Examining associations between gestational weight gain, birthweight and gestational age.

Kate Tilling, Corrie Macdonald-Wallis, Abigail Fraser, Laura D Howe, Tom Palmer and Debbie A Lawlor

Weight gain during pregnancy

- Maternal pre-pregnancy weight and gestational weight gain (GWG) associated with adverse perinatal health outcomes
- IOM guidelines:

Pre-pregnancy BMI	Recommended weight gain (kg)
<18.5kg/m2	12.5-18
18.5-24.9kg/m2	11.5-16
25-29.9kg/m2	7-11.5
>=30kg/m2	5-9

Measuring GWG

1) total weight gained

2) rate of weight change

3) compliance with IOM recommendations

- All require baseline and final weights taken at same gestational ages.
- None investigate pattern of weight change.
- Confounding with length of gestation

IOM and length of gestation

Length of gestation:

0.26 weeks shorter for <IOM rec

0.10 weeks longer for >IOM rec

Could be just artifact:

IOM based on difference between last and first weight measures

If born early, last weight measure will be lower.

ALSPAC study - GWG

- Prospectively recruited 14,541 women in Avon, UK with EDD 1/4/91-31/12/92
- 11,702 term, singleton, livebirths surviving to at least 1 yr of age consented to data abstraction
- 6 midwives abstracted data from obstetric medical records

ALSPAC study - GWG

1) Number of measures varies by gestational age:

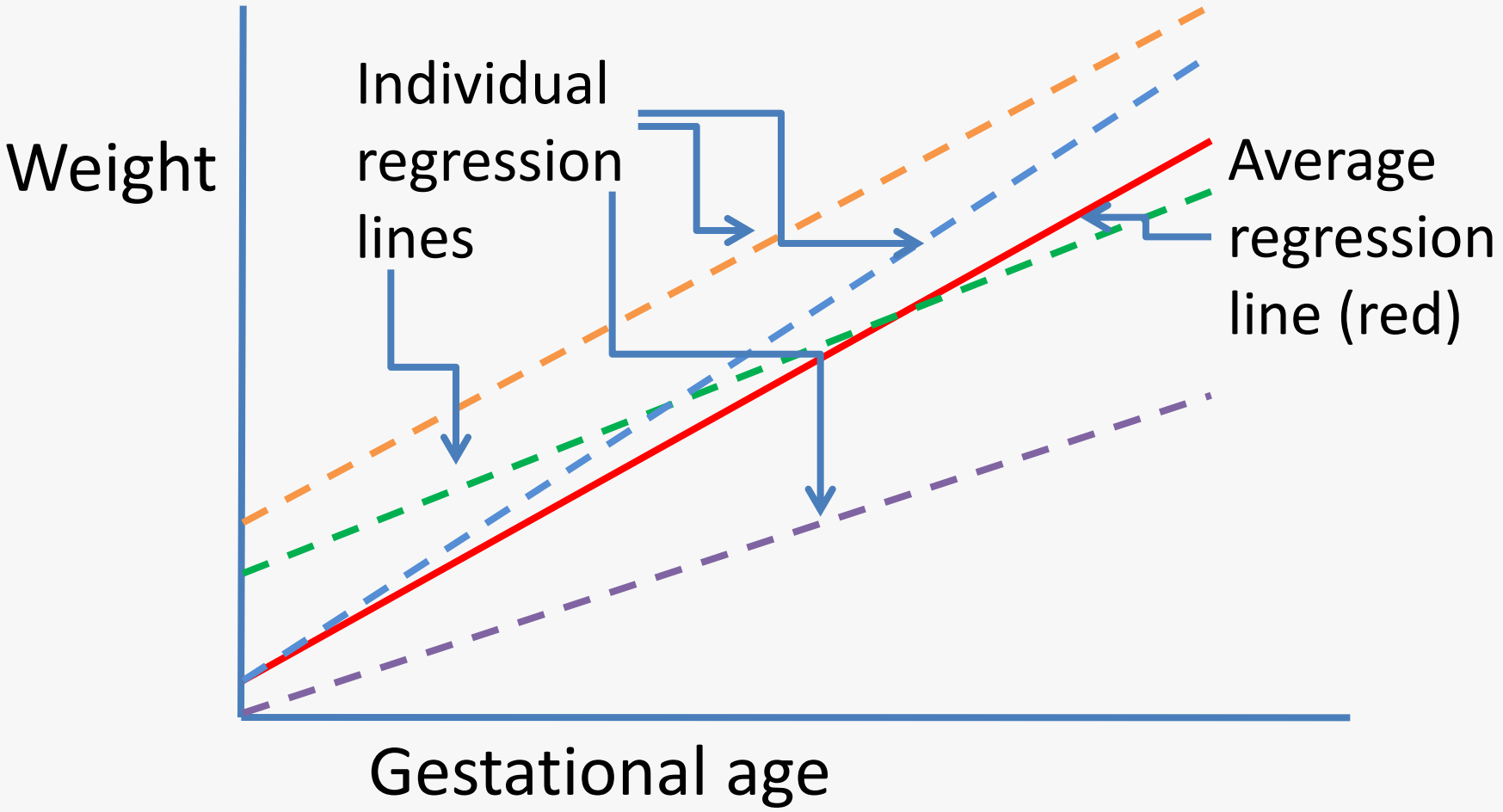
- 1106 women had weight <8 weeks
- 105 had weight>42 weeks.

2) Number of measures varies between women:

- Median number measures 10 (IQR 8, 11)

3) Measures on same woman correlated

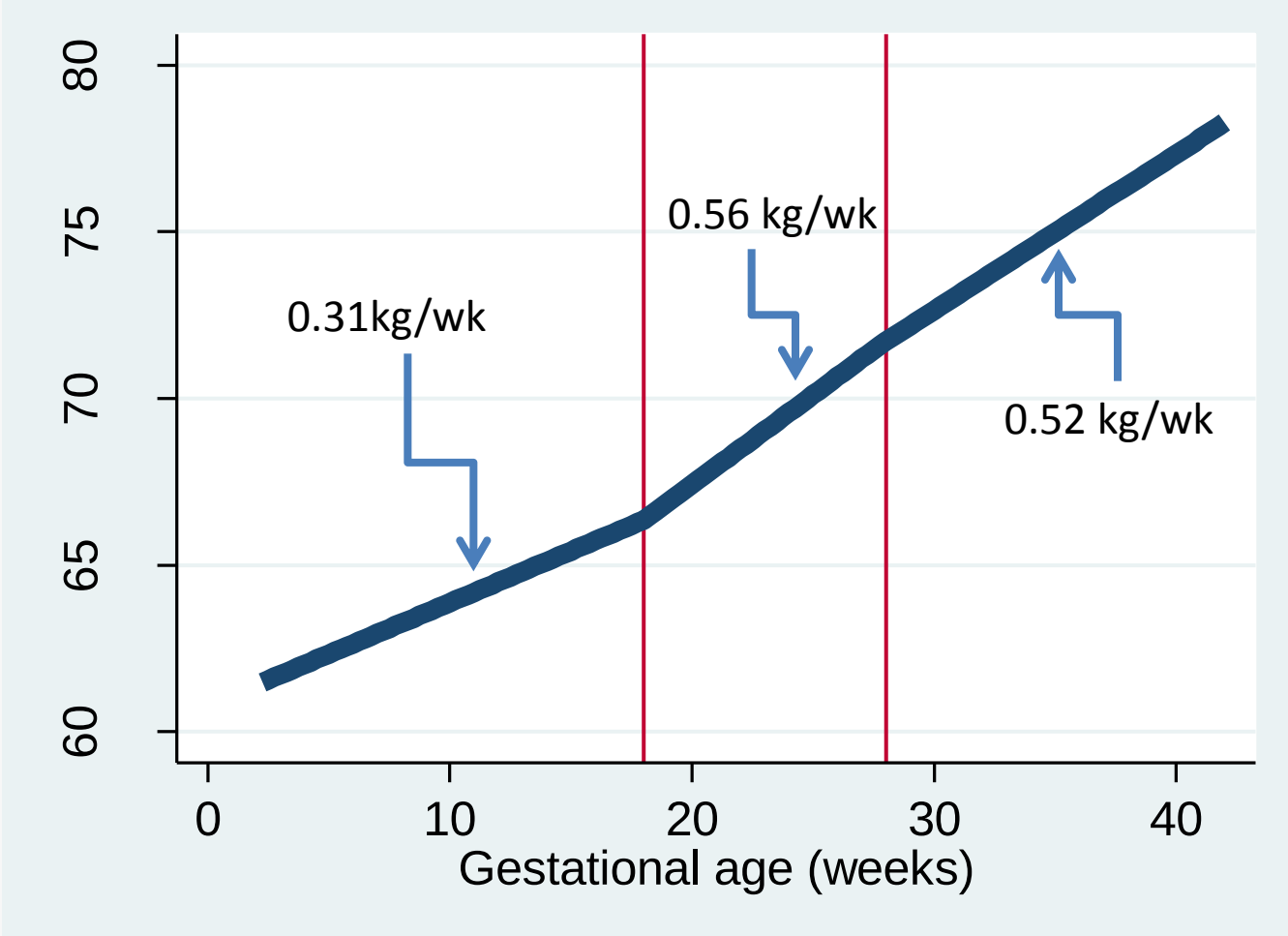
Multilevel models



Multilevel models

- Fractional polynomials used to find best-fitting pattern of weight gain
- Linear splines used to approximate curve
- Knots positioned at whole weeks of gestational age.
- Optimal knotpoints at 18 and 28 weeks
- For each individual, model estimates pre-pregnancy weight, weight gain from 0-18, 18-28 and 28-40 weeks

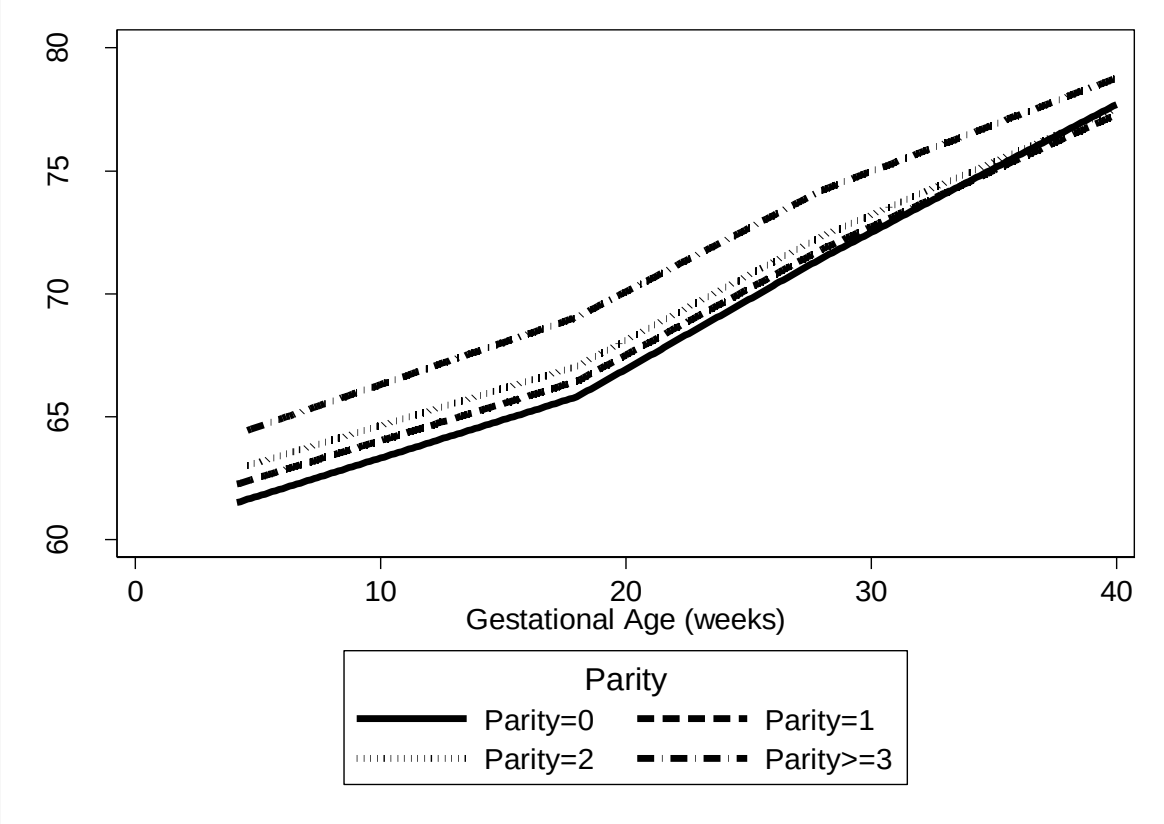
Pattern of weight gain



Model fit

Gestational age (weeks)	Number of measures	Actual weight (mean (sd))	Observed-predicted (mean (sd))	Observed-predicted (95% range)
<8	1,106	64.5 (12.4)	0.29 (0.7)	-0.8, 1.4
8-13	8,723	64.4 (11.9)	-0.02 (0.7)	-1.1, 1.0
13-18	11,023	65.6 (11.7)	-0.09 (0.7)	-1.3, 1.1
18-23	10,141	68.0 (11.8)	0.07 (0.8)	-1.1, 1.2
23-28	11,570	70.7 (11.8)	0.07 (0.8)	-1.2, 1.3
28-33	17,467	73.0 (11.8)	-0.06 (0.8)	-1.3, 1.2
33-38	20,273	75.4 (12.0)	0.02 (0.8)	-1.2, 1.2
>38	10,419	77.5 (12.1)	0.00 (0.7)	-1.1, 1,2

Parity and weight gain



Birthweight and GWG

BWT Mean=3.45kg, SD=0.52kg N= 9398

1) Regression of BWT on pre-pregnancy weight, IOM guidelines and covariates

BWT increased by 0.006kg for each 1kg increase in pre-pregnancy weight

BWT decreased by 0.17kg if GWG<IOM rec

BWT increased by 0.11kg if GWG>IOM rec

2) Regression of BWT on observed first and last weights

Joint Model GWG/BWT

GWG

Weightij= (a+uoi)+(b+u1i)s1i+(c+u2i)s2i

+(d+u2i)s3i+other covariates

BWT

BWTi=(α+vi)+other covariates

Joint Model GWG/BWT

Random effects matrix – allows BWT and GWG to be correlated

Estimate variances and covariances of:

uoi

u1i

u2i

u2i

v_i

Joint Model GWG/BWT

Use random effects matrices to calculate regression coefficients.

$$\beta(\text{BWT/pre-pregnancy weight}) = \frac{\text{Covariance(BWT/pre-pregnancy weight)}}{\text{Variance(pre-pregnancy weight)}}$$

Can also calculate adjusted regression coefficients

$$\beta(\text{BWT/Wt gain 0-18wks|pre-pregnancy weight}) = \frac{\text{cov(BWT/GWG018)*var(ppgWT)-cov(GWG018/ppgWT)*cov(ppgWT/BWT)}}{\text{var(GWG018)*var(ppgWT)-cov2(GWG018\ppgWT)}}$$

Confidence intervals?

Non-linear combination of variances and covariances

Draw from the random effects matrix and use centiles of the realisations

Both implemented within Stata

Joint Model GWG/BWT

Fixed effects

GWG greater in	BWT greater in
Nulliparous women	Multiparous women
Non-smokers	Non-smokers
Women who give up smoking	
Taller women	Taller women
Mothers of male offspring	Male offspring

Joint Model GWG/BWT

Random effects variance/covariance matrix:

	BWT cons	Pre-pg wt	GWG 0-18	GWG 18-28	GWG 28-40
BWT cons	0.24				
Pre-pg wt	0.89	138			
GWG 0-18	0.013	-1.02	0.05		
GWG 18-28	0.015	-0.45	0.012	0.04	
GWG 28-40	0.011	0.023	0.005	0.018	0.04

Joint Model GWG/BWT

Regression of birthweight (mean 3.4 (0.52) kg) on:

GWG	Mean (SD)	Unadjusted	Adjusted for previous GWG
Pre-pregnancy wt (kg)	60.7 (12.3)	0.006 (0.0004)	
Wt gain 0-18 weeks (kg/wk)	0.31 (0.18)	0.26 (0.03)	0.47 (0.03)
Wt gain 18-28 weeks (kg/wk)	0.54 (0.17)	0.42 (0.03)	0.42 (0.04)
Wt gain28-40 weeks (kg/wk)	0.47 (0.20)	0.26 (0.03)	0.03 (0.03)

Joint model GWG/BWT

Use random effects matrices to calculate regression coefficients.

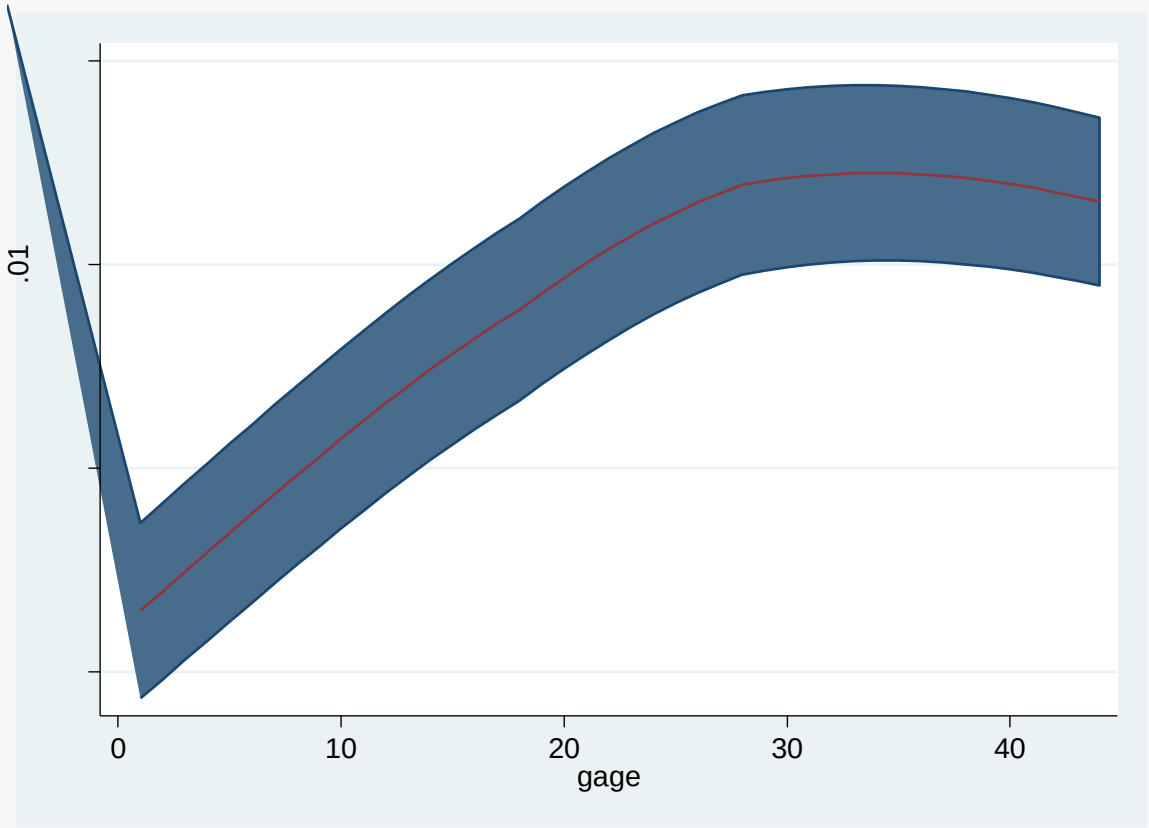
E.g. β(BWT/weight at time t)

and

β(BWT/weight at time t, adjusting for pre-pregnancy weight)

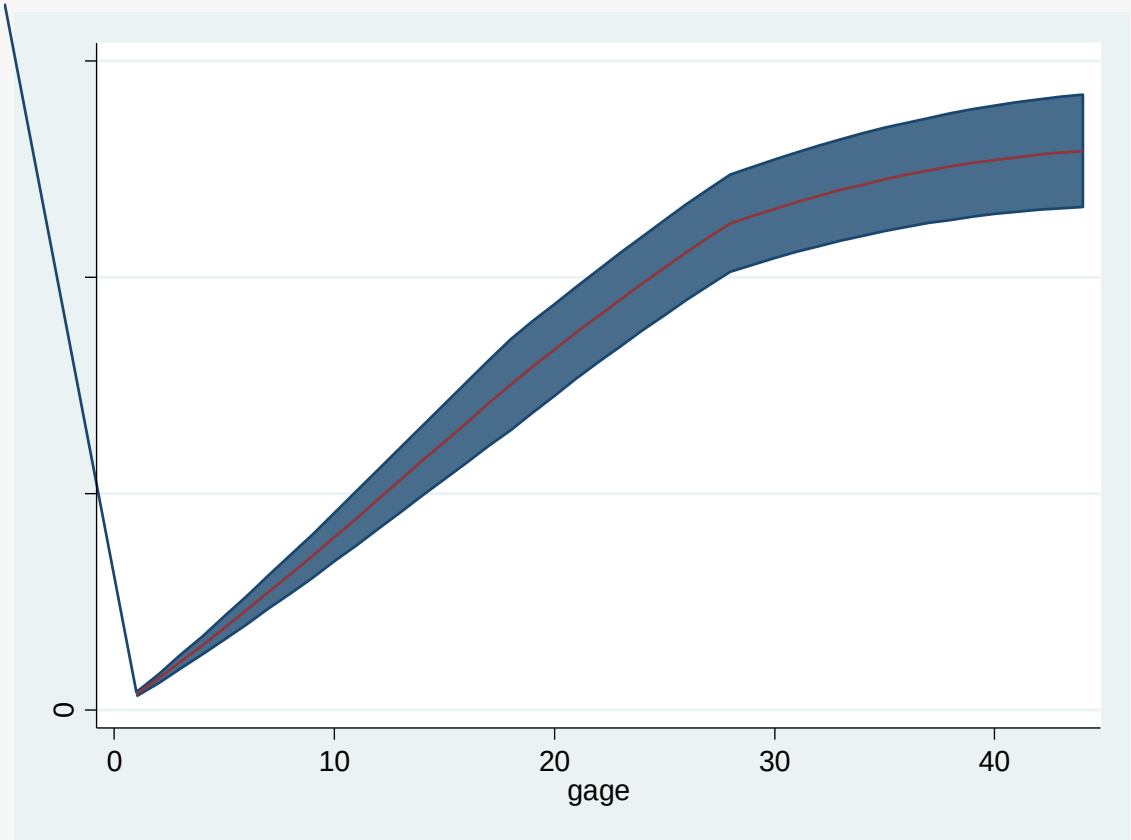
Joint model GWG/BWT

Unadjusted regression coefficients for BWT on GWG with gestational age



Joint model GWG/BWT

Regression coefficients for BWT on GWG with gestational age, adjusted for pre-pregnancy wt



Other outcomes

Interest in whether GWG related to:

- CVD outcomes in mother
- Growth in offspring
- CVD outcomes in offspring
- Cognitive outcomes in offspring

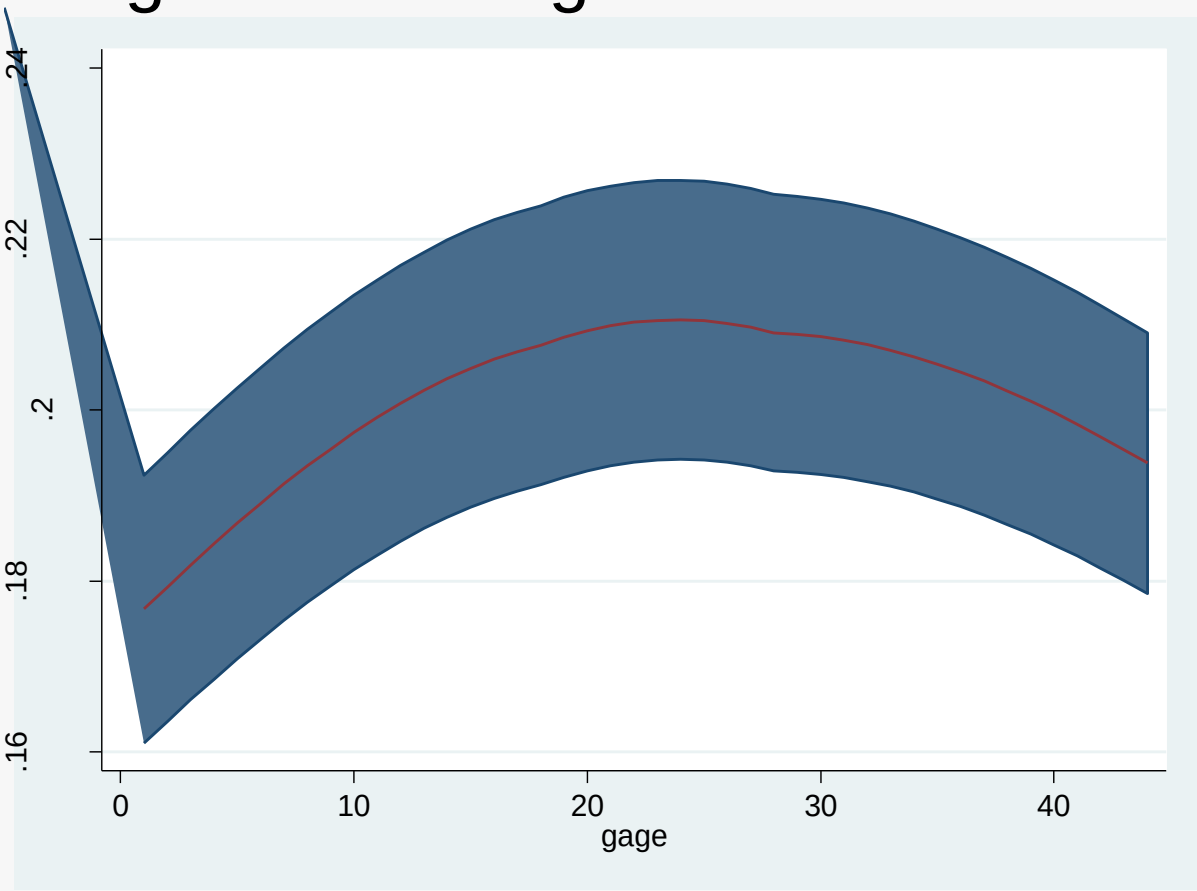
Joint Model GWG/Wt at age 9

Regression of offspring wt at age 9 (34.7 (sd 7.4) kg) on:

GWG	Mean (SD)	Unadjusted	Adjusted for previous GWG
Pre-pregnancy wt (kg)	60.7 (12.3)	0.17 (0.008)	
Wt gain 0-18 weeks (kg/wk)	0.31 (0.18)	0.31 (0.57)	4.69 (0.59)
Wt gain 18-28 weeks (kg/wk)	0.54 (0.17)	0.78 (0.59)	1.95 (0.67)
Wt gain28-40 weeks (kg/wk)	0.47 (0.20)	2.59 (0.50)	1.43 (0.64)

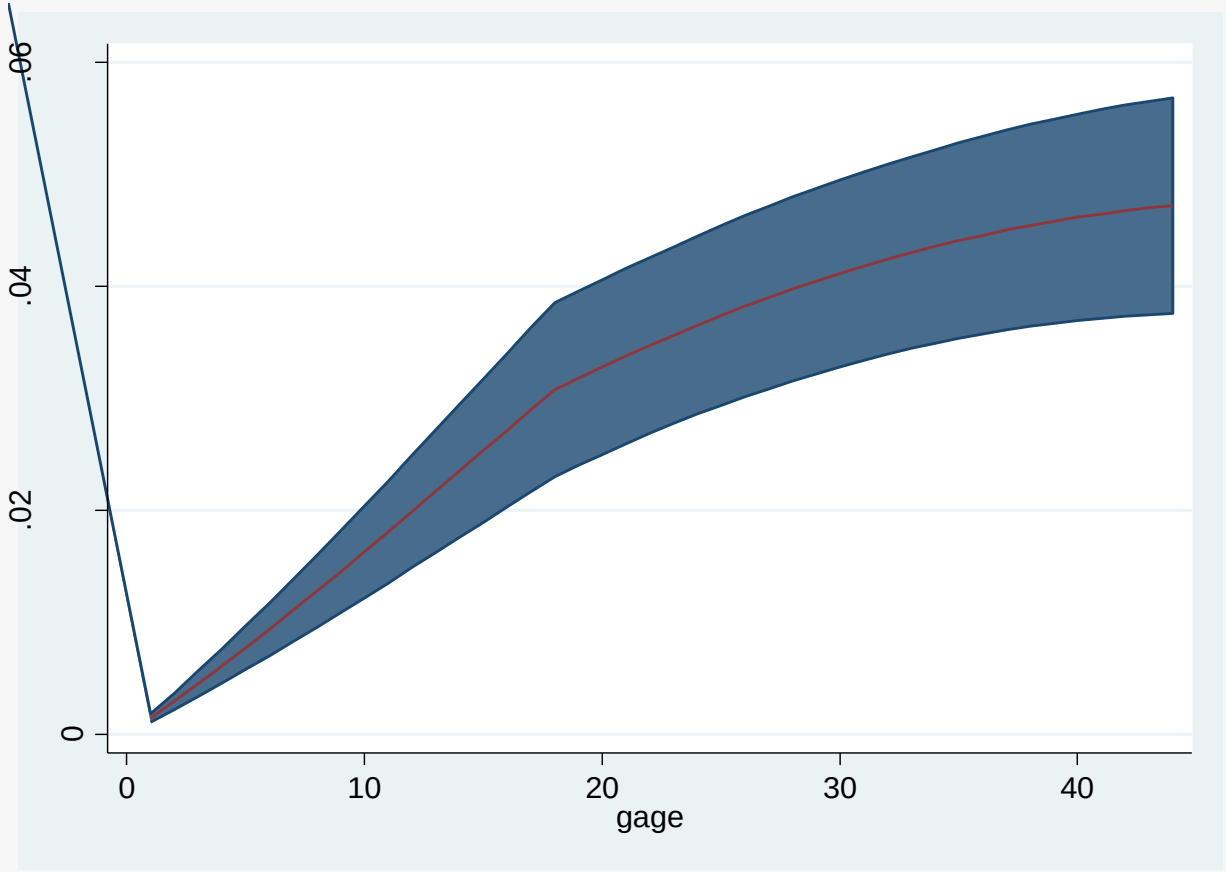
Joint model GWG/WT at 9

Unadjusted regression coefficients for WT at 9 on GWG with gestational age



Joint model GWG/BWT

Regression coefficients for WT at 9 on GWG with gestational age, adjusted for pre-pregnancy wt



Joint models

Can be formulated to give equivalent results to SEMs

Assume:

- Normal distributions
- Linear relationships
- No interactions

One alternative

Use level-2 residuals as exposures

Lifecourse models (Mishra et al IJE)

- *A structured approach to modelling the effects of binary exposure variables over the life course*
  Gita Mishra *et al*, Int J Epidemiol. 2009 April; 38(2): 528–537.

- Methods:
  - Fit saturated model for outcome on binary exposures
  - Compare this (P-values) to nested, simpler models corresponding to specific hypotheses

BWT as outcome, continuous exposures

Model	AIC	R-squared
Indep effects	12440.7	17.3%
Saturated	12390.3	17.8%
Accumulation	12495.7	16.8%
Critical period - early	12606.3	15.8%
Critical period - mid	12570.1	16.1%
Sensitive period – late*	12438.7	17.3%

* Early=mid, no effect of late GWG

Conclusions

- Can model several outcomes jointly (have also modelled with length of gestation)
- Calculating regression coefficients straightforward (expressions get complex)
- Confidence intervals – either nlcom or simulation give results similar to equivalent SEMs
- Avoids problem of length of gestation being related to total weight gain
- Lifecourse models – need alternative metrics?