Title

Previous pregnancy loss has an adverse impact on distress and behaviour in subsequent pregnancy.

Author's names

Fergus P McCarthy, Rona Moss-Morris, Ali S Khashan , Robyn A North, Philip N Baker, Gus Dekker, Lucilla Poston, Lesley ME McCowan, James J Walker, Louise C Kenny, Keelin O'Donoghue.

Author's details

Dr Fergus P McCarthy, The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork University Maternity Hospital, Wilton, Cork, Ireland.

Professor Rona Moss-Morris, Head of Health Psychology, Chair in Psychology as applied to Medicine, King's College London, United Kingdom.

Dr Ali S Khashan, The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork University Maternity Hospital, Wilton, Cork, Ireland.

Professor Robyn A North, Professor of Maternal and Fetal Medicine, Division of Women's Health, Women's Health Academic Centre, King's College London, and King's Health Partners, United Kingdom.

Professor Lucilla Poston, Division of Women's Health, Women's Health Academic Centre, King's College London, and King's Health Partners, United Kingdom.

Professor Lesley M E McCowan, Professor of Obstetrics and Gynaecology Department of Obstetrics and Gynaecology, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand.

Professor Philip N Baker, Director of the National Centre for Growth & Development, and Professor of Maternal and Fetal Health, Liggins Institute, University of Auckland, New Zealand and Honorary Professor of Maternal and Fetal Health, University of Manchester, United Kingdom

Professor Gus Dekker, Women's and Children's Division Lyell McEwin Hospital, University of Adelaide, Adelaide, South Australia.

Professor James J Walker, Professor of Obstetrics and Gynaecology, St James University Hospital, Leeds, United Kingdom.

Professor Louise C Kenny, Professor of Obstetrics and Consultant Obstetrician and Gynaecologist, Director of The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork University Maternity Hospital, Wilton, Cork, Ireland.

Dr Keelin O'Donoghue, Consultant Obstetrician and Gynaecologist, The Irish Centre for Fetal and Neonatal Translational Research (INFANT), University College Cork, Cork University Maternity Hospital, Wilton, Cork, Ireland.

On behalf of the SCOPE consortium

Corresponding author

Dr Fergus McCarthy, address: as above.

Tel: +353874169946. Fax: +353214920500 Email: Fergus.mccarthy@ucc.ie

Extended abstract

Title:

Previous pregnancy loss has an adverse impact on distress and behaviour in subsequent pregnancy.

Abstract

Study question:

Do women with previous miscarriages or terminations have higher levels of distress, perceived stress and unhelpful behaviours in pregnancy and if so, is the magnitude of any observed changes related to the number of previous miscarriages or terminations of pregnancy.

Summary answer:

Women with previous miscarriages or terminations of pregnancy have higher levels of distress, perceived stress and unhelpful behaviours in pregnancy.

What is known already:

Miscarriage affects approximately 20% of pregnancies and as many as a further 20% of pregnancies undergo termination. Previous pregnancy loss (miscarriage or termination) is associated with significant depression and anxiety.

Study design, size, duration

We utilised data from 5575 healthy nulliparous women with singleton pregnancies recruited to the Screening for Pregnancy Endpoints (SCOPE) study, a prospective cohort study performed between November 2004 and January 2011.

Participants/materials, setting, methods:

Patients were interviewed and primary outcomes recorded at 15 and 20 weeks' gestation. Primary outcomes were Short form State- Trait Anxiety Inventory (STAI) score measuring anxiety (range 6-24), Perceived Stress Scale score (PSS, range 0-30), Edinburgh Postnatal Depression Scale (EPDS) score (range 0-30 or categories a-c) and pregnancy related behaviour measured using behavioural responses to pregnancy score (limiting/resting [range 0-20] and all-or-nothing [range 0-28]).

Main results and the role of chance:

Of the 5690 women who were recruited to the SCOPE study, 4331 women (78%) had no history of miscarriage or termination, 559 (10%) had one and 94 (2%) had two previous miscarriages. 415 (8%) had one and 66 (1%) had two previous terminations of pregnancy. Women with one previous miscarriage had increased anxiety (adjusted mean difference 1.85; 0.61, 3.09), perceived stress (adjusted mean difference 0.76; 0.48, 1.03) and depression (adjusted mean difference 0.62; 0.00, 1.23 and adjusted OR 1.26; 1.08, 1.45 for continuous and categorical scores respectively) scores at 15 weeks' gestation. Significant changes were also seen at 20 weeks' gestation in all of anxiety (adjusted mean difference 1.15; 0.73, 1.56), stress (adjusted mean difference

0.62; 0.23, 1.01) and depression (adjusted mean difference 0.44; 0.00, 0.88 and adjusted OR 1.13; 1.00, 1.28 for continuous and categorical scores respectively). Women with either two previous miscarriages or two previous terminations displayed altered behavioural responses to pregnancy. In those with two previous terminations, increased limiting/resting responses to pregnancy scores (adjusted mean difference 4.12; 0.51, 7.73) and increased all-or-nothing response scores (adjusted mean difference 3.97; 0.84, 7.10) at 15 weeks' gestation were observed.

In women with two previous miscarriages changes were observed in limiting/resting behavioural response to pregnancy score (adjusted mean difference 5.23; 0.71, 9.76).

Limitations, reasons for caution:

Although every effort was made to record accurate previous pregnancy losses it was not feasible to confirm the history of previous pregnancy loss by hospital records. This may have introduced recall bias.

Wider implications of the findings:

This study highlights the psychological implications of miscarriage and termination of pregnancy, effects which persist long after the event. Further research is needed to determine whether support may help women deal with these additional adverse effects of pregnancy loss.

Study funding/competing interest(s):

New Zealand; New Enterprise Research Fund, Foundation for Research Science and Technology; Health Research Council; Evelyn Bond Fund, Auckland District Health Board Charitable Trust. Australia; Premier's Science and Research Fund, South Australian Government. Ireland; Health Research Board. Leeds: Cerebra Charity, Carmarthen, United Kingdom Manchester: National Health Service NEAT Grant, United Kingdom. Manchester Biotechnology and Biological Sciences Research

Council, United Kingdom. Manchester: University of Manchester Proof of Concept Funding, United Kingdom King's: Guy's and St Thomas' Charity, United Kingdom, King's and Manchester: Tommy's - The Baby Charity, United Kingdom.
All authors declare: no financial support from any organisation for the submitted work or any competing interests. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
Trial registration number: N/A

Introduction

Miscarriage affects approximately 20% of pregnancies (Regan and Rai, 2000) and, in some regions including England and Wales as many as a further 20% of pregnancies undergo termination (Department of Health). Pregnancy loss can have significant psychological implications for a couple and can impact adversely on relationships (Johnson and Baker, 2004, Kashanian, et al., 2006, Kong, et al., 2010, Lok, et al., 2010). Depression, anxiety and grief are important consequences of miscarriage (Lok and Neugebauer, 2007, Nakano, et al., 2013). Women who have experienced a miscarriage have been shown to experience subsequent mental distress while women who have undergone termination of pregnancy have been shown to have feelings of guilt, shame and anxiety up to five years after the termination (Broen, et al., 2004, Broen, et al., 2005). Factors influencing the development of subsequent anxiety and depression include recent life events and a history of previous psychiatric illness (Broen, et al., 2006). Some studies suggest that women with a history of miscarriage suffer more from pregnancy-specific anxieties in the first trimester of a new pregnancy than pregnant women with no history of miscarriages (Bergner, et al., 2008) while other studies suggest that these anxiety effects last only up to four months

following miscarriage (Geller, et al., 2004).

Recently published research investigated the association between previous pregnancy losses and adverse pregnancy outcomes in subsequent pregnancy (McCarthy, et al., 2013). In this follow on study of a large prospective cohort of nulliparous women with a singleton pregnancy, we investigated the association between spontaneous miscarriage or termination of pregnancy and distress and behaviour in subsequent pregnancy. We hypothesised that women with previous miscarriage or termination would have higher levels of distress and would display altered behavioural responses to pregnancy.

Methods

SCOPE (Screening for Pregnancy Endpoints) is a prospective, multicentre cohort study with the main aim of developing screening tests to predict pre-eclampsia, small for gestational age infants, and spontaneous preterm birth (North, et al., 2011). Methods are described in detail elsewhere (McCarthy, et al., 2013). In brief, participants were healthy nulliparous women with singleton pregnancies recruited between November 2004 and January 2011 in Auckland, New Zealand, Adelaide, Australia, Cork, Ireland, and Manchester, Leeds and London, United Kingdom. Women were recruited at 15±1 weeks' gestation as previously described.(McCowan, et al., 2009, North, et al., 2011) Women were excluded if they were considered to be at high risk of pre-eclampsia, small for gestational age babies, or spontaneous preterm birth because of underlying medical conditions, gynaecological history, three or more previous miscarriages, three or more terminations of pregnancy, or had received interventions, such as aspirin, that might modify pregnancy outcome.

Ethical approval was obtained from local ethics committees [New Zealand AKX/02/00/364, Australia REC 1712/5/2008, London, Leeds and Manchester 06/MRE01/98 and Cork ECM5(10)05/02/08] and all women provided written informed consent.

SCOPE participants were interviewed and examined by SCOPE research midwives at 15±1 and 20±1 weeks' gestation. At the time of interview, data were entered on an internet accessed central database with a complete audit trail (MedSciNet). Participants were followed up prospectively, with pregnancy outcome data collected by research midwives. Primary outcomes, reported at the 15±1 week and 20±1 week interview, were anxious mood measured using the short form of the State Trait Anxiety Index (STAI) (Marteau and Bekker, 1992), how much stress the individual feels they are currently experiencing measured using the Perceived Stress Scale (PSS) (Cohen, et al., 1983), depressed mood measured using the Edinburgh Postnatal Depression Scale (EPDS) (Peindl, et al., 2004) and pregnancy related behaviour measured using the Behavioural Response to Pregnancy Questionnaire, a modified version of the Behavioural Response to Illness Questionnaire (Spence, et al., 2005) (Table 1). The Behavioural Reponses to Pregnancy has two subscales, all-or-nothing behaviour - a pattern of alternating extremes of behaviour characterised by a cyclical response of pushing oneself to keep going until this no longer feels physically possible. Limiting/resting behaviour refers to a tendency to curtail activities of daily living in response to symptoms or to respond to symptoms by resting, e.g."I have avoided my usual activities". Each of the primary outcomes was analysed as a continuous variable with the exception of the EPDS which was also analysed as a categorical variable using ordered logistic regression. The EPDS is the only primary outcome to have recognised cut-offs which relate to risk of depression (see Table 1)

196 and has been extensively studied during pregnancy as well as postnatally.(Austin, et
197 al., 2005, Austin, et al., 2005, Stewart, et al., 2013)
198 Miscarriage was defined as spontaneous pregnancy loss less than 20 weeks' gestation.
199 Student's t-test was used to compare continuous variables and χ^2 was used to compare
200 categorical variables in relation to previous miscarriage(s) only and previous
201 termination(s) only. In all the statistical tests women with no previous pregnancies
202 represented the reference group. Linear regression and ordered logistic regression (for
203 EPDS categorical variable) were used to analyse the continuous and categorical
204 variables respectively. All regression models were adjusted for maternal age,
205 smoking, alcohol consumption, ethnicity, body mass index (BMI), infant sex, marital
206 status and income. The models were further adjusted for any clustering effect of
207 SCOPE centres using the "cluster" option in Stata which specifies that the standard
208 errors allow for intragroup correlation, relaxing the usual requirement that the
209 observations be independent. That is, the observations are independent across centres
210 but not necessarily within groups.
211 Analyses were performed to assess the effect of previous miscarriages or terminations
212 of pregnancy on primary outcomes. This was done by generating a three-category
213 variable; 1) no previous miscarriage or termination; 2) one previous miscarriage or
214 termination and 3) 2 previous miscarriages or terminations.
215 Women who had previous terminations of pregnancy were excluded from the
216 miscarriage analyses. Similar women with previous miscarriages were excluded from
217 the termination of pregnancy analysis. All statistical analyses were performed in
218 STATA 10.0.
219
220 **Results**

Of the 5690 women who were recruited to the SCOPE study 5575 (98%) were included in this study (Table II). 4331 women (78%) had no history of miscarriage or termination, 559 (10%) had one and 94 (2%) had two previous miscarriages. 415 (8%) had one and 66 (1%) had two previous terminations of pregnancy. Women with previous miscarriages or terminations tended to be older and more likely to be overweight compared with those with no miscarriages or terminations (Table III). Women with one previous miscarriage had increased anxiety (adjusted mean difference 1.85; 0.61, 3.09), stress (adjusted mean difference 0.76; 0.48, 1.03) and depression (adjusted mean difference 0.62; 0.00, 1.23 and adjusted OR 1.26; 1.08, 1.45 for continuous and categorical scores respectively) scores at 15 weeks' gestation (Table IV). Behavioural response to pregnancy scores were not significantly different (adjusted mean difference 2.03; -3.20, 7.27 and adjusted mean difference 1.25; -4.22, 6.73 for limiting/resting and all-or-nothing responses to pregnancy respectively). Significant changes were also seen at 20 weeks' gestation in all of anxiety (adjusted mean difference 1.15; 0.73, 1.56), stress (adjusted mean difference 0.62; 0.23, 1.01) and depression (adjusted mean difference 0.44; 0.00, 0.88 and adjusted OR 1.13; 1.00, 1.28 for continuous and categorical scores respectively).

In women with two previous miscarriages significant changes were observed in depression scores at 15 weeks gestation (adjusted OR 1.65; 1.01, 2.70) and in a limiting/resting behavioural response to pregnancy score (adjusted mean difference 5.23; 0.71, 9.76). No differences were observed in women with two previous miscarriages at 20 weeks gestation in any of the measured outcomes.

In contrast to women with previous miscarriages, women with previous terminations did not display differences in anxiety scores compared to women with no previous terminations. Stress and depression scores were however significantly different in

246 women with previous terminations. Stress scores were significantly elevated at 15
247 weeks gestation in women with both one (adjusted mean difference 0.65; 0.08, 1.23)
248 and two (adjusted mean difference 1.43; 0.00, 2.87) previous terminations (Table V).
249 No differences were observed at 20 weeks gestation. Elevated depression scores were
250 also observed in women with one (adjusted OR 1.25; 1.08, 1.45) and two (adjusted
251 OR 1.67; 1.28, 2.18) previous terminations. These scores remained elevated at 20
252 weeks gestation (adjusted OR 1.64; 1.01, 2.68 and 1.81; 1.25, 2.62 for one and two
253 previous terminations respectively). Women with two previous terminations displayed
254 altered behavioural responses to pregnancy having increased limiting/resting
255 responses to pregnancy scores (adjusted mean difference 4.12; 0.51, 7.73) and
256 increased all-or-nothing response scores (adjusted mean difference 3.97; 0.84, 7.10) at
257 15 weeks' gestation.
258
259 **Discussion**
260 This study has demonstrated that previous pregnancy loss is associated with higher
261 levels of distress, perceived stress and unhelpful behaviours in subsequent pregnancy.
262 These changes are seen regardless of whether or not the pregnancy loss was a
263 previous miscarriage or termination. The magnitude of these effects appear to be
264 related to the number of previous pregnancy losses with higher losses associated with
265 higher observed differences in score variables. The observed differences in score
266 variables were generally higher at 15 weeks' gestation compared with 20 weeks
267 gestation suggesting that women may perceive the early pregnancy period as a higher
268 risk time. Women with previous miscarriages but not terminations also reported
269 significantly elevated anxiety scores, most likely a reflection of the unpredictability of
270 miscarriage and increased risk of recurrence in subsequent pregnancies.

There was also evidence that those with two, but not one, previous pregnancy losses have more extreme behavioural responses to pregnancy. Women with either two previous miscarriages or two terminations reported significantly higher levels of limiting activity and resting in response to pregnancy at 15 weeks gestation. Those with two terminations also reported an increased tendency to fluctuate between over doing things and then needing prolonged periods of rest (all-or-nothing behaviours). These differences in behavioural patterns were not evident at 20 weeks' gestation suggesting that early pregnancy may be perceived to be a higher risk period resulting in behavioural changes. It is possible that these behavioural responses relate to obstetric advice given to women with previous miscarriage to rest, although there is no evidence that these behaviours improve pregnancy outcomes.(Crowther, 2001, McCall, et al., 2013) However, it is unlikely to explain the results for women with previous terminations of pregnancy.

The strengths of our study are that detailed information about cognitive, behavioural and emotional factors in pregnancy was collected prospectively and pregnancy outcome data were available in more than 99% of participants. A limitation is the use of self reported scales and questionnaires as indicators of depression etc rather than a clinical diagnosis. Although we have reported significantly different scores in women with previous pregnancy losses, the actual clinical effect of these differences remains unclear and requires further research. The majority of pregnancy losses in this study were early first trimester losses. Therefore, these findings may not be applicable to later (second trimester) pregnancy losses.

In conclusion, there is evidence to suggest that women with previous pregnancy losses display increased stress, anxiety (miscarriage only), depression scores and altered behavioural responses to pregnancy. The magnitude of these effects was generally

higher in early pregnancy (15 weeks' gestation) compared with 20 weeks' gestation and higher in women with two miscarriages or terminations compared with women with one miscarriage or termination. Although we have demonstrated significant associations between previous miscarriage or termination of pregnancy loss and subsequent cognitive, behavioural and emotional ill-health, an interpretation of any causal effect of miscarriage or termination of pregnancy is not possible and further studies are necessary to explore this. Further research is also needed to explore whether interventions may be justified in order to provide additional supportive care to women with previous pregnancy losses to help them manage their distress and provide guidance and support for appropriate activity levels during pregnancy to avoid excessive inactivity and distress in the early periods of gestation which may be associated with adverse pregnancy outcomes.(Dunkel Schetter and Tanner, 2012)

Acknowledgments

We thank the pregnant women who participated in the SCOPE study, Rennae Taylor for coordinating the New Zealand SCOPE study, Nicolai Murphy for coordinating the Irish SCOPE study, Annette Briley for coordinating the UK SCOPE centres, Denise Healy for coordinating the Australian SCOPE study and all other SCOPE research midwives.

Contributors

FMC is guarantor. All authors had a role in conception and design of the study. FMC, AK, RMM, KOD and LK interpreted the data. All authors took part in drafting the article or revising it for critically important intellectual content and all gave final approval of the version to be published.

Funding

New Zealand SCOPE Study—New Enterprise Research Fund, Foundation for Research Science and Technology; Health Research Council; Evelyn Bond Fund, Auckland District Health Board Charitable Trust.

Australian SCOPE Study—Premier's Science and Research Fund, South Australian Government. The study sponsors had no role in study design, data analysis, or writing this report.

Ireland SCOPE Study- Health Research Board.

Manchester: National Health Service NEAT Grant, United Kingdom

Manchester Biotechnology and Biological Sciences Research Council, United Kingdom

King's: Guy's and St Thomas' Charity, United Kingdom

King's and Manchester: Tommy's - The Baby Charity, United Kingdom

Manchester: University of Manchester Proof of Concept Funding, United Kingdom

Competing interests

None declared.

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Table I: Cognitive, behavioural and emotional health scores and their interpretations.

Psychological and behavioural scales	**Score range and interpretation**
Edinburgh Postnatal Depression Scale (EPDS) (Peindl, et al., 2004)	As a continuous measure (0-30), where a higher score indicates a higher probability of depression OR As a categorical variable with the following 3 categories a. EPDS <5: unlikely to experience depression post partum b. EPDS 5-9: increased risk of depression in the next year c. EPDS >9: very likely depressed
Perceived Stress Scale (Cohen, et al., 1983)	0-40, with high scores representing higher perceived stress (feelings of lack of control)
Behavioural Responses to Pregnancy (adapted from the Behavioural Response to Illness Questionnaire (Spence, et al., 2005))	Two subscales: 1. Limiting/resting behaviour (0-20) 2. All-or-Nothing behaviour (0-28)
Short form State-Trait Anxiety Inventory (Marteau and Bekker, 1992)	6-24, with high scores indicating high state anxiety (i.e. current anxiety)

Table II: Participants recruited

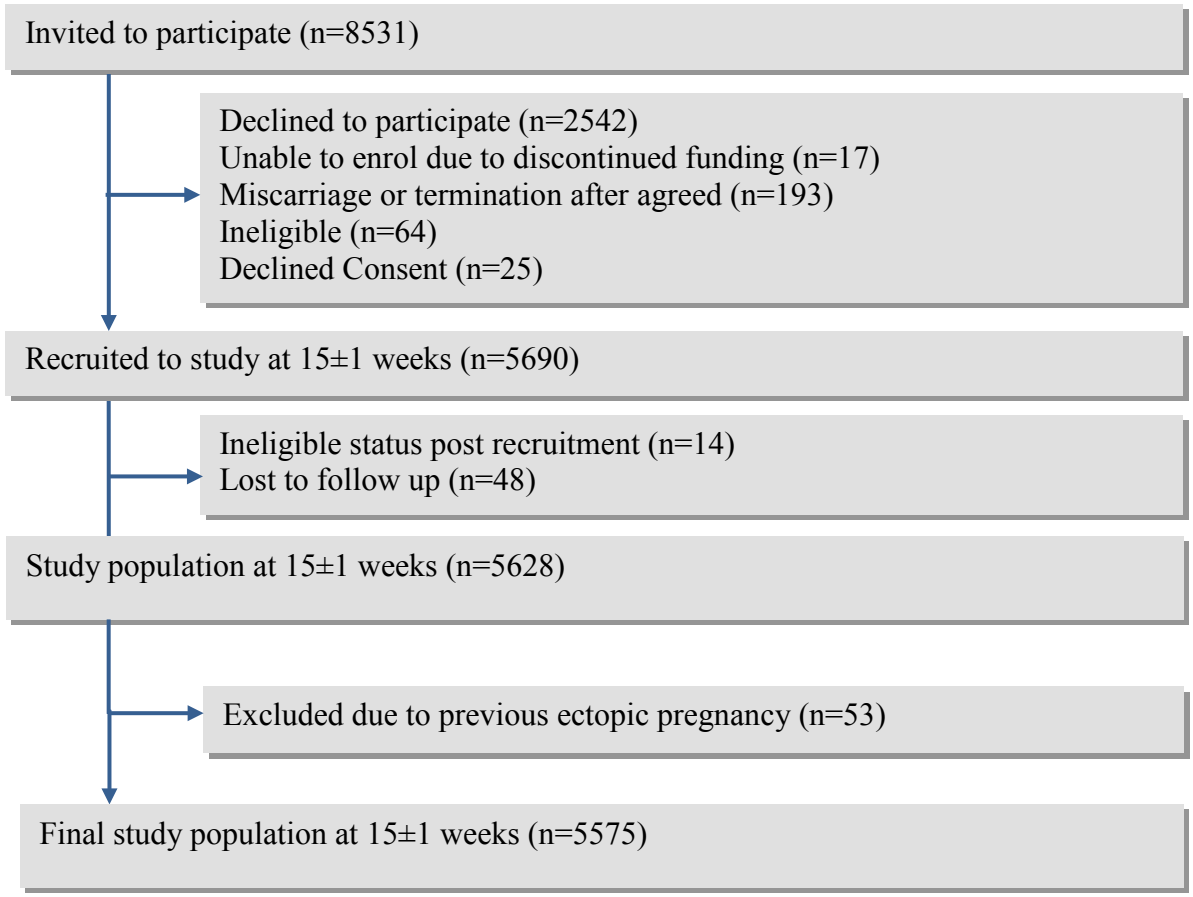

Table III: Characteristics of participants and pregnancy outcomes by number of pregnancies and mode of pregnancy loss.

Variable	**1st pregnancy (n=4331)**	**1 miscarriage (n=559)**	**2 miscarriages (n=94) †**	**P-value***	**1 TOP (n=415) ^†**	**2 TOP (n=66) ^†**	**P-value***
Maternal age (SD)	28.4(5.4)	29.6(5.5)	30.5(5.5)	<0.001	28.6(5.5)	28.9(5.2)	0.14
Ethnic origin				0.38			0.02
White	3910(90)	517(92)	82(87)		355(85)	59(89)	
Indian	106(3)	9(2)	3(3)		11(3)	1(2)	
Other	315(7)	33(6)	9(10)		49(12)	6(9)	
Married/ Cohabitating	3901(90)	525(94)	90(96)	0.003	372(89)	55(83)	0.19
Body mass index; n(%)				0.008			0.04
≤18.5	69(2)	8(1)	2(2)		3(1)	0	
18.6-24.9	2452(57)	283(51)	41(44)		224(53)	28(42)	
25-29.9	1185(27)	182(33)	28(30)		119(29)	21(32)	
>35	625(14)	86(15)	23(24)		69(17)	17(26)	

Table III continued: Characteristics of participants and pregnancy outcomes by number of pregnancies and mode of pregnancy loss.

Variable	1st pregnancy (n=4331)	1 miscarriage (n=559)	2 miscarriages (n=94) †	P-value*	1 TOP (n=415)^†	2 TOP (n=66) ^†	P-value*
Income				0.37			0.20
<25k	436(10)	49(9)	7(8)		33(8)	8(12)	
25k-74k	1386(32)	189(34)	39(41)		163(39)	21(31)	
75k-124k	1602(37)	191(34)	28(29)		137(33)	26(40)	
>124k	488(11)	75(13)	11(12)		43(10)	5(8)	
unknown	419(10)	55(10)	9(10)		39(10)	6(9)	
Alcohol**				0.06			0.94
No alcohol in pregnancy	1647(38)	237(42)	45(47)		163(39)	25(38)	
Quit in first trimester	2333(52)	277(50)	41(44)		206(50)	33(50)	
Continued to drink	451(10)	45(8)	8(9)		46(11)	8(12)	
Smoking**				0.03			<0.001
Never smoked	3329(77)	415(74)	77(82)		295(71)	30(46)	
Quit in pregnancy	583(13)	70(13)	6(6)		68(16)	16(24)	
Continued to smoke	419(10)	74(13)	11(12)		52(13)	20(30)	

Data are mean (SD) or number %. P values are for comparisons between the groups using student t-test or $\chi 2$ test, $P<0.05$. *Women in first pregnancies as reference group. **At 15±1 weeks ^TOP: Termination of pregnancy. Additional demographics available at (McCarthy, et al., 2013).

Table IV: Association between previous miscarriage and primary outcomes

Scale	Gestation measured (weeks)	One previous miscarriage only (n=559)		Two previous miscarriages only (n =94)	
		Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)	Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)
State Trait Anxiety[a]	15 20	1.78 (0.53, 3.02) 1.12 (0.65, 1.59)	1.85 (0.61, 3.09) 1.15 (0.73, 1.56)	1.39 (-2.40, 5.18) 0.46 (-1.72, 2.63)	1.58 (-1.98, 5.14) 0.45 (-1.62, 2.52)
Perceived Stress Scale[a]	15 20	0.68 (0.40, 0.97) 0.57 (0.14, 0.99)	0.76 (0.48, 1.03) 0.62 (0.23, 1.01)	0.73 (-2.04, 3.51) 1.31 (-1.00, 3.62)	0.88 (-2.08, 3.84) 1.30 (-1.24, 3.84)
EPDS [a](continuous)	15 20	0.57 (0.00, 1.16) 0.40 (-0.06, 0.86)	0.62 (0.00, 1.23) 0.44 (0.00, 0.88)	1.32 (-0.66, 3.29) 0.73 (-1.61, 3.07)	1.44 (-0.65, 3.53) 0.74 (-1.77, 3.25)
EPDS [b](categorical, OR)	15 20	1.21 (1.05, 1.39) 1.12 (1.01, 1.23)	1.26 (1.08, 1.45) 1.13 (1.00, 1.28)	1.55 (0.99, 2.42) 1.51 (0.80, 2.87)	1.65 (1.01, 2.70) 1.53 (0.75, 3.12)
Limiting response[a]	15 20	2.24 (-2.39, 6.88) 0.15 (-9.40,9.69)	2.03 (-3.20, 7.27) 0.27(-10.32, 10.86)	0.15 (-9.40, 9.69) 1.56 (-31.21, 34.32)	5.23 (0.71, 9.76) 1.96 (-30.55, 34.47)
All or nothing response[a]	15 20	1.42 (-3.56, 6.40) 1.27 ((-5.91, 8.44)	1.25 (-4.22, 6.73) 1.52 (-6.79, 9.84)	2.66 (-2.17, 7.50) -0.20 (-34.07, 33.67)	3.25 (-1.95, 8.44) 0.19 (-33.61, 33.99)

[a]Score variables are analysed using linear regression (95% CI).
[b] Edinburgh Postnatal Depression Score categorical variable presented as odds ratio and calculated using ordered logistic regression.
The reference group was primigravid women (no previous pregnancy losses). All regression models were adjusted for maternal age, smoking, alcohol consumption, ethnicity, BMI, infant sex, marital status and income. All analyses were adjusted for potential clustering effect of SCOPE centres.

Table V: Association between previous termination of pregnancy and primary outcomes

Scale	Gestation measured (weeks)	One previous termination (n= 415)		Two previous terminations (n =66)	
		Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)	Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)
State Trait Anxiety[a]	15 20	0.77 (-0.16, 1.70) 0.71 (-0.33, 1.75)	0.72 (-0.34, 1.79) 0.51 (-1.03, 2.06)	-0.13 (-2.98, 2.71) 2.22 (0.05, 4.40)	-0.67 (-3.64, 2.30) 1.54 (-0.89, 3.98)
Perceived Stress Scale[a]	15 20	0.82 (0.19, 1.45) 1.04 (0.19, 1.88)	0.65 (0.08, 1.23) 0.82 (-0.06, 1.71)	2.11 (0.86, 3.37) 2.08 (-0.37, 4.53)	1.43 (0.00, 2.87) 1.43 (-0.95, 3.82)
EPDS [a](continuous)	15 20	0.62 (0.07, 1.18) 0.88 (0.47, 1.30)	0.55 (-0.11, 1.20) 0.75 (0.23, 1.26)	2.07 (0.94, 3.21) 2.23 (1.03, 3.43)	1.66 (0.81, 2.51) 1.74 (0.50, 2.99)
EPDS [b](categorical, OR)	15 20	1.17 (1.00, 1.37) 1.39 (1.13, 1.71)	1.25 (1.08, 1.45) 1.64 (1.01, 2.68)	1.89 (1.44, 2.48) 2.20 (1.57, 3.08)	1.67 (1.28, 2.18) 1.81 (1.25, 2.62)
Limiting response[a]	15 20	-8.84 (-20.41, 2.73) -4.21 (-12.91, 4.49)	-6.12 (-17.43, 5.19) -3.78 (-10.85, 3.29)	3.74 (0.10, 7.38) 6.03 (-4.59, 16.64)	4.12 (0.51, 7.73) 6.21 (-5.09, 17.51)
All or nothing response[a]	15 20	-8.51 (-20.41, 3.39) -2.03 (-13.46, 9.38)	-5.84 (-17.39, 5.70) -1.49 (-11.14, 8.17)	3.78 (0.08, 7.49) 5.87 (-6.01, 17.75)	3.97 (0.84, 7.10) 6.51 (-5.87, 18.89)

[a]Score variables are analysed using linear regression (95% CI).
[b] Edinburgh Postnatal Depression Score categorical variable presented as odds ratio and calculated using ordered logistic regression.
The reference group was primigravid women (no previous pregnancy losses). All regression models were adjusted for maternal age, smoking, alcohol consumption, ethnicity, BMI, infant sex, marital status and income. All analyses were adjusted for potential clustering effect of SCOPE centres.