level*	Linear regression	Continuous	Leucocytes						NS	+
Brighenti (2005)	Blood level	Mann Whitney U test	Continuous	C-reactive protein (Q4 vs Q1-3)						NS	-
D'Adamo (2012)	Blood level	Regression	Continuous	sTNF-alphaR1		Beta	**-1300**	**-2605**	**-6**	**<0.05**	+++
				IL-6		Beta	-9.8	-23.9	4.3	0.20	+++
Graydon (2012)	Supplement intake	ANOVA	Supplement (10mg lutein + 5mg zeaxanthin) for 8 weeks vs. placebo	C-reactive protein						NS	randomized

Hozawa (2007)	Blood level*	Regression	Per SD	C-reactive protein		Beta	**-0.05**			**0.03**	+++
				Fibrinogen		Beta	-0.06			0.11	+++
				Leukocytes[3]		Beta	**-0.10**			**<0.01**	+++
Rowley (2003)	Blood level*	Linear regression	Continuous	C-reactive protein (per tertile increase)						0.23	++
Sundl (2009)	Blood level*	Linear regression	Continuous	(log)IL-6[4]			↓			**0.04**	-
				C-reactive protein						NS	-
Suzuki (2010)	Blood level*	Linear regression	Continuous (ln)	C-reactive protein	Men	Beta (S)	-0.094			0.36	+++
					Women	Beta (S)	-0.015			0.78	+++
				IL-6	Men	Beta (S)	-0.106			0.30	+++
					Women	Beta (S)	**-0.129**			**0.02**	+++
				TNF-alpha	Men	Beta (S)	-0.104			0.31	+++
					Women	Beta (S)	0.019			0.73	+++
van Herpen-Broekmans (2004)	Blood level	Linear regression	Continuous	(ln) C-reactive protein		Beta	-0.95	-2.71	0.81[5]	0.29	++
				Fibrinogen		Beta	-0.36	-1.22	0.50[5]	0.41	++
				(ln)leucocytes		Beta	-0.08	-0.47	0.31[5]	0.68	++
Wang (2013)	Supplement intake	ANCOVA	Supplements for 12 weeks vs placebo	C-reactive protein	10mg lutein					NS	randomized
					20mg lutein		**-0.14**	**0.02**	**0.25**	**<0.02**	randomized
	Blood level	Pearson correlation	Supplements for 12 weeks vs placebo	C-reactive Protein	10 mg	Correlation coefficient	**-0.45**			**<0.01**	-
					20 mg	Correlation coefficient	**-0.44**			**<0.01**	-
Wang (2014)	Blood level*	Linear regression	Continuous	(ln) C-reactive Protein		Beta	**-1.1324**			**<0.01**	+++
	Dietary intake*	Linear regression	Continuous	(ln) C-reactive Protein		Beta	-0.0160			0.55	+++
Xu (21012)[A]	Blood level	Spearman correlation	Continuous	IFN-gamm		Correlation coefficient	0.096			NS	+
				IL-6		Correlation coefficient	0.053			NS	+
Xu (2012)[B]	Supplement intake	T-test	Supplements (20mg) for 3 months, vs placebo	IL-6 (pg/ml)		Beta	-113.0	-265.05	39.11	0.14	randomized
Yeon (2012)	Blood level*	Pearson correlation	Continuous (ln)	IL-1beta in LPS-activated PBMCS		Correlation coefficient	**-0.5801**			**<0.05**	++

Growth and body composition										
Fetal life and childhood										
Capeding (2010)	Supplement intake	ANCOVA	Lutein fortified vs regular formula	Weight					NS	randomized
				Length					NS	randomized
				Head circumference					NS	randomized
Masters (2007)	Blood level*	Linear regression	Cord blood	Birth weight					NS	++
				Birth length					NS	++
				Head circumference					NS	++
Melikian (2001)	Blood level*	T-test	Tertiles (T3 vs T1)	Weight		↑			**<0.01**	+
				Weight velocity					NS	+
				Height		↑			**<0.01**	+
				Height velocity					NS	+
Adults										
Ben Amara (2014)	Blood level*	Linear regression	Continuous	BMI					NS	+
				Waist circumference					NS	+
Coyne (2009)	Blood level*	Logistic regression	Quartiles	Abdominal adiposity	OR	Q2: 0.91 Q3: 1.17 Q4: 0.77	Q2: 0.67 Q3: 0.72 Q4: 0.36	Q2: 1.25 Q3: 1.91 Q4: 1.67	0.72 (P trend)	++
Olea (2012)	Dietary intake*	T-test	Sufficient vs insufficient intake	% fatty mass excess					1.00	-
				Height					0.90	-
				Weight					0.08	-
				BMI		↑			**<0.05**	-
				brachial perimeter					0.07	-
				waist perimeter		↑			**<0.05**	-
				hip perimeter					0.09	-
Sluijs (2009)	Dietary intake*	Linear regression	Quartiles	Waist circumference	Beta	Q2: -0.04 Q3: 0.20 Q4: -0.47	Q2: -2.68 Q3: -2.49 Q4: -3.33	Q2: 2.60 Q3: 2.88 Q4: 2.30	0.50 (P trend)	+++
				Visceral fat	Beta	Q2: -0.01 Q3: -0.01 Q4: 0.01	Q2: -0.04 Q3: -0.04 Q4: -0.04	Q2: 0.03 Q3: 0.03 Q4: 0.04	0.88 (P trend)	+++
				Subcutaneous fat	Beta	Q2: -0.02 Q3: -0.03 Q4: -0.04	Q2: -0.07 Q3: -0.08 Q4: -0.09	Q2: 0.02 Q3: 0.01 Q4: 0.01	**0.04 (P trend)**	+++
				BMI		Q2: 0.01	Q2: -0.96	Q2: 0.97	0.99	+++

						Beta	Q3: 0.32 Q4: 0.05	Q3: -0.66 Q4: -0.96	Q3: 1.30 Q4: 1.06	(P trend)	
Sugiura (2008)	Blood level	Linear regression	Continuous (ln)	BMI		Beta	**-0.097**			**<0.01**	++
Suzuki (2011)	Blood level*	Partial correlation	Continuous (ln)	Waist circumference	Men	Correlation coefficient	-0.054			NS	++
					Women	Correlation coefficient	**-0.192**			**<0.01**	++
Wang (2013)	Supplement intake	ANCOVA	Supplements (10 or 20mg) for 12 weeks vs placebo	BMI						0.85	randomized
				Weight						0.47	randomized
				Waist circumference						0.64	randomized
				Body fat %						0.30	randomized
Waters (2009)	Blood level	Pearson Product Moment Correlation	Continuous	Waist circumference		Correlation coefficient	**-0.45**			**<0.05**	-
				BMI		Correlation coefficient	**-0.44**			**<0.05**	-
Insulin resistance											
Adults											
Ben Amara (2014)	Blood level*	Linear regression	Continuous	HOMA-IR						NS	+
				Fasting glucose						NS	+
				Fasting insulin						NS	+
Blondin (2013)	Blood level*	Linear regression	Continuous (ln)	(ln)HOMA-IR		Beta	-0.011	-0.058	0.036	0.64	++
				(ln) fasting glucose		Beta	-0.012	-0.045	0.020	0.45	++
				(ln) fasting insulin		Beta	-0.008	-0.008	0.036	0.72	++
Coyne (2005)	Blood level*	Linear regression	Quintiles	Fasting plasma glucose						0.07 (P trend)	+++
				2-hour postload plasma glucose			↓			**0.03 (P trend)**	+++
				fasting insulin			↓			**<0.01 (P trend)**	+++
				Glucose tolerance status (normal, impaired, diabetes)			↓			**0.03 (P trend)**	+++
Coyne (2009)	Blood level*	Logistic regression	Quartiles	High fasting glucose		OR	Q2: 0.95 Q3: 1.09 Q4: 0.57	Q2: 0.75 Q3: 0.64 Q4: 0.33	Q2: 1.20 Q3: 1.88 Q4: 1.00	0.13 (P trend)	++

Ford (2000)	Blood level*	NM	Mean levels per status	Glucose tolerance status						0.46	+++
		Regression	Continuous (ln)	Fasting glucose		Beta	-0.00105	-0.00252	0.00042[5]	0.18	+++
				2-hour glucose		Beta	-0.00050	-0.00124	0.0002448[5]	0.20	+++
				Fasting insulin		Beta	**-0.00079**	**-0.00153**	**-0.0000452[5]**	**<0.05**	+++
Granado-Lorencio (2006)	Blood level	Spearman correlation	Continuous	HbA1c < 7.1%		Correlation coefficient	0.31			NS	-
	Dietary intake	Spearman correlation	Continuous	HbA1c < 7.1%		Correlation coefficient	-0.13			NS	-
Hozawa (2006)	Blood level*	Linear regression	Per SD	Insulin concentration	Current smokers	Beta	-0.01	-0.7744	0.7544[5]	0.98	+++
					Non-smokers	Beta	-0.27	-0.6816	0.1416[5]	0.19	+++
				HOMA-IR	Current smokers	Beta	0.03	-0.2052	0.2652[5]	0.80	+++
					Non-smokers	Beta	-0.09	-0.2076	0.0276[5]	0.09	+++
Olea (2012)	Dietary intake*	T-test	Sufficient vs insufficient intake	Glucose						0.90	-
Sluijs (2009)	Dietary intake*	Linear regression	Quartiles	Fasting serum (ln)glucose		Beta	Q2: 0.01 Q3: 0.04 Q4: 0.02	Q2: -0.03 Q3: -0.01 Q4: -0.02	Q2: 0.05 Q3: 0.08 Q4: 0.06	0.42 (P trend)	+++
				Fasting serum (ln) insulin		Beta	Q2:-0.02 Q3: 0.07 Q4: 0.07	Q2: -0.16 Q3: -0.07 Q4: -0.08	Q2: 0.11 Q3: 0.21 Q4: 0.21	0.17 (P trend)	+++
				(ln)HOMA-IR		Beta	Q2:-0.01 Q3:-0.11 Q4:-0.11	Q2: -0.16 Q3: -0.26 Q4: -0.28	Q2: 0.14 Q3: 0.05 Q4: 0.06	0.16 (P trend)	+++
Sugiura (2006)	Blood level	Logistic regression	Tertiles	High HOMA-IR	male	OR	T2: 0.71 T3: 0.61	T2: 0.29 T3: 0.24	T2: 1.74 T3: 1.54	0.28 (P trend)	+++
					female	OR	T2: 1.35 T3: 0.76	T2: 0.77 T3: 0.41	T2: 2.36 T3: 1.40	0.37 (P trend)	+++
Sugiura (2008)	Blood level	Linear regression	Continuous (ln)	Fasting plasma glucose		Beta	-0.018			0.57	++
Suzuki (2011)	Blood level*	Partial correlation	Continuous (ln)	fasting serum glucose	men	Correlation coefficient	-0.009			NS	++
					women	Correlation coefficient	0.028			NS	++
Xu (2012)[B]	Supplement intake	T-test	Supplements (20mg) for 3 months, vs placebo	Blood glucose						0.66	randomized

Blood lipids Adults										
Ben Amara (2014)	Blood level*	Linear regression	Continuous	Total-c					NS	+
				HDL-c					NS	+
				LDL-c					NS	+
Coyne (2009)	Blood level*	Logistic regression	Quartiles	High triglycerides		OR	Q2: 1.00 Q3: 1.37 Q4: 1.19	Q2: 0.53 Q3: 0.85 Q4: 0.57	Q2: 1.90 Q3: 2.22 Q4: 2.48	0.37 (P trend)	++
				Low HDL-c		OR	Q2: 0.90 Q3: 0.55 Q4: 0.47	Q2: 0.45 Q3: 0.26 Q4: 0.21	Q2: 1.80 Q3: 1.18 Q4: 1.05	**0.04** **(P trend)**	++
Olea (2012)	Dietary intake*	T-test	Sufficient vs insufficient intake	Total-c						0.08	-
				HDL-c			↓			**0.01**	-
				LDL-c						0.3	-
				Triglycerides						0.7	-
Renzi (2012)	Blood level	Pearson correlation	Continuous	Total-c		Correlation coefficient	0.21			<0.09	+
				HDL-c		Correlation coefficient	**0.36**			**<0.01**	+
				LDL-c		Correlation coefficient	0.10			NS	+
				Triglycerides		Correlation coefficient	-0.01			NS	+
Ribaya-Mercado (1995)	Blood level*	Correlation	Continuous	Total plasma lipids (cholesterol + triglycerides)		Correlation coefficient	0.42			0.065	-
Street (1994)	Blood level	Linear regression	Mean levels per category	Total-c (>240mg/dl, 200-239 mg/dl, <200 mg/dl)			↑			**<0.01** **(P trend)**	-
Sluijs (2009)	Dietary intake*	Linear regression	Quartiles	HDL-c		Beta	Q2: 0.05 Q3:-0.03 Q4:0.03	Q2: -0.02 Q3: -0.11 Q4: -0.04	Q2: 0.12 Q3: 0.04 Q4: 0.11	0.28 (P trend)	+++
				Triglycerides		Beta	Q2:-0.10 Q3: 0.01 Q4:-0.01	Q2: -0.25 Q3: -0.15 Q4: -0.18	Q2: 0.06 Q3: 0.17 Q4: 0.15	0.32 (P trend)	+++
Sugiura (2008)	Blood level	Linear regression	Continuous (ln)	HDL-c		Beta	**0.222**			**<0.01**	++
				Triglycerides		Beta	0.022			0.48	++
Suzuki (2011)	Blood level*	Partial correlation	Continuous (ln)	(ln)Triglycerides	men	Correlation coefficient	-0.051			NS	++
					women	Correlation coefficient	-0.093			NS	++
				HDL-c	men	Correlation coefficient	**0.124**			**<0.05**	++
					women	Correlation coefficient	**0.176**			**<0.01**	++

Wang (2013)	Supplement intake	ANCOVA	Supplements (10 or 20mg) for 12weeks vs placebo	Total-c			0.62	randomized
				HDL-c			0.78	randomized
				LDL-c			0.96	randomized
				Triglycerides			0.56	randomized
Wang (2014)	Blood level*	Linear regression	Continuous	(ln) HDL-c	Beta	**0.2831**	**<0.01**	+++
				(ln) LDL-c	Beta	**-0.1106**	**<0.01**	+++
	Dietary intake*	Linear regression	Continuous	(ln) HDL-c	Beta	**0.0095**	**<0.01**	+++
				(ln) LDL-c	Beta	**-0.0083**	**<0.01**	+++
Xu (2012)[A]	Blood level	Spearman correlation	Continuous	HDL-c	Correlation coefficient	0.021	NS	+
				LDL-c	Correlation coefficient	0.018	NS	+
				Triglycerides	Correlation coefficient	-0.064	NS	+
Xu (2012)[B]	Supplement intake	T-test	Supplements (20mg) for 3 months, vs placebo	LDL-c			0.27	randomized
				HDL-c			0.95	randomized
				Triglycerides			0.06	randomized

Footnote: *measured together with zeaxanthin ↓: Negative association ↑: Positive association

[1]Adjustment level was categorized as followed; unadjusted –; 4 covariates or less +; 5 to 8 covariates ++, 9 or more covariates +++

[2]Different measures (carotid artery stiffness parameter, pressure-strain elasticity modulus, arterial compliance, pulse wave velocity, systolic maximum diameter minus diastolic minimum diameter)

[3]Association with leukocytes was cross-sectional.

[4]IL-6 available in n=35

[5]Confidence interval calculated based on reported standard error.

ANCOVA: Analysis of covariance, ANOVA: Analysis of variance, IMT: Intima media thickness, HOMA: homeastasis model assessment, IR: Insulin resistance, S: Standardized,

INF: interferon, LPS: lipopolysaccharida, PBMCS: peripheral blood mononuclear cells, TNF: tumor necrosis factor, IL: interleukin, Ln: natural logarithm, c: cholesterol, OR: Odds Ratio, NM: not mentioned, NS: not significant

Supplementary Material S2.1.4. Details on applied quality score

The quality score is composed of 5 items, and each item was allocated 0, 1 or 2 points. This allowed a total score between 0 and 10 points, 10 representing the highest quality. The following items are included in the score:

1. **Study design**
   0 for cross-sectional studies
   1 for longitudinal studies (retrospective or prospective) or non-randomized intervention studies
   2 for randomized intervention studies

2. **Population**
   Observational studies
   0 if n <500
   1 if n 500 to 2000
   2 if n >2000

   Intervention studies
   0 if n<50
   1 is n 50 to 100
   2 if n>100

3. **Exposure**
   Observational studies
   0 if the study used a one-day food record, a one-day 24h recall, an inappropriate FFQ or if not reported
   1 if the study used an appropriate FFQ, multiple day food records or multiple 24h recalls
   2 if the study used a biomarker

   Intervention studies
   0 if the intervention was only dietary advice or supplement use was not blinded
   1 if the intervention (supplement) was adequately single-blinded
   2 if the intervention (supplement) is adequately double-blinded

4. **Outcome (see table below)**

	0	1	2
Growth and adiposity			
Anthropometric and adiposity measures (e.g. weight, skinfold thickness)	If self-reported, inappropriate measurement method or not reported	If retrieved from medical records	If appropriate measurement method was used as part of study protocol.
Cardiovascular health			
Measurements (e.g. atherosclerosis, blood pressure (BFP))	If not reported or inappropriate measurement method (e.g. at home BP measure) or self-reported	Basically appropriate measurement method, but not adequately performed, for example single measurement of BP or not measured at rest, or from medical records	If appropriate measurement method was used as part of the study. For BP: minimum of 2 measurements at rest
Cardiovascular diseases (e.g. hypertension, events, mortality)	If not reported or if diagnosis was based on a proxy for disease (e.g. use of medication not specific for the disease(e.g. beta-blocking agents, anti-coagulants) or symptoms)	If diagnosis was self-reported or from medical records	If diagnosis was made in study using appropriate measurement method (see above) or from registries
Metabolic health and inflammatory markers			
Lab measures (e.g. bloodlipids, insulin, inflammatory markers)	Inappropriate measurement method, self-report or not reported	If lab measurement was not performed as part of study (e.g. from medical records) or non-fasting for insulin, glucose and lipids	If lab measurement was performed as part of the study and after 12h or overnight fast for lipids, glucose and insulin

Metabolic diseases (e.g. diabetes, metabolic syndrome)	If not reported or if diagnosis was based on a proxy for disease (i.e. use of medication that is not specific to the disease or symptoms)	If diagnosis was self-reported or retrieved from reports (e.g. medical records) not collected specifically for study or was based on the use of disease-specific medication (e.g. antidiabetic medication)	If diagnosis was made during study using adequate test or official registries were checked by a researcher

5. Adjustments

0 if findings are not controlled** for at least age and gender

1 if findings are controlled for age and gender

2 if an intervention study is adequately randomized or if findings are additionally controlled for covariates:

Dietary lutein: (minimally 4 out of 8)	**Blood level of lutein: (minimally 3 out of 6)**
- energy intake	- smoking
- supplement use	- other carotenoids
- smoking	- any measure of body weight (if this is not the outcome)
- other carotenoids	- physical activity
- any measure of body weight (if this is not the outcome)	- any measure of socioeconomic status
- physical activity	- race/ethnicity
- any measure of socioeconomic status	
- race/ethnicity	

** 'Controlled for' here refers to: adjusted for in the statistical analyses (e.g. with multiple regression); stratified for in the analyses (e.g. boys and girls separately); or narrow selection criteria of study participants on this covariate (e.g. including only 7 year old children would count as sufficiently controlling for age and including girls only does not require controlling for sex).

Supplementary Material S2.1.5. Assigned quality scores for the included studies

Author (year)	Study design	Population	Exposure assessment	Outcome assessment	Adjustments	Total
Almushatat (2006)	0	0	2	2	0	**4**
Ascherio (1999)	1	2	1	2	2	**8**
Bates (2011)	1	1	2	1	1	**6**
Ben Amara (2014)	0	0	2	2	1	**5**
Beydoun (2011)	0	2	2	2	2	**8**
Beydoun (2012)	0	1	2	2	2	**7**
Blondin (2013)	1	0	2	2	2	**7**
Brighenti (2005)	0	0	2	2	0	**4**
Buijsse (2008)	1	1	0	2	2	**6**
Capeding (2010)	2	2	2	2	2	**10**
Coyne (2005)	0	1	2	2	2	**7**
Coyne (2009)	0	1	2	2	2	**7**
D'Adamo (2012)	1	0	2	2	1	**6**
D'Odorico (2000)	1	0	2	2	1	**6**
Dwyer (2001)	1	0	2	2	2	**7**
Ford (2000)	0	2	2	2	2	**8**
Ford (2002)	0	2	2	2	2	**8**
Gey (2010)	1	2	2	2	0	**7**
Granado-Lorencio (2006)	1	0	2	2	0	**5**[1]
Graydon	2	1	1	2	2	**8**
Hak (2003)	1	1	2	2	2	**8**
Hak (2004)	1	0	2	2	2	**7**
Hirvonen (2000)	1	2	0	2	2	**7**
Hozawa (2006)	1	2	2	2	2	**9**
Hozawa (2007)	1	2	2	2	2	**9**[1]
Hozawa (2009)	1	2	2	2	2	**9**
Iribarren (1997)	0	0	2	2	2	**6**
Ito (2006)	1	2	2	2	1	**8**
Kabagambe (2005)	0	2	1	2	2	**7**
Karppi (2011)	0	1	2	2	2	**7**
Kataja-Tuomola (2011)	1	2	1	2	2	**8**
Klipstein-Grobusch (2000)	0	0	2	2	1	**5**
Knekt (2004)	1	2	0	2	2	**7**
Koh (2011)	1	1	2	2	2	**8**
Masters (2007)	0	0	2	2	1	**5**
Mayne (2004)	1	0	2	2	1	**6**
Melikian (2001)	1	0	2	2	0	**5**
Montonen (2004)	1	2	1	1	2	**7**
Murr (2009)	0	1	2	2	0	**5**
Nakamura (2006)	0	1	2	2	2	**7**
Nieto (2000)	1	0	2	2	1	**6**
Olea (2012)	0	0	0	1	0	**1**
Osganian (2003)	1	2	1	2	2	**8**
Polidori (2007)	0	0	2	2	2	**6**
Renzi (2012)	0	0	2	2	1	**5**
Rerksuppaphol	0	0	2	1	0	**3**
Ribaya-Mercado (1995)	0	0	2	2	0	**4**
Rowley (2003	0	0	2	2	2	**6**
Ruiz Rejon (2002)	0	0	2	2	0	**4**
Sesso (2004)	1	1	2	2	2	**8**
Sesso (2005)	1	1	2	2	2	**8**
Shardell (2011)	1	2	2	2	2	**9**
Sluijs (2009)	0	0	1	2	2	**5**
Street(1994)	1	0	2	2	1	**6**[1]
Sugiura (2006)	0	1	2	2	2	**7**
Sugiura (2008)	0	1	2	2	2	**7**
Sundl (2009)	0	0	2	2	0	**4**
Suzuki (2010)	0	0	2	2	2	**6**
Suzuki (2011)	0	1	2	2	1	**6**

Tavani (2006)	0	1	1	2	2	**6**
Tornwall (2000)	1	2	1	2	2	**8**
Van Herpen-Broekmans (2004)	0	0	2	2	1	**5**
Wang (2006)	1	1	2	1	2	**7**
Wang (2013)	2	2	2	2	2	**10**[1]
Wang (2014)	0	2	2	2	2	**8**[1]
Waters (2009)	0	0	2	0	0	**2**
Xu (2012)[a]	0	0	2	2	1	**5**[1]
Xu (2012)[b]	2	1	2	2	2	**9**
Yeon (2011)	1	0	2	2	1	**6**
Zou (2011)	0	0	2	2	1	**5**
Zou (2014)	1	0	2	2	1	**6**

[1]Highest attained QS, QS for other exposures/outcomes as following:
Granado-Lorencio (2006): for dietary lutein QS=4
Hozawa (2007): for leukocytes QS=8
Street (1994): for blood pressure QS=5, for cholesterol QS=4
Wang (2013): for body composition QS=8, for blood levels of lutein and inflammatory outcomes QS=5
Wang (2014): for dietary lutein and CRP QS=7, for blood level lutein and blood lipids QS=7, for dietary lutein and blood lipids QS=6.
Xu (2012)[a]: for blood lipids QS=4.

Supplementary Material S2.2.1. Details of the search strategy

	Before deduplication	After deduplication
Embase.com	3234	3211
Medline in ovidsp	1559	834
Web-of-Science	999	564
PubMed publisher	57	51
Cochrane central	27	0
Google Scholar	200	159
Total	**6076**	**4819**

Embase.com

(Choline/de OR 'choline alfoscerate'/de OR 'choline bitartrate'/de OR citicoline/de OR phosphorylcholine/de OR phosphatidylcholine/de OR ((beta NEXT/1 cholin*) OR 'alpha lecithin' OR amonita OR 'b cholin' OR bilineurine OR biocholine OR biocolina OR 'brassel 1000' OR bursine OR ceraxon OR cholin OR choline OR cholinephosphate OR cidifos OR cidiphos OR citicholine OR citicolin* OR cyticholin* OR cytocholine OR diacylglycerophosphocholine OR diacylglycerophosphorylcholine OR diacylphosphatidylcholine OR diphosphocholine OR 'egg lecithin' OR fagine OR fosfatidylcholine OR fosfolutein OR glycerophosphatidylcholine OR glycerophosphocholine OR glycerylphosphorylcholine OR granulestin OR hepacholine OR kelecin OR laevocholine OR lecithin* OR lecithol OR levocholine OR lipotril OR luridine OR maxicholine OR nicholin OR phosphatidylcholine* OR phosphocholine OR phospholipon OR phosphorylcholine OR rexort OR sauran OR sincaline OR sinkron OR sintoclar OR somazina OR topcithin OR urocholine OR vegelecithin OR 'Vitamine B4'):ab,ti) AND ((((('cardiovascular disease'/exp NOT ('cardiovascular disease'/exp/dm_cn OR 'congenital disorder'/exp)) OR ((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital):ab,ti) OR 'non insulin dependent diabetes mellitus'/de OR ((diabetes NEAR/6 ('type 2' OR 'type ii' OR 'non insulin' OR noninsulin)) OR ((glucose OR insulin) NEAR/3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*))):ab,ti) OR (hypertension/exp OR (('blood pressure') OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) NEAR/3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*):ab,ti) OR (obesity/exp OR 'body mass'/de OR 'body fat'/de OR 'waist circumference'/de OR 'waist hip ratio'/de 'Metabolic Syndrome X'/de OR 'dual energy X ray absorptiometry'/de OR (obesity OR obese OR 'over weight' OR overweight OR adiposity OR dexa OR dxa OR 'dual energy X ray absorptiometry' OR 'dual x ray absorptiometry' OR 'metabolic syndrome' OR 'body mass index' OR BMI OR Quetelet OR (body NEXT/1 (composition* OR fat* OR weight*)) OR 'ponderal index' OR (weight NEXT/1 gain*) OR 'abdominal fat' OR (fat NEAR/3 (mass OR percentage*) OR skinfold* OR (waist NEAR/3 (hip OR circumference*))):ab,ti)) OR (autacoid/de OR chemokine/exp OR 'prostaglandin derivative'/de OR 'C reactive protein '/de OR (autacoid* OR chemokine* OR prostaglandin* OR ((inflammat*) NEAR/3 (marker* OR mediator*)) OR 'C reactive protein' OR 'creactive protein' OR crp OR 'c reaction protein'):ab,ti) OR ('anthropometric parameters'/de OR 'body height'/de OR 'body size'/de OR 'head circumference'/de (((body) NEAR/3 (height OR size)) OR 'head circumference' OR (height NEAR/3 age)):ab,ti) OR ('respiratory tract disease'/exp OR 'respiratory function'/exp OR 'lung function test'/exp OR 'cystic fibrosis'/de OR (((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) NEAR/3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis):ab,ti) OR ('mental disease'/exp OR Epilepsy/exp OR cognition/exp OR 'mental function'/de OR 'brain function'/de OR memory/de OR (((cognit* OR learn* OR brain* OR neurolog* OR mental*) NEAR/3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention NEAR/3 Defic*) OR adhd OR epilep* OR cognit* OR dement*):ab,ti) OR ('nonalcoholic fatty liver'/de OR ((nonalcoholic OR 'non alcoholic') NEAR/3 ('fatty liver' OR steatohepatitis)):ab,ti)) AND (Epidemiology/exp OR 'cohort analysis'/de OR 'prospective study'/de OR 'follow up'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'case control study'/de OR 'intervention study'/de OR 'clinical study'/de OR 'clinical trial'/exp OR (((Hazard OR odds OR risk*) NEXT/1 Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect* OR intervent* OR clinical) NEXT/1 (stud* OR trial*)) OR (case* NEAR/3 control*) OR (Cross NEXT/1 section*)):ab,ti) NOT ([animals]/lim NOT [humans]/lim)

Medline in ovidsp

(Choline/ OR Glycerylphosphorylcholine/ OR exp Phosphatidylcholines/ OR (beta cholin* OR "alpha lecithin" OR amonita OR "b cholin" OR bilineurine OR biocholine OR biocolina OR "brassel 1000" OR bursine OR ceraxon OR cholin OR choline OR cholinephosphate OR cidifos OR cidiphos OR citicholine OR citicolin* OR cyticholin* OR cytocholine OR diacylglycerophosphocholine OR diacylglycerophosphorylcholine OR diacylphosphatidylcholine OR diphosphocholine OR "egg lecithin" OR fagine OR fosfatidylcholine OR fosfolutein OR glycerophosphatidylcholine OR glycerophosphocholine OR glycerylphosphorylcholine OR granulestin OR hepacholine OR kelecin OR laevocholine OR lecithin* OR lecithol OR levocholine OR lipotril OR luridine OR maxicholine OR nicholin OR phosphatidylcholine* OR phosphocholine OR phospholipon OR phosphorylcholine OR rexort OR sauran OR sincaline OR sinkron OR sintoclar OR somazina OR topcithin OR urocholine OR vegelecithin OR "Vitamine B4").ab,ti.) AND ((((exp "cardiovascular diseases"/ NOT (exp cardiovascular diseases/cn OR exp "Congenital Abnormalities"/)) OR ((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital).ab,ti.) OR "Diabetes Mellitus, Type 1"/ OR ((diabetes ADJ6 ("type 2" OR "type ii" OR "non insulin" OR noninsulin)) OR ((glucose OR insulin) ADJ3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*))).ab,ti.) OR (exp hypertension/ OR (("blood pressure") OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) ADJ3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*).ab,ti.) OR (exp obesity/ OR "Body Mass Index"/ OR exp "Body Fat Distribution"/ OR exp "Adipose Tissue"/ OR "waist circumference"/ OR "Waist-Hip Ratio"/ OR "Metabolic Syndrome X"/ OR "Absorptiometry, Photon"/ OR (obesity OR obese OR "over weight" OR overweight OR adiposity OR dexa OR dxa OR "dual energy X ray absorptiometry" OR "dual x ray absorptiometry" OR "metabolic syndrome" OR "body mass index" OR BMI OR Quetelet OR (body ADJ (composition* OR fat* OR weight*)) OR "ponderal index" OR (weight ADJ gain*) OR "abdominal fat" OR (fat ADJ3 (mass OR percentage*)) OR skinfold* OR (waist ADJ3 (hip OR circumference*))).ab,ti.) OR (exp autacoids/ OR exp chemokines/ OR "C-Reactive Protein"/ OR (autacoid* OR chemokine* OR prostaglandin* OR (inflammat* ADJ3 (marker* OR mediator*)) OR "C reactive protein" OR "creactive protein" OR crp OR "c reaction protein").ab,ti.) OR ("Body Weights and Measures"/ OR "Body Constitution"/ OR "Skinfold Thickness"/ OR exp "body size"/ OR (((body) ADJ3 (height OR size)) OR head circumference OR (height ADJ3 age)).ab,ti.) OR (exp "respiratory tract diseases"/ OR exp "Respiratory Physiological Phenomena"/ OR exp "Respiratory Function Tests"/ OR "cystic fibrosis"/ OR (((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) ADJ3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis).ab,ti.) OR (exp "Mental Disorders"/ OR exp Epilepsy/ OR exp cognition/ OR exp "Mental Processes"/ OR exp memory/ OR exp "Memory Disorders"/ OR (((cognit* OR learn* OR brain* OR neurolog* OR mental*) ADJ3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention ADJ3 Defic*) OR adhd OR epilep* OR cognit* OR dement*).ab,ti.) OR (((nonalcoholic OR 'non alcoholic') ADJ3 ('fatty liver' OR steatohepatitis)).ab,ti.)) AND (exp Epidemiologic Studies/ OR "Intervention Studies"/ OR "clinical trial".pt. OR (((Hazard OR odds OR risk*) ADJ Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect* OR intervent* OR clinical) ADJ (stud* trial*)) OR (case* ADJ3 control*) OR (Cross ADJ section*)).ab,ti.) NOT (exp animals/ NOT humans/)

Cochrane central

(((beta NEXT/1 cholin*) OR 'alpha lecithin' OR amonita OR 'b cholin' OR bilineurine OR biocholine OR biocolina OR 'brassel 1000' OR bursine OR ceraxon OR cholin OR choline OR cholinephosphate OR cidifos OR cidiphos OR citicholine OR citicolin* OR cyticholin* OR cytocholine OR diacylglycerophosphocholine OR diacylglycerophosphorylcholine OR diacylphosphatidylcholine OR diphosphocholine OR 'egg lecithin' OR fagine OR fosfatidylcholine OR fosfolutein OR

glycerophosphatidylcholine OR glycerophosphocholine OR glycerylphosphorylcholine OR granulestin OR hepacholine OR kelecin OR laevocholine OR lecithin* OR lecithol OR levocholine OR lipotril OR luridine OR maxicholine OR nicholin OR phosphatidylcholine* OR phosphocholine OR phospholipon OR phosphorylcholine OR rexort OR sauran OR sincaline OR sinkron OR sintoclar OR somazina OR topcithin OR urocholine OR vegelecithin OR 'Vitamine B4'):ab,ti) AND ((((((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital):ab,ti) OR ((diabetes NEAR/6 ('type 2' OR 'type ii' OR 'non insulin' OR noninsulin)) OR ((glucose OR insulin) NEAR/3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*))):ab,ti) OR (('blood pressure' OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) NEAR/3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*):ab,ti) OR ((obesity OR obese OR 'over weight' OR overweight OR adiposity OR dexa OR dxa OR 'dual energy X ray absorptiometry' OR 'dual x ray absorptiometry' OR 'metabolic syndrome' OR 'body mass index' OR BMI OR Quetelet OR (body NEXT/1 (composition* OR fat* OR weight*)) OR 'ponderal index' OR (weight NEXT/1 gain*) OR 'abdominal fat' OR (fat NEAR/3 (mass OR percentage*)) OR skinfold* OR (waist NEAR/3 (hip OR circumference*))):ab,ti) OR ((autacoid* OR chemokine* OR prostaglandin* OR ((inflammat*) NEAR/3 (marker* OR mediator*)) OR 'C reactive protein' OR 'creactive protein' OR crp OR 'c reaction protein'):ab,ti) OR ((((body) NEAR/3 (height OR size)) OR 'head circumference' OR (height NEAR/3 age)):ab,ti)) OR ((((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) NEAR/3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis):ab,ti) OR ((((cognit* OR learn* OR brain* OR neurolog* OR mental*) NEAR/3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention NEAR/3 Defic*) OR adhd OR epilep* OR cognit* OR dement*):ab,ti) OR (((nonalcoholic OR 'non alcoholic') NEAR/3 ('fatty liver' OR steatohepatitis)):ab,ti)) AND ((((Hazard OR odds OR risk*) NEXT/1 Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect*) NEXT/1 stud*) OR (case* NEAR/3 control*) OR (Cross NEXT/1 section*)):ab,ti)

Web-of-Science

TS=(((beta cholin* OR 'alpha lecithin' OR amonita OR 'b cholin' OR bilineurine OR biocholine OR biocolina OR 'brassel 1000' OR bursine OR ceraxon OR cholin OR choline OR cholinephosphate OR cidifos OR cidiphos OR citicholine OR citicolin* OR cyticholin* OR cytocholine OR diacylglycerophosphocholine OR diacylglycerophosphorylcholine OR diacylphosphatidylcholine OR diphosphocholine OR 'egg lecithin' OR fagine OR fosfatidylcholine OR fosfolutein OR glycerophosphatidylcholine OR glycerophosphocholine OR glycerylphosphorylcholine OR granulestin OR hepacholine OR kelecin OR laevocholine OR lecithin* OR lecithol OR levocholine OR lipotril OR luridine OR maxicholine OR nicholin OR phosphatidylcholine* OR phosphocholine OR phospholipon OR phosphorylcholine OR rexort OR sauran OR sincaline OR sinkron OR sintoclar OR somazina OR topcithin OR urocholine OR vegelecithin OR 'Vitamine B4')) AND ((((((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital)) OR ((diabetes NEAR/6 ("type 2" OR "type ii" OR "non insulin" OR noninsulin)) OR ((glucose OR insulin) NEAR/3 (level* OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit* OR insensitivity* OR resistance OR homeosta*)))) OR (("blood pressure" OR hypertensi* OR ((cholesterol OR LDL* OR HDL* OR triglyceride* OR lipoprotein* OR lipid*) NEAR/3 (plasma OR blood OR serum OR level* OR profile*)) OR hyperlip* OR dyslip*)) OR ((obesity OR obese OR "over weight" OR overweight OR adiposity OR dexa OR dxa OR "dual energy X ray absorptiometry" OR "dual x ray absorptiometry" OR "metabolic syndrome" OR "body mass index" OR BMI OR Quetelet OR (body composition* OR body fat* OR body weight*) OR "ponderal index" OR (weight gain*) OR "abdominal fat" OR (fat NEAR/3 (mass OR percentage*)) OR skinfold* OR (waist NEAR/3 (hip OR circumference*)))) OR ((autacoid* OR chemokine* OR prostaglandin* OR ((inflammat*) NEAR/3 (marker* OR mediator*)) OR "C reactive protein" OR "creactive protein" OR crp OR "c reaction protein")) OR ((((body) NEAR/3 (height OR size)) OR "head circumference" OR (height NEAR/3 age)))) OR ((((respirat* OR breath* OR pulmonar* OR lung* OR airway* OR bronchopulmon*) NEAR/3 (disease* OR function* OR disorder* OR obstruct*)) OR COPD OR bronchitis)) OR ((((cognit* OR learn* OR brain* OR neurolog* OR mental*) NEAR/3 (disorder* OR disease* OR function* OR develop* OR impair*)) OR memor* OR dyslex* OR (Attention NEAR/3 Defic*) OR adhd OR epilep* OR cognit* OR dement*)) OR (((nonalcoholic OR "non alcoholic") NEAR/3 ("fatty liver" OR steatohepatitis)))) AND ((((Hazard OR odds OR risk*) Ratio*) OR ((Prospectiv* OR Populat* OR Observat* OR Retrospect* OR clinical) NEAR/1 (stud* OR trial*)) OR (case* NEAR/3 control*) OR (Cross section*))) NOT (Animal* NOT human*))

PubMed publisher

(Choline[mh] OR Glycerylphosphorylcholine[mh] OR Phosphatidylcholines[mh] OR (beta cholin*[tiab] OR alpha lecithin OR amonita OR b cholin OR bilineurine OR biocholine OR biocolina OR brassel 1000 OR bursine OR ceraxon OR cholin OR choline OR cholinephosphate OR cidifos OR cidiphos OR citicholine OR citicolin*[tiab] OR cyticholin*[tiab] OR cytocholine OR diacylglycerophosphocholine OR diacylglycerophosphorylcholine OR diacylphosphatidylcholine OR diphosphocholine OR egg lecithin OR fagine OR fosfatidylcholine OR fosfolutein OR glycerophosphatidylcholine OR glycerophosphocholine OR glycerylphosphorylcholine OR granulestin OR hepacholine OR kelecin OR laevocholine OR lecithin*[tiab] OR lecithol OR levocholine OR lipotril OR luridine OR maxicholine OR nicholin OR phosphatidylcholine*[tiab] OR phosphocholine OR phospholipon OR phosphorylcholine OR rexort OR sauran OR sincaline OR sinkron OR sintoclar OR somazina OR topcithin OR urocholine OR vegelecithin OR Vitamine B4)) AND ((((cardiovascular diseases[mh] NOT (cardiovascular diseases[mh]cn OR Congenital Abnormalities[mh])) OR ((cardiovascular OR cardiac OR heart OR vascular OR cardiometabolic) NOT congenital)) OR Diabetes Mellitus, Type 1[mh] OR ((diabetes AND (type 2 OR type ii OR non insulin OR noninsulin)) OR ((glucose OR insulin) AND (level*[tiab] OR concentration OR plasma OR blood OR serum OR metabolism OR tolerance OR intolerance OR sensitivit*[tiab] OR insensitivity*[tiab] OR resistance OR homeosta*[tiab])))) OR (hypertension[mh] OR ((blood pressure) OR hypertensi*[tiab] OR ((cholesterol OR LDL*[tiab] OR HDL*[tiab] OR triglyceride*[tiab] OR lipoprotein*[tiab] OR lipid*[tiab]) AND (plasma OR blood OR serum OR level*[tiab] OR profile*[tiab])) OR hyperlip*[tiab] OR dyslip*[tiab])) OR (obesity[mh] OR Body Mass Index[mh] OR Body Fat Distribution[mh] OR Adipose Tissue[mh] OR waist circumference[mh] OR Waist-Hip Ratio[mh] OR Metabolic Syndrome X[mh] OR Absorptiometry, Photon[mh] OR (obesity OR obese OR over weight OR overweight OR adiposity OR dexa OR dxa OR dual energy X ray absorptiometry OR dual x ray absorptiometry OR metabolic syndrome OR body mass index OR BMI OR Quetelet OR (body composition*[tiab] OR body fat*[tiab] OR body weight*[tiab]) OR ponderal index OR (weight gain*[tiab]) OR abdominal fat OR (fat AND (mass OR percentage*[tiab])) OR skinfold*[tiab] OR (waist AND (hip OR circumference*[tiab])))) OR (autacoids[mh] OR chemokines[mh] OR C-Reactive Protein[mh] OR (autacoid*[tiab] OR chemokine*[tiab] OR prostaglandin*[tiab] OR (inflammat*[tiab] AND (marker*[tiab] OR mediator*[tiab])) OR C reactive protein OR creactive protein OR crp OR c reaction protein)) OR (Body Weights and Measures[mh] OR Body Constitution[mh] OR Skinfold Thickness[mh] OR body size[mh] OR (((body) AND (height OR size)) OR head circumference OR (height AND age))) OR (respiratory tract diseases[mh] OR Respiratory Physiological Phenomena[mh] OR Respiratory Function Tests[mh] OR cystic fibrosis[mh] OR (((respirat*[tiab] OR breath*[tiab] OR pulmonar*[tiab] OR lung*[tiab] OR airway*[tiab] OR bronchopulmon*[tiab]) AND (disease*[tiab] OR function*[tiab] OR disorder*[tiab] OR obstruct*[tiab])) OR COPD OR bronchitis)) OR (Mental Disorders[mh] OR Epilepsy[mh] OR cognition[mh] OR Mental Processes[mh] OR memory[mh] OR Memory Disorders[mh] OR (((cognit*[tiab] OR learn*[tiab] OR brain*[tiab] OR neurolog*[tiab] OR mental*[tiab]) AND (disorder*[tiab] OR disease*[tiab] OR function*[tiab] OR develop*[tiab] OR impair*[tiab])) OR memor*[tiab] OR dyslex*[tiab] OR (Attention AND Defic*[tiab]) OR adhd OR epilep*[tiab] OR cognit*[tiab] OR dement*[tiab]))) AND (Epidemiologic Studies[mh] OR Intervention Studies[mh] OR clinical trial.pt. OR ((Hazard Ratio*[tiab] OR odds Ratio*[tiab] OR risk Ratio*[tiab]) OR ((Prospectiv*[tiab] OR Populat*[tiab] OR Observat*[tiab] OR Retrospect*[tiab] OR intervent*[tiab] OR clinical) AND (studies[tiab] OR study[tiab] OR trial*[tiab])) OR (case*[tiab] AND control*[tiab]) OR (Cross section*[tiab]))) AND publisher[sb]

Google Scholar

Choline cardiac|heart|diabetes |hypertension|obesity|"body fat|mass|weight|height|size"|overweight|adiposity|COPD|bronchitis|"brain|mental disease|function"|Epilepsy|cognition|memory|adhd cohort|prospective|"follow up"|longitudinal|retrospective

Supplementary Material S2.2.2. Details on applied quality score

The quality score is composed of 5 items, and each item was allocated 0, 1 or 2 points.
This allowed a total score between 0 and 10 points, 10 representing the highest quality.
The following items are included in the score:

1. **Study design**
   0 for cross-sectional studies
   1 for longitudinal studies (retrospective or prospective) or non-randomized intervention studies
   2 for randomized intervention studies

2. **Population**
   Observational studies
   0 if n <500
   1 if n 500 to 2000
   2 if n >2000

   Intervention studies
   0 if n<50
   1 is n 50 to 100
   2 if n>100

3. **Exposure**
   Observational studies
   0 if the study used a one-day food record, a one-day 24h recall, an inappropriate FFQ or if not reported
   1 if the study used an appropriate FFQ, multiple day food records or multiple 24h recalls
   2 if the study used a biomarker

   Intervention studies
   0 if the intervention was only dietary advice or supplement use was not blinded
   1 if the intervention (supplement) was adequately single-blinded
   2 if the intervention (supplement) was adequately double-blinded

4. **Outcome (see table below)**

	0	1	2
Neurological			
Neurological diseases (ie. Parkinson, Alzheimer)	If not reported or if diagnosis was based on a proxy for disease (e.g. use of medication that is not specific to the disease or symptoms)	If diagnosis was self-reported or retrieved from reports (e.g. medical record) not collected specifically for study or was based on the use of disease-specific medication (e.g.L-dopa for Parkinson)	If diagnosis was made during study using appropriate test or official registries were checked by a researcher
Cognitive function tests (ie. MMSE, MDRS)	If not reported or inappropriate test was used	If appropriate test was done, but not as part of research protocol or by staff not qualified to do test.	If appropriate test was done as part of research protocol.
Pulmonary			
Pulmonary diseases (ie. Asthma, COPD)	If not reported or if diagnosis was based on a proxy for disease (e.g. use of medication that is not specific to the disease or symptoms)	If diagnosis was self-reported or retrieved from reports (e.g.medical record) not collected specifically for study or was based on the use of disease-specific medication	If diagnosis was made during study using appropriate test or official registries were checked by a researcher
Pulmonary function tests (ie. FEV1, FVC)	If not reported or inappropriate test was used	If appropriate test was done, but not as part of research	If appropriate test was done as part of research protocol.

		protocol or by staff not qualified to do test.	
Growth and adiposity			
Anthropometric and adiposity measures (ie. Weight, skinfold thickness)	If self-reported, inappropriate measurement method or not reported	If retrieved from medical records	If appropriate measurement method was used as part of study protocol.
Cardiovascular health			
Measurements (ie. Atherosclerosis, blood pressure)	If not reported or inappropriate measurement method (e.g. at home blood pressure measurement) or self-reported	Basically appropriate measurement method, but not adequately performed, for example single measurement of blood pressure or not measured at rest, or from medical records	If appropriate measurement method was used as part of the study. For blood pressure: minimum of 2 measurements at rest.
Cardiovascular diseases (ie hypertension, events, mortality)	If not reported or if diagnosis was based on a proxy for disease (e.g. use of medication not specific for the disease (e.g.beta-blocking agents, anti-coagulants) or symptoms)	If diagnosis was self-reported or from medical records	If diagnosis was made in study using appropriate measurement method (see above) or from registries
Metabolic health and inflammatory markers			
Laboratory measures (ie. Lipids, insulin, inflammatory markers)	Inappropriate measurement method, self-report or not reported	If lab measurement was not performed as part of study (e.g.from medical records) or non-fasting for insulin, glucose and lipids	If lab measurement was performed as part of the study and after 12h or overnight fast for lipids, glucose and insulin
Metabolic diseases (ie diabetes, metabolic syndrome)	If not reported or if diagnosis was based on a proxy for disease (e.g. use of medication that is not specific to the disease or symptoms)	If diagnosis was self-reported or retrieved from reports (e.g.medical records) not collected specifically for study or was based on the use of disease-specific medication (e.g.antidiabetic medication)	If diagnosis was made during study using adequate test or official registries were checked by a researcher

5. **Adjustments**

0 if findings are not controlled** for at least age and gender

1 if findings are controlled for:

- age
- gender

2 if an intervention study is adequately randomized or if findings are additionally controlled for covariates:

Dietary choline: (min 4 out of 8)	**Blood level of choline: (min 3 out of 6)**
- energy intake	- Cholesterol level
- cholesterol intake	- alcohol use
- supplement use	- any measure of body weight (if this is not the outcome)
- alcohol use	- physical activity
- any measure of body weight (if this is not the outcome)	- any measure of socioeconomic status
- physical activity	- race/ethnicity
- any measure of socioeconomic status	
- race/ethnicity	

** 'Controlled for' here refers to: adjusted for in the statistical analyses (e.g. with multiple regression); stratified for in the analyses (e.g. boys and girls separately); or narrow selection criteria of study participants on this covariate (e.g. including only 7 year old children would count as sufficiently controlling for age and including girls only does not require controlling for sex).

Supplementary Material S2.2.3. Assigned quality scores for the included studies

First author (year)	Study design	Population size	Exposure assessment	Outcome assessment	Adjustment	Total
Benton (2004)	2	2	2	2	2	**10**
Bertoia (2014)	1	1	1	2	2	**7**
Bidulescu (2007)	1	2	1	2	2	**8**
Boeke (2013)	1	1	1	2	2	**7**
Buchman (2001)	0	0	2	0	0	**2**
Carmichael (2010)	1	1	1	2	2	**7**
Cheatham (2012)	2	1	2	2	2	**9**
Chen (2013)	0	0	2	2	1	**5**
Dalmeijer (2008)	1	2	1	2	2	**8**[1]
Davis (1980)	2	0	2	2	2	**8**
Detopoulou (2008)	0	2	1	2	1	**6**
Deuster (2002)	2	0	2	2	2	**8**
Drachman (1982)	2	0	2	2	2	**8**
Evans (2007)	2	0	2	1	2	**7**
Ferrannini (2013)	1	2	2	2	1	**8**
Floegel (2012)	1	2	2	1	2	**8**
Harris (1983)	2	0	2	2	2	**8**[2]
Hogeveen (2013)	1	0	2	1	1	**5**
Imajo (2012)	0	0	2	2	0	**4**
Ivorra (2012)	0	0	2	0	1	**3**
Jiang (2012)	2	0	2	1	2	**7**
Kalhan (2010)	0	0	2	2	1	**5**
Killgore (2009)	2	0	0	0	2	**4**
Kupke (1983)	0	0	2	0	0	**2**
Ladd (1993)	2	1	2	2	2	**9**
Mapstone (2014)	1	0	2	2	1	**6**
Meikle (2013)	0	1	2	2	1	**6**[3]
Mills (2014)	1	1	2	2	1	**7**
Mohs (1980)	2	0	2	2	2	**8**
Nurk (2012)	0	2	2	2	1	**7**
Olthof (2005)	2	0	2	2	2	**8**
Poly (2011)	2	1	1	2	1	**7**
Ried (2013)	0	2	2	2	1	**7**[4]
Sanz-Cortés (2013)	0	0	2	2	1	**5**
Schriewer (1984)	0	2	2	1	0	**5**[5]
Shaw (2004)	1	1	1	2	2	**7**
Shaw (2014)	1	0	2	2	1	**6**
Signore (2008)	1	0	2	2	2	**7**
Simonsson (1982)	1	0	0	2	0	**3**
Sitaram (1978)	2	0	2	2	2	**8**
Sorgatz (1988)	2	1	2	2	2	**9**
Stegemann (2014)	1	1	2	2	1	**7**
Strain (2013)	0	0	2	2	1	**5**
Spiers (1996)	2	1	2	2	2	**9**
Veenema (2008)	2	0	0	2	2	**6**
Villamor (2012)	1	1	1	2	2	**7**
Wallace (2012)	2	0	2	2	2	**8**
Wu (2012)	1	0	2	2	2	**7**
Yan (2012)	0	0	2	2	1	**5**[6]
Zeisel (1991)	2	0	2	2	2	**8**

[1]Score for cardiovascular outcomes. QS for metabolic outcomes is 6.
[2]Score for intervention study. QS for longitudinal study is 5.
[3]Score for USA cohort. QS for Australian cohort is 5.
[4]Score for COPD. QS for asthma is 6.
[5]Score for metabolic outcomes. QS for body composition and cardiovascular outcomes is 4.
[6]Score for metabolic outcomes. QS for body composition is 2.

Supplementary Material S3.1.1. Food groups in PCA

Food group	Components
Potatoes and other tubers	Potatoes (cooked or fried) and french fries
Vegetables	Endive, purslane, turnip tops, lettuce, chard, spinach, chicory, eggplant, avocado, cucumber, paprika, corn, pickle, tomatoes, beans, snow peas, courgette, tomato sauce, carrots, beetroots, cabbages, mushrooms, green peas, onions, leek, garlic, bean sprouts, celery, atjar tjampoer and crudités
Fruits	Apple, strawberries, apricot, pineapple, red berries, banana, blackberries, lemon, grapes, raspberries, cherries, grapefruit, tangerine, peach, pear, prunes, orange, applesauce, kiwi, mango, rhubarb, melon, nectarine, canned fruit and dried fruit
Dairy products - high fat	Whole milk, full-fat yoghurt drink, full-fat yogurt, cheese 40-60+, cream cheese, full-fat quark, pudding, sour cream, whipped cream and crème fraiche
Dairy products - low fat	Skimmed and semi-skimmed milk, skimmed and semi-skimmed yoghurt drink, skimmed and semi-skimmed yogurt, cheese 20-30+ and low-fat quark
Cereals and cereal products - high-fiber	Brown rice, whole wheat pasta, whole wheat/brown/rye bread, muesli, seitan, oatmeal, wheat germ, and bran
Cereals and cereal products - low fiber	White rice, couscous, bulgur, white bread, rusk, croissants, corn flakes, crackers, rice cake, toast, pancakes, raisin bread, bami and white pasta
Meat and meat products	Red meat, poultry, organ meat and meat products
Fish and shellfish	Fish, fish products and shellfish
Eggs and egg products	Egg (cooked or fried)
Vegetable oils	Olive oil, nut oil, salad oil, sesame oil, sunflower oil, soybean oil and peanut oil
Margarine and butter	Margarine (solid and liquid), butter
Sugar, confectionary and cakes	Chocolate, candy, chocolate sprinkles, cake, pastry and biscuits
Snacks	Peanuts, beer nuts, trail mix, pretzels and chips
Coffee and tea	Coffee, cappuccino, espresso, English tea, green tea and herbal tea
Sugar containing beverages	Coke/Fanta/Sprite soft drinks, isotonic drinks, fruit juices and vegetable juices
Light soft drinks and water	Coke/Fanta/Sprite light soft drinks and water
Alcoholic beverages	Beer, wine, mixed drinks and liquor
Condiments and sauces	Chili/tomato/barbecue/shaslick/peanut/garlic/whisky/soy/salad sauce, salad dressing, mayonnaise, fish/egg/meat/Russian salad, sandwich spread, marmite, salt, spices/herbs and flavor powder
Soups and bouillon	Soup or bouillon with or without meat, meal soup and lentil soup
Nuts, seeds and olives	Nut butter, tahini, poppy seed, sesame, pumpkin seeds, sunflower seeds, pine nuts, mixed seeds and olives
Soy products	Tofu, tempeh, soymilk, soy chunks, soy dessert, vegetable burgers and quorn
Legumes	Legumes and tempeh

Supplementary Material S3.1.2. Details of the multiple imputation procedure

Software used	SPSS 22.0 for Windows
Imputation method and key settings	Fully conditional specification (Markov chain Monte Carlo method) Maximum iterations 10
No of imputed data sets created	10
Variables included in the imputation procedure: (imputed or used as predictors of missing data)	Maternal age, BMI, education level, parity, household income, marital status, gestational age at dietary assessment, pregnancy related comorbidities, alcohol use during pregnancy, smoking during pregnancy, use of folic acid supplementation, blood levels folic acid, stress during pregnancy, vomiting during pregnancy, feeling nauseous during pregnancy, 'Vegetable, fish and oil' dietary pattern, 'Fruits, nuts and high-fiber cereals' dietary pattern and 'Margarine, snacks and sugar' dietary pattern Paternal age, BMI and education level Child gender, gestational age at birth, birth weight, weight and height at 8 time points between age 1 and age 6 and age at all these measurements, diseases (wheezing, lower respiratory tract infections and eczema) between age 6 months and 4 year, breastfeeding, hospitalization in first year of life, TV watching at age 2, TV watching at age 4, playing outside at age 4, participation in sports at age 6, BMI, total body fat percentage, android/gynoid fat mass ratio, fat free mass index and fat mass index at age 6
Treatment of non-normally distributed variables	Predictive mean matching
Treatment of binary/categorical variables	Logistic regression models

Supplementary Material S3.1.3. Basic characteristics of participants before and after multiple imputation

	Original data	Imputed data
Maternal characteristics		
Age, y	31.7 ± 4.2	*No missings*
Pre-pregnancy BMI, kg/m^2	23.3 ± 3.9	23.3 ± 3.9
Gestational age at enrolment, weeks	13.6 (9.9-21.5)	*No missings*
Education,		
Primary or secondary	1,019 (38%)	1,044 (39%)
Higher	1,640 (62%)	1,651 (61%)
Missing	*36 (1%)*	
Household income,		
<2200 (Euro)	591 (24%)	676 (25%)
>2200 (Euro)	1,893 (76%)	2,019 (75%)
Missing	*211 (8%)*	
Parity,		
0	1,665 (62%)	1,667 (62%)
≥1	1,026 (38%)	1,028 (38%)
Missing	*4 (0.1%)*	
Smoking,		
Never during pregnancy	1,886 (76%)	2,044 (76%)
Until pregnancy was known	236 (9%)	260 (10%)
Continued throughout pregnancy	363 (15%)	391 (15%)
Missing	*210 (8%)*	
Alcohol,		
Never during pregnancy	776 (31%)	838 (31%)
Until pregnancy was known	413 (17%)	451 (17%)
Continued throughout pregnancy	1,278 (52%)	1,406 (52%)
Missing	*228 (9%)*	
Folic acid use,		
No	203 (9%)	266 (10%)
Start first 10 weeks	734 (33%)	901 (33%)
Start periconceptional	1,281 (58%)	1,528 (57%)
Missing	*477 (18%)*	
Total energy intake (FFQ), kcal/day	2,153 ± 503	*No missings*
Stress during pregnancy, global severity index	0.12 (0.00-0.77)	0.12 (0.00-0.77)
Child characteristics		
Gender, boys	1,351 (50%)	*No missings*
Age at centre visit (months)	72 (68-89)	*No missings*

Supplementary Material S3.1.4. Basic characteristics of included and excluded participants

	Participants in analysis	Participants not in analysis
Maternal characteristics		
Age, y	31.7 ± 4.2	30.5 ± 5.1
Pre-pregnancy BMI, kg/m^2	23.3 ± 3.9	23.1 ± 4.0
Gestational age at enrolment, weeks	13.6 (9.9-21.5)	13.5 (9.5-27.8)
Education,		
Primary or secondary	1,019 (37.8%)	697 (50.7%)
Higher	1,640 (61.7%)	679 (49.3%)
Missing	*36 (1.3%)*	*26 (1.9%)*
Household income,		
<2200 (Euro)	591 (23.8%)	360 (33.1%)
>2200 (Euro)	1,893 (76.2%)	728 (51.9%)
Missing	*211 (7.8%)*	*314 (22.4%)*
Parity,		
0	1,665 (61.9%)	769 (55.2%)
≥1	1,026 (38.1%)	623 (44.8%)
Missing	*4 (0.1%)*	*10 (0.1%)*
Smoking,		
Never during pregnancy	1,886 (75.9%)	875 (67.3%)
Until pregnancy was known	236 (9.5%)	113 (8.7%)
Continued throughout pregnancy	363 (14.6%)	313 (24.1%)
Missing	*210 (7.8%)*	*101 (7.2%)*
Alcohol,		
Never during pregnancy	776 (28.8%)	525 (40.7%)
Until pregnancy was known	413 (15.3%)	208 (16.1%)
Continued throughout pregnancy	1,278 (51.8%)	558 (43.2%)
Missing	*228 (8.5%)*	*111 (8.5%)*
Folic acid use,		
No	203 (9.2%)	192 (13.7%)
Start first 10 weeks	734 (33.1%)	380 (33.7%)
Start periconceptional	1,281 (57.8%)	555 (49.2%)
Missing	*477 (17.7%)*	*275 (19.6%)*
Total energy intake (FFQ), kcal/day	2,153 ± 503	2,125 ± 539
Stress during pregnancy, global severity index	0.12 (0.00-0.77)	0.12 (0.00-0.77)

Supplementary Material S3.1.5. Associations between maternal dietary patterns and offspring fat free mass index and fat mass index at 6 years (n=2,520).

	Fat Free Mass Index (SD) β (95% CI)		**Fat Mass Index (SD)** β (95% CI)	
	Crude	Multivariable model[a]	Crude	Multivariable model[a]
'Vegetable, fish and oil' dietary pattern				
Quartile 1 – low adherence	Reference	Reference	Reference	Reference
Quartile 2	0.02 (-0.08, 0.12)	-0.02 (-0.12, 0.08)	**-0.16 (-0.25, -0.08)***	-0.07 (-0.16, 0.01)
Quartile 3	0.01 (-0.09, 0.11)	-0.04 (-0.14, 0.07)	**-0.22 (-0.30, -0.13)***	**-0.09 (-0.17, -0.00)***
Quartile 4 – high adherence	0.07 (-0.03, 0.17)	0.00 (-0.10, 0.11)	**-0.24 (-0.32, -0.15)***	-0.09 (-0.18, 0.00)
P for trend	0.35	0.79	**<0.01**	0.30
'Nuts, soy and high-fiber cereals' dietary pattern				
Quartile 1 – low adherence	Reference	Reference	Reference	Reference
Quartile 2	0.03 (-0.08, 0.13)	0.01 (-0.09, 0.11)	**-0.15 (-0.24, -0.06)***	-0.06 (-0.14, 0.03)
Quartile 3	0.08 (-0.03, 0.18)	0.06 (-0.05, 0.16)	**-0.14 (-0.23, -0.05)***	0.01 (-0.08, 0.09)
Quartile 4 – high adherence	**0.13 (0.03, 0.23)****	0.12 (-0.01, 0.23)	**-0.16 (-0.25, -0.07)***	0.04 (-0.05, 0.13)
P for trend	**<0.01**	**<0.01**	**<0.01**	0.25
'Margarine, snacks and sugar' dietary pattern				
Quartile 1 – low adherence	Reference	Reference	Reference	Reference
Quartile 2	0.06 (-0.04, 0.16)	0.01 (-0.10, 0.11)	-0.01 (-0.09, 0.08)	0.02 (-0.06, 0.11)
Quartile 3	-0.01 (-0.10, 0.10)	-0.10 (-0.23, 0.03)	-0.01 (-0.08, 0.08)	0.03 (-0.08, 0.13)
Quartile 4 – high adherence	0.00 (-0.10, 0.10)	-0.16 (-0.33, 0.01)	-0.02 (-0.10, 0.07)	0.03 (-0.11, 0.17)
P for trend	0.66	**<0.01**	0.90	0.33

Results from multivariable linear regression analyses, based on imputed data. Values are regression coefficients (95% confidence interval) and reflect differences in age- and gender specific SD scores of fat free mass index or fat mass index of the child for quartiles 2 to 4, as compared to quartile 1.

Trend tests were performed by using adherence score (SD scores) as a continuous variable in the model.

[a] Multivariable model: adjusted for maternal age at intake, gestational age at dietary assessment, smoking during pregnancy, alcohol drinking during pregnancy, maternal folic acid use, maternal educational level, family income, parity, maternal pre-pregnancy BMI, maternal stress during pregnancy, gender of the child, breast feeding, watching television at 2 years of age and participation in sports at 6 years of age.

* p<0.01 for comparison with reference category.

Supplementary Material S4.1.1. Crude associations of lutein and beta-carotene intake at 13 months with body composition at age 6[1]

Table A. Associations of lutein (adjusted for beta-carotene)

	Height n=2044 *SD change (95% CI)*	Weight n=2044 *SD change (95% CI)*	BMI n=2044 *SD change (95% CI)*	FMI n=1964 *SD change (95% CI)*	FFMI n=1964 *SD change (95% CI)*	AG ratio n=1964 *SD change (95% CI)*	Body fat% n=1964 *SD change (95% CI)*
Q1 Low intake	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Q2	0.10 (-0.02; 0.22)	**0.10 (0.00; 0.20)***	0.08 (-0.01; 0.18)	0.05 (-0.04; 0.14)	0.07 (-0.05; 0.18)	0.05 (-0.06; 0.16)	0.04 (-0.06; 0.14)
Q3	0.09 (-0.03; 0.20)	0.09 (-0.00; 0.18)	0.08 (-0.01; 0.17)	0.04 (-0.05; 0.13)	0.10 (-0.02; 0.21)	-0.03 (-0.13; 0.07)	0.02 (-0.07; 0.12)
Q4 High intake	0.04 (-0.08; 0.15)	**0.10 (0.01; 0.20)***	**0.13 (0.03; 0.22)****	0.05 (-0.04; 0.14)	**0.13 (0.01; 0.24)***	0.01 (-0.10; 0.11)	0.02 (-0.08; 0.12)
Continuous (per SD)	*0.01 (-0.03; 0.05)*	*0.03 (-0.00; 0.07)*	***0.04 (0.01; 0.07)****	*0.03 (-0.00; 0.06)*	*0.03 (-0.01; 0.07)*	*0.00 (-0.03; 0.04)*	*0.02 (-0.02; 0.05)*

Table B. Associations of lutein (unadjusted for beta-carotene)

	Height n=2044 *SD change (95% CI)*	Weight n=2044 *SD change (95% CI)*	BMI n=2044 *SD change (95% CI)*	FMI n=1964 *SD change (95% CI)*	FFMI n=1964 *SD change (95% CI)*	AG ratio n=1964 *SD change (95% CI)*	Body fat% n=1964 *SD change (95% CI)*
Q1 Low intake	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Q2	-0.02 (-0.14; 0.09)	0.04 (-0.05; 0.13)	-0.06 (-0.04; 0.16)	0.06 (-0.03; 0.14)	0.05 (-0.06; 0.16)	0.06 (-0.05; 0.16)	0.04 (-0.06; 0.14)
Q3	0.01 (-0.10; 0.13)	0.08 (-0.01; 0.18)	**0.11 (0.02; 0.21)***	0.07 (-0.02; 0.16)	0.09 (-0.02; 0.20)	0.01 (-0.10; 0.11)	0.05 (-0.05; 0.14)
Q4 High intake	-0.02 (-0.13; 0.10)	**0.12 (0.03; 0.22)***	**0.19 (0.09; 0.29)****	**0.10 (0.01; 0.19)***	**0.16 (0.05; 0.27)****	0.01 (-0.10; 0.11)	0.06 (-0.04; 0.16)
Continuous (per SD)	*0.00 (-0.04; 0.04)*	***0.05 (0.02; 0.09)****	***0.08 (0.04; 0.11)****	***0.05 (0.01; 0.08)****	***0.06 (0.02; 0.10)****	*0.01 (-0.03; 0.05)*	*0.03 (-0.00; 0.07)*

Table C. Associations of beta-carotene

	Height n=2044 *SD change (95% CI)*	Weight n=2044 *SD change (95% CI)*	BMI n=2044 *SD change (95% CI)*	FMI n=1964 *SD change (95% CI)*	FFMI n=1964 *SD change (95% CI)*	AG ratio n=1964 *SD change (95% CI)*	Body fat% n=1964 *SD change (95% CI)*
Q1 Low intake	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Q2	-0.04 (-0.15; 0.08)	0.04 (-0.06; 0.13)	0.06 (-0.04; 0.16)	0.06 (-0.03; 0.15)	0.05 (-0.06; 0.16)	0.07 (-0.03; 0.17)	0.05 (-0.04; 0.15)
Q3	-0.03 (-0.15; 0.08)	0.05 (-0.04; 0.15)	0.09 (-0.01; 0.18)	0.08 (-0.01; 0.17)	0.06 (-0.05; 0.17)	0.04 (-0.06; 0.14)	0.07 (-0.03; 0.16)
Q4 High intake	0.01 (-0.10; 0.13)	**0.14 (0.04; 0.23)****	**0.19 (0.09; 0.29)***	0.09 (-0.00; 0.18)	**0.19 (0.08; 0.30)****	0.01 (-0.10; 0.12)	0.05 (-0.05; 0.14)
Continuous (per SD)	*0.00 (-0.04; 0.04)*	***0.05 (0.02; 0.08)****	***0.07 (0.04; 0.11)***	***0.04 (0.01; 0.07)****	***0.06 (0.02; 0.10)****	*0.01 (-0.02; 0.05)*	*0.03 (-0.01; 0.06)*

AG = android/gynoid, BMI = body mass index, FMI = fat mass index, FFMI = fat free mass index

[1]Values are linear regression coefficients (95% confidence interval) and reflect the difference in outcome (age and gender specific SD scores) for mid-low, mid-high and high intake, as compared to low intake of energy and beta carotene adjusted lutein intake.

*P<0.05, **P<0.01

Continuous model reflects the difference in outcome (age and gender specific SD scores) per SD increase of energy and beta carotene adjusted lutein intake.

Models are adjusted for age at dietary assessment.

Supplementary Material S4.1.2. Crude associations of lutein and beta-carotene intake at 13 months with cardiometabolic health at age 6[1]

Table A. Associations of lutein (adjusted for beta-carotene)

	Systolic blood pressure n=1969 *SD change (95% CI)*	Diastolic blood pressure n=1969 *SD change (95% CI)*	HDL cholesterol n=1390 *SD change (95% CI)*	Triglycerides n=1387 *SD change (95% CI)*	Insulin n=1383 *SD change (95% CI)*	Cardiometabolic risk factor score n=1305 *SD change (95% CI)*
Q1 Low intake	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Q2	-0.02 (-0.15; 0.10)	-0.07 (-0.19; 0.05)	-0.05 (-0.20; 0.10)	-0.09 (-0.24; 0.06)	-0.06 (-0.21; 0.09)	-0.02 (-0.17; 0.13)
Q3	0.09 (-0.03; 0.21)	0.02 (-0.09; 0.14)	0.09 (-0.05; 0.23)	-0.24 (-0.39; 0.10)	-0.10 (-0.24; 0.04)	-0.13 (-0.27; 0.01)
Q4 High intake	-0.00 (-0.12; 0.12)	-0.04 (-0.16; 0.08)	0.04 (-0.10; 0.19)	-0.02 (-0.17; 0.13)	-0.03 (-0.17; 0.12)	-0.09 (-0.23; 0.05)
Continuous (per SD)	*0.00 (-0.04; 0.04)*	*-0.01 (-0.05; 0.04)*	*0.02 (-0.03; 0.08)*	*-0.04 (-0.09; 0.02)*	*-0.02 (-0.07; 0.04)*	*-0.04 (-0.10; 0.01)*

Table B. Associations of lutein (unadjusted for beta-carotene)

	Systolic blood pressure n=1969 *SD change (95% CI)*	Diastolic blood pressure n=1969 *SD change (95% CI)*	HDL cholesterol n=1390 *SD change (95% CI)*	Triglycerides n=1387 *SD change (95% CI)*	Insulin n=1383 *SD change (95% CI)*	Cardiometabolic risk factor score n=1305 *SD change (95% CI)*
Q1 Low intake	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Q2	-0.02 (-0.14; 0.10)	-0.07 (-0.19; 0.05)	0.03 (-0.12; 0.18)	-0.13 (-0.28; 0.02)	-0.14 (-0.28; 0.01)	-0.14 (-0.28; 0.01)
Q3	0.02 (-0.10; 0.15)	-0.00 (-0.12; 0.12)	-0.03 (-0.18; 0.11)	-0.00 (-0.15; 0.15)	0.02 (-0.13; 0.17)	-0.00 (-0.15; 0.14)
Q4 High intake	-0.02 (-0.14; 0.10)	-0.04 (-0.16; 0.08)	0.13 (-0.02; 0.28)	**-0.19 (-0.34;-0.04)***	-0.06 (-0.21; 0.09)	**-0.19 (-0.34; -0.05)***
Continuous (per SD)	*0.00 (-0.04; 0.04)*	*-0.01 (-0.05; 0.03)*	***0.06 (0.01; 0.12)****	***-0.09 (-0.14;-0.04)***	*-0.02 (-0.07; 0.03)*	***-0.08 (-0.13; -0.03)****

Table C. Associations of beta-carotene

	Systolic blood pressure n=1969 *SD change (95% CI)*	Diastolic blood pressure n=1969 *SD change (95% CI)*	HDL cholesterol n=1390 *SD change (95% CI)*	Triglycerides n=1387 *SD change (95% CI)*	Insulin n=1383 *SD change (95% CI)*	Cardiometabolic risk factor score n=1305 *SD change (95% CI)*
Q1 Low intake	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
Q2	0.01 (-0.12; 0.13)	-0.05 (-0.17; 0.06)	-0.03 (-0.18; 0.12)	-0.05 (-0.20; 0.10)	-0.12 (-0.27; 0.02)	-0.06 (-0.20; 0.09)
Q3	-0.04 (-0.16; 0.09)	-0.09 (-0.21; 0.03)	0.07 (-0.22; 0.08)	0.04 (-0.11; 0.19)	0.03 (-0.12; 0.18)	-0.00 (-0.15; 0.14)
Q4 High intake	-0.01 (-0.14; 0.11)	-0.07 (-0.19; 0.05)	0.06 (-0.09; 0.21)	**-0.18 (-0.33;-0.03)***	-0.04 (-0.18; 0.11)	-0.14 (-0.28; 0.00)
Continuous (per SD)	*-0.01 (-0.05; 0.04)*	*-0.03 (-0.07; 0.02)*	*0.04 (-0.01; 0.09)*	***-0.07 (-0.12;-0.02)****	*-0.01 (-0.06; 0.04)*	***-0.06 (-0.11; -0.01)****

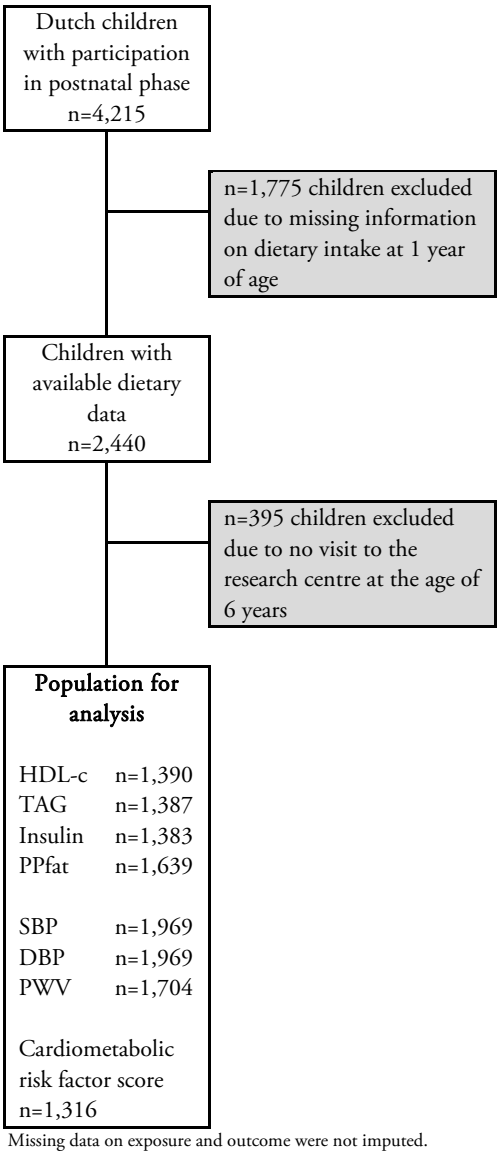
[1]Values are linear regression coefficients (95% confidence interval) and reflect the difference in outcome (age and gender specific SD scores) for mid-low, mid-high and high intake, as compared to low intake of energy and beta carotene adjusted lutein intake.

*P<0.05, **P<0.01

Continuous model reflects the difference in outcome (age and gender specific SD scores) per SD increase of energy and beta carotene adjusted lutein intake.

Crude models are adjusted for age at dietary assessment.

Supplementary Material S4.2.1. Flow chart of participants



Missing data on exposure and outcome were not imputed.
Missing data on covariates was imputed using the fully conditional specification (Markov chain Monte Carlo method) and predictive mean matching. Maximum number of iterations was 10 imputations and number of imputed datasets created 5 (default) .

Supplementary Material S4.2.2. Original data versus imputed data (n=2,371)[1]

	Original data	Imputed data
Child characteristics		
Sex		
Boys	49.9 (1,183)	*No missings*
Girls	50.1 (1,188)	*No missings*
Gestational age at birth (weeks)[2]	40.1 (35.9 – 42.3)	40.1 (35.9 – 42.3)
Birth weight (grams)	3492 (574)	3492 (574)
Dietary energy intake (kcal/day)	1306 (347)	*No missings*
Cakes & confectionary intake (gr/day)[2]	22 (2 – 80)	*No missings*
Sugar-containing beverage (servings/week)	7 (0 – 53)	*No missings*
Introduction of complementary feeding		
0-3 months	4.5 (106)	4.5 (106)
3-6 months	55.7 (1,316)	55.7 (1321)
After 6 months	39.8 (941)	39.9 (945)
Missing	*0.3 (8)*	-
History of allergy for cow's milk		
No	93.9 (2,188)	93.9 (2,226)
Yes	6.1 (142)	6.1 (145)
Missing	*7.1 (41)*	-
Hospitalization in the first year		
No	79.4 (1,514)	78.5 (1,860)
Yes	20.6 (394)	21.6 (511)
Missing	*19.5 (463)*	-
Breastfed		
Never	10.6 (227)	10.5 (250)
Partially in the first 4 months	60.6 (1,296)	60.6 (1437)
Exclusively for at least 4 months	28.8 (616)	28.8 (684)
Missing	*9.8 (232)*	-
TV watching (hours/day) at age 2yrs		
Less than 1	50.9 (1,128)	50.4 (1,195)
At least 1	49.1 (1,088)	49.6 (1,176)
Missing	*6.5 (155)*	-
Total body fat percentage	23.6 (4.6)	*Not imputed*
Fat mass index	3.5 (2.4 – 6.3)	*Not imputed*
Android/gynoid ratio	0.24 (0.05)	*Not imputed*
Maternal characteristics		
Maternal age (years)	31.9 (4.2)	*No missings*
Age of partner (years)	34.1 (5.2)	34.1 (5.2)
Mother BMI at intake (kg/m^2)	24.1 (4.0)	24.2 (4.0)
Folic acid use		
Never	7.7 (137)	8.1 (193)
Periconceptionally	62.5 (1,116)	62.2 (1,475)
Started in first 10 weeks	29.8 (532)	29.6 (702)
Missing	*24.7 (586)*	-
Educational level		
Lower	34.5 (808)	34.8 (824)
Higher	65.5 (1,536)	65.2 (1,547)
Missing	*1.1 (27)*	-
Net household income		
<2200 euros	20.3 (419)	21.3 (505)
>2200 euros	79.7 (1,640)	78.7 (1866)
Missing	*13.2 (312)*	-
Maternal comorbidities		
Pre-pregnancy	2.9 (49)	3.5 (82)
Pregnancy-related	7.2 (150)	7.6 (180)
Smoking during pregnancy		
Never	79.1 (1,710)	79.0 (1,873)
Until pregnancy was known	10.0 (216)	10.0 (238)
Continued	10.9 (236)	11.0 (260)
Missing	*8.8 (209)*	-

[1]Values are means (SD) or valid percentages (absolute numbers), unless indicated otherwise [2]Values are medians (95% range)
Due to rounding, numbers might not completely add up to total.

Supplementary Material S4.2.3. Association of sugar-containing beverage intake with BMI (kg/m²) at ages 2, 3, 4 and 6, by sex (n=2,371)

		Age 2			Age 3		
		Model A	Model B	Model C	Model A	Model B	Model C
Boys	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	0.01 (-0.17; 0.19)	-0.04 (-0.21; 0.14)	-0.03 (-0.21; 0.15)	-0.06 (-0.23; 0.12)	-0.09 (-0.26; 0.07)	-0.09 (-0.23;0.08)
	High intake ‡*15 servings/week*	-0.01 (-0.18; 0.18)	-0.03 (-0.21; 0.15)	-0.03 (-0.21; 0.15)	0.02 (-0.16; 0.20)	-0.04 (-0.22; 0.14)	-0.04 (-0.23; 0.15)
Trend		*p = 0.98*	*p = 0.75*	*p = 0.75*	*p = 0.94*	*p = 0.67*	*p = 0.67*
Girls	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	0.08 (-0.12; 0.26)	0.06 (-0.13; 0.24)	0.04 (-0.15; 0.23)	0.09 (-0.07; 0.26)	0.07 (-0.09; 0.23)	0.08 (-0.09; 0.24)
	High intake ‡*15 servings/week*	**0.22 (0.04; 0.41)***	**0.20 (0.02; 0.39)***	**0.21 (0.02; 0.40)***	**0.23 (0.06; 0.40)***	**0.17 (0.00; 0.34)***	**0.17 (0.00; 0.34)***
Trend		***p = 0.02***	***p = 0.03***	***p = 0.03***	***p = 0.01***	***p < 0.05***	***p = 0.03***

		Age 4			Age 6		
		Model A	Model B	Model C	Model A	Model B	Model C
Boys	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	-0.03 (-0.18; 0.12)	-0.06 (-0.21; 0.09)	-0.06 (-0.21; 0.09)	-0.06 (-0.27; 0.14)	-0.09 (-0.28; 0.10)	-0.06 (-0.26; 0.14)
	High intake ‡*15 servings/week*	0.00 (-0.15; 0.15)	-0.04 (-0.19; 0.11)	-0.04 (-0.20; 0.11)	0.05 (-0.16; 0.25)	-0.00 (-0.22; 0.22)	0.01 (-0.20; 0.22)
Trend		*p = 1.00*	*p=0.58*	*p=0.57*	*p = 0.66*	*p = 0.98*	*p = 0.92*
Girls	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	0.01 (-0.15; 0.17)	-0.02 (-0.17; 0.13)	-0.02 (-0.17; 0.14)	0.06 (-0.15; 0.28)	-0.01 (-0.22; 0.20)	-0.00 (-0.21; 0.20)
	High intake ‡*15 servings/week*	**0.22 (0.06; 0.39)****	**0.17 (0.01; 0.32)***	**0.17 (0.01; 0.33)***	**0.30 (0.09; 0.50)****	0.18 (-0.01; 0.38)	0.17 (-0.03; 0.36)
Trend		***p < 0.01***	***p = 0.04***	***p = 0.03***	***p < 0.01***	*p = 0.06*	*p = 0.09*

‡ Median intake within the category, energy-adjusted using the residual method and fixed to an intake of 1306 kcal/day.
Values are linear regression coefficients (95% confidence intervals) and reflect the increase in BMI for medium and high sugar-containing beverage intake, as compared to the lowest category.
Trend test was performed using categories of sugar-containing beverage intake as continuous variable in the model.
Model A was adjusted for age at the measurements.
Model B was additionally adjusted for gestational age at birth, birth weight (SDS), age of mother and father, net household income, maternal BMI, education, smoking, folic acid use, pre-pregnancy and pregnancy related comorbidities, child hospitalization in first year of life and history of allergy to cow's milk.
Model C contains all variables included in model B and was additionally adjusted for child's intake of sugar, confectionary, cakes and pastry, breastfeeding, time of introduction of complementary feeding, total energy intake and hours of TV watching.
*P-value <0.05; **P-value <0.01

Supplementary Material S4.2.4. Association of sugar-containing beverage intake with body composition at age 6, stratified by sex (n=2,001)

		Difference in total body fat percentage[1] *SD change (95% CI)*			**Difference in android/gynoid fat ratio[1]** *SD change (95% CI)*		
		Model A	Model B	Model C	Model A	Model B	Model C
Boys	Low intake ‡*3 servings/wk* n = 321	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/wk* n = 334	-0.05 (-0.20; 0.10)	-0.04 (-0.18; 0.11)	-0.07 (-0.22; 0.08)	0.00 (-0.08; 0.08)	0.00 (-0.15; 0.16)	0.00 (-0.16; 0.16)
	High intake ‡*15 servings/wk* n = 332	0.10 (-0.05; 0.25)	0.06 (-0.09; 0.22)	0.05 (-0.11; 0.20)	0.04 (-0.05; 0.12)	0.02 (-0.14; 0.18)	0.02 (-0.14; 0.18)
Trend		*p = 0.23*	*p = 0.40*	*p = 0.53*	*p = 0.93*	*p = 0.81*	*p = 0.77*
Girls	Low intake ‡*3 servings/wk* n = 339	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/wk* n = 331	0.06 (-0.09; 0.21)	0.00 (-0.14; 0.14)	-0.02 (-0.17; 0.12)	0.12 (-0.03; 0.27)	0.07 (-0.09; 0.22)	0.08 (-0.08; 0.23)
	High intake ‡*15 servings/wk* n = 344	**0.19 (0.04; 0.34)***	0.11 (-0.04; 0.25)	0.09 (-0.06; 0.23)	**0.20 (0.04; 0.35)***	0.14 (-0.01; 0.29)	0.14 (-0.02; 0.29)
Trend		***p = 0.01***	*p = 0.14*	*p = 0.25*	***p = 0.01***	*p = 0.08*	*p = 0.09*

‡ Median intake within the category, energy-adjusted using the residual method and fixed to an intake of 1306 kcal/day.

[1]Values are linear regression coefficients (95% confidence interval) and reflect the difference in total body fat percentage (SDS) or android/gynoid fat ratio (SDS) for medium and high sugar-containing beverage intake, compared to the lowest category.

Trend test was performed using categories of sugar-containing beverage intake as continuous variable in the model.

Model A was adjusted for age at the measurements and for child height at age 6 (SDS) (for android/gynoid ratio and body fat percentage).

Model B was additionally adjusted for gestational age at birth, birth weight (SDS), age of mother and father, net household income, maternal BMI, education, smoking, folic acid use, pre-pregnancy and pregnancy related comorbidities, child hospitalization in first year of life and history of allergy to cow's milk.

Model C contains all variables included in model B and was additionally adjusted for child's intake of sugar, confectionary, cakes and pastry, breastfeeding, time of introduction of complementary feeding, total energy intake and hours of TV watching.

*P-value <0.05

Supplementary Material S4.2.5. Associations of sugar-containing beverage intake at 13 months and weight and height at age 6, stratified by sex (n=2,371)

		Difference in weight[1] *SD change (95% CI)*	**Difference in height[1]** *SD change (95% CI)*
		Model C	Model C
Boys	Low intake ‡*3 servings/week* *n = 392*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week* *n = 393*	-0.03 (-0.12; 0.06)	0.13 (-0.01; 0.27)
	High intake ‡*15 servings/week* *n = 398*	0.03 (-0.06; 0.12)	**0.14 (0.00; 0.27)***
Trend		*p = 0.54*	***p < 0.05***
Girls	Low intake ‡*3 servings/week* *n = 394*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week* *n = 399*	0.01 (-0.08; 0.10)	-0.02 (-0.17; 0.13)
	High intake ‡*15 servings/week* *n = 395*	0.07 (-0.01; 0.16)	0.09 (-0.05; 0.23)
Trend		*p = 0.09*	*p = 0.19*

‡ Median intake within the category, energy-adjusted using the residual method and fixed to an intake of 1306 kcal/day.

[1]Values are linear regression coefficients (95% confidence interval) and reflect the difference in weight (SDS) or height (SDS) for medium and high sugar-containing beverage intake, compared to the lowest category.

Trend tests were performed using categories of sugar-containing beverage intake as continuous variable in the model.

Model C was adjusted for age at the measurements, gestational age at birth, weight at birth (SDS), age of mother, age of biological father, BMI of mother at intake, education of mother, smoking of mother during pregnancy, net household income, pre-pregnancy and pregnancy related comorbidities, child hospitalization in first year of life and history of allergy to cow's milk, child's intake of sugar, confectionary, cakes and pastry, breastfeeding, time of introduction of complementary feeding, total energy intake and hours of TV watching.

Model with child weight as outcome was additionally adjusted for child height (SDS)

*P-value <0.05

Supplementary Material S4.2.6. Association of sugar-containing beverage intake with risk of overweight/obesity at ages 2, 3, 4 and 6, stratified by sex

		Risk of overweight/obesity[1] *Odds ratios (95% CI)*					
		Age 2 (n=1,885)			**Age 3 (n=2,371)**		
		Model A	Model B	Model C	Model A	Model B	Model C
Boys	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	1.04 (0.56; 1.95)	0.96 (0.49; 1.86)	0.86 (0.43; 1.74)	0.85 (0.43; 1.67)	0.76 (0.37; 1.53)	0.78 (0.38; 1.60)
	High intake ‡*15 servings/week*	1.08 (0.59; 1.98)	1.15 (0.61; 2.16)	1.09 (0.57; 2.11)	0.79 (0.40; 1.56)	0.70 (0.34; 1.44)	0.71 (0.34; 1.48)
Trend		*p = 0.80*	*p = 0.67*	*p = 0.77*	*p = 0.49*	*p = 0.33*	*p = 0.36*
Girls	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	1.33 (0.76; 2.35)	1.21 (0.67; 2.19)	1.12 (0.61; 2.03)	1.47 (0.82; 2.64)	1.54 (0.84; 2.82)	1.56 (0.82; 2.94)
	High intake ‡*15 servings/week*	1.60 (0.91; 2.80)	1.47 (0.82; 2.65)	1.40 (0.76; 2.56)	1.61 (0.90; 2.87)	1.51 (0.82; 2.78)	1.48 (0.79; 2.77)
Trend		*p = 0.10*	*p = 0.19*	*p = 0.27*	*p = 0.11*	*p = 0.20*	*p = 0.25*

		Age 4 (n=2,371)			**Age 6 (n=2,371)**		
		Model A	Model B	Model C	Model A	Model B	Model C
Boys	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	0.88 (0.45; 1.69)	0.83 (0.42; 1.64)	0.78 (0.38; 1.57)	1.08 (0.62; 1.89)	1.04 (0.59; 1.82)	1.03 (0.57; 1.88)
	High intake ‡*15 servings/week*	0.66 (0.32; 1.38)	0.56 (0.26; 1.20)	0.51 (0.23; 1.13)	1.00 (0.55; 1.82)	0.90 (0.47; 1.72)	0.90 (0.44; 1.85)
Trend		*p = 0.27*	*p = 0.13*	*p = 0.10*	*p=0.99*	*p=0.73*	*p=0.75*
Girls	Low intake ‡*3 servings/week*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake ‡*8 servings/week*	1.10 (0.60; 2.01)	1.06 (0.55; 2.05)	0.95 (0.48; 1.87)	1.16 (0.74; 1.82)	1.08 (0.66; 1.76)	1.09 (0.67; 1.78)
	High intake ‡*15 servings/week*	1.44 (0.83; 2.50)	1.31 (0.74; 2.32)	1.24 (0.68; 2.23)	1.40 (0.89; 2.20)	1.22 (0.75; 1.99)	1.27 (0.78; 2.06)
Trend		*p = 0.18*	*p = 0.34*	*p = 0.45*	*p = 0.15*	*p = 0.42*	*p = 0.34*

‡ Median intake within the category, energy-adjusted using the residual method and fixed to an intake of 1306 kcal/day.

[1]Values are odds ratios (95% confidence interval) and reflect the risk for overweight/obesity for medium and high sugar-containing beverage intake, compared to the lowest category.

Trend test was performed using categories of sugar-containing beverage intake as continuous variable in the model.

Model A was adjusted for age at the measurements.

Model B was additionally adjusted for gestational age at birth, birth weight (SDS), age of mother and father, net household income, maternal BMI, education, smoking, folic acid use, pre-pregnancy and pregnancy related comorbidities, child hospitalization in first year of life and history of allergy to cow's milk.

Model C contains all variables included in model B and was additionally adjusted for child's intake of sugar, confectionary, cakes and pastry, breastfeeding, time of introduction of complementary feeding, total energy intake and hours of TV watching.

Supplementary Material S4.2.7. Association of absolute sugar-containing beverage intake with BMI (SD scores) at ages 2, 3, 4 and 6 stratified by sex (n=2,371) without total energy adjustment and standardization.

		Age 2	Age 3	Age 4	Age 6
Boys	Low intake	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake	0.05 (-0.09; 0.19)	-0.06 (-0.17; 0.06)	-0.02 (-0.12; 0.09)	0.02 (-0.10; 0.14)
	High intake	0.00 (-0.13; 0.14)	-0.02 (-0.15; 0.11)	-0.00 (-0.11; 0.10)	0.07 (-0.06; 0.20)
Trend		*p = 0.98*	*p = 0.75*	*p = 0.97*	*p =0.26*
Girls	Low intake	*Reference*	*Reference*	*Reference*	*Reference*
	Medium intake	0.10 (-0.03; 0.23)	0.05 (-0.08; 0.17)	0.05 (-0.07; 0.16)	0.07 (-0.04; 0.19)
	High intake	0.08 (-0.06; 0.22)	0.13 (-0.00; 0.27)	0.11 (-0.02; 0.24)	**0.14 (0.02; 0.25)***
Trend		*p = 0.25*	***p = 0.04***	*p = 0.09*	***p=0.02***

Values are linear regression coefficients (95% confidence intervals) and reflect the increase in BMI (SD scores) for medium and high sugar-containing beverage intake, as compared to the lowest category.
Trend test was performed using categories of sugar-containing beverage intake as continuous variable in the model.
Adjustments were made for age at measurements, gestational age at birth, birth weight (SDS), age of mother and father, net household income, maternal BMI, education, smoking, folic acid use, pre-pregnancy and pregnancy related comorbidities, child hospitalization in first year of life and history of allergy to cow's milk and child's intake of sugar, confectionary, cakes and pastry, breastfeeding, age at introduction of complementary feeding, and hours of TV watching.
*P-value <0.05

Supplementary Material S4.2.8. Association of absolute sugar-containing beverage intake with body composition at age 6, stratified by sex (n=2,001) without total energy adjustment and standardization.

		Difference in total body fat percentage *SD change (95% CI)*	Difference in android/gynoid fat ratio *SD change (95% CI)*
Boys	Low intake	*Reference*	*Reference*
	Medium intake	-0.02 (-0.17; 0.13)	-0.04 (-0.19; 0.12)
	High intake	0.06 (-0.10; 0.22)	0.02 (-0.14; 0.18)
Trend		*p = 0.45*	*p = 0.24*
Girls	Low intake	*Reference*	*Reference*
	Medium intake	0.10 (-0.03; 0.23)	0.10 (-0.06; 0.25)
	High intake	0.10 (-0.08; 0.21)	0.15 (-0.02; 0.31)
Trend		*p = 0.19*	*p = 0.05*

Values are linear regression coefficients (95% confidence interval) and reflect the difference in total body fat percentage (SDS) or android/gynoid fat ratio (SDS) for medium and high sugar-containing beverage intake, compared to the lowest category.
Trend test was performed using categories of sugar-containing beverage intake as continuous variable in the model.
Adjustments were made for age at measurements, gestational age at birth, birth weight (SDS), child height at age 6, age of mother and father, net household income, maternal BMI, education, smoking, folic acid use, pre-pregnancy and pregnancy related comorbidities, child hospitalization in first year of life and history of allergy to cow's milk and child's intake of sugar, confectionary, cakes and pastry, breastfeeding, age at introduction of complementary feeding, and hours of TV watching.

Supplementary Material S4.4.1. Components and cut-offs of the *a priori* diet quality score[1]

Food group	Cut-off level	Summary of included items
Vegetables	≥100 g	Fresh vegetables, frozen or canned vegetables
Fruit	≥150 g	Fresh fruit, canned fruit without added sugar
Bread and cereals	≥70 g	Whole-wheat bread or crackers, oatmeal, muesli without added sugar
Rice, pasta, potatoes, and legumes	≥70 g	Boiled or steamed potatoes, whole-wheat pasta, couscous, whole-grain rice, legumes
Dairy	≥350 g	Semi-skimmed and skimmed milk and yogurt without added sugars, soy milk without added sugars, low-fat and reduced-fat cheeses (20+ and 30+)
Meat, eggs and meat substitutes	≥35 g	Low-fat meat, eggs, tofu, tempeh
Fish	≥15 g	Fresh or canned fish
Fats and oils	≥25 g	Low-fat margarine products (≤16g saturated fat and ≤1g trans-fat per 100g), vegetable oils, liquid cooking or frying fat
Candy and snacks	≤ 20 g	Ice cream, potato chips, cookies, candy bars, fried snacks, cake
Sugar-sweetened beverages	≤ 100 g	Soft drinks, lemonade

[1]Reprinted from Voortman et al., 2015

Supplementary Material S4.4.2. Multivariable-adjusted associations of dietary patterns at 1 year of age with childhood height, weight, body fat percentage, and android/gynoid ratio at 6 years of age.

	Weight (SDS) *n* =2,026	Height (SDS) *n* = 2,026	BF% (SDS) *n* = 1,980	A/G ratio (SDS) *n* = 1,980
	β (95%CI)	β (95%CI)	β (95%CI)	β (95%CI)
Diet score				
Per SD	**0.06 (0.03; 0.10)****	**0.05 (0.01; 0.09)***	0.00 (-0.03; 0.03)	-0.00 (-0.04; 0.04)
Q1	*Reference*	*Reference*	*Reference*	*Reference*
Q2	0.04 (-0.05; 0.13)	-0.01 (-0.13; 0.10)	0.01 (-0.08; 0.10)	-0.04 (-0.14; 0.06)
Q3	0.04(-0.05; 0.14)	-0.02 (-0.14; 0.09)	-0.05 (-0.14; 0.04)	-0.06 (-0.16; 0.04)
Q4	**0.19 (0.10; 0.29)****	**0.15 (0.03;0.27)***	0.02 (-0.08; 0.11)	0.01 (-0.10; 0.11)
PCA Health-conscious pattern				
Per SD	0.03 (-0.01; 0.07)	0.01 (-0.04; 0.05)	-0.01 (-0.04; 0.03)	-0.01 (-0.05; 0.03)
Q1	*Reference*	*Reference*	*Reference*	*Reference*
Q2	0.04 (-0.06; 0.13)	0.05 (-0.07; 0.16)	0.01 (-0.09; 0.10)	0.02 (-0.08; 0.12)
Q3	**0.12 (0.02;0.21)***	0.11 (-0.01; 0.22)	-0.01 (-0.11; 0.08)	0.02 (-0.08; 0.12)
Q4	**0.13 (0.03;0.23)****	0.08 (-0.04; 0.20)	-0.01 (-0.11; 0.08)	-0.02 (-0.12; 0.09)
PCA Western pattern				
Per SD	0.00 (-0.04; 0.04)	0.00 (-0.05; 0.05)	-0.01 (-0.05; 0.04)	0.01 (-0.04; 0.06)
Q1	*Reference*	*Reference*	*Reference*	*Reference*
Q2	-0.01 (-0.11; 0.08)	-0.05 (-0.16; 0.07)	0.05 (-0.05; 0.14)	0.08 (-0.03; 0.18)
Q3	**0.11 (0.01; 0.20)***	0.04 (-0.07; 0.16)	0.03 (-0.07; 0.13)	0.08 (-0.02; 0.19)
Q4	0.03 (-0.08; 0.14)	0.02 (-0.11; 0.15)	-0.02 (-0.13; 0.09)	0.05 (-0.07; 0.17)
RRR pattern 1				
Per SD	**0.10 (0.06; 0.14)****	**0.05 (0.00; 0.10)***	**0.08 (0.04; 0.12)****	**0.07 (0.02; 0.11)****
Q1	*Reference*	*Reference*	*Reference*	*Reference*
Q2	**0.09 (0.00;0.19)***	0.04 (-0.08; 0.15)	**0.10 (0.01; 0.19)***	0.08 (-0.02; 0.18)
Q3	**0.14 (0.05;0.24)****	**0.12 (0.00; 0.24)***	0.08 (-0.01; 0.18)	0.06 (-0.04; 0.16)
Q4	**0.23 (0.13;0.33)****	**0.13 (0.01; 0.25)***	**0.14 (0.04; 0.24)****	**0.14 (0.03; 0.25)****
RRR pattern 2				
Per SD	0.02 (-0.02; 0.06)	0.02 (-0.03; 0.07)	**-0.05 (-0.09;-0.01)****	**-0.05 (-0.09;-0.00)***
Q1	*Reference*	*Reference*	*Reference*	*Reference*
Q2	-0.06 (-0.15; 0.04)	-0.03 (-0.15; 0.09)	-0.07 (-0.16; 0.03)	-0.07 (-0.17; 0.03)
Q3	**0.11 (0.01; 0.21)***	**0.13 (0.01; 0.25)***	-0.06 (-0.16; 0.04)	-0.03 (-0.14; 0.08)
Q4	0.04 (-0.07; 0.15)	0.01 (-0.12; 0.15)	**-0.12 (-0.23; -0.02)***	-0.12 (-0.23; 0.00)

Values are regression coefficients that reflect the difference in outcome (age- and sex-adjusted SD scores) per 1 SD increase in exposure and for quartiles of exposure compared to the lowest quartile, based on imputed data.

Models are adjusted for maternal age, BMI at enrollment, parity, folic acid supplement use, smoking and alcohol use during pregnancy; paternal smoking and education; household income; and child sex, breastfeeding in the first four months of life, timing of introduction of complementary feeding, age at dietary measurement, total energy intake at 1 year, and television watching at age 2 years. BF% and A/G ratio are additionally adjusted for child height.

Abbreviations: BF%, body fat percentage; A/G ratio, android/gynoid ratio; PCA, principal component analyses; RRR, reduced rank regression

*p<0.05, **p<0.01

Supplementary Material S4.4.3. Associations of dietary patterns at 1 year of age with childhood body composition at 6 years of age with various adjustment levels, and sensitivity analysis excluding breast/formulafed children

	BMI (SDS) *n* = 2,026 or 1,649	FMI (SDS) *n* = 1,980 or 1,609	FFMI (SDS) *n* = 1,980 or 1,609
	β (95%CI)	β (95%CI)	β (95%CI)
Diet quality score (per SD)			
Crude model – total population	**0.05 (0.02; 0.08)****	0.01 (-0.02; 0.04)	**0.07 (0.03; 0.11)****
Covariate adjusted (main model) – total population	**0.06 (0.02; 0.09)****	0.02 (-0.01; 0.05)	**0.06 (0.02; 0.10)****
Covariate adjusted (main model) – weaned children	**0.06 (0.02; 0.09)****	0.03 (-0.01; 0.06)	**0.05 (0.00; 0.09)***
Main model + baseline BMI –total population	**0.04 (0.01; 0.07)***	0.01 (-0.02; 0.04)	**0.05 (0.01; 0.08)***
Health-conscious pattern (PCA) (per SD)			
Crude model – total population	**0.04 (0.00; 0.07)***	0.00 (-0.03; 0.04)	**0.05 (0.01; 0.09)***
Covariate adjusted (main model) – total population	**0.04 (0.01; 0.08)***	0.01 (-0.03; 0.04)	**0.05 (0.01; 0.09)***
Covariate adjusted (main model) – weaned children	0.03 (-0.01; 0.07)	-0.00 (-0.04; 0.04)	0.03 (-0.02; 0.08)
Main model + baseline BMI –total population	0.03 (-0.00; 0.07)	0.00 (-0.03; 0.03)	**0.04 (0.00; 0.08)***
Western pattern (PCA) (per SD)			
Crude model – total population	0.04 (-0.01; 0.08)	**0.05 (0.01; 0.09)***	0.00 (-0.04; 0.05)
Covariate adjusted (main model) – total population	0.00 (-0.04; 0.05)	-0.01 (-0.05; 0.03)	0.02 (-0.04; 0.07)
Covariate adjusted (main model) – weaned children	-0.03 (-0.09; 0.02)	-0.04 (-0.09; 0.01)	0.00 (-0.06; 0.06)
Main model + baseline BMI –total population	0.01 (-0.03; 0.05)	-0.01 (-0.04; 0.03)	0.02 (-0.03; 0.07)
RRR pattern 1 (per SD)			
Crude model – total population	**0.14 (0.10; 0.18)****	**0.15 (0.11; 0.19)****	**0.08 (0.03; 0.13)****
Covariate adjusted (main model) – total population	**0.11 (0.07; 0.15)****	**0.10 (0.06; 0.13)****	**0.09 (0.04; 0.14)****
Covariate adjusted (main model) – weaned children	**0.09 (0.04; 0.13)****	**0.08 (0.04; 0.12)****	**0.07 (0.01; 0.12)***
Main model + baseline BMI –total population	**0.10 (0.06; 0.14)****	**0.09 (0.06; 0.13)****	**0.08 (0.03; 0.12)****
RRR pattern 2 (per SD)			
Crude model – total population	0.00 (-0.04; 0.04)	**-0.06 (-0.10; -0.03)****	**0.08 (0.03; 0.12)****
Covariate adjusted (main model) – total population	0.02 (-0.02; 0.06)	-0.03 (-0.07; 0.00)	**0.07 (0.02; 0.11)****
Covariate adjusted (main model) – weaned children	0.02 (-0.03; 0.06)	-0.03 (-0.07; 0.01)	0.05 (-0.00; 0.10)
Main model + baseline BMI –total population	0.01 (-0.03; 0.04)	**-0.04 (-0.07; -0.01)***	**0.06 (0.01; 0.10)****

Values are regression coefficients that reflect the difference in outcome (age- and sex-adjusted SD scores) per 1 SD increase in exposure, based on imputed data.
Weaned children were defined as children who no longer receive breast milk or a substantial amount of infant formula (i.e., more than 500 kcal/d).
Crude models are adjusted for child sex, age at dietary measurement and total energy intake at 1 year.
Covariate models are additionally adjusted for maternal age, BMI at enrollment, parity, folic acid supplement use, smoking and alcohol use during pregnancy; paternal smoking and education; household income; and child breastfeeding in the first four months of life, timing of introduction of complementary feeding, and television watching at age 2 years.
Baseline BMI adjusted models are additionally adjusted for BMI-SDS at the age of 1 year
Abbreviations: BMI, body mass index; FMI, fat mass index; FFMI, fat-free mass index; PCA, principal component analyses; RRR, reduced rank regression
*p<0.05, **p<0.01