# Identifying women who may benefit from higher-dose omega-3 supplementation during pregnancy to reduce their risk of prematurity: exploratory analyses from the ORIP trial

Lisa N Yelland, Thomas R Sullivan, Robert A Gibson, Lucy A Simmonds, Sagar K Thakkar, Fang Huang, Surabhi Devaraj, Karen P Best, Irma Silva Zolezzi, Maria Makrides

#### SUPPLEMENTARY MATERIAL

Fatty acid	Fatty acid name	Intervention %	Control %
Total saturates		2.8 - 6.1	34.2 - 35.0
Total monounsaturates		8.0 - 13.0	41.2 - 41.3
18:2 ω6	linoleic	0.4 – 0.6	19.8 - 20.0
20:4 ω6	arachidonic	2.3 - 3.5	0.1
22:5 ω6	docosapentaenoic	4.1 - 4.4	0.1
Total ω6		8.1 -8.9	20.0 – 20.2
18:3 ω3	α-linolenic	0.2 - 0.3	1.8 - 1.9
18:4 ω3	octadecatetraenoic	0.3 – 0.5	0.1
20:4 ω3	eicosatetraenoic	0.3 – 0.7	-
20:5 ω3	eicosapentaenoic	8.0 - 11.7	0.3
22:5 ω3	docosapentaenoic	2.3 –2.6	-
22:6 ω3	docosahexaenoic	55.9 – 58.8	1.0 - 1.1
Total ω3		68.2 – 74.0	3.2 – 3.4
Minor components		3.0 - 6.4	0.6 - 0.9

#### Table S1 Composition of study capsules

Note: The study capsules were manufactured by Efamol Ltd/Wassen International Ltd with oil supplied from Croda. The composition listed below is presented as a percentage of total fatty acids and is the range for the three batches used throughout the study. The average capsule fill weight is 500 mg.

Page **1** of **17** 

**Table S2** Predictors of interest measured at trial entry (<20 weeks' gestation), their definitions and</th>justification for any exclusions from the analysis

Predictor	Missing	Definition	Reason for Exclusion (if
	Data (%)		Applicable)
Use of	0.0	Was the mother taking dietary	
Supplements		supplements containing up to	
Containing		150mg/day of omega-3 LCPUFA in the	
omega-3 LCPUFA		last 3 months (yes/no). Women taking	
in Last 3 Months		more than 150mg/day were ineligible	
		for the trial. This variable was used to	
		stratify the randomisation, along with	
		enrolment centre.	
Age	0.0	Maternal age at trial entry in years.	
SEIFA Index of	0.2	SEIFA=Socio-Economic Indexes for	
Socioeconomic		Areas. Index of socioeconomic	
Disadvantage		disadvantage quintile is based on	
Quintile		Australian postcodes where mother	
		lives. This variable was included in the	
		analysis but may have limited value as	
		an equivalent measure may not be	
		available in other countries.	
Race	0.2	Self-reported and categorised as	
		Caucasian, Asian or Other for analysis.	
Completed	0.3	Did the mother complete secondary	
Secondary School		school (i.e. high school) to year 12 or	
		equivalent (yes/no).	
Completed	0.3	Did the mother complete any further	
Further Study		study, e.g. a certificate, diploma or	
		degree (yes/no).	
Highest	0.5	Highest qualification completed by	
Qualification		the mother, categorised as none,	
Completed		secondary school, certificate/diploma	
		or degree/higher degree.	
Number of Years	0.4	Number of years the mother spent in	
Spent in Full Time		full time education from year 1 or	
Education		grade 1, including primary school,	
		secondary school and any further	
		study, even if not completed.	
In Workforce	0.3	Has the mother been in the work	
During Last 12		force during the last 12 months	
Months		(yes/no).	
ANZSCO	0.4	ANZSCO=Australian and New Zealand	
Occupation Code		Standard Classification of	
		Occupations. Occupation codes are	
		based on the skill level and skill	
		specialisation of the mother's usual or	

Page **2** of **17** 

		regular occupation and range from 1	
		(managers) to 8 (labourers).	
		Categorised as 1-2, 3-5, 6-8 and not in	
		workforce for the analysis. This	
		variable was included in the analysis	
		but may have limited value as an	
		equivalent measure may not be	
		available in other countries.	
Currently	0.4	Is the mother currently employed	
Employed		(yes/no).	
Annual	23.7	Annual total household income	Many women (23.7%)
Household		before tax, asked in categories	chose not to disclose this
Income		ranging from \$20,000 or less to over	information, suggesting it
		\$205,000.	would not be a useful
			predictor in practice.
Current Weight	2.5	Mother's weight measured by study	
(kg)		staff on a calibrated scale to the	
		nearest 0.1kg.	
Usual Pre-	7.9	Self-reported based on recall and	Strongly related to current
pregnancy		recorded to the nearest 0.5kg.	weight (correlation
Weight (kg)			coefficient=0.97) and less
			preferred due to risk of
			recall bias and higher rates
			of missing data (7.9% vs
			2.5%).
Height (cm)	1.9	Mother's height measured by study	
		staff to the nearest 0.5cm.	
Current BMI	3.7	Calculated from mother's current	
		weight and height.	
Usual Pre-	9.1	Calculated from mother's usual pre-	Strongly related to current
pregnancy BMI		pregnancy weight and height.	BMI (correlation
			coefficient=0.96) and less
			preferred due to risk of
			recall bias and higher rates
			of missing data (9.1% vs
			3.7%).
Currently Smoke	0.3	Does the mother currently smoke	
Cigarettes		cigarettes (yes/no).	
Smoked	0.5	Did the mother smoke cigarettes in	
Cigarettes in 3		the 3 months leading up to the	
Months Leading		pregnancy (yes/no).	
up to Pregnancy			
Anyone Else	0.3	Does anyone other than the mother	
Living in House		who lives in the same house smoke	
Smokes		cigarettes (yes/no).	
•			

Page **3** of **17** 

Currently Drink	0.3	Does the mother currently drink	
Alcohol		alcohol (yes/no).	
How Often	0.4	How often the mother currently	Few women (2%) were
Currently Drink		drinks alcohol, categorised as	current drinkers, resulting
Alcohol		monthly or less, 2-4 times a month, 2-	in very small numbers
		3 times a week, 4 or more times a	when these were further
		week.	divided according to how
			often they drank.
Drank Alcohol in	0.4	Did the mother drink alcohol in the 3	
3 Months Leading		months leading up to the pregnancy	
up to Pregnancy		(yes/no).	
How Often Drank	0.4	How often the mother drank alcohol	
Alcohol in 3		in the 3 months leading up to the	
Months Leading		pregnancy, categorised as monthly or	
up to Pregnancy		less, 2-4 times a month, 2-3 times a	
		week, 4 or more times a week.	
Currently Taking	0.3	Is the mother currently taking any	
Dietary		dietary supplements (yes/no).	
Supplements			
Took Dietary	0.3	Did the mother take any dietary	
Supplements in 3		supplements in the 3 months leading	
Months Leading		up to the pregnancy (yes/no).	
up to Pregnancy			
Type I Diabetes	0.4	Has the mother been diagnosed with	Very few women (0.3%)
		type I diabetes by a doctor (yes/no).	had type I diabetes.
Type II Diabetes	0.4	Has the mother been diagnosed with	Very few women (0.8%)
		type II diabetes by a doctor (yes/no).	had type II diabetes.
Gestational	0.4	Has the mother been diagnosed with	Excluded from early
Diabetes in		gestational diabetes in a previous	preterm birth analyses
Previous		pregnancy by a doctor (yes/no).	only, since no women in
Pregnancy			the control group had both
			gestational diabetes in a
			previous pregnancy and an
			early preterm birth and
			hence an interaction
			analysis is not possible.
Pre-eclampsia or	0.4	Has the mother been diagnosed with	
Eclampsia in		pre-eclampsia or eclampsia in a	
Previous		previous pregnancy by a doctor	
Pregnancy		(yes/no).	
Born Preterm	4.7	Was the mother born preterm, i.e.	
		<37 weeks' gestation (yes/no).	
Any Previous	0.4	Has the mother had any previous	
Pregnancies		pregnancies (yes/no).	

Page **4** of **17** 

Any Previous	0.3	Has the mother had any previous	
Pregnancies		pregnancies that ended before 20	
Ending Before 20		weeks' gestation (yes/no).	
Weeks			
Any Previous	0.4	Has the mother had any previous	
Births >=20		births >=20 weeks' gestation (yes/no).	
Weeks			
Any Previous	0.3	Has the mother had any previous	Very few women (0.7%)
Stillbirths >=20		stillbirths >=20 weeks' gestation	had a previous stillbirth.
Weeks		(yes/no).	
Any Previous	0.4	Has the mother had any previous	Very few women (0.4%)
Neonatal Deaths		neonatal deaths during the first 28	had a previous neonatal
During First 28		days of life (yes/no).	death.
Days			
Any Previous	0.3	Has the mother had any previous	
Premature Births		preterm births >=20 weeks' gestation	
>=20 Weeks and		and <37 weeks' gestation (ves/no).	
<37 Weeks			
Used Fertility	03	Did the mother have fertility	
Treatments for	0.0	treatments to bein them become	
Current		pregnant for the current pregnancy	
Drognanov		(vos (no)	
	0.4	(yes/110).	
	0.4	Has the mother had any ultrasound	
Ultrasound Scans		scans for the current pregnancy	
for Current		(yes/no).	
Pregnancy			
Gestational Age	0.0	Gestational age at trial entry in	
(Weeks) at Trial		weeks.	
Entry			
ALA	4.8	Alpha linolenic acid in maternal	
		capillary whole blood collected on	
		chemically treated filter paper as	
		dried blood spots, expressed as a	
		percentage of total fatty acids.	
DHA	4.8	Docosahexaenoic acid in maternal	
		capillary whole blood collected on	
		chemically treated filter paper as	
		dried blood spots, expressed as a	
		percentage of total fatty acids.	
EPA	4.8	Eicosapentaenoic acid in maternal	
		capillary whole blood collected on	
		chemically treated filter paper as	
		dried blood spots, expressed as a	
		percentage of total fatty acids	
FPA + ΠΗΔ	4.8	Sum of EPA and DHA	
	4.8	Sum of ALA FPA DPA and DHA	
i otai omega-o	4.0		

Page **5** of **17** 

LA	4.8	Linoleic acid in maternal capillary	
		whole blood collected on chemically	
		treated filter paper as dried blood	
		spots, expressed as a percentage of	
		total fatty acids.	
AA	4.8	Arachidonic acid in maternal capillary	
		whole blood collected on chemically	
		treated filter paper as dried blood	
		spots, expressed as a percentage of	
		total fatty acids.	
DHA Status*	4.8	Low <2.0% of total fatty acids in	
		whole blood	
		Moderate 2.0-2.9%	
		Replete >2.9%	
EPA + DHA	4.8	Low <2.6% of total fatty acids in	
Status*		whole blood	
		Moderate 2.6-3.4%	
		Replete >3.4%	
Total omega-3	4.8	Low <4.2% of total fatty acids in	
Status*		whole blood	
		Moderate 4.2-4.9%	
		Replete >4.9%	

\* Status was defined previously using ORIP trial data as follows. Log binomial regression models were used to estimate the effect of randomised treatment group (expressed as a relative risk) on early preterm birth as a function of DHA, EPA + DHA or total omega-3 levels at baseline (treated as continuous variables and modelled using two-term fractional polynomials). Analyses were adjusted for the stratification variables (enrolment centre and use of n-3 supplements in the last 3 months) and used robust variance estimation to account for clustering of pregnancies due to women who participated in the trial during more than one pregnancy. Following identification of a statistically significant interaction effect between randomised treatment group and DHA, EPA + DHA or total omega-3, low status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk fell entirely below 1 and hence omega-3 supplementation appeared beneficial. Moderate status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk contained 1. Replete status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk contained 1. Replete status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk contained 1. Replete status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk contained 1. Replete status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk contained 1. Replete status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk contained 1. Replete status was defined as values of DHA, EPA + DHA or total omega-3 where the 95% confidence interval for the relative risk fell entirely above 1 and hence omega-3 supplementation appeared harmful.

Further details can be found in Simmonds LA, Sullivan TR, Skubisz M, et al. Omega-3 fatty acid supplementation in pregnancy-baseline omega-3 status and early preterm birth: exploratory analysis of a randomised controlled trial. *BJOG: an International Journal of Obstetrics and Gynaecology* 2020; 127: 975-981.

Page 6 of 17

### Table S3 Complete results of interaction analyses for early preterm birth

Predictor	Unadjusted Odds	Adjusted Odds	Adjusted	Adjusted
	Ratio (95% CI)*	Ratio (95% CI)*	P-value	Interaction
				P-value
Use of Supplements Containing				0.4106
omega-3 LCPUFA in Last 3				
Months				
No	1.21 (0.77, 1.89)	1.21 (0.77, 1.89)	0.4118	
Yes	0.71 (0.22, 2.27)	0.72 (0.22, 2.28)	0.5716	
Completed Secondary School				0.5557
No	0.91 (0.39, 2.13)	0.91 (0.39, 2.11)	0.8228	
Yes	1.22 (0.75, 1.96)	1.22 (0.75, 1.96)	0.4238	
Completed Further Study				0.3364
No	0.79 (0.33, 1.86)	0.79 (0.33, 1.86)	0.5848	
Yes	1.28 (0.79, 2.06)	1.28 (0.79, 2.06)	0.3201	
In Workforce During Last 12				0.4228
Months				
No	0.88 (0.41, 1.86)	0.87 (0.41, 1.85)	0.7255	
Yes	1.26 (0.77, 2.08)	1.26 (0.77, 2.08)	0.3592	
Currently Employed				0.5894
No	0.97 (0.47, 1.97)	0.96 (0.47, 1.96)	0.9172	
Yes	1.23 (0.73, 2.05)	1.23 (0.73, 2.05)	0.4361	
Currently Smoke Cigarettes				0.5602
No	1.08 (0.69, 1.69)	1.08 (0.69, 1.69)	0.7294	
Yes	1.57 (0.49, 5.03)	1.57 (0.49, 5.01)	0.4496	
Smoked Cigarettes in 3 Months				0.7314
Leading up to Pregnancy				
No	1.17 (0.73, 1.89)	1.17 (0.73, 1.89)	0.5117	
Yes	1.01 (0.43, 2.35)	0.99 (0.42, 2.31)	0.9808	
Anyone Else Living in House				0.5821
Smokes Cigarettes				
No	1.20 (0.74, 1.93)	1.20 (0.74, 1.93)	0.4580	
Yes	0.92 (0.40, 2.14)	0.91 (0.39, 2.12)	0.8320	
Currently Drink Alcohol				0.9788
No	1.13 (0.74, 1.72)	1.13 (0.74, 1.71)	0.5760	
Yes	1.19 (0.07, 19.58)	1.17 (0.07, 20.15)	0.9129	
Drank Alcohol in 3 Months				0.7946
Leading up to Pregnancy				
No	1.06 (0.60, 1.87)	1.06 (0.60, 1.89)	0.8310	
Yes	1.20 (0.66, 2.19)	1.19 (0.65, 2.18)	0.5745	
Currently Taking Dietary				0.8930
Supplements				
No	1.19 (0.50, 2.83)	1.20 (0.50, 2.85)	0.6834	
Yes	1.12 (0.70, 1.80)	1.12 (0.70, 1.80)	0.6421	

Page **7** of **17** 

Took Dietary Supplements in 3				0.7485
Months Leading up to				
Pregnancy				
No	1.09 (0.68, 1.75)	1.09 (0.68, 1.75)	0.7253	
Yes	1.28 (0.55, 3.00)	1.28 (0.55, 2.98)	0.5720	
Pre-eclampsia or Eclampsia in				0.9539
Previous Pregnancy				
No	1.13 (0.74, 1.74)	1.13 (0.73, 1.73)	0.5822	
Yes	1.19 (0.23, 6.04)	1.19 (0.23, 6.07)	0.8379	
Born Preterm				0.5296
No	1.13 (0.71, 1.79)	1.13 (0.71, 1.80)	0.6181	
Yes	0.77 (0.24, 2.45)	0.75 (0.24, 2.41)	0.6336	
Any Previous Pregnancies				0.7608
No	1.23 (0.57, 2.64)	1.25 (0.58, 2.67)	0.5715	
Yes	1.09 (0.67, 1.79)	1.08 (0.66, 1.77)	0.7510	
Any Previous Pregnancies				0.5967
Ending Before 20 Weeks				
No	1.02 (0.59, 1.76)	1.02 (0.59, 1.77)	0.9406	
Yes	1.29 (0.68, 2.45)	1.28 (0.68, 2.42)	0.4471	
Any Previous Births ≥20 Weeks				0.6470
No	1.23 (0.69, 2.17)	1.23 (0.70, 2.18)	0.4734	
Yes	1.02 (0.55, 1.88)	1.01 (0.55, 1.86)	0.9652	
Any Previous Premature Births				0.8247
≥20 Weeks and <37 Weeks				
No	1.10 (0.69, 1.75)	1.10 (0.69, 1.75)	0.6912	
Yes	1.24 (0.48, 3.22)	1.24 (0.48, 3.21)	0.6599	
Used Fertility Treatments for				0.3384
Current Pregnancy				
No	1.21 (0.78, 1.88)	1.21 (0.78, 1.87)	0.4043	
Yes	0.62 (0.17, 2.25)	0.62 (0.17, 2.25)	0.4672	
Had Any Ultrasound Scans for				0.4432
Current Pregnancy				
No	0.46 (0.04, 5.17)	0.46 (0.04, 5.12)	0.5257	
Yes	1.19 (0.78, 1.83)	1.19 (0.78, 1.83)	0.4127	
Age				0.5537
Omega-3	1.02 (0.96, 1.09)	1.02 (0.96, 1.09)	0.5030	
Control	1.05 (0.99, 1.12)	1.05 (0.99, 1.12)	0.1266	
Number of Years Spent in Full				0.9078
Time Education				
Omega-3	1.00 (0.90, 1.12)	1.00 (0.89, 1.12)	0.9694	
Control	0.99 (0.87, 1.14)	0.99 (0.86, 1.13)	0.8590	
Current Weight (kg)				0.4759
Omega-3	1.02 (1.00, 1.03)	1.02 (1.00, 1.03)	0.0407	
Control	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	0.1998	
Height (cm)				0.9959
	•		•	

Page **8** of **17** 

Omega-3         0.9           Control         0.9           Current BMI         0           Omega-3         1.0           Control         1.0           ALA         0           Omega-3         0.5           Control         0.8           EPA         0           Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	99 (0.94, 1.03)         99 (0.94, 1.03)         99 (0.94, 1.03)         99 (0.94, 1.03)         99 (0.94, 1.03)         99 (0.94, 1.03)         99 (0.94, 1.03)         99 (0.94, 1.03)         90 (0.94, 1.03)         90 (1.01, 1.10)         93 (1.00, 1.07)         96 (0.20, 1.56)         96 (0.20, 1.56)         96 (0.21, 3.47)         90 (0.25, 3.23)         90 (0.25, 3.23)         18 (0.88, 1.59)         52 (0.32, 0.85)         11 (0.91, 1.36)         51 (0.44, 0.85)	0.99 (0.94, 1.03) 0.99 (0.94, 1.03) 1.05 (1.01, 1.10) 1.03 (1.00, 1.07) 0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.5390 0.5056 0.0155 0.0873 0.2553 0.8120 0.0371 0.8831 0.3125 0.0093	0.4479 0.6262 0.1511 0.0055 0.0024
Control         0.9           Current BMI         0           Omega-3         1.0           Control         1.0           ALA         0           Omega-3         0.5           Control         0.8           EPA         0           Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	99 (0.94, 1.03)         06 (1.01, 1.10)         03 (1.00, 1.07)         06 (0.20, 1.56)         36 (0.21, 3.47)         04 (1.03, 9.00)         00 (0.25, 3.23)         18 (0.88, 1.59)         52 (0.32, 0.85)         11 (0.91, 1.36)         51 (0.44, 0.85)	0.99 (0.94, 1.03) 1.05 (1.01, 1.10) 1.03 (1.00, 1.07) 0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.5056 0.0155 0.0873 0.2553 0.8120 0.0371 0.8831 0.3125 0.0093 0.2552	0.4479 0.6262 0.1511 0.0055 0.0024
Current BMI         Image: Control         1.0           Omega-3         1.0         1.0           Control         1.0         1.0           ALA         0         0           Omega-3         0.5         0.5           Control         0.8         0.8           EPA         0         0.9           Control         0.9         0.9           EPA + DHA         0         0.9           Control         0.5         0.5           Total omega-3         1.1         0           Control         0.5         1.1           Control         0.5         0.5	06 (1.01, 1.10) 03 (1.00, 1.07) 56 (0.20, 1.56) 36 (0.21, 3.47) 04 (1.03, 9.00) 90 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	1.05 (1.01, 1.10) 1.03 (1.00, 1.07) 0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.0155 0.0873 0.2553 0.8120 0.0371 0.8831 0.3125 0.0093	0.4479 0.6262 0.1511 0.0055 0.0024
Omega-3         1.0           Control         1.0           ALA         0           Omega-3         0.5           Control         0.8           EPA         0           Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	06 (1.01, 1.10) 03 (1.00, 1.07) 56 (0.20, 1.56) 36 (0.21, 3.47) 04 (1.03, 9.00) 90 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	1.05 (1.01, 1.10) 1.03 (1.00, 1.07) 0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.0155 0.0873 0.2553 0.8120 0.0371 0.8831 0.3125 0.0093	0.6262
Control         1.0           ALA         0           Omega-3         0.5           Control         0.8           EPA         0           Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	03 (1.00, 1.07) 56 (0.20, 1.56) 36 (0.21, 3.47) 04 (1.03, 9.00) 50 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	1.03 (1.00, 1.07) 0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.0873 0.2553 0.8120 0.0371 0.8831 0.3125 0.0093	0.6262
ALA       0mega-3       0.5         Control       0.8         EPA       0mega-3       3.0         Control       0.9         EPA + DHA       0mega-3       1.1         Control       0.5       0.5         Total omega-3       1.1       0mega-3       1.1         Control       0.5       0.5       0.5         Total omega-3       1.1       0.5       0.5	56 (0.20, 1.56) 36 (0.21, 3.47) 04 (1.03, 9.00) 90 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.2553 0.8120 0.0371 0.8831 0.3125 0.0093	0.6262
Omega-3         0.5           Control         0.8           EPA         0           Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	56 (0.20, 1.56) 36 (0.21, 3.47) 04 (1.03, 9.00) 90 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	0.55 (0.20, 1.53) 0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.2553 0.8120 0.0371 0.8831 0.3125 0.0093	0.1511
Control         0.8           EPA	36 (0.21, 3.47) 04 (1.03, 9.00) 90 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	0.85 (0.21, 3.34) 3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.8120 0.0371 0.8831 0.3125 0.0093	0.1511
EPA         3.0           Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	04 (1.03, 9.00) 00 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.0371 0.8831 0.3125 0.0093	0.1511
Omega-3         3.0           Control         0.9           EPA + DHA         0           Omega-3         1.1           Control         0.5           Total omega-3         0.1           Omega-3         1.1           Control         0.5           Total omega-3         1.1           Control         0.6	04 (1.03, 9.00) 00 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	3.10 (1.07, 9.01) 0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.0371 0.8831 0.3125 0.0093	0.0055
Control0.9EPA + DHA0Omega-31.1Control0.5Total omega-31.1Omega-31.1Control0.6	00 (0.25, 3.23) 18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	0.91 (0.25, 3.34) 1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.8831	0.0055
EPA + DHAOmega-31.1Control0.5Total omega-31.1Omega-31.1	18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.3125 0.0093	0.0055
Omega-31.1Control0.5Total omega-31.1Omega-31.1	18 (0.88, 1.59) 52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	1.17 (0.86, 1.59) 0.52 (0.32, 0.85) 1.10 (0.90, 1.35)	0.3125 0.0093	0.0024
Control0.5Total omega-31.1Omega-31.1	52 (0.32, 0.85) 11 (0.91, 1.36) 51 (0.44, 0.85)	0.52 (0.32, 0.85)	0.0093	0.0024
Total omega-3Omega-31.1Control	11 (0.91, 1.36) 51 (0.44, 0.85)	1.10 (0.90, 1.35)	0.0000	0.0024
Omega-3 1.1	11 (0.91, 1.36) 51 (0.44, 0.85)	1.10 (0.90, 1.35)	0.0000	0.0024
Control	51 (0.44, 0.85)		0.3638	
0.0		0.61 (0.43, 0.85)	0.0033	
LA				0.8254
Omega-3 0.8	39 (0.78, 1.02)	0.89 (0.78, 1.01)	0.0804	
Control 0.9	91 (0.81, 1.02)	0.91 (0.80, 1.02)	0.1045	
AA				0.2265
Omega-3 1.0	09 (0.88, 1.35)	1.08 (0.87, 1.34)	0.4768	
Control 0.8	38 (0.68, 1.15)	0.88 (0.67, 1.15)	0.3383	
SEIFA Index of Socioeconomic				0.8690
Disadvantage Quintile				
1 (Most Disadvantaged) 1.5	57 (0.55 <i>,</i> 4.45)	1.57 (0.56, 4.45)	0.3943	
2 1.5	53 (0.55, 4.26)	1.55 (0.55, 4.31)	0.4050	
3 0.9	94 (0.42, 2.06)	0.93 (0.42, 2.06)	0.8621	
4 0.8	38 (0.35, 2.18)	0.88 (0.35, 2.20)	0.7878	
5 (Least Disadvantaged) 1.1	10 (0.41, 2.96)	1.09 (0.40, 2.93)	0.8676	
Race				0.7831
Other 1.7	72 (0.28, 10.42)	1.69 (0.28, 10.29)	0.5680	
Caucasian 1.0	03 (0.63, 1.69)	1.03 (0.63, 1.68)	0.9072	
Asian 1.3	33 (0.55, 3.18)	1.35 (0.56, 3.24)	0.5031	
Highest Qualification				0.3377
Completed				
Certificate/Diploma 1.7	71 (0.84, 3.50)	1.70 (0.83, 3.48)	0.1432	
Degree/Higher Degree 0.9	93 (0.48, 1.82)	0.93 (0.48, 1.82)	0.8366	
None 0.4	46 (0.12, 1.74)	0.46 (0.12, 1.75)	0.2558	
Secondary School 1.3	31 (0.40, 4.35)	1.30 (0.39, 4.31)	0.6669	
ANZSCO Occupation Code				0.8805
1-2 (Most Skilled) 1.3	33 (0.59, 3.01)	1.32 (0.58, 2.99)	0.5072	
3-5 1.2	21 (0.59, 2.49)	1.22 (0.59, 2.50)	0.5960	
6-8 (Least Skilled) 1.2	27 (0.34, 4.76)	1.27 (0.34, 4.75)	0.7251	
Not in Workforce 0.8	38 (0.41, 1.86)	0.87 (0.41, 1.85)	0.7180	

Page **9** of **17** 

How Often Drank Alcohol in 3				0.9652
Months Leading up to				
Pregnancy				
Never	1.06 (0.60, 1.87)	1.06 (0.60, 1.89)	0.8308	
Sometimes (up to once a	1.21 (0.60, 2.42)	1.20 (0.59, 2.41)	0.6180	
week)				
Often (twice a week or more)	1.20 (0.36, 3.95)	1.18 (0.36, 3.91)	0.7845	
Gestational Age (Weeks) at Trial				0.3219
Entry				
≤12	1.57 (0.66, 3.72)	1.56 (0.66, 3.69)	0.3145	
12.1-14	0.69 (0.34, 1.42)	0.69 (0.34, 1.42)	0.3182	
14.1-16	2.20 (0.67, 7.17)	2.19 (0.67, 7.14)	0.1935	
≥16	1.15 (0.52, 2.54)	1.15 (0.52, 2.53)	0.7309	
Total omega-3 Status				0.0074
Low	0.30 (0.10, 0.92)	0.30 (0.10, 0.93)	0.0366	
Moderate	1.05 (0.55, 2.00)	1.05 (0.55, 2.01)	0.8712	
Replete	2.61 (1.20, 5.67)	2.60 (1.20, 5.64)	0.0155	
EPA + DHA Status				0.0199
Low	0.54 (0.18, 1.56)	0.54 (0.19, 1.55)	0.2502	
Moderate	0.91 (0.53, 1.56)	0.91 (0.53, 1.57)	0.7293	
Replete	4.20 (1.40, 12.60)	4.17 (1.39, 12.54)	0.0109	
DHA Status				0.0500
Low	0.62 (0.19, 2.11)	0.63 (0.19, 2.14)	0.4607	
Moderate	0.93 (0.56, 1.55)	0.93 (0.56, 1.55)	0.7896	
Replete	4.53 (1.28, 15.94)	4.50 (1.28, 15.83)	0.0193	
Total omega-3 Status**				0.0150
Low	0.30 (0.10, 0.92)	0.30 (0.10, 0.93)	0.0365	
Lower Moderate	0.80 (0.31, 2.04)	0.79 (0.31, 2.03)	0.6284	
Upper Moderate	1.35 (0.55, 3.33)	1.37 (0.55, 3.39)	0.4984	
Replete	2.61 (1.20, 5.67)	2.60 (1.20, 5.64)	0.0155	
EPA + DHA Status**				0.0405
Low	0.54 (0.18, 1.56)	0.54 (0.19, 1.55)	0.2490	
Lower Moderate	0.74 (0.32, 1.69)	0.74 (0.32, 1.69)	0.4682	
Upper Moderate	1.05 (0.51, 2.17)	1.06 (0.51, 2.20)	0.8741	
Replete	4.20 (1.40, 12.60)	4.18 (1.39, 12.54)	0.0109	
DHA Status**				0.0618
Low	0.62 (0.19, 2.11)	0.63 (0.19, 2.14)	0.4600	
Lower Moderate	0.63 (0.27, 1.47)	0.63 (0.27, 1.47)	0.2852	
Upper Moderate	1.17 (0.61, 2.23)	1.18 (0.62, 2.25)	0.6221	
Replete	4.53 (1.28, 15.94)	4.50 (1.28, 15.84)	0.0192	
DHA Quartile***				0.0140
Q1	0.75 (0.35, 1.63)	0.75 (0.35, 1.63)	0.4711	
Q2	0.51 (0.22, 1.17)	0.51 (0.22, 1.17)	0.1139	
Q3	1.97 (0.84, 4.63)	1.97 (0.84, 4.63)	0.1210	
Q4	5.84 (1.29, 26.47)	5.83 (1.29, 26.45)	0.0222	

Page **10** of **17** 

\* Odds ratios for continuous predictors are the effect of a 1-unit increase in the predictor within each treatment group. Odds ratios > 1 indicate the odds of early preterm birth increase as the predictor increases, while odds ratios <1 indicate the odds of early preterm birth decrease as the predictor increases. Odds ratios for categorical predictors are comparing the omega-3 group to the control group within each category. Odds ratios <1 indicate the odds of early preterm birth are higher in the omega-3 group, while odds ratios <1 indicate the odds of early preterm birth are higher in the control group.

\*\* Moderate status category split into lower moderate (between the threshold for benefit and the null treatment effect) and upper moderate (between the null treatment effect and the threshold for harm).

\*\*\* DHA failed the Hosmer-Lemeshow goodness of fit test when considered as a linear predictor and hence it was categorised in quartiles.

Page 11 of 17

## Table S4 Complete results of interaction analyses for preterm birth

Predictor	Unadjusted Odds	Adjusted Odds	Adjusted	Adjusted
	Ratio (95% CI)*	Ratio (95% CI)*	P-value	Interaction
				P-value
Use of Supplements Containing				0.6493
omega-3 LCPUFA in Last 3				
Months				
No	0.82 (0.65, 1.03)	0.82 (0.65, 1.03)	0.0860	
Yes	0.71 (0.41, 1.23)	0.71 (0.41, 1.23)	0.2267	
Completed Secondary School				0.1564
No	0.59 (0.36, 0.96)	0.58 (0.35, 0.95)	0.0303	
Yes	0.86 (0.68, 1.08)	0.86 (0.68, 1.09)	0.2020	
Completed Further Study				0.0581
No	0.54 (0.34, 0.86)	0.54 (0.34, 0.86)	0.0093	
Yes	0.89 (0.70, 1.14)	0.89 (0.70, 1.13)	0.3549	
In Workforce During Last 12				0.0707
Months				
No	0.57 (0.37, 0.88)	0.56 (0.37, 0.87)	0.0097	
Yes	0.89 (0.70, 1.14)	0.89 (0.70, 1.14)	0.3627	
Currently Employed				0.1670
No	0.63 (0.42, 0.94)	0.63 (0.42, 0.94)	0.0226	
Yes	0.88 (0.68, 1.13)	0.88 (0.68, 1.13)	0.3105	
Currently Smoke Cigarettes				0.4716
No	0.82 (0.66, 1.02)	0.82 (0.66, 1.02)	0.0790	
Yes	0.62 (0.30, 1.28)	0.62 (0.30, 1.28)	0.1949	
Smoked Cigarettes in 3 Months				0.8710
Leading up to Pregnancy				
No	0.80 (0.63, 1.02)	0.81 (0.64, 1.02)	0.0731	
Yes	0.78 (0.48, 1.25)	0.77 (0.48, 1.24)	0.2801	
Anyone Else Living in House				0.1335
Smokes Cigarettes				
No	0.87 (0.68, 1.10)	0.87 (0.68, 1.10)	0.2421	
Yes	0.58 (0.36, 0.92)	0.58 (0.37, 0.92)	0.0219	
Currently Drink Alcohol				0.2180
No	0.78 (0.63, 0.97)	0.78 (0.63, 0.97)	0.0250	
Yes	2.09 (0.47, 9.25)	2.02 (0.45, 8.96)	0.3562	
Drank Alcohol in 3 Months				0.0404
Leading up to Pregnancy				
No	0.62 (0.45, 0.85)	0.62 (0.45, 0.86)	0.0035	
Yes	0.98 (0.74, 1.31)	0.97 (0.73, 1.30)	0.8608	
Currently Taking Dietary				0.3487
Supplements				
No	0.99 (0.60, 1.63)	0.99 (0.60, 1.64)	0.9818	
Yes	0.76 (0.60, 0.97)	0.76 (0.60, 0.96)	0.0234	

Page **12** of **17** 

onio open	BMJ	Open
-----------	-----	------

Took Dietary Supplements in 3				0.9601
Months Leading up to				
Pregnancy				
No	0.80 (0.63, 1.01)	0.80 (0.63, 1.01)	0.0598	
Yes	0.80 (0.50, 1.29)	0.81 (0.50, 1.30)	0.3755	
Gestational Diabetes in				0.2791
Previous Pregnancy				
No	0.82 (0.66, 1.02)	0.82 (0.66, 1.02)	0.0803	
Yes	0.50 (0.21, 1.21)	0.50 (0.21, 1.20)	0.1217	
Pre-eclampsia or Eclampsia in				0.8889
Previous Pregnancy				
No	0.80 (0.64, 1.00)	0.80 (0.64, 1.00)	0.0485	
Yes	0.85 (0.40, 1.80)	0.85 (0.40, 1.80)	0.6650	
Born Preterm				0.4843
No	0.81 (0.64, 1.03)	0.81 (0.64, 1.03)	0.0844	
Yes	0.65 (0.35, 1.22)	0.64 (0.34, 1.20)	0.1660	
Any Previous Pregnancies				0.0922
No	1.03 (0.71, 1.49)	1.04 (0.72, 1.50)	0.8530	
Yes	0.70 (0.54, 0.91)	0.70 (0.54, 0.91)	0.0080	
Any Previous Pregnancies				0.7164
Ending Before 20 Weeks				
No	0.82 (0.63, 1.07)	0.82 (0.63, 1.07)	0.1458	
Yes	0.76 (0.53, 1.08)	0.76 (0.53, 1.08)	0.1229	
Any Previous Births ≥20 Weeks				0.0357
No	1.03 (0.75, 1.42)	1.03 (0.75, 1.42)	0.8501	
Yes	0.65 (0.49, 0.87)	0.65 (0.49, 0.87)	0.0035	
Any Previous Premature Births				0.4601
≥20 Weeks and <37 Weeks				
No	0.76 (0.60, 0.96)	0.76 (0.60, 0.96)	0.0237	
Yes	0.95 (0.56, 1.59)	0.95 (0.56, 1.60)	0.8378	
Used Fertility Treatments for				0.3757
Current Pregnancy				
No	0.78 (0.63, 0.97)	0.78 (0.63, 0.97)	0.0249	
Yes	1.13 (0.49, 2.63)	1.15 (0.50, 2.66)	0.7419	
Had Any Ultrasound Scans for				0.9231
Current Pregnancy				
No	0.83 (0.33, 2.10)	0.84 (0.33, 2.13)	0.7121	
Yes	0.80 (0.64, 1.00)	0.80 (0.64, 1.00)	0.0458	
Age				0.3227
Omega-3	1.02 (0.99, 1.06)	1.03 (0.99, 1.06)	0.1328	
Control	1.00 (0.97, 1.03)	1.00 (0.97, 1.03)	0.8831	
Number of Years Spent in Full				0.4613
Time Education				
Omega-3	1.01 (0.95, 1.06)	1.01 (0.95, 1.07)	0.7588	
Control	0.98 (0.92, 1.03)	0.98 (0.92, 1.04)	0.4735	

Page **13** of **17** 

Current Weight (kg)				0.6098
Omega-3	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	0.0475	
Control	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)	0.0044	
Height (cm)				0.6440
Omega-3	0.99 (0.97, 1.02)	0.99 (0.97, 1.02)	0.4737	
Control	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)	0.8993	
Current BMI				0.7296
Omega-3	1.03 (1.01, 1.06)	1.03 (1.01, 1.06)	0.0136	
Control	1.04 (1.01, 1.06)	1.04 (1.01, 1.06)	0.0016	
ALA				0.2689
Omega-3	0.69 (0.34, 1.38)	0.68 (0.34, 1.37)	0.2847	
Control	1.16 (0.61, 2.23)	1.17 (0.61, 2.24)	0.6407	
DHA				0.6088
Omega-3	0.84 (0.64, 1.11)	0.83 (0.63, 1.09)	0.1839	
Control	0.76 (0.58, 1.00)	0.75 (0.57, 0.99)	0.0387	
EPA				0.6246
Omega-3	1.59 (0.85, 2.98)	1.56 (0.83, 2.94)	0.1716	
Control	1.28 (0.68, 2.41)	1.24 (0.65, 2.36)	0.5053	
EPA + DHA				0.5627
Omega-3	0.92 (0.74, 1.15)	0.91 (0.73, 1.14)	0.4069	
Control	0.84 (0.67, 1.05)	0.83 (0.66, 1.04)	0.1077	
Total omega-3				0.9368
Omega-3	0.92 (0.78, 1.08)	0.91 (0.77, 1.07)	0.2517	
Control	0.91 (0.76, 1.09)	0.90 (0.75, 1.08)	0.2573	
AA				0.3533
Omega-3	1.06 (0.92, 1.21)	1.05 (0.91, 1.21)	0.4872	
Control	0.97 (0.86, 1.10)	0.96 (0.85, 1.09)	0.5544	
SEIFA Index of Socioeconomic				0.2194
Disadvantage Quintile				
1 (Most Disadvantaged)	0.97 (0.59, 1.61)	0.99 (0.60, 1.64)	0.9657	
2	0.84 (0.50, 1.43)	0.84 (0.50, 1.42)	0.5184	
3	0.96 (0.64, 1.42)	0.95 (0.64, 1.42)	0.8057	
4	0.49 (0.31, 0.78)	0.49 (0.31, 0.78)	0.0028	
5 (Least Disadvantaged)	0.87 (0.52, 1.46)	0.86 (0.51, 1.45)	0.5708	
Race				0.4805
Other	0.48 (0.20, 1.13)	0.48 (0.20, 1.14)	0.0961	
Caucasian	0.83 (0.65, 1.07)	0.84 (0.65, 1.07)	0.1478	
Asian	0.82 (0.50, 1.34)	0.82 (0.50, 1.34)	0.4246	
Highest Qualification				0.3056
Completed				
Certificate/Diploma	0.91 (0.65, 1.28)	0.91 (0.65, 1.27)	0.5784	
Degree/Higher Degree	0.86 (0.61, 1.21)	0.86 (0.61, 1.21)	0.3929	
None	0.57 (0.26, 1.23)	0.57 (0.26, 1.24)	0.1533	
Secondary School	0.52 (0.29, 0.93)	0.52 (0.29, 0.93)	0.0278	
ANZSCO Occupation Code				0.2733

Page **14** of **17** 

1.2 (Most Skillod)	0.00 (0.62, 1.55)	0.00/0.62 1.54)	0.0601	Ι
3-5	0.99 (0.63, 1.55)	0.99 (0.03, 1.34)	0.5001	
6-8 (Least Skilled)	0.78 (0.46, 1.34)	0.78 (0.46, 1.33)	0.3631	
Not in Workforce	0.56 (0.37, 0.87)	0.56 (0.36, 0.87)	0.0091	
How Often Drank Alcohol in 3	0.50 (0.57, 0.07)	0.50 (0.50, 0.07)	0.0051	0.0987
Months Leading up to				0.0507
Pregnancy				
Never	0.62 (0.45, 0.85)	0.62 (0.45, 0.86)	0.0035	
Sometimes (up to once a	0.94 (0.68, 1.31)	0.94 (0.68, 1.30)	0.6897	
week)	0.0 . (0.00) 1.01)			
Often (twice a week or more)	1.15 (0.63, 2.09)	1.15 (0.63, 2.10)	0.6546	
Gestational Age (Weeks) at Trial				0.5112
Entry				
≤12	1.08 (0.67, 1.74)	1.09 (0.68, 1.75)	0.7317	
12.1-14	0.77 (0.53, 1.12)	0.77 (0.53, 1.12)	0.1757	
14.1-16	0.82 (0.52, 1.30)	0.82 (0.52, 1.29)	0.3861	
≥16	0.67 (0.45, 1.01)	0.67 (0.45, 1.02)	0.0601	
Total omega-3 Status				0.2295
Low	0.56 (0.34, 0.91)	0.56 (0.34, 0.92)	0.0208	
Moderate	0.88 (0.63, 1.25)	0.88 (0.62, 1.24)	0.4644	
Replete	0.92 (0.65, 1.30)	0.93 (0.66, 1.30)	0.6572	
EPA + DHA Status				0.4205
Low	0.62 (0.37, 1.05)	0.62 (0.37, 1.05)	0.0750	
Moderate	0.81 (0.60, 1.10)	0.81 (0.60, 1.10)	0.1819	
Replete	0.96 (0.65, 1.41)	0.96 (0.65, 1.42)	0.8459	
DHA Status				0.9069
Low	0.72 (0.38, 1.35)	0.73 (0.39, 1.36)	0.3194	
Moderate	0.82 (0.63, 1.08)	0.82 (0.62, 1.08)	0.1607	
Replete	0.86 (0.56, 1.32)	0.86 (0.56, 1.32)	0.4913	
Total omega-3 Status**				0.1767
Low	0.56 (0.34, 0.91)	0.56 (0.34, 0.92)	0.0208	
Lower Moderate	0.68 (0.41, 1.12)	0.68 (0.41, 1.12)	0.1279	
Upper Moderate	1.13 (0.70, 1.82)	1.12 (0.69, 1.82)	0.6436	
Replete	0.92 (0.65, 1.30)	0.93 (0.66, 1.30)	0.6568	
EPA + DHA Status**				0.4392
Low	0.62 (0.37, 1.05)	0.62 (0.37, 1.05)	0.0750	
Lower Moderate	0.71 (0.47, 1.07)	0.71 (0.47, 1.07)	0.1005	
Upper Moderate	0.96 (0.61, 1.50)	0.96 (0.61, 1.51)	0.8624	
Replete	0.96 (0.65, 1.41)	0.96 (0.65, 1.42)	0.8454	
DHA Status**				0.4355
Low	0.72 (0.38, 1.35)	0.73 (0.39, 1.37)	0.3208	
Lower Moderate	0.65 (0.43, 0.98)	0.65 (0.43, 0.97)	0.0359	
Upper Moderate	1.01 (0.69, 1.47)	1.01 (0.70, 1.47)	0.9465	
Replete	0.86 (0.56, 1.32)	0.86 (0.56, 1.32)	0.4906	
LA Quartile***				0.4478

Page **15** of **17** 

Q1	0.81 (0.55, 1.18)	0.81 (0.55, 1.19)	0.2779
Q2	1.02 (0.65, 1.58)	1.01 (0.65, 1.57)	0.9491
Q3	0.61 (0.39, 0.96)	0.61 (0.38, 0.96)	0.0331
Q4	0.88 (0.55, 1.41)	0.88 (0.55, 1.41)	0.6021

\* Odds ratios for continuous predictors are the effect of a 1-unit increase in the predictor within each treatment group. Odds ratios > 1 indicate the odds of preterm birth increase as the predictor increases, while odds ratios <1 indicate the odds of preterm birth decrease as the predictor increases. Odds ratios for categorical predictors are comparing the omega-3 group to the control group within each category. Odds ratios >1 indicate the odds of preterm birth are higher in the omega-3 group, while odds ratios <1 indicate the odds of preterm birth are higher in the control group.

\*\* Moderate status category split into lower moderate (between the threshold for benefit and the null treatment effect) and upper moderate (between the null treatment effect and the threshold for harm).

\*\*\* LA failed the Hosmer-Lemeshow goodness of fit test when considered as a linear predictor and hence it was categorised in quartiles.

**Table S5** Baseline characteristics of women for singleton pregnancies included in the analysis byalcohol use and parity

Baseline Characteristic	No Alcohol,	No Alcohol,	Alcohol, No	Alcohol,
	No Previous	Previous	Previous	Previous
	Birth (N=905)	Birth	Birth	Birth
		(N=1452)	(N=1429)	(N=1521)
Consumed omega-3 containing				
supplements in previous 3	105/905	156/1452	207/1429	242/1521
months: n/N (%)	(11.6%)	(10.7%)	(14.5%)	(15.9%)
Maternal age: Median (IQR)	28.0 (24.0-	31.0 (27.0-	29.0 (26.0-	32.0 (28.0-
	31.0)	34.0)	32.0)	35.0)
Gestational age (weeks) at trial	14.3 (12.7-	14.6 (12.9-	14.1 (12.7-	14.0 (12.7-
entry: Median (IQR)	16.9)	16.7)	16.4)	16.0)
White race: n/N (%)	497/905	856/1452	1238/1429	1332/1521
	(54.9%)	(59.0%)	(86.6%)	(87.6%)
Completed high school	756/905	1158/1452	1192/1429	1171/1521
education: n/N (%)	(83.5%)	(79.8%)	(83.4%)	(77.0%)
Currently employed: n/N (%)	669/904	852/1452	1270/1428	1048/1521
	(74.0%)	(58.7%)	(88.9%)	(68.9%)
Weight at trial entry (kg): Median	65.5 (58.0-	70.0 (61.0-	68.2 (60.6-	71.0 (62.2-
(IQR)	76.0)	82.4)	78.8)	84.0)
Smoked cigarettes leading up to	110/905	178/1447	253/1428	270/1521
pregnancy: n/N (%)	(12.2%)	(12.3%)	(17.7%)	(17.8%)
ALA: Median (IQR)	0.5 (0.4-0.7)	0.6 (0.5-0.7)	0.5 (0.4-0.7)	0.5 (0.4-0.7)
EPA: Median (IQR)	0.5 (0.3-0.6)	0.5 (0.4-0.6)	0.5 (0.4-0.6)	0.5 (0.4-0.6)
DPA: Median (IQR)	1.0 (0.8-1.1)	1.0 (0.8-1.1)	1.0 (0.9-1.1)	1.0 (0.9-1.1)
DHA: Median (IQR)	2.6 (2.2-3.1)	2.6 (2.2-3.0)	2.8 (2.4-3.2)	2.7 (2.3-3.0)
EPA + DHA: Median (IQR)	3.1 (2.7-3.6)	3.1 (2.7-3.6)	3.3 (2.9-3.8)	3.2 (2.8-3.6)
Total omega-3: Median (IQR)	4.7 (4.1-5.2)	4.7 (4.2-5.3)	4.9 (4.4-5.4)	4.8 (4.4-5.3)

Page 16 of 17

IQR, interquartile range; ALA, alpha-linolenic acid; EPA, eicosapentaenoic acid; DPA, docosapentaenoic acid; DHA, docosahexaenoic acid; Total omega-3 is the sum of ALA, EPA, DPA and DHA.

Page **17** of **17**