Supporting Women with Postnatal Weight MAnagemeNt

SWAN Feasibility Trial

Data Analysis Plan

Version 1.0

Professor Debra Bick

Chief Investigator

Mr Paul Seed

[redacted]

[redacted]

Local Principal Investigator

ISRCTN: 39186148

1. Introduction

1.1 Status of document

This is the first approved version of the SWAN data analysis plan (Version 1.0), incorporating changes made at the TSC on 12th April 2017. It should be read in conjunction with the current trial protocol, which describes all other aspects of the trial in greater detail. Relevant sections of the protocol are quoted or summarised here as appropriate.

1.2 Trial design

The trial is a two-arm feasibility randomised controlled trial (RCT) of lifestyle information and Slimming World®(Alfreton, UK) groups to promote weight management and positive lifestyle behaviour in postnatal women from an ethnically diverse inner city population.

Eligible women will be a) overweight (BMI 25–29.9 kg/m^2) or obese (BMI ≥30 kg/m^2) as identified at their first antenatal contact and b) women with excessive gestational weight gain (EGWG) when weighed at 36 weeks gestation, as defined using IoM criteria (Siega-Riz & Gray, 2013): > 18 kg if pre-pregnancy BMI<18.5 kg/m^2, >16kg if BMI 18.5 to 24.99 kg/m^2, >11.5 kg if BMI 25 to 29.99 kg/m^2, >9kg if BMI ≥ 30 kg/m^2**.**

1.3 General principle of analysis

We aim to recruit 190 over 6 months (7 – 8 women a week), and obtain complete data on 130 (68% retention). As this is a feasibility trial, attention will be paid mainly to the rates of recruitment and trial completion. However, the plan for analysing the main trial data is also explored below.

The main trial analysis will follow the intention-to-treat principle. Women will be analysed according to the original randomised allocation, irrespective of compliance and crossovers. Linear regression will be used for the primary outcome and other continuous measures. Where data are available, adjustment will be made for corresponding measurements made pre-randomisation (Vickers & Altman 2001). Binary regression with a log-link will be used to assess risk ratios for all binary (Yes/No) outcomes, adjusting for the most important potential confounders: maternal BMI, ethnicity, & parity. Following the most recent CONSORT guidelines and additional recommendations (Schultz et al. 2010; Moher et al. 2010), risk differences will also be estimated.

Significance tests will in general only be carried out in the feasibility study to test for differences in dropout rates between subject groups (Table 3.1), and will only be carried out in the main study for estimates of treatment effects. Baseline comparisons between randomized groups do not provide useful information (Altman & Doré 1990). Separate tests for changes over time in the two groups can result in entirely false and misleading conclusions about the differences between the groups ('comparing p-values'; Matthews & Altman, 1996).

No formal interim analysis is planned. The results of this feasibility study will be used to decide whether to seek funding for a full trial.

2. Participant flow and description of participants

2.1 Participant flow

A standard CONSORT flow chart will be produced, showing the total number of women approached, the numbers who declined and were found to be ineligible (with reasons where given) and the number randomised; the numbers in each group, the number who received and did not receive the randomised intervention (at least one session and as planned), who were excluded from the final analysis; and the total numbers analysed.

2.2 Description of participants

Key sociodemographic and obstetric information will be given for each group, and overall. This will include: age, parity, ethnicity (4 cats), IMD centiles, current pregnancy: gestation at delivery, gender, birthweight, birthweight centile (Table 2.1). Customised birthweight centiles will be used (Gardosi & Francis 2007) correcting the expected birthweight for maternal height, weight, ethnicity, & parity, neonatal gender and gestation at delivery. In order not to correct for pathological overweight, for obese women a healthy weight will be used, corresponding to a BMI of 30 kg/m^2. Following best practice (Altman & Doré, 1990) there will be no test for differences between randomised groups.

Table 2.1 Social, demographic and obstetric information on all women randomised

	Control arm	Intervention arm	All women
	(n=XX)	(n=XX)	(N=XX)
Age (years)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Height (m)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Weight (kg)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
BMI (kg/m2)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
SBP (mmHg)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
DBP (mmHg)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Entry criteria: Booking BMI (kg/m^2) & EGWG*			
< 30 kg, EGWG	*n (%)*	*n (%)*	*n (%)*
30-35, No EGWG	*n (%)*	*n (%)*	*n (%)*
30-35, EGWG	*n (%)*	*n (%)*	*n (%)*
35+, No EGWG	*n (%)*	*n (%)*	*n (%)*
35+, EGWG	*n (%)*	*n (%)*	*n (%)*
Ethnicity**			
White	*n (%)*	*n (%)*	*n (%)*
Black	*n (%)*	*n (%)*	*n (%)*
Asian	*n (%)*	*n (%)*	*n (%)*
Other	*n (%)*	*n (%)*	*n (%)*

IMD ***	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
(centile scale)			
IMD quintiles			
1 (least deprived)	*n (%)*	*n (%)*	*n (%)*
2	*n (%)*	*n (%)*	*n (%)*
3	*n (%)*	*n (%)*	*n (%)*
4	*n (%)*	*n (%)*	*n (%)*
5 (most deprived)	*n (%)*	*n (%)*	*n (%)*
Index pregnancy			
Gestation at delivery (weeks)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Gender (male)	*n (%)*	*n (%)*	*n (%)*
Birthweight	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Birthweight centile ****	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*

* EGWG : Excessive gestational weight gain, IoM criteria

** Ethnicity based on UK census categories

***IMD: Index of Multiple Deprivation (McLennan et al. 2010)

**** Customised birthweight centiles (Gardosi & Francis 2007),

3. Primary and secondary objectives

The primary aim of the trial is to assess the feasibility of conducting a future definitive RCT. Objectives reflect clarifying uncertainty in relation to various aspects of the study in order to inform progression to a definitive RCT. Objectives are measurable and time-bound to support project monitoring in line with our 2 year project plan. Further details are given in section 2.1 of the protocol.

Table 3.1 Differences in trial completion between trial arms, and by social, demographic and obstetric factors

	Control arm	Intervention arm	All women	Difference
	(n=XX)	(n=XX)	(n=XX)	(95% Confidence interval)
All women	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
Age groups				
<20	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
20-30	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
30+	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
				P= 0.xxx
Booking BMI (kg/m^2) & EGWG				
< 30 kg, EGWG	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*

30-35, No EGWG	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
30-35, EGWG	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
35+, No EGWG	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
35+, EGWG	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
				P= 0.xxx
Ethnicity*				
White	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
Black	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
Asian	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
Other	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
				P= 0.xxx
IMD quintiles **				
1 (least deprived)	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
2	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
3	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
4	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
5 (most deprived)	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
				P= 0.xxx
Birthweight				
SGA	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
<10th centile ***				
AGA	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
				P= 0.xxx
Prematurity				
<37 weeks	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
Term	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
				P= 0.xxx
Gender				
Female	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*
Male	*N (%)*	*N (%)*	*N (%)*	*D% (L% to H%)*

EGWG: Excessive gestational weight gain * Ethnicity is based on UK national census categories **IMD: Index of Multiple Deprivation (McLennan et al. 2010) *** Customised birthweight centiles (Gardosi & Francis 2007), adjusted for maternal height, weight, ethnicity, & parity, as well as neonatal gender and gestation at delivery.

3.1 Recruitment and retention

Recruitment will be assessed as the number randomised per month from the study centre; with 95% confidence intervals derived from the Poisson distribution. Retention will be assessed as the proportion of women randomised providing complete analysable data. Logistic regression will be used to investigate whether dropout rates are the same in each arm, with interaction tests to check whether there is differential dropout for each of the factors given in table 1 (e.g. whether obese women are more or less likely to drop out if included in the control arm).

3.2 Acceptability of trial procedures and intervention

This will be assessed partly by retention rates (section 3.1) and partly by qualitative assessment of the participants' opinions of the trial.

3.3 The impact of the intervention on maternal weight

This will be assessed by the maternal weight change from first antenatal visit to 12 months postnatally. As part of the preparation for the main trial, different methods of analysis will be compared. See section 4.1 below.

3.4 The influence of the intervention on secondary outcomes

Weight management, diet, physical activity, breastfeeding, smoking cessation, alcohol intake, physical and mental health, infant health, sleep patterns, body image, self-esteem and health-related quality of life will all be considered at 6 and 12 months.

3.5 Resource impacts across different agencies likely to be of relevance and identify data appropriate for economic evaluation in a definitive RCT

Self-report resource use (hospital and community) measured at baseline and follow-up (6 and 12 months) will be evaluated for acceptability among participants and analysed for the completeness of information recorded across specific service items. Data on contacts made with Slimming World weight management groups, collected via trial participant completion of an attendance log, will also be assessed against these criteria.

Pre-planned sub-group statistical analysis of resource use and costs for participants will be undertaken in alignment with analysis of primary-end point data in relation to different booking BMI categories (see section 4.1). This will be carried out with the sole intention of informing whether there might be sufficient grounds to evaluate within a main trial whether the cost-effectiveness of the intervention varies according to BMI at booking and whether participants experienced excessive gestational weight gain (exact definitions of sub-groups are provided in 4.1).

Based on the results of these analyses and other relevant factors, a decision will be made on whether to progress to a definitive RCT, following discussions with Core Project Team, SW, Expert PPI group, Trial Steering Committee (TSC), NIHR PHR programme team and other key stakeholders.

4 *Feasibility outcomes and clinical endpoints*

4.1 Feasibility outcomes

Our feasibility outcomes reflect MRC guidelines for complex interventions (UK MRC 2014) with some important exceptions due to the nature of this study and intervention proposed. The purpose is not to evaluate the intervention itself as Slimming World®(Alfreton, UK) weight management groups are a 'standardised' intervention, with robust mechanisms to ensure intervention fidelity. Due to the robust in-built quality assurance and evidence base for the intervention, process evaluation is not designed to answer some standard questions seen in complex evaluations regarding generalizability of the intervention to other contexts/settings, assurance that implementation/delivery of the intervention has been consistent across study sites, or to determine mechanisms of impact. This study reflects a pragmatic trial approach – evaluating the impact of the intervention in the hands of many, where women can choose which group to attend, and can switch groups if they like, exactly as they could if they were a 'standard' self-referred member of Slimming World.

Material in sections 4.2 and 4.3 refers to the planned data analysis in the main study. This should be regarded as provisional, and will be reconsidered in the light of the experience of the feasibility study.

4.2 Primary endpoint

The primary assessment likely to be used in a future definitive RCT will be the difference between study groups in weight 12 months postnatally. This will be adjusted for the antenatal weight at first booking, and for the last weight obtained in pregnancy. The use of the two together means that the estimate is also adjusted for gestational weight gain.

Because there are by design no systematic differences between the randomised groups in booking weight or gestational weight gain, the effect of the intervention on mean weight at 12 months postpartum is also its effect on post-pregnancy weight retention and on weight gain from pre-pregnancy weight.

Antenatal weight will be estimated as weight at first booking – 1.25 kg. Analysis will use multiple linear regression adjusting for baseline weight (Vickers & Altman, 2001). The change will also be expressed as % weight change or weight loss from booking weight.

We will also undertake in the main study pre-planned sub-group analysis of the primary assessment in women of different booking BMI categories: overweight (BMI 25–29.9 kg/m²), obese (BMI ≥30 kg/m²) and non-obese women with excessive GWG when weighed at 36 weeks. Interaction tests will be used to determine if the treatment effect varied by subgroup.

4.3 Secondary endpoint

Reduction of weight by 5% and 10% will be analysed as a binary variables, with both risk ratios and risk differences presented (see section 1.3 above). Retention of EGWG will be defined as BMI 12 months postpartum more than 1 kg/m^2 above estimated pre-pregnancy weight.

Aspects of healthy lifestyle and health behaviours will be assessed by questionnaire at 6 and 12 months, including diet and nutrition, breastfeeding, physical activity, smoking cessation and alcohol intake, self-esteem and body image. Where a standard questionnaire is used, a baseline measurement will be made, and this will be used in the analysis as a covariate (Vickers & Altman, 2001).

For certain areas, the relevant questions are to be developed during the feasibility study, prior to use in the main trial. See the protocol for more details.

Standard validated scales:

- Dietary intake: The Dietary Instrument for Nutritional Education (DINE©, University of Oxford) (Roe et al 1994)
- Physical activity: The International Physical Activity Short-Form (Craig et al. 2003)
- Mental health: Edinburgh Postnatal Depression Scale (Cox et al. 1987)
- Smoking: smoking status/cigarette dependence (Ussher et al. 2012)
- Alcohol consumption: Alcohol Use Disorders Identification Test (Barbor et al. 2001)
- Self-esteem: Rosenberg Self-Esteem Scale (Rosenberg 1965)
- Impact on body image (Fairburn & Beglin 1994)
- Resource utilisation and costs outcome measures: the EQ-5D (EuroQoL Group, 1990) and the Adult Service Use Schedule (Barrett et al. 2013)

Questions developed for the study

- Breastfeeding intent, uptake, and duration
- Sleep patterns
- Infant health
- Soft drink intake

Further questions on uptake of support for weight management will be 'tailored' for the intervention or standard care arm, to be included at 6 and 12 months. This will inform trial process outcomes. Topics to be covered include: when the women started Slimming World (8-16 weeks PN), number of groups attended (out of 12), how long they stayed (did they attend for the full 1 hour or leave early?), proportion attending at least 10 out of 12 sessions, as this is seen as necessary for full benefit.

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