

# Supplementary material

## Maternal fish consumption, fetal growth and the risks of neonatal complications: The Generation R Study.

Denise H.M. Heppel<sup>1,2,3</sup>, Eric A.P. Steegers<sup>4</sup>, Sarah Timmermans<sup>1,4</sup>, Hanneke den Breeijen<sup>1,2</sup>,  
Henning Tiemeier<sup>5</sup>, Albert Hofman<sup>2</sup>, Vincent W.V. Jaddoe<sup>1, 2, 3</sup>

<sup>1</sup>The Generation R Study Group, Erasmus Medical Centre, PO Box 2040, 3000 CA Rotterdam  
Rotterdam, The Netherlands.

<sup>2</sup>Department of Epidemiology, Erasmus Medical Centre, PO Box 2040, 3000 CA Rotterdam, The  
Netherlands.

<sup>3</sup>Department of Paediatrics, Erasmus Medical Centre, PO Box 2040, 3000 CA Rotterdam, The  
Netherlands.

<sup>4</sup>Department of Obstetrics and Gynaecology, Erasmus Medical Centre, PO Box 2040, 3000 CA  
Rotterdam, The Netherlands.

<sup>5</sup>Department of Psychiatrics, Erasmus Medical Centre, PO Box 2040, 3000 CA Rotterdam, The  
Netherlands.

**Table S1. Associations between weekly maternal total fish consumption and fetal growth and growth characteristics at birth, the Generation R Study Cohort, Rotterdam, The Netherlands.**

Total fish consumption	Trimester 2			Trimester 3			Birth		
	Head circumference (n=3307)			Head circumference (n=3276)			Head circumference (n=2775)		
	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI
0	653	Reference		641	Reference		541	Reference	
1-69 g/week	878	0.5	-0.1, 1.2	872	1.7	0.8, 2.7†	742	0.3	-0.0, 0.5
70-139 g/week	1061	-0.1	-0.7, 0.5	1058	0.6	-0.3, 1.5	895	0.1	-0.1, 0.4
140-209 g/week	494	0.1	-0.6, 0.8	487	1.8	0.8, 2.9†	422	0.2	-0.1 0.5
>210 g/week	221	0.5	-0.5, -1.4	218	0.9	-0.5, 2.3	175	0.1	-0.3 0.5
<i>P for trend</i>		<i>0.88</i>			<i>0.06</i>			<i>0.80</i>	
Total fish consumption	Femur length (n=3306)			Femur length (n=3310)			Birth length (n=2831)		
	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (cm)	95% CI
	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (cm)	95% CI
0	650	Reference		652	Reference		557	Reference	
1-69 g/week	877	0.0	-0.2, 0.2	879	0.1	-0.1, 0.3	758	0.4	0.1 0.7†

70-139 g/week	1064	-0.1	-0.3, 0.1	1067	0.0	-0.2, 0.2	911	0.1	-0.2, 0.4
140-209 g/week	494	-0.2	-0.4, 0.1	492	0.1	-0.2, 0.3	428	0.3	-0.1, 0.6
>210 g/week	221	0.0	-0.3, 0.3	220	-0.2	-0.6, 0.1	177	-0.1	-0.5, 0.4
<i>P for trend</i>		0.52			0.72			0.92	

Total fish consumption	Estimated fetal weight (n=3291)			Estimated fetal weight (n=3298)			Birth weight (n=3367)		
	n	Difference (g)	95% CI	n	Difference (g)	95% CI	n	Difference (g)	95% CI
0	647	Reference		651	Reference		667	Reference	
1-69 g/week	871	2.7	-1.6, 7.1	874	15.2	-3.8 34.2	894	34.8	-10.0, 79.5
70-139 g/week	1061	-0.1	-4.3, 4.1	1062	-8.1	-26.4, 10.1	1080	24.4	-18.6, 67.5
140-209 g/week	491	-0.9	-5.9, 4.1	491	7.5	-14.5 29.5	501	45.1	-6.7, 96.9
>210 g/week	221	4.9	-1.6, 11.5	220	-0.1	-10.2, 15.5	225	6.00	-28.6, 40.5
<i>P for trend</i>		0.84			0.80			0.36	

\* Values were based on multivariate linear regression models and reflect the difference and 95% Confidence Interval for each level of weekly total fish consumption compared to the reference group (0 g/week). Models were only adjusted for gestational age at measurement and fetal sex. Tests for trend were performed by including weekly total fish consumption as a continuous term in the regression model.

† *P* value <0.05

**Table S2. Associations between weekly maternal lean fish consumption and fetal growth and growth characteristics at birth, the Generation R Study Cohort, Rotterdam, The Netherlands.**

	Trimester 2			Trimester 3			Birth		
	Head circumference (n=3307)			Head circumference (n=3276)			Head circumference (n=2775)		
Lean fish consumption	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (cm)	95% CI
0	1239	Ref		1219	Ref		1017	Ref	
1-35 g/week	849	0.2	-0.3, 0.8	850	0.8	-0.0, 1.6	724	0.0	-0.1, 0.3
35-69 g/week	813	0.2	-0.3, 0.8	804	1.1	0.3, 2.0 <sup>†</sup>	697	0.1	-0.0, 0.4
>70 g/week	406	0.2	-0.5, 0.9	403	0.3	-0.8, 1.3	337	0.1	-0.2, 0.4
<i>P for trend</i>		0.34			0.08			0.39	
	Femur length (n=3306)			Femur length (n=3310)			Birth length (n=2831)		
Lean fish consumption	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (cm)	95% CI
0	1233	Ref		1234	Ref		1044	Ref	
1-35 g/week	853	0.0	-0.2, 0.2	857	0.1	-0.1, 0.3	742	0.1	-0.1, 0.4
35-69 g/week	814	-0.1	-0.3, 0.0	812	0.1	-0.1, 0.3	711	0.2	-0.1, 0.4

>70 g/week	406	-0.2	-0.6, 0.1	407	-0.1	-0.4, 0.1	334	0.0	-0.3, 0.4
<i>P for trend</i>		<i>0.16</i>			<i>0.46</i>			<i>0.51</i>	
	Estimated fetal weight (n=3291)			Estimated fetal weight (n=3298)			Birth weight (n=3367)		
Lean fish consumption		Difference			Difference			Difference	
	n	(g)	95% CI	n	(g)	95% CI	n	(g)	95% CI
0	1226	Ref		1230	Ref		1262	Ref	
1-35 g/week	849	0.4	-3.4, 4.1	852	4.8	-11.7, 21.2	869	24.6	-14.1, 63.2
35-69 g/week	810	-1.4	-5.2, 2.4	810	8.8	-7.9, 25.5	823	45.9	6.7, 85.2†
>70 g/week	406	0.0	-4.8, 4.8	406	-4.3	-25.4, 16.9	413	-11.4	-61.1, 38.4
<i>P for trend</i>		<i>0.74</i>			<i>0.88</i>			<i>0.58</i>	

\* Values were based on multivariate linear regression models and reflect the difference and 95% Confidence Interval for each level of weekly lean fish consumption compared to the reference group (0 g/week). Models were only adjusted for gestational age at measurement and fetal sex. Tests for trend were performed by including weekly lean fish consumption as a continuous term in the regression model.

† *P* value <0.05

**Table S3. Associations between weekly maternal fatty fish consumption and fetal growth and growth characteristics at birth, the Generation R Study Cohort, Rotterdam, The Netherlands.**

	Trimester 2			Trimester 3			Birth		
	Head circumference (n=3307)			Head circumference (n=3276)			Head circumference (n=2775)		
Fatty fish consumption	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI
0	1083	Ref		1064	Ref		912	Ref	
1-35 g/week	719	0.1	-0.5, 0.7	725	0.7	-0.1, 1.6	610	0.1	-0.2, 0.3
35-69 g/week	911	-0.2	-0.7, 0.4	900	-0.0	-0.8, 0.8	764	0.0	-0.2, 0.2
>70 g/week	594	-0.1	-0.7, 0.5	587	0.5	-0.4, 1.4	489	0.1	-0.2, 0.4
<i>P for trend</i>		0.68			0.25			0.75	
	Femur length (n=3306)			Femur length (n=3310)			Birth length (n=2831)		
Fatty fish consumption	n	Difference (mm)	95% CI	n	Difference (mm)	95% CI	n	Difference (cm)	95% CI
0	1097	Ref		1081	Ref		934	Ref	
1-35 g/week	723	-0.1	-0.2, 0.1	729	-0.0	-0.2, 0.2	626	0.1	-0.2, 0.4
35-69 g/week	911	-0.1	-0.3, 0.1	908	-0.1	-0.3, 0.1	774	0.1	-0.1, 0.4

>70 g/week	593	-0.1	-0.3, 0.1	592	-0.1	-0.3, 0.2	497	0.0	-0.2, 0.3
<i>P for trend</i>		0.39			0.46			0.99	
	Estimated fetal weight (n=3291)			Estimated fetal weight (n=3298)			Birth weight (n=3367)		
Fatty fish consumption		Difference			Difference			Difference	
	n	(g)	95% CI	n	(g)	95% CI	n	(g)	95% CI
0	1074	Ref		1077	Ref		1100	Ref	
1-35 g/week	719	-0.1	-4.1, 4.0	725	0.1	-17.6, 17.8	737	-6.8	-48.6, 35.0
35-69 g/week	910	-0.6	-4.3, 3.2	907	-10.6	-27.3, 6.0	928	19.0	-20.2, 58.1
>70 g/week	588	-0.9	-5.2, 3.4	589	-8.6	-27.5, 10.3	602	6.4	-38.0, 50.8
<i>P for trend</i>		0.72			0.38			0.40	

\* Values were based on multivariate linear regression models and reflect the difference and 95% Confidence Interval for each level of weekly fatty fish consumption compared to the reference group (0 g/week). Models were only adjusted for gestational age at measurement and fetal sex. Tests for trend were performed by including weekly fatty fish consumption as a continuous term in the regression model.

**Table S4. Associations between weekly maternal shellfish consumption and fetal growth and growth characteristics at birth, the Generation R Study Cohort, Rotterdam, The Netherlands.**

Shellfish consumption	Trimester 2			Trimester 3			Birth		
	Head circumference (n=3307)			Head circumference (n=3276)			Head circumference (n=2775)		
	Difference			Difference			Difference		
	n	(mm)	95% CI	n	(mm)	95% CI	n	(mm)	95% CI
0	2053	Ref		2027	Ref		1693	Ref	
1-13 g/week	604	0.2	-0.3, 0.8	609	0.8	-0.0, 1.6	520	-0.0	-0.2, 0.2
>14 g/week	650	0.1	-0.4, 0.7	640	0.2	-0.6, 1.0	561	0.0	-0.2, 0.3
<i>P for trend</i>		<i>0.40</i>			<i>0.50</i>			<i>0.83</i>	
Shellfish consumption	Femur length (n=3306)			Femur length (n=3310)			Birth length (n=2831)		
	Difference			Difference			Difference		
	n	(mm)	95% CI	n	(mm)	95% CI	n	(cm)	95% CI
0	2049	Ref		2046	Ref		1747	Ref	
1-13 g/week	608	-0.1	-0.2, 0.1	618	-0.0	-0.2, 0.2	528	0.0	-0.3, 0.3
>14 g/week	649	-0.2	-0.3, -0.0†	646	-0.2	-0.4, 0.0	556	-0.0	-0.3, 0.2
<i>P for trend</i>		<i>0.13</i>			<i>0.21</i>			<i>0.60</i>	

Shellfish consumption	Estimated fetal weight (n=3291)			Estimated fetal weight (n=3298)			Birth weight (n=3367)		
	n	Difference (g)	95% CI	n	Difference (g)	95% CI	n	Difference (g)	95% CI
0	2042	Ref		2040	Ref		2090	Ref	
1-13 g/week	604	-0.8	-4.7, 3.1	615	1.9	-15.1, 18.9	620	-12.5	-52.8, 27.7
>14 g/week	645	-0.9	-4.7, 2.9	643	-12.6	-29.3, 4.1	657	-28.8	-68.1, 10.6
<i>P for trend</i>		<i>0.64</i>			<i>0.19</i>			<i>0.20</i>	

\* Values were based on multivariate linear regression models and reflect the difference and 95% Confidence Interval for each level of weekly shellfish consumption compared to the reference group (0 g/week). Models were only adjusted for gestational age at measurement and fetal sex. Tests for trend were performed by including weekly shellfish consumption as a continuous term in the regression model.

† *P* value <0.05

**Table S5. Associations between fish consumption and risks of neonatal complications, the Generation R Study Cohort, Rotterdam, The Netherlands.**

Fish consumption	Neonatal complications											
	Preterm birth (n=334)				Low birth weight (n=138)				Small for gestational age (n=205)			
	n	cases	OR	95% CI	n	cases	OR	95% CI	n	cases	OR	95% CI
<b>Total fish consumption</b>												
0	668	34	Ref		667	34	Ref		667	51	Ref	
1-69 g/week	897	45	0.99	0.62, 1.56	894	29	0.49	0.25, 0.95†	893	57	0.81	0.55, 1.20
70-139 g/week	1085	47	0.85	0.54, 1.33	1080	46	0.84	0.47, 1.51	1079	60	0.70	0.48, 1.03
140-209 g/week	502	20	0.78	0.44, 1.37	501	16	0.66	0.30, 1.43	501	25	0.63	0.38, 1.02
>210 g/week	226	13	1.14	0.59, 2.20	225	13	0.93	0.39, 2.21	225	12	0.67	0.35, 1.28
<i>P for trend</i>			<i>0.54</i>				<i>0.86</i>				<i>0.10</i>	
<b>Lean fish consumption</b>												
0	1267	75	Ref		1262	62	Ref		1260	91	Ref	
1-35 g/week	869	32	0.61	0.40, 0.93†	869	27	0.67	0.37, 1.21	869	46	0.71	0.49, 1.02
35-69 g/week	828	38	0.77	0.51, 1.14	823	32	0.81	0.45, 1.44	823	37	0.60	0.41, 0.89†
>70 g/week	414	14	0.56	0.31, 1.00	413	17	1.22	0.62, 2.40	413	31	1.03	0.68, 1.58

<i>P for trend</i>		<i>0.49</i>				<i>0.85</i>				<i>0.54</i>		
Fatty fish consumption												
0	1104	58	Ref		1100	50	Ref		1099	75	Ref	
1-35 g/week	739	26	0.66	0.41, 1.06	737	18	0.66	0.34, 1.30	737	51	1.00	0.70, 1.45
35-69 g/week	931	48	0.98	0.66, 1.46	928	47	1.23	0.72, 2.13	927	49	0.75	0.52, 1.09
>70 g/week	604	27	0.84	0.53, 1.35	602	23	1.04	0.55, 1.98	602	30	0.71	0.46, 1.09
<i>P for trend</i>		<i>0.35</i>				<i>0.80</i>				<i>0.04†</i>		
Shellfish consumption												
0	2098	103	Ref		2090	87	Ref		2089	120	Ref	
1-13 g/week	620	24	0.78	0.50, 1.23	620	18	0.83	0.43, 1.57	620	44	1.24	0.87, 1.78
>14 g/week	660	32	0.99	0.66, 1.48	657	33	1.64	0.95, 2.83	656	41	1.08	0.75, 1.56
<i>P for trend</i>		<i>0.43</i>				<i>0.86</i>				<i>0.99</i>		

\* Values were based on multivariate logistic regression models and reflect the odds ratio and 95% Confidence interval for pregnancy complications for each level of fish consumption compared to the reference group (0 g/week). Models were only adjusted for gestational age at measurement and fetal sex. Tests for trend were performed by including weekly fish consumption as a continuous term in the regression model.

† *P* value <0.05