Supplemental Online Content

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

eMethods

Participant Selection

All pregnant individuals attending routine second trimester ultrasonography scans from 19.0 through 23.6 weeks' gestation were screened for eligibility under the Royal College of Obstetrics and Gynaecologists criteria of being at risk for SGA during pregnancy1.

In order to be eligible, they had to fulfill one major criterion and/or three minor criteria. Inclusion criteria were age 18 years or older, fluency in Spanish language, singleton pregnancy, positive fetal heart rate at the time of ultrasonography, and high risk of newborns with SGA according to the adapted criteria of the Royal College of Obstetricians and Gynaecologists for SGA. Exclusion criteria were fetal anomalies, including chromosomal abnormalities, structural malformations, and congenital infections, detected prenatally; neonatal malformations or congenital anomalies diagnosed after birth; inability to perform additional visits; participation in another trial; and maternal intellectual disability or other mental or major psychiatric disorders requiring therapy during pregnancy.

Participants were analyzed according to their randomization group, excluding from analysis those who withdrew consent for participation in the trial and those whose fetuses/neonates had a malformation diagnosed during pregnancy or in the postnatal period.

Randomization

Participants were randomized using an online central randomization service. Allocation concealment was ensured, as the service did not release the randomization code until the participant was recruited into the trial, which took place after eligibility had been confirmed and consent form signed. Randomization was requested by the investigator responsible for recruitment. A different investigator, responsible for allocation, generated the allocation sequence using an online central randomization about intervention allocation to the participant. Participants were randomly assigned to either Usual care, Mediterranean diet, or Mindfulness-Based Stress Reduction (stress reduction) with a 1:1:1 allocation as per computerized random number generator, with equal proportion in each group. The randomization strategy used in this trial was the simple randomization, restricting for an equal number of patients required in each treatment group at the end of the trial.

Mediation analyses

Parametric Mediation analyses was conducted to generate evidence about the mechanisms by which interventions may influence the outcomes. We defined as mediating variables the Mediterranean diet adherence score (obtained from a 17-item dietary assessment questionnaire) and Perceived Stress score (obtained from Perceived Stress scale, PSS). In addition, we performed models with the biomarkers of walnuts consumption (oleic acid concentration),extra virgin olive oil consumption (hydroxytyrosol concentration) and the maternal stress (cortisone/ cortisol ratio) at the final visit. We defined as outcomes cognitive and socio-emotional Bayley-III scores. The sample sizes of the biomarkers will be significantly reduced due to the number of subsample of participants who provided the biomarkers, randomly selected from the three study groups. Thus, the results should be considered with caution. The estimation of Average Causal Mediation Effects, Average Direct Effects, the Total Effects and the Proportion Mediated effects were computed for each of 1000 bootstrapped resamples, and the 95% confidence interval was computed by determining 2.5th and 97.5th percentiles for the resamples2. The mediation analysis was done with mediation package version 4.5.03.

eResults

Individuals non attending the Bayley Scales of Infant and Toddler Development assessment. Among all individuals included in the trial, 558 (47%) did not participate to the Bayley III assessment. Maternal and perinatal characteristics of individuals who refused/non-responded are displayed in eTable 1, showing similar characteristics among the study groups with the exception of SGA prevalence. Individuals who did not participate in the postnatal follow-up had similar maternal and perinatal characteristics as those who participated in the follow-up, with the exception for a younger maternal age (Non-participants 35.6 years vs. Participants 37.8 years, p<0.001), lower rate of white ethnicity (74.9% vs. 81.9%, p=0.04), and higher rate of low socio-economic status (9.0% vs. 4.8%, p=0.01) as compared to those who attended the postnatal follow-up.

Bayley Scales of Infant and Toddler Development, 3rd edition (Bayley-III)

Infants from the Mediterranean diet group had significantly higher scores in the cognitive and social-emotional domains, and those from the stress reduction group had significantly higher scores in the social-emotional domain, compared to controls when adjusting for maternal socioeconomic status and fetal sex (eTable 2).

The evaluation of Mediterranean diet adherence and maternal adherence to the Mediterranean diet intervention Participants belonged to the Mediterranean diet intervention showed higher scores to Mediterranean diet adherence and higher consumption of fatty acids at final assessment, compared to the usual care group (eTable 4); this was also reflected by related biomarkers of walnuts consumption, particularly α -Linolenic acid (eTable 5). Stress reduction group mothers also showed improvements in several fatty acids' intakes; however, they were not significantly different compared to the usual care group. Among the Mediterranean diet group participants, 155 (71.8%) women had high adherence to the intervention.

Infant Bayley-III and maternal fatty acids' intake and nutritional biomarkers

There was a positive association with several Bayley-III domains and Mediterranean diet adherence score (eFigure 1) and fatty acids' intake. We reported in eTable 6 the comparison between lower (T1) vs higher intake (T3) of fatty acids according to Spanish food consumption databases4,5: after adjustment by variables considered predictable of neurodevelopment at 24 months (mother's socioeconomic status, gestational age at delivery, birthweight, fetal sex, and breastfeeding over 4 months) and also by energy intake, a higher consumption of monounsaturated fatty acids (MUFA) was associated with higher score in the cognitive and motor domain; a higher consumption of saturated fatty acids (SFA) with a better motor score; a higher consumption of Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) with a better language domain; and finally, a higher consumption of trans-fatty acids with a higher social-emotional domain.

Regarding nutritional biomarkers in the whole study population, only oleic acid had positive associations with adaptive behavior domain (β (95%CI); 0.62 (0.19 to 1.03); p=0.004) (eTable 7).

The evaluation of stress and anxiety and maternal adherence to the stress reduction intervention

Women belonged to the stress reduction group had significantly lower State-Trait Anxiety Inventory (STAI) personality and STAI anxiety scores, and significantly higher scores on the Five Facet Mindfulness Questionnaire (FFMQ) observation, FFMQ non-judgmental and FFMQ non-reactivity scores at final assessment, compared to the usual care group (eTable 8). This was also reflected by the urinary biomarker related to stress: higher 24h urinary cortisone/cortisol ratio in the stress reduction group compared with the usual care group (eTable 8). Among the stress reduction group participants, 137 (63.7%) women had high adherence to the intervention (prespecified in the Statistical Analysis Plan).

Infant Bayley-III and maternal stress, well-being, and mindful state during pregnancy

Associations of infant Bayley-III cognitive domains with perceived stress, STAI personality and anxiety are displayed in eFigures 2, with maternal WHO-5 wellbeing in eFigure 3, with cortisone/cortisol in eFigure 4; and with FFMQ in eTable 9.

Mediation analysis

In the Mediterranean diet group, the intervention had significant total effect on Bayley cognitive domain (eFigure 5, Casual Model 1) and social-emotional domain (eFigure 6, Casual Model 2). Mediterranean diet adherence score at the final visit had a high proportion mediated on the cognitive domain (78%, eFigure 5), and it had low proportion mediated on the social-emotional domain (44%, eFigure 6). Casual Model 3 showed that the PSS measure at the final visit showed low proportion mediated on the Bayley social-emotional domain (6.7%, eFigure 7). Regarding the casual models with the biomarkers (available only in a subsample with reduced sample size), the intervention had borderline or non-significant total effects on the Bayley outcomes (eFigure 8, Casual Model 4 and eFigure 9, Casual Model 5). In Casual Model 4, oleic acid concentration at the final visit had a very low proportion mediated on the cognitive domain (0.5%) and on the social-emotional domain (11%) (eFigure 8). In Casual Model 5, the hydroxycortisol concentration at the final visit had low proportion mediated on the cognitive domain (3.2%) and the social-emotional domain (3.1%) (eFigure 9).

In the Stress reduction group, the intervention had significant total effect on the social-emotional domain in both Casual Model 2 and 3. The proportion mediated of the Mediterranean diet adherence score on social-emotional domain was very low (4.7%, eFigure 6), as well as proportion mediated of the PSS measure at the final visit (0.4%, eFigure 7). Regarding the casual model with the biomarker (available only in a subsample with reduced sample size) (eFigure10, Casual Model 6), the intervention did not have a significant effect on the social-emotional domain, and the cortisone/ cortisol ratio had low proportion mediated on the outcome (60%, eFigure 10).

eTable 1. Maternal, neonatal and infants' characteristics of individuals who did not participate in the Bayley Scales of Infant and Toddler Development, 3rd edition (Bayley-III) assessment, according to intervention groups (n=558)

	Mediterranean Diet	Stress reduction	Usual care	Mediterranean Diet vs. Usual care	Stress reduction vs. Usual care
	n=174	n=176	n=208	p value	p value
Maternal Characteristics					
Age (years)	35.5 (5.6)	35.7 (5.6)	35.6 (5.7)	0.88	0.81
Race and ethnicity				0.16	0.59
Afro-American	6 (3.4%)	5 (2.8%)	3 (1.4%)		
Asian	6 (3.4%)	1 (0.6%)	3 (1.4%)		
Latin American	23 (13.2%)	39 (22.2%)	39 (18.8%)		
Maghreb	2 (1.1%)	7 (4.0%)	6 (2.9%)		
White	137 (78.7%)	124 (70.5%)	157 (75.5%)		
Socio-economic statusa				0.97	0.15
Low	13 (7.5%)	22 (12.5%)	15 (7.2%)		
Medium	72 (41.4%)	74 (42.0%)	84 (40.4%)		
High	89 (51.1%)	80 (45.5%)	109 (52.4%)		
Education				0.93	0.15
None/primary	13 (7.5%)	22 (12.5%)	15 (7.2%)		
Secondary/technology	69 (39.7%)	70 (39.8%)	79 (38.0%)		
University	92 (52.9%)	84 (47.7%)	114 (54.8%)		
Cigarette smoking	46 (26.4%)	36 (20.5%)	57 (27.4%)	0.83	0.11
Alcohol intake	16 (9.2%)	19 (10.8%)	25 (12.0%)	0.37	0.71
Drugs consumption	3 (1.7%)	2 (1.1%)	3 (1.4%)	0.82	0.79
Neonatal Characteristics					
Sex				0.63	0.96
Female	84 (48.3%)	84 (47.7%)	97 (46.6%)		
Male	90 (51.7%)	92 (52.3%)	122 (53.4%)		
Gestational age at delivery (weeks)	39.6 (38.7 - 40.4)	39.7 (39.0 - 40.5)	39.4 (38.3 - 40.3)	0.11	0.007
Cesarean section	65 (37.6%)	67 (32.2%)	56 (29.8%)	0.24	0.93
Birthweight (g)	3180.1 (522.7)	3215.9 (474.1)	3090.3 (691.2)	0.16	0.04
Birthweight percentile	42.8 (30.3)	42.7 (30.5)	41.3 (31.2)	0.63	0.65
Small for gestational age (<10th centile)	20 (11.5%)	28 (15.9%)	48 (23.1%)	0.008	0.21
Apgar 5 minutes <7	1 (0.6%)	3 (1.7%)	3 (1.4%)	0.35	0.97
Umbilical artery pH	7.21 (0.08)	7.21 (0.08)	7.21 (0.09)	0.79	0.96
Neonatal Intensive Care Unit admission	10 (5.7%)	6 (3.4%)	16 (7.7%)	0.31	0.18

Data are expressed as mean (SD) or median (IQR) or n (%). aSocioeconomical status: low (never work or unemployed >2ys); medium (secondary studies & work); high (university studies & work).

eTable 2. Adjusted comparisons of Bayley Scales of Infant and Toddler Development examination (Bayley-III) of infants according to intervention groups (n=626)

	Mediterranean	Stress	Usual	Mediterranean	diet	Stress reduc	tion
	Mediterranean diet n=218 123.6 (17.8) 2 (0.9%) 107.9 (19.2) 15 (6.9%) 113.3 (14.4) 0 (0.0%) 108.6 (22.0) 24 (11.1%) 94.8 (16.3)	reduction	care	vs. Usual ca	re	vs. Usual ca	are
	n=218	n=215	n=193	Adjusted mean difference (95% CI)	p value	Adjusted mean difference (95% CI) p v	
3ayley-III domains							
Cognitive composite score	123.6 (17.8)	119.3 (19.6)	118.6 (18.3)	4.15 (0.71 to 7.60)	0.01	0.34 (-3.28 to 3.97)	0.18
Cognitive score below 85	2 (0.9%)	8 (3.7%)	7 (3.6%)		0.06		0.96
Language composite score	107.9 (19.2)	104.7 (17.7)	105.5 (17.0)	1.53 (-1.89 to 4.97)	0.38	-0.84 (-4.10 to 2.41)	0.60
Language score below 85	15 (6.9%)	19 (8.9%)	16 (8.5%)		0.55		0.86
Motor composite score	113.3 (14.4)	113.4 (13.9)	114.7 (13.8)	-1.78 (-4.51 to 0.95)	0.20	-1.46 (-4.16 to 1.23)	0.28
Motor score below 85	0 (0.0%)	1 (0.5%)	3 (1.6%)		0.06		0.27
Social-emotional composite score	108.6 (22.0)	108.2 (24.0)	103.4 (18.5)	4.52 (0.56 to 8.48)	0.02	4.38 (0.23 to 8.53)	0.03
Social-emotional score below 85	24 (11.1%)	23 (10.7%)	28 (14.5%)		0.30		0.25
Adaptive composite score	94.8 (16.3)	93.0 (16.5)	94.0 (15.5)	0.14 (-2.93 to 3.22)	0.92	-1.12 (-4.24 to 1.99)	0.47
Adaptive score below 85	50 (23.1%)	58 (26.9%)	51 (26.4%)		0.44		0.90

Data are expressed as mean (SD) or n (%). CI denotes for Confidence interval. p values were generated from a regression model adjusted for: socioeconomic status and fetal sex. Language n=620, Motor n=625, Social-Emotional=n=624, Adaptive behavior n=624.

eTable 3. Comparison of Bayley Scales of Infant and Toddler Development examination, 3rd edition (Bayley-III) comparing appropriate versus small for gestational age newborns (n=626)

	Appropriate for gestational age	Small for gestational age		
	n=519	n=107	Adjusted mean difference (95% CI)	p value
Bayley-III domains				
Cognitive composite score	120.5 (18.9)	121.0 (17.9)	-0.48 (-4.38 to 3.42)	0.80
Cognitive score below 85	31 (6.0%)	5 (4.7%)		0.60
Language composite score	105.9 (18.1)	106.9 (18.0)	-1.05 (-4.82 to 2.71)	0.58
Language score below 85	110 (21.5%)	27 (25.2%)		0.63
Motor composite score	113.8 (14.2)	113.5 (13.5)	0.33 (-2.59 to 3.26)	0.82
Motor score below 85	26 (5.0%)	7 (6.5%)		0.52
Social-emotional composite score	107.6 (22.3)	103.4 (18.9)	4.22 (-0.31 to 8.76)	0.07
Social-emotional score below 85	85 (16.4%)	17 (15.9%)		0.89
Adaptive composite score	94.2 (16.2)	92.7 (15.8)	1.42 (-1.93 to 4.79)	0.40
Adaptive score below 85	184 (35.6%)	43 (40.2%)		0.37

Data are expressed as mean (SD) or n (%). CI denotes for Confidence interval. p values were generated from a regression model adjusted for: socioeconomic status and fetal sex. Language n=620, Motor n=625, Social-Emotional=n=624, Adaptive behavior n=624

eTable 4. Maternal Mediterranean diet adherence and fatty acid intake at the final visit adjusted by baseline assessment per intervention group (n=543)

		Mediterranean diet	Stress reduction	Usual care		Mediterranean diet vs. Usual care	Stress reduction vs. Usual care	Mediterranean diet vs. Stress reduction
		(N=198)	(N=177)	(N=168)	рс	Adjusted mean difference (95% CI)	Adjusted mean difference (95% CI)	Adjusted mean difference (95% CI)
Mediterranean diet adherence score+	Baselinea	8.01 (2.62)	7.60 (2.62)	7.56 (2.61)				
	Finalb	12.4 (0.15)**	8.23 (0.15)*	7.90 (0.16)	<0.001	-4.45 (-4.88 to -4.02)	-0.33 (-0.76 to 0.10)	-4.12 (-4.53 to -3.70)
SFA – g/day	Baselinea	34.1 (10.1)	34.9 (9.78)	34.1 (9.23)				
	Finalb	36.8 (0.58)**	35.5 (0.61)	35.5 (0.63)	0.19	1.32 (-0.34 to 3.00)	0.02 (-1.69 to 1.74)	1.30 (-0.34 to 2.95)
MUFA – g/day	Baselinea	60.9 (15.0)	62.0 (14.8)	61.6 (15.5)				
	Finalb	67.2 (0.87)**	64.8 (0.92)*	63.1 (0.94)	0.006	4.04 (1.53 to 6.56)	1.64 (-0.94 to 4.22)	2.40 (-0.08 to 4.88)
PUFA – g/day	Baselinea	21.7 (7.59)	21.9 (7.52)	23.3 (8.28)				
	Finalb	28.3 (0.48)**	21.6 (0.51)	22.9 (0.52)	<0.001	5.38 (3.98 to 6.77)	-1.30 (-2.72 to 0.13)	6.67 (5.31 to 8.04)
α -Linoleic acid – g/day	Baselinea	14.2 (5.71)	14.3 (6.70)	15.4 (6.26)				
	Finalb	18.5 (0.36)**	14.1 (0.38)	15.3 (0.39)	<0.001	3.29 (2.24 to 4.34)	-1.16 (-2.24 to -0.08)	4.45 (3.42 to 5.48)
α -Linolenic acid – g/day	Baselinea	1.40 (0.58)	1.36 (0.63)	1.40 (0.62)				
	Finalb	2.38 (0.04)**	1.37 (0.04)	1.43 (0.04)	<0.001	0.95 (0.83 to 1.07)	-0.06 (-0.18 to 0.06)	1.01 (0.89 to 1.13)
EPA – g/day	Baselinea	0.17 (0.12)	0.15 (0.09)	0.15 (0.10)				
	Finalb	26.7 (0.01)**	0.17 (0.01)*	0.16 (0.01)	<0.001	0.10 (0.08 to 0.12)	0.01 (-0.02 to 0.03)	0.10 (0.08 to 0.12)
DHA – g/day	Baselinea	0.35 (0.28)	0.31 (0.23)	0.31 (0.24)				
	Finalb	0.60 (0.02)**	0.36 (0.02)*	0.34 (0.02)	<0.001	0.25 (0.20 to 0.30)	0.02 (-0.04 to 0.07)	0.23 (0.18 to 0.28)
Trans-fatty acids – g/day	Baselinea	1.67 (1.21)	1.65 (1.08)	1.68 (1.17)				
	Finalb	1.30 (0.07)**	1.60 (0.07)	1.68 (0.07)	<0.001	-0.38 (-0.57 to -0.19)	-0.08 (-0.27 to 0.12)	-0.30 (-0.49 to -0.11)

CI denotes Confidence interval, SFA Saturated fatty acids, MUFA Monounsaturated fatty acids, PUFA Polyunsaturated fatty acids, EPA Eicosapentaenoic acid, DHA Docosahexaenoic acid.

+Mediterranean diet adherence score was available for 612 participants (n=216 Mediterranean diet, n=206 Stress reduction, n=190 Usual care).

aBaseline values are observed means (SD). bFinal values are baseline-adjusted (least-squares) means (SE) and comparison among groups done with ANCOVA analysis. *P<0.05 and **P<0.001 final comparison adjusted for baseline values. cANCOVA analysis for the final assessment.

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eTable 5. Maternal biomarkers of Mediterranean diet adherence at the final visit adjusted by baseline assessment per intervention group (n=291)

		Mediterranean diet	Stress reduction	Usual care		Mediterranean diet vs. Usual care	Stress reduction vs. Usual care	Mediterranean diet vs. Stress reduction
		(N=95)	(N=105)	(N=91)	рс	Adjusted mean difference (95% CI)	Adjusted mean difference (95% CI)	Adjusted mean difference (95% CI)
Oleic acid µmol/g creatinine	Baselinea	20.92 (3.91)	20.86 (4.03)	21.20 (4.41)				
	Finalb	22.1 (0.28)*	22.5 (0.27)*	22.6 (0.29)*	0.29	-0.42 (0.22 to 0.38)	-0.07 (-0.83 to 0.69)	0.34 (-0.42 to 1.10)
α-Linoleic acid μmol/g creatinine	Baselinea	28.37 (4.12)	28.31 (4.36)	27.86 (3.49)				
	Finalb	28.3 (0.36)*	26.6 (0.34)*	27.1 (0.37)	0.002	1.12 (0.10 to 2.13)	-0.57 (-0.55 to 0.41)	-1.69 (-2.67 to -0.71)
α-Linolenic acid µmol/g creatinine	Baselinea	0.37 (0.16)	0.35 (0.14)	0.36 (0.14)				
	Finalb	0.54 (0.01)**	0.36 (0.01)	0.38 (0.01)	<0.001	0.15 (0.11 to 0.18)	-0.02 (-0.05 to 0.01)	-0.19 (-0.22 to -0.15)
OH-TY µmol/g creatinine	Baselinea	0.42 (1.60)	0.31 (0.86)	0.26 (0.83)				
	Finalb	1.64 (0.23)**	0.96 (0.22)*	1.21 (0.23)**	0.10	0.42 (-0.22 to 1.06)	-0.25 (-0.87 to 0.37)	-0.68 (1.30 to -0.05)
4'-O-Glu_OH-TY μmol/g creatinine	Baselinea	1.52 (2.03)	2.08 (3.98)	1.65 (3.36)				
	Finalb	1.96 (0.35)	1.68 (0.33)	1.60 (0.35)	0.81	0.34 (-0.64 to 1.32)	0.08 (-0.88 to 1.04)	-0.25 (-1.19 to 0.69)
3'-O-Glu_OH-TY µmol/g creatinine	Baselinea	2.24 (3.64)	1.90 (3.36)	1.84 (4.05)				
	Finalb	0.82 (0.18)**	1.10 (0.17)*	0.90 (0.18)*	0.56	-0.08 (-0.58 to 0.42)	0.19 (-0.30 to 0.68)	0.28 (-0.21 to 0.77)

OH-TY denotes Hydroxytyrosol, 4'-O-Glu-OH-TY, Urine 4-O-Glucose-Hydroxytyrosol Concentration; 3'-O-Glu-OH-TY, Urine 3-O-Glucose-Hydroxytyrosol Concentration. aBaseline values are observed as means (SD).

bFinal value are baseline-adjusted (least-square) means (SE) and comparison among groups done with ANCOVA analysis. *P<0.05 and **P<0.001 final comparison adjusted for baseline values. cANCOVA analysis for the final assessment.

eTable 6. Associations between fatty acids intake according to Spanish food consumption (tertiles) at final assessment during pregnancy (34-36 weeks' gestation) and the infant Bayley-III results in the whole study population (n=543)

Bayley-III assessment	I	Fatty acids tertile	T3 vs. T1			
	T1 (Low)	T2 (Medium)	T3 (High)	Adjusted mean difference (95% CI)	p value	
MUFA						
Cognitive	118.6 (19.1)	121.3 (18.0)	123.1 (18.3)	4.69 (0.94 to 8.44)	0.01	
Language	105.1 (17.3)	107.2 (18.3)	106.9 (17.6)	1.92 (-1.71 to 5.55)	0.30	
Motor	112.8 (14.5)	114.4 (14.6)	115.2 (12.9)	2.54 (-0.31 to 5.40)	0.08	
Social-Emotional	105.5 (23.0)	108.4 (21.2)	106.6 (21.5)	1.34 (-3.12 to 5.80)	0.55	
Adaptive behavior	93.4 (15.8)	92.8 (15.8)	96.1 (16.2)	2.89 (-0.36 to 6.13)	0.08	
PUFA						
Cognitive	120.6 (18.8)	120.3 (18.1)	122.2 (18.6)	1.81 (-1.96 to 3.58)	0.34	
Language	105.8 (18.0)	105.7 (16.9	107.7 (18.4)	2.06 (-1.57 to 5.70)	0.26	
Motor	114.1 (15.2)	114.2 (13.5)	114.0 (13.4)	-0.11 (-2.98 to 2.75)	0.93	
Social-Emotional	106.7 (22.3)	106.6 (21.7)	107.1 (21.8)	0.51 (-3.96 to 4.99)	0.82	
Adaptive behavior	93.7 (16.3)	94.6 (16.0)	94.0 (15.8)	0.48 (-2.79 to 3.74)	0.77	
SFA						
Cognitive	119.9 (18.4)	120.2 (19.5)	123.0 (17.5)	3.18 (-0.59 to 6.94)	0.09	
Language	106.3 (17.3)	106.9 (18.7)	106.1 (17.3)	-0.15 (-3.78 to 3.49)	0.93	
Motor	114.0 (14.7)	112.6 (13.9)	115.8 (13.3)	1.71 (-1.14 to 4.57)	0.23	
Social-Emotional	107.1 (22.8)	107.8 (21.9)	105.6 (21.1)	-1.10 (-5.58 to 3.38)	0.62	
Adaptive behavior	93.2 (15.9)	93.6 (15.2)	95.4 (16.9)	2.30 (-0.97 to 5.57)	0.16	
Linoleic acid		· · ·				
Cognitive	120.5 (19.2)	119.6 (17.3)	122.9 (18.8)	2.45 (-1.30 to 6.21)	0.20	
Language	105.3 (18.5)	105.7 (15.7)	108.1 (18.8)	2.73 (-0.90 to 6.36)	0.14	
Motor	114.0 (14.6)	114.9 (13.9)	113.5 (13.6)	-0.45 (-3.32 to 2.41)	0.75	
Social-Emotional	106.6 (22.3)	106.6 (22.6)	107.3 (20.9)	0.63 (-3.84 to 5.09)	0.61	
Adaptive behavior	93.2 (15.8)	94.2 (16.5)	94.8 (15.7)	1.71 (-1.54 to 4.97)	0.30	
Linolenic acid						
Cognitive	119.3 (18.3)	120.0 (18.9)	123.6 (18.0)	4.17 (0.42 to 7.93)	0.02	
Language	104.0 (17.4)	. ,	108.1 (18.4)	4.16 (0.54 to 7.78)	0.02	
Motor	113.6 (14.4)	115.9 (13.7)	112.9 (13.9)	-0.88 (-3.73 to 1.97)	0.54	
Social-Emotional	107.0 (22.8)	104.7 (21.9)	108.8 (20.9)	1.77 (-2.69 to 6.24)	0.43	
Adaptive behavior	92.7 (15.5)	94.4 (16.4)	95.1 (16.0)	2.35 (-0.91 to 5.61)	0.15	
EPA		. , ,				
Cognitive	118.7 (18.7)	122.3 (17.9)	122.1 (18.7)	3.27 (-0.49 to 7.04)	0.08	
Language	103.2 (16.0)	107.0 (18.4)	109.0 (18.4)	5.45 (1.82 to 9.08)	<0.001	
Motor	113.5 (13.9)	114.7 (14.3)	114.2 (14.0)	0.65 (-2.22 to 3.53)	0.65	
Social-Emotional	106.2 (22.8)	107.4 (21.3)	106.9 (21.6)	0.94 (-3.54 to 5.43)	0.68	
Adaptive behavior	92.6 (15.4)	94.2 (16.5)	95.5 (16.0)	2.72 (-0.55 to 5.99	0.10	
DHA	(/)	. ()	/	(
Cognitive	118.3 (18.8)	122.9 (17.6)	121.9 (18.8)	3.30 (-0.46 to 7.07)	0.08	
Language	102.6 (15.9)	107.1 (17.5)	109.5 (1901)	6.56 (2.94 to 10.2)	<0.001	
	113.4 (13.9)	114.9 (14.3)	114.1 (13.9)	0.61 (-2.27 to 3.49)	0.67	
Motor	110.7 (10.9)	117.0 (17.0)	114.1 (10.0)	0.01 (2.21 (0 0.40)	0.07	

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Social-Emotional	105.9 (22.8)	107.1 (20.7)	107.5 (22.2)	1.64 (-2.84 to 6.13)	0.47
Adaptive behavior	92.3 (15.3)	94.4 (16.3)	95.6 (16.3)	2.94 (-0.33 to 6.20)	0.07
Trans fat					
Cognitive	121.0 (18.7)	122.2 (18.0)	119.8 (18.8)	-0.98 (-4.74 to 2.79)	0.61
Language	108.2 (18.2)	107.1 (17.8)	103.8 (17.0)	-4.14 (-7.77 to -0.51)	0.02
Motor	114.2 (14.2)	115.2 (14.9)	113.0 (13.0)	-1.29 (-4.16 to 1.57)	0.37
Social-Emotional	110.1 (20.9)	106.8 (20.9)	103.6 (21.9)	-6.27 (-10.7 to -1.82)	0.01
Adaptive behavior	94.6 (16.5)	94.6 (15.4)	93.1 (16.2)	-1.42 (-4.69 to 1.84)	0.39

Bayley-III denotes for Bayley Scales of Infant and Toddler Development, 3rd edition, MUFA Monounsaturated fatty acids, PUFA Polyunsaturated fatty acids, SFA Saturated fatty acids, EPA Eicosapentaenoic acid, DHA Docosahexaenoic acid.

P values were generated from a regression model adjusted for: socioeconomic status and fetal sex.

eTable 7. Association between biomarkers related to Mediterranean diet at 34-36 weeks' gestation and the infant Bayley-III results in the whole study population (n=290)

Bayley-III domain	Oleic acid		a-Linoleic acid		a-Linolenic	acid	Hydroxytyrosol*		4'-O-Glu-OH-TY*		3'-O-Glu-OH	I-TY
			(ω 6)		(w 3)							
	β (95%CI)	p value	β (95%Cl)	p value	β (95%CI)	p value	β (95%Cl)	p value	β (95%CI)	p value	β (95%Cl)	p value
Cognitive	0.06 (-0.40 to 0.53)	0.79	0.09 (-0.39 to 0.58)	0.69	1.28 (-9.49 to 12.07)	0.81	-0.21 (-0.70 to 0.27)	0.38	0.25 (-0.61 to 1.11)	0.56	-0.57 (-1.29 to 0.14)	0.11
Language	0.31 (-0.12 to 0.76)	0.16	0.15 (-0.30 to 0.62)	0.50	3.71 (-6.51 to 13.94)	0.47	0.13 (-0.32 to 0.60)	0.56	-0.04 (-0.86 to 0.78)	0.92	-0.09 (-0.78 to 0.58)	0.78
Motor	0.14 (-0.21 to 0.49)	0.43	0.04 (-0.32 to 0.41)	0.81	2.37 (-5.74 to 10.49)	0.56	-0.23 (-0.60 to 0.13)	0.20	0.44 (-0.20 to 1.09)	0.18	-0.45 (-0.99 to 0.08)	0.10
Socio-emotional	0.50 (-0.05 to 1.07)	0.08	-0.18 (-0.78 to 0.40)	0.53	7.20 (-5.81 to 20.22)	0.27	-0.50 (-1.09 to 0.08)	0.09	-0.64 (-1.68 to 0.40)	0.23	0.27 (-0.60 to 1.14)	0.54
Adaptative behavior	0.61 (0.19 to 1.03)	0.004	0.20 (-0.24 to 0.64)	0.37	1.08 (-8.64 to 10.82)	0.82	0.22 (-0.22 to 0.66)	0.32	0.34 (-0.43 to 1.12)	0.38	-0.01 (-0.66 to 0.64)	0.96

Bayley-III denotes for Bayley Scales of Infant and Toddler Development, 3rd edition, SE: standard error, 4'-O-Glu-OH-TY: Urine 4-O-Glucose-Hydroxytyrosol Concentration, 3'-O-Glu-OH-TY: Urine 3-O-Glucose-Hydroxytyrosol Concentration, 3'-O-Glucose-Hydroxytyrosol Conce

P values were generated from a regression model adjusted for: socioeconomic status and fetal sex.

eTable 8. Maternal lifestyle questionnaires and biological sample related to maternal stress, well-being and mindful state at the final visit adjusted by baseline assessment per intervention group

		Mediterranean diet	Stress reduction	Usual care		Mediterranean diet vs. Usual care	Stress reduction vs. Usual care	Mediterranean diet vs. Stress reduction
					рс	Adjusted mean difference (95% CI)	Adjusted mean difference (95% CI)	Adjusted mean difference (95% CI)
Perceived stress scale score	Baselinea	15.6 (7.41)	16.1 (7.32)	15.8 (7.58)				
	Finalb	15.5 (0.36)	16.4 (0.36)	16.7 (0.37)	0.01	-1.26 (-2.28 to - 0.23)	-0.35 (-0.36 to 0.66)	-0.90 (-1.89 to 0.09)
State-trait Anxiety Inventory (personality)	Baselinea	14.0 (7.45)	15.6 (8.51)	15.2 (9.07)		,	,	
	Finalb	14.0 (0.37)	13.6 (0.37)	15.1 (0.38)	0.001	-1.03 (-2.06 to 0.008)	-1.45 (-2.48 to - 0.41)	0.42 (-0.59 to 1.43)
State-trait Anxiety Inventory (anxiety)	Baselinea	12.8 (8.05)	14.1 (8.50)	13.4 (8.70)		,	,	
	Finalb	13.7 (0.42)	12.6 (0.42)	15.2 (0.44)*	<0.001	-1.53 (-1.72 to 0.66)	-2.60 (-3.79 to - 1.40)	1.06 (-0.09 to 2.21)
WHO Five well-being index	Baselinea	67.4 (14.36)	65.4 (15.75)	64.4 (17.47)				
	Finalb	66.3 (0.90)	66.2 (0.91)	64.9 (0.94)	0.04	1.34 (-1.20 to 3.88)	1.28 (-1.26 to 3.82)	0.06 (-2.44 to 2.56)
FFMQ: Observation	Baselinea	23.8 (5.67)	23.6 (6.32)	23.1 (5.74)				
	Finalb	24.4 (0.34)	27.9 (0.35)**	24.2 (0.36)	<0.001	0.12 (-0.86 to 1.1)	3.66 (2.68 to 4.64)	-3.54 (-4.50 to - 2.57)
FFMQ: Description	Baselinea	33.0 (4.75)	31.3 (5.93)	32.4 (5.46)				
	Finalb	32.2 (0.30)	32.5 (0.30)	32.0 (0.31)	0.34	0.12 (-0.72 to 0.96)	0.48 (-0.36 to 1.32)	-0.36 (-1.18 to 0.46)
FFMQ: Awareness	Baselinea	31.5 (6.31)	29.7 (6.66)	31.7 (5.85)				
	Finalb	30.0 (0.39)	31.2 (0.39)	30.7 (0.41)	0.35	-0.71 (-1.80 to 0.38)	0.48 (-0.63 to 1.59)	-1.20 (-2.27 to - 0.12)
FFMQ: Non-judgmental	Baselinea	30.6 (4.91)	29.5 (5.86)	30.5 (5.59)				,
	Finalb	30.2 (0.31)	31.6 (0.31)*	30.0 (0.32)	0.05	0.20 (-0.68 to 1.08)	1.60 (0.71 to 2.48)	-1.39 (-2.25 to - 0.52)
FFMQ: Non-reactivity	Baselinea	23.0 (4.78)	22.1 (4.81)	22.6 (4.83))
	Finalb	22.7 (0.26)	25.1 (0.27)**	23.0 (0.28)	<0.001	-0.35 (-1.09 to 0.39)	2.10 (1.33 to 2.86)	-2.45 (-3.19 to - 1.70)
Cortisone/Cortisol	Baselinea	1.06 (0.69)	1.32 (0.77)	1.02 (0.48)				
	Finalb	1.67 (0.10)**	1.67 (0.06)**	1.38 (0.10)*	0.001	0.29 (0.01 to 0.56)	0.29 (0.05 to 0.52)	-0.004 (-0.23 to 0.23)

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PSS denotes for Perceived Stress Scale, STAI: State-Trait Anxiety Inventory, WHO-5: WHO Five Well-being Index; FFMQ, Five Facet Mindfulness Questionnaire, SE: standard error.

PSS was available for total 591 data (n=201 Mediterranean diet, 201 Stress reduction, 189 Usual care); STÅl and WHO were available for 587 participants (n=201 Mediterranean diet, 202 Stress reduction, 184 Usual care); FFMQ was available for 587 participants (n=203 Mediterranean diet, 200 Stress reduction, 184 Usual care); Cortisone/ Cortisol was available for 166 participants (n=36 Usual care, 37 Mediterranean diet, 93 Stress reduction).

*P<0.05 and **P<0.001 final comparison adjusted for baseline values. aBaseline values are observed as means (SD). bFinal value are baseline-adjusted (least-square) means (SE) and comparison among groups done with ANCOVA analysis. cANCOVA analysis for the final assessment.

eTable 9. Association between maternal mindful state (FFMQ) at final assessment during pregnancy (34-36 weeks' gestation) and the infant Bayley-III results in the whole study population (n=587)

					FFMQ					
	Observation		Description		Awareness	Awareness			Non-reactivity	
BSID assessment	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value
Cognitive	0.04 (-0.17 to 0.25)	0.69	0.10 (-0.18 to 0.38)	0.48	-0.15 (-0.36 to 0.06)	0.18	0.07 (-0.20 to 0.34)	0.60	-0.10 (-0.41 to 0.21)	0.53
Language	0.01 (-0.20 to 0.22)	0.90	0.41 (0.13 to 0.68)	0.003	0.03 (-0.18 to 0.24)	0.73	0.21 (-0.04 to 0.46)	0.12	0.23 (-0.06 to 0.52)	0.13
Motor	0.04 (-0.13 to 0.21)	0.58	0.33 (0.11 to 0.54)	0.003	0.12 (-0.05 to 0.29)	0.17	0.07 (-0.12 to 0.26)	0.50	0.23 (-0.005 to 0.46)	0.06
Socio-emotional	0.25 (-0.004 to 0.50)	0.06	0.32 (-0.01 to 0.66)	0.06	0.24 (-0.01 to 0.49)	0.08	0.26 (-0.05 to 0.57)	0.11	0.26 (-0.11 to 0.63)	0.18
Adaptive behavior	0.11 (-0.08 to 0.30)	0.26	0.40 (0.15 to 0.65)	0.001	0.21 (0.01 to 0.40)	0.03	0.15 (-0.08 to 0.38)	0.22	0.10 (-0.17 to 0.37)	0.45

	Observation Description				FFMQ Awareness		Non-judgeing	n Non-reactivity			
BSID assessment	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	
Cognitive	0.04 (-0.17 to 0.25)	0.69	0.10 (-0.18 to 0.38)	0.48	-0.15 (-0.36 to 0.06)	0.18	0.07 (-0.20 to 0.34)	0.60	-0.10 (-0.41 to 0.21)	0.53	
Language	0.01 (-0.20 to 0.22)	0.90	0.41 (0.13 to 0.68)	0.003	0.03 (-0.18 to 0.24)	0.73	0.21 (-0.04 to 0.46)	0.12	0.23 (-0.06 to 0.52)	0.13	
Motor	0.04 (-0.13 to 0.21)	0.58	0.33 (0.11 to 0.54)	0.003	0.12 (-0.05 to 0.29)	0.17	0.07 (-0.12 to 0.26)	0.50	0.23 (-0.005 to 0.46)	0.06	
Socio-emotional	0.25 (-0.004 to 0.50)	0.06	0.32 (-0.01 to 0.66)	0.06	0.24 (-0.01 to 0.49)	0.08	0.26 (-0.05 to 0.57)	0.11	0.26 (-0.11 to 0.63)	0.18	
Adaptive behavior	0.11 (-0.08 to 0.30)	0.26	0.40 (0.15 to 0.65)	0.001	0.21 (0.01 to 0.40)	0.03	0.15 (-0.08 to 0.38)	0.22	0.10 (-0.17 to 0.37)	0.45	

					FFMQ					
	Observation		Description		Awareness		Non-judgeing		Non-reactivity	
Bayley-III assessment	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value
Cognitive	0.04 (-0.17 to 0.27)	0.67	0.11 (-0.17 to 0.39)	0.44	-0.15 (-0.38 to 0.07)	0.19	0.08 (-0.19 to 0.35)	0.56	-0.09 (-0.42 to 0.22)	0.54
Language	0.08 (-0.14 to 0.31)	0.46	0.38 (0.11 to 0.65)	0.005	0.02 (-0.19 to 0.24)	0.83	0.21 (-0.05 to 0.47)	0.11	0.31 (0.003 to 0.63)	0.04
Motor	0.06 (-0.11 to 0.24)	0.47	0.32 (0.1 to 0.54)	0.003	0.12 (-0.05 to 0.29)	0.18	0.09 (-0.11 to 0.31)	0.36	0.24 (-0.006 to 0.49)	0.05
Socio-emotional	0.20 (-0.07 to 0.48)	0.14	0.30 (-0.02 to 0.64)	0.06	0.25 (-0.02 to 0.52)	0.07	0.24 (-0.08 to 0.57)	0.14	0.21 (-0.17 to 0.6)	0.28
Adaptive behavior	0.14 (-0.06 to 0.35)	0.17	0.38 (0.13 to 0.63)	0.002	0.22 (0.01 to 0.42)	0.03	0.16 (-0.07 to 0.41)	0.18	0.13 (-0.15 to 0.42)	0.37

Bayley-III denotes for Bayley Scales of Infant and Toddler Development, 3rd edition, SE: standard error.

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P values were generated from a regression model adjusted for: socioeconomic status and fetal sex.

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eFigure 1. Associations between maternal Mediterranean diet adherence scores during pregnancy and the infant Bayley-III domain scores

Mediter	Mediterranean diet adherence score β (95%Cl)						
Co	gnitive			•		0	.72 (0.31 to 1.13)
La	nguage					0	.90 (0.51 to 1.29)
Mo	tor					0	.18 (–0.14 to 0.50)
So	cial-emotional		+	-		0	.40 (–0.09 to 0.89)
Ad	aptive			-		0	.33 (-0.04 to 0.69)
	<	-1	0	1	2	3	

Negative association Positive association

eFigure 2. Associations between maternal stress/anxiety questionnaires and the infant Bayley-III scores

PSS		<i>В</i> (95%СІ)
Cognitive	- - :	-0.33 (-0.54 to -0.12)
Language		-0.48 (-0.68 to -0.28)
Motor	- - - ¦	-0.26 (-0.42 to -0.11)
Social-emotional		-0.14 (-0.39 to 0.11)
Adaptive		-0.28 (-0.46 to -0.10)
	-1 -0.5 0 0.5	1

Negative association Positive association

STAI personality		β (95%CI)
Cognitive		-0.23 (-0.42 to -0.04)
Language		-0.29 (-0.47 to -0.11)
Motor		-0.16 (-0.30 to -0.02)
Social-emotional		-0.23 (-0.46 to -0.01)
Adaptive		-0.29 (-0.45 to -0.12)
	1 –0.5 0 0.5	→

Negative association Positive association

STAI anxiety		<i>β</i> (95%Cl)
Cognitive		-0.18 (-0.37 to 0.01)
Language		-0.31 (-0.49 to -0.13)
Motor		-0.14 (-0.28 to 0.01)
Social-emotional		-0.07 (-0.29 to 0.15)
Adaptive		-0.23 (-0.40 to -0.06)
	1 –0.5 0 0.5	>

Negative association Positive association

PSS denotes for Perceived Stress Scale; data were available for 591 participants (n=201 Mediterranean diet, 201 Stress reduction, 189 Usual care).

STAÍ denoted for State-Trait Anxiety Inventory; data were available for 587 participants (n=201 Mediterranean diet, 202 Stress reduction, 184 Usual care).

eFigure 3. Associations between infant Bayley-III scores and maternal WHO-5 score

WHO-5	Low well-being	High well-being	Adjus	ted mean difference (95%Cl)
Cognitive	118.4 (18.8)	121.5 (18.4)		-2.05 (-5.69 to 1.58)
Language	102.4 (17.4)	107.6 (17.9)	e	-3.98 (-7.43 to -0.53)
Motor	112.8 (14.0)	114.3 (14.0)		-1.12 (-3.91 to 1.67)
Social-emotional	101.6 (20.3)	108.1 (22.1)	e	-5.44 (-9.75 to -1.12)
Adaptive	90.0 (17.5)	95.1 (15.3)	_ - _	-4.78 (-7.95 to -1.61)
			-20 -15 -10 -5 0 5	

WHO-5 denotes for WHO Five Well-being Index. Data were available for 587 participants (n=203 Mediterranean diet, 198 Stress reduction, 186 Usual care)

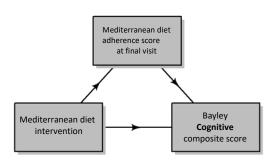
eFigure 4. Associations between infant Bayley-III scores and maternal 24h-urinary cortisone/cortisol ratio

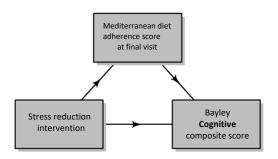
Cor	tisone/ Cortisol		ß (95%Cl)
	Cognitive	<u>+</u>	2.51 (-0.86 to 5.88)
	Language		3.15 (0.01 to 6.30)
	Motor		1.11 (-1.53 to 3.77)
	Social-emotional		-0.28 (-4.27 to 3.70)
	Adaptive		-1.76 (-4.76 to 1.24)
	-	15 – 10 –5 0 5 10 1	15

Data was available for 166 participants (n=37 Mediterranean diet, 93 Stress reduction, 36 Usual care)

eFigure 5. Mediation analysis models of intervention mechanisms*, Casual Model .

Casual Model 1



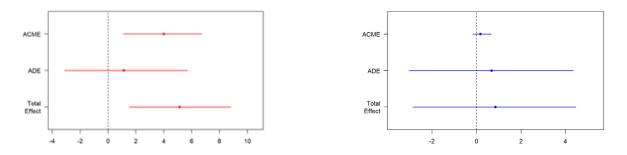


Parameters 1**

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	4.005	1.115	6.72	0.002
AADE	1.13	-3.107	5.69	0.62
Total Effect	5.135	1.54	8.8	0.006
Prop. Mediated	0.78	0.209	2.51	0.008

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	0.178	-0.161	0.66	0.34
AADE	0.676	-3.025	4.35	0.68
Total Effect	0.855	-2.854	4.46	0.61
Prop. Mediated	0.208	-1.153	1.52	0.72

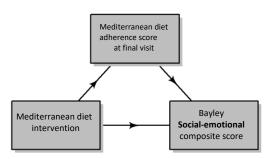
Effect Decomposition 1

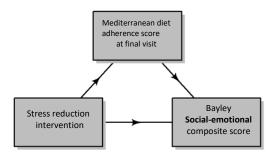


*Causal models of intervention mechanisms, model parameters and effect decomposition. The causal models panel shows the hypothesized mechanisms of each intervention. The red lines represent the effect of the Mediterranean diet intervention and blue lines represent Stress reduction intervention. The effect decomposition panel shows how the average total effect of the intervention on the outcome is decomposed into the indirect effect, and the direct effect.

eFigure 6. Mediation analysis models of intervention mechanisms*, Casual Model 2

Casual Model 2



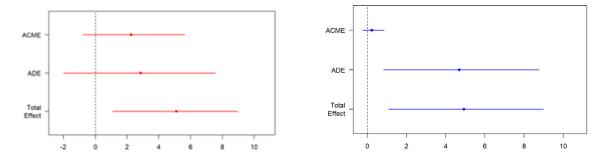


Parameters 2**

	Estimate	95% CI	95%CI	p-value
		Lower	Upper	p varue
ACME	2.252	-0.761	5.62	0.13
AADE	2.849	-2.004	7.56	0.26
Total Effect	5.102	1.082	8.98	0.01
Prop. Mediated	0.441	-0.169	2.21	0.14

	Estimate	95% CI	95%CI	
		Lower	Upper	p-value
ACME	0.2321	-0.2336	0.86	0.29
AADE	4.6959	0.8338	8.76	0.01
Total Effect	4.928	1.0878	8.97	0.01
Prop. Mediated	0.0471	-0.0669	0.25	0.31

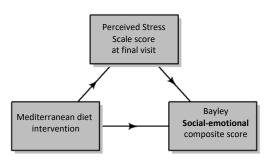
Effect Decomposition 2

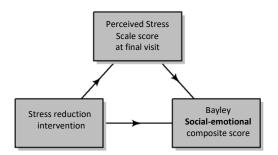


*Causal models of intervention mechanisms, model parameters and effect decomposition. The causal models panel shows the hypothesized mechanisms of each intervention. The red lines represent the effect of the Mediterranean diet intervention and blue lines represent Stress reduction intervention. The effect decomposition panel shows how the average total effect of the intervention on the outcome is decomposed into the indirect effect, and the direct effect.

eFigure 7. Mediation analysis models of intervention mechanisms*, Casual Model 3

Casual Model 3



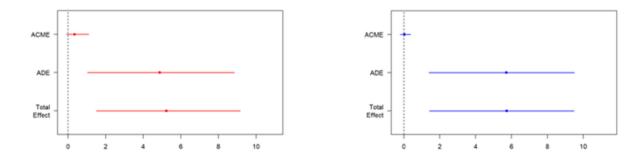


Parameters 3**

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	0.3488	-0.0904	1.1	0.16
AADE	4.8808	1.0294	8.85	0.01
Total Effect	5.2296	1.5089	9.15	0.01
Prop. Mediated	0.0667	-0.0262	0.31	0.17

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	0.02381	-0.20477	0.37	0.81
AADE	5.71055	1.39291	9.51	0.004
Total Effect	5.73436	1.42227	9.48	0.004
Prop. Mediated	0.00415	-0.04586	0.1	0.81

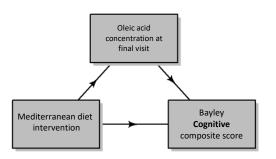
Effect Decomposition 3

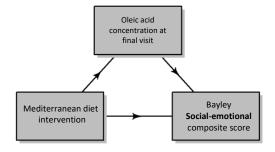


*Causal models of intervention mechanisms, model parameters and effect decomposition. The causal models panel shows the hypothesized mechanisms of each intervention. The red lines represent the effect of the Mediterranean diet intervention and blue lines represent Stress reduction. The effect decomposition panel shows how the average total effect of the intervention on the outcome is decomposed into the indirect effect, and the direct effect.

eFigure 8. Mediation analysis models of intervention mechanisms*, Casual Model 4

Casual Model 4, sample size N=185



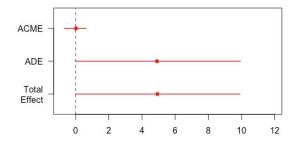


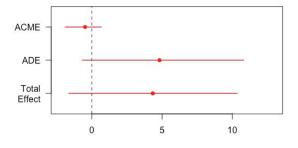
Parameters 4**

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	0.02472	-0.55268	0.61	0.95
ADE	4.90221	0.329	9.96	0.044
Total Effect	4.92693	0.10161	9.91	0.04
Prop. Mediated	0.00502	-0.18028	0.18	0.962

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	-0.475	-1.741	0.7	0.416
ADE	4.814	-0.683	10.84	0.086
Total Effect	4.339	-1.474	10.37	0.132
Prop. Mediated	-0.11	-1.294	0.96	0.528

Effect Decomposition 4

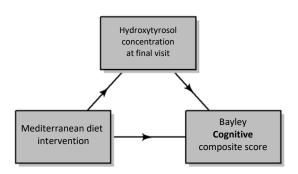


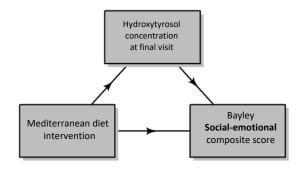


*Causal models of intervention mechanisms, model parameters and effect decomposition. The causal models panel shows the hypothesized mechanisms of each intervention. The red lines represent the effect of the Mediterranean diet intervention and blue lines represent Stress reduction intervention. The effect decomposition panel shows how the average total effect of the intervention on the outcome is decomposed into the indirect effect, and the direct effect.

eFigure 9. Mediation analysis models of intervention mechanisms*, Casual Model 5

Casual Model 5, sample size N=185



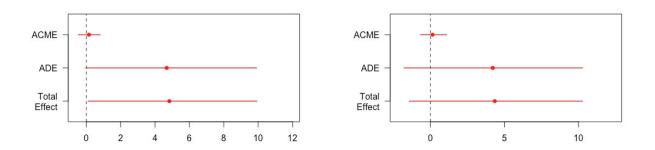


Parameters 5**

	Estimate	95% CI	95%CI	p-value
		Lower	Upper	
ACME	0.153	-0.5406	0.93	0.724
ADE	4.6804	-0.6023	9.94	0.092
Total Effect	4.8334	-0.4476	10.12	0.068
Prop. Mediated	0.0317	-0.2684	0.43	0.764

	Estimate	95% CI Lower	95%CI Upper	p-value
ACME	0.1365	-0.5114	1.08	0.70
ADE	4.2073	-1.9148	10.16	0.17
Total Effect	4.3438	-1.8629	10.21	0.15
Prop. Mediated	0.0314	-0.521	0.75	0.74

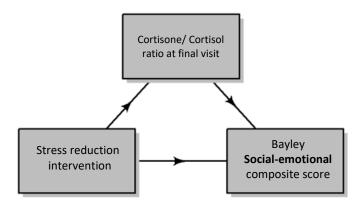
Effect Decomposition 5



*Causal models of intervention mechanisms, model parameters and effect decomposition. The causal models panel shows the hypothesized mechanisms of each intervention. The red lines represent the effect of the Mediterranean diet intervention and blue lines represent Stress reduction intervention. The effect decomposition panel shows how the average total effect of the intervention on the outcome is decomposed into the indirect effect, and the direct effect.

eFigure 10. Mediation analysis models of intervention mechanisms*, Casual Model 6

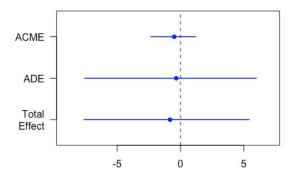
Casual Model 6, sample size N=129



Parameters 6**

	Estimate	95% CI	95%CI	p-value
		Lower	Upper	-
ACME	-0.492	-2.519	1.15	0.53
ADE	-0.333	-7.464	6.54	0.95
Total Effect	-0.825	-7.854	5.72	0.84
Prop. Mediated	0.596	-2.353	4.84	0.95

Effect Decomposition 6



*Causal models of intervention mechanisms, model parameters and effect decomposition. The causal models panel shows the hypothesized mechanisms of each intervention. The red lines represent the effect of the Mediterranean diet intervention and blue lines represent Stress reduction intervention. The effect decomposition panel shows how the average total effect of the intervention on the outcome is decomposed into the indirect effect, and the direct effect.

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