## THE ALSPAC STUDY

## **OBSTETRIC DATA**

# Data abstracted from antenatal medical records

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Documentation giving frequencies, background and instructions for use.

Obstetric data – description of variables and their derivation for all variables where data have been abstracted on all eligible participants

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#### 1. BACKGROUND

Data are abstracted from routine antenatal medical records (i.e. they are not measurements conducted specifically for research).

Data were only abstracted for women who had indicated at recruitment that they were happy for the medical records to be obtained and data taken from them and added to the ALSPAC dataset.

Funding for these abstractions has been from a number of separate projects and therefore abstractions have taken place over a number of years.

Two grants awarded in 2006 (US NIH) and 2009 (Wellcome Trust) to DA Lawlor and colleagues provided funds to complete abstraction of selected data from obstetric records from all remaining eligible women. These selected data included most of the antenatal variables (including repeat measurements of weight, blood pressure, glycosuria and proteinuria) and pregnancy variables that had been previously collected, but did not include some of the more detailed antenatal measurements that had been the focus of some previous sub-studies and only included a small number of the labour related data and none of the immediate postnatal data that had been previously collected for some sub-studies.

These data, collected using funds from these two recent grants, have been combined with equivalent data collected previously on the same variables from a number of other funding sources. Thus, this document describes the obstetric variables, including a number of variables that we have derived, that are available on all eligible women (those who gave consent for abstraction) for variables that are collected in all collection sweeps.

At some stage in the future (currently date unknown) we hope that a built file will be made of other obstetric data collected on subgroups and separate documentation will describe those data.

#### 2. DATA

Data are available on a total of 13,706 women (13,899 offspring) [Note: As will all data this does not mean all 13,706 women have complete data; some will have missing data for some fields].

Below we first describe derivation of some newly derived variables and then each variable in the dataset (including our derived variables) is described using histograms, mean (SD) or median (IQR) for continuous variables and N (%) for categorical variables; information is provided about numbers for each variable so that the amount of missing data can be deduced.

#### Accuracy of data abstraction

The following comments refer only to the abstractions funded by the two recent grants. Data were entered from medical records directly onto an electronic database that 'flagged' when a result considered to be outside physiological ranges was entered (Table 1; shows the ranges used for each measurement). If an attempt was made to enter a result that was outside any of these ranges for a variable a 'bubble' appeared on the computer screen indicating that this was the case and requesting that the value was correct. The outside of normal range value could be entered if the abstractor was sure this was as written in the notes, but the abstractor was then also required to enter a comment in a free text box stating that they had checked and

that this value was as written in the medical records and giving any other comment (e.g. if there was a supporting clinical diagnosis or some explanation for the value). All data were abstracted from obstetric medical records by six trained research midwives. There was no between-midwife variation in mean values of the data abstracted and error rates were consistently <1% in repeated data entry checks.

Table 1: Ranges used to check validity of data

Variable	Acceptable range	Comment
Date of	1/1/1990 to	Reflects range of plausible dates of
measurements	31/3/1993	pregnancies for recruited ALSPAC
		women
Date LMP	1/6/1989-31/8/1992	Reflects range of plausible dates of
		last period for pregnant women
		recruited to ALSPAC
Expected Date of	1/1/1991 - 31/3/1993	As above, reflects what would be
Delivery		plausible given dates of recruitment
		of women
Weight	40-150kg	Considered plausible range of
		weights through pregnancy
Systolic BP	70-270mmHg	Considered plausible range of SBP
		through pregnancy
Diastolic BP	40-130mmHg	Considered plausible range of DBP
		through pregnancy
Haemoglobin	7-16.2 g/dL	Considered plausible range of Hb
		through pregnancy
Haemoglobin when	4-9.9 g/dL	Definition of anaemia in pregnancy
result reported as		at the time
'anaemia'		
Weight of placenta	100-2200g	Considered plausible range of
		values for placental weight

## Missing data

In the past missing data have been recorded in ALSPAC with values such as -99, -88, -77 etc. For the last 5 years with new data collection this practice has stopped – missing data are left missing. We adopted this approach in the new data collection and have therefore changed all values of -99, -88, etc. in the existing data to missing. Total values for each variable therefore represent the actual valid existing data for each variable that is described in this document.

### **Derived variables using repeat measurements**

All BP, weight, proteinuria and glycosuria measurements that were taken routinely as part of antenatal care by midwives or obstetricians have been used in the derivation of hypertensive disorder of pregnancy variables, glycosuria/gestational diabetes variables and also variables that can be used to examine risk factors for and consequences of changes in these variables through pregnancy.

The date at which each measurement was undertaken together with the recorded (in the medical records) expected date of delivery was used to derive the gestational age at each measurement and repeat measurements are stored with gestational age (in days and week).

#### **Gestational age**

Gestational age, at the time of each measurement, was calculated using the expected date of delivery (EDD) as reported in the medical record (for most, given the dates of ALSPAC recruitment (when few women had dating scans), this will have been based on the mothers LMP).

Gestational age in days was calculated as:

280 - (EDD- date of measure)

Once that was calculated we generated a second variable of gestational age in **completed** weeks by taking the rounded <u>down</u> integer of gestational age in days divided by 7.

#### Hypertensive disorder of pregnancy in ALSPAC

There was a median of 14 and interquartile range of 11 to 16 measurements of BP per woman in the dataset.

For deriving the 3 hypertensive disorder of pregnancy variables (hypertensive disorder of pregnancy, gestational hypertension and preeclampsia) all clinic data were used – i.e. individual BP and proteinuria measurements from all clinics that each woman attended.

The outcomes were defined according to the International Society for the Study of Hypertension in Pregnancy (ISSHP):

**Hypertensive disorder of pregnancy** (combines gestational hypertension and pre-eclampsia):

Systolic blood pressure >139mmHg OR diastolic blood pressure >89mmHg on at least 2 occasions after 20 weeks of gestation in women who had not previously been diagnosed with hypertension outside of pregnancy . The `healthy' (coded 0) group includes those who had a previous diagnosis of hypertension prior to pregnancy (referred to from now on as pre-existing hypertension; see below for how this information was obtained). This follows the ISSHP definition (which states that those with existing hypertension are not classified as having HDP).

### Pre-eclampsia

Hypertensive disorder of pregnancy (as above) PLUS at least 1+ proteinuria on dipstick testing (Albustix; Ames Co, Elkhart, Ind) occurring at the same time as the episodes of raised blood pressure. As with hypertensive disorder of pregnancy (and in accordance with ISSHP), the 'healthy' (coded 0) group for this variable includes those with no evidence of HDP, those with pre-existing hypertension AND in addition those with gestational hypertension (see below). Thus, it compares preeclampsia to no preeclampsia. For some analyses investigators may want to compare

preeclampsia to a group with no evidence of hypertensive disorder of pregnancy. Such a variable can be easily derived from the provided variables.

#### **Gestational hypertension**

Is hypertensive disorder of pregnancy but without preeclampsia (i.e. the same elevated blood pressure but with no concurrent proteinuria; note that it is possible that women defined as having gestational hypertension – i.e. fulfilling ISSHP for this – did have at least two episodes of at least 1+ proteinuria after 20 weeks of pregnancy but at a different time to when they were noted to have elevated blood pressure). In the database the 'healthy' (coded 0) group for this variable excludes those with preeclampsia but includes those with pre-existing hypertension.

### **Pre-existing hypertension**

Pre-existing hypertension was derived from a questionnaire (not the obstetric data abstraction) that women completed at the time of recruitment. A question in this questionnaire asked whether the woman had ever been diagnosed with hypertension, if they answered yes, a second question asked whether this diagnosis was only when they were pregnant or whether they had been diagnosed with hypertension outside of pregnancy. Those who responded that they had been diagnosed with hypertension outside of pregnancy are defined as 'pre-existing hypertension'. Women who had answered that they had never had hypertension or that they had had hypertension only in pregnancy were included in the 'healthy' (coded 0) group. (NB: we have no way of verifying this diagnosis or of checking that those who responded no to the question regarding hypertension truly do not have hypertension as we do not have an actual measure of blood pressure in these women before they became pregnant. However, the trajectory of BP change in this group shows they start pregnancy with higher blood pressure than all other groups of women (preeclampsia, gestational hypertension and normal) but then join a similar trajectory to those with gestational hypertension from ~ 20 weeks and stay on this trajectory. These findings offer some validity to this self report; they are in paper 4 of the work currently in progress list at the end of this document).

## Pre-eclampsia superimposed on existing hypertension

Indicates women who had been diagnosed with hypertension prior to pregnancy and had high blood pressure as above (used in the diagnosis of HDP) along with proteinuria on 2 occasions after 20 weeks gestation. The 'healthy' (coded 0) group includes all other women.

#### **Proteinuria**

Proteinuria of at least 1+ (= 30mg/dl) on dipstick testing (Albustix; Ames Co, Elkhart, Ind) occurring on two occasions after 20 weeks gestation. This variable includes women who had a previous diagnosis of hypertension in both of its categories – i.e. this is simply a variable that corresponds to whether they had these two episodes of proteinuria or not.

#### Number of blood pressure measurements

HDP variables were derived according to 2 SBP/DBP measurements after 20 weeks gestation and therefore women with no blood pressure measurements or only one measurement available would automatically be classed as not having a HDP. We have therefore derived a variable indicating the number of complete blood pressure measurements (SBP and DBP, with a visit date available) which each woman had during pregnancy and classed this as 0, 1 or  $\geq$  2. This allows women with less than 2 blood pressure measurements to be excluded, or can be used for sensitivity analyses.

#### Deriving change in BP during pregnancy variables

The BP data are clustered within women, and thus all analyses used multilevel models with two levels (antenatal visit within woman) to take into account the correlation between BP measures on the same woman.

#### General summary

Using the entire cohort of women with term pregnancies (≥37 weeks gestation) fractional polynomial curves were fitted to the data to obtain the average shape of the trajectories of SBP and DBP with gestational age. These were used to determine the approximate positions of knots (indicating changes in slope) in linear spline random effects models with SBP and DBP as outcomes and gestational age in weeks as the exposure. The best-fitting linear spline models had 3 knots at 18, 30 and 36 weeks gestation.

#### Details

The data were divided into 2 week intervals by gestational age, starting from 4 weeks gestation (there was little data prior to this time), and in cases where an individual had multiple blood pressure measurements within any 2 week interval, one measurement was chosen at random from this interval for inclusion in the sample for analysis. This was to prevent individuals with a high number of antenatal visits (those likely to be ill or have complications of pregnancy) from having too great an influence on the models. After this process there remained a median of 10 BP measurements per woman, with a range of 1 to 18.

Fractional polynomial curves, as described by Royston<sup>1</sup>, were fitted to the data to describe the shape of the average pattern of BP change with gestational age . Fractional polynomials are similar to conventional polynomials such as quadratic or cubic curves, but have a wider (infinite) range of possible powers of X and so provide more flexibility in shape. The models take the form  $Y = \beta_0 + \beta_1 X^{P1} + \beta_2 X^{P2} + ... + \beta_n X^{Pn}$ , where P1, ..., Pn are powers of time, X; we restricted to the powers: -2, -1, -0.5, 0, 0.5, 1, 2, 3 and considered fractional polynomials up to degree 2, meaning that up to two powers of time could be included in the models. This set of powers and degree of polynomial has been found to be sufficient to adequately describe most data. Separate models were fitted with SBP and DBP as the outcome variables (Y) and for each model gestational age in weeks was used as the exposure variable (X). The models had two levels: antenatal visit and individual, since there were multiple antenatal visits per woman. An individual-level random effect was included and the

powers of time were also allowed to vary at the individual level. The best-fitting model was selected as the model with the highest log-likehood.

We used the shape of the best-fitting fractional polynomial model for each of SBP and DBP to determine the approximate position and number of knot points in a linear spline random effects model. Models with 2 or 3 knots were considered and the final positioning and number of knots was selected as that which optimally fulfilled the criteria of a high model log-likelihood, a close fit to the fractional polynomial curve and good fit of the model predicted values to observed values over the whole course of pregnancy. The linear spline models had two levels, as above, and each contained an individual-level random effect and random slope parameters on each of the splines. The selected models for both SBP and DBP had 3 knots at 18, 30 and 36 weeks gestation. These main models were used to describe the average patterns of SBP and DBP change for the whole cohort of women. 90% of the predicted values from these models lay within around 14 mmHg of the actual measurements for the SBP model and within around 10 mmHg of the actual measurements for the DBP model for each 2 week period of gestation except at the very beginning of gestation where the limits were slightly wider for the DBP model.

The random effects for each individual are initially obtained as deviations from the average. In the dataset these have been converted (using the prediction model coefficients with the deviations) to more meaningful variables that represent BP in mmHg for the baseline/constant (BP at 8 weeks gestation; we set the predicted model baseline to 8 weeks as there was little data prior to this time point and BP may change dramatically even from very early in pregnancy) and BP change per completed week of gestation (mmHg/week) for each of the slopes.

Thus there are 10 BP variables from these models:

Systolic blood pressure (SBP) mmHg at 8 weeks
Change SBP mmHg/week between 8 and 18 weeks gestation
Change SBP mmHg/week between 18 and 30 weeks gestation
Change SBP mmHg/week between 30 and 36 weeks gestation
Change SBP mmHg/week between 36 weeks gestation and birth
Diastolic blood pressure (DBP) mmHg at 8 weeks
Change DBP mmHg/week between 8 and 18 weeks gestation
Change DBP mmHg/week between 18 and 30 weeks gestation
Change DBP mmHg/week between 30 and 36 weeks gestation
Change DBP mmHg/week between 36 weeks gestation and birth

NB: since the knot points are precise it is appropriate to describe the change variables as above e.g. between 8 and 18 weeks and then between 18 and 30 weeks

We have also included the standard errors of the random effects and the number of blood pressure measurements each woman contributed to the spline models for each period of gestation. This is the number of blood pressure measurements remaining after one measurement was randomly selected from each 2 week period.

Either the standard errors or number of measurements in each period could be used as weights to do a sensitivity analysis taking into account the different degrees of uncertainty in the random effects estimates.

### Latent classes for proteinuria changes in pregnancy

Latent classes for proteinuria changes were derived for women who had a term (≥37 weeks) singleton or twin live birth and did not have a previous diagnosis of hypertension, existing diabetes or experience gestational diabetes or pre-eclampsia during the pregnancy. These therefore provide information on patterns of proteinuria in 'healthy' pregnant women without pre-eclampsia. Gestation was divided into six periods: ≤20 weeks, 21-24 weeks, 25-28 weeks, 29-32 weeks, 33-36 weeks and ≥37 weeks and 6 variables representing the maximum degree of proteinuria each woman experienced on any dipstick measurement in each of the 6 periods were derived. These were used as indicators in the latent class analysis. The first period of gestational age is larger than the others since few women experienced any proteinuria prior to 20 weeks. Models with 1 to 8 classes were fitted and the best-fitting model was selected as that which minimised the Bayesian Information Criterion (BIC), maximised the model entropy and satisfied the assumption that variables were independent conditional on the latent class.

### Latent class analysis of all eligible women:

In latent class analysis of all eligible women six binary indicators of maximum proteinuria in each of the six periods of gestational age were used, defining maximum proteinuria as "nil/trace" or "1+ or more". The best-fitting model had two latent classes. Class 1 (98.8%) had a low probability of experiencing proteinuria throughout pregnancy and Class 2 (1.2%) had a higher probability of proteinuria, which was greatest in late pregnancy.

#### Latent class analysis of only women who ever experienced proteinuria:

To define different patterns of occurrence of proteinuria another latent class analysis was completed restricting to only those women who had at least one measurement of at least 1+ proteinuria during pregnancy. For this analysis maximum degree of proteinuria in each of the 6 periods of gestation was defined in three categories as "nil/trace", "1+" or "2+ or more". The best-fitting model had five latent classes, which represent the timing of onset of proteinuria. Class 1 (9.0%) experienced proteinuria in early pregnancy (≤ 20 weeks gestation), Class 2(9.3%) had onset of proteinuria between 21 and 28 weeks, Class 3 (12.2%) had proteinuria onset between 33 and 36 weeks and Class 5 (44.9%) had proteinuria onset at 37 weeks gestation or later.

For each of the latent class analyses variables indicating each woman's most probable latent class have been derived. Variables representing each woman's probability of belonging to each of the latent classes have also been derived.

#### Deriving gestational weight change in pregnancy

For gestational weight change in pregnancy the exact same statistical methods as those described above for BP were used. Here we allowed the baseline from the predicted model to be gestational age = 0 weeks which we define as pre-pregnancy weight (strictly speaking given how gestational age is defined this is  $\sim$  2weeks prior to conception). For these analyses we also restricted data to those women who delivered at term only. The knots produced from the modelling result in 4 variables:

Pre-pregnancy weight (kg)
Change in weight between 0 and 18 weeks (kg/week)
Change in weight between 18 and 28 weeks (kg/week)
Change in weight between 28 weeks and birth(kg/week)

NB: since the knot points are precise it is appropriate to describe the change variables as above e.g. between 0 and 18 weeks and then between 18 and 28 weeks

Variables indicating the standard errors of the random effects for gestational weight change, and the number of weight measurements each woman contributed to the spline models for each period of gestation have been produced. These can be used as weights in sensitivity analyses as described for blood pressure change above.

#### Absolute weight gain

Two variables were derived for absolute weight gain, one using the actual weight measurements in pregnancy and the other using predictions from the linear spline models for gestational weight change. The first variable was derived as the difference between the last obstetric weight measurement and the first obstetric weight measurement. This was derived for all women who had at least one weight measurement prior to 18 weeks gestation and after 28 weeks gestation. The second variable was derived as the difference between the predicted weight at the time of delivery and the predicted pre-pregnancy weight (at gestational age = 0 weeks). This could only be derived for term pregnancies as the spline models were only fitted for women with term pregnancies.

### Average weight gain

Using the two absolute weight gain variables described above we also generated two average (i.e. kg / week of gestation) total weight gain variables. The first was derived as the difference between the last obstetric weight measurement and the first obstetric weight measurement divided by the difference in gestational age at the first and last weight measurement. The second was derived as the difference between the predicted weight at the time of delivery and the predicted prepregnancy weight (at gestational age = 0 weeks) divided by the gestational age at birth of the baby (as the first predicted measure is = 0).

### 2010 US Institute of Medicine categories of gestational weight gain.

US Institute of Medicine (IOM) recommendations for weight gain in pregnancy are increasingly used in research and we have derived a variable indicating which IOM (2010) category each woman belongs to (see table below for how these are defined).

Pre-pregnancy BMI	Range of absolute weight gain in kg
Underweight (<18.5kg/m²)	12.5-18
Normal weight (18.5-24.9kg/m <sup>2</sup> )	11.5-16
Overweight (25-29.9kg/m <sup>2</sup> )	7-11.5
Obese (>=30kg/m²)	5-9

To allocate women to IOM categories of lower than (category 1), recommended (0) and higher than recommended (2) GWG we used the absolute weight gain variables described above, combined with pre-pregnancy BMI based on the predicted pre-pregnancy weight from the multilevel models (see below) and maternal report of height. We derived one IOM category variable using absolute weight gain from measured weights and one using absolute weight gain from predicted weights.

#### Existing diabetes, gestational diabetes and glycosuria

At recruitment, women were asked about existing diabetes and any previous history of gestational diabetes. Information on glycosuria (recorded as none, trace, +, ++, +++ or more) was abstracted from the records of each antenatal clinic visit made by the woman (median number, 14 per woman). Glycosuria was defined as a record of at least ++ (equal to 13.9 mmol/l or 250 mg/100 ml) on at least two occasions at any time during the pregnancy. Women were classified into one of four mutually exclusive categories: no evidence of glycosuria or diabetes; existing diabetes before the pregnancy; gestational diabetes (i.e. a diagnosis in the medical records of gestational diabetes in any woman with no history of existing diabetes); and glycosuria (i.e. ++ glycosuria on two occasions in women with no evidence of existing or gestational diabetes).

## Early pregnancy haemoglobin

There were fewer repeat measurements of haemoglobin than other repeat measurements and it is likely that women with repeat measurements are those who were found to be anaemic at an earlier visit or unwell in some other way. As well as providing all of the repeat data for each women we have derived a variable that is the 'early pregnancy' Hb, defined as the first measurement of Hb when this occurs before 18 weeks (women with a first measurement after 18 weeks are not included in this derived variable).

#### **Number of antenatal visits**

We have generated a variable that gives the total number of recorded antenatal clinic visits. This is defined as any recorded encounter with a health professional in the medical records. At any one encounter different measurements may have been conducted.

#### 3. DESCRIPTION OF VARIABLES

Below each variable in the dataset is described

#### **Antenatal repeated measurements**

The following have repeated measurements for each woman. The data is in wide format so for each measure there are 49 variables (labelled variablename1-variablename49) representing up to 49 antenatal visits. The 49 variables are in order of visit date, however please be aware that any antenatal measurements where the date was missing will appear after the other measurements so the last measurement in the list is not necessarily from the final visit.

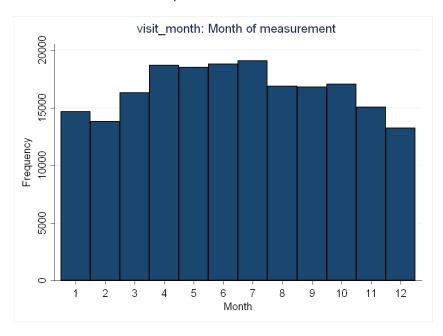
#### Month of measurement: visit month\*

\* 1-49 These are the months on which repeat measurements were collected; women in the dataset have up to 49 measurements (visits) for one or more variables. At any one visit the woman does not necessarily have all repeat measurements. She will have BP at some, weight at some, etc.

Total number of observations: 199,001

Median number of observations per woman: 14 IQR: 12 to 17

N with at least one observation: 13,575



Year of measurement: visit\_year\*

Median number of observations per woman: 14 IQR: 12 to 17

visit_year	Frequency	Percent	Cumulative percent
1990	5,383	2.71	2.71
1991	101,437	50.97	53.68
1992	92,109	46.29	99.96
1993	72	0.04	100.00
Total number of observations	199,001	100.00	

Care status: v1dab1b\_care\_status\*

This describes where a measurement (visit) took place.

Median number of observations per woman: 14 IQR: 12 to 17

N with at least one observation: 13,584

v1dab1b_care_status	Frequency	Percent	Cumulative percent
1. ANC	127,178	63.97	63.97
2. Inpatient	24,976	12.56	76.53
3. Home visit	9,748	4.90	81.43
4. Hospital/consultant clinic visit	36,917	18.57	100.00
Total number of observations	198,819	100.00	

Weight (kg): v1dab1c\_weight\*

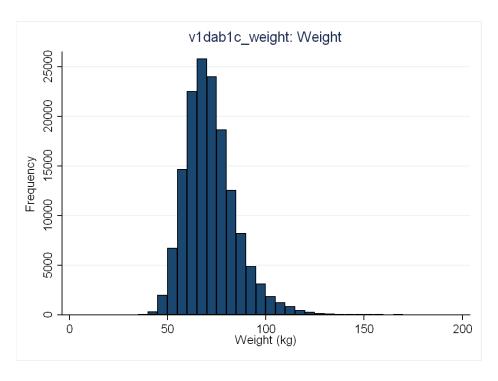
This is the weight at each measurement/visit available for a woman.

Total number of observations: 148,446

Mean: 71.87kg SD: 13.01kg

Median number of observations per woman: 12 IQR: 9 to 13

N with at least one observation: 13,469



Protein in urine: v1dab1d\_protein\*

This is the value of the proteinuria stix test at each repeat measurement/visit.

Median number of observations per woman: 12 IQR: 9 to 14

v1dab1d_protein	Frequency	Percent	Cumulative percent
0. Nil	148,665	92.27	92.27
1. Trace	6,742	4.18	96.46
2. +	2,267	1.41	97.86
3. ++	821	0.51	98.37
4. +++ or more	245	0.15	98.52
5. Blood	2,378	1.48	100.00
Total number of observations	161,118	100.00	

## Glycosuria, glucose in the urine: v1dab1e\_glycosuria\*

This is the value of the glycosuria stix test at each repeat measurement/visit. As can be seen in the table two different types of stix (with different scales) were used. The majority used the + scale, with a small number using % scale. On the advice of Prof Scott Nelson (Muirhead Professor of Obstetrics at Glasgow University) and after obtaining information from the manufacturers in our papers we converted the % to + values as follows (the values in brackets give the approximate quantity of glucose being detected at each level):

¼ % = + = 250 mg/dL ½ % = ++ = 500 mg/dL 1 % = +++ = 1000 mg/dL

Median number of observations per woman: 12 IQR: 9 to 14

N with at least one observation: 13,203

v1dab1e_glycosuria	Frequency	Percent	Cumulative percent
0. None	154,105	95.74	95.74
1. Trace to +	3,960	2.46	98.20
2. ++	2,023	1.26	99.45
3. +++ or more	705	0.44	99.89
4. Quarter of percent	102	0.06	99.96
5. Half of percent	29	0.02	99.97
6. One percent or more	43	0.03	100.00
Total	160,967	100.00	

Oedema: v1dab1f\_oedema\*

This gives the extent of oedema at each measurement/visit

Median number of observations per woman: 13 IQR: 11 to 16

v1dab1f_oedema	Frequency	Percent	Cumulative percent
0. None	169,394	93.46	93.46
1. Ankles only	3,315	1.83	95.29
2. Hands only	1,639	0.90	96.19
3. Face only	67	0.04	96.23
4. Generalised	344	0.19	96.42
5. Not otherwise specified	2,330	1.29	97.70
6. More than one site	4,161	2.30	100.00
Total number of observations	181,250	100.00	

## Systolic blood pressure (mm Hg): v1dab1g\_systolic\_bp\*

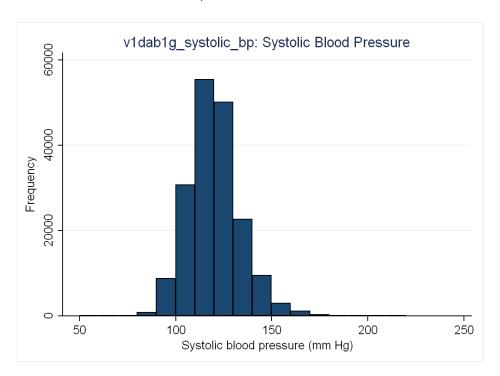
This gives the systolic blood pressure measurement at each measurement/visit

Total number of observations: 182,787

Mean: 115.73 mm Hg SD: 13.73 mm Hg

Median number of observations per woman: 13 IQR: 11 to 16

N with at least one observation: 13,273



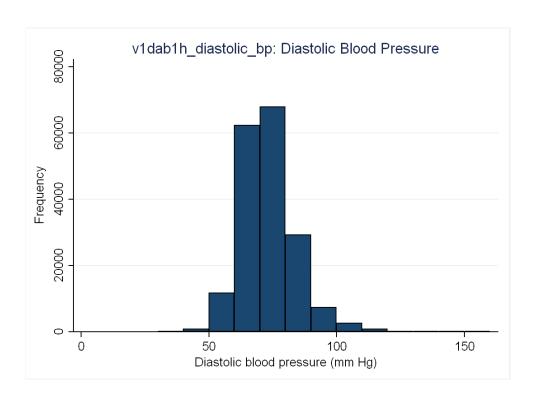
## Diastolic blood pressure (mm Hg): v1dab1h\_diastolic\_bp\*

This gives the diastolic blood pressure measurement at each measurement/visit.

Number of observations: 182,997

Mean: 69.17 mm Hg SD: 10.91 mm Hg

Median number of observations per woman: 13 IQR: 11 to 16



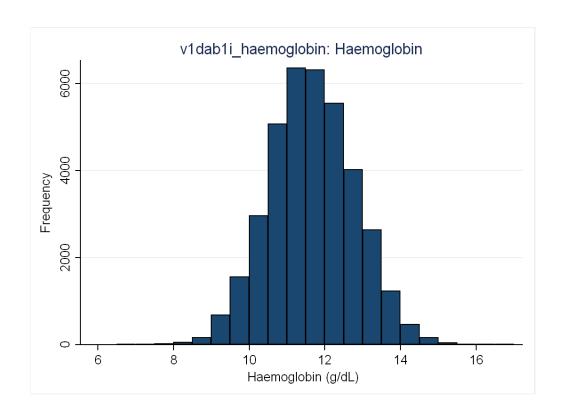
## Haemoglobin (Hb): v1dab1i\_haemoglobin\*

This gives the haemoglobin value for samples taken at each measurement/visit. There were 5 values of 64, 70, 96, 99, 111. It is possible that these have a missing decimal place (i.e. real values are 6.4, 7.0 etc) but it is also possible that they are diastolic (or for higher systolic) blood pressure measurements entered incorrectly on the form. Since it is not possible to determine just what these should be we have changed them to missing. There are also 2 values of 0 and 1; these have also been changed to missing.

Number of observations: 37,344

Mean: 11.62 g/dL SD: 1.13 g/dL

Median number of observations per woman: 3 IQR: 2 to 3

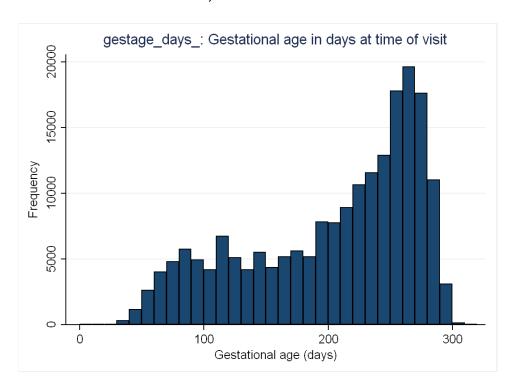


Gestational age in days at time of visit (derived variable): gestage\_days\_\* This gives the gestational age in days at each measurement/visit.

Number of observations: 198,705

Median: 225 IQR: 150 to 260

Median number of observations per woman: 14 IQR: 12 to 17

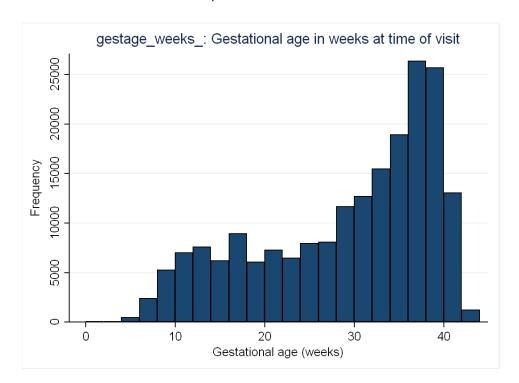


## Gestational age in weeks at time of visit (derived variable): gestage\_weeks\_\* This gives the gestational age in completed weeks at each measurement/visit.

Number of observations: 198,705

Median: 32 IQR: 21 to 37

Median number of observations per woman: 14 IQR: 12 to 17

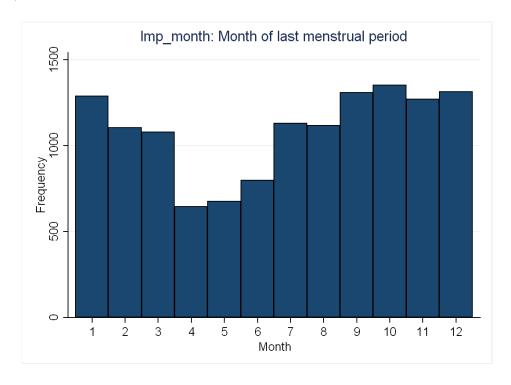


## **Basic measures**

The following variables are recorded once for each woman.

## Month of first day of last menstrual period: <a href="mailto:lmp\_month">lmp\_month</a>

N: 13,097



## Year of first day of last menstrual period: Imp\_year

Year of first day of last	Freq.	Percent	Cumulative percent
menstrual period			
1989	1	0.01	0.01
1990	3,612	27.58	27.59
1991	7,908	60.38	87.97
1992	1,576	12.03	100.00
Total	13,097	100.00	

## Was mother certain of last menstrual period date: v1dab2b\_certain\_period

Was the mother certain of	Frequency	Percent	Cumulative percent
LMP date?			
1. Yes	10,912	82.66	82.66
2. No	2,175	16.48	99.14
3. Unsure	114	0.86	100.00
Total	13,201	100.00	

## Month of final clinical estimate of expected date of delivery: edd month

The clinical estimated date of delivery reflects clinical practice at the time. Most will have been determined on the basis of the woman's LMP, with some having information on early ultrasound scans. We do not know who had scans or exactly how the expected date of delivery was estimated by clinicians for each woman.

N: 13,607



## Year of final clinical estimate of expected date of delivery: edd\_year

Year of final clinical estimate of	Frequency	Percent	Cumulative percent
expected date of delivery			
1991	5,586	41.05	41.05
1992	7,959	58.49	99.54
1993	62	0.46	100.00
Total	13,607	100.00	

## Mother's blood group:

ABO: v1dab3a\_abo

Mother's blood group: ABO	Frequency	Percent	Cumulative percent
1. A	5,839	43.01	43.01
2. B	1,225	9.02	52.03
3. 0	6,097	44.91	96.94
4. AB	416	3.06	100.00
Total	13,577	100.00	

Rhesus: v1dab3b\_rhesus

Mother's blood group: rhesus	Frequency	Percent	Cumulative percent
1. Positive	11,242	82.79	82.79
2. Negative	2,337	17.21	100.00
Total	13,579	100.00	

Rubella immune: v1dab3c\_rubella

Total	13,077	100.00	
2. No	117	0.89	100.00
1. Yes	12,960	99.11	99.11
Mother's blood group: rubella immune	Frequency	Percent	Cumulative percent

## Was hypertension/pre-eclampsia diagnosed at any time during the pregnancy:

v1dab5\_hypertension

Abstracters entered yes for this variable if there was any evidence in the notes of preeclampsia or hypertension being noted or diagnosed. It cannot distinguish between existing hypertension, gestational hypertension, preeclampsia, or indeed one elevated measurement of blood pressure. It is maintained in the dataset, but we would recommend the derived variables for hypertensive disorder of pregnancy that we have derived from the repeat blood pressure and proteinuria values are used in research rather than this variable.

Was hypertension/pre- eclampsia diagnosed during the	Frequency	Percent	Cumulative percent
pregnancy?			
1. Yes	939	6.99	6.99
2. No	12,492	93.01	100.00
Total	13,431	100.00	

### Amniocentesis noted during pregnancy before the onset of labour:

This variable indicates whether or not a woman had an amniocentesis during pregnancy. We do not have results of this.

### v1dab6b1\_amniocentesis

Amniocentesis noted during	Frequency	Percent	Cumulative percent
pregnancy			
1. Yes	338	2.47	2.47
2. No	13,367	97.53	100.00
Total	13,705	100.00	

### Blood sugars noted during pregnancy before the onset of labour:

This variable indicates whether or not a woman had blood glucose test during pregnancy. We do not have results of this.

v1dab6g\_blood\_sugars

Blood sugars noted during	Frequency	Percent	Cumulative percent
pregnancy			
1. Yes	1,042	7.60	7.60
2. No	12,664	92.40	100.00
Total	13,706	100.00	

## Chorionic villus sampling noted during pregnancy before the onset of labour:

This variable indicates whether or not a woman had a CVS during pregnancy. We do not have results of this.

v1dab6i\_chorionic\_villus

Chorionic villus sampling noted during pregnancy	Frequency	Percent	Cumulative percent
1. Yes	99	0.72	0.72
2. No	13,607	99.28	100.00
Total	13,706	100.00	

## Diabetes noted during pregnancy before the onset of labour:

This variable indicates whether or not a woman had a diagnosis of diabetes made during pregnancy. We have used this variable in the derivation of a categorical variable (healthy, existing diabetes, gestational diabetes, glycosuria) as described above.

v1dab6k\_diabetes

Diabetes noted during	Frequency	Percent	Cumulative percent
pregnancy			
1. Yes	112	0.82	0.82
2. No	13,594	99.18	100.00
Total	13,706	100.00	

### **Excessive vomiting noted during pregnancy before the onset of labour:**

This variable describes whether a woman was diagnosed with excessive vomiting during pregnancy

v1dab6m\_exc\_vomiting

Excessive vomiting noted	Frequency	Percent	Cumulative percent
during pregnancy			
1. Yes	113	0.82	0.82
2. No	13,593	99.18	100.00
Total	13,706	100.00	

## Random blood sugar noted during pregnancy before the onset of labour:

This variable describes whether a woman had a random blood glucose test taken during pregnancy

v1dab6z\_rnd\_blood\_sugar

Random blood sugar noted	Frequency	Percent	Cumulative percent
during pregnancy			
1. Yes	1,432	10.45	10.45
2. No	12,274	89.55	100.00
Total	13,706	100.00	

## Was the mother admitted to hospital during this pregnancy:

This variable indicates whether the woman was admitted to hospital during pregnancy (for any reason). We do not have information on the diagnosis for these admissions.

v1dab10a\_hosp\_admission

Was the mother admitted to hospital during this pregnancy?	Frequency	Percent	Cumulative percent
1. Yes	8,718	64.57	64.57
2. No	4,784	35.43	100.00
Total	13,502	100.00	

## What was the method of delivery:

Women with multiple births may have had different methods of delivery for each baby (qlet = A, B, C) so this variable is summarised by number of offspring rather than number of women

v1dac6\_method\_delivery

What was the method of delivery?	Frequency	Percent	Cumulative percent
0. Spontaneous	10,344	75.64	75.64
<ol> <li>Assisted breech</li> </ol>	197	1.44	77.08
2. Breech, extraction	9	0.07	77.15
3. Caesarean section	1,508	11.03	88.18
4. Forceps	723	5.29	93.46
5. Vacuum extraction	728	5.32	98.79
6. Other	166	1.21	100.00
Total offspring	13,675	100.00	

## Anaemia noted as having occurred during the first 14 days postpartum: v1dad1a1\_anaemia

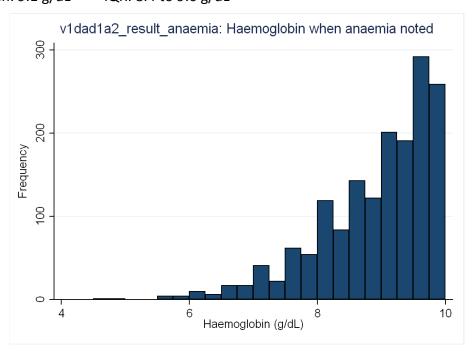
Anaemia noted to have occurred during the first 14 days postpartum	Frequency	Percent	Cumulative percent
1. Yes	1,658	12.10	12.10
2. No	12,039	87.90	100.00
Total	13,697	100.00	

**Haemoglobin when anaemia noted:** This variable only has data in women where a diagnosis of anaemia – post partum (see above variable) was noted in the notes and it is the corresponding haemoglobin value written in the notes at the time that that diagnosis was made in the notes.

v1dad1a2\_result\_anaemia

N with measurement: 1650

Median: 9.1 g/dL IQR: 8.4 to 9.6 g/dL



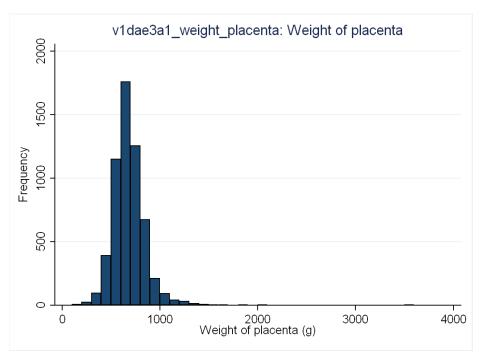
## Weight of placenta (g): v1dae3a1\_weight\_placenta

This variable is summarised by number of offspring as some women had multiple pregnancies with more than one placenta.

There is one extreme outlier of 3600g. This is for a woman who had twins with one placenta. Since this is a plausible weight we have left it in the dataset.

N offspring with measurement: 5,769

Mean: 661.5g SD: 167.4g



Placenta not weighed: v1dae3a2\_not\_wghtd\_placenta

This variable is summarised by number of offspring.

Placenta not weighed	Frequency	Percent	Cumulative percent
8. Ticked	7,875	100.00	100.00
Total offspring	7,875	100.00	

### Place of delivery: da050

This variable is only available for women whose medical records were included in the first set of abstractions.

Place of delivery	Frequency	Percent	Cumulative percent
bmh/st. michaels	3,190	38.29	38.29
southmead	4,402	52.84	91.13
weston	363	4.36	95.49
home	208	2.50	97.98
other	168	2.02	100.00
Total	8,331	100.00	

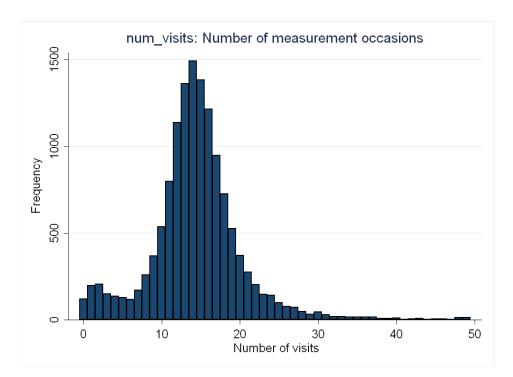
## **Summary of our derived variables**

Below we summarise the variables that we have derived (derivation methods described above)

Number of antenatal visits num\_visits this gives the total number of antenatal visits.

Number of observations (=participants with data): 13,706

Median: 14 IQR: 12 to 17



## **Hypertension in pregnancy (derived variables)**

## **Pre-existing hypertension:**

prev\_hyp

Previously been diagnosed with	Frequency	Percent	Cumulative percent
hypertension outside of pregnancy			
0. No	11,582	96.29	96.29
1. Yes	446	3.71	100.00
Total	12,028	100.00	

## Hypertensive disorder of pregnancy (gestational hypertension or pre-eclampsia): HDP

High blood pressure after 20 weeks without pre-existing	Frequency	Percent	Cumulative percent
hypertension			
0. No <sup>a</sup>	11,469	83.68	83.68
1. Yes	2,237	16.32	100.00
Total	13,706	100.00	

<sup>&</sup>lt;sup>a</sup> This group includes all women who had pre-existing hypertension(see above for definition of HDP)

## Preeclampsia:

preeclampsia

Preeclampsia without pre-existing hypertension	Frequency	Percent	Cumulative percent
0. No <sup>a</sup>	13,409	97.83	97.83
1. Yes	297	2.17	100.00
Total	13,706	100.00	

<sup>&</sup>lt;sup>a</sup> This group includes women who had pre-existing hypertension and women who had gestational hypertension

## **Gestational hypertension:**

gesthyp

Gestational hypertension without	Frequency	Percent	Cumulative percent
pre-existing hypertension			
No <sup>a</sup>	11,469	85.53	85.53
Yes	1,940	14.47	100.00
Total	13,409	100.00	

<sup>&</sup>lt;sup>a</sup> This group does NOT include those with pre-eclampsia but includes women who had pre-existing hypertension

### Pre-eclampsia superimposed on pre-existing hypertension:

sup preeclampsia

Preeclampsia superimposed on	Frequency	Percent	Cumulative percent
existing hypertension			
0. No <sup>a</sup>	13,675	99.77	99.77
1. Yes	31	0.23	100.00
Total	13,706	100.00	

<sup>&</sup>lt;sup>a</sup> This group includes all other women, including those who had pre-existing hypertension but who did not go on to develop preeclampia (according to ISSHP criteria) and those with gestational hypertension or pre-eclampsia who did not have pre-existing hypertension

## Proteinuria of 1+ or more on 2 occasions after 20 weeks gestation<sup>a</sup>: proturi

Proteinuria (1+ or more) after 20	Frequency	Percent	Cumulative percent
weeks gestation			
0. No	13,147	95.92	95.92
1. Yes	559	4.08	100.00
Total	13,706	100.00	

<sup>&</sup>lt;sup>a</sup> This variable is classified by proteinuria only, so women who had pre-existing hypertension may be included in either category

## Number of blood pressure measurements across pregnancy: num\_bp

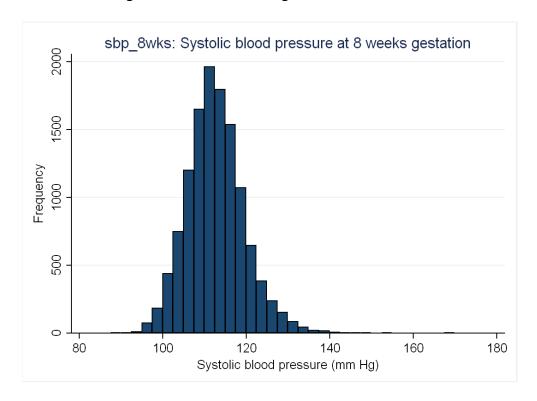
Number of blood pressure	Frequency	Percent	Cumulative percent
measurements across pregnancy			
0. None	443	3.23	3.23
1. One	149	1.09	4.32
2. Two or more	13,114	95.68	100.00
Total	13,706	100.00	

## **Blood pressure change (derived variables)**

## SBP at 8 weeks gestation (mm Hg): sbp\_8wks

N: 12,302

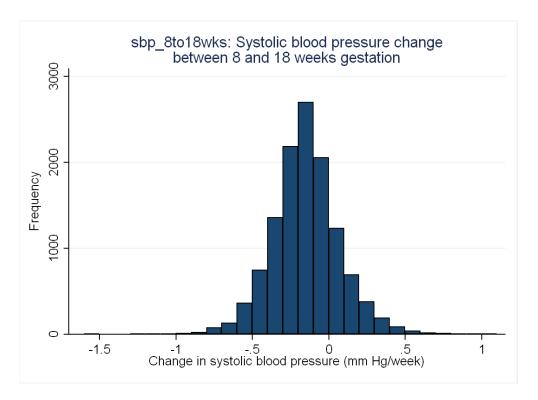
Mean: 112.74 mm Hg SD: 6.92 mm Hg



SBP change 8-18 weeks gestation (mm Hg/week): sbp\_8to18wks

N: 12,302

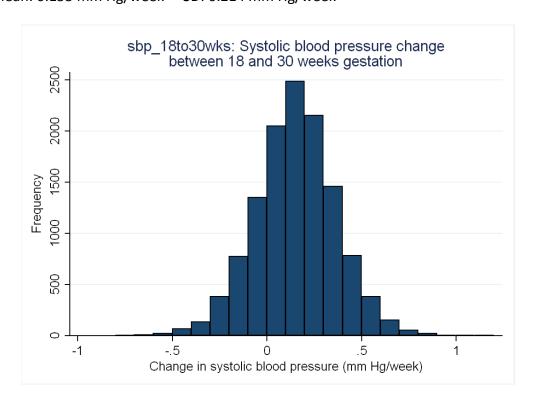
Mean: -0.150 mm Hg/week SD: 0.220 mm Hg/week



SBP change 18-30 weeks gestation (mm Hg/week): sbp\_18to30wks

N: 12,302

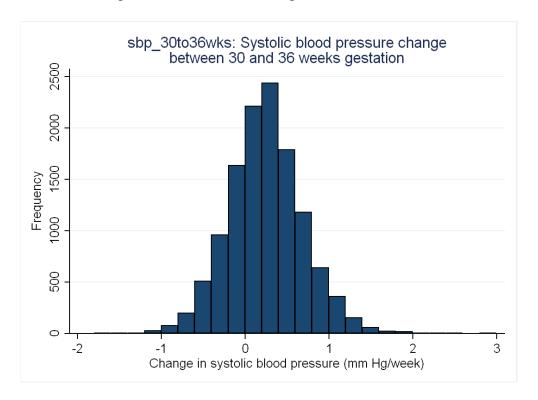
Mean: 0.153 mm Hg/week SD: 0.214 mm Hg/week



SBP change 30-36 weeks gestation (mm Hg/week): sbp\_30to36wks

N: 12,302

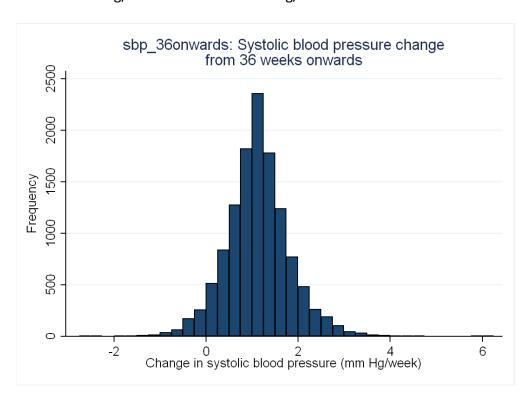
Mean: 0.250 mm Hg/week SD: 0.445 mm Hg/week



## SBP change 36 weeks onwards (mm Hg/week): sbp\_36onwards

N: 12,302

Mean: 1.134 mm Hg/week SD: 0.692 mm Hg/week



## Standard error of estimate of SBP at 8 weeks (mm Hg): sbp\_8wks\_se

N: 12,302

Median: 5.328 mm Hg IQR: 4.895 to 5.702 mm Hg

## Standard error of estimate of SBP change 8-18 weeks (mm Hg/week):

sbp\_8to18wks\_se:

N: 12,302

Median: 0.562 mm Hg/week IQR: 0.540 to 0.575 mm Hg/week

### Standard error of estimate of SBP change 18-30 weeks (mm Hg/week):

sbp\_18to30wks\_se

N: 12,302

Median: 0.386 mm Hg/week IQR: 0.379 to 0.395 mm Hg/week

## Standard error of estimate of SBP change 30-36 weeks (mm Hg/week):

sbp 30to36wks se

N: 12,302

Median: 0.758 mm Hg/week IQR: 0.748 to 0.771 mm Hg/week

## Standard error of estimate of SBP change 36 weeks onwards (mm Hg/week):

sbp\_36onwards

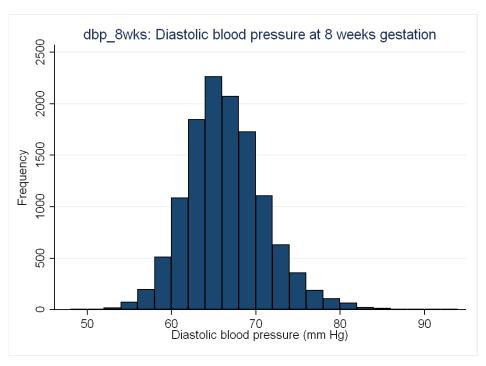
N: 12,302

Median: 1.351 mm Hg/week IQR: 1.277 to 1.427 mm Hg/week

## DBP at 8 weeks gestation (mm Hg): dbp\_8wks

N: 12,302

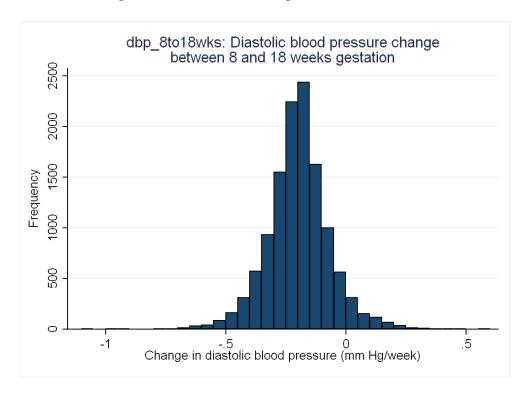
Mean: 66.49 mm Hg SD: 4.70 mm Hg



DBP change 8-18 weeks gestation (mm Hg/week): dbp\_8to18wks

N: 12,302

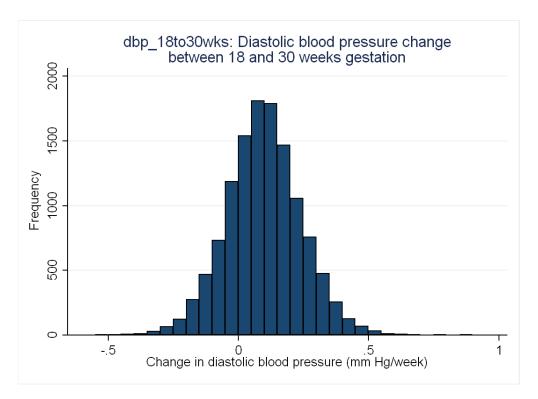
Mean: -0.197 mm Hg/week SD: 0.129 mm Hg/week



DBP change 18-30 weeks gestation (mm Hg/week): dbp\_18to30wks

N: 12,302

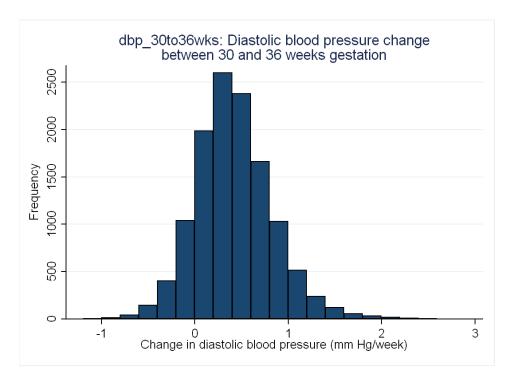
Mean: 0.099 mm Hg/week SD: 0.144 mm Hg/week



DBP change 30-36 weeks gestation (mm Hg/week): dbp\_30to36wks

N: 12,302

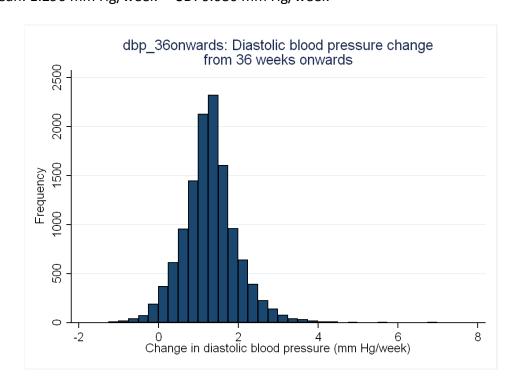
Mean: 0.423 mm Hg/week SD: 0.416 mm Hg/week



## DBP change 36 weeks onwards (mm Hg/week): dbp\_36onwards

N: 12,302

Mean: 1.296 mm Hg/week SD: 0.680 mm Hg/week



Standard error of estimate of DBP at 8 weeks (mm Hg): dbp\_8wks\_se

N: 12,302

Median: 3.823 mm Hg IQR: 3.528 to 4.086 mm Hg

Standard error of estimate of DBP change 8-18 weeks (mm Hg/week):

dbp\_8to18wks\_se:

N: 12,302

Median: 0.384 mm Hg/week IQR: 0.370 to 0.392 mm Hg/week

Standard error of estimate of DBP change 18-30 weeks (mm Hg/week):

dbp\_18to30wks\_se

N: 12,302

Median: 0.270 mm Hg/week IQR: 0.265 to 0.276 mm Hg/week

Standard error of estimate of DBP change 30-36 weeks (mm Hg/week):

dbp\_30to36wks\_se

N: 12,302

Median: 0.602 mm Hg/week IQR: 0.593 to 0.613 mm Hg/week

Standard error of estimate of DBP change 36 weeks onwards (mm Hg/week):

dbp\_36onwards

N: 12,302

Median: 1.150 mm Hg/week IQR: 1.068 to 1.240 mm Hg/week

Number of blood pressure measurements in the first period of gestation (up to 18

weeks): bp1num

N: 12,302

Median: 2 IQR: 1 to 3

Number of blood pressure measurements in the second period of gestation (18 to

30 weeks): bp2num

N: 12,302

Median: 3 IQR: 3 to 4

Number of blood pressure measurements in the third period of gestation (30 to 36

weeks): bp3num

N: 12,302

Median: 3 IQR: 2 to 3

## Number of blood pressure measurements in the fourth period of gestation (36 weeks onwards): bp4num

N: 12,302

Median: 2 IQR: 2 to 3

## Proteinuria latent classes (derived variables)

## Latent class analysis of all women:

Most likely latent class: prot\_LCA\_all\_class

LCA of all women: most likely class	Frequency	Percent	Cumulative percent
1. Class 1: Low probability of proteinuria	11,511	98.80	98.80
2. Class 2: High probability of proteinuria	140	1.20	100.00
Total	11,651	100.00	

Probability of membership of Class 1: prot LCA all pclass1

N: 11,651

Median: 0.993 IQR: 0.992 to 0.993

**Probability of membership of Class 2:** prot\_LCA\_all\_pclass2

N: 11,651

Median: 0.007 IQR: 0.007 to 0.008

## Latent class analysis of women who ever had proteinuria:

Most likely latent class: prot\_LCA\_ever\_class

LCA of women with any proteinuria:	Frequency	Percent	Cumulative percent
most likely class			
1. Class 1: proteinuria up to 20 weeks	101	9.00	9.00
2. Class 2: proteinuria onset 21-28 weeks	104	9.27	18.27
3. Class 3: proteinuria onset 29-32 weeks	137	12.21	30.48
4. Class 4: proteinuria onset 33-36 weeks	276	24.60	55.08
5. Class 5: proteinuria onset 37+ weeks	504	44.92	100.00
Total	1,122	100.00	

Probability of membership of Class 1: prot\_LCA\_ever\_pclass1

N: 1,122

Median: 0.000 IQR: 0.000 to 0.985

Probability of membership of Class 2: prot\_LCA\_ever\_pclass2

N: 1,122

Median: 0.000 IQR: 0.000 to 1.000

## Probability of membership of Class 3: prot LCA ever pclass3

N: 1,122

Median: 0.000 IQR: 0.000 to 1.000

## Probability of membership of Class 4: prot LCA ever pclass4

N: 1,122

Median: 0.000 IQR: 0.000 to 0.992

## **Probability of membership of Class5:** prot\_LCA\_ever\_pclass5

N: 1,122

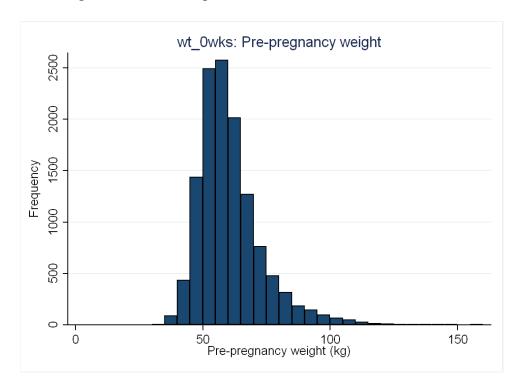
Median: 0.000 IQR: 0.000 to 1.000

## **Gestational weight change (derived variables)**

## Pre-pregnancy weight (kg): wt\_0wks

N: 12,484

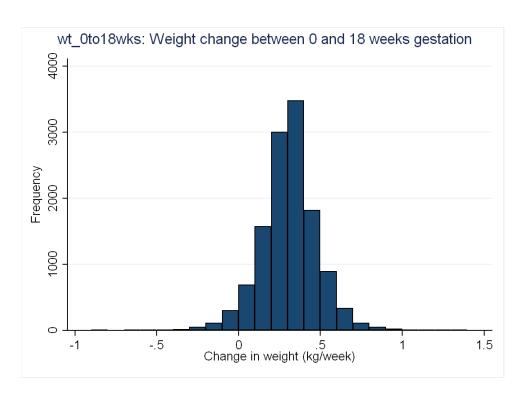
Mean: 60.79 kg SD: 12.56 kg



## Weight change between 0 and 18 weeks gestation (kg/week): wt\_0to18wks

N: 12,484

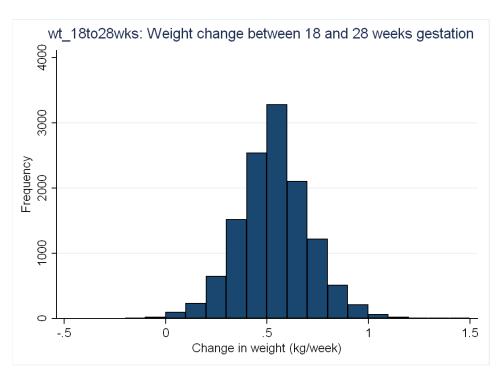
Mean: 0.309 kg/week SD: 0.173 kg/week



Weight change between 18 and 28 weeks gestation (kg/week): wt\_18to28wks

N: 12,484

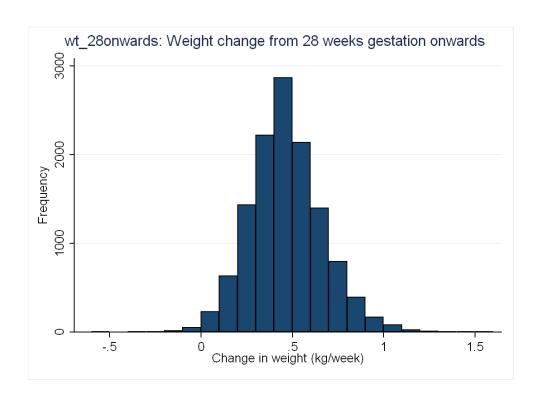
Mean: 0.537 kg/week SD: 0.176 kg/week



Weight change from 28 weeks gestation onwards (kg/week): wt\_28onwards

N: 12,484

Mean: 0.468 kg/week SD: 0.198 kg/week



## Standard error of estimate of pre-pregnancy weight (kg): wt Owks se

N: 12,484

Median: 2.158 kg IQR: 1.689 to 2.775 kg

## Standard error of estimate of weight change between 0 and 18 weeks (kg/week): wt\_0to18wks\_se:

N: 12,484

Median: 0.139 kg/week IQR: 0.114 to 0.172 kg/week

## Standard error of estimate of weight change between 18 and 28 weeks (kg/week): wt\_18to28wks\_se

N: 12,484

Median: 0.082 kg/week IQR: 0.078 to 0.089 kg/week

## Standard error of estimate of weight change from 28 weeks onwards (kg/week): wt 28onwards se

N: 12,484

Median: 0.078 kg/week IQR: 0.070 to 0.090 kg/week

## Number of weight measurements in the first period of gestation (up to 18 weeks): wt1num

N: 12,484

Median: 2 IQR: 1 to 3

## Number of weight measurements in the second period of gestation (18 to 28 weeks): wt2num

N: 12,484

Median: 2 IQR: 2 to 3

## Number of weight measurements in the third period of gestation (28 weeks onwards): wt3num

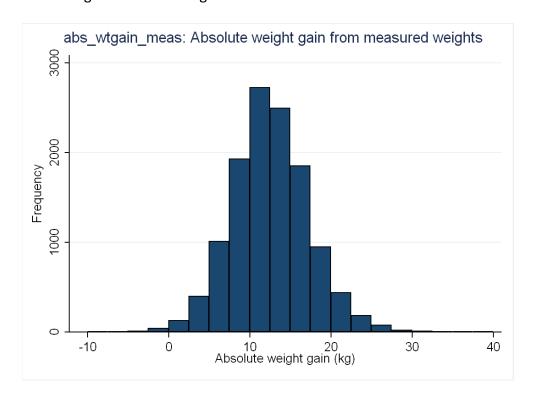
N: 12,484

Median: 5 IQR: 4 to 6

## Absolute weight gain from last minus first weight measurement: abs\_wtgain\_meas

N: 12,287

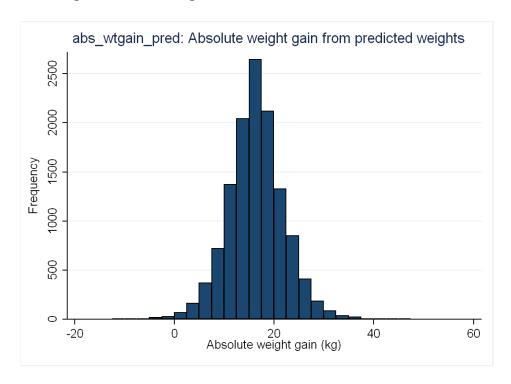
Mean: 12.49 kg SD: 4.73 kg



## Absolute weight gain from spline model predictions: abs\_wtgain\_pred

N: 12,484

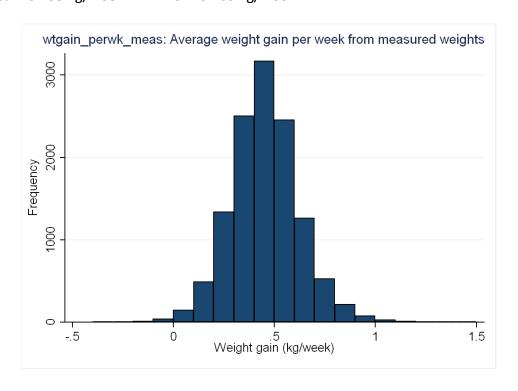
Mean: 16.42 kg SD: 5.60 kg



## Average weight gain per week across pregnancy from first and last weight measurements: wtgain perwk meas

N: 12,287

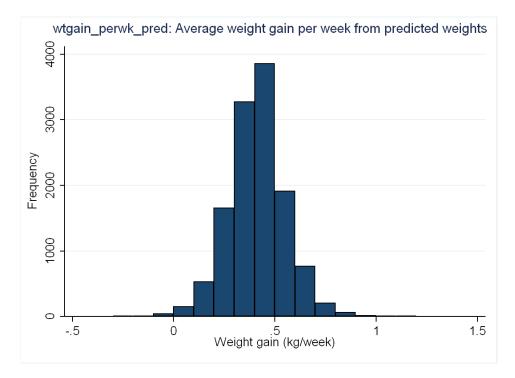
Mean: 0.455 kg/week SD: 0.169 kg/week



## Average weight gain per week across pregnancy from predicted weights at 0 weeks and delivery: wtgain perwk pred

N: 12,484

Mean: 0.413 kg/week SD: 0.140 kg/week



## Institute of Medicine categories of gestational weight gain from measured weights: IOMadequate\_meas

IOM categories of gestational weight gain using last minus first weight measurement	Frequency	Percent	Cumulative percent
Recommended	4,005	38.95	38.95
Less than recommended	3,468	33.73	72.67
More than recommended	2,810	27.33	100.00
Total	10,283	100.00	

## Institute of Medicine categories of gestational weight gain from predicted weights: IOMadequate\_pred

IOM categories of gestational weight gain using predicted weights	Frequency	Percent	Cumulative percent
Recommended	3,196	28.89	28.89
Less than recommended	1,390	12.57	41.46
More than recommended	6,475	58.54	100.00
Total	11,061	100.00	

## **Diabetes in pregnancy (derived variables)**

## Glycosuria of 2+ or more on two occasions: glycosuria

Glycosuria (2+ or more) on two occasions	Frequency	Percent	Cumulative percent
2. No	13,185	96.20	96.20
3. Yes	521	3.80	100.00
Total	13,706	100.00	

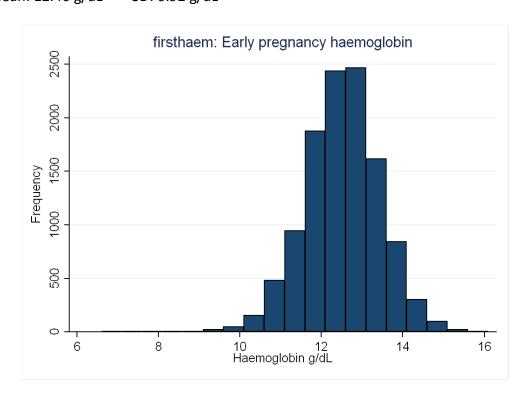
## Categories of diabetes in pregnancy: pregnancy\_diabetes

Diabetes in	Frequency	Percent	Cumulative percent
pregnancy			
0. No glycosuria or diabetes	11,773	95.86	95.86
<ol> <li>Existing diabetes</li> </ol>	47	0.38	96.25
2. Gestational diabetes	57	0.46	96.71
3. Glycosuria	404	3.29	100.00
Total	12,281	100.00	

## Early pregnancy haemoglobin (derived variable): firsthaem

N: 11,336

Mean: 12.46 g/dL SD: 0.92 g/dL



The cleaning of the obstetric data and deriving of these variables was done by:
Corrie Macdonald-Wallis
Debbie A Lawlor
Abigail Fraser
Kate Tilling

For more information contact Debbie A Lawlor – d.a.lawlor@bristol.ac.uk

The final version of this report (and associated datafile) was completed 31<sup>st</sup> October 2011

#### 4. COMPLETED RESEARCH USING THESE DATA

Below we list publications that have used these data; submitted papers and work in progress using these data at the time of completing this report.

The published work provides additional methodological detail that might help researchers wanting to use these data.

### Published/ in press journal papers

- 1. Macdonald-Wallis C, Lawlor DA, Tilling K. Multivariate multilevel spline models for parallel growth processes: application to blood pressure in pregnancy. *Statistics in Medicine* 2011, in press (accepted October 2011).
- 2. Patel D, Fraser A, Davey Smith G, Lindsay RS, Sattar N, Nelson SM, Lawlor DA. Associations of gestational diabetes, existing diabetes and glycosuria with offspring obesity and cardiometabolic outcomes. *Diabetes Care* 2011, in press (accepted October 2011).
- 3. Fraser A, Nelson SM, Macdonald-Wallis C, Cherry L, Butler E, Sattar N, Lawlor DA. Associations of pregnancy complications with calculated CVD risk and cardiovascular risk factors in middle age: the Avon Longitudinal Study of Parents and Children. *Circulation* 2011, in press (accepted August 2011).
- 4. Macdonald-Wallis C, Tilling K, Fraser A, Nelson SM, Lawlor DA. Established pre-eclampsia risk factors are related to patterns of blood pressure change in normal term pregnancy: findings from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Journal of Hypertension* 2011, 29:1703-1711.
- 5. Lawlor DA, Macdonald-Wallis C, Fraser A, Nelson SM, Hingorani A, Davey Smith G, Sattar N, Deanfield J. Hypertensive disorders of pregnancy and offspring vascular, inflammatory and lipid outcomes in childhood: findings from the Avon Longitudinal Study of Parents and Children. *European Heart Journal* 2011; doi:10.1093/eurheart/ehr300.
- 6. Macdonald-Wallis C, Lawlor DA, Heron J, Fraser A, Nelson SM, Tilling K. Relationships of Risk Factors for Pre-eclampsia with Patterns of Occurrence of Isolated Gestational Proteinuria During Normal Term Pregnancy. *PLoS ONE* 6(7): e22115. doi:10.1371/journal.pone.0022115.
- 7. Lawlor DA, Fraser A, MacDonald-Wallis C, Palmer T, Davey Smith G, Tilling K. Maternal and offspring adiposity related genetic variants and gestational weight gain. *American Journal of Clinical Nutrition* 2011; 94:149-55.

- 8. Fraser A, Tilling K, Macdonald-Wallis C, Sattar N, Nelson SM, Lawlor DA. Associations of pre-pregnancy weight and gestational weight gain with mothers' BMI, waist circumference and blood pressure measured 16 years post-pregnancy: the Avon Longitudinal Study of Parents and Children. *American Journal of Clinical Nutrition* 2011; 93: 1285-92.
- Geelhoed JJM, Fraser A, Tilling K, Benfield L, Davey Smith G, Sattar N, Nelson S, Lawlor DA. Preeclampsia and gestational hypertension are associated with childhood blood pressure, independently of family adiposity measures: the Avon Longitudinal Study of Parents and Children. *Circulation* 2010, 122:1192-1199.
- 10. Fraser A, Tilling K, Macdonald-wallis C, Sattar N, Brion M-J, Benfield L, Ness A, Deanfield J, Hingorani A, Nelson SM, Davey Smith G, Lawlor DA. Association of maternal weight gain in pregnancy with offspring obesity and metabolic and vascular traits in childhood. *Circulation* 2010;121:2557-2564.
- 11. Lawlor DA, Fraser A, Lindsay RS, Ness A, Dabelea D, Catalano P, Davey Smith G, Sattar N, Nelson SM. The association of existing diabetes, gestational diabetes and glycosuria in pregnancy with macrosomia and offspring body mass index, waist and fat mass in later childhood: findings from a prospective pregnancy cohort. *Diabetologia* 2010;53:89-97

### **Submitted papers**

- 1. Macdonald-Wallis C, Lawlor DA, Fraser A, May M, Nelson SM, Tilling K. Blood pressure change in normotensive, gestational hypertensive, preeclamptic and essential hypertensive pregnancies: the Avon Longitudinal Study of Parents and Children. Submitted to European Heart Journal, October 2011.
- Macdonald-Wallis C, Tilling K, Fraser A, Nelson SM, Lawlor DA. Relationship of gestational weight gain with subsequent changes in blood pressure and risk of hypertensive disorders of pregnancy: the Avon Longitudinal Study of Parents and Children. Submitted to International Journal of Epidemiology, October 2011.
- 3. Gage S, Lawlor DA, Tilling K, MacDonald-Wallis C, Fraser A. Gestational weight gain and offspring intelligence: findings from the Avon Longitudinal Study of Parents and Children. Submitted to American Journal of Epidemiology, September 2011.
- 4. Fraser A, Nelson SM, Macdonald-Wallis C, Lawlor DA. The associations of existing diabetes, gestational diabetes and glycosuria in pregnancy with offspring cognition and educational attainment. Submitted Epidemiology, June 2011.
- 5. Fraser A, Tilling K, Henderson J, Grannell R, MacDonald-Wallis C, Lawlor DA. The association of gestational weight gain and offspring asthma. Submitted to International Journal of Obesity, April 2011.

### 5. APPROVED ON-GOING RESEARCH USING THESE DATA

The following are a list of projects that have been approved by exec. and that use these data as major (exposure / outcome) variables. Approved work using these data as covariables or in ways that are not key to the research are not listed. The list was

complete at the time of writing this report (31<sup>st</sup> October 2011). For details of subsequent approved studies please go to the ALSPAC website where all approved research proposals (using any of the study data) are published.

- 1. Macdonald-Wallis C, Lawlor DA, Tilling K, Nelson SM. Development of BP change in pregnancy normograms, association of BP change in pregnancy with maternal and offspring later cardiometabolic health. Approved January 2009 (as part of DA Lawlor grant submission to Wellcome Trust); submitted as Corrie's postdoc fellowship application to MRC and Wellcome Trust. Work starting 2012.
- Macdonald-Wallis C, Lawlor DA, Tilling K, Evans D, et al. Maternal and offspring GWAS and blood pressure change in normal term pregnancy. Exec approved 2009 WT mums GWAS grant to DA Lawlor & included in C Macdonald-Wallis fellowship application to MRC / WT September/October 2011. Replication samples agreed September 2011.
- 3. Lawlor DA, Evans D, Paternoster L, et al. Maternal and offspring GWAS and gestational weight gain in term pregnancy. Exec approved 2009 WT mums GWAS grant to DA Lawlor. Analysis plan and discovery and replication samples agreed October 2011.
- 4. Fraser A, Nelson SM, Macdonald-Wallis C, Cherry L, Butler E, Sattar N, Lawlor DA. Associations of pregnancy complications with carotid intima media thickness in middle age. Exec approved 2007 BHF mums grant to DA Lawlor & in 2008 fellowship to A Fraser. Work will start in Spring 2012 when CIMT data ready.
- 5. Macali N, Tilling K, et al. Association of maternal eating disorders with gestational weight gain. Exec. approved July 2011; data October 2011.
- 6. Morales E, Relton C, Lawlor DA, Davey Smith G et al. Association of gestational weight gain with DNA methylation in cord blood. Exec. approved July 2011; data sent October 2011.
- 7. Fraser A, Williams D, Fraser W, Nelson S, Lawlor DA. Associations of pregnancy vitamin D and calcium with HDP, preterm delivery, and small for gestational age. Exec. approved 2008 MRC vitamin D grant to DA Lawlor. Work started July 2011; paper likely to be submitted November 2011.
- 8. Fraser A, Williams D, Fraser W, Nelson S, Lawlor DA. Associations of pregnancy vitamin D and calcium with pregnancy diabetes. Exec. approved 2008 MRC vitamin D grant to DA Lawlor. Work started October 2011; paper likely to be submitted Spring 2012.
- Macdonald-Wallis C, Tilling K, Nelson SM, Lawlor DA. Maternal blood pressure change in pregnancy and perinatal outcomes. Exec. approved 2009 WT obstetric data abstraction grant to DA Lawlor.
- 10. Pre-eclampsia GWAS collaboration being led by colleagues in LSHTM, Cambridge and US – ALSPAC as one contributing study. Exec approved 2009 WT mums GWAS grant to DA Lawlor.
- 11. Tsosi R, Jeffreys M, Lawlor DA, et al. Pre-eclampsia and breast cancer risk. Exec approved 2009. Data sent January 2010.