SUPPLEMENTAL MATERIAL

Web Appendix

Details of random effects statistical modelling to determine gestational weight gain parameters

The sample was limited to mothers of offspring born at term (at least 37 weeks gestation) and alive. We divided the gestational period into 2-week stages, from 4 weeks onwards. Where an individual woman had more than one measurement in one of these two-week periods, one was chosen randomly for inclusion in the sample.

Thus, each woman could contribute a maximum of 20 weight measures to the model. Deletion of obvious errors in weights and dates, and elimination of repeat measures within the two week period, gave a sample for model development of 12,484 women with a total of 114,988 weight measures.

There was little evidence that patterns of gestational weight gain (GWG) differed markedly between mothers of female and male offspring; predicted mean pre-pregnancy weight was 0.479 (0.05, 0.91) kg greater for mothers of male compared to female offspring ($p = 0.025$) but otherwise there were no differences. One model was constructed for mothers of both female and male offspring, and interactions between sex of offspring and gestational weight gain included. Multilevel models (with two levels: antenatal visit, within mother) were used to relate weight at each visit to gestational age of the child at that visit. Fractional polynomials were used to derive the best-fitting function to describe the pattern of weight gain with gestational age. However, although fractional polynomials provide a flexible way to examine such relationships, they do not provide parameters that are clinically relevant or easily interpreted. For example, here the best-fitting polynomial had powers of 2 and 3, indicating that weight was related to gestational age squared and gestational age cubed. We therefore used the best-fitting fractional polynomial to derive a piecewise linear spline model.

Here, the best approximation to the fractional polynomial was provided by a spline model with three linear portions: from 0 to 18 weeks gestation; from 19 to 28 weeks gestation; and, from 29 weeks gestation to birth.

The positioning of the knots was chosen by varying the positions of the knots (in whole gestational weeks) around the approximate times and selecting the model with the smallest residuals throughout the range of gestational age. This linear spline multilevel model enabled estimation of the individual pre-pregnancy weight and weight gain during each period, for each woman. In addition, the model allowed variation in measurement between occasions and within subjects, thereby capturing the change in the variance of measurements with age. The model was estimated using maximum likelihood estimation within MLWiN.1. The final multilevel spline model is shown below.

Multilevel spline model:

$weight_{ij}=\beta 0i+\beta 1i age0to18_{ij}+\beta 2i age18to28_{ij}+\beta 3i age29plus_{ij}+e_{ij}$ where, for mother i (i=1 to 12,484) at measurement occasion j (j=1 to 18):

$\beta 0i$=individual estimate of weight at gestational age=0 for the ith mother

$\beta 1i$= individual estimate of rate of weight gain during the first 18 weeks for the ith mother

$\beta 2i$=individual estimate of rate of weight gain during weeks 18-28 for the ith mother

$\beta 3i$=individual estimate of rate of weight gain after week 28 for the ith mother

$age0to18_{ij}$= the value of the first linear spline at the gestational age of the jth observation for the ith mother

$age18to28_{ij}$= the value of the second linear spline at the gestational age of the jth observation for the ith mother

$age29tomax_{ij}$= the value of the third linear spline at the gestational age of the jth observation for the ith mother

e_{ij} = measurement error

Table 1 shows the fit of this model when compared to the measured weights at each time point. It shows high level of agreement between predicted and actual weight, demonstrating the goodness of fit of the model.

With analyses restricted to births occurring between 37-44 weeks there were between 1 and 18 measures of weight per woman, with average 11.2 (median 10, sd 3.7, IQR 8, 11). In the first period (0-18 weeks) there were between 0 and 7 measures per woman, with an average of 2.0 (median 2, sd 1.01, IQR 1, 3). In the second period (18-28 weeks) there were between 0 and 5 measures per woman, with an average of 2.2 (median 2, sd 1.0, IQR 2, 3). In the third period (29+ weeks) there were between 0 and 8 measures per woman, with an average of 4.9 (median 5, sd 1.6, IQR 4,6). All mother-offspring pairs are included in the analyses provided the mother has at least one measure of gestational weight. This approach to modelling repeat measurements provides estimated coefficients in each gestational age period even if the woman has no measurements in that particular period. This is because the overall model uses all data and will use the woman's values in other periods to give a predicted coefficient for the period where she has no data based on the overall model using data from all women. If women with few weight measurements differed from those with more measurements (in particular those who had measurements in all periods) in such a way that associations with outcomes differed between the two groups then our results would be biased. In order to explore this possibility we conducted sensitivity analyses in which predicted GWG derived from multilevel models were repeated with only those women who had at least 2, 4 and 3 measures in each time period respectively (i.e. total of at least 9 per woman across pregnancy).

Web Figure 1 shows the pattern predicted by the multilevel fractional polynomial model. This shows that the final spline model used in the analyses fits closed to the fractional polynomial fitted to the data in the multilevel model. Web-figure 2 shows the difference between predicted and observed weight plotted against the average of predicted and observed weight .The difference between predicted and actual weight gets very slightly smaller as weight increases – an average difference of 0.004kg for women of weight 70kg, with an average difference of -0.31kg for women of weight 168kg (the maximum weight in our dataset, indicating that for these women predicted weight is on average 0.31kg lower than measured weight) and 0.12kg for women of weight 36kg (the minimum weight in our dataset, indicating that for these women predicted weight is on average 0.12kg higher than measured weight).

Web Table 1: Fit of the model (predicted weight) to actual weight at each time Period, in Avon Longitudinal Study of Parents And Children, Bristol, UK.

Gestational age (weeks)	Number of measurements	Weight (mean (SD)) kg	Predicted weight (mean(SD)) kg	Difference (actual-predicted) (median) kg	90% limits of agreement (kg)[b]
<=4	23	65.89 (12.95)	65.59 (12.94)	0.10	-0.55, 1.25
5-6	178	64.55 (13.54)	64.30 (13.53)	0.29	-0.88, 1.53
7-8	1,206	64.53 (12.30)	64.25 (12.27)	0.29	-0.73, 1.28
9-10	3,154	64.36 (12.20)	64.27 (12.15)	0.11	-0.91, 0.99
11-12	4,810	64.37 (12.16)	64.41 (12.09)	-0.01	-1.11, 0.91
13-14	5,457	64.69 (11.84)	64.84 (11.78)	-0.12	-1.30, 0.94
15-16	4,646	65.39 (12.15)	65.53 (12.11)	-0.15	-1.32, 1.06
17-18	6,587	66.02 (11.87)	66.02 (11.82)	-0.01	-1.11, 1.14
19-20	4,722	67.26 (12.18)	67.19 (12.14)	0.06	-0.99, 1.19
21-22	5,790	68.03 (11.94)	67.98 (11.90)	0.06	-1.20, 1.26
23-24	5,061	69.35 (12.24)	69.28 (12.18)	0.09	-1.30, 1.37
25-26	5,770	70.07 (11.96)	69.96 (11.91)	0.11	-1.18, 1.42
27-28	6,035	71.46 (11.98)	71.46 (11.91)	-0.002	-1.14, 1.15
29-30	8,307	72.26 (12.04)	72.30 (11.97)	-0.03	-1.14, 1.08
31-32	8,907	73.17 (12.16)	73.24 (12.13)	-0.08	-1.30, 1.17
33-34	9,769	74.00 (12.05)	74.08 (12.03)	-0.08	-1.39, 1.23
35-36	10,286	74.99 (12.31)	75.00 (12.30)	-0.004	-1.26, 1.25
37-38	10,927	75.95 (12.29)	75.90 (12.24)	0.05	-1.11, 1.20
39-40	9,215	76.97 (12.35)	76.96 (12.30)	0.003	-1.11, 1.17
41-42	3,991	78.28 (12.46)	78.33 (12.35)	-0.9	-1.20, 1.14
>42	147	80.69 (15.04)	80.82 (14.76)	-0.20	-1.51, 1.59

Abbreviations: SD: Standard Deviation
a Total number of measurements in each strata of gestational age (i.e. number of women*number of measurements that woman had)
b These indicate the range within which 90% of the differences lie in this sample

Web Table 2. Associations of Institute Of Medicine Categories of Maternal Gestational Weight Gain With Offspring Cognition, adjustment for birthweight and SEA (IQ and late school results) in Avon Longitudinal Study of Parents And Children, Bristol, UK.

Outcome		Less than recommended GWG			As rec. GWG	More than recommended GWG		
	Model	Mean SD difference	Odds Ratio	95% CI	Ref.	Mean SD difference	Odds Ratio	95% CI
SEA[c] N=,5832	1 [a]	-0.054		-0.107, -0.002	0	-0.006		-0.062, 0.050
IQ at 8[c] N=5,191	1 [a]	-0.002		-0.062, 0.057	0	0.047		-0.018, 0.112
	2 [b]	-0.002		-0.065, 0.062	0	0.060		0.021, 0.159
Final-exam results N=7,339	1 [a]		0.90	0.79, 1.01	1		0.98	0.86, 1.12
	2 [b]		0.88	0.75, 1.02	1		1.00	0.86, 1.17

Abbreviations: BMI: Body Mass Index, CI: Confidence Interval, GWG: Gestational Weight Gain, IOM: Institute of Medicine, IQ: Intelligence Quotient, rec.: Recommended, Ref.: Reference category, SEA: School Entry Assessment, SD: Standard Deviation.

a Model 1 - adjusted for gestational age, maternal age, age at outcome assessment, gender, prepregnancy BMI, parity, maternal smoking, maternal education, mode of delivery and birthweight

b Model 2 - as model 2 plus additional adjustment for standardised School Entry Assessment

c Standardised. SEA SD=3.26, IQ SD=16.47

Web Table 3. Multivariable Associations of Prepregnancy Weight and Gestational Weight Gain With Offspring Cognition, in Avon Longitudinal Study of Parents And Children, Bristol, UK – adjustment for birthweight and SEA (IQ and late school results)

		Prepregnancy weight			0-18 weeks				18-28 weeks				28+ weeks			
Outcome	Mod-el	Mean SD diff per 1 kg	Odds Ratio	95%CI	Mean SD diff per 400g/wk		95%CI		Mean SD diff per 400g/wk		95%CI		Mean SD diff per 400g/wk		95%CI	
SEA [c]	1[a]	-0.004		-0.006, -0.003	0.048		-0.006, 0.124		0.056		-0.005, 0.116		0.017		-0.044, 0.078	
IQ at 8[c] N=5,191	1[a]	-0.005		-0.008, -0.003	0.038		-0.024, 0.100		0.036		-0.033, 0.105		0.064		-0.006, 0.133	
	2[b]	-0.002		-0.004, 0.000	0.069		0.004, 0.135		0.037		-0.036, 0.111		0.069		-0.007, 0.145	
					BMI<25		BMI≥25		BMI<25		BMI≥25		BMI<25		BMI≥25	
					OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Adequate late school results N=7,339	1[a]		0.98	0.980.99	0.87	0.75, 1.01	1.32	1.06, 1.65	1.01	0.86, 1.18	1.12	0.87, 1.44	1.00	0.85, 1.17	1.48	1.14, 1.92
	2[b]		0.99	0.98,0.99	0.82	0.69, 0.99	1.34	1.04, 1.74	1.06	0.97, 1.29	1.20	0.88, 1.63	1.00	0.82, 1.23	1.42	1.03, 1.96

Abbreviations: BMI: Body Mass Index, CI: confidence interval, diff: difference, IQ: Intelligence Quotient, prepreg: prepregnancy, SD: Standard deviation, SEA: School Entry Assessment.

a Model 1 - adjusted for gestational age, maternal age, age at outcome assessment, gender, prepregnancy weight, GWG in previous period, parity, maternal smoking, maternal education, mode of delivery and birthweight

b Model 2 - as model 1 plus additional adjustment for SEA

c Standardised. SEA SD=3.26, IQ SD=16.47

Web Table 4. Characteristics of participants included and excluded from analyses, in Avon Longitudinal Study of Parents And Children, Bristol UK.

	Included in analyses *n*=8650			**Excluded from analyses**			**Total excluded *n***	***P*-value ***
	Mean (SD)	%	*n*	Mean (SD)	%	*n*		
Maternal age at birth (years)	28.6 (4.8)			26.9 (5.1)			2250	<0.001
Did not smoke at all during pregnancy		78	6758		66	1307	1979	<0.001
Maternal education – no higher education		86	7410		91	1557	1706	<0.001
Manual social class		18	1523		26	280	1085	<0.001
No previous pregnancies		47	4044		40	723	1827	<0.001
Caesarean section		11	909		9	164	1855	0.03
Pre pregnancy weight (kg)	60.8 (12.3)			60.8 (13.2)			2250	0.83
Weight gain 0-18 weeks	0.31 (0.18)			0.30 (0.17)			2250	<0.001
Weight gain 18-28 weeks	0.54 (0.17)			0.53 (0.18)			2250	0.007
Weight gain after 28 weeks	0.47 (0.20)			0.46 (0.20)			2250	0.10
Males		51	4403		52	1161	2250	0.56
Gestational age (weeks)	39.8 (1.3)			39.8 (1.3)			2250	0.51
Birth weight (g)	3486.2 (471.3)			3422.3 (496.9)			1415	<0.001
IOM adequate		38	3323		34	764	2250	<0.001
SEA	13.1 (3.1)			12.0 (3.3)			1551	<0.001

IQ age 8, (N=5191)	105.1 (16.4)			101.4 (16.6)			816	<0.001
Achieved 5 GCSEs A*-C (N=7339)		44	3212		59	1116	1883	<0.001

Abbreviations: GCSE: General Certificate of Secondary Education, IOM: Institute of Medicine, IQ: Intelligence Quotients, SD: Standard Deviation, SEA: School Entry Assessment

* chi squared or regression analysis as appropriate

Web Table 5. Associations of Institute Of Medicine categories of maternal Gestational Weight Gain with high and low GCSE achievement, in Avon Longitudinal Study of Parents And Children, Bristol, UK. *n*=7,339

Outcome	Model	Less than recommended		As recommended	More than recommended	
		Odds Ratio	95%CI	Odds Ratio	Odds Ratio	95%CI
9 A*/A grades	1 [a]	0.97	0.78, 1.22	1	0.91	0.71, 1.17
	2 [b]	1.02	0.80, 1.29	1	1.03	0.79, 1.34
	3 [c]	1.11	0.87, 1.41	1	0.97	0.74, 1.26
	4 [d]	0.98	0.71, 1.34	1	1.07	0.76, 1.51
0 A*-C grades						
	1 [a]	1.28	1.10, 1.51	1	1.20	1.02, 1.42
	2 [b]	1.18	1.00, 1.40	1	1.23	1.04, 1.47
	3 [c]	1.13	0.95, 1.34	1	1.29	1.08, 1.54
	4 [d]	1.12	0.91, 1.37	1	1.17	0.95, 1.44

Abbreviations: CI: Confidence Interval, GCSE: General Certificate of Secondary Education.
a Model 1 - adjusted for gestational age, age at exposure measurement and gender
b Model 2 - as model 1 plus additional adjustment for maternal age, parity, maternal smoking, maternal education and mode of delivery
c Model 3 as model 2 plus additional adjustment for birth weight
d Model 4 as model 2 plus additional adjustment for standardised School Entry Assessment Score

Web Table 6. Associations of Institute Of Medicine categories of maternal Gestational Weight Gain with offspring cognition in mother-offspring pairs with complete data, in Avon Longitudinal Study of Parents And Children, Bristol, UK. *n*=3,340

Outcome	Model	Less than recommended			As recommended	More than recommended		
		Mean SD difference	Odds Ratio	95%CI	Reference	Mean SD difference	Odds Ratio	95%CI
SEA [e]	1[a]	-0.055		-0.124, 0.013	0	-0.049		-0.121, 0.023
	2[b]	-0.044		-0.011, 0.022	0	-0.039		-0.109, 0.030
	3[c]	-0.028		-0.095, 0.039	0	-0.052		-0.122, 0.176
IQ at 8[e]	1[a]	-0.028		-0.106, 0.049	0	0.039		(0.043, 0.121
	2[b]	-0.018		-0.091, 0.055	0	0.052		-0.025, 0.013
	3[c]	0.009		-0.065, 0.083	0	0.030		-0.048, 0.107
	4[d]	0.000		-0.067, 0.066	0	0.072		0.002, 0.142
Final-exam results	1[a]		0.92	0.77, 1.08	1		0.97	0.82, 1.16
	2[b]		0.94	0.79, 1.13	1		0.98	0.81, 1.17
	3[c]		0.97	0.81, 1.16	1		0.95	0.79, 1.15
	4[d]		0.92	0.77, 1.08	1		0.97	0.82, 1.16

Abbreviations: CI: Confidence Interval, GCSE: General Certificate of Secondary Education, IQ: Intelligence Quotient, SEA: School Entry Assessment, SD: Standard Deviation.
a Models 1 - adjusted for gestational age, age at exposure measurement and gender
b Model 2 - as model 1 plus additional adjustment for maternal age, parity, maternal smoking, maternal education and mode of delivery
c Model 3 as model 2 plus additional adjustment for birth weight
d Model 4 as model 2 plus additional adjustment for standardised School Entry Assessment Score

e Standardised. SEA SD=3.26, IQ SD=16.47

Web Table 7. Multivariable associations of prepregnancy weight and GWG with offspring cognition in mother-offspring pairs with complete data, in Avon Longitudinal Study of Parents And Children, Bristol, UK. *n*=3,340

Outcome	Prepregnancy weight			0-18 weeks		18-28 weeks		29+ weeks	
	Mean difference per 1 kg	Odds Ratio	95%CI	Mean difference per 400 g/week	95%CI	Mean difference per 400 g/week	95%CI	Mean difference per 400 g/week	95%CI
SEA [f] Model 1 [a]	-0.005		-0.007, -0.003	0.074	0.006, 0.143	0.118	0.047, 0.188	0.210	0.172, 0.248
Model 2 [b]				0.036	-0.036, 0.108	0.105	0.025, 0.185	0.230	0.188, 0.272
Model 3 [c]	-0.003		-0.005, -0.001	0.031	-0.038, 0.101	0.078	0.000, 0.155	0.215	0.174, 0.256
Model 4 [d]	-0.004		-0.006, -0.001	0.015	-0.055, 0.086	0.063	-0.016, 0.142	0.222	0.181, 0.262
IQ [f] Model 1 [a]	-0.007		-0.009, -0.004	0.145	0.069, 0.221	0.171	0.094, 0.249	0.046	0.003, 0.089
Model 2 [b]				0.099	0.019, 0.178	0.129	0.041, 0.417	0.022	-0.026, 0.069
Model 3 [c]	-0.004		-0.007, -0.001	0.091	0.016, 0.166	0.096	0.012, 0.180	0.002	(0.043, 0.047

Model 4 [d]	-0.005		-0.008, -0.003	0.054		-0.023, 0.130		0.058		-0.027, 0.144		0.122		-0.033, 0.057	
Model 5 [e]	-0.004		-0.006, -0.001	0.095		0.026, 0.163		0.082		0.005, 0.158		-0.067		-0.138, -0.055	
Final-exam results				BMI<25		BMI≥25		BMI<25		BMI≥25		BMI<25		BMI≥25	
Model 1 [a]		0.99	0.98, 0.99	0.82	0.66, 1.01	1.55	1.17, 2.06	0.98	0.80, 1.21	1.76	1.29, 2.39	1.78	0.98, 1.41	1.61	1.23, 2.10
Model 2 [b]				0.82	0.66, 1.01	1.50	1.12, 2.02	1.08	0.86, 1.36	1.53	1.07, 2.18	1.27	1.00, 1.62	1.46	1.01, 2.11
Model 3 [c]		0.99	0.98, 1.00	0.86	0.69, 1.08	1.43	1.05, 1.96	1.01	0.79, 1.28	1.45	0.99, 2.12	1.06	0.83, 1.37	1.45	0.98, 2.13
Model 4 [d]		0.99	0.98, 1.00	0.83	0.66, 1.05	1.36	0.99, 1.87	0.97	0.76, 1.25	1.39	0.95, 2.05	1.06	0.82, 1.36	1.43	0.97, 2.11
Model 5 [e]		0.99	0.98, 1.00	0.87	0.69, 1.10	1.42	1.02, 1.99	1.00	0.78, 1.30	1.44	0.96, 2.16	1.05	0.81, 1.37	1.41	0.93, 2.13

Abbreviations:: Body Mass Index, CI: confidence interval, GCSE: General Certificate of Secondary Education, GWG: Gestational weight gain, IQ: Intelligence Quotient, SEA: School Entry Assessment.

a Model 1 - adjusted for gestational age, age at exposure measure and gender

b Model 2 - as model 1 plus additional adjustment for prepregnancy weight and GWG in previous period

c Model 3 - as model 2 plus additional adjustment for maternal age, parity, maternal smoking, maternal education and mode of delivery

d Model 4 - as model 3 with additional adjustment for birth weight

e Model 5 – as model 3 with additional adjustment for SEA

f Standardised. SEA SD=3.26, IQ SD=16.47

Web Table 8. Multivariable associations of Institute Of Medicine categories of maternal Gestational Weight Gain with GCSE results from poisson regression models, in Avon Longitudinal Study of Parents And Children, Bristol, UK.

Final-exam results N=7,339	Model	Less than recommended		As recommended	More than recommended	
		Risk Ratio	95%CI		Risk Ratio	95%CI
	1 [a]	0.91	0.87, 1.00	1	0.95	0.89, 1.01
	2 [b]	0.94	0.89, 1.00	1	0.96	0.91, 1.01
	3 [c]	0.96	0.91, 1.01	1	0.97	0.91, 1.02
	4 [d]	0.95	0.90, 1.01	1	0.95	0.90, 1.01

Abbreviations: CI: Confidence Interval, GCSE: General Certificate of Secondary Education.
a Models 1 - adjusted for gestational age, maternal age, age at outcome assessment and gender
b Model 2 - as model 1 plus additional adjustment for parity, maternal smoking, maternal education and mode of delivery
c Model 3 - as model 2 plus additional adjustment for birthweight
d Model 4 - as model 2 plus additional adjustment for standardised School Entry Assessment

Web Table 9. Multivariable associations of prepregnancy weight and GWG with offspring GCSE results from poisson regression models, in Avon Longitudinal Study of Parents And Children, Bristol, UK.

5A*-C GCSE	Prepregnancy weight		0-18 weeks				18-28 weeks				28+ weeks			
			BMI <25		BMI ≥25		BMI <25		BMI ≥25		BMI <25		BMI ≥25	
	Risk Ratio	95% CI	Risk Ratio	95% CI	Risk Ratio	95% CI	Risk Ratio	95% CI	Risk Ratio	95% CI	Risk Ratio	95% CI	Risk Ratio	95% CI
Model 1 [a]	0.99	0.99, 0.99	0.96	0.91, 1.01	1.26	1.14, 1.39	1.01	0.95, 1.06	1.28	1.16, 1.41	1.05	1.00, 1.10	1.27	1.16, 1.39
Model 2 [b]			0.95	0.90, 1.01	1.18	1.06, 1.31	1.04	0.98, 1.10	1.15	1.01, 1.30	1.07	1.01, 1.14	1.28	1.13, 1.45
Model 3 [c]	0.99	0.99, 1.00	0.96	0.91, 1.02	1.17	1.06, 1.29	1.01	0.95, 1.08	1.07	0.95, 1.21	1.00	0.94, 1.06	1.21	1.07, 1.37
Model 4 [d]	0.99	0.99, 0.99	0.96	0.90, 1.01	1.15	1.03, 1.27	1.01	0.95, 1.07	1.06	0.95, 1.20	1.00	0.94, 1.06	1.21	1.07, 1.36
Model 5 [e]	0.99	0.99, 1.00	0.94	0.89, 1.01	DNC	DNC	1.02	0.95, 1.09	DNC	DNC	1.00	0.93, 1.07	DNC	DNC

Abbreviations: BMI: Body Mass Index, CI: confidence interval, DNC: did not converge, GCSE: General Certificate of Secondary Education, GWG: Gestational weight gain, IQ: Intelligence Quotient, SEA: School Entry Assessment.

a Model 1 - adjusted for gestational age, age at exposure measure and gender

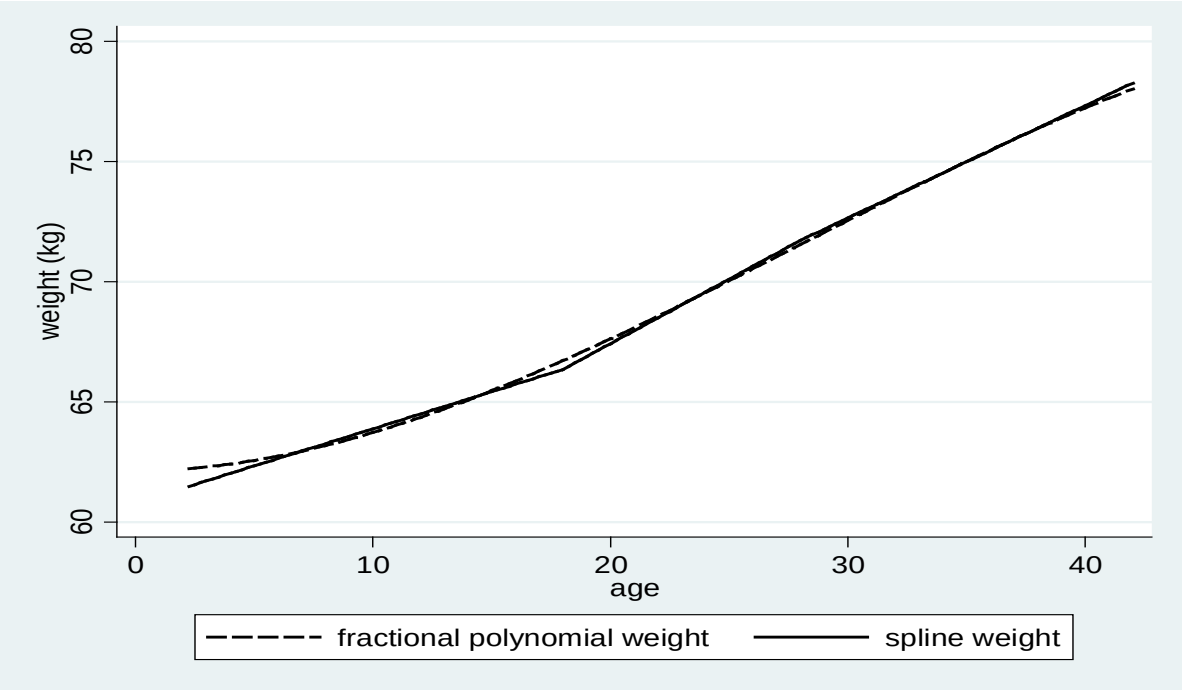
b Model 2 - as model 1 plus additional adjustment for prepregnancy weight and GWG in previous period

c Model 3 - as model 2 plus additional adjustment for maternal age, parity, maternal smoking, maternal education and mode of delivery

d Model 4 - as model 3 with additional adjustment for birth weight

e Model 5 – as model 3 with additional adjustment for SEA

Web Figure 1: Graph showing the pattern predicted by the fractional polynomial for the multilevel model and the spline that was fitted to the data



Web Figure 2: Bland-Altman plot showing the difference between predicted and observed weight plotted against the average of predicted and observed weight, with 95% limits of agreement