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Cohort profile: The Southampton Women's Survey

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How did the study come about?

Inverse associations between birthweight and later risk of major chronic diseases, notably cardiovascular disease, diabetes, and osteoporosis, have been found in various studies.[1] Birthweight is determined by length of gestation and the combination of the early trajectory of fetal growth and the capacity of the fetal supply line to maintain this trajectory in late gestation. Studies in early pregnancy, assisted reproductive technology, and animal experiments indicate that both genetic and environmental factors are important in establishing the fetal growth trajectory and the fetal supply line; environmental factors include transgenerational influences and the mother's body composition, endocrine profile, diet, and physical activity around the time of conception.[2] As these influences may change during early pregnancy, there is a need to characterize women before conception. The Southampton Women's Survey (SWS) was thus established to measure the pre-pregnant characteristics of women aged 20–34 years living in the city and then follow-up those women who subsequently become pregnant.

Although the original focus was on fetal development, more recent research has shown that post-natal growth, and the way in which it interacts with intrauterine growth, is also associated with the risk of chronic disease risk in later life.[3] Thus the SWS children are being followed through infancy and childhood to examine how their pre-natal growth interacts with their post-natal growth, and how both affect the children's risk factors for a range of chronic diseases.

What does it cover?

The objectives of the SWS are:

(i) To characterize the influence of the mother's own fetal growth and of her diet, body composition, and endocrine profile before and during pregnancy on: (a) the early trajectory of fetal growth; (b) the maintenance of this growth trajectory in late gestation; (c) placental and fetal adaptive responses, including altered regional blood flow and body composition in the fetus; and

(ii) To examine how maternal and intrauterine factors interact with the offspring's genes and post-natal environment to influence: (a) weight gain, head growth, and linear growth in infancy; (b) the pathways of growth and development during childhood that lead to poor adult health; and (c) respiratory function and asthma in childhood, as well as levels of risk factors for adult cardiovascular disease, type 2 diabetes, and osteoporosis.

Using this information, we aim to inform the development of interventions to optimize fetal, infant, and childhood growth and development.

Who is in the sample?

Between 1998 and 2002 all general practitioners in Southampton were asked to help us recruit their female patients aged 20–34 years to the study. A small team of the SWS staff acted under contract to the GPs to recruit the women. The team members were provided with a list of eligible women, excluding any that the GP felt should not be approached. A letter and a leaflet explaining the study were sent to each woman, followed by a telephone call. If the woman was willing to take part, an appointment was made for an SWS nurse to visit her in her home. If the woman could not be contacted by telephone, a repeat letter was sent to ask for updated contact details. Where there was no response we attempted to visit the home to ascertain whether the woman still lived there or not. The study was extensively publicized locally and we recruited women not registered with GPs or who were registered with an incorrect address by approaching women at local events and in supermarkets in the city. Of those women contacted about the study, 12 579 (75%) agreed and were interviewed by a research nurse. All interviews were conducted between April 1998 and October 2002.

How often have they been followed-up?

Figure 1 shows an outline of the structure of the SWS.

At the end of the interview, each woman was given a card and pre-paid envelope, and a fridge magnet that gave the Survey office freephone number. She was encouraged to use these to contact the office if she became pregnant. Additionally she was asked to provide written consent for her GP or local maternity hospital to notify the SWS team if she became pregnant.

Women who become pregnant are recruited into the pregnancy phase of the SWS. They visit the SWS Ultrasound Unit at the Princess Anne Hospital in Southampton at 11, 19, and 34 weeks gestation where fetal and placental size and blood

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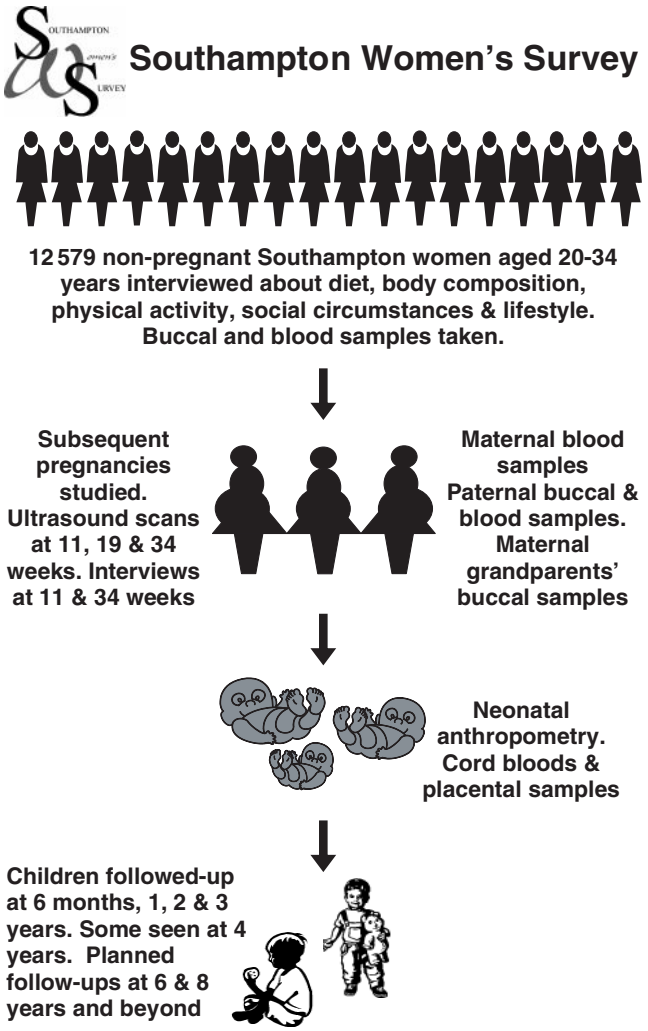

Figure 1 Schematic representation of the Southampton Women's Survey

flows are measured using ultrasound. At 11 and 34 weeks, the women are interviewed by research nurses, and anthropometric measurements of the baby are made within 48 h of birth. By the end of May 2005, 2567 babies had been born to SWS women.

The offspring are followed-up at home at 6 months, and 1, 2, and 3 years of age. At 4 years a sub-sample is seen for a DXA scan and cognitive function assessment. Plans are being developed to see the children at 6 and 8 years of age.

What has been measured?

Table 1 gives details of the types of information collected at each stage of the Survey.

The main focus of the interviews has been on diet and body composition. There is an additional interest in physical activity, social circumstances, and lifestyle. Data on allergies, atopy, and childhood illnesses are collected to enable examination of risk factors for asthma and atopy in the children. Skin prick testing is performed on the women when their children reach 1 year of age, and on the children at 1 and 3 years.

Diet is assessed at each stage of the SWS using administered food frequency questionnaires. A 100-item questionnaire was used to assess the diets of women before and during pregnancy. This questionnaire records the average intake of the listed foods over a 3 month period preceding the interview.[4] Three new food frequency questionnaires have been developed to assess the diet of the offspring at 6 months, 1 year, and 3 years of age. Additional dietary information is obtained in prospective records kept by the women before pregnancy and at 11 weeks gestation (24 h food diaries), on behalf of the children at 3 years of age (2 day diary), and retrospectively for the infants at 6 months of age (24 h recall). This open-ended information allows an examination of meal patterns and yields detailed information on the nature of foods eaten.

Body composition of the women and their children has been assessed by anthropometry. Regular studies to monitor inter-observer variation have been performed. At 11 and 34 weeks gestation, ultrasound is used to measure the women's heel bone density. Also during pregnancy, grip strength is assessed in the women and their partners. When the children reach 3 years of age, bioelectrical impedance is used to assess body composition, and their blood pressure is measured.

Venous blood samples were taken from the women following the initial interview (during the luteal phase of her menstrual cycle) and two samples are taken during pregnancy. One sample is taken from the woman's partner during her pregnancy. Urine samples were also collected from the women at the same time as the non-pregnant blood sample. Buccal samples obtained by mouthwash were collected from the women at initial interview and from the partners and parents of the women who become pregnant. Umbilical cord blood samples are collected at birth, and samples of the placenta and membranes are used for functional studies with biopsies stored for later morphometry and molecular analyses. The women's blood samples are analysed for red cell folate and a full blood count, and aliquots are stored at -80°C for later analysis. DNA is extracted from buccal and blood samples providing scope for genetic analyses of each woman, her baby, her baby's father, and her parents.

For subsets of the cohort, additional data have been collected. Part way through the initial recruitment of the women a depression component was incorporated into the study. Some 5513 women have completed the GHQ12[5] with an additional question about perceived financial strain. These women were also asked for their written consent to examine their medical notes for diagnoses of depression and treatment for it in the 2 years after the interview. This allows us to examine the relationship between incident depression and a variety of risk factors about which information was collected in the initial SWS recruitment interview.

For all women whose children are followed-up at 6 months of age, the Edinburgh Postnatal Depression questionnaire is administered. Using this we will examine the effects of the mother's sense of well-being on the child's growth and development and explore risk factors for low spirits in the post-partum period.

To study premenstrual syndrome we asked 1481 women in the SWS to complete a daily diary for 6 weeks recording their menstrual symptoms; 974 women completed these diaries. No previous study of premenstrual syndrome in the community has been conducted of this size, and this component of the SWS

Table 1 Data collected at each stage of the Southampton Women's Survey

	Pre-pregnant	11 weeks	19 weeks	34 weeks	Birth	6 month	1 year	2 year	3 year	4 year
Woman										
Occupation/employment	•			•	•		•	•		
Activity and exercise	•	•		•						
Food frequency questionnaire	•	•		•						
Prospective diet record	•	•								
Food supplements	•	•	•	•	•	•				
General diet questions	•									
Dietary changes		•								
Alcohol consumption	•	•		•						
Smoking	•	•		•		•		•		
General health	•					•		•		
Menstrual cycle and LMP	•	•								
Medications		•		•						
Pregnancies and illnesses		•								
Appetite and nausea		•		•						
Examination										
Body measurements	•	•		•		•				
Grip strength			•							
Heel ultrasound		•		•						
Skin prick testing							•			
Biological samples										
Buccal	•									
Blood	•	•		•						
Demographics/social										
Family background	•									
Education	•									
Ethnic group	•									
Marital status	•									
Housing	•							•		
Household heating						•		•		
Household composition	•							•		
Childcare arrangements	•							•		
Benefits	•							•		
Income/household/shopping								•		
Obstetrics										
Delivery/labour					•					
Obstetric history					•					
Family medical history					•					
BP/weights/urine analyses					•					
Pregnancy complications					•					
Woman's partner										
Asthma/eczema		•								
Height/weight/date of birth		•								
Occupation/employment	•	•						•		
Biological samples										
Blood			•							
Buccal			•							
Woman's parents										
Buccal samples			•							

Table 1 continued

	Pre-pregnant	11 weeks	19 weeks	34 weeks	Birth	6 month	1 year	2 year	3 year	4 year
Infant/Child										
Supplement use						•	•		•	•
Milk or formula feeding					•	•	•			
Food frequency questionnaire						•	•		•	•
24 h dietary recall						•				
Prospective food diary									•	
Introduction of foods						•	•			
(Dummy &) bottle use						•	•			
Eating behaviour/dietary restraint									•	
Illnesses						•	•	•	•	•
Antibiotics							•			
Skin conditions						•	•		•	
Allergies						•	•			
Sleeping arrangements						•	•	•		
Sleep/activity									•	
TV watching								•		
Physical activity									•	•
Immunizations									•	
Parenting									•	
Cognitive function										•
Examination										
Gender					•					
Fetal anthropometry		•	•	•						
Body measurements					•	•	•	•	•	•
Placental weight/appearance					•					
DXA scan					•					•
Skin examination						•	•			
Skin prick testing							•		•	
Dental eruption							•	•		
Blood pressure									•	
Bio-electrical impedance									•	
Grip strength										•
Biological samples										
Umbilical cord blood					•					
Umbilical cord					•					
Placenta and membranes					•					

enables us to link premenstrual symptoms to information on dietary and lifestyle factors that was collected at initial interview.

Women who become pregnant are allocated to be approached for one of two substudies. The general practices in the city were randomly linked to the two studies and women are allocated to a study on the basis of the general practice at which they are registered. Women in the first study, which is now complete, were asked if they would be willing for their babies to take part in a study of infant lung function at ~6 weeks of age. Women in the other study are asked if they are willing for their baby to undergo a DXA scan as soon as possible after birth for bone densitometry and body composition assessment. Some 150 infants successfully completed an infant lung function assessment, and 880 have had a DXA scan to date; children in this latter group are the focus for the 4 year DXA scans and cognitive function assessment.

Women who at initial interview said they anticipated trying for a baby within the next 12 months are being approached for a detailed study of protein metabolism before and during pregnancy. This builds on work showing that women with higher rates of protein turnover in pregnancy had longer babies.[6] The SWS provides an opportunity to recruit a group of women who are likely to become pregnant and to obtain longitudinal measures of protein metabolism before conception and during pregnancy, which can then be related to fetal development.

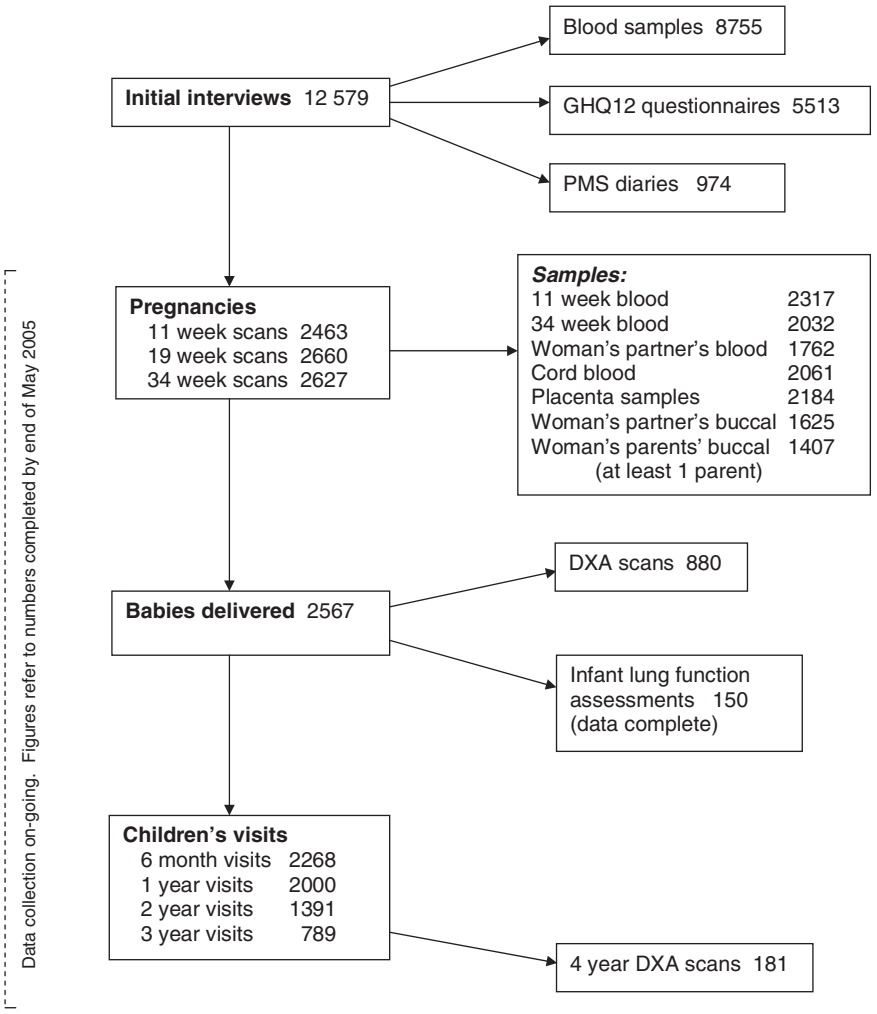

Figure 2 Progress with the Southampton Women's Survey

What is attrition like?

Of those women identified as becoming pregnant, 89% have agreed to be followed-up during pregnancy. To date, follow-up of the children of these pregnancies has been 95, 93, 86, and 81% at 6 months, 1, 2 and 3 years of age, respectively. Figure 2 shows the numbers of interviews and samples collected at each stage of the study and Figure 3 shows the evolution of the cohort in terms of the numbers of initial interviews, births, and children's follow-up interviews during each calendar year.

What has it found?

Data collection and analysis are ongoing and papers are currently in preparation. Analyses of fetal, placental, and infant growth are in progress. Some of the findings that have been published to date are summarized below.

Principal components analysis was used to examine the dietary data and the first principal component could be interpreted as a score of how 'prudent' the woman's diet was. This score was positively associated with the women's educational levels and the taking of strenuous exercise, but negatively associated with smoking, the amount of time spent watching television, and the number of children in the household.[7]

In a subset of the SWS, we found that fetuses of women who were slimmer before pregnancy and who had lower 'prudent' diet scores had greater liver blood flow at 36 weeks gestation, shunting less blood away from the liver through the ductus venosus. This diversion of the liver blood flow may contribute to the observed increase in risk factors for cardiovascular disease in people who were born to mothers with lower body fat stores in pregnancy.[8]

An assessment of the infant lung function data in relation to birthweight and change in weight over the first few weeks of life has shown that babies who are smaller at birth or who had high post-natal weight gain have poorer lung function.[9]

Analysis of the data on bone mass derived from the DXA scans has confirmed that maternal body composition, nutrition, and smoking are factors that influence bone development *in utero*. In addition, poor calcium and vitamin D status during pregnancy has been linked with excessive skeletal loss in the mother and impaired bone mineral accrual in the offspring. The pronounced seasonal variation in pregnancy bone loss supports vitamin D deficiency as an important contributor to materno-fetal calcium transport.[10]

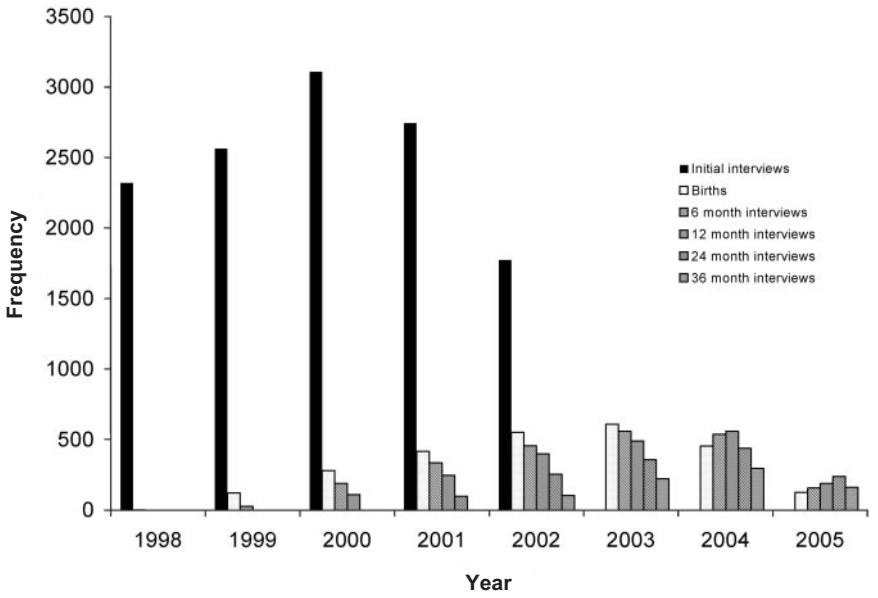

Figure 3 Numbers of initial interviews, births, and children's follow-up visits by calendar year
Note: Data collection commenced on April 6, 1998, initial interviews stopped after October 31, 2002, and all data for 2005 are until the end of May only.

What are the main strengths and weaknesses?

The most important feature of the SWS is that it has information collected on the women before conception. Women were recruited from the general population whether or not they were planning a pregnancy, making the study unique in the Western world. Another strength of the SWS is the detailed longitudinal measurements of fetal anthropometry, enabling derivation of rates of fetal growth in early, mid, and late pregnancy.

No single city can be truly representative of the general population. Southampton is in the more affluent southern part of England, but a comparison of the Townsend Indices of Deprivation[11] for the enumeration districts of Southampton with those for England and Wales shows Southampton to be somewhat more deprived than average. Approximately 94% of the population are white, somewhat higher than the figure of 88% for women aged 20–34 years in England and Wales in 2001[12]; 31% of SWS women were smokers at the time of the initial interview, compared with 33% of women aged 20–34 years in Britain[13]; 21% had university degrees, comparable with the findings from the Labour Force Survey of 22% for women of working age in England.[14]

A disadvantage of the study is that recruitment of pregnancies has necessarily been over a prolonged period (Figure 3). Many stages of the study are being conducted concurrently: pregnancy scanning and interviews, obstetric measurements, and all children follow-up interviews. Complete data on children at any specific age will not, therefore, be available until the entire cohort has reached that age.

Where can I find out more and what is the potential for collaboration?

Collaboration is encouraged but the data are still being collected and are not currently available for access by other researchers. The initial contact point for collaborations is Professor Cyrus Cooper (cc@mrc.soton.ac.uk). The SWS has a website, mainly focused on information for the participants of the Survey and the general public, at www.swsurvey.soton.ac.uk. Some information is also available on the website of the MRC Epidemiology Resource Centre at www.mrc.soton.ac.uk. Additionally, a freelance photographer spent a day with each of a group of SWS participants, photographing their lives to give a pictorial record to accompany the scientific findings. A selection of her photographs can be viewed at www.wellcome.ac.uk/en/magdasegal.

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