

BMJ Open

Evaluation of Health in Pregnancy grants in Scotland: a natural experiment

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-006547
Article Type:	Protocol
Date Submitted by the Author:	04-Sep-2014
Complete List of Authors:	Dundas, Ruth; University of Glasgow, MRC/CSO Social and Public Health Sciences Unit Ouédraogo, Samiratou; University of Glasgow, MRC/CSO Social and Public Health Sciences Unit Bond, Lyndal; Centre of Excellence in Intervention and Prevention Science, Briggs, Andrew; University of Glasgow, Health Economics & Health Technology Assessment Institute of Health & Wellbeing Chalmers, James; NHS National Services Scotland, Information Services Division Gray, Ron; University of Oxford, National Perinatal Epidemiology Unit Wood, Rachael; NHS National Services Scotland, Information Services Division Leyland, Alastair; University of Glasgow, MRC/CSO Social and Public Health Sciences Unit
Primary Subject Heading:	Health policy
Secondary Subject Heading:	Epidemiology, Public health, Health economics, Research methods
Keywords:	EPIDEMIOLOGY, Reproductive medicine < GYNAECOLOGY, HEALTH ECONOMICS, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, NEONATOLOGY, Maternal medicine < OBSTETRICS

SCHOLARONE™
Manuscripts

PROJECT PROTOCOL

Title: Evaluation of Health in Pregnancy grants in Scotland: a natural experiment

Authors: Ruth Dundas¹, Samiratou Ouédraogo¹, Lyndal Bond², Andrew H Briggs³, James Chalmers⁴, Ron Gray⁵, Rachael Wood⁴, Alastair H Leyland¹

Affiliations:

¹ MRC/CSO Social and Public Health Sciences Unit, University of Glasgow, Glasgow, UK

² Centre of Excellence in Intervention and Prevention Science, Melbourne, Australia

³ Health Economics and Health Technology Assessment, University of Glasgow, Glasgow, UK

⁴ Information Services Division, NHS National Services Scotland, Edinburgh, UK

⁵ National Perinatal Epidemiology Unit, University of Oxford, UK

Correspondence to:

Ruth Dundas

MRC/CSO Social and Public Health Sciences Unit, University of Glasgow

200 Renfield Street, Glasgow G2 3QB, Scotland

Tel: +44 141 353 7541 Email: ruth.dundas@glasgow.ac.uk

Keywords: Low birthweight; interrupted time series; multilevel analysis; Health in Pregnancy grant; natural experiment.

ABSTRACT

Introduction

A substantial proportion of low birthweight (LBW) is attributable to the mother's cultural and socioeconomic circumstances. Early childhood programmes have been widely developed to improve child outcomes. In the UK, the Health in Pregnancy (HiP) grant, a universal conditional cash transfer of £190, was introduced for women reaching the 25th week of pregnancy with a due date on/or after 6th April 2009 and subsequently withdrawn for women reaching the 25th week of pregnancy on/or after 1st January 2011. The current study focuses on the evaluation of the effectiveness and cost-effectiveness of the HiP grant.

Methods and analysis

The population under study will be all singleton births in Scotland over the periods of January 2004 to March 2009 (pre-intervention), April 2009 to April 2011 (intervention) and May 2011 to December 2013 (post-intervention). Data will be extracted from the Scottish maternity and neonatal database. The analysis period 2004-2013 should yield over 585,000 births. The primary outcome will be birthweight among singleton births. Other secondary outcomes will include gestation at booking, booking before 25 weeks; measures of size and stage; gestational age at delivery; weight-for-dates, term at birth; birth outcomes and maternal smoking. The main statistical method we will use is interrupted time series. Outcomes will be measured on individual births nested within mothers, with mothers themselves clustered within datazones. Multilevel regression models will be used to determine whether the outcomes changed during the period in which the HiP grants was in effect. Subgroup analyses will be conducted for those groups most likely to benefit from the payments.

Ethics and dissemination

Approval for data collection, storage and release for research purpose has been given (6th of May 2014, PAC38A/13) by the Privacy Advisory Committee. The results of this study will be disseminated through peer-reviewed publications in journals, national and international conferences.

ARTICLE SUMMARY

Article focus

- To evaluate the effectiveness and cost-effectiveness of Health in Pregnancy grant (HiP) in Scotland.

Key messages

- We will assess the difference in birthweight for babies born to those mothers who were eligible for the HiP grant with babies born before the HiP grant was introduced or after it was withdrawn using interrupted time series multilevel analysis.
- Subgroup analyses will be conducted for those groups seen as having the greatest potential to benefit from the payments such as those living in the most deprived areas, those in the lowest social classes, lone mothers, primiparous women, teen mothers, mothers from ethnic minorities and selected combinations of these groups.
- As part of the project an economic model will be developed based on a review of the literature to relate birthweight changes to long-term cost and health outcomes (in terms of QALYs).

Strengths and limitations of this study

The strengths of this study are:

- This is the first study evaluating the effect and the cost-effectiveness of the HiP grant in Scotland. It will use routinely available vital event and maternal and neonatal health records that are known to have high completeness and accuracy.
- The evaluation of the HiP grant using an interrupted time series design will enable us to analyse birthweight trends in Scotland and detect whether the intervention has had an effect over and above the underlying temporal trend. The use of interrupted time series will overcome other biases such as the autocorrelation of repeated measurements (measurement taken close together are related), seasonal effects (birthweight varies according to month of birth), the duration of the intervention (we will have pre-intervention intervention and post-intervention), and random variation in the measurement (birthweight).

The limitations of this study

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47
- 48
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60
- This study will evaluate the effect and the cost-effectiveness of the HiP grant, birthweight and other birth outcomes in Scotland using obstetric as well as maternal data. However, these outcomes may be influenced by many factors, not all of which are routinely captured (such as maternal diet, maternal work and psychological stress, abuse, exposure to toxic substance).¹¹
- The HiP grant was money given to pregnant women with no constraint on its use. The use of routine data gives us no indication on how the money was spent.

INTRODUCTION

Low birthweight (LBW) due to preterm birth, intrauterine growth restriction, or being born small for gestational age (SGA), is commonly associated with perinatal mortality and impaired development¹⁻¹¹. Despite the improvement of the mortality in LBW babies over the past three decades, more than 70% of all neonatal mortality in Europe is found in infants weighing less than 2500 grams (g).¹²

LBW refers to birth weights below 2500 g,¹³ irrespective of the gestational age of the infant. In most developed countries, the prevalence of LBW has increased due to several reasons: the number of multiple births with the increased risks of pre-term births and low birth weight partly as a result of the rise in fertility treatments; older age at childbearing and increases in the use of delivery management techniques such as induction of labour and caesarean delivery, which have increased the survival rates of low birth weight babies.¹⁴ About one in 20 babies born in Europe in 2010 weighed less than 2500 g at birth.¹² With LBW estimated at 7.0% of live births in England and Wales, 6.5% in Scotland and 5.7% of live births in Northern Ireland, prevalence of LBW in the countries of the United Kingdom (UK) tended to be higher than in the rest of Europe.^{12 15} Moreover, compared with other Western European countries, the UK has an incidence of LBW (<2500g) and very LBW (<1500g) in the top third. The proportion of pre-term birth (<37 weeks) is also high compared with other Western European countries.

Considerable attention has been focused on the causal determinants of LBW, in order to identify potentially modifiable factors. A substantial proportion of LBW is attributable to the mother's cultural and socioeconomic circumstances such as socioeconomic status (SES), harmful behaviours (smoking and excessive alcohol consumption) and poor nutrition during pregnancy.^{11 16-18} In a study of social class inequalities in perinatal outcomes in Scotland, Fairley and Leyland¹⁹ reported a percentage of 5.8% LBW in unskilled social class (V) compared to 2.9% in professional social class (I) between 1995 and 2000. The systematic review and meta-analyses of social inequality and infant health in the UK performed by Weightman et al.²⁰ found that the odds ratio for low birth weight was 1.79 (95% CI 1.43 to 2.24) in the lowest compared to the highest social class. This effect may vary with maternal factors such as age and smoking status. Smoking during pregnancy reduces birthweight by 162 to 377 g, depending on daily consumption (larger reduction for heavy smokers) and the trimester in which exposure occurs (larger reduction during the last trimester).^{18 21-22}

1
2
3 The association between maternal nutrition and birth outcome is complex and is influenced
4 by many biologic, socioeconomic, and demographic factors, which vary widely in different
5 populations.²³⁻²⁴ However, it has been reported that favourable prenatal nutrition associated
6 with adequate prenatal care can have a positive impact on birth outcomes and morbidity in
7 adult life.²⁵⁻²⁶ Indeed, the developmental model of the origins of chronic disease proposes the
8 causal influence of undernutrition *in utero* on coronary heart disease and stroke in adult life.⁷⁻
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

9 An improvement in fetal nutrition may therefore have far reaching consequences in terms of
the prevention of disease. A review of maternal nutrition and birth outcomes identified
improving maternal nutrition as being beneficial to the prevention of adverse birth outcomes
in lower social class groups.²⁴
A number of early childhood programmes have been developed to improve child outcomes.
There is mixed evidence that these programmes do provide such improvement. In a meta-
analysis of the effect of interventions in pregnancy on maternal and obstetric outcomes,
Thangaratinam et al. concluded that dietary and lifestyle interventions in pregnancy reduced
maternal gestational weight gain but had less effect on outcomes related to fetal weight and
other morbidity and mortality.²⁷ Glassman et al.²⁸ who reported the results of conditional cash
transfer programmes increasingly being adopted and scaled in developing countries, found
that the programmes have increased the uptake of maternal and newborn health services,
especially skilled attendance at delivery and antenatal monitoring. However, the impact of the
programs on maternal and newborn mortality has not been well documented. Therefore, they
recommended more rigorous impact evaluations that document impact pathways and take
factors, such as cost-effectiveness, into account. Other studies evaluating payments to
influence health behaviour found financial incentives were effective in increasing infrequent
behaviours such as attending clinic appointments particularly in low-income groups, and
recommended payments as being more effective than information and less restrictive than
legislation.²⁹⁻³¹ In Canada, Brownell et al. have evaluated a complex programme on a prenatal
benefit provided to families on low income during pregnancy.³² They found that the receipt
of this prenatal benefit was associated with a reduction in incidence of both low birthweight
babies and preterm births. They suggested that efforts should be made to ensure all low-
income women receive the income supplement.

In the UK, the Health in Pregnancy (HiP) grant was introduced for women reaching the 25th
week of pregnancy with a due date on/or after 6th April 2009. It was subsequently withdrawn
for women reaching the 25th week of pregnancy on/or after 1st January 2011. The HiP grant

1
2
3 was a universal conditional cash transfer of £190 for women reaching 25 weeks of pregnancy
4 if they had sought health advice from a doctor or midwife. It was designed to provide
5 additional financial support, in the last months of pregnancy, towards a healthy lifestyle
6 including diet, and it was suggested that the link to the requirement for pregnant women to
7 seek health advice from a professional may provide a greater incentive for expectant mothers
8 to seek the recommended health advice at the appropriate time. The grant was paid and
9 administered by Her Majesty's Revenue and Customs (HMRC) on receipt of a claim form
10 partly completed by the midwife or doctor. Advice was offered as normal by doctors and
11 midwives. Payment was made directly into a bank account with a telephone helpline
12 available to provide support through the claims process including options for payment in the
13 event of difficulties opening a bank account. Take up of the grant was said to be about the
14 same level as for child benefit (98-99%, personal communication, HMRC).

15
16
17
18
19
20
21
22 The current study focuses on the evaluation of the effectiveness and cost-effectiveness of the
23 HiP grant. As a primary outcome, we will consider the difference in birthweight for babies
24 born to those mothers who were eligible for the HiP grant with babies born before the HiP
25 grant was introduced or after it was withdrawn. Specific questions the research project will
26 address are:
27
28
29
30

- 31
32
33
34
35
36
37
38
39
40
41
42
43
- Were there differential impacts of the intervention for particular subgroups defined by socioeconomic (defined in terms of both area deprivation and individual occupational social class), demographic (marital status, age, maternal height), or obstetric (parity, previous caesarean section) factors or for selected combination of these groups?
 - Was the HiP grant cost-effective? How did cost-effectiveness vary across important subgroups identified as having differential outcomes?

44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The principle of universalism in the allocation of social benefits, that is the availability of social benefits to everyone as of right, is contrasted with allocation on a selective basis (targeted) in which benefits are allocated on the basis of need as determined by means testing of income.³³ The advantage of universal benefits is that they are easy to administer and can be efficiently delivered. The major disadvantage is that they are expensive, because they are delivered to those who do not need them as much as to those who do. However, the use of targeting involves some mechanism that discriminates between the poor and the non-poor. As such it always runs the danger of committing either type I errors which occur when someone

1
2
3 who deserves the benefits is denied them (underpayment, false positives), or type II errors,
4 which occur when benefits are paid to someone who does not deserve them (overpayment,
5 leakage).³⁴ The HiP grant represented an attempt to influence behaviour – appropriate and
6 timely receipt of antenatal care advice – by means of a relatively modest, universally applied
7 cash transfer. The evaluation of the effectiveness of such a payment may inform other
8 policies aiming to change behaviour.
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

METHODS AND ANALYSIS

Study design

The HiP grant will be evaluated as a natural experiment using interrupted time series analysis to compare outcomes before the introduction of the intervention in Scotland and immediately after its withdrawal with those during the period for which it existed.

The Medical Research Council (MRC) has issued guidelines regarding the use of natural experiments to evaluate population health interventions when exposure to the intervention has not been manipulated by the researchers (Table 1).³⁵⁻³⁶

Table 1: Guidance for use of natural experiments to evaluate population health interventions

When to use a natural experimental approach?	How does the evaluation of HiP* grant meet these criteria?
<ul style="list-style-type: none"> ▪ There is a reasonable expectation that the intervention will have a significant health impact, but scientific uncertainty about the size or nature of the effects. 	<ul style="list-style-type: none"> ▪ The HiP grant represented an attempt to influence behaviour – appropriate and timely receipt of antenatal care advice. With the sample size we are using in this evaluation study, we are able to detect small changes in birthweight.
<ul style="list-style-type: none"> ▪ Natural experimental study is the most appropriate method for studying a given type of intervention. 	<ul style="list-style-type: none"> ▪ The HiP grant was a universally applied cash transfer available for all pregnant women with no discrimination between socioeconomic classes. This policy was not introduced using a randomised allocation
<ul style="list-style-type: none"> ▪ It is possible to obtain the relevant data from an appropriate study population, comprising groups with different levels of exposure to the intervention. 	<ul style="list-style-type: none"> ▪ The uptake of the HiP grant was thought to be 98-99%. The linked Scottish birth dataset has 98% coverage of births and the primary outcome, birthweight, is well measured, 99.9% complete and accurate. Exposure is determined by the dates for which the HiP grant was in existence.
<ul style="list-style-type: none"> ▪ The intervention or the principles behind it have the potential for replication, scalability or generalisability. 	<ul style="list-style-type: none"> ▪ The HiP grant is replicable everywhere in countries with similar health systems.

HiP* grant: Health in Pregnancy grant

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The guidance advocates a number of designs including regression discontinuity designs such as interrupted time series. The interrupted time series approach is a powerful tool used for evaluating the impact of a policy change or quality improvement programme on the rate of an outcome in a defined population of individuals.³⁷⁻³⁹ This approach will allow us to use a comparison group of pregnant women who delivered before the HiP grant was introduced, an intervention group who received the HiP grant and an additional post-intervention group who delivered after the HiP grant was withdrawn. It will also allow adjustment for seasonality, temporal trends and the socio-demographic and obstetric characteristics of the mother.

Study population

The population under study will be all singleton births in Scotland over the periods of January 2004 to March 2009 (pre-intervention), April 2009 to April 2011 (intervention) and May 2011 to December 2013 (post-intervention).

The Scottish maternity and neonatal database is a comprehensive record linkage system. Probabilistic linkage procedures are used to add a unique identifier to all datasets to ensure all relevant records relating to an individual can be linked as required. It facilitates the linkage of a number of records from the system of Scottish Morbidity Records (SMR) including mother's obstetric records (SMR02) and the baby's birth and neonatal information from Scottish Birth Records (SBR). Further links to the stillbirth and infant Death Survey and the National Records of Scotland (NRS) birth, stillbirth and infant death records can be carried out. The coverage is almost all births in Scotland. From NRS data, we know of all registered births in Scotland (ie 100%). We have suitable record linked data on 98% of these births. These will nearly all be hospital births; a fairly high proportion of the missing records are home births.

There is an average of about 56,000 births per year in Scotland. The analysis period 2004-2013 should yield over 585,000 births. The analysis period 2006-2013 should yield over 455,000 births.

We have chosen to use data from the Scotland for this evaluation for the following reasons. First, data are available at a national level on the approximately 56,000 deliveries per year. Second, Scotland has a long history of collecting high quality routine data; the coverage, completeness and quality of the data are considered to be very high. Third, the concentration of deprivation within parts of Scotland is unique within the UK. For example six of the ten most deprived electoral constituencies in the UK are in Scotland and using a UK wide Cartstairs index, the Scotland's population is over-represented in the bottom 5 deciles compared to England. Fourth, data on smoking at booking have been routinely recorded in Scotland for a number of years. This is not yet the case in England and Wales. The data can be linked to NRS civil registration data, which provides an estimate of completeness and contributes further information such as social class. The results will be generalisable to the rest of the UK and internationally. If the HiP grant proved beneficial in Scotland then there is every good reason to believe that a similar impact on outcomes could be achieved elsewhere and certainly in countries with similar health systems and comparable circumstances. Likewise, if the intervention was found to have been more effective for specific subgroups then we might expect subgroups to show greater benefits in other settings.

Study variables

Individual level and area level variables will be used in this study.

Individual level variables will include: birthweight, date of birth, sex, gestational age at delivery, preterm (delivery before the 37th week of pregnancy), weight-for-dates, 5 min Apgar score, crown to heel length, and head circumference. We will distinguish between spontaneous pre-term births and induced pre-term births. A potential reason for induced pre-term births is evidence of poor fetal growth; a proportion of these babies would become more severely growth retarded (more extremely small for gestational age) or stillborn.

Since maternal factors influence fetal growth,¹¹ individual level variables related to the mother will be examined: parity, age, height, weight at booking, diabetes, smoking status, gestation at booking, booking before 25 weeks, and marital status. Individual socioeconomic position will also be included using data from the birth registrations at NRS. NRS collects occupation for both father and mother for births registered to married couples and jointly

1
2
3 registered by unmarried couples. Only mother's occupation is recorded for sole registered
4 births. The National Statistics Socio-economic Classification (NS-SEC)⁴⁰ will be used to
5 classify the individual socioeconomic position.
6
7

8
9 Marital status is an important variable as single mothers have consistently been shown to
10 have poorer birth outcomes.^{17 19} We are particularly interested in single mothers and social
11 class. Social class for lone mothers is an amalgamation of socioeconomic position and lone
12 parenthood.
13
14

15
16 Although the routinely collected data on ethnicity are incomplete and of dubious quality,
17 ethnicity remains important for birthweight and other neonatal outcomes.⁴¹⁻⁴² We will
18 therefore, within the constraints of the data, include ethnicity and undertake all analyses on
19 the subgroup of mother from a minority ethnic background. Within this subgroup, we will
20 examine the possibility of further distinction between ethnic groups.
21
22
23

24
25 Birthweight varies according to the socioeconomic status of the area of residence.²⁰ The
26 Scottish Index of Multiple Deprivation (SIMD) will be used and included as area level
27 variables in the analysis. The SIMD is the Scottish Government's official tool for identifying
28 those places in Scotland suffering from deprivation.⁴³ It is a weighted sum of different
29 domains: income; employment; health; education; housing and geographical access (and
30 crime, added in the SIMD 2012). The SIMD provides a comprehensive picture of material
31 deprivation in small areas within Scotland. The index ranks 6505 areas from the most
32 deprived to the least deprived and measures the degree of deprivation of an area relative to
33 that of other areas. The areas employed by the SIMD are datazones and are small: the 6505
34 datazones have a mean population of 780 people. The reason for employing small area
35 geography at this scale is to permit identification of relatively small pockets of deprivation.
36 The health domain includes an indicator of the proportion of live singleton births that is
37 LBW. The outcomes of this project include birthweight and LBW and so it would not be
38 appropriate to use the health domain or the composite index which includes the health
39 domain. The income domain will therefore be used to assess inequalities at the area level.
40 This domain contributes 28% to the overall index and is highly correlated with the overall
41 SIMD. The income domain of the SIMD identifies areas where there are concentrations of
42 individuals and families living on low incomes. This is done by looking at the numbers of
43 people, both adult and children, who are receiving, or are dependent on, benefits related to
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 income or tax credits. Each mother will be assigned to a datazone and its income domain
4 through her home postcode. Previous studies investigating inequalities in birthweight have
5 shown that area deprivation performs as well as or better than individual social class in
6 describing the extent of inequalities in the population.⁴⁴⁻⁴⁵ However, Fairley et al. who
7 studied the influence of both individual and area based socioeconomic status on temporal
8 trends in Caesarean sections between 1980 and 2000 in Scotland found that maternal social
9 class and area deprivation are different indicators of socioeconomic status which exhibit
10 independent effects on the probability of a woman receiving a Caesarean section.⁴⁶ The
11 multilevel analysis will allow us to analyse the effect of both parental social class and SMID
12 and the effect of their interaction on birthweight.

13 We will adjust the analyses on the urban or rural status of the mother's area of residence.
14 Indeed, Kent et al reported higher adverse birth outcome rates in isolated rural and more
15 population dense areas.⁴⁷ They showed that these disparities are being maintained or
16 increasing over time in Alabama. Shankardass et al also found that the patterns of association
17 between socioeconomic position and LGA, spontaneous preterm birth and perinatal death
18 varied depending on urbanicity in Nova Scotia (Canada).⁴⁸

31 Outcome measures

32 Primary Outcome

33 The primary outcome will be birthweight among singleton births. This is influenced by many
34 factors including maternal nutrition and one of the intentions of the HiP grant was to improve
35 this.

36 Secondary Outcomes

37 The following secondary outcomes will be assessed:

- 38 - Gestation at booking,
- 39 - Booking before 25 weeks,
- 40 - Measures of size: crown to heel length, head circumference,
- 41 - Measures of stage: gestational age at delivery, weight-for-dates (standardised; small
42 for gestational age babies are those weighted less than the 5th centile weight, or large

1
2
3 for gestational age weighted more than the 90th centile weight), term at birth (pre-
4 term, babies are born at less than 37 weeks gestation; term babies are those born
5 between 37-42 weeks gestation and post-term babies are born after 42 weeks
6 gestation),
7
8

- 9
10 - Birth outcomes: mode of delivery, stillbirths, neonatal deaths, 5 minutes Apgar score.
11 Although there is some debate concerning the robustness of the Apgar score as an
12 outcome, it is in common use and we will therefore present results for this outcome
13 within the context of the wide debate on the subject.
14
15
16

17
18 Due in part to the introduction of smoking ban in Scotland in 2006, an additional outcome of
19 interest is maternal smoking. Maternal smoking is collected at booking and during pregnancy.
20 The health advice given when receiving the HiP grant might have an impact on smoking rates
21 during pregnancy over and above that of the smoke-free legislation. We will analyse the
22 temporal change in smoking rate by socioeconomic class and its effect on outcomes.
23
24
25
26
27
28

29 **Sample size**

30
31 The data are clustered in small areas, 6505 datazones. The sample size calculation takes this
32 clustering into account. Assuming an average of 56,000 singleton live births per year, and
33 allowing for the clustering within the 6505 datazones in Scotland (average population 780 per
34 datazone) with an estimated intraclass correlation coefficient of 0.05, we have power of 0.90
35 to detect an effect of 7g change in birthweight at a 95% significance level. This is not to say
36 that 7g is a clinically important threshold; rather, it is indicative of the power of the study.
37 The large national data set available to us will allow for subgroup analysis. In the 20% most
38 deprived areas, we will have power of 0.80 to detect an effect of 13g; among the 26% of
39 single mothers, we will have power of 0.80 to detect an effect of 11g. To put these small
40 effects into context, 50g is the estimated mean birthweight reduction reported in the meta-
41 analysis of the effect of interventions in pregnancy on maternal and obstetric outcomes.²⁷
42
43
44
45
46
47
48
49

50
51 We anticipate item non-response for some outcomes and explanatory variables. Our primary
52 outcome measure, birthweight, has a completion rate of 99.9%. There is high completion rate
53 (<1.5% missing) for all obstetric variables, with the exception of crown to heel length (15%
54 missing) and head circumference (12% missing). The item non-response ranges from 8% for
55
56
57
58
59
60

maternal smoking to 20% for marital status. We will use multiple imputation to account for missing data and all analyses will compare the results of analyses of complete cases and multiple imputation. Imputed models will be constructed such that they contain as many relevant predictor variables as possible. The more variables that are used the greater the amount of information available on which estimations are made. We will use all (or as many as possible) obstetric and maternal variables in an imputation model to predict the missing values. It is difficult to identify in advance the number of multiple imputed datasets we will need to construct but it is likely to be between 5 and 10. We will then analyse these datasets identically and combine the results to get the estimates and standard errors for the multiple imputed data. These results will be compared to the complete case analysis results.

It is difficult to be specific about the missing data mechanism until we see the data but much is likely to be missing completely at random (MCAR, e.g. certain hospitals are less likely to collect specific items) or missing at random (MAR, when the missingness is related to known variables and, conditional on these, is assumed to be unrelated to unmeasured variables).

Data analysis plan

Statistical analysis

Descriptive statistics of all variables will be presented as mean, standard deviation, minimum, median and maximum for continuous variables and as proportions when the variables are categorical.

The main statistical design we will use is interrupted time series. Segmented regression analysis will allow an estimation of the size of the effect of the HiP grant at different time points, as well as changes in the trend of the effect over time after its implementation.

Outcomes will be measured on individual births, which are nested within mothers, with mothers themselves clustered within datazones and Health Boards. Multilevel univariable and multivariable models will be used to determine whether the outcomes changed during the period in which the HiP grants were in effect. Multilevel linear regression will be used when the outcome is continuous and multilevel binomial logistic regression when the outcome is dichotomous. Multilevel multinomial logistic regression will be used for the multi-category outcomes mode of delivery and 5 minutes Apgar score.

1
2
3 All analyses will be adjusted for temporal trends and seasonal variations in outcomes in
4 addition to maternal age, sex of child, parity, marital status, height, weight at booking,
5 diabetes, smoking status, gestation at booking, maternal diabetes, social class, maternal
6 smoking and area deprivation.
7
8

9
10 The effect of HiP grant on birthweight might have a carryover effect after the withdrawal of
11 the grant. In other words, post-intervention the slope in birthweight might not fall back to the
12 same rate as pre-intervention. This could be due to women who have given birth during the
13 intervention subsequently having a birth postintervention but still heeding the health advice
14 given during their first pregnancy. We will carry out an additional analysis only on
15 primiparous women to avoid such contamination.
16
17

18 We will analyse pre-term births stratified by mode of delivery and stratified according to
19 whether the birth was induced or spontaneous.
20

21 We will repeat the main analyses including (i.e adjusting for the effect of) ethnicity along
22 with other covariates and compare the results with analyses excluding ethnicity to gauge the
23 impact of this on our results. We note that the quality of this variable (including the
24 completeness of recording) is poorer than for other variables and that only 1-2% of mothers
25 delivering in Scotland are from minority ethnic backgrounds.
26
27

28 The simplest model for the intervention effect will include a dummy variable “intervention”
29 covering the period from the introduction to the withdrawal of HiP grants, with adjustment
30 for relevant factors such as marital status. (More complex models of the effect of the
31 intervention will include an interaction of the intervention with the temporal trend). Before
32 carrying out specific subgroup analysis, we will identify differential effects by fitting
33 interaction terms. An assessment as to whether there is a differential effect of the intervention
34 for single women, for example, will involve a test of the significance of the intervention
35 between marital status and the intervention effect. If the interaction is significant this will aid
36 our understanding of the generalisability to other populations, including the rest of the UK.
37 Subgroup analyses will be conducted for those groups seen as having the greatest potential to
38 benefit from the payments such as those living in the most deprived areas, those in the lowest
39 social classes, lone mothers, primiparous women, teen mothers, mothers from ethnic
40 minorities and selected combinations of these groups. For each group we will replicate the
41 main analysis. This reduction in sample size for sub-group analyses will result in fewer
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 women/births being available but the same number of areas (datazones) will be analysed
4 (apart from analyses restricted to those living in the most deprived areas).
5
6

7 An increase in birthweight, although desirable at a population level, may not be a beneficial
8 outcome if the baby were already at risk of being large for gestational age (LGA). Separate
9 subgroup analyses will therefore be conducted for women seen to be at high risk of delivering
10 a LGA baby (women with diabetes) and for the remainder of the population. Given that some
11 subgroups may contain small numbers, and bearing in mind the potential importance of the
12 intervention, we will report the results of all subgroup analyses and not just those that reach
13 statistical significance to avoid false negatives. The above process will involve conducting
14 many tests, which will not be independent of each other. Rather than adjusting confidence
15 intervals or p-values to account for this we will present the results of all analyses and caution
16 the user regarding the interpretation of the results. Indeed, some statisticians recommend
17 never correcting for multiple comparisons while analyzing data.⁴⁹⁻⁵⁰ According to Rothman,⁴⁹
18 reducing the type I error for null associations increases the type II error for those associations
19 that are not null. He recommends a policy of not making adjustments for multiple
20 comparisons because it will lead to fewer errors of interpretation when the data under
21 evaluation are not random numbers but actual observations on nature.
22
23
24
25
26
27
28
29
30
31
32

33 The HiP grant was introduced and withdrawn at the same time as other interventions that may
34 have an impact on birthweight. Healthy Start is a means tested voucher scheme for pregnant
35 women. If they are in receipt of certain benefits or under 18 years old, then they are eligible
36 for free vitamins and vouchers to be spent on fruits and vegetables. This scheme replaced the
37 means tested parts of the Welfare Food Scheme in the UK (including Scotland in 2006) and is
38 still currently in place. During this period, there were policy changes in the optimal timing of
39 first booking appointments due to changes in blood tests offered to pregnant women in the
40 Pregnancy Screening Programme. These changes were first discussed in 2008 and had to be
41 implemented by all Health Boards by March 2011.⁵¹⁻⁵² Early booking is a HEAT target of the
42 Scottish Government (Health improvement for the people of Scotland Efficiency and
43 governance improvements, Access to services, Treatment appropriate to individuals H11.1).
44 At least 80% of pregnant women in each SIMD quintile will have booked for antenatal care
45 by the 12th week of gestation by March 2015.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 A further piece of legislation that may affect birthweight is the introduction of the smoking
4 ban in public places in Scotland in March 2006. Mackay et al⁵³ reported a reduction in the
5 prevalence of current smoking among women who conceived after the introduction of the
6 legislation prohibiting smoking. They also reported a reduction in small and very small for
7 gestational age, as well as in absolute low birth weight after the legislation. We will carry out
8 a further analysis restricting the pre-intervention HiP grant period to April 2006-March 2009.
9

10
11
12 It is possible that harm may have occurred due to the cash transfer. The £190 was given to
13 pregnant women with no restriction as to how it should be spent, and we do not know how
14 the money was used. We are examining how the intervention group differed; birthweight
15 could have reduced or increased. We will carry out 2-sided hypothesis tests to ensure that we
16 are able to detect any such potential harmful effect.
17

18
19 We will conduct sensitivity analyses to increase the probability that any observed effect can
20 be attributed to the HiP grant. The timing of the HiP grant is well defined and fixed, therefore
21 using the interrupted time series approach any effects within that window can be observed.
22

23 We plan to carry out 3 analyses for this.

- 24 1- We will extend this window for some months before April 2009 (births before the HiP
25 grant was introduced).
- 26 2- We will extend this window for some months after April 2011 (births after the HiP
27 grant was withdrawn).
- 28 3- We will extend the window both before and after the HiP grant period. In each case
29 we would expect to see a dilution of any effects of the HiP grant.
30

31
32 The statistical analysis plan detailing the outcomes and the covariates, which will be
33 considered for adjustment in the statistical models are presented in table 2.
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 2: Analysis plan detailing the outcomes and the covariates that will be considered for adjustment in the statistical models

Primary outcome	Secondary outcomes											Maternal smoking during this pregnancy
	Booking status			Measures of stage			Measures of size		Other birth outcomes			
	Birth-weight	Gestation at booking	Booking before 25 weeks	Gestational age at delivery	Term at birth	Weight-for-dates	Head circumference Crown to heel length	Mode of delivery	Still-birth	5 minutes Apgar score	Neonatal death	
Covariates												
I- Measured covariates												
A- Socio-demographic determinants												
A-1. Related to the baby												
Date of birth	X	X	X	X	X	X	X	X	X	X	X	X
Sex	X			X	X	X	X	X	X	X	X	
Gestational age at delivery	X						X	X	X	X	X	
Birthweight							X			X	X	
Mode of delivery										X	X	
A-2. Related to the mother												
Hip grant	X	X	X	X	X	X	X	X	X	X	X	X
Age	X	X	X	X	X	X	X	X	X	X	X	X
Weight at booking	X	X	X	X	X	X	X	X	X	X	X	
Height	X			X	X	X	X	X	X	X	X	
Ethnic group	X	X	X	X	X	X	X	X	X	X	X	X

Parity	X	X	X	X	X	X	X	X	X	X	X	X
Marital status	X	X	X	X	X	X	X	X	X	X	X	X
Social class	X	X	X	X	X	X	X	X	X	X	X	X
B- Medical risks of the current pregnancy and before pregnancy												
Diabetes	X	X	X	X	X	X	X	X	X	X	X	X
Hypertension	X	X	X	X	X	X	X	X	X	X	X	X
Infection	X			X	X	X	X	X	X	X	X	X
Congenital anomalies	X			X	X	X	X	X	X	X	X	X
Induction of labour									X	X	X	
Duration of labour									X	X	X	
C- Medical risks related to previous pregnancies												
Previous spontaneous abortions		X	X						X			
Previous stillbirths		X	X						X			
Previous neonatal deaths		X	X								X	
D- Environmental and behavioural risks												
Income domain of the SIMD	X	X	X	X	X	X	X	X	X	X	X	X
Urban/rural status of the area of residence	X	X	X	X	X	X	X	X	X	X	X	X
Booking status (gestational age at booking, booking before 25 weeks)	X			X	X	X	X	X	X	X	X	X

1													
2													
3													
4													
5	Smoking status												
6	(Before and												
7	during												
8	pregnancy)	X	X	X	X	X	X	X	X	X	X	X	
9	Typical weekly												
10	alcohol												
11	consumption												
12	(Before and												
13	during												
14	pregnancy)	X	X	X	X	X	X	X	X	X	X	X	X
15	Drug misuse												
16	during this												
17	pregnancy	X	X	X	X	X	X	X	X	X	X	X	X
18													
19	II- Unmeasured covariates												
20	Maternal weight gain												
21	Maternal nutrition												
22	Maternal education												
23	Maternal exposure to stress												
24	Maternal physical activity												
25	Exposure to toxic substances												
26	Birth interval												
27	History of pre-term birth												
28													
29													
30	Statistical methods												
31	Multilevel linear												
32	regression	X	X		X			X					
33	Multilevel binomial												
34	logistic regression			X			X		X		X		X
35	Multilevel multinomial												
36	logistic regression					X		X		X			
37													
38													
39													
40													
41													21
42													
43													
44													
45													
46													
47													
48													
49													

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

X: variables which will be considered for adjustment in the statistical analysis

For peer review only

Economic analysis

The cost-effectiveness analysis will be based around relating the estimated cost of the intervention (£190 for HiP grant plus the costs of administering the grant) to the observed benefits of the programme (birthweight changes and changes in secondary endpoints such as stillbirths) from the natural experiment. As part of the project an economic model will be developed based on a review of the literature to relate birthweight changes (and any secondary outcomes affected by the HiP grant identified in this study) to long-term cost and health outcomes (in terms of QALYs). Other potential outcomes (such as the effect of birthweight on long term educational outcomes) will be summarised, but may not be included in the cost-per-QALY analysis. The review will inform only the relationship between birthweight and long-term outcomes, the effectiveness of the HiP grant will be taken only from the current study.

The perspective taken will be that of the UK National Health Service in the first instance. For this particular intervention it will be important to consider two further perspectives: the broader Public Sector (due to the relationship between LBW and social care/educational development), and society as whole (since the HiP grant is a transfer payment and therefore there is no net cost to society of transferring the grant from Government to individuals beyond the administration costs).

Of particular interest will be the relative cost-effectiveness of the programme between different socioeconomic groups identified in the main analysis. This may lead to differential policy recommendations for different socioeconomic groups. Uncertainty in the modelling of long-term outcomes will be subject to extensive sensitivity analysis to explore the robustness of the cost-effectiveness analysis.

IMPLICATIONS

Maternal nutrition plays a crucial role in influencing fetal growth and birth outcomes. It is a modifiable risk factor of public health importance in the effort to prevent adverse birth outcomes, particularly among low-income populations.²⁴ According to Barker, “*the seeds of inequalities in health in the next century are being sown today, in inner cities and other communities where adverse influences impact upon the growth, nutrition and health of mothers and their infants*”.⁵⁴

The HiP grant was cash given to the pregnant women with no constraint on its use. However, economic theory would suggest that cash transfers are more efficient than “vouchers” or subsidies, which try to target the expenditure in the “appropriate expenditure”. This is because vouchers, for example, free up disposable income if they displace planned expenditure. This evaluation study may show the HiP grant increased birthweight across the population. If so, then a benefit would be to recommend the re-introduction of a universal cash transfer or, if we believed more evidence was needed that the HiP grants were delivering this benefit, the development of a randomized controlled trial for a similar cash transfer. An additional benefit will be the relative cost-effectiveness of the HiP grant between different socioeconomic groups identified in the main analysis. This may lead to differential policy recommendations for different socioeconomic groups with consequent reduction in health inequalities.

ETHICS AND DISSEMINATION

Ethical approval is not required as there is no primary data collection. Indeed, the information from maternal and birth records from all hospitals in Scotland are routinely collected. Approval for data collection, storage and release for research purpose has been given (6th May 2014; PAC38A/13) by the Privacy Advisory Committee, an Advisory Committee to NHS National Service Scotland and the Registrar General.

The results of this study will be disseminated through peer-reviewed publications in public health research journals, national and international conferences.

AUTHOR'S CONTRIBUTIONS

Ruth Dundas was involved in the conception of the study design, literature search and prepared the first draft of the study protocol. She will contribute to the statistical analysis and the interpretation of the results.

Samiratou Ouédraogo contributed to the literature search and the preparation of the present protocol paper. She will be responsible for the statistical analysis and contribute to the interpretation of the results.

Lyndal Bond was involved in the conception of the study design. She will contribute to the interpretation of the results.

Andrew H Briggs designed the health economic analysis aspect of the protocol. He will oversee the cost-effectiveness analysis and assist with writing the health economic paper.

James Chalmers was involved in the conception of the study design.

Ron Gray was involved in the conception of the study design. He will contribute to the interpretation of the results.

Rachael Wood will contribute to the interpretation of the results.

Alastair H Leyland was involved in the conception of the study design, literature search and contributed to all sections. He will contribute to the statistical analysis and the interpretation of the results.

All authors read and approved the final manuscript.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

COMPETING INTERESTS

We declare that we have no conflicts of interest.

For peer review only

FUNDING STATEMENT

This project was funded by the National Institute for Health Research Public Health Research Board (project number 12/3070/02). The Social and Public Health Sciences Unit is core funded by the Medical Research Council (MC_UU_12017/5) and the Chief Scientist Office of the Scottish Government Health Directorates (SPHSU2).

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Public Health Research Board, NIHR, NHS or the Department of Health.

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

REFERENCE LIST

1. Frankel S, Elwood P, Sweetnam P, et al. Birthweight, body-mass index in middle age, and incident coronary heart disease. *Lancet* 1996;348(9040):1478-80.
2. Leon DA, Lithell HO, Vagero D, et al. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15 000 Swedish men and women born 1915-29. *BMJ* 1998;317(7153):241-5.
3. Reyes L, Manalich R. Long-term consequences of low birth weight. *Kidney Int Suppl* 2005(97):S107-11.
4. Class QA, Rickert ME, Lichtenstein P, et al. Birth weight, physical morbidity, and mortality: a population-based sibling-comparison study. *Am J Epidemiol* 2014;179(5):550-8.
5. Hendryx M, Luo J, Knox SS, et al. Identifying multiple risks of low birth weight using person-centered modeling. *Womens Health Issues* 2014;24(2):e251-6.
6. Barker DJ. Birth weight and hypertension. *Hypertension* 2006;48(3):357-8.
7. Barker DJ, Eriksson JG, Forsen T, et al. Fetal origins of adult disease: strength of effects and biological basis. *Int J Epidemiol* 2002;31(6):1235-9.
8. Barker DJ. In utero programming of chronic disease. *Clin Sci (Lond)* 1998;95(2):115-28.
9. Barker DJ. The fetal and infant origins of adult disease. *BMJ* 1990;301(6761):1111.
10. Negrato C, Gomes M. Low birth weight: causes and consequences. *Diabetol Metab Syndr* 2013;5(1):49.
11. Valero De Bernabe J, Soriano T, Albaladejo R, et al. Risk factors for low birth weight: a review. *Eur J Obstet Gynecol Reprod Biol* 2004;116(1):3-15.

- 1
2
3 12. EURO-PERISTAT. “Babies’ health: mortality and morbidity during pregnancy and in the
4 first year of life” in “The European Perinatal Health Report 2010”. 2013.
5 <http://www.europeristat.com/images/doc/Peristat%202013%20V2.pdf>. (Accessed 28
6 August 2014)
7
8
9
10
11 13. World Health Organisation. International Statictical Classification of Diseases and
12 Related Health Problems- ICD-10. 10th Revision. Geneva: World Health
13 Organisation, 2010. <http://www.who.int/classifications/icd/en/>. (Accessed 28 August
14 2014)
15
16
17
18
19 14. OECD. “Infant health: Low birth weight”, in Health at a Glance: Europe 2012. In:
20 Publishing O, ed., 2012. [http://www.oecd-](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest&checksum=368A07F542E03A0442EFDEB9B002B6AE)
21 [ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accnam](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest&checksum=368A07F542E03A0442EFDEB9B002B6AE)
22 [e=guest&checksum=368A07F542E03A0442EFDEB9B002B6AE](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest&checksum=368A07F542E03A0442EFDEB9B002B6AE) (Accessed 28
23 August 2014)
24
25
26
27
28
29 15. Macfalane A, Dattani N. European Perinatal Health Report: highlights from a United
30 Kingdom perspective. London, 2013. [http://www.europeristat.com/images/Euro-](http://www.europeristat.com/images/Euro-peristat%20UK%20briefing.pdf)
31 [peristat%20UK%20briefing.pdf](http://www.europeristat.com/images/Euro-peristat%20UK%20briefing.pdf). (Accessed 28 August 2014)
32
33
34
35
36 16. Madden D. The relationship between low birth weight and socioeconomic status in
37 Ireland. *J Biosoc Sci* 2014;46(2):248-65.
38
39
40
41 17. Frimmel W, Pruckner GJ. Birth weight and family status revisited: evidence from
42 Austrian register data. *Health Econ* 2014;23(4):426-45.
43
44
45
46 18. Huxley R. Smoking, birthweight, and mortality across generations. *Eur Heart J*
47 2013;34(44):3398-9.
48
49
50 19. Fairley L, Leyland AH. Social class inequalities in perinatal outcomes: Scotland 1980-
51 2000. *J Epidemiol Community Health* 2006;60(1):31-6.
52
53
54
55
56
57
58
59
60

- 1
2
3 20. Weightman AL, Morgan HE, Shepherd MA, et al. Social inequality and infant health in
4 the UK: systematic review and meta-analyses. *BMJ Open* 2012;2(3) 2012 Jun
5 14;2(3):e000964.
6
7
8
9
10 21. Juarez SP, Merlo J. Revisiting the effect of maternal smoking during pregnancy on
11 offspring birthweight: a quasi-experimental sibling analysis in Sweden. *PLoS One*
12 2013;8(4):e61734.
13
14
15
16 22. Zdravkovic T, Genbacev O, McMaster MT, et al. The adverse effects of maternal
17 smoking on the human placenta: a review. *Placenta* 2005;26 Suppl A:S81-6.
18
19
20
21 23. Villar J, Merialdi M, Gulmezoglu AM, et al. Nutritional interventions during pregnancy
22 for the prevention or treatment of maternal morbidity and preterm delivery: an
23 overview of randomized controlled trials. *J Nutr* 2003;133(5 Suppl 2):1606S-25S.
24
25
26
27 24. Abu-Saad K, Fraser D. Maternal nutrition and birth outcomes. *Epidemiol Rev*
28 2010;32(1):5-25.
29
30
31
32 25. Wu G, Imhoff-Kunsch B, Girard AW. Biological mechanisms for nutritional regulation of
33 maternal health and fetal development. *Paediatr Perinat Epidemiol* 2012;26 Suppl 1:4-
34 26.
35
36
37
38 26. Mason JB, Saldanha LS, Ramakrishnan U, et al. Opportunities for improving maternal
39 nutrition and birth outcomes: synthesis of country experiences. *Food Nutr Bull*
40 2012;33(2 Suppl):S104-37.
41
42
43
44
45 27. Thangaratinam S, Rogozinska E, Jolly K, et al. Effects of interventions in pregnancy on
46 maternal weight and obstetric outcomes: meta-analysis of randomised evidence. *BMJ*
47 2012;344:e2088.
48
49
50
51 28. Glassman A, Duran D, Fleisher L, et al. Impact of Conditional Cash Transfers on
52 Maternal and Newborn Health. *J Health Popul Nutr* 2013;4:19.
53
54
55
56
57
58
59
60

- 1
2
3 29. Sutherland K, Christianson JB, Leatherman S. Impact of targeted financial incentives on
4 personal health behavior: a review of the literature. *Med Care Res Rev* 2008;65(6
5 Suppl):36S-78S.
6
7
8
9
10 30. Marteau TM, Ashcroft RE, Oliver A. Using financial incentives to achieve healthy
11 behaviour. *BMJ* 2009;338:b1415.
12
13
14 31. Giles EL, Robalino S, McColl E, et al. The effectiveness of financial incentives for health
15 behaviour change: systematic review and meta-analysis. *PLoS One* 2014;9(3):e90347.
16
17
18 32. Brownell M, Chartier M, Au W, et al. Evaluation of the Health Baby Program. Winnipeg,
19 MB: Manitoba Centre for Health Policy. 2010.
20
21
22
23 33. Neil G. Universal to selective. *Transformation of the Welfare State: The Silent Surrender*
24 of Public Responsibility: Oxford University Press, 2002:20.
25
26
27
28 34. Mkandawire T. Targeting and Universalism in poverty reduction. . Secondary Targeting
29 and Universalism in poverty reduction. 2005.
30 <http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EE>
31 <http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EE>
32 [A0B0C12570FF00493EAA/\\$file/mkandatarget.pdf](http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EE). (Accessed 28 August 2014)
33
34
35
36 35. Craig P, Cooper C, Gunnell D, et al. Using natural experiments to evaluate population
37 health interventions: new Medical Research Council guidance. *J Epidemiol*
38 *Community Health* 2012;66(12):1182-6.
39
40
41
42 36. Council MR. Using natural experiments to evaluate population health interventions:
43 guidance for producers and users of evidence.
44 [http://www.behaviourworksaustralia.org/wp-](http://www.behaviourworksaustralia.org/wp-content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf)
45 [content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf](http://www.behaviourworksaustralia.org/wp-content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf)
46
47
48 (Accessed 28 August 2014)
49
50
51
52 37. Einarsdottir K, Kemp A, Haggard FA, et al. Increase in caesarean deliveries after the
53 Australian Private Health Insurance Incentive policy reforms. *PLoS One*
54 2012;7(7):e41436.
55
56
57
58
59
60

- 1
2
3 38. Ramsay CR, Matowe L, Grilli R, et al. Interrupted time series designs in health
4 technology assessment: lessons from two systematic reviews of behavior change
5 strategies. *Int J Technol Assess Health Care* 2003;19(4):613-23.
6
7
8
9
10 39. Penfold RB, Zhang F. Use of interrupted time series analysis in evaluating health care
11 quality improvements. *Acad Pediatr* 2013;13(6 Suppl):S38-44.
12
13
14 40. Statistics OfN. The National Statistics Socio-economic Classification (NS-SEC rebased
15 on the SOC2010). . Secondary The National Statistics Socio-economic Classification
16 (NS-SEC rebased on the SOC2010). [http://www.ons.gov.uk/ons/guide-](http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html)
17 [method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-](http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html)
18 [ns-sec--rebased-on-soc2010--user-manual/index.html](http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html). (Accessed 28 August 2014)
19
20
21
22
23
24 41. Scholmerich VL, Erdem O, Borsboom G, et al. The association of neighborhood social
25 capital and ethnic (minority) density with pregnancy outcomes in the Netherlands.
26 *PLoS One* 2014;9(5):e95873.
27
28
29
30 42. Margerison-Zilko C. The Contribution of Maternal Birth Cohort to Term Small for
31 Gestational Age in the United States 1989-2010: an Age, Period, and Cohort
32 Analysis. *Paediatr Perinat Epidemiol* 2014;28(4):312-21
33
34
35
36
37 43. The Scottish Government. Scottish Index of Multiple Deprivation 2012: A national
38 Statistics publication for Scotland 2012. [http://22fa0f74501b902c9f11-](http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf)
39 [8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_201212](http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf)
40 [17.pdf](http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf). (Accessed 28 August 2014)
41
42
43
44
45 44. Pattenden S, Dolk H, Vrijheid M. Inequalities in low birth weight: parental social class,
46 area deprivation, and "lone mother" status. *J Epidemiol Community Health*
47 1999;53(6):355-8.
48
49
50
51 45. Spencer N, Bambang S, Logan S, et al. Socioeconomic status and birth weight:
52 comparison of an area-based measure with the Registrar General's social class. *J*
53 *Epidemiol Community Health* 1999;53(8):495-8.
54
55
56
57
58
59
60

- 1
2
3 46. Fairley L, Dundas R, Leyland AH. The influence of both individual and area based
4 socioeconomic status on temporal trends in Caesarean sections in Scotland 1980-
5 2000. BMC Public Health 2011;11:330.
6
7
8
9
10 47. Kent ST, McClure LA, Zaitchik BF, et al. Area-level risk factors for adverse birth
11 outcomes: trends in urban and rural settings. BMC Pregnancy Childbirth 2013;13:129.
12
13
14 48. Shankardass K, O'Campo P, Dodds L, et al. Magnitude of income-related disparities in
15 adverse perinatal outcomes. BMC Pregnancy Childbirth 2014;14:96.
16
17
18
19 49. Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology
20 1990;1(1):43-6.
21
22
23
24 50. Greenland S. Multiple comparisons and association selection in general epidemiology. Int
25 J Epidemiol 2008;37(3):430-4.
26
27
28
29 51. National Service Division. Pregnancy Screening Programmes.
30 <http://www.nsd.scot.nhs.uk/services/screening/pregscreening/index.html>. (Accessed
31 28 August 2014)
32
33
34
35 52. NHS Health Scotland. Your guide to screening tests during pregnancy.
36 [http://www.healthscotland.com/uploads/documents/3985-](http://www.healthscotland.com/uploads/documents/3985-YourGuideToScreeningTestsDuringPregnancy_1.pdf)
37 [YourGuideToScreeningTestsDuringPregnancy_1.pdf](http://www.healthscotland.com/uploads/documents/3985-YourGuideToScreeningTestsDuringPregnancy_1.pdf). (Accessed 28 August 2014)
38
39
40
41 53. Mackay DF, Nelson SM, Haw SJ, et al. Impact of Scotland's smoke-free legislation on
42 pregnancy complications: retrospective cohort study. PLoS Med 2012;9(3):e1001175.
43
44
45
46 54. Barker DJ. The foetal and infant origins of inequalities in health in Britain. J Public
47 Health Med 1991;13(2):64-8.
48
49
50
51
52
53
54
55
56
57
58
59
60

BMJ Open

Evaluation of Health in Pregnancy grants in Scotland: a protocol for a natural experiment

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-006547.R1
Article Type:	Protocol
Date Submitted by the Author:	23-Sep-2014
Complete List of Authors:	Dundas, Ruth; University of Glasgow, MRC/CSO Social and Public Health Sciences Unit Ouédraogo, Samiratou; University of Glasgow, MRC/CSO Social and Public Health Sciences Unit Bond, Lyndal; Centre of Excellence in Intervention and Prevention Science, Briggs, Andrew; University of Glasgow, Health Economics & Health Technology Assessment Institute of Health & Wellbeing Chalmers, James; NHS National Services Scotland, Information Services Division Gray, Ron; University of Oxford, National Perinatal Epidemiology Unit Wood, Rachael; NHS National Services Scotland, Information Services Division Leyland, Alastair; University of Glasgow, MRC/CSO Social and Public Health Sciences Unit
Primary Subject Heading:	Health policy
Secondary Subject Heading:	Epidemiology, Public health, Health economics, Research methods
Keywords:	EPIDEMIOLOGY, Reproductive medicine < GYNAECOLOGY, HEALTH ECONOMICS, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, NEONATOLOGY, Maternal medicine < OBSTETRICS

SCHOLARONE™
Manuscripts

PROJECT PROTOCOL

Title: Evaluation of Health in Pregnancy grants in Scotland: a protocol for a natural experiment

Authors: Ruth Dundas¹, Samiratou Ouédraogo¹, Lyndal Bond², Andrew H Briggs³, James Chalmers⁴, Ron Gray⁵, Rachael Wood⁴, Alastair H Leyland¹

Affiliations:

¹ MRC/CSO Social and Public Health Sciences Unit, University of Glasgow, Glasgow, UK

² Centre of Excellence in Intervention and Prevention Science, Melbourne, Australia

³ Health Economics and Health Technology Assessment, University of Glasgow, Glasgow, UK

⁴ Information Services Division, NHS National Services Scotland, Edinburgh, UK

⁵ National Perinatal Epidemiology Unit, University of Oxford, UK

Correspondence to:

Ruth Dundas

MRC/CSO Social and Public Health Sciences Unit, University of Glasgow

200 Renfield Street, Glasgow G2 3QB, Scotland

Tel: +44 141 353 7541 Email: ruth.dundas@glasgow.ac.uk

Keywords: Low birthweight; interrupted time series; multilevel analysis; Health in Pregnancy grant; natural experiment.

ABSTRACT

Introduction

A substantial proportion of low birthweight (LBW) is attributable to the mother's cultural and socioeconomic circumstances. Early childhood programmes have been widely developed to improve child outcomes. In the UK, the Health in Pregnancy (HiP) grant, a universal conditional cash transfer of £190, was introduced for women reaching the 25th week of pregnancy with a due date on/or after 6th April 2009 and subsequently withdrawn for women reaching the 25th week of pregnancy on/or after 1st January 2011. The current study focuses on the evaluation of the effectiveness and cost-effectiveness of the HiP grant.

Methods and analysis

The population under study will be all singleton births in Scotland over the periods of January 2004 to March 2009 (pre-intervention), April 2009 to April 2011 (intervention) and May 2011 to December 2013 (post-intervention). Data will be extracted from the Scottish maternity and neonatal database. The analysis period 2004-2013 should yield over 585,000 births. The primary outcome will be birthweight among singleton births. Other secondary outcomes will include gestation at booking, booking before 25 weeks; measures of size and stage; gestational age at delivery; weight-for-dates, term at birth; birth outcomes and maternal smoking. The main statistical method we will use is interrupted time series. Outcomes will be measured on individual births nested within mothers, with mothers themselves clustered within datazones. Multilevel regression models will be used to determine whether the outcomes changed during the period in which the HiP grants was in effect. Subgroup analyses will be conducted for those groups most likely to benefit from the payments.

Ethics and dissemination

Approval for data collection, storage and release for research purpose has been given (6th of May 2014, PAC38A/13) by the Privacy Advisory Committee. The results of this study will be disseminated through peer-reviewed publications in journals, national and international conferences.

ARTICLE SUMMARY

Article focus

- To evaluate the effectiveness and cost-effectiveness of Health in Pregnancy grant (HiP) in Scotland.

Key messages

- We will assess the difference in birthweight for babies born to those mothers who were eligible for the HiP grant with babies born before the HiP grant was introduced or after it was withdrawn using interrupted time series multilevel analysis.
- Subgroup analyses will be conducted for those groups seen as having the greatest potential to benefit from the payments such as those living in the most deprived areas, those in the lowest social classes, lone mothers, primiparous women, teen mothers, mothers from ethnic minorities and selected combinations of these groups.
- As part of the project an economic model will be developed based on a review of the literature to relate birthweight changes to long-term cost and health outcomes (in terms of QALYs).

Strengths and limitations of this study

The strengths of this study are:

- This is the first study evaluating the effect and the cost-effectiveness of the HiP grant in Scotland. It will use routinely available vital event and maternal and neonatal health records that are known to have high completeness and accuracy.
- The evaluation of the HiP grant using an interrupted time series design will enable us to analyse birthweight trends in Scotland and detect whether the intervention has had an effect over and above the underlying temporal trend. The use of interrupted time series will overcome other biases such as the autocorrelation of repeated measurements (measurement taken close together are related), seasonal effects (birthweight varies according to month of birth), the duration of the intervention (we will have pre-intervention intervention and post-intervention), and random variation in the measurement (birthweight).

The limitations of this study

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47
- 48
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60
- This study will evaluate the effect and the cost-effectiveness of the HiP grant, birthweight and other birth outcomes in Scotland using obstetric as well as maternal data. However, these outcomes may be influenced by many factors, not all of which are routinely captured (such as maternal diet, maternal work and psychological stress, abuse, exposure to toxic substance).¹¹
- The HiP grant was money given to pregnant women with no constraint on its use. The use of routine data gives us no indication on how the money was spent.

INTRODUCTION

Low birthweight (LBW) due to preterm birth, intrauterine growth restriction, or being born small for gestational age (SGA), is commonly associated with perinatal mortality and impaired development¹⁻¹¹. Despite the improvement of the mortality in LBW babies over the past three decades, more than 70% of all neonatal mortality in Europe is found in infants weighing less than 2500 grams (g).¹²

LBW refers to birth weights below 2500 g,¹³ irrespective of the gestational age of the infant. In most developed countries, the prevalence of LBW has increased due to several reasons: the number of multiple births with the increased risks of pre-term births and low birth weight partly as a result of the rise in fertility treatments; older age at childbearing and increases in the use of delivery management techniques such as induction of labour and caesarean delivery, which have increased the survival rates of low birth weight babies.¹⁴ About one in 20 babies born in Europe in 2010 weighed less than 2500 g at birth.¹² With LBW estimated at 7.0% of live births in England and Wales, 6.5% in Scotland and 5.7% of live births in Northern Ireland, prevalence of LBW in the countries of the United Kingdom (UK) tended to be higher than in the rest of Europe.¹²⁻¹⁵ Moreover, compared with other Western European countries, the UK has an incidence of LBW (<2500g) and very LBW (<1500g) in the top third. The proportion of pre-term birth (<37 weeks) is also high compared with other Western European countries.

Considerable attention has been focused on the causal determinants of LBW, in order to identify potentially modifiable factors. A substantial proportion of LBW is attributable to the mother's cultural and socioeconomic circumstances such as socioeconomic status (SES), harmful behaviours (smoking and excessive alcohol consumption) and poor nutrition during pregnancy.^{11,16-18} In a study of social class inequalities in perinatal outcomes in Scotland, Fairley and Leyland¹⁹ reported a percentage of 5.8% LBW in unskilled social class (V) compared to 2.9% in professional social class (I) between 1995 and 2000. The systematic review and meta-analyses of social inequality and infant health in the UK performed by Weightman et al.²⁰ found that the odds ratio for low birth weight was 1.79 (95% CI 1.43 to 2.24) in the lowest compared to the highest social class. This effect may vary with maternal factors such as age and smoking status. Smoking during pregnancy reduces birthweight by 162 to 377 g, depending on daily consumption (larger reduction for heavy smokers) and the trimester in which exposure occurs (larger reduction during the last trimester).^{18,21-22}

1
2
3 The association between maternal nutrition and birth outcome is complex and is influenced
4 by many biologic, socioeconomic, and demographic factors, which vary widely in different
5 populations.²³⁻²⁴ However, it has been reported that favourable prenatal nutrition associated
6 with adequate prenatal care can have a positive impact on birth outcomes and morbidity in
7 adult life.²⁵⁻²⁶ Indeed, the developmental model of the origins of chronic disease proposes the
8 causal influence of undernutrition *in utero* on coronary heart disease and stroke in adult life.⁷⁻
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

9 An improvement in fetal nutrition may therefore have far reaching consequences in terms of
the prevention of disease. A review of maternal nutrition and birth outcomes identified
improving maternal nutrition as being beneficial to the prevention of adverse birth outcomes
in lower social class groups.²⁴
A number of early childhood programmes have been developed to improve child outcomes.
There is mixed evidence that these programmes do provide such improvement. In a meta-
analysis of the effect of interventions in pregnancy on maternal and obstetric outcomes,
Thangaratinam et al. concluded that dietary and lifestyle interventions in pregnancy reduced
maternal gestational weight gain but had less effect on outcomes related to fetal weight and
other morbidity and mortality.²⁷ Glassman et al.²⁸ who reported the results of conditional cash
transfer programmes increasingly being adopted and scaled in developing countries, found
that the programmes have increased the uptake of maternal and newborn health services,
especially skilled attendance at delivery and antenatal monitoring. However, the impact of the
programs on maternal and newborn mortality has not been well documented. Therefore, they
recommended more rigorous impact evaluations that document impact pathways and take
factors, such as cost-effectiveness, into account. Other studies evaluating payments to
influence health behaviour found financial incentives were effective in increasing infrequent
behaviours such as attending clinic appointments particularly in low-income groups, and
recommended payments as being more effective than information and less restrictive than
legislation.²⁹⁻³¹ In Canada, Brownell et al. have evaluated a complex programme on a prenatal
benefit provided to families on low income during pregnancy.³² They found that the receipt
of this prenatal benefit was associated with a reduction in incidence of both low birthweight
babies and preterm births. They suggested that efforts should be made to ensure all low-
income women receive the income supplement.

In the UK, the Health in Pregnancy (HiP) grant was introduced for women reaching the 25th
week of pregnancy with a due date on/or after 6th April 2009. It was subsequently withdrawn
for women reaching the 25th week of pregnancy on/or after 1st January 2011. The HiP grant

1
2
3 was a universal conditional cash transfer of £190 for women reaching 25 weeks of pregnancy
4 if they had sought health advice from a doctor or midwife. It was designed to provide
5 additional financial support, in the last months of pregnancy, towards a healthy lifestyle
6 including diet, and it was suggested that the link to the requirement for pregnant women to
7 seek health advice from a professional may provide a greater incentive for expectant mothers
8 to seek the recommended health advice at the appropriate time. The grant was paid and
9 administered by Her Majesty's Revenue and Customs (HMRC) on receipt of a claim form
10 partly completed by the midwife or doctor. Advice was offered as normal by doctors and
11 midwives. Payment was made directly into a bank account with a telephone helpline
12 available to provide support through the claims process including options for payment in the
13 event of difficulties opening a bank account. Take up of the grant was said to be about the
14 same level as for child benefit (98-99%, personal communication, HMRC).

15
16
17
18
19
20
21
22
23 The current study focuses on the evaluation of the effectiveness and cost-effectiveness of the
24 HiP grant. As a primary outcome, we will consider the difference in birthweight for babies
25 born to those mothers who were eligible for the HiP grant with babies born before the HiP
26 grant was introduced or after it was withdrawn. Specific questions the research project will
27 address are:
28
29
30

- 31
32
33
34
35
36
37
38
39
40
41
42
43
- Were there differential impacts of the intervention for particular subgroups defined by socioeconomic (defined in terms of both area deprivation and individual occupational social class), demographic (marital status, age, maternal height), or obstetric (parity, previous caesarean section) factors or for selected combination of these groups?
 - Was the HiP grant cost-effective? How did cost-effectiveness vary across important subgroups identified as having differential outcomes?

44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The principle of universalism in the allocation of social benefits, that is the availability of social benefits to everyone as of right, is contrasted with allocation on a selective basis (targeted) in which benefits are allocated on the basis of need as determined by means testing of income.³³ The advantage of universal benefits is that they are easy to administer and can be efficiently delivered. The major disadvantage is that they are expensive, because they are delivered to those who do not need them as much as to those who do. However, the use of targeting involves some mechanism that discriminates between the poor and the non-poor. As such it always runs the danger of committing either type I errors which occur when someone

1
2
3 who deserves the benefits is denied them (underpayment, false positives), or type II errors,
4 which occur when benefits are paid to someone who does not deserve them (overpayment,
5 leakage).³⁴ The HiP grant represented an attempt to influence behaviour – appropriate and
6 timely receipt of antenatal care advice – by means of a relatively modest, universally applied
7 cash transfer. The evaluation of the effectiveness of such a payment may inform other
8 policies aiming to change behaviour.
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

METHODS AND ANALYSIS

Study design

The HiP grant will be evaluated as a natural experiment using interrupted time series analysis to compare outcomes before the introduction of the intervention in Scotland and immediately after its withdrawal with those during the period for which it existed.

The Medical Research Council (MRC) has issued guidelines regarding the use of natural experiments to evaluate population health interventions when exposure to the intervention has not been manipulated by the researchers (Table 1).³⁵⁻³⁶

Table 1: Guidance for use of natural experiments to evaluate population health interventions

When to use a natural experimental approach?	How does the evaluation of HiP* grant meet these criteria?
<ul style="list-style-type: none"> ▪ There is a reasonable expectation that the intervention will have a significant health impact, but scientific uncertainty about the size or nature of the effects. 	<ul style="list-style-type: none"> ▪ The HiP grant represented an attempt to influence behaviour – appropriate and timely receipt of antenatal care advice. With the sample size we are using in this evaluation study, we are able to detect small changes in birthweight.
<ul style="list-style-type: none"> ▪ Natural experimental study is the most appropriate method for studying a given type of intervention. 	<ul style="list-style-type: none"> ▪ The HiP grant was a universally applied cash transfer available for all pregnant women with no discrimination between socioeconomic classes. This policy was not introduced using a randomised allocation
<ul style="list-style-type: none"> ▪ It is possible to obtain the relevant data from an appropriate study population, comprising groups with different levels of exposure to the intervention. 	<ul style="list-style-type: none"> ▪ The uptake of the HiP grant was thought to be 98-99%. The linked Scottish birth dataset has 98% coverage of births and the primary outcome, birthweight, is well measured, 99.9% complete and accurate. Exposure is determined by the dates for which the HiP grant was in existence.
<ul style="list-style-type: none"> ▪ The intervention or the principles behind it have the potential for replication, scalability or generalisability. 	<ul style="list-style-type: none"> ▪ The HiP grant is replicable everywhere in countries with similar health systems.

HiP* grant: Health in Pregnancy grant

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The guidance advocates a number of designs including regression discontinuity designs such as interrupted time series. The interrupted time series approach is a powerful tool used for evaluating the impact of a policy change or quality improvement programme on the rate of an outcome in a defined population of individuals.³⁷⁻³⁹ This approach will allow us to use a comparison group of pregnant women who delivered before the HiP grant was introduced, an intervention group who received the HiP grant and an additional post-intervention group who delivered after the HiP grant was withdrawn. It will also allow adjustment for seasonality, temporal trends and the socio-demographic and obstetric characteristics of the mother.

Study population

The population under study will be all singleton births in Scotland over the periods of January 2004 to March 2009 (pre-intervention), April 2009 to April 2011 (intervention) and May 2011 to December 2013 (post-intervention).

The Scottish maternity and neonatal database is a comprehensive record linkage system.⁴⁰⁻⁴¹ Probabilistic linkage procedures are used to add a unique identifier to all datasets to ensure all relevant records relating to an individual can be linked as required. It facilitates the linkage of a number of records from the system of Scottish Morbidity Records (SMR) including mother's obstetric records (SMR02) and the baby's birth and neonatal information from Scottish Birth Records (SBR).⁴² Further links to the stillbirth and infant Death Survey and the National Records of Scotland (NRS) birth, stillbirth and infant death records can be carried out. The coverage is almost all births in Scotland.⁴³ From NRS data, we know of all registered births in Scotland (ie 100%). We have suitable record linked data on 98% of these births.⁴⁴ These will nearly all be hospital births; a fairly high proportion of the missing records are home births.

There is an average of about 56,000 births per year in Scotland.⁴⁵ The analysis period 2004-2013 should yield over 585,000 births. The analysis period 2006-2013 should yield over 455,000 births.

We have chosen to use data from the Scotland for this evaluation for the following reasons. First, data are available at a national level on the approximately 56,000 deliveries per year. Second, Scotland has a long history of collecting high quality routine data. The coverage, completeness and quality of the data are considered to be very high.⁴⁶ Third, the concentration of deprivation within parts of Scotland is unique within the UK.⁴⁷ And using a UK wide Cartstairs index, the Scotland's population is over-represented in the bottom 5 deciles compared to England.⁴⁸ Fourth, data on smoking at booking have been routinely recorded in Scotland for a number of years.⁴⁹ This is not yet the case in England and Wales. The data can be linked to NRS civil registration data, which provides an estimate of completeness and contributes further information such as social class. The results will be generalisable to the rest of the UK and internationally. If the HiP grant proved beneficial in Scotland then there is every good reason to believe that a similar impact on outcomes could be achieved elsewhere and certainly in countries with similar health systems and comparable circumstances. Likewise, if the intervention was found to have been more effective for specific subgroups then we might expect subgroups to show greater benefits in other settings.

Study variables

Individual level and area level variables will be used in this study.

Individual level variables will include: birthweight, date of birth, sex, gestational age at delivery, preterm (delivery before the 37th week of pregnancy), weight-for-dates, 5 min Apgar score, crown to heel length, and head circumference. We will distinguish between spontaneous pre-term births and induced pre-term births. A potential reason for induced pre-term births is evidence of poor fetal growth; a proportion of these babies would become more severely growth retarded (more extremely small for gestational age) or stillborn.

Since maternal factors influence fetal growth,¹¹ individual level variables related to the mother will be examined: parity, age, height, weight at booking, diabetes, smoking status, gestation at booking, booking before 25 weeks, and marital status. Individual socioeconomic position will also be included using data from the birth registrations at NRS.⁵⁰ NRS collects occupation for both father and mother for births registered to married couples and jointly registered by unmarried couples.⁵¹ Only mother's occupation is recorded for sole registered

1
2
3 births. The National Statistics Socio-economic Classification (NS-SEC)⁵² will be used to
4 classify the individual socioeconomic position.
5
6

7 Marital status is an important variable as single mothers have consistently been shown to
8 have poorer birth outcomes.¹⁷⁻¹⁹ We are particularly interested in single mothers and social
9 class. Social class for lone mothers is an amalgamation of socioeconomic position and lone
10 parenthood.
11
12

13 Although the routinely collected data on ethnicity are incomplete and of dubious quality,^{46,53}
14 ethnicity remains important for birthweight and other neonatal outcomes.⁵⁴⁻⁵⁵ We will
15 therefore, within the constraints of the data, include ethnicity and undertake all analyses on
16 the subgroup of mother from a minority ethnic background. Within this subgroup, we will
17 examine the possibility of further distinction between ethnic groups.
18
19
20
21
22

23 Birthweight varies according to the socioeconomic status of the area of residence.²⁰ The
24 Scottish Index of Multiple Deprivation (SIMD) will be used and included as area level
25 variables in the analysis. The SIMD is the Scottish Government's official tool for identifying
26 those places in Scotland suffering from deprivation.⁵⁶ It is a weighted sum of different
27 domains: income; employment; health; education; housing and geographical access (and
28 crime, added in the SIMD 2012). The SIMD provides a comprehensive picture of material
29 deprivation in small areas within Scotland. The index ranks 6505 areas from the most
30 deprived to the least deprived and measures the degree of deprivation of an area relative to
31 that of other areas. The areas employed by the SIMD are datazones and are small: the 6505
32 datazones have a mean population of 780 people. The reason for employing small area
33 geography at this scale is to permit identification of relatively small pockets of deprivation.
34 The health domain includes an indicator of the proportion of live singleton births that is
35 LBW. The outcomes of this project include birthweight and LBW and so it would not be
36 appropriate to use the health domain or the composite index which includes the health
37 domain. The income domain will therefore be used to assess inequalities at the area level.
38 This domain contributes 28% to the overall index and is highly correlated with the overall
39 SIMD. The income domain of the SIMD identifies areas where there are concentrations of
40 individuals and families living on low incomes. This is done by looking at the numbers of
41 people, both adult and children, who are receiving, or are dependent on, benefits related to
42 income or tax credits.⁵⁷ Each mother will be assigned to a datazone and its income domain
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

through her home postcode. Previous studies investigating inequalities in birthweight have shown that area deprivation performs as well as or better than individual social class in describing the extent of inequalities in the population.⁵⁸⁻⁵⁹ However, Fairley et al. who studied the influence of both individual and area based socioeconomic status on temporal trends in Caesarean sections between 1980 and 2000 in Scotland found that maternal social class and area deprivation are different indicators of socioeconomic status which exhibit independent effects on the probability of a woman receiving a Caesarean section.⁶⁰ The multilevel analysis will allow us to analyse the effect of both parental social class and SMID and the effect of their interaction on birthweight.

We will adjust the analyses on the urban or rural status of the mother's area of residence. Indeed, Kent et al reported higher adverse birth outcome rates in isolated rural and more population dense areas.⁶¹ They showed that these disparities are being maintained or increasing over time in Alabama. Shankardass et al also found that the patterns of association between socioeconomic position and LGA, spontaneous preterm birth and perinatal death varied depending on urbanicity in Nova Scotia (Canada).⁶²

Outcome measures

Primary Outcome

The primary outcome will be birthweight among singleton births. This is influenced by many factors including maternal nutrition and one of the intentions of the HiP grant was to improve this.

Secondary Outcomes

The following secondary outcomes will be assessed:

- Gestation at booking,
- Booking before 25 weeks,
- Measures of size: crown to heel length, head circumference,
- Measures of stage: gestational age at delivery, weight-for-dates (standardised; small for gestational age babies are those weighted less than the 5th centile weight, or large for gestational age weighted more than the 90th centile weight), term at birth (pre-

1
2
3 term, babies are born at less than 37 weeks gestation; term babies are those born
4 between 37-42 weeks gestation and post-term babies are born after 42 weeks
5 gestation),
6
7

- 8
9 - Birth outcomes: mode of delivery, stillbirths, neonatal deaths, 5 minutes Apgar score.
10 Although there is some debate concerning the robustness of the Apgar score as an
11 outcome, it is in common use and we will therefore present results for this outcome
12 within the context of the wide debate on the subject.
13
14

15
16 Due in part to the introduction of smoking ban in Scotland in 2006, an additional outcome of
17 interest is maternal smoking. Maternal smoking is collected at booking and during pregnancy.
18 The health advice given when receiving the HiP grant might have an impact on smoking rates
19 during pregnancy over and above that of the smoke-free legislation. We will analyse the
20 temporal change in smoking rate by socioeconomic class and its effect on outcomes.
21
22
23
24
25
26
27

28 **Sample size**

29
30 The data are clustered in small areas, 6505 datazones. The sample size calculation takes this
31 clustering into account. Assuming an average of 56,000 singleton live births per year, and
32 allowing for the clustering within the 6505 datazones in Scotland (average population 780 per
33 datazone) with an estimated intraclass correlation coefficient of 0.05, we have power of 0.90
34 to detect an effect of 7g change in birthweight at a 95% significance level. This is not to say
35 that 7g is a clinically important threshold; rather, it is indicative of the power of the study.
36 The large national data set available to us will allow for subgroup analysis. In the 20% most
37 deprived areas, we will have power of 0.80 to detect an effect of 13g; among the 26% of
38 single mothers, we will have power of 0.80 to detect an effect of 11g. To put these small
39 effects into context, 50g is the estimated mean birthweight reduction reported in the meta-
40 analysis of the effect of interventions in pregnancy on maternal and obstetric outcomes.²⁷
41
42
43
44
45
46
47
48

49 We anticipate item non-response for some outcomes and explanatory variables. Our primary
50 outcome measure, birthweight, has a completion rate of 99.9%. There is high completion rate
51 (<1.5% missing) for all obstetric variables,⁴⁶ with the exception of crown to heel length (15%
52 missing) and head circumference (12% missing). The item non-response ranges from 8% for
53 maternal smoking to 20% for marital status. We will use multiple imputation to account for
54
55
56
57
58
59
60

1
2
3 missing data and all analyses will compare the results of analyses of complete cases and
4 multiple imputation.⁶³ Imputed models will be constructed such that they contain as many
5 relevant predictor variables as possible. The more variables that are used the greater the
6 amount of information available on which estimations are made. We will use all (or as many
7 as possible) obstetric and maternal variables in an imputation model to predict the missing
8 values. It is difficult to identify in advance the number of multiple imputed datasets we will
9 need to construct but it is likely to be between 5 and 10. We will then analyse these datasets
10 identically and combine the results to get the estimates and standard errors for the multiple
11 imputed data. These results will be compared to the complete case analysis results.
12
13

14
15
16 It is difficult to be specific about the missing data mechanism until we see the data but much
17 is likely to be missing completely at random (MCAR, e.g. certain hospitals are less likely to
18 collect specific items) or missing at random (MAR, when the missingness is related to known
19 variables and, conditional on these, is assumed to be unrelated to unmeasured variables).
20
21
22
23
24
25
26
27

28 **Data analysis plan**

29 **Statistical analysis**

30
31
32 Descriptive statistics of all variables will be presented as mean, standard deviation, minimum,
33 median and maximum for continuous variables and as proportions when the variables are
34 categorical.
35
36

37
38 The main statistical design we will use is interrupted time series.⁶⁴ Segmented regression
39 analysis will allow an estimation of the size of the effect of the HiP grant at different time
40 points, as well as changes in the trend of the effect over time after its implementation.
41
42

43
44 Outcomes will be measured on individual births, which are nested within mothers, with
45 mothers themselves clustered within datazones and Health Boards. Multilevel univariable and
46 multivariable models will be used to determine whether the outcomes changed during the
47 period in which the HiP grants were in effect. Multilevel linear regression will be used when
48 the outcome is continuous and multilevel binomial logistic regression when the outcome is
49 dichotomous. Multilevel multinomial logistic regression will be used for the multi-category
50 outcomes mode of delivery and 5 minutes Apgar score.
51
52
53
54
55
56
57
58
59
60

1
2
3 All analyses will be adjusted for temporal trends and seasonal variations in outcomes in
4 addition to maternal age, sex of child, parity, marital status, height, weight at booking,
5 diabetes, smoking status, gestation at booking, maternal diabetes, social class, maternal
6 smoking and area deprivation.
7
8

9
10 The effect of HiP grant on birthweight might have a carryover effect after the withdrawal of
11 the grant. In other words, post-intervention the slope in birthweight might not fall back to the
12 same rate as pre-intervention. This could be due to women who have gave birth during the
13 intervention subsequently having a birth postintervention but still heeding the health advice
14 given during their first pregnancy. We will carry out an additional analysis only on
15 primiparous women to avoid such contamination.
16
17

18 We will analyse pre-term births stratified by mode of delivery and stratified according to
19 whether the birth was induced or spontaneous.
20

21 We will repeat the main analyses including (i.e adjusting for the effect of) ethnicity along
22 with other covariates and compare the results with analyses excluding ethnicity to gauge the
23 impact of this on our results. We note that the quality of this variable (including the
24 completeness of recording) is poorer than for other variables and that only 1-2% of mothers
25 delivering in Scotland are from minority ethnic backgrounds.
26
27

28 The simplest model for the intervention effect will include a dummy variable “intervention”
29 covering the period from the introduction to the withdrawal of HiP grants, with adjustment
30 for relevant factors such as marital status. (More complex models of the effect of the
31 intervention will include an interaction of the intervention with the temporal trend). Before
32 carrying out specific subgroup analysis, we will identify differential effects by fitting
33 interaction terms. An assessment as to whether there is a differential effect of the intervention
34 for single women, for example, will involve a test of the significance of the intervention
35 between marital status and the intervention effect. If the interaction is significant this will aid
36 our understanding of the generalisability to other populations, including the rest of the UK.
37 Subgroup analyses will be conducted for those groups seen as having the greatest potential to
38 benefit from the payments such as those living in the most deprived areas, those in the lowest
39 social classes, lone mothers, primiparous women, teen mothers, mothers from ethnic
40 minorities and selected combinations of these groups. For each group we will replicate the
41 main analysis. This reduction in sample size for sub-group analyses will result in fewer
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

women/births being available but the same number of areas (datazones) will be analysed (apart from analyses restricted to those living in the most deprived areas).

An increase in birthweight, although desirable at a population level, may not be a beneficial outcome if the baby were already at risk of being large for gestational age (LGA). Separate subgroup analyses will therefore be conducted for women seen to be at high risk of delivering a LGA baby (women with diabetes) and for the remainder of the population. Given that some subgroups may contain small numbers, and bearing in mind the potential importance of the intervention, we will report the results of all subgroup analyses and not just those that reach statistical significance to avoid false negatives. The above process will involve conducting many tests, which will not be independent of each other. Rather than adjusting confidence intervals or p-values to account for this we will present the results of all analyses and caution the user regarding the interpretation of the results. Indeed, some statisticians recommend never correcting for multiple comparisons while analyzing data.⁶⁵⁻⁶⁶ According to Rothman,⁶⁵ reducing the type I error for null associations increases the type II error for those associations that are not null. He recommends a policy of not making adjustments for multiple comparisons because it will lead to fewer errors of interpretation when the data under evaluation are not random numbers but actual observations on nature.

The HiP grant was introduced and withdrawn at the same time as other interventions that may have an impact on birthweight. Healthy Start is a means tested voucher scheme for pregnant women. If they are in receipt of certain benefits or under 18 years old, then they are eligible for free vitamins and vouchers to be spent on fruits and vegetables. This scheme replaced the means tested parts of the Welfare Food Scheme in the UK (including Scotland in 2006) and is still currently in place. During this period, there were policy changes in the optimal timing of first booking appointments due to changes in blood tests offered to pregnant women in the Pregnancy Screening Programme. These changes were first discussed in 2008 and had to be implemented by all Health Boards by March 2011.⁶⁷⁻⁶⁸ Early booking is a HEAT target of the Scottish Government (Health improvement for the people of Scotland Efficiency and governance improvements, Access to services, Treatment appropriate to individuals H11.1).⁶⁹ At least 80% of pregnant women in each SIMD quintile will have booked for antenatal care by the 12th week of gestation by March 2015.

1
2
3 A further piece of legislation that may affect birthweight is the introduction of the smoking
4 ban in public places in Scotland in March 2006. Mackay et al ⁷⁰ reported a reduction in the
5 prevalence of current smoking among women who conceived after the introduction of the
6 legislation prohibiting smoking. They also reported a reduction in small and very small for
7 gestational age, as well as in absolute low birth weight after the legislation. We will carry out
8 a further analysis restricting the pre-intervention HiP grant period to April 2006-March 2009.
9

10
11
12
13
14 It is possible that harm may have occurred due to the cash transfer. The £190 was given to
15 pregnant women with no restriction as to how it should be spent, and we do not know how
16 the money was used. We are examining how the intervention group differed; birthweight
17 could have reduced or increased. We will carry out 2-sided hypothesis tests to ensure that we
18 are able to detect any such potential harmful effect.
19

20
21
22
23 We will conduct sensitivity analyses to increase the probability that any observed effect can
24 be attributed to the HiP grant. The timing of the HiP grant is well defined and fixed, therefore
25 using the interrupted time series approach any effects within that window can be observed.
26

27
28 We plan to carry out 3 analyses for this.
29

- 30 1- We will extend this window for some months before April 2009 (births before the HiP
31 grant was introduced).
32
- 33 2- We will extend this window for some months after April 2011 (births after the HiP
34 grant was withdrawn).
35
- 36 3- We will extend the window both before and after the HiP grant period. In each case
37 we would expect to see a dilution of any effects of the HiP grant.
38
39
40
41

42
43 The statistical analysis plan detailing the outcomes and the covariates, which will be
44 considered for adjustment in the statistical models are presented in table 2.
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 2: Analysis plan detailing the outcomes and the covariates that will be considered for adjustment in the statistical models

Primary outcome	Secondary outcomes											Maternal smoking during this pregnancy
	Booking status		Measures of stage			Measures of size		Other birth outcomes				
	Birth-weight	Gestation at booking	Booking before 25 weeks	Gestational age at delivery	Term at birth	Weight-for-dates	Head circumference Crown to heel length	Mode of delivery	Still-birth	5 minutes Apgar score	Neonatal death	
Covariates												
I- Measured covariates												
A- Socio-demographic determinants												
A-1. Related to the baby												
Date of birth	X	X	X	X	X	X	X	X	X	X	X	X
Sex	X			X	X	X	X	X	X	X	X	
Gestational age at delivery	X						X	X	X	X	X	
Birthweight							X			X	X	
Mode of delivery										X	X	
A-2. Related to the mother												
Hip grant	X	X	X	X	X	X	X	X	X	X	X	X
Age	X	X	X	X	X	X	X	X	X	X	X	X
Weight at booking	X	X	X	X	X	X	X	X	X	X	X	
Height	X			X	X	X	X	X	X	X	X	
Ethnic group	X	X	X	X	X	X	X	X	X	X	X	X

5	Parity	X	X	X	X	X	X	X	X	X	X	X	X
6	Marital status	X	X	X	X	X	X	X	X	X	X	X	X
7	Social class	X	X	X	X	X	X	X	X	X	X	X	X
9	B- Medical risks of the current pregnancy and before pregnancy												
12	Diabetes	X	X	X	X	X	X	X	X	X	X	X	X
13	Hypertension	X	X	X	X	X	X	X	X	X	X	X	X
14	Infection	X			X	X	X	X	X	X	X	X	X
15	Congenital anomalies	X			X	X	X	X	X	X	X	X	X
16	Induction of labour								X	X	X	X	
17	Duration of labour								X	X	X	X	
21	C- Medical risks related to previous pregnancies												
23	Previous spontaneous abortions		X	X						X			
24	Previous stillbirths		X	X						X			
25	Previous neonatal deaths		X	X								X	
27	D- Environmental and behavioural risks												
29	Income domain of the SIMD	X	X	X	X	X	X	X	X	X	X	X	X
30	Urban/rural status of the area of residence	X	X	X	X	X	X	X	X	X	X	X	X
31	Booking status (gestational age at booking, booking before 25 weeks)	X			X	X	X	X	X	X	X	X	X

1													
2													
3													
4													
5	Smoking status												
6	(Before and												
7	during												
8	pregnancy)	X	X	X	X	X	X	X	X	X	X	X	
9	Typical weekly												
10	alcohol												
11	consumption												
12	(Before and												
13	during												
14	pregnancy)	X	X	X	X	X	X	X	X	X	X	X	X
15	Drug misuse												
16	during this												
17	pregnancy	X	X	X	X	X	X	X	X	X	X	X	X
18													
19	II- Unmeasured covariates												
20	Maternal weight gain												
21	Maternal nutrition												
22	Maternal education												
23	Maternal exposure to stress												
24	Maternal physical activity												
25	Exposure to toxic substances												
26	Birth interval												
27	History of pre-term birth												
28													
29													
30	Statistical methods												
31	Multilevel linear												
32	regression	X	X		X			X					
33	Multilevel binomial												
34	logistic regression			X			X		X		X		X
35	Multilevel multinomial												
36	logistic regression					X		X		X			
37													
38													
39													
40													
41													21
42													
43													
44													
45													
46													
47													
48													
49													

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

X: variables which will be considered for adjustment in the statistical analysis

For peer review only

Economic analysis

The cost-effectiveness analysis will be based around relating the estimated cost of the intervention (£190 for HiP grant plus the costs of administering the grant) to the observed benefits of the programme (birthweight changes and changes in secondary endpoints such as stillbirths) from the natural experiment. As part of the project an economic model will be developed based on a review of the literature to relate birthweight changes (and any secondary outcomes affected by the HiP grant identified in this study) to long-term cost and health outcomes (in terms of QALYs). Other potential outcomes (such as the effect of birthweight on long term educational outcomes) will be summarised, but may not be included in the cost-per-QALY analysis. The review will inform only the relationship between birthweight and long-term outcomes, the effectiveness of the HiP grant will be taken only from the current study.

The perspective taken will be that of the UK National Health Service in the first instance. For this particular intervention it will be important to consider two further perspectives: the broader Public Sector (due to the relationship between LBW and social care/educational development), and society as whole (since the HiP grant is a transfer payment and therefore there is no net cost to society of transferring the grant from Government to individuals beyond the administration costs).

Of particular interest will be the relative cost-effectiveness of the programme between different socioeconomic groups identified in the main analysis. This may lead to differential policy recommendations for different socioeconomic groups. Uncertainty in the modelling of long-term outcomes will be subject to extensive sensitivity analysis to explore the robustness of the cost-effectiveness analysis.

IMPLICATIONS

Maternal nutrition plays a crucial role in influencing fetal growth and birth outcomes. It is a modifiable risk factor of public health importance in the effort to prevent adverse birth outcomes, particularly among low-income populations.²⁴ According to Barker, “*the seeds of inequalities in health in the next century are being sown today, in inner cities and other communities where adverse influences impact upon the growth, nutrition and health of mothers and their infants*”.⁷¹

The HiP grant was cash given to the pregnant women with no constraint on its use. However, whether cash transfers are more efficient than “vouchers” or subsidies, which try to target the “appropriate expenditure”, remains a controversial topic in economics.⁷² This is because vouchers, for example, free up disposable income if they displace planned expenditure. This evaluation study may show the HiP grant increased birthweight across the population. If so, then a benefit would be to recommend the re-introduction of a universal cash transfer or, if we believed more evidence was needed that the HiP grants were delivering this benefit, the development of a randomized controlled trial for a similar cash transfer. An additional benefit will be the relative cost-effectiveness of the HiP grant between different socioeconomic groups identified in the main analysis. This may lead to differential policy recommendations for different socioeconomic groups with consequent reduction in health inequalities.

ETHICS AND DISSEMINATION

Ethical approval is not required as there is no primary data collection. Indeed, the information from maternal and birth records from all hospitals in Scotland are routinely collected. Approval for data collection, storage and release for research purpose has been given (6th May 2014; PAC38A/13) by the Privacy Advisory Committee, an Advisory Committee to NHS National Service Scotland and the Registrar General.

The results of this study will be disseminated through peer-reviewed publications in public health research journals, national and international conferences.

AUTHOR'S CONTRIBUTIONS

Ruth Dundas was involved in the conception of the study design, literature search and prepared the first draft of the study protocol. She will contribute to the statistical analysis and the interpretation of the results.

Samiratou Ouédraogo contributed to the literature search and the preparation of the present protocol paper. She will be responsible for the statistical analysis and contribute to the interpretation of the results.

Lyndal Bond was involved in the conception of the study design. She will contribute to the interpretation of the results.

Andrew H Briggs designed the health economic analysis aspect of the protocol. He will oversee the cost-effectiveness analysis and assist with writing the health economic paper.

James Chalmers was involved in the conception of the study design.

Ron Gray was involved in the conception of the study design. He will contribute to the interpretation of the results.

Rachael Wood will contribute to the interpretation of the results.

Alastair H Leyland was involved in the conception of the study design, literature search and contributed to all sections. He will contribute to the statistical analysis and the interpretation of the results.

All authors read and approved the final manuscript.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

COMPETING INTERESTS

We declare that we have no conflicts of interest.

For peer review only

FUNDING STATEMENT

This project was funded by the National Institute for Health Research Public Health Research Board (project number 12/3070/02). The Social and Public Health Sciences Unit is core funded by the Medical Research Council (MC_UU_12017/5) and the Chief Scientist Office of the Scottish Government Health Directorates (SPHSU2).

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Public Health Research Board, NIHR, NHS or the Department of Health.

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

REFERENCE LIST

1. Frankel S, Elwood P, Sweetnam P, et al. Birthweight, body-mass index in middle age, and incident coronary heart disease. *Lancet* 1996;348(9040):1478-80.
2. Leon DA, Lithell HO, Vagero D, et al. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15 000 Swedish men and women born 1915-29. *BMJ* 1998;317(7153):241-5.
3. Reyes L, Manalich R. Long-term consequences of low birth weight. *Kidney Int Suppl* 2005(97):S107-11.
4. Class QA, Rickert ME, Lichtenstein P, et al. Birth weight, physical morbidity, and mortality: a population-based sibling-comparison study. *Am J Epidemiol* 2014;179(5):550-8.
5. Hendryx M, Luo J, Knox SS, et al. Identifying multiple risks of low birth weight using person-centered modeling. *Womens Health Issues* 2014;24(2):e251-6.
6. Barker DJ. Birth weight and hypertension. *Hypertension* 2006;48(3):357-8.
7. Barker DJ, Eriksson JG, Forsen T, et al. Fetal origins of adult disease: strength of effects and biological basis. *Int J Epidemiol* 2002;31(6):1235-9.
8. Barker DJ. In utero programming of chronic disease. *Clin Sci (Lond)* 1998;95(2):115-28.
9. Barker DJ. The fetal and infant origins of adult disease. *BMJ* 1990;301(6761):1111.
10. Negrato C, Gomes M. Low birth weight: causes and consequences. *Diabetol Metab Syndr* 2013;5(1):49.
11. Valero De Bernabe J, Soriano T, Albaladejo R, et al. Risk factors for low birth weight: a review. *Eur J Obstet Gynecol Reprod Biol* 2004;116(1):3-15.
12. EURO-PERISTAT. "Babies' health: mortality and morbidity during pregnancy and in the first year of life" in "The European Perinatal Health Report 2010". 2013.

1
2
3 <http://www.europeristat.com/images/doc/Peristat%202013%20V2.pdf>. (Accessed 28 August
4 2014).

5
6
7
8 13. World Health Organisation. International Statictical Classification of Diseases and
9 Related Health Problems- ICD-10. 10th Revision. Geneva: World Health Organisation, 2010.
10 <http://www.who.int/classifications/icd/en/>. (Accessed 28 August 2014).

11
12
13
14 14. OECD. “Infant health: Low birth weight”, in Health at a Glance: Europe 2012. In:
15 Publishing O, ed., 2012. <http://www.oecd->
16 [ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest)
17 [&checksum=368A07F542E03A0442EFDEB9B002B6AE](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest) . (Accessed 28 August 2014).

18
19
20
21 15. Macfalane A, Dattani N. European Perinatal Health Report: highlights from a United
22 Kingdom perspective. London, 2013. <http://www.europeristat.com/images/Euro->
23 [peristat%20UK%20briefing.pdf](http://www.europeristat.com/images/Euro-peristat%20UK%20briefing.pdf). (Accessed 28 August 2014).

24
25
26
27 16. Madden D. The relationship between low birth weight and socioeconomic status in
28 Ireland. *J Biosoc Sci* 2014;46(2):248-65.

29
30
31
32 17. Frimmel W, Pruckner GJ. Birth weight and family status revisited: evidence from
33 Austrian register data. *Health Econ* 2014;23(4):426-45.

34
35
36
37 18. Huxley R. Smoking, birthweight, and mortality across generations. *Eur Heart J*
38 2013;34(44):3398-9.

39
40
41
42 19. Fairley L, Leyland AH. Social class inequalities in perinatal outcomes: Scotland 1980-
43 2000. *J Epidemiol Community Health* 2006;60(1):31-6.

44
45
46
47 20. Weightman AL, Morgan HE, Shepherd MA, et al. Social inequality and infant health in
48 the UK: systematic review and meta-analyses. *BMJ Open* 2012;2(3):e000964.

49
50
51
52 21. Juarez SP, Merlo J. Revisiting the effect of maternal smoking during pregnancy on
53 offspring birthweight: a quasi-experimental sibling analysis in Sweden. *PLoS One*
54 2013;8(4):e61734.
55
56
57

- 1
2
3 22. Zdravkovic T, Genbacev O, McMaster MT, et al. The adverse effects of maternal
4 smoking on the human placenta: a review. *Placenta* 2005;26(Suppl A):S81-6.
5
6
7
8 23. Villar J, Merialdi M, Gulmezoglu AM, et al. Nutritional interventions during pregnancy
9 for the prevention or treatment of maternal morbidity and preterm delivery: an overview of
10 randomized controlled trials. *J Nutr* 2003;133(5 Suppl 2):1606S-25S.
11
12
13
14 24. Abu-Saad K, Fraser D. Maternal nutrition and birth outcomes. *Epidemiol Rev*
15 2010;32(1):5-25.
16
17
18
19 25. Wu G, Imhoff-Kunsch B, Girard AW. Biological mechanisms for nutritional regulation of
20 maternal health and fetal development. *Paediatr Perinat Epidemiol* 2012;26(Suppl 1):4-26.
21
22
23
24 26. Mason JB, Saldanha LS, Ramakrishnan U, et al. Opportunities for improving maternal
25 nutrition and birth outcomes: synthesis of country experiences. *Food Nutr Bull*
26 2012;33(Suppl 2):S104-37.
27
28
29
30 27. Thangaratinam S, Rogozinska E, Jolly K, et al. Effects of interventions in pregnancy on
31 maternal weight and obstetric outcomes: meta-analysis of randomised evidence. *BMJ*
32 2012;344:e2088.
33
34
35
36 28. Glassman A, Duran D, Fleisher L, et al. Impact of Conditional Cash Transfers on
37 Maternal and Newborn Health. *J Health Popul Nutr* 2013;4:19.
38
39
40
41 29. Sutherland K, Christianson JB, Leatherman S. Impact of targeted financial incentives on
42 personal health behavior: a review of the literature. *Med Care Res Rev* 2008;65(Suppl
43 6):36S-78S.
44
45
46
47 30. Marteau TM, Ashcroft RE, Oliver A. Using financial incentives to achieve healthy
48 behaviour. *BMJ* 2009;338:b1415.
49
50
51
52 31. Giles EL, Robalino S, McColl E, et al. The effectiveness of financial incentives for health
53 behaviour change: systematic review and meta-analysis. *PLoS One* 2014;9(3):e90347.
54
55
56
57
58
59
60

- 1
2
3 32. Brownell M, Chartier M, Au W, et al. Evaluation of the Healthy Baby Program.
4 Winnipeg, MB: Manitoba Centre for Health Policy. 2010. [http://mchp-](http://mchp-appserv.cpe.umanitoba.ca/reference/Healthy_Baby.pdf)
5 [appserv.cpe.umanitoba.ca/reference/Healthy_Baby.pdf](http://mchp-appserv.cpe.umanitoba.ca/reference/Healthy_Baby.pdf). (Accessed 22 September 2014).
6
7
8
9
10 33. Neil G. Universal to selective. Transformation of the Welfare State: The Silent Surrender
11 of Public Responsibility: Oxford University Press 2002:20.
12
13
14 34. Mkandawire T. Targeting and Universalism in poverty reduction. Secondary Targeting
15 and Universalism in poverty reduction. 2005.
16 <http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EEA0B0>
17 [C12570FF00493EAA/\\$file/mkandatarget.pdf](http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EEA0B0). (Accessed 28 August 2014).
18
19
20
21
22 35. Craig P, Cooper C, Gunnell D, et al. Using natural experiments to evaluate population
23 health interventions: new Medical Research Council guidance. *J Epidemiol Community*
24 *Health* 2012;66(12):1182-6.
25
26
27
28
29 36. Medical Research Council. Using natural experiments to evaluate population health
30 interventions: guidance for producers and users of evidence.
31 [http://www.behaviourworksaustralia.org/wp-](http://www.behaviourworksaustralia.org/wp-content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf)
32 [content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf](http://www.behaviourworksaustralia.org/wp-content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf). (Accessed 28
33 August 2014).
34
35
36
37
38 37. Einarsdottir K, Kemp A, Haggard FA, et al. Increase in caesarean deliveries after the
39 Australian Private Health Insurance Incentive policy reforms. *PLoS One* 2012;7(7):e41436.
40
41
42
43 38. Ramsay CR, Matowe L, Grilli R, et al. Interrupted time series designs in health
44 technology assessment: lessons from two systematic reviews of behavior change strategies.
45 *Int J Technol Assess Health Care* 2003;19(4):613-23.
46
47
48
49
50 39. Penfold RB, Zhang F. Use of interrupted time series analysis in evaluating health care
51 quality improvements. *Acad Pediatr* 2013;13(6 Suppl):S38-44.
52
53
54
55
56
57
58
59
60

- 1
2
3 40. Administrative Data Liaison Service. Maternity and Neonatal Linked Database.
4 <http://www.adls.ac.uk/nhs-scotland/maternity-and-neonatal-linked-database/?detail>.
5
6 (Accessed 16 September 2014).
7
8
- 9 41. Kendrick SW and Clarke JA. The Scottish Record Linkage System. Health Bulletin 1993
10 51(2):72-79.
11
12
- 13 42. Administrative Data Liaison Service. Scottish Birth Record. [http://www.adls.ac.uk/nhs-](http://www.adls.ac.uk/nhs-scotland/sbr-scottish-birth-record/?detail)
14 [scotland/sbr-scottish-birth-record/?detail](http://www.adls.ac.uk/nhs-scotland/sbr-scottish-birth-record/?detail). (Accessed 16 September 2014).
15
16
- 17 43. Administrative Data Liaison Service. Birth registrations. [http://www.adls.ac.uk/national-](http://www.adls.ac.uk/national-records-of-scotland/birth-registrations/?detail)
18 [records-of-scotland/birth-registrations/?detail](http://www.adls.ac.uk/national-records-of-scotland/birth-registrations/?detail). (Accessed 16 September 2014).
19
20
- 21 44. Information Service Division. Birth in Scottish Hospitals.
22 <http://www.isdscotland.org/Health-Topics/Maternity-and-Births/Births/Background.asp>.
23
24 (Accessed 16 September 2014).
25
26
- 27 45. General Register Office for Scotland. Vital Events-Births. [http://www.gro-](http://www.gro-scotland.gov.uk/statistics/theme/vital-events/births/index.html)
28 [scotland.gov.uk/statistics/theme/vital-events/births/index.html](http://www.gro-scotland.gov.uk/statistics/theme/vital-events/births/index.html). (Accessed 16 September
29 2014).
30
31
- 32 46. National Health Service Scotland. Data Quality Assurance Assessment of Maternity Data
33 (SMR02). Scotland report April 2010.
34
35 [http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DQA-Assessment-of-Maternity-Data-](http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DQA-Assessment-of-Maternity-Data-SMR02-2008-to-2009.pdf)
36 [SMR02-2008-to-2009.pdf](http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DQA-Assessment-of-Maternity-Data-SMR02-2008-to-2009.pdf). (Accessed 11 September 2014).
37
38
- 39 47. Taulbut M, Walsh D. Poverty, parenting and poor early years' experiences in Scotland,
40 England and three city regions. 2013. [http://socialwelfare.bl.uk/subject-areas/services-client-](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty__parenting_and_poor_health.pdf)
41 [groups/families/glasgowcentreforpopulationhealth/164762Poverty__parenting_and_poor_hea](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty__parenting_and_poor_health.pdf)
42 [lth.pdf](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty__parenting_and_poor_health.pdf). (Accessed 11 September 2014).
43
44
- 45 48. Carstairs V, Morris R. Deprivation: explaining differences in mortality between Scotland
46 and England and Wales. Brit Med J 1989;299:886-889.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 49. NHS National Services Scotland. Births in Scottish Hospital: Smoking and Pregnancy
4 <http://www.isdscotlandarchive.scot.nhs.uk/isd/2911.html>. (Accessed 16 September 2014).
5
6
7
8 50. General Register Office for Scotland. Vital Events-General Background Informations.
9 <http://www.gro-scotland.gov.uk/statistics/theme/vital-events/births/index.html>. (Accessed 16
10 September 2014).
11
12
13 51. General Register Office for Scotland. Vital Events-General Background Informations:
14 Occupation and social class / socio-economic classification. [http://www.gro-](http://www.gro-scotland.gov.uk/files2/stats/vital-events/ve-occupation-social-classification.pdf)
15 [scotland.gov.uk/files2/stats/vital-events/ve-occupation-social-classification.pdf](http://www.gro-scotland.gov.uk/files2/stats/vital-events/ve-occupation-social-classification.pdf). (Accessed 16
16 September 2014).
17
18
19
20 52. The National Statistics Socio-economic Classification (NS-SEC rebased on the
21 SOC2010). [http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-](http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html)
22 [classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-](http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html)
23 [manual/index.html](http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html). (Accessed 28 August 2014).
24
25
26
27
28
29 53. Aspinall PJ, Jacobson B. Why poor quality of ethnicity data should not preclude its use
30 for identifying disparities in health and healthcare. *Qual Saf Health Care* 2007;16(3):176-80.
31
32
33 54. Scholmerich VL, Erdem O, Borsboom G, et al. The association of neighborhood social
34 capital and ethnic (minority) density with pregnancy outcomes in the Netherlands. *PLoS One*
35 2014;9(5):e95873.
36
37
38
39 55. Margerison-Zilko C. The Contribution of Maternal Birth Cohort to Term Small for
40 Gestational Age in the United States 1989-2010: an Age, Period, and Cohort Analysis.
41 *Paediatr Perinat Epidemiol* 2014;28(4):312-21.
42
43
44
45 56. The Scottish Government. Scottish Index of Multiple Deprivation 2012: A national
46 Statistics publication for Scotland 2012. [http://22fa0f74501b902c9f11-](http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf)
47 [8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf](http://22fa0f74501b902c9f11-8b3fbddfa1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf).
48
49 (Accessed 28 August 2014).
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 57. The Scottish Government. Scottish Index of Multiple Deprivation 2012: Technical notes.
4 <http://simd.scotland.gov.uk/publication-2012/technical-notes/domains-and->
5 [indicators/income-domain/](http://simd.scotland.gov.uk/publication-2012/technical-notes/domains-and-). (Accessed 16 September 2014).
6
7
8
9
10 58. Pattenden S, Dolk H, Vrijheid M. Inequalities in low birth weight: parental social class,
11 area deprivation, and "lone mother" status. *J Epidemiol Community Health* 1999;53(6):355-
12 8.
13
14
15 59. Spencer N, Bambang S, Logan S, et al. Socioeconomic status and birth weight:
16 comparison of an area-based measure with the Registrar General's social class. *J Epidemiol*
17 *Community Health* 1999;53(8):495-8.
18
19
20
21 60. Fairley L, Dundas R, Leyland AH. The influence of both individual and area based
22 socioeconomic status on temporal trends in Caesarean sections in Scotland 1980-2000. *BMC*
23 *Public Health* 2011;11:330.
24
25
26
27
28 61. Kent ST, McClure LA, Zaitchik BF, et al. Area-level risk factors for adverse birth
29 outcomes: trends in urban and rural settings. *BMC Pregnancy Childbirth* 2013;13:129.
30
31
32
33 62. Shankardass K, O'Campo P, Dodds L, et al. Magnitude of income-related disparities in
34 adverse perinatal outcomes. *BMC Pregnancy Childbirth* 2014;14:96.
35
36
37
38 63. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in
39 epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393.
40
41
42
43 64. Shadish WR, Cook TD, Campbell DT. Quasi-experiments: Interrupted time-series
44 designs. In *Experimental and quasi-experimental designs for generalized causal inference*.
45 Boston: Houghton-Mifflin 2002:171-206.
46
47
48
49 65. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology*
50 1990;1(1):43-6.
51
52
53
54 66. Greenland S. Multiple comparisons and association selection in general epidemiology. *Int*
55 *J Epidemiol* 2008;37(3):430-4.
56
57
58
59
60

- 1
2
3 67. National Service Division. Pregnancy Screening Programmes.
4 <http://www.nsd.scot.nhs.uk/services/screening/pregscreening/index.html>. (Accessed 28
5 August 2014)
6
7
8
9
10 68. NHS Health Scotland. Your guide to screening tests during pregnancy.
11 [http://www.healthscotland.com/uploads/documents/3985-](http://www.healthscotland.com/uploads/documents/3985-YourGuideToScreeningTestsDuringPregnancy_1.pdf)
12 [YourGuideToScreeningTestsDuringPregnancy_1.pdf](http://www.healthscotland.com/uploads/documents/3985-YourGuideToScreeningTestsDuringPregnancy_1.pdf). (Accessed 28 August 2014).
13
14
15
16 69. The Scottish Government. NHS Performance Targets.
17
18 [http://www.scotland.gov.uk/Topics/Health/Quality-Improvement-Performance/NHS-](http://www.scotland.gov.uk/Topics/Health/Quality-Improvement-Performance/NHS-Performance-Targets)
19 [Performance-Targets](http://www.scotland.gov.uk/Topics/Health/Quality-Improvement-Performance/NHS-Performance-Targets). (Accessed 16 September 2014).
20
21
22
23 70. Mackay DF, Nelson SM, Haw SJ, et al. Impact of Scotland's smoke-free legislation on
24 pregnancy complications: retrospective cohort study. PLoS Med 2012;9(3):e1001175.
25
26
27
28 71. Barker DJ. The foetal and infant origins of inequalities in health in Britain. J Public
29 Health Med 1991;13(2):64-8.
30
31
32
33 72. Gentilini U. Cash and food transfers: A Primer. World Food Programme. 2007.
34 https://www.wfp.org/sites/default/files/OP18_Cash_and_Food_Transfers_Eng%2007.pdf
35 (Accessed 16 September 2014).
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

PROJECT PROTOCOL

Title: Evaluation of Health in Pregnancy grants in Scotland: [a protocol for](#) a natural experiment

Authors: Ruth Dundas¹, Samiratou Ouédraogo¹, Lyndal Bond², Andrew H Briggs³, James Chalmers⁴, Ron Gray⁵, Rachael Wood⁴, Alastair H Leyland¹

Affiliations:

¹ MRC/CSO Social and Public Health Sciences Unit, University of Glasgow, Glasgow, UK

² Centre of Excellence in Intervention and Prevention Science, Melbourne, Australia

³ Health Economics and Health Technology Assessment, University of Glasgow, Glasgow, UK

⁴ Information Services Division, NHS National Services Scotland, Edinburgh, UK

⁵ National Perinatal Epidemiology Unit, University of Oxford, UK

Correspondence to:

Ruth Dundas

MRC/CSO Social and Public Health Sciences Unit, University of Glasgow

200 Renfield Street, Glasgow G2 3QB, Scotland

Tel: +44 141 353 7541 Email: ruth.dundas@glasgow.ac.uk

Keywords: Low birthweight; interrupted time series; multilevel analysis; Health in Pregnancy grant; natural experiment.

ABSTRACT

Introduction

A substantial proportion of low birthweight (LBW) is attributable to the mother's cultural and socioeconomic circumstances. Early childhood programmes have been widely developed to improve child outcomes. In the UK, the Health in Pregnancy (HiP) grant, a universal conditional cash transfer of £190, was introduced for women reaching the 25th week of pregnancy with a due date on/or after 6th April 2009 and subsequently withdrawn for women reaching the 25th week of pregnancy on/or after 1st January 2011. The current study focuses on the evaluation of the effectiveness and cost-effectiveness of the HiP grant.

Methods and analysis

The population under study will be all singleton births in Scotland over the periods of January 2004 to March 2009 (pre-intervention), April 2009 to April 2011 (intervention) and May 2011 to December 2013 (post-intervention). Data will be extracted from the Scottish maternity and neonatal database. The analysis period 2004-2013 should yield over 585,000 births. The primary outcome will be birthweight among singleton births. Other secondary outcomes will include gestation at booking, booking before 25 weeks; measures of size and stage; gestational age at delivery; weight-for-dates, term at birth; birth outcomes and maternal smoking. The main statistical method we will use is interrupted time series. Outcomes will be measured on individual births nested within mothers, with mothers themselves clustered within datazones. Multilevel regression models will be used to determine whether the outcomes changed during the period in which the HiP grants was in effect. Subgroup analyses will be conducted for those groups most likely to benefit from the payments.

Ethics and dissemination

Approval for data collection, storage and release for research purpose has been given (6th of May 2014, PAC38A/13) by the Privacy Advisory Committee. The results of this study will be disseminated through peer-reviewed publications in journals, national and international conferences.

ARTICLE SUMMARY

Article focus

- To evaluate the effectiveness and cost-effectiveness of Health in Pregnancy grant (HiP) in Scotland.

Key messages

- We will assess the difference in birthweight for babies born to those mothers who were eligible for the HiP grant with babies born before the HiP grant was introduced or after it was withdrawn using interrupted time series multilevel analysis.
- Subgroup analyses will be conducted for those groups seen as having the greatest potential to benefit from the payments such as those living in the most deprived areas, those in the lowest social classes, lone mothers, primiparous women, teen mothers, mothers from ethnic minorities and selected combinations of these groups.
- As part of the project an economic model will be developed based on a review of the literature to relate birthweight changes to long-term cost and health outcomes (in terms of QALYs).

Strengths and limitations of this study

The strengths of this study are:

- This is the first study evaluating the effect and the cost-effectiveness of the HiP grant in Scotland. It will use routinely available vital event and maternal and neonatal health records that are known to have high completeness and accuracy.
- The evaluation of the HiP grant using an interrupted time series design will enable us to analyse birthweight trends in Scotland and detect whether the intervention has had an effect over and above the underlying temporal trend. The use of interrupted time series will overcome other biases such as the autocorrelation of repeated measurements (measurement taken close together are related), seasonal effects (birthweight varies according to month of birth), the duration of the intervention (we will have pre-intervention intervention and post-intervention), and random variation in the measurement (birthweight).

The limitations of this study

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47
- 48
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60
- This study will evaluate the effect and the cost-effectiveness of the HiP grant, birthweight and other birth outcomes in Scotland using obstetric as well as maternal data. However, these outcomes may be influenced by many factors, not all of which are routinely captured (such as maternal diet, maternal work and psychological stress, abuse, exposure to toxic substance).¹¹
- The HiP grant was money given to pregnant women with no constraint on its use. The use of routine data gives us no indication on how the money was spent.

INTRODUCTION

Low birthweight (LBW) due to preterm birth, intrauterine growth restriction, or being born small for gestational age (SGA), is commonly associated with perinatal mortality and impaired development¹⁻¹¹. Despite the improvement of the mortality in LBW babies over the past three decades, more than 70% of all neonatal mortality in Europe is found in infants weighing less than 2500 grams (g).¹²

LBW refers to birth weights below 2500 g,¹³ irrespective of the gestational age of the infant. In most developed countries, the prevalence of LBW has increased due to several reasons: the number of multiple births with the increased risks of pre-term births and low birth weight partly as a result of the rise in fertility treatments; older age at childbearing and increases in the use of delivery management techniques such as induction of labour and caesarean delivery, which have increased the survival rates of low birth weight babies.¹⁴ About one in 20 babies born in Europe in 2010 weighed less than 2500 g at birth.¹² With LBW estimated at 7.0% of live births in England and Wales, 6.5% in Scotland and 5.7% of live births in Northern Ireland, prevalence of LBW in the countries of the United Kingdom (UK) tended to be higher than in the rest of Europe.¹²⁻¹⁵ Moreover, compared with other Western European countries, the UK has an incidence of LBW (<2500g) and very LBW (<1500g) in the top third. The proportion of pre-term birth (<37 weeks) is also high compared with other Western European countries.

Considerable attention has been focused on the causal determinants of LBW, in order to identify potentially modifiable factors. A substantial proportion of LBW is attributable to the mother's cultural and socioeconomic circumstances such as socioeconomic status (SES), harmful behaviours (smoking and excessive alcohol consumption) and poor nutrition during pregnancy.^{11 16-18} In a study of social class inequalities in perinatal outcomes in Scotland, Fairley and Leyland¹⁹ reported a percentage of 5.8% LBW in unskilled social class (V) compared to 2.9% in professional social class (I) between 1995 and 2000. The systematic review and meta-analyses of social inequality and infant health in the UK performed by Weightman et al.²⁰ found that the odds ratio for low birth weight was 1.79 (95% CI 1.43 to 2.24) in the lowest compared to the highest social class. This effect may vary with maternal factors such as age and smoking status. Smoking during pregnancy reduces birthweight by 162 to 377 g, depending on daily consumption (larger reduction for heavy smokers) and the trimester in which exposure occurs (larger reduction during the last trimester).^{18,21-22}

1
2
3
4
5
6
7 The association between maternal nutrition and birth outcome is complex and is influenced
8 by many biologic, socioeconomic, and demographic factors, which vary widely in different
9 populations.²³⁻²⁴ However, it has been reported that favourable prenatal nutrition associated
10 with adequate prenatal care can have a positive impact on birth outcomes and morbidity in
11 adult life.²⁵⁻²⁶ Indeed, the developmental model of the origins of chronic disease proposes the
12 causal influence of undernutrition *in utero* on coronary heart disease and stroke in adult life.⁷⁻
13

14
15 ⁹ An improvement in fetal nutrition may therefore have far reaching consequences in terms of
16 the prevention of disease. A review of maternal nutrition and birth outcomes identified
17 improving maternal nutrition as being beneficial to the prevention of adverse birth outcomes
18 in lower social class groups.²⁴

19
20 A number of early childhood programmes have been developed to improve child outcomes.
21 There is mixed evidence that these programmes do provide such improvement. In a meta-
22 analysis of the effect of interventions in pregnancy on maternal and obstetric outcomes,
23 Thangaratinam et al. concluded that dietary and lifestyle interventions in pregnancy reduced
24 maternal gestational weight gain but had less effect on outcomes related to fetal weight and
25 other morbidity and mortality.²⁷ Glassman et al.²⁸ who reported the results of conditional cash
26 transfer programmes increasingly being adopted and scaled in developing countries, found
27 that the programmes have increased the uptake of maternal and newborn health services,
28 especially skilled attendance at delivery and antenatal monitoring. However, the impact of the
29 programs on maternal and newborn mortality has not been well documented. Therefore, they
30 recommended more rigorous impact evaluations that document impact pathways and take
31 factors, such as cost-effectiveness, into account. Other studies evaluating payments to
32 influence health behaviour found financial incentives were effective in increasing infrequent
33 behaviours such as attending clinic appointments particularly in low-income groups, and
34 recommended payments as being more effective than information and less restrictive than
35 legislation.²⁹⁻³¹ In Canada, Brownell et al. have evaluated a complex programme on a prenatal
36 benefit provided to families on low income during pregnancy.³² They found that the receipt
37 of this prenatal benefit was associated with a reduction in incidence of both low birthweight
38 babies and preterm births. They suggested that efforts should be made to ensure all low-
39 income women receive the income supplement.

40
41 In the UK, the Health in Pregnancy (HiP) grant was introduced for women reaching the 25th
42 week of pregnancy with a due date on/or after 6th April 2009. It was subsequently withdrawn
43 for women reaching the 25th week of pregnancy on/or after 1st January 2011. The HiP grant
44
45
46
47
48
49

1
2
3
4
5
6
7 was a universal conditional cash transfer of £190 for women reaching 25 weeks of pregnancy
8 if they had sought health advice from a doctor or midwife. It was designed to provide
9 additional financial support, in the last months of pregnancy, towards a healthy lifestyle
10 including diet, and it was suggested that the link to the requirement for pregnant women to
11 seek health advice from a professional may provide a greater incentive for expectant mothers
12 to seek the recommended health advice at the appropriate time. The grant was paid and
13 administered by Her Majesty's Revenue and Customs (HMRC) on receipt of a claim form
14 partly completed by the midwife or doctor. Advice was offered as normal by doctors and
15 midwives. Payment was made directly into a bank account with a telephone helpline
16 available to provide support through the claims process including options for payment in the
17 event of difficulties opening a bank account. Take up of the grant was said to be about the
18 same level as for child benefit (98-99%, personal communication, HMRC).

19
20
21
22
23
24 The current study focuses on the evaluation of the effectiveness and cost-effectiveness of the
25 HiP grant. As a primary outcome, we will consider the difference in birthweight for babies
26 born to those mothers who were eligible for the HiP grant with babies born before the HiP
27 grant was introduced or after it was withdrawn. Specific questions the research project will
28 address are:
29
30

- 31
32
33
34
35
36
37
38
39
40
41
- Were there differential impacts of the intervention for particular subgroups defined by socioeconomic (defined in terms of both area deprivation and individual occupational social class), demographic (marital status, age, maternal height), or obstetric (parity, previous caesarean section) factors or for selected combination of these groups?
 - Was the HiP grant cost-effective? How did cost-effectiveness vary across important subgroups identified as having differential outcomes?

42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The principle of universalism in the allocation of social benefits, that is the availability of social benefits to everyone as of right, is contrasted with allocation on a selective basis (targeted) in which benefits are allocated on the basis of need as determined by means testing of income.³³ The advantage of universal benefits is that they are easy to administer and can be efficiently delivered. The major disadvantage is that they are expensive, because they are delivered to those who do not need them as much as to those who do. However, the use of targeting involves some mechanism that discriminates between the poor and the non-poor. As such it always runs the danger of committing either type I errors which occur when someone

1
2
3
4
5
6
7 who deserves the benefits is denied them (underpayment, false positives), or type II errors,
8 which occur when benefits are paid to someone who does not deserve them (overpayment,
9 leakage).³⁴ The HiP grant represented an attempt to influence behaviour – appropriate and
10 timely receipt of antenatal care advice – by means of a relatively modest, universally applied
11 cash transfer. The evaluation of the effectiveness of such a payment may inform other
12 policies aiming to change behaviour.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

METHODS AND ANALYSIS

Study design

The HiP grant will be evaluated as a natural experiment using interrupted time series analysis to compare outcomes before the introduction of the intervention in Scotland and immediately after its withdrawal with those during the period for which it existed.

The Medical Research Council (MRC) has issued guidelines regarding the use of natural experiments to evaluate population health interventions when exposure to the intervention has not been manipulated by the researchers (Table 1).³⁵⁻³⁶

Table 1: Guidance for use of natural experiments to evaluate population health interventions

When to use a natural experimental approach?	How does the evaluation of HiP* grant meet these criteria?
<ul style="list-style-type: none"> ▪ There is a reasonable expectation that the intervention will have a significant health impact, but scientific uncertainty about the size or nature of the effects. 	<ul style="list-style-type: none"> ▪ The HiP grant represented an attempt to influence behaviour – appropriate and timely receipt of antenatal care advice. With the sample size we are using in this evaluation study, we are able to detect small changes in birthweight.
<ul style="list-style-type: none"> ▪ Natural experimental study is the most appropriate method for studying a given type of intervention. 	<ul style="list-style-type: none"> ▪ The HiP grant was a universally applied cash transfer available for all pregnant women with no discrimination between socioeconomic classes. This policy was not introduced using a randomised allocation
<ul style="list-style-type: none"> ▪ It is possible to obtain the relevant data from an appropriate study population, comprising groups with different levels of exposure to the intervention. 	<ul style="list-style-type: none"> ▪ The uptake of the HiP grant was thought to be 98-99%. The linked Scottish birth dataset has 98% coverage of births and the primary outcome, birthweight, is well measured, 99.9% complete and accurate. Exposure is determined by the dates for which the HiP grant was in existence.
<ul style="list-style-type: none"> ▪ The intervention or the principles behind it have the potential for replication, scalability or generalisability. 	<ul style="list-style-type: none"> ▪ The HiP grant is replicable everywhere in countries with similar health systems.

HiP* grant: Health in Pregnancy grant

1
2
3
4
5
6
7
8
9 The guidance advocates a number of designs including regression discontinuity designs such
10 as interrupted time series. The interrupted time series approach is a powerful tool used for
11 evaluating the impact of a policy change or quality improvement programme on the rate of an
12 outcome in a defined population of individuals.³⁷⁻³⁹ This approach will allow us to use a
13 comparison group of pregnant women who delivered before the HiP grant was introduced, an
14 intervention group who received the HiP grant and an additional post-intervention group who
15 delivered after the HiP grant was withdrawn. It will also allow adjustment for seasonality,
16 temporal trends and the socio-demographic and obstetric characteristics of the mother.
17
18
19
20
21
22

23 Study population

24
25 The population under study will be all singleton births in Scotland over the periods of
26 January 2004 to March 2009 (pre-intervention), April 2009 to April 2011 (intervention) and
27 May 2011 to December 2013 (post-intervention).
28
29

30 The Scottish maternity and neonatal database is a comprehensive record linkage system.⁴⁰⁻⁴¹
31 Probabilistic linkage procedures are used to add a unique identifier to all datasets to ensure all
32 relevant records relating to an individual can be linked as required. It facilitates the linkage of
33 a number of records from the system of Scottish Morbidity Records (SMR) including
34 mother's obstetric records (SMR02) and the baby's birth and neonatal information from
35 Scottish Birth Records (SBR).⁴² Further links to the stillbirth and infant Death Survey and the
36 National Records of Scotland (NRS) birth, stillbirth and infant death records can be carried
37 out. The coverage is almost all births in Scotland.⁴³ From NRS data, we know of all
38 registered births in Scotland (ie 100%). We have suitable record linked data on 98% of these
39 births.⁴⁴ These will nearly all be hospital births; a fairly high proportion of the missing
40 records are home births.
41
42
43
44
45

46
47 There is an average of about 56,000 births per year in Scotland.⁴⁵ The analysis period 2004-
48 2013 should yield over 585,000 births. The analysis period 2006-2013 should yield over
49 455,000 births.
50
51
52
53
54

We have chosen to use data from the Scotland for this evaluation for the following reasons. First, data are available at a national level on the approximately 56,000 deliveries per year. Second, Scotland has a long history of collecting high quality routine data; ~~the~~ The coverage, completeness and quality of the data are considered to be very high.⁴⁶ Third, the concentration of deprivation within parts of Scotland is unique within the UK.⁴⁷ ~~For~~ And ~~example six of the ten most deprived electoral constituencies in the UK are in Scotland and~~ using a UK wide Cartstairs index, the Scotland's population is over-represented in the bottom 5 deciles compared to England.⁴⁸ ~~Four~~ Fourth, data on smoking at booking have been routinely recorded in Scotland for a number of years.⁴⁹ This is not yet the case in England and Wales. The data can be linked to NRS civil registration data, which provides an estimate of completeness and contributes further information such as social class. The results will be generalisable to the rest of the UK and internationally. If the HiP grant proved beneficial in Scotland then there is every good reason to believe that a similar impact on outcomes could be achieved elsewhere and certainly in countries with similar health systems and comparable circumstances. Likewise, if the intervention was found to have been more effective for specific subgroups then we might expect subgroups to show greater benefits in other settings.

Study variables

Individual level and area level variables will be used in this study.

Individual level variables will include: birthweight, date of birth, sex, gestational age at delivery, preterm (delivery before the 37th week of pregnancy), weight-for-dates, 5 min Apgar score, crown to heel length, and head circumference. We will distinguish between spontaneous pre-term births and induced pre-term births. A potential reason for induced pre-term births is evidence of poor fetal growth; a proportion of these babies would become more severely growth retarded (more extremely small for gestational age) or stillborn.

Since maternal factors influence fetal growth,¹¹ individual level variables related to the mother will be examined: parity, age, height, weight at booking, diabetes, smoking status, gestation at booking, booking before 25 weeks, and marital status. Individual socioeconomic position will also be included using data from the birth registrations at NRS.⁵⁰ NRS collects occupation for both father and mother for births registered to married couples and jointly

1
2
3
4
5
6
7 registered by unmarried couples.⁵¹ Only mother's occupation is recorded for sole registered
8 births. The National Statistics Socio-economic Classification (NS-SEC)⁴⁰⁻⁵² will be used to
9 classify the individual socioeconomic position.
10

11 Marital status is an important variable as single mothers have consistently been shown to
12 have poorer birth outcomes.¹⁷⁻¹⁹ We are particularly interested in single mothers and social
13 class. Social class for lone mothers is an amalgamation of socioeconomic position and lone
14 parenthood.
15
16

17
18 Although the routinely collected data on ethnicity are incomplete and of dubious quality,^{46,53}
19 ethnicity remains important for birthweight and other neonatal outcomes.⁵⁴⁻⁵⁵ We will
20 therefore, within the constraints of the data, include ethnicity and undertake all analyses on
21 the subgroup of mother from a minority ethnic background. Within this subgroup, we will
22 examine the possibility of further distinction between ethnic groups.
23
24

25
26 Birthweight varies according to the socioeconomic status of the area of residence.²⁰ The
27 Scottish Index of Multiple Deprivation (SIMD) will be used and included as area level
28 variables in the analysis. The SIMD is the Scottish Government's official tool for identifying
29 those places in Scotland suffering from deprivation.⁴³⁻⁵⁶ It is a weighted sum of different
30 domains: income; employment; health; education; housing and geographical access (and
31 crime, added in the SIMD 2012). The SIMD provides a comprehensive picture of material
32 deprivation in small areas within Scotland. The index ranks 6505 areas from the most
33 deprived to the least deprived and measures the degree of deprivation of an area relative to
34 that of other areas. The areas employed by the SIMD are datazones and are small: the 6505
35 datazones have a mean population of 780 people. The reason for employing small area
36 geography at this scale is to permit identification of relatively small pockets of deprivation.
37 The health domain includes an indicator of the proportion of live singleton births that is
38 LBW. The outcomes of this project include birthweight and LBW and so it would not be
39 appropriate to use the health domain or the composite index which includes the health
40 domain. The income domain will therefore be used to assess inequalities at the area level.
41 This domain contributes 28% to the overall index and is highly correlated with the overall
42 SIMD. The income domain of the SIMD identifies areas where there are concentrations of
43 individuals and families living on low incomes. This is done by looking at the numbers of
44 people, both adult and children, who are receiving, or are dependent on, benefits related to
45
46
47
48
49
50
51
52
53

1
2
3
4
5
6
7 income or tax credits.⁵⁷ Each mother will be assigned to a datazone and its income domain
8 through her home postcode. Previous studies investigating inequalities in birthweight have
9 shown that area deprivation performs as well as or better than individual social class in
10 describing the extent of inequalities in the population.⁵⁸⁻⁵⁹ However, Fairley et al. who
11 studied the influence of both individual and area based socioeconomic status on temporal
12 trends in Caesarean sections between 1980 and 2000 in Scotland found that maternal social
13 class and area deprivation are different indicators of socioeconomic status which exhibit
14 independent effects on the probability of a woman receiving a Caesarean section.⁶⁰ The
15 multilevel analysis will allow us to analyse the effect of both parental social class and SMID
16 and the effect of their interaction on birthweight.

17
18 We will adjust the analyses on the urban or rural status of the mother's area of residence.
19 Indeed, Kent et al reported higher adverse birth outcome rates in isolated rural and more
20 population dense areas.⁶¹ They showed that these disparities are being maintained or
21 increasing over time in Alabama. Shankardass et al also found that the patterns of association
22 between socioeconomic position and LGA, spontaneous preterm birth and perinatal death
23 varied depending on urbanicity in Nova Scotia (Canada).⁶²

31 Outcome measures

32 Primary Outcome

33
34 The primary outcome will be birthweight among singleton births. This is influenced by many
35 factors including maternal nutrition and one of the intentions of the HiP grant was to improve
36 this.

39 Secondary Outcomes

40
41 The following secondary outcomes will be assessed:

- 42 - Gestation at booking,
- 43 - Booking before 25 weeks,
- 44 - Measures of size: crown to heel length, head circumference,
- 45 - Measures of stage: gestational age at delivery, weight-for-dates (standardised; small
46 for gestational age babies are those weighted less than the 5th centile weight, or large

1
2
3
4
5
6
7 for gestational age weighted more than the 90th centile weight), term at birth (pre-
8 term, babies are born at less than 37 weeks gestation; term babies are those born
9 between 37-42 weeks gestation and post-term babies are born after 42 weeks
10 gestation),
11

- 12 - Birth outcomes: mode of delivery, stillbirths, neonatal deaths, 5 minutes Apgar score.
13 Although there is some debate concerning the robustness of the Apgar score as an
14 outcome, it is in common use and we will therefore present results for this outcome
15 within the context of the wide debate on the subject.
16
17
18
19

20 Due in part to the introduction of smoking ban in Scotland in 2006, an additional outcome of
21 interest is maternal smoking. Maternal smoking is collected at booking and during pregnancy.
22 The health advice given when receiving the HiP grant might have an impact on smoking rates
23 during pregnancy over and above that of the smoke-free legislation. We will analyse the
24 temporal change in smoking rate by socioeconomic class and its effect on outcomes.
25
26
27
28
29

30 **Sample size**

31 The data are clustered in small areas, 6505 datazones. The sample size calculation takes this
32 clustering into account. Assuming an average of 56,000 singleton live births per year, and
33 allowing for the clustering within the 6505 datazones in Scotland (average population 780 per
34 datazone) with an estimated intraclass correlation coefficient of 0.05, we have power of 0.90
35 to detect an effect of 7g change in birthweight at a 95% significance level. This is not to say
36 that 7g is a clinically important threshold; rather, it is indicative of the power of the study.
37 The large national data set available to us will allow for subgroup analysis. In the 20% most
38 deprived areas, we will have power of 0.80 to detect an effect of 13g; among the 26% of
39 single mothers, we will have power of 0.80 to detect an effect of 11g. To put these small
40 effects into context, 50g is the estimated mean birthweight reduction reported in the meta-
41 analysis of the effect of interventions in pregnancy on maternal and obstetric outcomes.²⁷
42
43
44
45
46
47

48 We anticipate item non-response for some outcomes and explanatory variables. Our primary
49 outcome measure, birthweight, has a completion rate of 99.9%. There is high completion rate
50 (<1.5% missing) for all obstetric variables,⁴⁶ with the exception of crown to heel length (15%
51 missing) and head circumference (12% missing). The item non-response ranges from 8% for
52
53
54

1
2
3
4
5
6
7 maternal smoking to 20% for marital status. We will use multiple imputation to account for
8 missing data and all analyses will compare the results of analyses of complete cases and
9 multiple imputation.⁶³ Imputed models will be constructed such that they contain as many
10 relevant predictor variables as possible. The more variables that are used the greater the
11 amount of information available on which estimations are made. We will use all (or as many
12 as possible) obstetric and maternal variables in an imputation model to predict the missing
13 values. It is difficult to identify in advance the number of multiple imputed datasets we will
14 need to construct but it is likely to be between 5 and 10. We will then analyse these datasets
15 identically and combine the results to get the estimates and standard errors for the multiple
16 imputed data. These results will be compared to the complete case analysis results.

17
18 It is difficult to be specific about the missing data mechanism until we see the data but much
19 is likely to be missing completely at random (MCAR, e.g. certain hospitals are less likely to
20 collect specific items) or missing at random (MAR, when the missingness is related to known
21 variables and, conditional on these, is assumed to be unrelated to unmeasured variables).

22 23 24 25 26 27 28 29 30 **Data analysis plan**

31 32 Statistical analysis

33
34 Descriptive statistics of all variables will be presented as mean, standard deviation, minimum,
35 median and maximum for continuous variables and as proportions when the variables are
36 categorical.

37
38 The main statistical design we will use is interrupted time series.⁶⁴ Segmented regression
39 analysis will allow an estimation of the size of the effect of the HiP grant at different time
40 points, as well as changes in the trend of the effect over time after its implementation.

41
42 Outcomes will be measured on individual births, which are nested within mothers, with
43 mothers themselves clustered within datazones and Health Boards. Multilevel univariable and
44 multivariable models will be used to determine whether the outcomes changed during the
45 period in which the HiP grants were in effect. Multilevel linear regression will be used when
46 the outcome is continuous and multilevel binomial logistic regression when the outcome is
47 dichotomous. Multilevel multinomial logistic regression will be used for the multi-category
48 outcomes mode of delivery and 5 minutes Apgar score.

1
2
3
4
5
6
7 All analyses will be adjusted for temporal trends and seasonal variations in outcomes in
8 addition to maternal age, sex of child, parity, marital status, height, weight at booking,
9 diabetes, smoking status, gestation at booking, maternal diabetes, social class, maternal
10 smoking and area deprivation.
11

12
13 The effect of HiP grant on birthweight might have a carryover effect after the withdrawal of
14 the grant. In other words, post-intervention the slope in birthweight might not fall back to the
15 same rate as pre-intervention. This could be due to women who have gave birth during the
16 intervention subsequently having a birth postintervention but still heeding the health advice
17 given during their first pregnancy. We will carry out an additional analysis only on
18 primiparous women to avoid such contamination.
19
20

21
22 We will analyse pre-term births stratified by mode of delivery and stratified according to
23 whether the birth was induced or spontaneous.
24
25

26 We will repeat the main analyses including (i.e adjusting for the effect of) ethnicity along
27 with other covariates and compare the results with analyses excluding ethnicity to gauge the
28 impact of this on our results. We note that the quality of this variable (including the
29 completeness of recording) is poorer than for other variables and that only 1-2% of mothers
30 delivering in Scotland are from minority ethnic backgrounds.
31
32

33
34 The simplest model for the intervention effect will include a dummy variable “intervention”
35 covering the period from the introduction to the withdrawal of HiP grants, with adjustment
36 for relevant factors such as marital status. (More complex models of the effect of the
37 intervention will include an interaction of the intervention with the temporal trend). Before
38 carrying out specific subgroup analysis, we will identify differential effects by fitting
39 interaction terms. An assessment as to whether there is a differential effect of the intervention
40 for single women, for example, will involve a test of the significance of the intervention
41 between marital status and the intervention effect. If the interaction is significant this will aid
42 our understanding of the generalisability to other populations, including the rest of the UK.
43
44 Subgroup analyses will be conducted for those groups seen as having the greatest potential to
45 benefit from the payments such as those living in the most deprived areas, those in the lowest
46 social classes, lone mothers, primiparous women, teen mothers, mothers from ethnic
47 minorities and selected combinations of these groups. For each group we will replicate the
48 main analysis. This reduction in sample size for sub-group analyses will result in fewer
49
50
51
52
53

women/births being available but the same number of areas (datazones) will be analysed (apart from analyses restricted to those living in the most deprived areas).

An increase in birthweight, although desirable at a population level, may not be a beneficial outcome if the baby were already at risk of being large for gestational age (LGA). Separate subgroup analyses will therefore be conducted for women seen to be at high risk of delivering a LGA baby (women with diabetes) and for the remainder of the population. Given that some subgroups may contain small numbers, and bearing in mind the potential importance of the intervention, we will report the results of all subgroup analyses and not just those that reach statistical significance to avoid false negatives. The above process will involve conducting many tests, which will not be independent of each other. Rather than adjusting confidence intervals or p-values to account for this we will present the results of all analyses and caution the user regarding the interpretation of the results. Indeed, some statisticians recommend never correcting for multiple comparisons while analyzing data.⁶⁵⁻⁶⁶ According to Rothman,⁶⁵ reducing the type I error for null associations increases the type II error for those associations that are not null. He recommends a policy of not making adjustments for multiple comparisons because it will lead to fewer errors of interpretation when the data under evaluation are not random numbers but actual observations on nature.

The HiP grant was introduced and withdrawn at the same time as other interventions that may have an impact on birthweight. Healthy Start is a means tested voucher scheme for pregnant women. If they are in receipt of certain benefits or under 18 years old, then they are eligible for free vitamins and vouchers to be spent on fruits and vegetables. This scheme replaced the means tested parts of the Welfare Food Scheme in the UK (including Scotland in 2006) and is still currently in place. During this period, there were policy changes in the optimal timing of first booking appointments due to changes in blood tests offered to pregnant women in the Pregnancy Screening Programme. These changes were first discussed in 2008 and had to be implemented by all Health Boards by March 2011.⁶⁷⁻⁶⁸ Early booking is a HEAT target of the Scottish Government (Health improvement for the people of Scotland Efficiency and governance improvements, Access to services, Treatment appropriate to individuals H11.1).⁶⁹

At least 80% of pregnant women in each SIMD quintile will have booked for antenatal care by the 12th week of gestation by March 2015.

1
2
3
4
5
6
7 A further piece of legislation that may affect birthweight is the introduction of the smoking
8 ban in public places in Scotland in March 2006. Mackay et al ⁷⁰ reported a reduction in the
9 prevalence of current smoking among women who conceived after the introduction of the
10 legislation prohibiting smoking. They also reported a reduction in small and very small for
11 gestational age, as well as in absolute low birth weight after the legislation. We will carry out
12 a further analysis restricting the pre-intervention HiP grant period to April 2006-March 2009.
13
14

15
16 It is possible that harm may have occurred due to the cash transfer. The £190 was given to
17 pregnant women with no restriction as to how it should be spent, and we do not know how
18 the money was used. We are examining how the intervention group differed; birthweight
19 could have reduced or increased. We will carry out 2-sided hypothesis tests to ensure that we
20 are able to detect any such potential harmful effect.
21
22

23
24 We will conduct sensitivity analyses to increase the probability that any observed effect can
25 be attributed to the HiP grant. The timing of the HiP grant is well defined and fixed, therefore
26 using the interrupted time series approach any effects within that window can be observed.
27 We plan to carry out 3 analyses for this.
28
29

- 30 1- We will extend this window for some months before April 2009 (births before the HiP
31 grant was introduced).
- 32
33 2- We will extend this window for some months after April 2011 (births after the HiP
34 grant was withdrawn).
- 35
36 3- We will extend the window both before and after the HiP grant period. In each case
37 we would expect to see a dilution of any effects of the HiP grant.
38
39

40
41 The statistical analysis plan detailing the outcomes and the covariates, which will be
42 considered for adjustment in the statistical models are presented in table 2.
43
44
45
46
47
48
49
50
51
52
53
54

Table 2: Analysis plan detailing the outcomes and the covariates that will be considered for adjustment in the statistical models

	Primary outcome	Secondary outcomes											
		Booking status		Measures of stage			Measures of size		Other birth outcomes			Maternal smoking during this pregnancy	
	Birth-weight	Gestation at booking	Booking before 25 weeks	Gestational age at delivery	Term at birth	Weight-for-dates	Head circumference Crown to heel length	Mode of delivery	Still-birth	5 minutes Apgar score	Neonatal death		
Covariates													
I- Measured covariates													
A- Socio-demographic determinants													
A-1. Related to the baby													
Date of birth	X	X	X	X	X	X	X	X	X	X	X	X	X
Sex	X			X	X	X	X	X	X	X	X	X	
Gestational age at delivery	X						X	X	X	X	X		
Birthweight							X			X	X		
Mode of delivery										X	X		
A-2. Related to the mother													
Hip grant	X	X	X	X	X	X	X	X	X	X	X	X	X
Age	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight at booking	X	X	X	X	X	X	X	X	X	X	X		
Height	X			X	X	X	X	X	X	X	X		
Ethnic group	X	X	X	X	X	X	X	X	X	X	X		X

1													
2													
3													
4													
5													
6													
7													
8	Parity	X	X	X	X	X	X	X	X	X	X	X	X
9	Marital status	X	X	X	X	X	X	X	X	X	X	X	X
10	Social class	X	X	X	X	X	X	X	X	X	X	X	X
11	B- Medical risks of the current pregnancy and before pregnancy												
12													
13													
14	Diabetes	X	X	X	X	X	X	X	X	X	X	X	X
15	Hypertension	X	X	X	X	X	X	X	X	X	X	X	X
16	Infection	X		X	X	X	X	X	X	X	X	X	X
17	Congenital anomalies	X		X	X	X	X	X	X	X	X	X	X
18	Induction of labour								X	X	X	X	X
19	Duration of labour								X	X	X	X	X
20													
21	C- Medical risks related to previous pregnancies												
22													
23	Previous spontaneous abortions		X	X					X				
24	Previous stillbirths		X	X					X				
25	Previous neonatal deaths		X	X							X		
26													
27	D- Environmental and behavioural risks												
28													
29	Income domain of the SIMD	X	X	X	X	X	X	X	X	X	X	X	X
30	Urban/rural status of the area of residence	X	X	X	X	X	X	X	X	X	X	X	X
31	Booking status (gestational age at booking, booking before 25 weeks)	X			X	X	X	X	X	X	X	X	X
32													
33													
34													
35													
36													
37													
38													20
39													
40													
41													
42													
43													
44													
45													
46													
47													
48													
49													

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Smoking status
(Before and
during
pregnancy)
Typical weekly
alcohol
consumption
(Before and
during
pregnancy)
Drug misuse
during this
pregnancy

X	X	X	X	X	X	X	X	X	X	X	X	
X	X	X	X	X	X	X	X	X	X	X	X	X
X	X	X	X	X	X	X	X	X	X	X	X	X

II- Unmeasured covariates

Maternal weight gain
Maternal nutrition
Maternal education
Maternal exposure to stress
Maternal physical activity
Exposure to toxic substances
Birth interval
History of pre-term birth

Statistical methods

Multilevel linear
regression
Multilevel binomial
logistic regression
Multilevel multinomial
logistic regression

X	X		X			X					
			X		X			X		X	X
					X		X		X		

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

X: variables which will be considered for adjustment in the statistical analysis

For peer review only

Economic analysis

The cost-effectiveness analysis will be based around relating the estimated cost of the intervention (£190 for HiP grant plus the costs of administering the grant) to the observed benefits of the programme (birthweight changes and changes in secondary endpoints such as stillbirths) from the natural experiment. As part of the project an economic model will be developed based on a review of the literature to relate birthweight changes (and any secondary outcomes affected by the HiP grant identified in this study) to long-term cost and health outcomes (in terms of QALYs). Other potential outcomes (such as the effect of birthweight on long term educational outcomes) will be summarised, but may not be included in the cost-per-QALY analysis. The review will inform only the relationship between birthweight and long-term outcomes, the effectiveness of the HiP grant will be taken only from the current study.

The perspective taken will be that of the UK National Health Service in the first instance. For this particular intervention it will be important to consider two further perspectives: the broader Public Sector (due to the relationship between LBW and social care/educational development), and society as whole (since the HiP grant is a transfer payment and therefore there is no net cost to society of transferring the grant from Government to individuals beyond the administration costs).

Of particular interest will be the relative cost-effectiveness of the programme between different socioeconomic groups identified in the main analysis. This may lead to differential policy recommendations for different socioeconomic groups. Uncertainty in the modelling of long-term outcomes will be subject to extensive sensitivity analysis to explore the robustness of the cost-effectiveness analysis.

IMPLICATIONS

Maternal nutrition plays a crucial role in influencing fetal growth and birth outcomes. It is a modifiable risk factor of public health importance in the effort to prevent adverse birth outcomes, particularly among low-income populations.²⁴ According to Barker, “*the seeds of inequalities in health in the next century are being sown today, in inner cities and other communities where adverse influences impact upon the growth, nutrition and health of mothers and their infants*”.⁷¹

The HiP grant was cash given to the pregnant women with no constraint on its use. However, whether cash transfers are more efficient than “vouchers” or subsidies, which try to target the “appropriate expenditure”, remains a controversial topic in economics.⁷² ~~However, economic theory would suggest that cash transfers are more efficient than “vouchers” or subsidies, which try to target the expenditure in the “appropriate expenditure”.~~ This is because vouchers, for example, free up disposable income if they displace planned expenditure. This evaluation study may show the HiP grant increased birthweight across the population. If so, then a benefit would be to recommend the re-introduction of a universal cash transfer or, if we believed more evidence was needed that the HiP grants were delivering this benefit, the development of a randomized controlled trial for a similar cash transfer. An additional benefit will be the relative cost-effectiveness of the HiP grant between different socioeconomic groups identified in the main analysis. This may lead to differential policy recommendations for different socioeconomic groups with consequent reduction in health inequalities.

ETHICS AND DISSEMINATION

Ethical approval is not required as there is no primary data collection. Indeed, the information from maternal and birth records from all hospitals in Scotland are routinely collected. Approval for data collection, storage and release for research purpose has been given (6th May 2014; PAC38A/13) by the Privacy Advisory Committee, an Advisory Committee to NHS National Service Scotland and the Registrar General.

The results of this study will be disseminated through peer-reviewed publications in public health research journals, national and international conferences.

AUTHOR'S CONTRIBUTIONS

Ruth Dundas was involved in the conception of the study design, literature search and prepared the first draft of the study protocol. She will contribute to the statistical analysis and the interpretation of the results.

Samiratou Ouédraogo contributed to the literature search and the preparation of the present protocol paper. She will be responsible for the statistical analysis and contribute to the interpretation of the results.

Lyndal Bond was involved in the conception of the study design. She will contribute to the interpretation of the results.

Andrew H Briggs designed the health economic analysis aspect of the protocol. He will oversee the cost-effectiveness analysis and assist with writing the health economic paper.

James Chalmers was involved in the conception of the study design.

Ron Gray was involved in the conception of the study design. He will contribute to the interpretation of the results.

Rachael Wood will contribute to the interpretation of the results.

Alastair H Leyland was involved in the conception of the study design, literature search and contributed to all sections. He will contribute to the statistical analysis and the interpretation of the results.

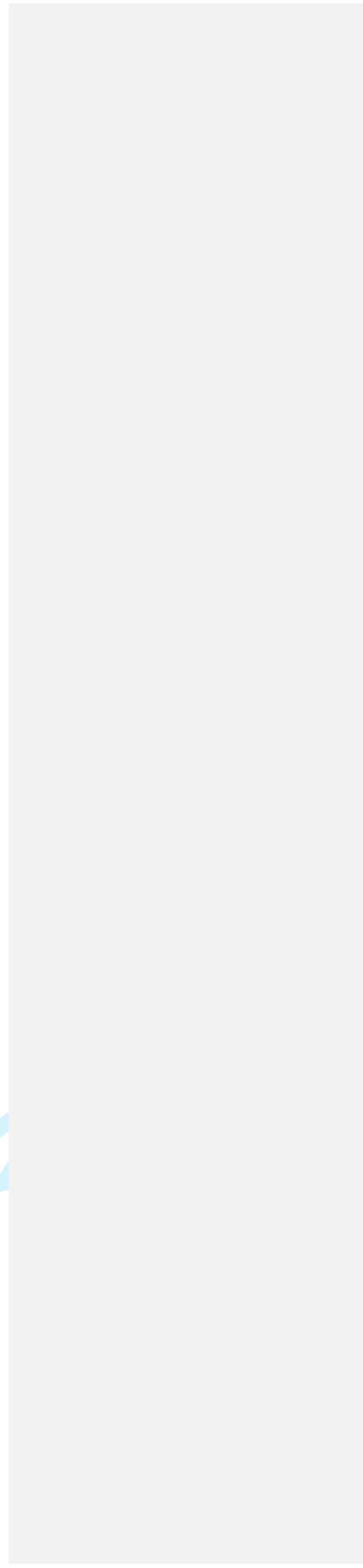
All authors read and approved the final manuscript.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

COMPETING INTERESTS

We declare that we have no conflicts of interest.

For peer review only



FUNDING STATEMENT

This project was funded by the National Institute for Health Research Public Health Research Board (project number 12/3070/02). The Social and Public Health Sciences Unit is core funded by the Medical Research Council (MC_UU_12017/5) and the Chief Scientist Office of the Scottish Government Health Directorates (SPHSU2).

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Public Health Research Board, NIHR, NHS or the Department of Health.

REFERENCE LIST

1. Frankel S, Elwood P, Sweetnam P, et al. Birthweight, body-mass index in middle age, and incident coronary heart disease. *Lancet* 1996;348(9040):1478-80.
2. Leon DA, Lithell HO, Vagero D, et al. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15 000 Swedish men and women born 1915-29. *BMJ* 1998;317(7153):241-5.
3. Reyes L, Manalich R. Long-term consequences of low birth weight. *Kidney Int Suppl* 2005(97):S107-11.
4. Class QA, Rickert ME, Lichtenstein P, et al. Birth weight, physical morbidity, and mortality: a population-based sibling-comparison study. *Am J Epidemiol* 2014;179(5):550-8.
5. Hendryx M, Luo J, Knox SS, et al. Identifying multiple risks of low birth weight using person-centered modeling. *Womens Health Issues* 2014;24(2):e251-6.
6. Barker DJ. Birth weight and hypertension. *Hypertension* 2006;48(3):357-8.
7. Barker DJ, Eriksson JG, Forsen T, et al. Fetal origins of adult disease: strength of effects and biological basis. *Int J Epidemiol* 2002;31(6):1235-9.
8. Barker DJ. In utero programming of chronic disease. *Clin Sci (Lond)* 1998;95(2):115-28.
9. Barker DJ. The fetal and infant origins of adult disease. *BMJ* 1990;301(6761):1111.
10. Negrato C, Gomes M. Low birth weight: causes and consequences. *Diabetol Metab Syndr* 2013;5(1):49.
11. Valero De Bernabe J, Soriano T, Albaladejo R, et al. Risk factors for low birth weight: a review. *Eur J Obstet Gynecol Reprod Biol* 2004;116(1):3-15.
12. EURO-PERISTAT. "Babies' health: mortality and morbidity during pregnancy and in the first year of life" in "The European Perinatal Health Report 2010". 2013.

1
2
3
4
5
6
7 <http://www.europeristat.com/images/doc/Peristat%202013%20V2.pdf>. (Accessed 28 August
8 2014).

9
10
11 13. World Health Organisation. International Statictical Classification of Diseases and
12 Related Health Problems- ICD-10. 10th Revision. Geneva: World Health Organisation, 2010.
13 <http://www.who.int/classifications/icd/en/>. (Accessed 28 August 2014).

14
15
16 14. OECD. "Infant health: Low birth weight", in Health at a Glance: Europe 2012. In:
17 Publishing O, ed., 2012. [http://www.oecd-](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest)
18 [ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest)
19 [&checksum=368A07F542E03A0442EFDEB9B002B6AE](http://www.oecd-ilibrary.org/docserver/download/8112121e.pdf?expires=1404136197&id=id&accname=guest) . (Accessed 28 August 2014).

20
21
22 15. Macfalane A, Dattani N. European Perinatal Health Report: highlights from a United
23 Kingdom perspective. London, 2013. [http://www.europeristat.com/images/Euro-](http://www.europeristat.com/images/Euro-peristat%20UK%20briefing.pdf)
24 [peristat%20UK%20briefing.pdf](http://www.europeristat.com/images/Euro-peristat%20UK%20briefing.pdf). (Accessed 28 August 2014).

25
26
27
28
29 16. Madden D. The relationship between low birth weight and socioeconomic status in
30 Ireland. J Biosoc Sci 2014;46(2):248-65.

31
32
33 17. Frimmel W, Pruckner GJ. Birth weight and family status revisited: evidence from
34 Austrian register data. Health Econ 2014;23(4):426-45.

35
36
37 18. Huxley R. Smoking, birthweight, and mortality across generations. Eur Heart J
38 2013;34(44):3398-9.

39
40
41 19. Fairley L, Leyland AH. Social class inequalities in perinatal outcomes: Scotland 1980-
42 2000. J Epidemiol Community Health 2006;60(1):31-6.

43
44
45 20. Weightman AL, Morgan HE, Shepherd MA, et al. Social inequality and infant health in
46 the UK: systematic review and meta-analyses. BMJ Open 2012;2(3):e000964.

47
48
49 21. Juarez SP, Merlo J. Revisiting the effect of maternal smoking during pregnancy on
50 offspring birthweight: a quasi-experimental sibling analysis in Sweden. PLoS One
51 2013;8(4):e61734.

- 1
2
3
4
5
6
7 22. Zdravkovic T, Genbacev O, McMaster MT, et al. The adverse effects of maternal
8 smoking on the human placenta: a review. *Placenta* 2005;26(Suppl A):S81-6.
9
10
11 23. Villar J, Merialdi M, Gulmezoglu AM, et al. Nutritional interventions during pregnancy
12 for the prevention or treatment of maternal morbidity and preterm delivery: an overview of
13 randomized controlled trials. *J Nutr* 2003;133(5 Suppl 2):1606S-25S.
14
15
16 24. Abu-Saad K, Fraser D. Maternal nutrition and birth outcomes. *Epidemiol Rev*
17 2010;32(1):5-25.
18
19
20 25. Wu G, Imhoff-Kunsch B, Girard AW. Biological mechanisms for nutritional regulation of
21 maternal health and fetal development. *Paediatr Perinat Epidemiol* 2012;26(Suppl 1):4-26.
22
23
24 26. Mason JB, Saldanha LS, Ramakrishnan U, et al. Opportunities for improving maternal
25 nutrition and birth outcomes: synthesis of country experiences. *Food Nutr Bull* 2012;33(Suppl 2):S104-37.
26
27
28
29
30 27. Thangaratinam S, Rogozinska E, Jolly K, et al. Effects of interventions in pregnancy on
31 maternal weight and obstetric outcomes: meta-analysis of randomised evidence. *BMJ*
32 2012;344:e2088.
33
34
35 28. Glassman A, Duran D, Fleisher L, et al. Impact of Conditional Cash Transfers on
36 Maternal and Newborn Health. *J Health Popul Nutr* 2013;4:19.
37
38
39 29. Sutherland K, Christianson JB, Leatherman S. Impact of targeted financial incentives on
40 personal health behavior: a review of the literature. *Med Care Res Rev* 2008;65(Suppl 6):36S-78S.
41
42
43
44
45 30. Marteau TM, Ashcroft RE, Oliver A. Using financial incentives to achieve healthy
46 behaviour. *BMJ* 2009;338:b1415.
47
48
49 31. Giles EL, Robalino S, McColl E, et al. The effectiveness of financial incentives for health
50 behaviour change: systematic review and meta-analysis. *PLoS One* 2014;9(3):e90347.
51
52
53
54

- 1
2
3
4
5
6
7 32. Brownell M, Chartier M, Au W, et al. Evaluation of the Healthy Baby Program.
8 Winnipeg, MB: Manitoba Centre for Health Policy. 2010. [http://mchp-
10 appserv.cpe.umanitoba.ca/reference/Healthy_Baby.pdf](http://mchp-
9 appserv.cpe.umanitoba.ca/reference/Healthy_Baby.pdf). (Accessed 22 September 2014).
11
12 33. Neil G. Universal to selective. Transformation of the Welfare State: The Silent Surrender
13 of Public Responsibility: Oxford University Press; 2002:20.
14
15 34. Mkandawire T. Targeting and Universalism in poverty reduction. —Secondary Targeting
16 and Universalism in poverty reduction. 2005.
17 [http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EEA0B0
19 C12570FF00493EAA/\\$file/mkandatarget.pdf](http://www.unrisd.org/80256B3C005BCCF9/%28httpAuxPages%29/955FB8A594EEA0B0
18 C12570FF00493EAA/$file/mkandatarget.pdf). (Accessed 28 August 2014).
20
21 35. Craig P, Cooper C, Gunnell D, et al. Using natural experiments to evaluate population
22 health interventions: new Medical Research Council guidance. J Epidemiol Community
23 Health 2012;66(12):1182-6.
24
25 36. ~~Council MR~~ Medical Research Council. Using natural experiments to evaluate population
26 health interventions: guidance for producers and users of evidence.
27 [http://www.behaviourworksaustralia.org/wp-
29 content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf](http://www.behaviourworksaustralia.org/wp-
28 content/uploads/2012/10/NaturalExperimentsGuidance_MRC-guidance.pdf). (Accessed 28
30 August 2014).
31
32 37. Einarsdottir K, Kemp A, Hagggar FA, et al. Increase in caesarean deliveries after the
33 Australian Private Health Insurance Incentive policy reforms. PLoS One 2012;7(7):e41436.
34
35 38. Ramsay CR, Matowe L, Grilli R, et al. Interrupted time series designs in health
36 technology assessment: lessons from two systematic reviews of behavior change strategies.
37 Int J Technol Assess Health Care 2003;19(4):613-23.
38
39 39. Penfold RB, Zhang F. Use of interrupted time series analysis in evaluating health care
40 quality improvements. Acad Pediatr 2013;13(6 Suppl):S38-44.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Formatted: English (U.K.)

Field Code Changed

Field Code Changed

1
2
3
4
5
6
7 [40. Administrative Data Liaison Service. Maternity and Neonatal Linked Database.](http://www.adls.ac.uk/nhs-scotland/maternity-and-neonatal-linked-database/?detail)
8 [http://www.adls.ac.uk/nhs-scotland/maternity-and-neonatal-linked-database/?detail.](http://www.adls.ac.uk/nhs-scotland/maternity-and-neonatal-linked-database/?detail)

Field Code Changed

9 [\(Accessed 16 September 2014\).](#)

10
11
12 [41. Kendrick SW and Clarke JA. The Scottish Record Linkage System. Health Bulletin 1993](#)
13 [51\(2\):72-79.](#)

14
15
16 [42. Administrative Data Liaison Service. Scottish Birth Record.](#) [http://www.adls.ac.uk/nhs-](http://www.adls.ac.uk/nhs-scotland/sbr-scottish-birth-record/?detail)
17 [scotland/sbr-scottish-birth-record/?detail.](http://www.adls.ac.uk/nhs-scotland/sbr-scottish-birth-record/?detail) [\(Accessed 16 September 2014\).](#)

Field Code Changed

18
19
20 [43. Administrative Data Liaison Service. Birth registrations.](#) [http://www.adls.ac.uk/national-](http://www.adls.ac.uk/national-records-of-scotland/birth-registrations/?detail)
21 [records-of-scotland/birth-registrations/?detail.](http://www.adls.ac.uk/national-records-of-scotland/birth-registrations/?detail) [\(Accessed 16 September 2014\).](#)

22
23
24 [44. Information Service Division. Birth in Scottish Hospitals.](#)

25 [http://www.isdscotland.org/Health-Topics/Maternity-and-Births/Births/Background.asp.](http://www.isdscotland.org/Health-Topics/Maternity-and-Births/Births/Background.asp)

Field Code Changed

26 [\(Accessed 16 September 2014\).](#)

27
28
29
30 [45. General Register Office for Scotland. Vital Events-Births.](#) [http://www.gro-](http://www.gro-scotland.gov.uk/statistics/theme/vital-events/births/index.html)
31 [scotland.gov.uk/statistics/theme/vital-events/births/index.html.](http://www.gro-scotland.gov.uk/statistics/theme/vital-events/births/index.html) [\(Accessed 16 September](#)
32 [2014\).](#)

33
34
35 [46. National Health Service Scotland. Data Quality Assurance Assessment of Maternity Data](#)
36 [\(SMR02\). Scotland report April 2010.](#)

37 [http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DOA-Assessment-of-Maternity-Data-](http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DOA-Assessment-of-Maternity-Data-SMR02-2008-to-2009.pdf)
38 [40 \[SMR02-2008-to-2009.pdf.\]\(http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DOA-Assessment-of-Maternity-Data-SMR02-2008-to-2009.pdf\) \[\\(Accessed 11 September 2014\\).\]\(#\)](http://www.isdscotlandarchive.scot.nhs.uk/isd/files//DOA-Assessment-of-Maternity-Data-
39 <a href=)

Field Code Changed

41
42 [47. Taulbut M, Walsh D. Poverty, parenting and poor early years' experiences in Scotland,](#)
43 [England and three city regions. 2013.](#) [http://socialwelfare.bl.uk/subject-areas/services-client-](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty_parenting_and_poor_health.pdf)
44 [groups/families/glasgowcentreforpopulationhealth/164762Poverty_](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty_parenting_and_poor_health.pdf)
45 [parenting_and_poor_hea](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty_parenting_and_poor_health.pdf)
46 [lth.pdf.](http://socialwelfare.bl.uk/subject-areas/services-client-groups/families/glasgowcentreforpopulationhealth/164762Poverty_parenting_and_poor_health.pdf) [\(Accessed 11 September 2014\).](#)

47
48
49 [48. Carstairs V, Morris R. Deprivation: explaining differences in mortality between Scotland](#)
50 [and England and Wales. Brit Med J 1989;299:886-889.](#)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

49. NHS National Services Scotland. Births in Scottish Hospital: Smoking and Pregnancy <http://www.isdscotlandarchive.scot.nhs.uk/isd/2911.html>. (Accessed 16 September 2014).

50. General Register Office for Scotland. Vital Events-General Background Informations. <http://www.gro-scotland.gov.uk/statistics/theme/vital-events/births/index.html>. (Accessed 16 September 2014).

51. General Register Office for Scotland. Vital Events-General Background Informations: Occupation and social class / socio-economic classification. <http://www.gro-scotland.gov.uk/files2/stats/vital-events/ve-occupation-social-classification.pdf>. (Accessed 16 September 2014).

52. The National Statistics Socio-economic Classification (NS-SEC rebased on the SOC2010). <http://www.ons.gov.uk/ons/guide-method/classifications/current-standard-classifications/soc2010/soc2010-volume-3-ns-sec--rebased-on-soc2010--user-manual/index.html>. (Accessed 28 August 2014).

53. Aspinall PJ, Jacobson B. Why poor quality of ethnicity data should not preclude its use for identifying disparities in health and healthcare. *Qual Saf Health Care* 2007;16(3):176-80.

54. Scholmerich VL, Erdem O, Borsboom G, et al. The association of neighborhood social capital and ethnic (minority) density with pregnancy outcomes in the Netherlands. *PLoS One* 2014;9(5):e95873.

55. Margerison-Zilko C. The Contribution of Maternal Birth Cohort to Term Small for Gestational Age in the United States 1989-2010: an Age, Period, and Cohort Analysis. *Paediatr Perinat Epidemiol* 2014;28(4):312-21.

56. The Scottish Government. Scottish Index of Multiple Deprivation 2012: A national Statistics publication for Scotland 2012. http://22fa0f74501b902c9f11-8b3fbddf1e1fab453a8e75cb14f3396.r26.cf3.rackcdn.com/simd_448749_v7_20121217.pdf. (Accessed 28 August 2014).

1
2
3
4
5
6
7 [57. The Scottish Government. Scottish Index of Multiple Deprivation 2012: Technical notes.](http://simd.scotland.gov.uk/publication-2012/technical-notes/domains-and-indicators/income-domain/)
8 [http://simd.scotland.gov.uk/publication-2012/technical-notes/domains-and-](http://simd.scotland.gov.uk/publication-2012/technical-notes/domains-and-indicators/income-domain/)
9 [indicators/income-domain/.](http://simd.scotland.gov.uk/publication-2012/technical-notes/domains-and-indicators/income-domain/) (Accessed 16 September 2014).

Field Code Changed

10
11
12 58. Pattenden S, Dolk H, Vrijheid M. Inequalities in low birth weight: parental social class,
13 area deprivation, and "lone mother" status. *J Epidemiol Community Health* 1999;53(6):355-
14 8.

15
16
17 59. Spencer N, Bambang S, Logan S, et al. Socioeconomic status and birth weight:
18 comparison of an area-based measure with the Registrar General's social class. *J Epidemiol*
19 *Community Health* 1999;53(8):495-8.

20
21
22 60. Fairley L, Dundas R, Leyland AH. The influence of both individual and area based
23 socioeconomic status on temporal trends in Caesarean sections in Scotland 1980-2000. *BMC*
24 *Public Health* 2011;11:330.

25
26
27 61. Kent ST, McClure LA, Zaitchik BF, et al. Area-level risk factors for adverse birth
28 outcomes: trends in urban and rural settings. *BMC Pregnancy Childbirth* 2013;13:129.

29
30
31 62. Shankardass K, O'Campo P, Dodds L, et al. Magnitude of income-related disparities in
32 adverse perinatal outcomes. *BMC Pregnancy Childbirth* 2014;14:96.

33
34
35
36
37 [63. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, Wood AM,](#)
38 [Carpenter JR. Multiple imputation for missing data in epidemiological and clinical research:](#)
39 [potential and pitfalls. *BMJ* 2009;338:b2393.](#)

40
41
42
43 64. Shadish WR, Cook TD, Campbell DT. Quasi-experiments: Interrupted time-series
44 designs. In *Experimental and quasi-experimental designs for generalized causal inference*.
45 Boston: Houghton-Mifflin 2002:171-206.

46
47
48 65. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology*
49 1990;1(1):43-6.

66. Greenland S. Multiple comparisons and association selection in general epidemiology. *Int J Epidemiol* 2008;37(3):430-4.

67. National Service Division. Pregnancy Screening Programmes. <http://www.nsd.scot.nhs.uk/services/screening/pregscreening/index.html>. (Accessed 28 August 2014)

68. NHS Health Scotland. Your guide to screening tests during pregnancy. http://www.healthscotland.com/uploads/documents/3985-YourGuideToScreeningTestsDuringPregnancy_1.pdf. (Accessed 28 August 2014).

69. The Scottish Government. [NHS Performance Targets](http://www.scotland.gov.uk/Topics/Health/Quality-Improvement-Performance/NHS-Performance-Targets).

<http://www.scotland.gov.uk/Topics/Health/Quality-Improvement-Performance/NHS-Performance-Targets>. (Accessed 16 September 2014).

70. Mackay DF, Nelson SM, Haw SJ, et al. Impact of Scotland's smoke-free legislation on pregnancy complications: retrospective cohort study. *PLoS Med* 2012;9(3):e1001175.

71. Barker DJ. The foetal and infant origins of inequalities in health in Britain. *J Public Health Med* 1991;13(2):64-8.

72. Gentilini U. [Cash and food transfers: A Primer. World Food Programme. 2007.](https://www.wfp.org/sites/default/files/OP18_Cash_and_Food_Transfers_Eng%2007.pdf) https://www.wfp.org/sites/default/files/OP18_Cash_and_Food_Transfers_Eng%2007.pdf (Accessed 16 September 2014).