Is Reassurance Scanning Reassuring?
Anxiety levels, worries and attitudes of women with a history of recurrent miscarriage and standard risk women to early serial ultrasound scanning in a new pregnancy

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Is Reassurance Scanning Reassuring?

Anxiety levels, worries and attitudes of women with a history of recurrent miscarriage and standard risk women to early serial ultrasound scanning in a new pregnancy

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Abstract

Recurrent miscarriage affects 1% of all women and for many the cause will remain unexplained and a significant cause of distress. Evidence suggests that supportive care alone in the setting of an Early Pregnancy Unit increases the likelihood of a subsequent successful outcome to 76%. The mechanism of supportive care is not known and psychological support is poorly defined. Ultrasound examination in the absence of symptoms suggestive of further miscarriage is often the consistent feature of supportive care. Women with recurrent miscarriage have had many scans in previous pregnancies and the result has often been bad news. Is repeated scanning in women who are anxious about the outcome supportive? The work presented here examines the hypothesis that women with a history of recurrent miscarriage have higher background anxiety levels than women who have not had previous pregnancy loss (standard risk) and there is a more significant decrease in anxiety levels in recurrent miscarriage women when measured post scan than standard risk women.

Anxiety levels were assessed at 8 time points using the Stait-Trait Anxiety Inventory (STAI); pre and post ultrasound scan at 6,8 and 10 weeks and at the intervening 7 and 9 weeks at home. Worries were evaluated using the Cambridge Worry Scale (CWS) before the 6 week and after the 10 week scan, coping mechanisms were assessed using the Miller Behavioural Style Scale (MBSS) before the 6 week scan and attitudes towards the scans and pregnancy were evaluated before the 6 week and after the 10 weeks scan using semantic differentiation scales.

Anxiety levels were significantly higher before each scan in the recurrent miscarriage group compared to the standard risk group ($p<0.001$, $p=0.001$, $p<0.001$). Anxiety levels significantly decreased by a greater amount in the recurrent miscarriage group ($p=0.012$, $p=0.025$, $p=0.001$), this was short lived as anxiety increased again by 7 and 9 weeks independent of scanning. After the 10-week scan anxiety levels in both groups were not significantly different. Using mixed model analysis the number of children significantly reduced anxiety levels pre scan. The main worry before

the 10-week scan was of miscarriage in both groups, this worry did significantly reduce by 10 weeks, but was still the leading cause of worry in the recurrent miscarriage group. All participants were significantly more positive towards the pregnancy and scans after the 10-week scan.

This data demonstrates that anxiety levels are higher in women with recurrent miscarriage when compared to women with no previous adverse pregnancy outcomes. It provides evidence that in women with recurrent miscarriage and standard risk, scanning lowers anxiety levels immediately following the scan and that women have increased positivity as a result of scanning.

Acknowledgements

Working on this thesis has allowed me to combine two passions of mine: early pregnancy scanning and recurrent miscarriage. It has allowed me the opportunity to experience and learn a little about clinical research. I have found it stimulating, challenging and enjoyable.

If has been a privilege to work alongside many wonderful and inspiring colleagues and patients, in particular all of the staff of the Early Pregnancy and Acute Gynaecology Unit at St Thomas Hospital. Thank you all for allowing me to be a part of the team, for all your support in abundance and for looking out for recruits for this study. A big thank you to Myra Colendres for stepping in to scan in my absence and for her unwavering friendship. I would like to thank Myra Hunter for her advice in the early stages of this project 'conception'. Thank you to Paul Seed for his statistical advice. Special thanks must go to my supervisors Professor Jane Sandall and Dr Jude Hamilton for their support, belief, trust and guidance.

Thank you to all of the participants in this study. It has been an honour to have been entrusted with your care. Thank you for sharing your stories and completing so many questionnaires in spite of the emotional rollercoaster that many of you were going through.

Thank you to my parents for their support and invaluable help, the girls loved having their Nana and Grandad around!

Finally I would like to thank Rachael for all of her support, encouragement, patience and understanding. I could not have completed this without you.

Sarah

October 2017

Dedication

I would like to dedicate this thesis to Rachael and our girls Emily, Katie and Olivia. You have all given me the determination and strength to keep going.

I would also like to dedicate this to my parents Beryl and Phillip Merritt, who have always been encouraging and supportive in everything that I do.

Declaration

The work presented is that of the author, who performed all but 5 of the scans, scored all of the questionnaires and performed all the statistical analysis.

Abbreviations

AFI	Amniotic Fluid Index
AFP	Alpha Fetoprotein
ALARA	As Low As Reasonably Possible
ANC	Antenatal Clinic
APEU	Association Of Early Pregnancy Units
APS	Anti phospholipid Syndrome
BDI	Beck Depression Inventory
BMI	Body Mass Index
BMUS	British Medical Ultrasound Society
CI	Confidence Interval
CRL	Crown Rump Length
CWS	Cambridge Worry Scale
DASS-21	Depression, anxiety and stress scale
DGH	District General Hospital
ED	Emergency Department
EP	Ectopic Pregnancy
EPAGU	Early Pregnancy and Acute Gynaecology Unit
EPU	Early Pregnancy Unit
ESHRE	The European Society of Human Reproduction and Embryology
FH	Fetal Heart

GDG	Guideline Development Group
GP	General Practitioner
GSTFT	Guy's and St Thomas' Foundation Trust
GSTT	Guy's and St Thomas' NHS Trust
hCG	Human chorionic gonadotropin
HADS	Hospital Anxiety and Depression Scale
IMD	Index of Multiple Deprivation
ISUOG	International Society of Ultrasound in Obstetrics and Gynaecology
IUP	Intrauterine Pregnancy
IUS	Intolerance of uncertainty scale
LGBTQ	Lesbian, Gay Bisexual, Transgender, Questioning
LMP	Last Menstrual Period
MBRRACE	Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK
MBSS	Miller Behavioural Style Scale
MDI	Major Depression Index
MI	Mechanical Index
NICE	National Institute of Clinical Excellence
NT	Nuchal Translucency
p	Probability
PCOS	Poly Cystic Ovarian Syndrome

POC	Products of Conception
PUL	Pregnancy of Unknown Location
PTS	Post Traumatic Stress
PTSD	Post Traumatic Stress Disorder
RCOG	Royal College of Obstetricians and Gynaecologists
RPOC	Retained Products of Conception
SLE	Systemic Lupus Erythematosis
S-anxiety	State anxiety
SCL-90-R	Symptom checklist 90
STAI	State Trait Anxiety Inventory
T-anxiety	Trait anxiety
TAS	Trans abdominal Ultrasound Scan
TI	Thermal Index
TLC	Tender Loving Care
TVS	Trans Vaginal Ultrasound Scan
UK	United Kingdom
USA	United States of America
VIUP	Viable Intrauterine Pregnancy
VTE	Venous Thromboembolism
WHO	World Health Organisation

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Chapter 1 Introduction

1.1 Early pregnancy

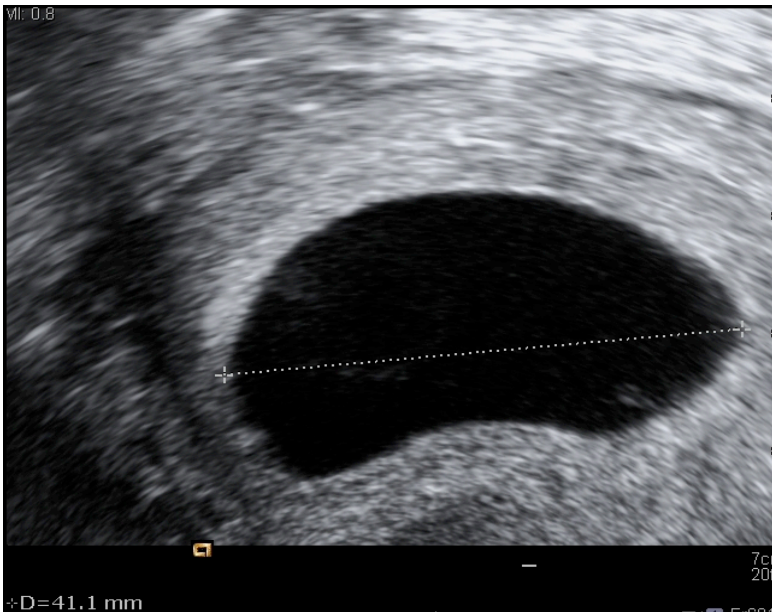
1.1.1 Early Pregnancy

The period of early pregnancy covers from the time of fertilisation through until typically 12 weeks gestation by menstrual dates based on a 28 day cycle assuming that ovulation has occurred on the 14th day. This coincides with the end of the first trimester. It is around this time at 11 weeks and four days to 13 weeks and five days gestation that women normally undergo their first pregnancy ultrasound scan, other wise known as the nuchal scan as part of combined screening which screens for the three major chromosomal abnormalities which could affect the fetus. For many women this is the first time that they will 'see their baby' and that their expected due date will be confirmed and if they have not already had pregnancy booking with a midwife, this will be the first time they will see a health care professional (fetal medicine specialist, sonographer or nurse/midwife sonographer) regarding the pregnancy. However for other women the period of early pregnancy is a time for concern in the form of symptoms such as pain and bleeding which may or may not signify an early pregnancy loss, or an anxious time despite no physical symptoms due to a loss in a previous pregnancy. With increasing access to early pregnancy information whether it is from organisation leaflets, books, websites or blogs, women are more aware of early pregnancy symptoms, including those that can be associated with problems such as miscarriage and ectopic pregnancy. With easier access to Early Pregnancy Units (EPUs) and ultrasound scans more women are presenting in early pregnancy expecting review by an expert and an ultrasound scan during which they can see the 'baby' themselves. However often the women's approach, expectations and reason for the ultrasound scan can be different to the clinicians (1) and women may be unprepared for the result if there is bad news, which may indicate that pre scan counselling is not adequate/occurs at all. There are important psychological factors involved with scanning and in particular previous pregnancy loss and women need to be aware of what the scan can and importantly cannot achieve (2).

1.1.2 Early Pregnancy Development

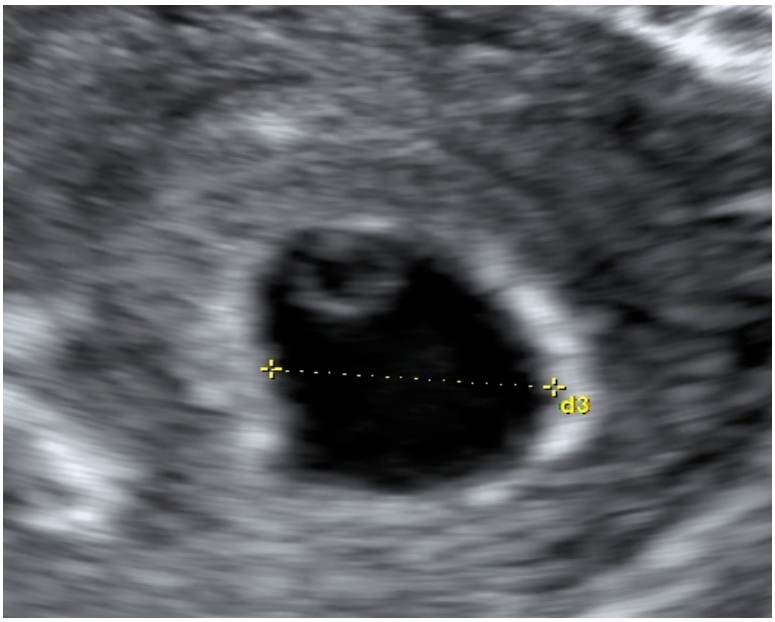
In order to understand early pregnancy and miscarriage it is important to consider normal development. The conceptus is regarded as an embryo until nine weeks and six days and a fetus from 10 weeks until birth. Due to the presence of ultrasound the development stages in early pregnancy can be seen clearly especially as the embryo/fetus can be visualised in its entirety on the screen during this time and that the development is visibly dramatic, organogenesis is completed by week 12.

Figure 1: The gestational sac at 4+6 weeks gestation



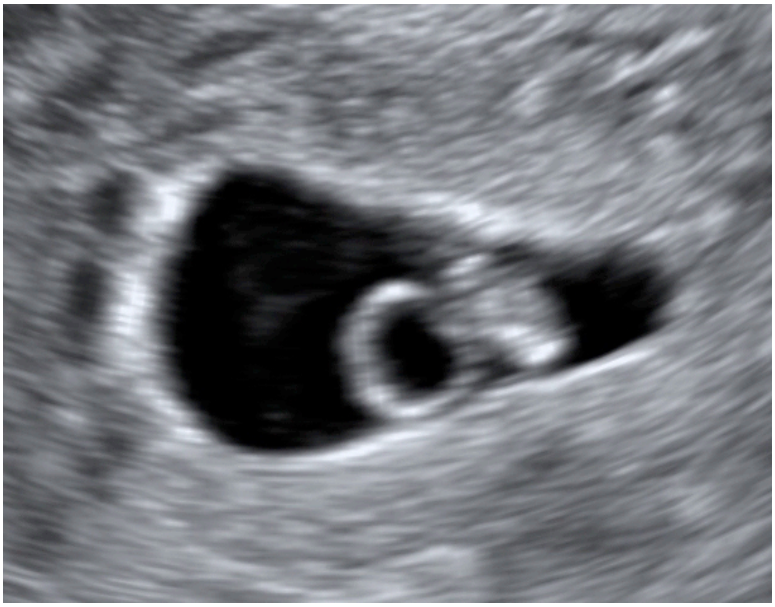
The gestational sac within which the embryo grows is visible from 4 weeks gestation

Figure 2: The gestational sac containing a yolk sac at 5 weeks gestation



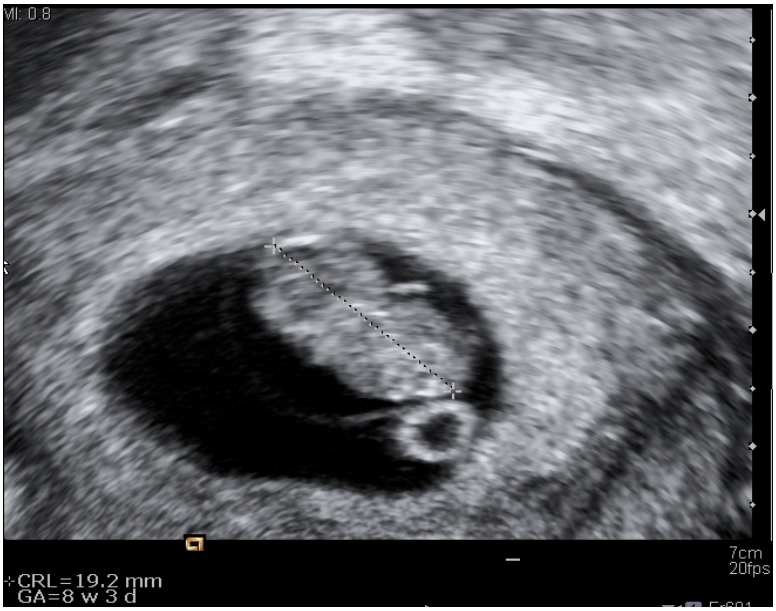
The yolk sac is visible from 5 weeks gestation

Figure 3: the embryo at 6 weeks gestation positioned next to the yolk sac



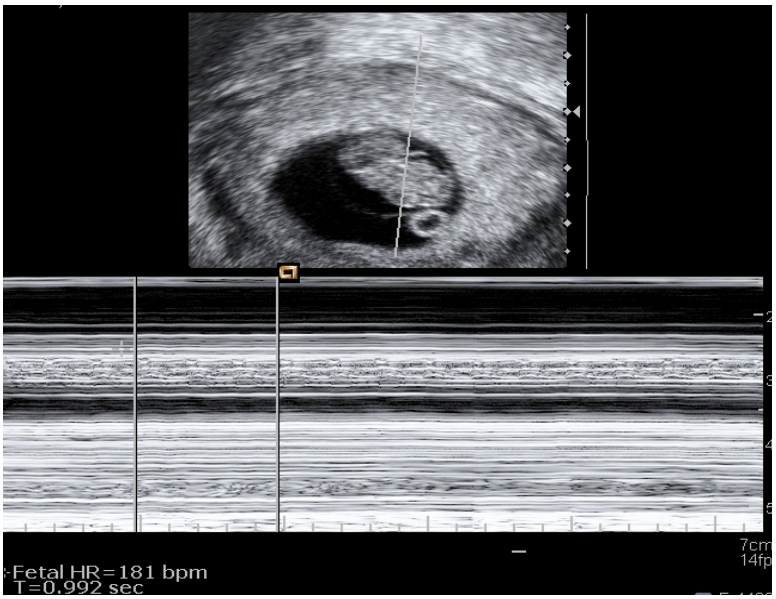
The embryo can first be seen at 5+4 weeks as a 2mm echogenic line, growing to 4mm at 6 weeks. Here it lies along side the yolk sac. The heartbeat can normally be seen at this stage.

Figure 4: The embryo at 8+3 weeks gestation



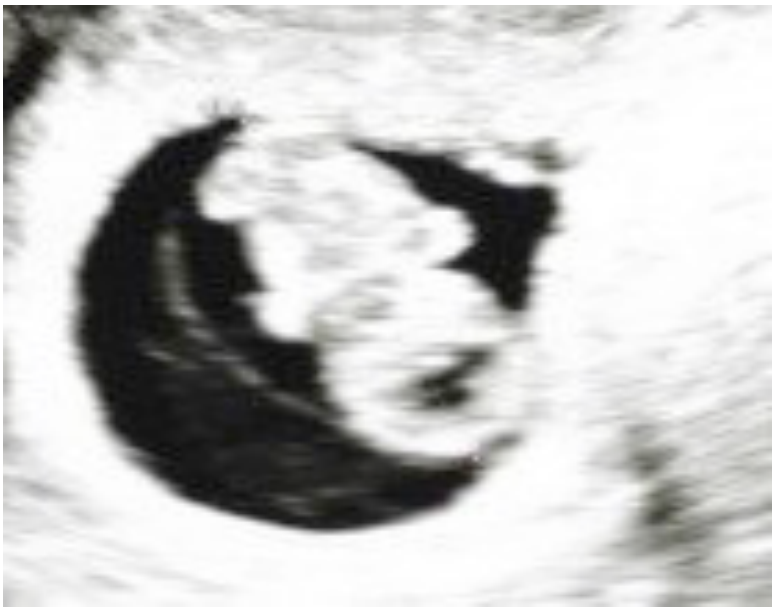
The amniontic sac is just visible

Figure 5: The embryo at 8+3 with m-mode measuring the FH



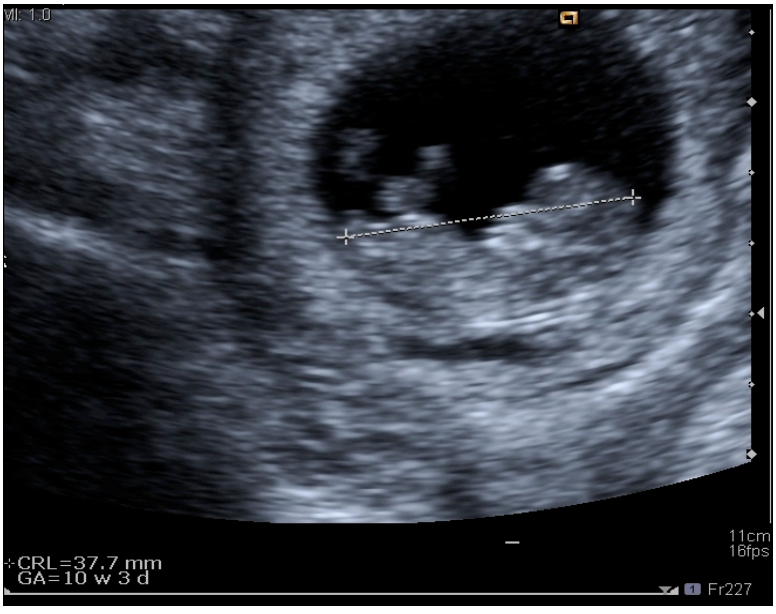
In early pregnancy the heartbeat is measure using M-mode, which detects movement. Doppler should not be used until after 11 weeks as there is a risk of too much heat being transmitted to the embryo

Figure 6: The embryo at 8+5 weeks gestation



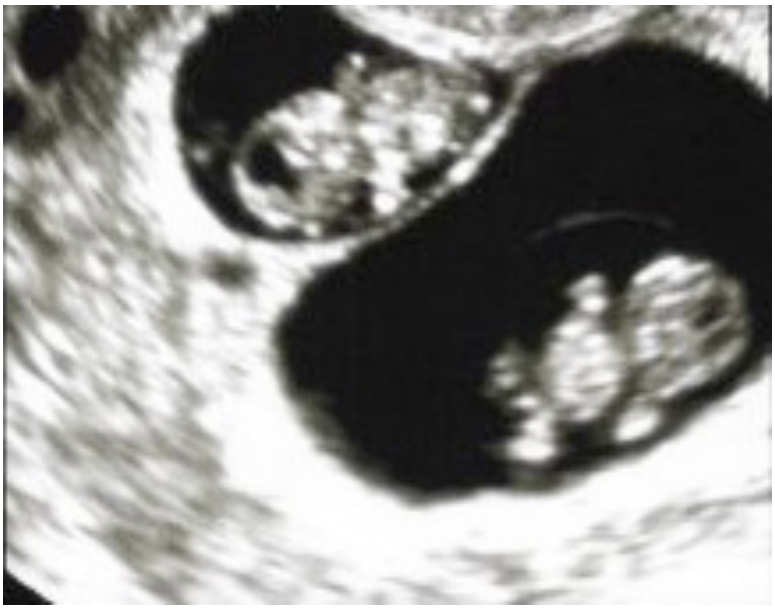
The limb buds are visible in this image from 8 weeks gestation as is the amniotic sac which eventually fuses with the gestational sac.

Figure 7: The embryo at 10 +3 weeks gestation



The fetus can now be imaged trans abdominally, limbs can be seen as can a profile

Figure 8: Twin pregnancy



This is a dichorionic diamniotic (two gestational sacs and 2 placentas) at 8+4 weeks gestation

1.1.3 Early pregnancy units

The majority of gynaecological emergencies which occur are due to early pregnancy complications and many women present to their General Practitioner (GP) or to hospital with symptoms of pain and bleeding, the latter affecting about 20% of clinically recognised pregnancies (3). Such symptoms are often perceived by women to be associated with miscarriage or ectopic pregnancy, prompting concern and need for review.

Table 1 Indications for referral to EPU

Pain	Pregnancy related pain can occur secondary to the corpus luteum, or pregnancy loss
Bleeding	Occurs in 20% of clinically detectable pregnancies can occur in ongoing pregnancies
Loss of pregnancy symptoms	Women report loss of breast tenderness, reduction/cessation of vomiting. This can also occur during an ongoing pregnancy
Hyperemesis	Vomiting can be associated with multiple and molar pregnancies
Dating Scans	Women who are uncertain of their last menstrual period dates (LMP)
Previous Ectopic Pregnancy	All asymptomatic women with a previous ectopic pregnancy are offered a scan at 6 weeks gestation to ensure correct pregnancy location due to the risk of another EP
Previous miscarriage/ Recurrent Miscarriage	Women who have recurrent miscarriage (3 or more consecutive miscarriages can attend for ultrasound scan/s in a subsequent pregnancy in an EPU. The specialist recurrent miscarriage clinic may be located within EPU.

Although the majority of pregnancies will progress normally and result in a live birth, pregnancy loss is common and it has been recognised that such women should be managed within a dedicated EPU (4), where they can be assessed by a team specialising in the management of early pregnancy problems to facilitate preferably “one stop” diagnosis and provide, for the majority, outpatient care. Previously such women were seen in the Emergency Department (ED) waiting a long time to be reviewed sometimes by healthcare professionals not trained in early pregnancy problems (5) and with limited access to diagnostic facilities, often being unnecessarily admitted to hospital for inpatient investigations (6). EPUs allow access to transvaginal ultrasound scanning (TVS), laboratory investigations and instigation of appropriate management and follow- up,

providing continuity of care and emotional support. Combined miscarriage and ectopic pregnancies were responsible for the deaths of 11 women in the 2006-2008 confidential enquiry into maternal death (7), highlighting the importance of accurate early pregnancy management. Since the establishment of EPUs in the early 1990s (6), there are now over 200 registered with the Association of Early Pregnancy Units (AEPU) (8). The standards of these units however vary in the quality of service offered and management protocols (9). The Royal College of Obstetricians and Gynaecologists (RCOG) produced a working party report (10) in 2008 in which they set out standards in early pregnancy care, looking specifically at early pregnancy loss, recurrent miscarriage and ectopic pregnancy. It acknowledged the vulnerability of women experiencing pregnancy losses, and not only the physical but resultant psychological distress. Trained staff specialising in miscarriage and recurrent miscarriage can offer support and continuity of care. Some EPUs have a dedicated recurrent miscarriage clinic located within it.

1.1.4 Miscarriage

Miscarriage is the loss of a pregnancy before 24 weeks gestation (11), the recognised gestation at which a fetus is viable. Early pregnancy miscarriage is the loss of a pregnancy before 12 weeks gestation. Miscarriage occurs in 20% of clinically detectable pregnancies (12). Over 80% of miscarriages occur prior to 12 weeks gestation (13).

1.1.5 Aetiology of sporadic miscarriage

In the majority of cases the cause is unknown, purely as many products of conception (POC) are either not examined histologically or have cytogenetics performed.

Causes :

- Fetal chromosomal- 50%

Risk Factors:

• Maternal medical conditions	Diabetes Mellitus (poorly controlled) Systemic Lupus Erythematousus, Anti Phospholipid Syndrome
• Socio- demographic	Increased maternal age, obesity, smoking, alcohol, recreational drugs
• Anatomical	Uterine anomalies (later miscarriages)
• Infection	Listeria, toxoplasmosis, varicella zoster, malaria

1.1.6 Diagnosis of Miscarriage

The introduction of ultrasound has led to more miscarriages being diagnosed without clinical examination (6). There are different types of miscarriage and dependant upon when a woman presents within the miscarriage process and is scanned will depend on what is seen on ultrasound.

Table 2 Different types of miscarriage and corresponding ultrasound findings

Type of miscarriage	Ultrasound Findings
Threatened	Viable intrauterine pregnancy (VIUP)
Inevitable	Cervical os is open, the embryo/fetus if present may still be alive
Incomplete	Retained Products of Conception (RPOC) are seen
Complete	There is no evidence of RPOC in a woman who has previously had an IUP seen on scan
Delayed	Either: Empty gestational sac of >25mm Or A Crown Rump Length (CRL) of > 7mm and no heart beat Or No significant change from previous scan after two weeks with an empty sac or one week with an embryo

Diagnosis of early pregnancy loss is advised to be made using a TVS ensuring a clear image. The scan operator should be trained in early pregnancy scanning and follow the strict diagnostic criteria listed above. The NICE guideline (14) on Ectopic pregnancy and miscarriage state that If either the gestational sac is empty but less than 25mm in diameter or an embryo is present and the CRL is < 7mm on TVS a repeat scan is advised a minimum of 7 days after the first (14). If either an empty gestational sac is >25 mm or the CRL is > 7mm with no heart beat on TVS a diagnosis of miscarriage can be made but NICE advise seeking a second opinion on the viability of the pregnancy or rescanning a minimum of 7 days after the first scan.

1.1.7 Management of Miscarriage

Women who are diagnosed with a miscarriage can be offered 3 main types of management with appropriate counselling to each one: expectant, where the products of conception (POC) are given medications to expel the POC or surgical management either by manual vacuum aspiration under a local anaesthetic or curettage under a general anaesthetic. All women with miscarriage should be treated with dignity and respect and given information about support and counselling services (14).

1.2 Recurrent miscarriage

1.2.1 Recurrent miscarriage- Definition and Incidence

Several definitions of recurrent miscarriage exist. The RCOG define it as the loss of 3 or more consecutive miscarriages before 24 weeks' gestation (11). This definition refers to all pregnancies, including pregnancies visible and diagnosed on ultrasound scan, failing PULs and those pregnancies confirmed with a urine or serum hCG where a scan may never have taken place. The calculated incidence of having three consecutive, 'sporadic' miscarriages is 0.34%, where as recurrent miscarriage has been found to affect approximately 1% of fertile women. Recurrent miscarriage is more common than by chance alone which suggests some cases of recurrent miscarriage may have an underlying, associated pathology. The risk of further miscarriage also increases by more than would be expected by chance after two previous losses, although not by the same degree as after three (15) (16). In 2018 the Guideline Development Group (GDG) of The European Society of Human Reproduction and Embryology (ESHRE) defined recurrent miscarriage as two or more pregnancy losses and did not specify that these had to be consecutive (17). The prevalence of recurrent miscarriage, using this definition is 2.6% (18). Regardless of how recurrent miscarriage is defined, repeated pregnancy loss is recognized as a significant cause of distress in couples trying to conceive.

1.2.2 Epidemiology of Recurrent Miscarriage

Recurrence risk of miscarriage increases with maternal age and the number of previous miscarriages. The numbers of oocytes are highest during female fetal development at 10-12 weeks gestation totalling between 6-7 million (19). From this stage on the number of oocytes decrease, two million are left at birth and approximately 300000 by puberty. Each month after this a cohort of follicles begin to develop, with usually one becoming dominant, eventually ovulating. Over 99% of all follicles will undergo apoptosis and not ovulate. The supply of oocytes is exhausted leading to menopause. The quality of these remaining oocytes year by year worsens resulting in an increase in the number of miscarriages particularly over the age of 35 years, there is also a recognised risk with increasing paternal age of over 40 years (20).

Having had a previous miscarriage increases the risk of future pregnancy failure. Regan et al (21) observed that in 407 women from the general population, the overall incidence of miscarriage was 12%. This decreased to 5 and 4% for primigravid women and mutiparous women with no previous pregnancy loss respectively, whilst 24% of those who had experienced any previous number of miscarriages, miscarried again. In a woman who has had three consecutive miscarriages her risk of miscarrying again increases to 40% (11). The risk of miscarriage increases with rising number of previous miscarriages, independent of maternal age (16). After four previous miscarriages the miscarriage risk was 54.3% compared to 10.7 % in women with no previous miscarriage. See table 3 below. Similar findings are observed by Magnus et al (15) who show that miscarriage rates increase almost four times after three consecutive previous miscarriages compared to no previous miscarriages, regardless of maternal age. Having a living child is not a protective factor against recurrent miscarriage (22).

Table 3 Adapted from Recurrence risk in Norway between 2009 and 2013 after consecutive miscarriages (15) and Knudsen et al (16) risk of subsequent pregnancy ending in miscarriage 1980-1984 in Denmark

	Norway		**Denmark**
Previous miscarriages	% of miscarriages	Adjusted odds ratio (95% CI)	% of miscarriages (95% CI)
0	11.6	ref	10.7 (10.3-11.2)
1	19.8	1.54 (1.48 to 1.60)	15.9 (15.4-16.4)
2	27.7	2.21 (2.03 to 2.41)	25.1 (23.4-27.0)
≥ 3	41.9	3.97 (3.29 to 4.78)	45.0 (39.8-50.4)

1.2.3 Risk Factors for Recurrent miscarriage

Investigations have been able to detect associated factors in up to 50% of cases of recurrent miscarriage (23).

Table 4 Factors associated with recurrent miscarriage

Risk Factors	
Antiphospholipid antibody syndrome	Present in 15% of women with recurrent miscarriage
Genetic Factors	Parental chromosomal rearrangements (2-5% of recurrent miscarriage) or fetal chromosomal abnormalities (30-57%)
Anatomical Factors	Congenital uterine malformation and cervical weakness
Endocrine	Poorly controlled diabetes, thyroid disease, PCOS
Immune	Possible bias towards a T-helper-1 cytocine response
Infective	Role unclear in recurrent miscarriage
Inherited Thrombophilias	Eg deficiencies in protein C and antithrombin III. Presumed mechanism of thrombosis of the uteroplacental circulation.

1.2.4 Management of recurrent miscarriage with an identifiable underlying association

All women should be offered care by a healthcare professional with expertise in recurrent miscarriage, where possible in a recurrent miscarriage clinic (11).

Table 5 Recommended investigations and treatment for women with recurrent miscarriage

Investigation		Treatment
Antiphospholipid antibodies	Two positive tests ≥12 weeks apart of either lupus anticoagulant or anticardiolipin antibodies confirms diagnosis	Consider low dose aspirin and heparin
Karyotyping	Cytogenetics on POC of the third and subsequent miscarriages Parental karyotype after cytogenetics of the POC shows an unbalanced structural chromosomal abnormality	Genetic counselling
Anatomical Factors	TVUS to asses anatomy or hysteroscopy/laparoscopy if required for definitive diagnosis	No evidence that surgical correction reduces miscarriage rate
Thrombophilias	Screening for inherited thrombophilia's in women with second trimester miscarriage	Heparin may improve the live birth rate with second trimester miscarriage

1.2.5 Unexplained recurrent miscarriage

It is increasingly thought that the majority of women with recurrent miscarriage have no identifiable cause after investigation (24) (25). Regardless of figures, these women are deemed to have unexplained recurrent miscarriage and it remains a distressing and discouraging diagnosis for couples involved. Not identifying a cause can be difficult for both the clinician and couple and it is important that the clinician should be clear about the prognosis. It is very easy for the doctor to feel frustrated and obliged to intervene and initiate medical treatment (26). There is no evidence that

therapeutic intervention improves pregnancy outcome. Despite this and the existence of guidelines advising on recurrent miscarriage adherence to the recommended guidance is often poor (27). Although the chance of recurrence does increase with maternal (and paternal) age and number of miscarriages, it has been found that with supportive care alone in the settling of a dedicated early pregnancy unit the likelihood of a subsequent successful outcome for these couples is around 74% (those not miscarrying) (22) and 75% (survival after 28 weeks) (28).

The mechanism of this psychological support is proven within the midwifery setting where continuity of care helps support women; meeting physical and psychological health needs. A Cochrane review of midwife led continuity models of care included 15 trials (29). Those women undergoing midwife-led continuity of care were less likely to have interventions, had less preterm births before 37 weeks, and there were fewer fetal losses before and after 24 weeks. Measurement of women's satisfaction was reported narratively, and there was a higher rate of maternal satisfaction in midwife–led continuity groups. This was further examined in the project 20 work, examining midwives' insight into continuity of care (30). Overall they found that midwives felt continuity of care was beneficial to women and had a positive impact on their outcomes, by building trust and responding to each woman's individual physical, emotional and social needs.

1.3 Supportive Care

1.3.1 Definition

Supportive care is the care given to couples with a history of recurrent miscarriage in a subsequent pregnancy. The concept of what constitutes supportive care is ill defined (31). Examples of supportive care from the literature include:

- Review in a specialist Early Pregnancy Unit
- Consistency of care by specialist gynaecologist/team in recurrent miscarriage

- Serial ultrasound scans
- Serum hCG and progesterone monitoring
- Counselling and 'psychological' support
- Life style and diet advice
- Stress reduction physiotherapy
- Alternative therapy including relaxation tapes
- Admission to hospital at gestation previously coinciding with miscarriage
- Bed rest
- Admission to hospital if symptomatic/requested by patient

1.3.2 Evidence

The evidence concerning supportive care is very limited and current guidelines and papers discussing the management of unexplained recurrent miscarriage are based on a few non-randomised and older studies (32) (22, 28, 33)

Stray- Pederson and Stray-Pederson (32) found a 86% successful pregnancy outcome in women with a history of unexplained recurrent miscarriage and who had then received specific antenatal counselling and psychological support as opposed to 33% who did not. The 'tender loving care' was however restricted to those who lived within a 'reasonable' distance from the hospital and the study design has been criticised (26). The TLC was stated as consisting of psychological support and weekly medical examinations, to rest as much as possible, avoid coitus and for bed rest for at least 2 weeks at the gestational age in which they had experienced their earlier miscarriages. It is unclear exactly what psychological support was given and how it was evaluated. The trial itself was small; 37 participants receiving TLC and 24 who did not. There is no evidence to support bed rest

helps reduce/prevent miscarriage and comes with the risk of women developing venous thromboembolism (VTE). At the time of the study APS was not routinely screened for so it is difficult to guarantee that all of those participants particularly in the non TLC group did in fact have unexplained recurrent miscarriage. Untreated APS could account for the higher miscarriage rate. The fact that those women who lived geographically closer to the hospital were allocated to TLC indicates a degree of bias.

Liddell et al (33) addressed the role of supportive care, observing that 86% of the 44 women with unexplained recurrent miscarriage and receiving supportive care (weekly visits from 5-13 weeks gestation, comprising of scanning and βhCG levels additionally access to stress reduction physiotherapy, relaxation tape and liberal admission to the miscarriage inpatient room) were successful. This was compared to 33% success rate in pregnancy outcome in a control group of only 9 women with unexplained recurrent miscarriage who received no formal supportive care. βhCG levels are elevated prior to the pregnancy being visible on scan and are not predictive of location of pregnancy and could give false reassurance. Although typically a rising βhCG of 66% in 48 hours is often associated with a viable intrauterine pregnancy (VIUP) it can also be associated with ectopic pregnancies and pregnancies that will fail (34). βhCG levels can vary and lower rising levels can also be associated with on-going pregnancies, but could unnecessarily increase worries in a woman with a history of recurrent miscarriage. Blood tests themselves are invasive and there is no evidence to support the use of βhCG supplementation if low levels are detected to prevent a miscarriage in a woman with recurrent miscarriage (11).

Similar results were noted during the Clifford et al (35) study, which primarily looked at LH suppression, followed by low dose ovulation induction and possible association with reduction of miscarriage rate. They found that this had no benefit but at the same time as a secondary measure saw a live birth rate of 76% in the control group who ovulated spontaneously and received supportive care consisting of weekly scans and review by a specialist team. However within this control group of 46 women, 20 received progesterone luteal phase support and only 26 participants

received a placebo i.e. had no intervention. This was then followed by a 1997 (22) study by the same team, looking primarily at pregnancy outcome in unexplained miscarriage with supportive care only, consisting of weekly scanning for viability and growth in a dedicated early pregnancy clinic. The miscarriage rate in this group was 26% compared to 51% who did not attend the clinic. For the 41 women who did not receive specialist supportive care, these women simply did not attend the clinic in a subsequent early pregnancy rather than being randomised to no follow up and were then contacted by phone or letter to document the pregnancy outcome. It is not clear within the study as to what care these women did or did not receive including whether they attended another specialist clinic elsewhere.

Brigham et al (28) offered fortnightly scans and "followed clinic protocol" to recurrent miscarriage women in a subsequent pregnancy in their study examining pregnancy outcome following idiopathic recurrent miscarriage. They found that of the 222 women there was a 75% live birth rate. Although they state that this success "has been obtained with the provision of tender loving care and ultrasound in early pregnancy" it does not allude to what TLC was received.

Table 6: Miscarriage rates in women receiving supportive care versus no supportive care

Study	**TLC Group**		**Control**	
	Number of participants	Miscarriage rate (%)	Number of participants	Miscarriage rate (%)
Stray-Pederson and Stray-Pederson (1984)	37	14	24	67
Liddell et al (1991)	44	14	9	67
Clifford et al (1997)	160	26	41	51
Brigham et al (1999)	222	25	-	-

What is evident from the studies, which have been conducted examining supportive care is that, supportive care differed in each study and it was not always clear what the supportive care consisted of which makes it difficult to know what should be offered to women with a history of recurrent miscarriage. None of the studies were randomised, there were elements of bias in allocating participants to the control group and the numbers of participants were very small particularly in the control groups. Despite the limited data, it is on these studies that conclusions have been drawn and evidence used, for current practise recommendations.

1.3.3 In practice

The RCOG Green-top Guideline (11) on the management of recurrent miscarriage advises that

> "women with unexplained recurrent miscarriage have an excellent prognosis for future pregnancy outcome without pharmacological intervention if offered supportive care alone in the setting of a dedicated early pregnancy assessment unit."

In their working part report (10) from 2008 the RCOG include within their standards for recurrent miscarriage:

> "Arrangements should be in place for women with a future confirmed pregnancy test to attend an EPAU for an ultrasound scan and to receive shared antenatal care in a high-risk obstetric unit"

Other than advising that women "attend an EPAU for an ultrasound scan", neither document elaborates on what supportive care should consist of. Hospitals differ in the care and support of such women in subsequent pregnancies; and review in early pregnancy units is not always available. In many hospitals ultrasound examination is the consistent factor of supportive care, whether this is a single or serial scans. Each hospital may have its own guideline, but adherence to guidelines within the arena of investigating and managing recurrent miscarriage does not occur (27). Additionally none of the studies so far have defined what supportive care should be, and the study populations and difference in what was being offered in support differ enabling it difficult to tailor a guideline, which could easily be followed by all.

Musters et al (36) attempted to identify what women with a history of recurrent miscarriage want in terms of supportive care in a subsequent pregnancy. They conducted semi structured in-depth interviews with 15 women by phone in Amsterdam using both open ended and topic list questions. When asked women preferred having early, repeated scans, βhCG monitoring, lifestyle advise, counselling and a clear pathway of care for the first 12 weeks of their pregnancy. Timing of when the participants' preference as to when first βhCG would be taken was added to the list of questions for all participants when suggested by a participant as what they wanted in supportive care. This is an example of a service user asking for an intervention for which there is no evidence to support its use. By then directly asking other participants when they want their first βhCG it may falsely convey that this is an accepted, helpful measure which if a woman who has had recurrent miscarriage thinks it will be helpful then she is more likely to agree that it should be part of supportive care. Many of the topic list questions may have acted in the same way creating a bias.

It is difficult for a clinician to explain to a couple that no pharmacological intervention is required in a case of unexplained recurrent miscarriage and then be unable to explain exactly how supportive care works. Although studies have been invaluable in showing that pharmacological intervention is not warranted in unexplained recurrent miscarriage none of them have explained what emotional/ psychological care was given. This is important as both single spontaneous and recurrent miscarriages are associated with an increased rate of psychiatric morbidity, including depression and heightened anxiety (37-39).

1.4 Psychological Factors

1.4.1 Mental Health in pregnancy

Pregnancy for many is a time of joy and excitement, an event that is often planned, sometimes long awaited for. For all it is a major life-changing event where physiological and psychological change occurs and this transition period to motherhood can be can be associated with increased levels of anxiety and emotion. Women are additionally at increased risk of depression and deaths from

suicide in pregnancy and the postnatal period has been well documented and was previously the leading cause of indirect maternal death. The 2015 Mothers and Babies: Reducing risk through Audits and Confidential Enquiries (MBRACE) (40) focused on the psychiatric causes of maternal death and in lieu of this report and recognition of the importance of suicide in pregnancy the World Health Organisation (WHO) now classify it as a direct cause of death. Consequently MBRACE have also changed the classification in their report from indirect to direct (41).

1.4.1.1 Pregnancy Worries

Many studies have focused on anxiety levels in pregnancy and have used various measures (42-44) to do this. It is not always apparent however as to what women are worrying about. As a consequence Green et al (45) developed the Cambridge Worry Scale to measure what pregnant women were worried about and to what extent they were worried. In their 2003 (46) study they used the CWS to measure worry at 3 stages, 16 weeks gestation, 22 weeks gestation and at 35 weeks gestation. They found that the mean CWS scores for each item in the scale were higher at the first stage, dropped for the second stage and again rose in the third stage. They observed that the highest mean scores were for the following items across the stages: the possibility of something being wrong with the baby, the possibility of miscarriage (not included in the third stage), giving birth and money problems. In a further study (47) using the CWS, the major worries were about the possibility of something being wrong with the baby, giving birth and miscarriage followed by financial matters. These results are similar to the Green at al study. Rather than a longitudinal study, the participants in the later study had varying gestations of 8 to 42 weeks, and were then divided into groups for gestational comparison, which means there would not be the same consistency in thought process. What they also observed in their study is that women also had concerns about the maternity services, which are not, included in the CWS e.g. hospital overbooked, staff being too busy. Further use of the CWS, Penacoba-Puente et al 2011 (48) on women at mean gestational age of 14.4 weeks and then again at 34.3 showed that the main concern at both stages was the possibility of something being wrong with the baby. They observed that first pregnancy, unplanned pregnancy and history of previous miscarriage were factors which

negatively influenced women's worries. Less than half the women who completed the scale at 14 weeks completed it again at 34 weeks so it is not a true reflection of a longitudinal study.

1.4.1.1.1 Screening

The CWS in each of the three studies discussed indicates that predominantly women are most worried about the health of their baby. Such occasions that could precipitate anxiety and worry is screening for chromosomal problems and fetal anomaly assessments. In their extensive systematic review of the psychosocial aspects of genetic screening of pregnant women and newborns Green et al (49) observed that studies have increased knowledge of screening but have not increased anxiety levels, that anxiety whilst raised in women receiving positive screening results there is insufficient evidence of a beneficial effect of receiving negative results. Additionally they observed from the literature that anxiety in screen positive women falls on subsequent negative results but some residual anxiety may remain and that the way in which screening is offered may affect the anxiety in screen negative women. This last observation suggests that whilst informing women of the chance that there may be a problem with the baby, it may cause a previously unknown awareness and therefore increase anxiety levels.

Muller et al (50) compared levels of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) during pregnancy and puerperium between women offered NT screening and a control group who were not offered screening and then comparing levels between women accepting and those declining screening. They found that informing women and offering the NT screening didn't increase their anxiety levels and that women either undergoing the NT or those who were offered it and declined screening were significantly less anxious than those not offered screening at all. At the time of this study women under the age of 36 in the Netherlands are not offered screening.

Watson et al (51), used the short form of the Spielberger Sate-Trait Anxiety Inventory to assess the anxiety levels in women where soft markers (e.g. echogenic bowel, cardiac echogenic foci, renal dilatation) were seen on ultrasound scan and a control group with no markers visualised. They found that in the women where markers had been seen they had significantly elevated levels of anxiety after the scan, which then reduced at 30 weeks gestation and at one-month post delivery to normal range. Additionally they observed that women who were informed during the scan that although markers were present that the baby would probably be all right had significantly less anxiety than those not told this. The sample size in this study was very small and focused on one centre and therefore may not be transferrable to the general population.

With the advent of new screening tests not only will we possibly see varying anxiety levels but increased surveillance and intervention, which could also affect anxiety and worry during pregnancy.

1.4.2 Anxiety as a possible cause of miscarriage and recurrent miscarriage

Stress is thought to have a role to play in causing miscarriage (52). Studies have shown when mice are exposed to stress they miscarry (53). Psychological factors have been found to influence immunological function (54). Models have been proposed providing a framework within which psycho-neuro-cytokine/endocrine pathways can be investigated and targeted for prevention of miscarriage (55). Within the realms of sporadic miscarriage decidual tissue has been found to contain significantly higher numbers of MCT+, CD8+ and tumour necrosis factor-α TNFα cells in women with high stress scores (56).

In a retrospective review of the National Comorbidity Survey of the United States (57) it was found that pre-existing mental illness was significantly associated with both stillbirth and miscarriage. However an anxiety disorder alone was not significantly associated with fetal loss.

Sugiura-Ogasawara et al (58) looked at depression as a potential cause of recurrent miscarriage. They prospectively gave self-report questionnaires to assess mental health to 61 women with a history of two consecutive first trimester miscarriages. Of the 45 women who conceived, ten miscarried again. They found that those women who miscarried again were significantly associated with depressive symptoms and that depression was a statistically significant predictor of subsequent pregnancy outcome.

1.4.3 Psychological sequelae in women with a history of sporadic miscarriage

A loss of a pregnancy no matter the gestation is often associated with a grieving process. A woman who loses a pregnancy through miscarriage will grieve depending on what the loss means to her (59). Previously and still to some extent miscarriage is not openly talked about and can be dismissed as not being a "real" pregnancy loss (60) or that it can not be compared to a woman who has had a third trimester stillbirth. The most common reaction is initially grief and approximately 40% of women will suffer from grief following a miscarriage (60, 61). Grief encompasses emotions including sadness, yearning for the lost baby, a need to talk about the loss, guilt with self blame and a search for a 'meaningful explanation about the loss' (60-62). Miscarriage often occurs without warning, it can be sudden and in early pregnancy there is sometimes no identifiable baby. No funeral takes place, there is no official chance to mourn and often family members and friends are unaware of the pregnancy and so there can be little or no support from those she is closest to. It has been recognised that as soon as a woman knows she is pregnant, she may prepare for her future life with that baby including hopes and dreams (63). The grief reaction can be akin to the loss of a loved one (61). The grief process can vary but can last 2 to 3 years (60, 62).

Women with miscarriage have depression and anxiety rates of 12-50% and 22-41% respectively (60, 62). Signs of depression include low self-esteem, sadness, loss of appetite and sleep disturbance.

Thapar and Thapar (37) used the general health questionnaire and hospital anxiety and depression scale to ascertain the psychological sequelae after a miscarriage in women who had an evacuation of the products of conception under a general anaesthesia and compared their scoring to women who had booked in antenatal clinic. They observed that women who had miscarried were significantly more anxious and scored higher on the depression scale than pregnant women. However the gestations of women attending the ANC varied and only in those who were less than 16 weeks pregnant was there a significant difference in anxiety and depression scores. Additionally some of those women attending the ANC could have had a past history of pregnancy loss which would bias the results.

Klier et al (64) attempted to show that women with a history of miscarriage suffer from minor depressive disorders. The miscarriage group consisted of women attending a medical centre with spontaneous miscarriage and the control group, women from the same area with no history of pregnancy in the last 12 months. Whilst 5.2 % of miscarrying women were classified with a minor depressive disorder versus 1% of the controls, neither groups had many cases of minor depression and therefore statistical analysis was difficult.

Longitudinal studies examining psychological morbidity have found that depression and anxiety can persist at 12, 13 months and 5 years post miscarriage (61, 65, 66). Further studies have shown that depression and anxiety associated with miscarriage can persist after the birth of a subsequent child (67). The anxiety and depression found in a subsequent pregnancy has been observed to be higher in the first trimester and decreases during the course of the pregnancy (68). Both these facts suggest the need for follow up and counselling post miscarriage, that it helps reduce grief, self blame and worry (69) plus a reduction in anxiety and improvement of a more positive mood (70) and it has been found that women want to be seen, and are more satisfied if there is follow-up soon after the miscarriage (71).

1.4.4 Anxiety and depression after recurrent miscarriage

It is recognised that a single pregnancy loss impacts on psychological morbidity (as above) and it is suggested that those women who have recurrent miscarriage "the intensity of the grief and association of continued distress becomes more common" and that recurrent miscarriage "leaves a cumulative impact, which can manifest in various aspects of a woman's functioning" (59). Certainly it has long since been recognised that clinicians caring for women who have experienced recurrent miscarriage, either in the acute setting or afterwards for investigation and review in recurrent miscarriage clinic, have observed that women are unhappy, feel depressed, anxious and have low self esteem (39, 59). Male partners do grieve but not as much as the female partner (72) (73), overall a couple's relationship has not previously been found to be negatively affected by recurrent miscarriage (74). Pre pregnancy counselling in women with recurrent miscarriage does not significantly reduce levels of psychological distress (75).

In the past two decades more studies have looked at women's and their partner's psychological state after recurrent miscarriage. In particular the studies have attempted to elicit empirical data to quantify the reactions and psychological consequences of recurrent miscarriage.

Klock et al (38) were one of the first to examine psychological distress in women experiencing recurrent miscarriage. They recruited 57 women from their recurrent miscarriage clinic (2 or more miscarriages, mean 3.3) and used several measures to assess psychological distress, including the Beck Depression Inventory (BDI) and the STAI. They found that 32% of women could be classified as being depressed (based on a score of 14 or more on the BDI). The STAI results showed that the participants had higher levels of both acute (state) and chronic (trait) anxiety. They also observed that having a living child was not a protective against feeling of psychological distress. This study was however restricted by several factors; the response rate was 57%, the final sample size of 57 was small, (40 women with 3 miscarriages and 14 with 2) and there was no correlation with the STAI and BDI results with other possible confounding factors such as time since last miscarriage, all of which could bias results.

In 2002 Craig et al (39) assessed the psychiatric morbidity in 81 women with recurrent miscarriage attending for their first clinic review also using the BDI, STAI, the general health questionnaire (GHG) and their own locally developed miscarriage specific questionnaire. Of the 81 women, 17 had suffered 2 miscarriages and 64 women had experienced 3 losses. They found no significant difference between these 2 groups with regard to their psychological data and amongst those who had living children and those who did not, replicating the findings in Klock et al (38). Similarly to Klock et al, Craig et al found that 33% of participants could be classified as depressed based on scoring 14 or above on the BDI. Additionally Craig and colleagues found that 21% of participants had levels of anxiety that were either the same as or higher than a typical psychiatric outpatient population. Due to the small number of women who were also undergoing or had undergone IVF in the study the impact of this factor could not be assessed, additionally the ethnicity of those attending the clinic were predominantly Caucasian (90%) which is a bias and not reflective of their local population. Neither study made use of a control group for direct comparison with women with no pregnancy loss.

An Israeli study (76) used the STAI to examine anxiety and quality of life in women with recurrent miscarriage (2 or more miscarriages). All of the participants had mild to moderate levels of anxiety. There was no significant difference between anxiety levels in those women with unexplained recurrent miscarriage and those with an identifiable cause. They found age had no affect on psychological morbidity. They calculated the ratio of children to pregnancies for each woman in the study to try to ascertain the relationship between the number of children, pregnancies and the levels of anxiety and quality of life. They found that women with more living children had higher anxiety levels. This study included women with explained and unexplained recurrent miscarriage and although they found no difference in anxiety levels between the two groups the two groups are often treated differently in their management in subsequent pregnancies. Additionally there was a small sample size of initially 41 completing the questionnaires at the beginning of their clinic visit and only 54% completed the same questionnaires after their medical investigations were complete. It is

difficult for them to draw conclusions regarding age and anxiety levels as their participants were all relatively young and so anxiety levels attributed to possible concerns with future subfertility secondary to older age group would not be accounted for.

A Brazilian group (77) looked at quality of life, depression and anxiety amongst women in a subsequent pregnancy with a history of recurrent miscarriage, fetal death, preterm birth or early neonatal death and compared their results with a control group with no such adverse outcomes and matched for number of living children. They used the short from quality of life questionnaire and the Depression and Anxiety Scale at 18 and 24 weeks gestation. They found that women with previous poor outcomes had higher levels of anxiety and poorer quality of life than those in the control group. However there was nothing in the results to distinguish between the anxiety levels in women who had had recurrent miscarriage and those for example who had had a early neonatal death. The questionnaires were given at 18 and 24 weeks therefore beyond the period of early miscarriage when most miscarriages occur and where anxiety levels would probably be higher, and therefore these women may be less anxious at a later gestation. There were also significant differences in the higher risk group and the control group with regards to number of pregnancies, smokers and number of previous deliveries, which can bias results.

None of the afore mentioned studies have discussed the extent to which women's anxiety is linked to the desire to be a mother. Magee et al (78) primarily looked at the investment that women with a history of recurrent miscarriage put into becoming a parent. They hypothesised that in the case of some women experiencing recurrent miscarriage, they are so intent on the goal of being a mother, they invest heavily in this one goal and have little time for any other of life's goals, that they have no co existing protective factors which can lower their vulnerability to distress. Using different measures given to non-pregnant women with recurrent miscarriage who did not have children attending the recurrent miscarriage clinic, they found that 51% of women were within the clinically anxious and 10% depressed. They described a variation in distress in the participants which could not be attributed directly to the number of miscarriages experienced or the time since last

miscarriage. They observed that women who were relatively over-invested in the parent role showed higher levels of distress when compared to women who had recognisable other goals. Additionally women who had negative child related thoughts about the future and no positive thoughts of non-child related matters had the highest levels of distress. The main limitations of this study is that the finding can't be applied to those women who have children and have recurrent miscarriage.

1.5 Ultrasound scanning in pregnancy

The use of transabdominal ultrasound (TA) scanning is well established within pregnancy in the developed world. The 20 week anomaly scan became routine in the early 1990s and although the 12 week nuchal scan was developed in 1985 (79) it did not come into routine use until the late 1990s in the United Kingdom. The introduction of scanning was met with much scepticism as its use was quickly established as routine before it was proved to be a safe procedure and its benefits were confirmed (80). Previously women were only scanned with clinical indications such as raised serum biochemistry, which highlighted them as being 'high risk' for fetal abnormality, these women were counselled regarding the need for scan which may detect a problem with the fetus. Concerns were raised over the safety of scanning when used as routine, its cost implications and whether appropriate counselling for all women was conducted pre scan, taking into account that the majority of routine scans would be performed for 'low risk' women (81). The use of ultrasound scans, when guidelines are adhered to is deemed to be safe, and invaluable for use as a diagnostic tool, and both the anomaly and nuchal scan, the latter as part of combined screening, are recommended to be performed for all women as part of the NICE guidelines for antenatal care (82). Additionally to its use of identifying structural abnormalities and screening for chromosomal problems, ultrasound scanning is used antenatally to identify complications such as placenta praevia, fetal growth including intra uterine fetal growth restriction, and measurement of the Amniotic Fluid Index (AFI).

1.5.1 Safety of Ultrasound in pregnancy

Ultrasound is used for a large number of clinical purposes both within and outside of pregnancy, predominantly as a diagnostic tool. There has been no proven harm to humans (83, 84) and consequently new imaging modes and approaches to scanning have been developed; however to generate the scan image, ultrasound uses energy, which means that both thermal and mechanical effects are produced. Data looking at scan safety in pregnancy has been based on older studies but more recent technological advances mean that now much higher energy ultrasound levels are used. The ALARA (as low as reasonably achievable) principle should be used in the operators approach to ultrasound i.e. to use the lowest power in the shortest amount of time to obtain the scan images required (83). On balance though it is important to be able to complete an ultrasound examination to ensure accurate diagnosis and subsequent management is correct e.g. diagnosis of an ectopic pregnancy or diagnosis of a fetal abnormality.

It is therefore essential that the operator be trained and understands the thermal and mechanical bio-effects of ultrasound including being able to interpret both the Thermal Index (TI) and Mechanical Index (MI) displays on the screen which indicate the potential for tissue temperature rise and non thermal bioeffects respectively (83-85). Additionally the operator should understand the machine settings and the power that use of the settings generates. The operator should also be able to scan to determine an accurate diagnosis as ultrasound is operator dependant and it is based on the operators findings that care and management pathways can be decided.

Within pregnancy real time B-mode scanning is used to generate a moving image there and then, which has a low thermal output and is considered safe to use throughout pregnancy (85). It is within early pregnancy that there is more potential for damage to come to an embryo or fetus as it is so small. Doppler ultrasound with its higher thermal output should be avoided. The transvaginal probe is used in pregnancy up to the gestation of 9 weeks and 6 days pregnant and will generate more heat of which the operator should be aware.

1.5.2 Souvenir Scanning

Based upon safety, professional bodies including The British Medical Ultrasound Society (BMUS) (83), The International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) (84) and the Royal College of Obstetricians and Gynaecologists (RCOG) (86) advise against recreational or souvenir scans i.e. those scans done without clinical reason and more often or not to obtain photos and possible videos of the embryo or fetus. The potential risks of scanning should always be weighed up against the reason for the scan, which should be diagnostic and therefore clinically indicated. To purchase photos of the developing embryo or fetus is not a medical reason for the scan and should not be encouraged. Such images can however be obtained at the end of a clinically indicated scan, as this does not increase any risk significantly. It is very easy to search the internet or see adverts for 3 or 4D scans the latter of which uses huge amounts of energy. Advertising with slogans stating that there is easily accessible scanning and that future parents can bond better if they have seen their baby in 3D or look for family resemblances before its born can entice future parents into having these non clinically indicated scans.

1.5.3 Trans Vaginal Ultrasound scanning

With easier access to the growing number of EPU in the UK, more women present either directly or by referral with early pregnancy problems including pain, bleeding, hyperemesis gravidarum and loss of pregnancy symptoms and expect to be assessed including having an ultrasound scan. The majority of these women are under ten weeks of gestation. To assess the pregnancy accurately a TVS is used rather than the traditional abdominal approach. TVS was developed in the 1980s and is an increasingly used modality. The RCOG guideline on early pregnancy loss (12) advises that all EPUs should have access to TVS. It utilises a higher frequency probe, leading to improved resolution and a much more detailed clearer image. The position of the probe allows the target of the scan to be closer in proximity, enabling better visualisation. It bypasses the problems found with TA including the need for a full bladder (a cause of discomfort) high body mass index (BMI), poorer resolution and image quality. TVS is considered the first line investigation in early pregnancy and is used to determine pregnancy location (intrauterine- IUP versus ectopic pregnancy- EP), viability and detects multiple pregnancy and determines chronicity. Usually a

pregnancy, which is intrauterine and will proceed healthily is first visualised as a small empty gestational sac at 4 weeks and three days gestation, using TVS in a woman with a regular 28 day cycle. The appearance of the yolk sac occurs at 5 weeks, with visualisation of the embryo at 5 weeks and 3 days with or without a heart beat. If detected the heart beat is typically slow which at a later gestation can indicate a failing pregnancy. A rescan is performed a week later to confirm whether or not the heart beat has increased as expected. Confirmation of viability is related to gestational age and therefore the timing of a scan is important. In asymptomatic low risk women waiting until 49 days (post LMP) to scan would reduce the numbers of Pregnancy on Unknown Location (PULs) and unknown viability scans (87). Although as LMPs can be inaccurate, TVS should be available to all symptomatic women presenting in early pregnancy regardless of gestation, to either identify an extra uterine pregnancy or failing pregnancy, either of which may require medical intervention. In 90% of cases of suspected early pregnancy complications, a single TVS scan can provide all the information required for further management (6). Early pregnancy scans are also performed in asymptomatic women who have had previous ectopic pregnancies to ensure correct pregnancy location or recurrent miscarriage for 'reassurance'.

A TVS is by its nature a more 'invasive' procedure, but studies have shown that it is both an acceptable and well tolerated investigative tool (88-90). Acceptance of a TVS varied from 55.2 to 98.2%, however to take into context, it was only within the two studies showing over 98% acceptance that the scan was performed in early pregnancy within an EPU in symptomatic women. Where women were less willing to have a TVS occurred within studies where routine scans were performed at 12-13 weeks (88) for nuchal assessment and at 23 weeks for the anomaly scan (89), where all women were offered a TVS as part of a study for prediction of preterm delivery. In both of these studies women had already had a TAS, so it is of less surprise that less women agreed 88.1% and 54.2% respectively. Although within both the majority of women who agreed to have the TVS found it an acceptable procedure. The main reason for initially declining was perceived fear of miscarriage as a result of the TVS (88). The majority of women do not find the procedure painful (88, 90, 91) and would have a further TVS if required (88-90).

Although there are undoubtedly many benefits to scans there are also drawbacks, which may not be considered by the operator or the woman prior to the scan. Although the real time nature of scanning usually allows an immediate diagnosis and the parents to see their baby for the first time, it is operator dependant, whereby the images are interpreted there and then by the operator, which carries with it responsibility and pressure to make a diagnosis and draw a correct conclusion. A diagnosis cannot in all cases be made on a single scan and the diagnosis can also be dependant on the true gestation. Therefore a final diagnosis may not be made at the first scan or if the operator is unable to interpret what they see.

1.5.4 Psychological factors and ultrasound scans

Ultrasound scanning was introduced as routine within obstetrics before the potential psychological impact was known. Whether a scan has a positive or negative effect on the woman and on her attitudes towards the pregnancy or embryo/fetus can be dependant on the expectations of the woman, the experience of the scan itself, her previous experiences and the final scan diagnosis.

1.5.4.1 Women's expectation of scans

To the clinician the ultrasound scan is a diagnostic or screening investigative tool, performed for medical reasons, the results of which may bring bad news such as miscarriage, ectopic pregnancy or a fetal abnormality. To many women the ultrasound scan is not an investigation or a medical procedure but an opportunity to 'see their baby' thereby confirming the pregnancy and to purchase a photograph (1). Women are often accompanied by partners, family members or friends turning the diagnostic procedure into more of a social event (92) something not usually associated with medical investigations. The very introduction of obstetric scans as routine may imply that the procedure was 'valuable, safe and acceptable' (93), potentially allowing women to undergo a scan without realising the possibility of a problem being discovered (94). In her 2007 paper Nicol (1), discussed the vulnerability of first-time expectant mothers during routine ultrasound scans and noted that this group of women were "not aware of the potential of an early scan to demonstrate these problems" (i.e. miscarriage, structural/functional problems), this was despite the fact they had

been given information to read prior to the scan. Some women commented that they “put it (the information) to the back of their minds’ and their belief that scan were part of the “treatment’ of pregnancy and had no “choice” but to have the scan. It is true that in the United Kingdom the 12 and 22 week scans are recommended within the NICE guidelines (82) as part of routine antenatal care for all women, and that a scan does not require written consent but women should be given an informed choice, just as in any other screening procedure. Nicol argues that the later is impossible “within the obstetric and ultrasound environment due to influences of hospital and social cultures”. The letter for the nuchal scan often arrives before the midwifery booking appointment, and there may not always be a chance to discuss the scan, its risks and benefits and what it may or may not show and any information accompanying it may not be read or interpreted correctly. A date for the scan is sent in the assumption that all women will want the scan and that any information included. When offered a scan very few women will decline (94). In their review of women’s views of pregnancy ultrasound Garcia et al (2), found that ultrasound scans were appealing to women, but that they often lacked information regarding the aim of the scan and the accompanying limitations. They concluded that the very appeal of the scans in the first place might mean women are often unprepared for adverse findings.

Eurenius et al (92) examined parental opinions regarding the aim of a second trimester ultrasound scan. When asked to give yes/no responses to specific questions, they observed that 97% of women believed that the purpose of the scan was to determine multiple gestation, 91% thought it was to estimate the age of the pregnancy whilst 89% agreed it was to see if the baby had any malformations. Only 71% thought it was to see if the baby was alive, the latter perhaps suggesting that the women did not think there was a possibility of a delayed miscarriage. When asked regarding their expectations 99% again said it was to know if there was more than one baby and 87% to know if the baby had a malformation. The higher numbers agreeing with the detection of multiple gestation and dating the pregnancy reflect that they were informed beforehand that this was the purpose of the scan. They were additionally informed that the purpose was not to detect abnormalities but some serious malformations may be observed, despite this a large number of both women and men agreed that this was still the purpose of the scan indicating that they were

aware that this could be a problem or merely the possibility entering their minds when it was mentioned.

All of these studies have been aimed at women attending for the routine antenatal scans and who are asymptomatic. In women who have symptoms of pain or bleeding in early pregnancy or who have had previous pregnancy losses or a bad pregnancy outcome often present expecting or requesting an early scan. The 'normalisation' of scans in pregnancy has led to a need for visual proof of the pregnancy.

1.5.4.2 Women's attitudes to the fetus and pregnancy and ultrasound scan

Asymptomatic women without a past history of miscarriage have been shown to have a short term increase in positive attitudes towards their fetus and pregnancy when scanned late in the first trimester, particularly if visual and vocal reassurance was given (95). Tsoi et al (42) observed a similar level of increased positivity towards the fetus and pregnancy by both women deemed high risk of fetal abnormality and those low risk following a second trimester ultrasound scan. Although it should be said that none of those women deemed high risk were found to have an abnormal fetus. For some couples the sight of their fetus on scan at a routine second trimester scan made them think of it as a baby and them their selves as parents (94). The presence of a heartbeat also increases positivity towards the fetus by women and more so than if a heart beat was not seen (96). This reinforces the point that asymptomatic women should not be scanned before 6 weeks as a heartbeat may not be seen before this gestation in a healthy pregnancy.

Sikorski et al (97), observed that women can have less positive attitudes towards the fetus and were more concerned about fetal wellbeing if they had less scans. However this study was aimed at examining two antenatal visit schedules and so these women also had less antenatal care than their counterparts, which may explain some of the negativity.

1.5.4.3 Anxiety levels and ultrasound scan

Studies looking at the anxiety levels of pregnant women before and after ultrasound examination have been aimed at women undergoing prenatal screening (98) and the comparison between ultrasound prenatal screening in higher versus low risk women (42). Both found that state anxiety was reduced post scan in all women and that there was a greater reduction of state anxiety following scanning in the high-risk group when compared to the low risk group. However in their study examining anxiety levels of pregnant women pre and post routine ultrasound as part of prenatal care Zlotogorski et al (98) only included married subjects, no distinction was made between primiparous women and multiparous, nor those who had had a previous pregnancy loss. Many had already had more than one ultrasound scan (mean=2.37 scans) and the gestations of participants varied from 4 to 41 weeks all of which could influence women's anxiety levels.

Following on from their study examining the short term psychological effects of scanning in women with a raised serum alpha fetoprotein (42), Hunter et al (43) found that anxiety levels and attitude towards the fetus and pregnancy 4 to 5 weeks post scan were maintained, although there was some return of the initial anxiety about the pregnancy and fetus on follow up. The response rate of the questionnaire sent to all participants was approximately 60% so it is not clear whether the 40% who did not respond did indeed have higher anxiety levels, which may even have prevented them from replying. Gestational ages were also different between the groups and the women with high levels of AFP had had significantly more scans in the pregnancy already. However this high risk group of women still had higher anxiety levels despite having previous scans (42).

Eurenius et al (92) used questionnaires to ascertain that women experiencing routine second trimester scans showed low levels of anxiety before the scans except from those who had had 'problems' at earlier scans. The anxiety scale used was not discussed or indication given that it was validated in pregnancy. Additionally the previous 'problems' were not elaborated on and it was not clear whether the participants had had previously pregnancy loss, which could effect their anxiety levels pre scan.

Elekin et al (94) performed qualitative interviews for couples examining mother's and father's experiences of routine scan and found that they explained a feeling of 'reassurance' at the moment that they were informed by the scan operator during the scan that the scan results were normal. Only women with a partner were included in the study and no distinction was made between primiparous and multiparous women or if any couples had had previous pregnancy loss or complications which could influence their experience of the scan. It is not clear if the level of feedback at each scan differed between participants which could affect the participants understanding of the scan and the interviewer had not worked with ultrasound before which may reduce their pre understanding of the subject. It is not clear if the questions were open ended or directed, some answers to questions given from each interview influenced the next participants interview, generating new questions, which could generate some bias.

Previous concerns have been raised that the ultrasound scan itself may increase anxiety levels. Those studies observing a reduction in anxiety levels can suggest that the thought of the scan itself is responsible for increasing anxiety levels before and that the decrease post scan is merely a return to normal baseline levels (99). In these women a transient rise in anxiety may occur settling post scan.

In their study assessing the short term psychological effects of early scans, Campbell et al (95), observed that there was no support for the view that scanning causes distress regardless of level of feedback during the scan in a group of low risk women. The emotional impact measured by the subjective stress scale given to all of the participants post scan showed that neither group said they felt worried, nervous unsafe, frightened, panicky or scared stiff. However the emotional state at the time of the scan could have been influenced by the level of feedback that participants were given during their scan; 50/67 in the high feed back felt wonderful versus 7 of the low feedback group who mainly felt comfortable (14/64) or fine (15/64). Their study was conducted using only women who were either married or in a stable relationship which is not a reflection of the population of women assessing pregnancy scans.

1.5.5 Scanning in recurrent miscarriage

Ultrasound scans in subsequent pregnancies of those women with recurrent miscarriage are performed without a clinical indication i.e. asymptomatic of early pregnancy problems such as pain or bleeding. We assume that the justification for performing such scans is providing reassurance of an on-going viable pregnancy (100) (101). Detection of fetal cardiac activity on ultrasound scan is usually associated with a low rate of miscarriage and in a selected population of 222 women with a history of recurrent miscarriage Brigham et al (28) showed a 3% (6/222) miscarriage rate after cardiac activity was previously detected on scan. The number of scans provided in a subsequent pregnancy and the gestation at which they commence varies from hospital to hospital. In some of the studies looking at supportive care scans have been performed on a weekly basis (33) (22). This in everyday practise is probably unrealistic and difficult to achieve due to cost and staffing issues.

We know that women who have had a previous miscarriage (102) are more anxious in a subsequent pregnancy. Although we may expect that these women will be 'reassured' following a positive scan result, from clinical observation this is not always the case. These women have been scanned many times and the outcome of these scans has usually been to relay bad news. Can an intervention that women, associate with previous negative outcomes, serve to reduce anxiety, be supportive and improve the likelihood of an ongoing pregnancy?

1.6 Hypothesis

Women with recurrent miscarriage (two or more consecutive miscarriages) will have higher levels of background anxiety in a subsequent early pregnancy period than standard risk women (women who have never had a previous adverse pregnancy outcome). This will be reflected by higher anxiety scores measured by the State- Trait Anxiety Inventory (STAI).

Women with recurrent miscarriage are offered serial ultrasound scanning in early pregnancy. These scans are not usually available to standard risk women. Women with recurrent miscarriage will have higher anxiety scores (based on the STAI) before the scans and are expected to have a more significant decrease in anxiety levels when measured post scan than standard risk women

1.7 Aims

- To assess the effects of serial scanning in the first ten weeks of pregnancy on the anxiety levels of women with a history of recurrent miscarriage and standard risk women
- To examine anxiety levels at the mid point between serial scans to assess how long any change in anxiety levels persists
- To explore the attitude to serial scanning in the first 10 weeks of gestation
- To explore the attitude to pregnancy in the first 10 weeks of gestation

Chapter 2 Materials and Methods

2.1 Study design

Participants were prospectively recruited from July 2011 until December 2012. This was a longitudinal observational, case controlled study, using quantitative methodology. Ethical approval for this study was obtained from the central REC and R&D approval obtained from Guys and St Thomas' NHS Foundation Trust. Four patients of the EPAGU and an EPAGU senior staff nurse were asked to review the length of the questionnaire sets and time taken to complete to confirm acceptability, prior to the study commencing. Each participant was allocated a study number at the time of consent, which served to anonymise the data throughout.

2.1.1 Powering the Study

Full data was required on 96 subjects (48 per group) in order to estimate a mean difference of 8 points (12 versus 4) in the State-Trait scale, (Standard Deviation 10) (42). Using the instrument manual of Spielberger et al (103), a correlation between repeated measures of 0.27 was anticipated. Using standard formulae, the Standard deviation of the difference would be 12.88 and 48 subjects would be needed to detect a difference of 8 points with 90% power at 5% significance level. To achieve this, we aimed to recruit 120 women, allowing for 12 dropouts per group.

2.2 Participant Recruitment

2.2.1 Recurrent Miscarriage Group

Women with a history of proven unexplained recurrent miscarriage were recruited from the recurrent miscarriage clinic prior to a subsequent pregnancy or when she contacted the EPAGU to arrange her first scan. Those recruited from clinic were not pregnant at that stage and were given both verbal and written information by one of the investigators and written consent obtained for women who agreed to participate. For those who conceived the participant rang the EPAGU at four to five weeks of pregnancy by her LMP. The first scan was arranged when she was estimated to be in her sixth week of gestation. Those women recruited when they rang to book a scan were four to

five weeks pregnant by their LMP and were called back by one of the investigating team to discuss the study and sent an information leaflet via email or post. If the woman agreed to take part in the study written consent was taken on the day she attended for the first scan in her sixth week of gestation.

2.2.2 Standard Risk Group

This group consisted of women who had never experienced a previous pregnancy loss (ectopic pregnancy, miscarriage, stillbirth or neonatal death). They were recruited by from advertising posters, website adverts and information leaflets via three means: advert of nappy valley.com, local GP practices and advert on Tommies website. A phone number and secure email address were provided and potential participants communicated the study contact numbers as soon as possible after missing a period and with a positive pregnancy test. They were asked to provide their LMP and their gestation calculated from this. They all received a phone call or email by one of the investigating team in reply to confirm eligibility and involvement in the study. Information leaflets were emailed or posted to potential participants and each were asked to attend one hour before their first scan to meet with one of the study team where written consent was taken.

2.2.3 Inclusion criteria

2.2.3.1 Recurrent Miscarriage Group

Women who

- have had two or more consecutive unexplained miscarriages.
- Are aged between 18-45 years at recruitment
- Are up to six completed weeks' gestation (6 weeks and six days) at recruitment
- are willing and able to give informed consent
- are willing and able to comply with follow up

2.2.3.2 Standard Risk Group

Women

- with no previous pregnancy loss, or adverse obstetric outcome including miscarriage, ectopic pregnancy, intrauterine or neonatal death
- have either one child or no children
- between 18-45 years at recruitment
- up to six completed weeks of gestation at recruitment
- who are willing and able to give informed consent
- who are willing and able to comply with follow up

2.2.4 Exclusion criteria

2.2.4.1 Recurrent miscarriage Group

Women with

- less than two consecutive miscarriages
- previous miscarriages with a proven association:

    I. Antiphospholipid syndrome (lupus anticoagulant and/or anticardiolipin antibody positive [IgG or IgM]

    II. Intrauterine abnormalities (as assessed by ultrasound, hysterosonography, hysterosalpingogram, or hysteroscopy

    III. Fibroids distorting uterine cavity

    IV. Abnormal parental karyotype

    V. Other identifiable causes of recurrent miscarriages (tests performed only if clinically indicated) e.g., diabetes, thyroid disease and systemic lupus erythematosus (SLE)

- less than 18 years of age or aged 46 or above at recruitment
- more than seven weeks gestation at recruitment.
- Non English speaking participants (it is not possible to translate the questionnaires into multiple languages and they have not been validated for such use)

2.2.4.2 Standard Risk Group

Women

- with one or more previous pregnancy losses, or adverse obstetric outcome including miscarriage, ectopic pregnancy, intrauterine or neonatal death
- Have had more than one previous successful pregnancy
- less than 18 years of age or aged 46 or above at recruitment
- more than seven weeks gestation at recruitment
- Non English speaking participants (it is not possible to translate the questionnaires into multiple languages and they have not been validated for such use)

2.3 Location of study

All of the interviews and pre and post scan questionnaires were conducted within the EPAGU based within the department of women's health at St Thomas' Hospital part of Guy's and St Thomas' NHS Foundation Trust. The EPAGU provides early pregnancy care to women with women with symptoms of pain and or bleeding with a positive pregnancy test up until 17+6 weeks of gestation. It is a nurse led unit with a consultant lead and clinical fellow. There are two dedicated scan rooms, a three bedded trolley area and four consultation rooms, including a procedure room. There is a dedicated 'quiet' room which is used to counsel women after or during early pregnancy loss and an outpatient hyperemesis room. Referral sources include self-referral, GP, A&E, private

scan clinics and sexual health clinics. Women can also be seen if they have an acute gynaecological problem or symptoms suggestive of such. It also provides outpatient medical and expectant management of miscarriage and ectopic pregnancy, follow up scans for pregnancy viability and scans for women with a previous history of ectopic pregnancy to confirm pregnancy location. The specialist dedicated scan clinic for women with a history of recurrent miscarriage is led by a nurse specialist and clinical fellow, where women are scanned at 6,8 and 10 weeks of pregnancy as per hospital policy. The interview or completion of questionnaires took place within one of the consultation rooms or scan rooms conducted by one of the investigating team.

Participants in the recurrent miscarriage or standard risk group who had either a scan which was inconclusive regarding viability or location of the pregnancy or had symptoms of pain or bleeding, all of which could increase the number of scans performed outside the study number, were scanned where possible (other than in an emergency situation or if attending another hospital) by a member of the investigating team. If any participants in the study were found to have a miscarriage or ectopic pregnancy during the course of the study, they were withdrawn from further participation within the study. All were appropriately counselled as to management options by a trained member of staff following the departmental guidelines. The gestation at which she miscarried was recorded on the study database.

All contact details and names were entered onto one database with a unique participant number. This database was held solely on a password secure GSTT computer. A separate excel database with participant number only was created (Microsoft office) onto which scan and questionnaire data was entered. Patient data was managed according to the data protection policy of GSTT and King's College London. All original completed questionnaires and hard printed scan reports were kept securely in a locked filing cabinet in a locked office within EPAGU.

2.4 Measures

2.4.1 Ultrasound Scans

All scans were performed at the EPAGU at St Thomas' Hospital in the department of women's health. The machines used were: Voluson E8, TV probe 3D RIC5-9-D, TA probe C4-8-D. The machines were calibrated to operating specifications. Scans were carried out in B-mode 2d. Where a heart beat was present, this was assessed using M-mode and not colour or pulsed wave Doppler as per safety guidelines (83). Members of the investigating team performed the scans. Each operator had at least one year's experience of early pregnancy scanning, a postgraduate certification in early pregnancy scanning or MRCOG and specialised in early pregnancy care. Explanation of each scan occurred prior to each scan and feedback in the form of verbal and written report were provided at and during each scan. All participants were offered the opportunity to see their pregnancy on the scan screen and explanation given for what was seen on the screen and what was considered normal for the gestation. If the participant's menstrual cycle was either longer or shorter than expected, gestational dates were recalculated based on the measurement of the crown rump length (CRL) in mm. The scans occurring prior to 10 weeks of gestation were transvaginal scans, the scan occurring after 10 weeks of gestation was a trans abdominal scan. Each scan was performed at approximately 2-week intervals as per existing unit protocol for women with a history of recurrent miscarriage. The ultrasound probes were cleaned in between use following departmental guidelines. Latex or latex free disposable probe sheaths were used during trans vaginal ultrasound dependent on the participants response to the latex allergy question prior to scanning. All scan findings were entered onto the Astraia (MS SQL Server JTDS) database used by GSTT. The ultrasound reports were generated from this as standard. All participants were given a copy of the scan report for their own record.

2.4.2 Questionnaires

Questionnaire bundles were provided before and after each scan (6,8,10 weeks gestation) and in between at 7 and 9 weeks.

Before each of the immediate pre and post scan hospital questionnaires were completed, the investigator reiterated the written instructions on the front of the questionnaire pack verbally. During the longer pre 6-week questionnaire, the investigator left the room to allow the participant to complete it with no feeling of pressure. There were no time constraints during the completion of any of the questionnaires. The STAI S-anxiety questionnaire was given to participants to complete at home one week after the 6 and 8 week scans i.e. at 7 and 9 weeks gestation. Each participant brought this back with her at her next pre arranged scan appointment and handed it to the investigator.

2.4.2.1 Demographics

All participants were required at the pre 6 week scan questionnaire bundle to initially provide information including age, ethnicity, postcode, marital status, highest qualification, occupation, nicotine/alcohol use, medical and psychiatric history. Additionally obstetric history including; number of live children, number of miscarriages (where applicable), time since last miscarriage, time taken to conceive and infertility treatment prior to conception. Demographic questions were asked after the MBSS.

2.4.2.2 Spielberger State- Trait Anxiety Inventory (STAI)

The State-Trait Anxiety Inventory is a self-evaluation questionnaire consisting of 40 items or statements that measure anxiety levels. The first 20 items require the participant to describe their emotional state at a particular moment in time, participants are asked “how do you feel right here and now”, this is a measure of state anxiety (S-anxiety). The second 20 items require the participants to describe their usual emotional state; participants are asked “how do you generally feel”, a measure of trait anxiety (T-anxiety). Both scales contain anxiety present and anxiety absent items represented by directly worded and reversed worded statements respectively.

Figure 9: State anxiety Statements

State Anxiety	
Anxiety present items (directly worded)	Anxiety Absent Items (indirectly worded)
I am tense	I am calm
I feel strained	I feel secure
I feel upset	I am at ease

Figure 10: Trait anxiety Statements

Trait Anxiety	
Anxiety present items (directly worded)	Anxiety Absent Items (indirectly worded)
I feel nervous and restless	I feel pleasant
I wish I could be as happy as others seem to be	I feel satisfied with myself
I feel like a failure	I feel rested

Whilst completing the S- anxiety scale participants tick the response that describes the intensity of their feelings for each item:

1. not at all
2. somewhat
3. moderately so
4. very much so

Whilst completing the T- anxiety scale the participants tick the response that indicates the frequency of their feelings for each item

1. almost never
2. sometimes
3. often
4. almost always

Scores for both S and T anxiety can range from 20-80 based on a four point Likert scale for each item, 80 indicating maximum high anxiety levels and 20 minimum low anxiety levels. The scoring weight for the anxiety present/directly worded statements are the same as the number ticked by the participant on the test form, i.e.

	Not at all	Somewhat	Moderately	Very much
I am tense	□1	□2	□3	☑4

The above answer would score 4 and represent high anxiety.

The scoring weight for the anxiety absent/indirect worded statements are reversed i.e. any responses marked 1,2,3, 4 are scored 4,3,2,1 respectively e.g.

	Not at all	Somewhat	Moderately	Very much
I am calm	□1	□2	□3	☑4

The above answer would score 1 and represent low anxiety.

The Scoring key supplied with the State-Trait Anxiety Inventory for Adults manual (103) was used for scoring by hand. The weighted scores for each participant questionnaire were added up to give a total and overall score between 20-80. This figure was entered onto the database. The individual weighted scores and total scores were checked three times to ensure that the correct score was recorded.

Participants were asked to complete the STAI S and T scales prior to their 6-week USS scan and after their 10-week ultrasound scan. Additionally participants were required to complete the S anxiety scale before and after each scan and again at 7 and 9 weeks gestation at home.

The S-anxiety scale is administered first as it is sensitive and the participants' answers could be influenced by the emotions caused by the T- anxiety scale. The STAI has been validated for use in pregnancy and has previously been used within the miscarriage and scanning setting. The mean state anxiety scores for healthy working adults is 35.72 for men and 35.20 for women and for male neuropsychiatric patients the mean is 47.74 (103).

Permission to use the STAI was granted on purchasing the manual and questionnaires from the Mind Garden Inc.

2.4.2.3 The Cambridge Worry Scale

The CWS was developed to examine women's concerns regarding the health of their baby within the context of other worries both within and outside of pregnancy. It was devised initially for use in early pregnancy. It consists of 16 statements regarding common pregnancy and everyday worries. Participants are asked to respond using the six point Likert-type scale ranging from 0 "not a worry" to 5 "extremely worried". Participants are asked to tick one box next to the number, which best describes to how much extent the statement is a worry to them at that moment in time.

Examples of everyday worries:

	Not a worry					Major worry
Your Housing	☐0	☐1	☑2	☐3	☐4	☐5
Money Problems	☑0	☐1	☐2	☐3	☐4	☐5

Examples of pregnancy related worries:

	Not a worry					Major worry
Giving birth	☐0	☑1	☐2	☐3	☐4	☐5
The possibility of miscarriage	☐0	☐1	☐2	☐3	☑4	☐5

The scoring was dependent on the numerical value of the box ticked i.e. if the box with 2 next to it is ticked the score for this item will be 2. The mean scores for each item in both groups of participants was calculated and ranking of worry items determined.

Participants were asked to complete the CWS before the six week scan immediately after completing the STAI and again after the 10 week scan immediately after completing the STAI.

Permission was granted directly from Professor Jo Green to use the scale for the purpose of this research study.

2.4.2.4 The Miller Behavioural Style Scale

The MBSS is a self-report written questionnaire designed to identify whether participants would actively seek out information about an uncontrollable stressful situation (Monitor) or avoid and distract from any information gathering (Blunter). The scale consists of four hypothetical stress-evoking scenes (dental visit, taken hostage, potential dismissal from job and aeroplane malfunction during a flight) each with 8 statements describing responses to the stressful scenario. Participants are asked to tick which response or responses they might take in each scenario as to their preferred information coping style. Participants can choose to tick as many statements as they wish from each scenario. Of each 8 statements per scenario, four represent monitoring and four represent blunting responses i.e. is the participant an information seeker wanting to maximise their knowledge or would rather avoid knowing the extent of the situation or problem? The participants are blinded as to which statements represent either monitoring or blunting strategies. The Monitoring and Blunting response statements are intermingled with each other with no pattern within each scenario.

For example in response to being asked regarding having a fear of the dentist and having dental work carried out, one response option is:

> I would ask the dentist exactly what work was going to be done.

This is categorised as a Monitoring response.

Another response to the same scenario is:

> I would take a tranquilizer or have a drink before going.

This is categorised as a Blunting response.

It is possible that the participant can tick a mixture of both monitoring and blunting options.

The scoring key indicates which statements are Monitoring (M) and which are Blunting (B). The MBSS can be scored in three different ways following the scoring key: the total monitoring score which can range from 0-16, the total blunting score which can also range from 0-16 or a total difference score which is calculated from subtracting the sum of the blunting score from the sum of the monitoring score (M-B, which can range from -16 to 16). To calculate the total monitoring score, the researcher simply adds the number of statements marked M together and to calculate the total blunting score the researcher simply adds the number of statements marked B together. These scores are used to calculate the total difference score if required.

For the purposes of this project the monitoring score was used based on its utility with regard to predictive value (104).

Participants were asked to complete the MBSS before the 6 week scan immediately after completing the CWS.

The MBSS is validated for use in pregnancy and has previously been used in non-medical and medical settings including ultrasound scan in pregnancy.

Permission was granted to use the MBSS from Dr Miller and her associates for the sole purpose of this research project.

2.4.2.5 Semantic Differentiation Scale

Participants were asked to complete seven-point differentiation scales designed to measure their attitude towards the ultrasound scan and to their pregnancy. Each question consisted of three pairs of words with the opposite meaning separated by the scale. Participants were asked to circle the number, which they thought indicated how they were feeling regarding the scan and the pregnancy.

For example with regard to the participants feelings towards the scan:

Reassuring 1 2 3 4 5 6 7 Worrying

For example with regard to the participant's feelings towards their pregnancy:

Calm 1 2 3 4 5 6 7 Nervous

The same questions were asked within the pre six week scan questionnaire bundle after the MBSS and then again at the post ten week scan questionnaire bundle after the CWS. The questions were scored according to the number circled.

2.4.2.6 Additional questions

Prior to the semantic differentiation scale at the pre 6 week scan questionnaire bundle participants were asked what the scans are going to give you and asked to circle the answer that they felt they most agreed with:

Good news Bad news Not sure

In order to gain additional information participants were directly asked after their ten week scan as to how many scans they would have ideally liked and given a choice of:

Daily, weekly, every two weeks, monthly, any time I was worried, none or other.

They were also asked two 5-point Likert scale questions: had the participant found the scans reassuring and if the participant thinks she benefitted from seeing a dedicated team throughout her early pregnancy. For each question the participants were requested to circle the most appropriate answer which best describes how they feel either:

Strongly agree, agree, neither, disagree or strongly disagree.

Table 7: showing the timing of questionnaires given to participants throughout the study

	Demographics	**State-Trait S-anxiety and T-anxiety**	S-anxiety	**The Cambridge Worry Scale**	The Miller Behavioural Style Scale	**Pre scan attitude to scan questions**	**Post scan attitude to scan questionnaire**
Pre 6 week scan EPAGU	X	X		X	X	X	
Post 6 week scan EPAGU			X				
7 weeks gestation Home			X				
Pre 8 week scan EPAGU			X				
Post 8 week scan EPAGU			X				
9 weeks gestation Home			X				
Pre 10 weeks scan EPAGU			X				
Post 10 week scan EPAGU		X		X			X

2.5 Statistical Analysis

Descriptive data are given in numbers and percentages.

For the STAI results, to ensure that parametric tests can be used to analyse the results, q-q plots of each S-anxiety and T-anxiety score and the mean change of scores within both participant groups were performed that showed a normal distribution see appendix 4.

IBM SPSS (statistical package for the social sciences) versions 22 and 24 were used in all statistical analysis, licensed through King's College London.

Paired t- tests were used to compare mean S and T anxiety scores and change scores within each group. Unpaired t-tests were used to compare mean S and T- anxiety scores and change scores between each group using unequal variance.

Simple and multiple linear regression analysis was used for prediction of each scan change score. To increase the power, mixed models was used to assess the prediction of variables on the combined pre scan S- anxiety, the post scan S- anxiety and the change scores.

For the CWS paired t- tests were used to compare the mean item scores at 6 weeks and 10 weeks within the same group. Unpaired t-tests were used to compare the mean CWS scores between each group.

The mean and median scores for monitoring were calculated and the mean compared using unpaired t test between the groups.

The wilcoxan- signed test was used to assess whether there was a median difference between the semantic scale scores within each group.

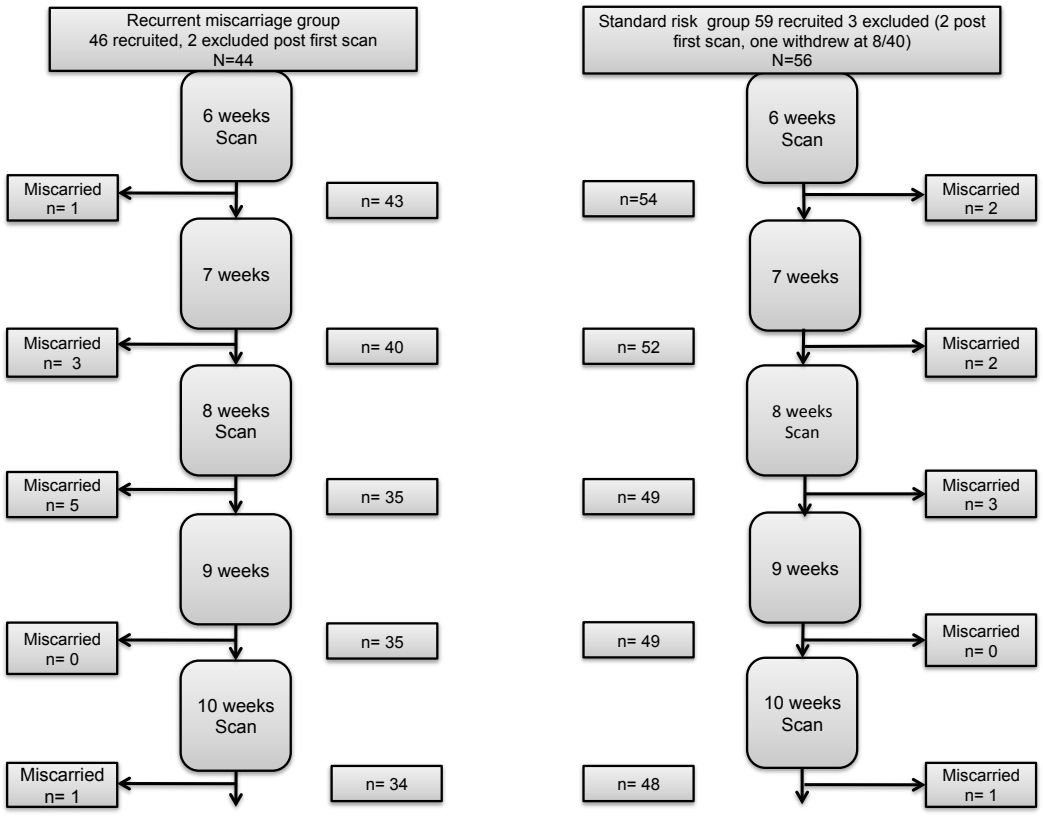
Chapter 3 Results

3.1 Recruitment

3.1.1 Participants

During this longitudinal observational study participants were recruited in the methods described previously from July 2011 until December 2012. A target of 48 participants per group was set over this time period.

Figure 11: Flowchart showing participants recruited to both miscarriage and standard risk groups



A total of 47 women were approached to take part in the study, one declined to participate. A total of 46 participants were recruited to the recurrent miscarriage group, 2 were excluded following the 6 weeks scan as one had a delayed positive lupus anticoagulant result which showed a possible cause of her miscarriages and she did not therefore fulfil the criteria of having unexplained recurrent

miscarriage. The other believed that she was 6 weeks pregnant by dates, but was found to be 10 weeks gestation on her initial scan. Forty-four participants entered the recurrent miscarriage arm of the study, 1 participant miscarried after her 6 week scan, 3 before their 8 weeks scan, 5 were found to have miscarried at their 8 week scan and 1 at her 10 week scan. This is a 22.7% miscarriage rate. A total of 34 participants in the recurrent miscarriage group completed the study.

Of the 59 participants recruited into the standard risk arm of the study, 2 were excluded after the first scan, 1 as she failed to declare a previous miscarriage until after completing the first questionnaire and having the first scan, and the other as she was found to have a large asymptomatic ectopic pregnancy for which she underwent surgery. A further participant failed to attend for her 8-week scan and did not respond to attempts to contact her. There were 56 women who entered the standard risk arm of the study, 2 were found to have miscarried at the 6 week scan, 2 miscarried before their 8 week scan, 3 were found to have miscarried at their 8 week scan and 1 women was diagnosed with miscarriage at her 10 week scan. This equates to a 14.3% miscarriage rate, their data was excluded from analysis and no further questionnaires were undertaken. Forty-eight participants completed the study. All standard risk participants were volunteers; therefore nobody declined to take part.

3.2 Demographics

3.2.1 General Demographics

The general demographics for both study groups is shown in the table below.

Table 8: General demographics of participants in the recurrent miscarriage and standard risk groups

	Recurrent Miscarriage n=34 Mean (SD) or n (%)	Standard Risk n=48 Mean (SD) or n (%)	P values
Age	34 (4.3)	31.1 (4.6)	0.51 (T-test)
Ethnicity			0.536 (Chi)
White	30 (88%)	40 (83%)	
Asian	1 (3%)	2 (4%)	
Black	1 (3%)	1 (2%)	
Other	2 (6%)	5 (10%)	
Marital status			
Single	0 (0%)	2 (4%)	0.434 (Chi)
Married	27 (79%)	31 (65%)	
Civil partnership	0 (0%)	1 (2%)	
Partner	7 (21%)	13 (27%)	
Other	0 (0%)	1 (2%)	
Qualifications			0.224 (Chi)
GCSE	1 (2.9%)	3 (6%)	
A Level	3 (8.8%)	10 (21%)	
Degree	29 (85%)	31 (65%)	
None of these	1 (2.9%)	4 (8.3%)	
Smoker			0.660 (Fishers)
Yes	1 (3%)	1 (2%)	
No	33 (97%)	47(98%)	
Hx of Depression			0.433 (Fishers)
Yes	5 (15%)	9 (19%)	
No	29 (85%)	39 (81%)	
Hx of fertility Treatment			0.593 (Fishers)
Yes	0 (0%)	1 (2%)	
No	34 (100)	47 (98%)	
Primiparous	17 (50%)	24 (50%)	

.

There were no significant differences in the demographics between the two groups. Participants in the recurrent miscarriage group were marginally older and more had a degree as their highest qualification than those on the low risk group. The majority of participants in both groups were

married, caucasian and there were similar numbers of participants in both groups with a history of depression.

3.2.2 Deprivation score

The deprivation scores were calculated using participant postcodes entered onto the Department for Communities and Local Government English indices of deprivation 2010 postcode lookup tool (105). Two recurrent miscarriage participants failed to fill in their postcodes in full, n=32. The IMD quintiles and ranks are shown in table 8 below.

Table 9: Indices of multiple deprivation ranks in each group

Quintile	Quintile description	Ranks	Recurrent Miscarriage	Standard Risk Group
1	10 to 20% most deprived	1 to 6568	8	5
2	20 to 40%	6569 to 13137	16	10
3	40 to 60%	13138 to 19706	5	13
4	60 to 80%	19707 to 26275	1	11
5	10 to 20% least deprived	26276 to 32844	2	7

Rank 1= most deprived

Rank 5= least deprived

Twenty-seven (84.4%) of the recurrent miscarriage participants live in the top 50% of deprived areas. All but two of these participants lived in the immediate area served by GSTT.

Two of the standard risk group did not complete their postcode in full, n=46.

Twenty (43%) of standard risk participants live in the top 50% of deprived areas

More women from the standard risk group lived in areas least deprived. Participants from this group lived in the immediate area and further afield into East of England including Cambridge (Rank of 5) and Essex, one participant travelled from mid Devon.

3.3 Analysis of anxiety scores over time

3.3.1 Distribution of results

The main tool for the quantitative analysis is the STAI recorded pre and post 6,8 and 10 week scans and at 7 and 9 weeks. To ensure that parametric tests can be used to analyse these results, q-q plots were performed to show the distribution of results of each STAI score and the mean change of scores within the recurrent miscarriage groups and standard risk groups combined, see appendix 4.

3.3.2 Stait Trait Inventory

3.3.2.1 T anxiety

The trait anxiety (T anxiety) was assessed before the 6 week scan and after the 10 week scan. Paired T test was used to compare the T-anxiety scores within each of the study groups.

Table 10: Comparison of the Trait anxiety scores within each group using paired T test

Group	Pre 6 week Scan T-anxiety Mean (SD)	Post 10 week scan T-anxiety Mean (SD)	T-anxiety Change (SD) (CI)	P value
Recurrent Miscarriage n=34	40.5 (8.4)	34.4 (8.8)	3.5 (5.0) 1.7-5.2	**<0.001**
Standard Risk n=48	37.0 (8.2)	32.9 (8.6)	1.5 (5.1) -0.18-2.99	**0.047**

The T- anxiety score within both groups was significantly lower post 10 week scan than pre 6 week.

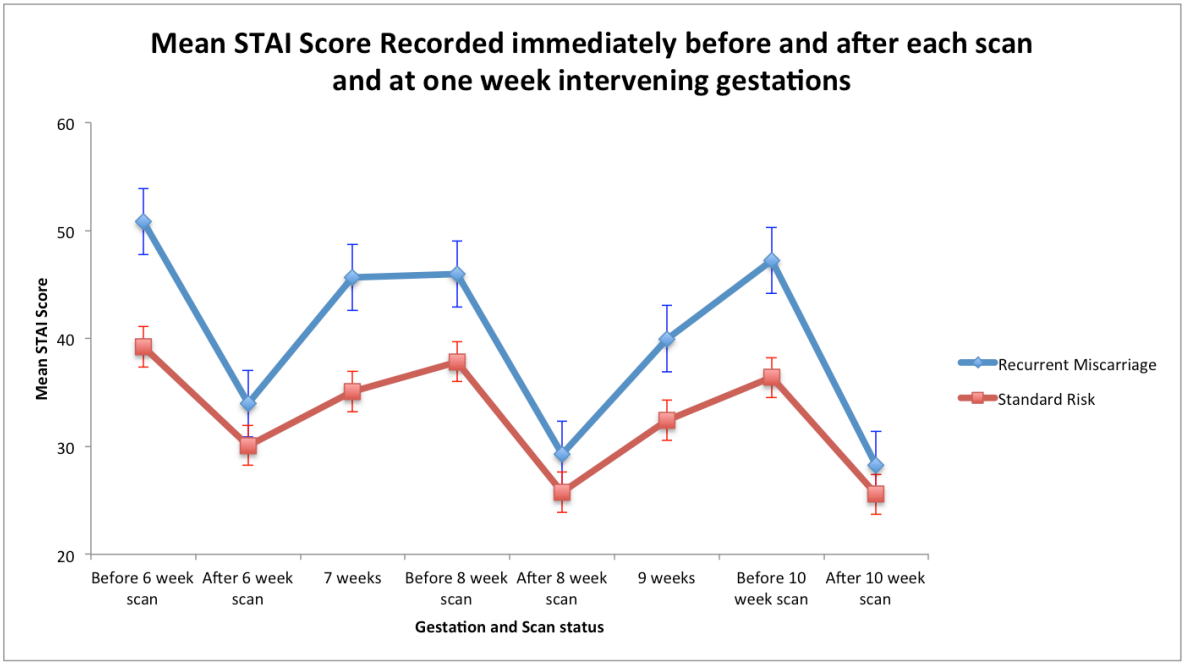
Table 11: Comparison of the Trait anxiety scores between the recurrent miscarriage and standard risk groups using unpaired T tests

T- anxiety score	Recurrent miscarriage Mean (SD)	Standard risk Mean (SD)	Mean difference & 95% CI	P value
Pre 6 week scan	40.5 (8.4)	34.4 (8.8)	6.2 (2.3-10.0)	**0.002**
Post 10 week scan	37.0 (8.2)	32.9 (8.6)	4.2 (0.417-7.9)	**0.03**

The T-anxiety scores were significantly lower in the standard risk group than the recurrent miscarriage group on both occasions.

3.3.2.2 S anxiety

Figure 12: Graph showing the trend of mean S-anxiety scores at each pre and post scan and the intervening 7 and 9 weeks gestation. Error bars represent standard errors.



Before each scan the recurrent miscarriage group had higher mean S-anxiety scores than the standard risk group. Immediately after the scans S-anxiety levels were reduced in all participants but in particular within the recurrent miscarriage group by 16.6 points as opposed to 9.1 points in the standard risk group. Post scan levels of S-anxiety were similar in each group. S-anxiety levels increased at 7 and 9 weeks in both sets of participants, marking the half way points between each scan, this can be seen with divergence on the graph. The S-anxiety levels further increased immediately prior to the scans within each group. Those participants in the recurrent miscarriage group had S-anxiety levels which increased again more quickly.

Within the recurrent miscarriage groups the pre 6 week S-anxiety result was significanty higher than all of the questionnaire interventions other than that at pre 10 weeks (p= 0.116) indicating that anxiety levels pre 10 weeks were almost similar to those seen before the first scan at 6 weeks. There was no significant difference between the S-anxiety results at 7 weeks and pre 8 week scan, 7 week and pre 10 week scan and pre 8 and pre 10 week scan. There were significant differences in the mean S-anxiety scores pre and post each scan i.e each time a scan occured the S-anxiety was significantly lower than it was pre scan.

Within the standard risk group the pre 6 week S-anxiety score was significantly higher than all of the other intervention scores except the pre 8 week S-anxiety score where it was similar. The S-anxiety scores pre 8 and 10 weeks were not significantly different and the post 8 and 10 week scores were also similar.

There were four participants in the standard risk groups whose S-anxiey score increased post 6 weeks scan. With all of these women although they believed that their LMP estimated them to be 6+0 to 6+6 weeks gestation, their cycles were longer meaning that their gestations varied from 4+5 to 5+5. Although an intrauterine pregnancy was confirmed in each case, the pregnancy was either too early for an embryo to be seen or the heart beat was not evident. These women were reassured that this was a normal finding of earlier pregnancies at this gestation. All of these pregnancies developed normaly thoughout the period of their involvement in the study. A further five participants in the standard risk group had similar S-anxiety scores pre and post 10 week scan. With each of these participants their scores were very close to 20 which marks the lowest level a score could be.

One participant in the recurrent miscarriage group had a higher S-anxiety score post 6 week scan, her actual cyle was also longer making her 5+4 weeks gestation and no heart beat was evident. Her subsequent scans showed a normally developing pregnancy.

Unpaired T-test was used to compare the mean S-anxiety scores between the recurrent miscarriage group and the standard risk group.

(Equal variances are assumed as the significance for Levene's test for equality of variances is >0.05.)

Table 12: Comparison of mean S-anxiety scores between women with a history of recurrent miscarriage and women with no previous pregnancy loss at each assessment

S-anxiety Score	Recurrent miscarriage Mean (SD)	Standard risk Mean (SD)	Mean difference & 95% CI	P value
Pre 6 week scan	50.8 (13.3)	39.2 (10.5)	11.6 (6.4-16.9)	**<0.001**
Post 6 week scan	33.9 (10.9)	30.1 (11.6)	3.9 (-1.2-8.9)	0.128
7 week	45.6 (11.3)	35.1 (9.1)	10.6 (6.0-15.1)	**<0.001**
Pre 8 week scan	46.0 (10.1)	37.9 (11.4)	8.1 (3.3-13.0)	**0.001**
Post 8 week scan	29.3 (7.4)	25.8 (6.2)	3.5 (0.5-6.6)	**0.026**
9 week	40.0 (11.9)	32.4 (8.6)	7.6 (2.9-12.2)	**0.003**
Pre 10 week scan	47.2 (12.3)	36.4 (12.5)	10.9 (5.3-16.4)	**<0.001**
Post 10 week scan	28.3 (7.5)	25.6 (5.8)	2.7 (-0.19-5.7)	0.08

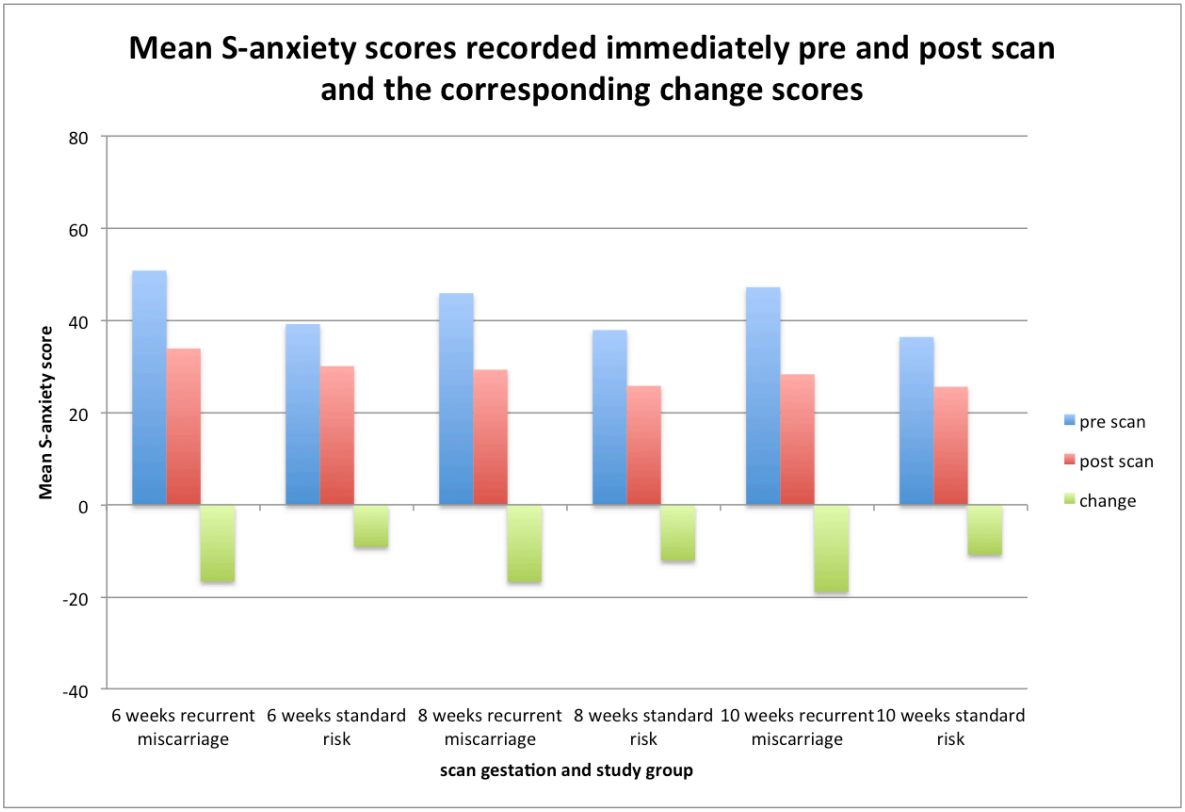
No significant difference in S-anxiety score was found between the post scan anxiety results between each group at 6 and 10 weeks. There was a significant difference at 8 weeks post scan. Women with a history of recurrent miscarriage have significantly higher levels of anxiety before each scan (6,8 and 10 weeks) and at the intervening 7 and 9 weeks.

Table 13: Comparison of mean S-anxiety scores pre and post scan within each group at each assessment using paired t tests. P <0.001 for all comparisons

Group	Scan Gestation (weeks)	Pre Scan S-anxiety Mean (SD)	Post Scan S-anxiety Mean (SD)	S-anxiety Change between scans (SD) (CI)
Recurrent Miscarriage **n=34**	6 n=34	50.8 (13.3)	33.9 (10.9)	16.6 (13.2) 12-21.3
	8 n=34	45.9 (10.1)	29.3 (7.4)	16.7 (8.3) 13.8-19.6
	10 n=34	47.2 (12.3)	28.3 (7.5)	18.9 (10.6) 15.2-22.6

Group	Scan Gestation (weeks)	Pre Scan S-anxiety Mean (SD)	Post Scan S-anxiety Mean (SD)	S-anxiety Change between scans (SD) (CI)
Standard Risk **n=48**	6 n=48	39.2 (10.5)	30.08 (11.6)	9.1 (12.6) 5.4-12.8
	8 n=48	37.9 (11.4)	25.8 (6.2)	12.1 (9.6) 9.3-14.9
	10 n=48	36.4 (12.5)	25.6 (5.8)	10.8 (10.2) 7.8-13.8

Figure 13: Graph showing pre and post scan s –anxiety scores and corresponding change scores within each group



Within both groups the change in S-anxiety levels from before to after the three scans at each gestation were significantly different i.e. anxiety levels post scan were significantly lower than before the scan. There was no significant difference between the mean change scores when compared to each other in each group i.e. the reduction levels in S-anxiety were similar after each scan in the individual groups.

Unpaired t tests were used to assess the changes in S-anxiety associated with scanning and comparison of groups.

Table 14: change of S-anxiety scores between women with a history of recurrent miscarriage and women with no previous pregnancy loss

S-anxiety Score	Recurrent miscarriage Mean (SD)	Standard risk Mean (SD)	Mean difference & 95% CI	P value
Pre 6 week-post 6 week scan	16.6 (13.2)	9.1 (12.6)	7.5 (1.8-13.3)	**0.012**
Pre 8 week-post 8 week scan	16.7 (8.3)	12.1 (9.7)	4.6 (0.5-8.7)	**0.025**
Pre 10 week-post 10 week scan	18.9 (10.6)	10.8 (10.2)	8.1 (3.5-12.7)	**0.001**

Women with a history of recurrent miscarriage had significantly higher change scores from pre to post scan than women with no previous pregnancy loss.

3.3.2.3 Summary of anxiety

- Participants with a history of recurrent miscarriage have significantly higher s- anxiety scores than participants with no previous pregnancy loss before each scan and after the 8 week scan and at 7 and 9 weeks gestation.

- Immediately after each scan, s-anxiety is reduced in all participants. The drop in anxiety levels, that is the change score, from pre scan to post scan is significant with each scan at 6,8 and 10 weeks gestation within both groups. The change scores are significantly larger, i.e. the anxiety levels drop more in the recurrent miscarriage group when compared to the standard risk group.

- There is a short-lived effect of the scan in reducing anxiety in both groups as anxiety levels were found to increase in-between scans at 7 and 9 weeks gestation in both groups, more so in the recurrent miscarriage groups.

- The t- anxiety scores were significantly lower after the 10-week scan than before the 6-week scan in both groups. The t- anxiety scores were significantly higher in the recurrent miscarriage group when compared to the standard risk group.

3.4 Prediction of anxiety levels

A Multiple regression analysis was conducted to predict the STAI change scores at the 6,8 and 10 week scans from number of previous miscarriages, number of children, the number of months since the last miscarriage and the monitoring score within each of the study groups. None of the variables were significant in predicting the STAI change score at the 6-week scan. The unstandardized regression coefficient and 95% confidence intervals can be seen in the table below (adjusted results). Within the recurrent miscarriage group, the higher the number of miscarriages, the more months since the last miscarriage and the higher the monitoring score are associated with a larger change score i.e. less anxious after the scan but not significantly so. The number of children carries a non significant negative weight indicating that after accounting for the other variables, those participants with more children had a lower change score after their 6 week scan i.e. their anxiety levels did not decrease as much. Within the standard risk group the monitoring score was not predictive of the STAI 6 week change score and the participants with children also had lower change scores, although not significantly so.

Table 15: Summary of Multiple Regression Analysis (adjusted) and Simple Linear Regression (unadjusted) for prediction of the 6 week STAI change score

	Recurrent Miscarriage		**Standard Risk**	
	Unadjusted b (CI)	Adjusted b (CI)	Unadjusted b (CI)	Adjusted b (CI)
Number of children	1.34 (-5.49- 8.17)	-1.16 (-10.78- 8.46)	-5.50 (-12.69- 1.69)	-4.83 (-11.86- 2.21)
Number of miscarriages	-3.73 (-16.9- 9.45)	1.41 (-4.23- 7.04)		
Months since last miscarriage	0.04 (-0.21- 0.30)	0.08 (-0.28- 0.41)		
Monitoring score	0.62 (-1.33- 2.57)	0.94 (-1.51- 3.39)	1.09 (0.01- 2.16)	1.01 (-0.06- 2.08)

b= unstandardized regression coefficient

For adjusted scores: R^2 = 0.04 Recurrent miscarriage, R^2 = 0.12 for the Standard risk

For unadjusted scores in the recurrent miscarriage group; R^2= 0.005 (number of children); 0.011 (number of miscarriages), 0.004 (number of moths since last miscarriage), 0.013 (Monitoring score). R^2 in standard group; 0.05 (number of children); 0.08 (monitoring score)

None of the variables when simple linear regression (unadjusted) was performed had a significant correlation with the 6-week STAI change score. The number of children however has a positive correlation as opposed to negative when assessed with the other variables in multiple regression. The number of miscarriages when used as a variable on its own now has a negative association although not significant, which suggests that on its own the more miscarriages a participant has the smaller the change score i.e. the lower the drop in their anxiety.

Table 16: Summary of Multiple Regression Analysis for prediction and Simple Linear Regression (unadjusted) of the 8 week STAI change score

	Recurrent miscarriage		**Standard Risk**	
	Unadjusted b (CI)	Adjusted b (CI)	Unadjusted b (CI)	Adjusted b (CI)
Number of children	-6.99 (-5.00- 3.60)	-0.93 (-6.88- 5.03)	-1.71 (-7.35- 3.93)	-1.69 (-7.43- 4.05)
Number of miscarriages	-0.52 (-2.95- 1.91)	-0.25 (-3.73- 3.24)		
Months since last miscarriage	-0.06 (-0.22- 0.097)	0.01 (-0.20- 0.23)		
Monitoring score	0.86 (-0.31- 2.03)	0.93 (-0.56- 2.42)	0.06 (-0.81- 0.92)	0.03 (-0.85- 0.90)

b= unstandardized regression coefficient

For adjusted scores: R^2 = 0.074 recurrent miscarriage, R^2 = 0.008 standard risk

For unadjusted scores in the recurrent miscarriage group; R^2 = 0.003(number of children); 0.006 (number of miscarriages), 0.02 (number of moths since last miscarriage), 0.067 (Monitoring score). R^2 in standard group; 0.008 (number of children); 0.00 (monitoring score)

None of the variables had a positive association/predictor for STAI change score at 8 weeks gestation in either group. Both the number of miscarriages and number of children were negatively associated indicating lower change scores in the recurrent miscarriage group in the multiple and simple regression.

When multiple regression was performed for predicting the 10 week STAI change score the monitoring score added statistically significantly to the prediction p=0.003in the recurrent miscarriage group. This indicates that if a participant had a higher monitoring score the larger the change score i.e. the less anxious after a scan, see table 17 below.

Table 17: Summary of Multiple Regression Analysis for prediction of the 10 week STAI change score

	Recurrent miscarriage		Standard Risk	
	Unadjusted b (CI)	Adjusted b (CI)	Unadjusted b (CI)	Adjusted b (CI)
Number of children	-2.48 (-7.89- 2.93)	-2.46 (-9.05- 4.14)	-2.96 (-8.86- 2.95)	-2.57 (-8.46- 3.33)
Number of miscarriages	-1.82 (-4.86- 1.21)	-1.38 (-5.24- 2.47)		
Months since last miscarriage	-0.14 (-0.32- 0.05)	0.04 (-0.20- 0.27)		
Monitoring score	1.78 * (0.37- 3.18)	1.80 ** (0.15- 3.45)	0.63 (-0.26- 1.52)	0.59 (-0.31- 1.49)

b= unstandardized regression coefficient

R2 =0.229 recurrent miscarriage, R2 = 0.058 standard risk

For unadjusted scores in the recurrent miscarriage group; R^2 = 0.0.03(number of children); 0.05 (number of miscarriages), (number of moths since last miscarriage), 0.17 (Monitoring score). R^2 in standard group; 0.02 (number of children); 0.04 (monitoring score)

p= 0.015*, p= 0.033**

When performing simple linear regression the monitoring score was again found to be a significant predictor of the STAI change score at 10 weeks gestation in the recurrent miscarriage group p=0.015.

There were no significant predictors within the standard risk group.

3.4.1 Linear Mixed Model analysis

The sample sizes are small. To increase the power of the analysis, the pre scan s-anxiety scores from the 6, 8 and 10 week scans have been combined, the post s-anxiety scores from the 6,8 and 10 week scans have been combined and the change scores have been combined from each of the scans for all the participants in each group.

Linear mixed models was then used to examine whether the same variables, used in the multiple and simple linear regression, can predict the anxiety score pre scan, post scan and the change score in each group.

By combining all of the recurrent miscarriage group's (n=34) pre scan s-anxiety scores together, post scan s-anxiety scores together and change scores together, linear mixed models has been used to examine whether the variables can predict the anxiety score pre scan, post scan and the change score in each group. By adding each of the scores together there were a total of 102 sets of results in each of these three constants. Within the recurrent miscarriage group the number of children the participant had had a negative significant prediction (p=0.018) on anxiety levels pre scan i.e. the more children, the less anxious the recurrent miscarriage participants were. The monitoring score was also a significant predictor (p=0.004) of the s-anxiety pre scan in the recurrent miscarriage group; the higher the monitoring score, the higher the anxiety levels were in participants before the 6,8 and 10 week scans (see table 18 below). The monitoring score also significantly predicted the change score in the recurrent miscarriage group (p=0.007), the higher the monitor the larger the drop in s-anxiety from pre to post scan, meaning the more reassured the participant was after the scan. The number of miscarriages and the time since last miscarriage does not predict higher s-anxiety levels, pre scan, post scan or the change score.

Table 18: Mixed Model analysis

	Pre scan		Post scan		Change score	
	Recurrent Miscarriage Group	Standard Risk	Recurrent Miscarriage Group	Standard Risk	Recurrent Miscarriage Group	Standard Risk
	Estimates (CI)	Estimates (CI)	Estimates (CI)	Estimates (CI)	Estimates (CI)	Estimates (CI)
Number of Children	-6.42* (-11.65--1.14)	-4.02** (-7.98--0.06)	-1.52 (-5.04-1.98)	0.86 (-1.64-3.36)	-4.9 (-10.04-0.23)	-4.34*** (-7.80- -0.89)
Number of miscarriages	0.81 (-2.22-3.84)		-0.45 (-2.48-1.58)		1.45 (-1.52-4.42)	
Months since last miscarriage	0.12 (-0.12-0.42)		-0.05 (-0.25-0.14)		0.19 (-0.10-0.47)	
Monitoring score	2.06❖ (0.70-3.43)	0.28 (-0.32-0.88)	0.23 (-0.66-1.12)	-0.08 (-0.46-0.30)	1.85❖❖ (0.52-3.17)	0.32 (-0.20-0.85)

P values *= 0.018, **=0.047, *=0.014, ❖=0.004, ❖❖=0.007**

Within the standard risk group, the number of children was negatively significantly associated with the s- anxiety levels pre scan (p=0.047), the more children the participants had the less anxious they were pre 6, 8 and 10 week scan. The number of children was also negatively significantly associated with the change score with the standard risk group, meaning that the participants within the standard risk group had a smaller drop in anxiety from pre to post scan if they had more children. The monitoring score did not predict the s-anxiety results. There was no evidence that any of the variables could predict the s-anxiety levels post scan in either group.

3.4.2 Summary of prediction of anxiety levels

Within both groups the number of children the participant had a negatively significant prediction (p=0.018 recurrent miscarriage, p=0.047 standard risk) on anxiety levels pre scan i.e. the more children, the less anxious the participants were before their scans.

3.5 Assessment of worries

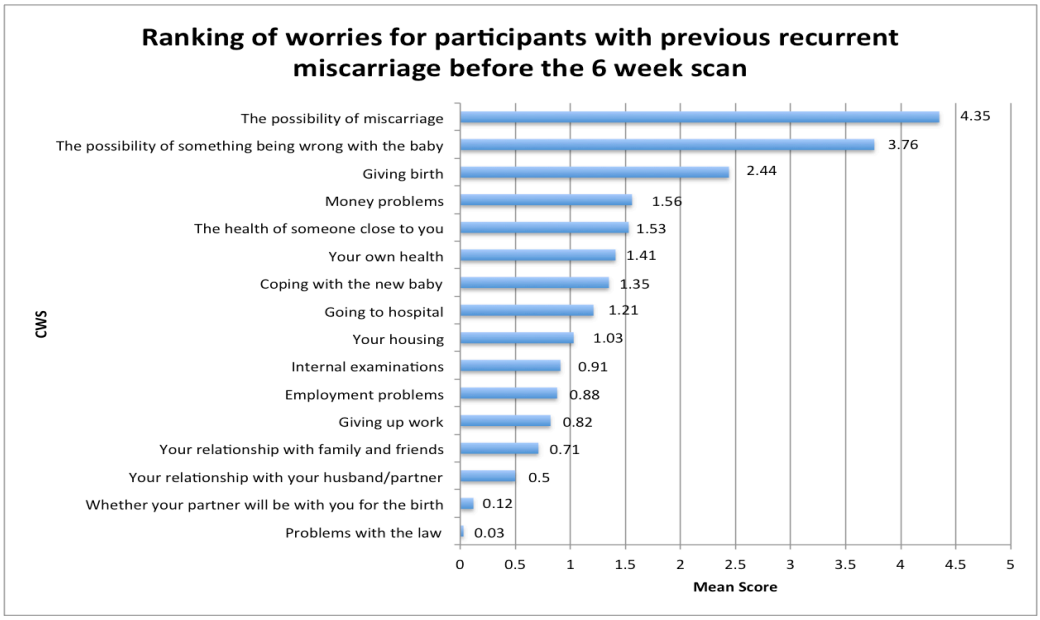
Within the recurrent miscarriage group of the 16 items in the CWS the risk of miscarriage and the possibility of something being wrong with the baby were both major worries (scored 4or 5 on the scale) pre 6 week scan. 82.4% of women had major worries regarding the risk of miscarriage before the 6 week scan. After the 10 week scan 44.2% of participants still were classified as having major worries regarding miscarriage. Only one participant (2.9%) was not particularly worried before the 6 week scan (scored 1) no participants scored 0 for risk of miscarriage. Within the same group, 61.8% of participants scored 4 or 5, before the 6 week scan, indicating major worry regarding the possibility of something being wrong with the baby. After the 10 week scan 44.1% of women still had major worries. Worries about giving birth was the only other item on the scale which scored a 4 or a 5 both pre 6 week (20.5%) and post 10 week scan (23.5%).

The standard risk group showed similar worries, although not to the same extent. There were 41.7% of participants who considered the risk of miscarriage a major worry pre 6 week scan although this dropped to 18.8% post 10 week scan. Worries of something being wrong with the baby were of major concern for 33.4% of participants pre 6 week scan, dropping to 10.4% post 10 week scan. Giving birth was a major worry to 31.3% of participants pre 6 week scan and to 20.9% of women after the 10 week scan. Coping with a new baby was a major worry to 20.9% of standard risk participants pre 6 week scan and to 12.6% of participants after the 10 week scan. The majority of standard risk women did not express high levels of worry for the majority of the items in the scale.

3.5.1 Ranking of Means

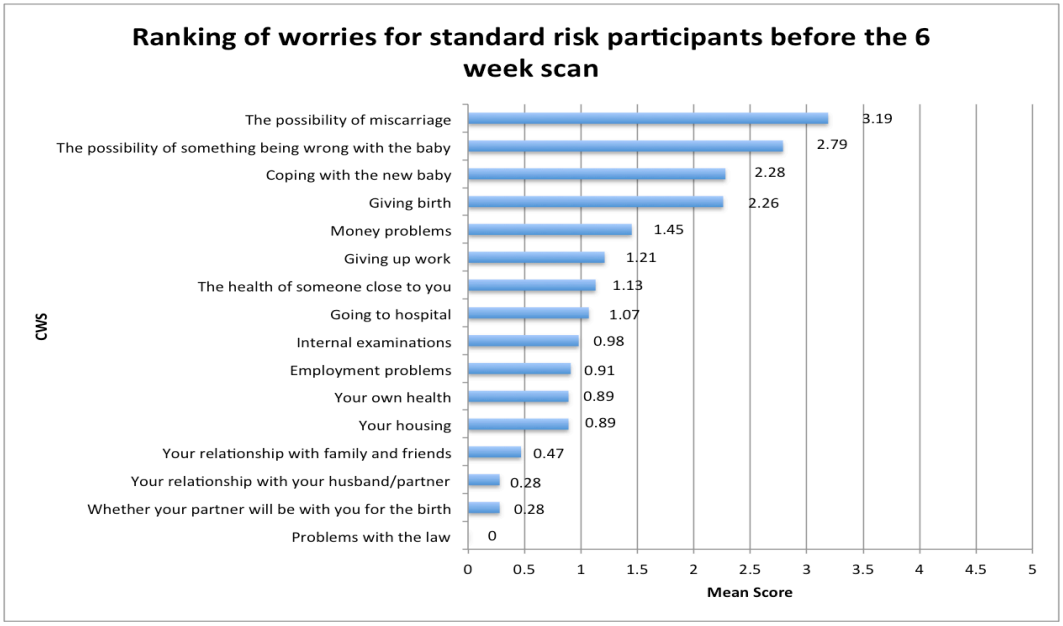
The mean CWS scores across the items were calculated for both groups of participants before the 6 week scan and post the 10 week scan and plotted on the graphs in figures 14-17 below.

Figure 14: The ranking of the mean CWS scores in the recurrent miscarriage group before the 6 week scan



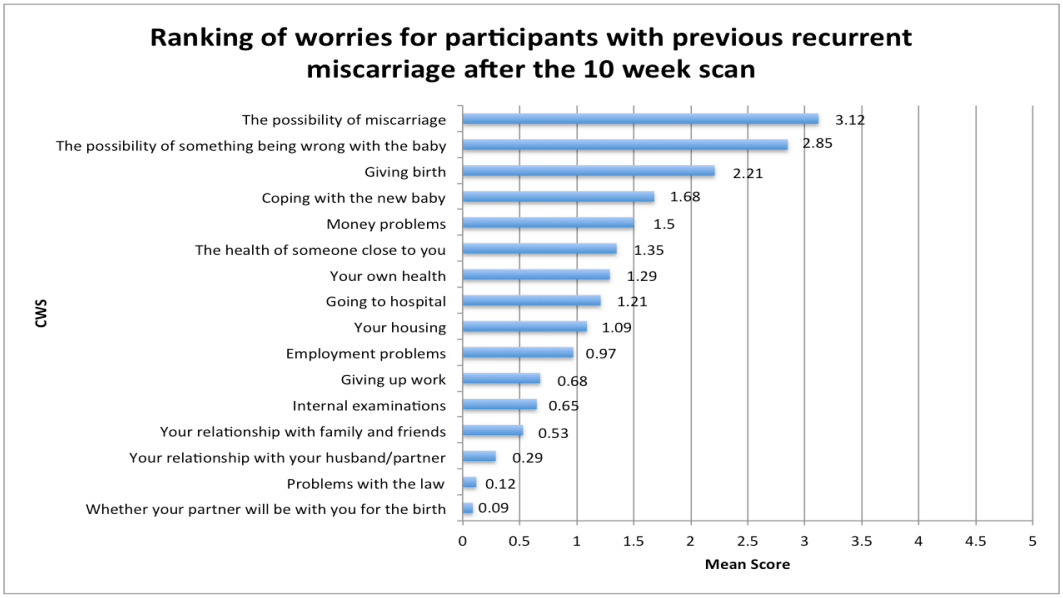
The most common worry was that of miscarriage in the recurrent miscarriage group prior to the 6 week scan, followed by the possibility of something being wrong with the baby and giving birth.

Figure 15: The ranking of the mean CWS scores in the standard risk group before the 6 week scan



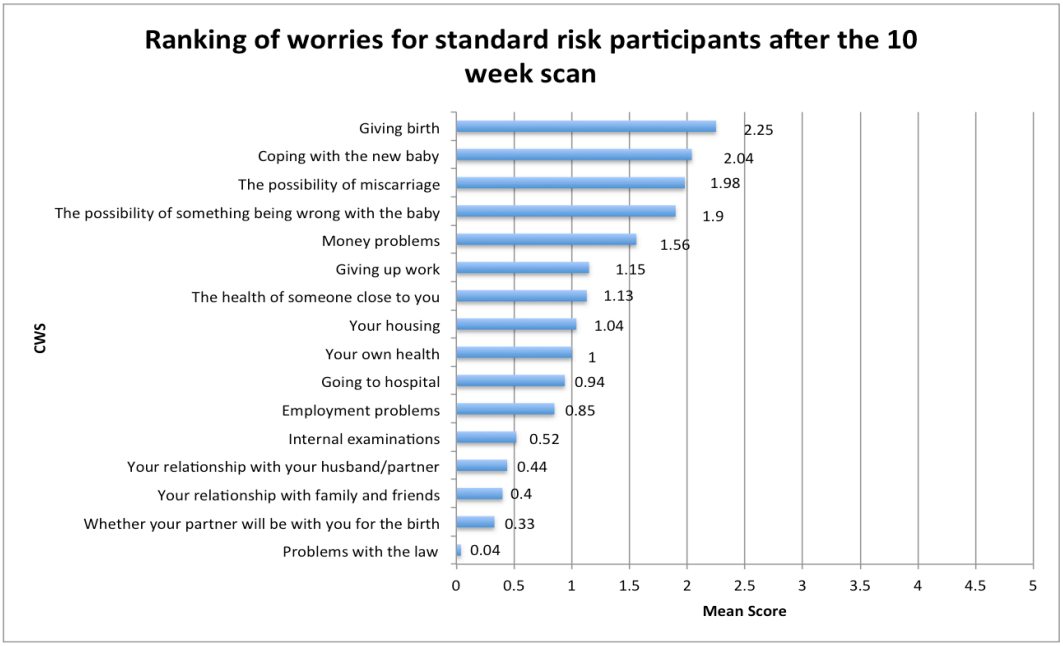
The most common worry in the standard risk group prior to the 6 weeks scan was the possibility of miscarriage followed by something being wrong with the baby, coping with the new baby and giving birth.

Figure 16: The ranking of the mean CWS scores in the recurrent miscarriage group after the 10 week scan



The possibility of miscarriage was still the primary worry for participants in the recurrent miscarriage group post the 10 week scan followed by something being wrong with the baby, giving birth and coping with the new baby.

Figure 17: The ranking of the mean CWS scores in the standard risk group after the 10 week scan



Giving birth was the major worry for participants in the standard risk group after their 10 week scan followed by coping with the new baby, the possibility of miscarriage and the possibility of something being wrong with the baby.

3.5.2 Comparing the means

Pre 6 week and post 10 week CWS score means for each of the 16 questions were compared using paired t- test within each group and presented in table 19 below.

Table 19: Comparison of the mean CWS scores pre 6 week and post 10 week scans within the recurrent miscarriage group

CWS	Pre 6 week	Post 10 week	Mean difference & (95% CI)
Your housing	1.03 (1.47)	1.09 (1.311)	-0.059 (-0.44-0.32)
Money problems	1.56 (1.397)	1.50 (1.397)	0.059 (-0.225-0.343)
Problems with the law	0.03 (0.171)	00.12 (0.537)	-0.88 (-0.287-0.111)
Your relationship with husband/partner	0.50 (0.749)	0.29 (0.906)	0.206 (-0.166- 0.578)
Your relationship with family and friends	0.71 (0.906)	0.53 (0.929)	0.176 (-0.93- 0.546)
Your own health	1.41 (1.048)	1.29 (1.219)	0.118 (-0.292-0.527)
The health of someone close to you	1.53 (1.261)	1.35 (1.252)	0.176 (-0.240-0.593)
Employment problems	0.88 (1.122)	0.97 (1.167)	-.088 (-0.503-0.327)
The possibility of something being wrong with the baby	3.76 (1.372)	2.85 (1.438)	**0.912* (0.387-1.437)**
Going to hospital	1.21 (1.219)	1.21 (1.386)	0.00 (-595- 0.595)
Internal examinations	0.45 (0.522)	1.55 (1.753)	-1.091 (-2.346- 0.164)
Giving birth	2.44 (1.599)	2.21 (1.553)	0.235 (-0.168-0.639)
Coping with a new baby	1.35 (1.346)	1.68 (1.319)	-.0324 (-0.715-0.067)
Giving up work	0.82 (0.936)	0.68 (1.173)	0.147 (-0.198-0.492)
Partner will be with you for the birth	0.12 (0.409)	0.09 (0.288)	0.029 (-0.106-0.165)
Risk of miscarriage	4.35 (1.012)	3.12 (1.610)	**1.235** (0.719-1.751)**

***p= 0.001, **p=<0.001**

Comparison of the mean CWS scores for each item before the 6 week and after the 10 week scans within the recurrent miscarriage group showed that there was a significantly lower score i.e. less of a worry after the 10 week scans for the items risk of miscarriage and the possibility of something being wrong with the baby. Problems with the law, employment problems, internal examinations and coping with a new baby had a higher mean score after the 10 week scan than before the 6 week scan but not significantly so.

Table 20: Comparison of the mean CWS scores pre 6 week and post 10 week scans within the standard risk group

CWS	Pre 6 week	Post 10 week	Mean difference & (95% CI)
Your housing	0.89 (1.418)	1.06 (1.538)	-0.170 (-0.410-0.069)
Money problems	1.45 (1.457)	1.55 (1.427)	-0.106 (-4.37-0.225)
Problems with the law	0.00	0.04 (0.204)	-0.043 (-0.102-0.017)
Your relationship with husband/partner	0.28 (0.615)	0.43 (0.801)	-0.149 (-0.322-0.024)
Your relationship with family and friends	0.47 (0.718)	0.38 (0.644)	0.085 (-0.116-0.287)
Your own health	0.89 (0.914)	1.00 (1.063)	-0.106 (0.361-0.148)
The health of someone close to you	1.13 (1.361)	1.13 (1.541)	0.000 (-0.318-0.318)
Employment problems	0.91 (1.299)	0.87 (1.096)	0.043 (-0.354-0.439)
The possibility of something being wrong with the baby	2.79 (1.503)	1.87 (1.135)	**0.915* (0.543-1.286)**
Going to hospital	1.07 (1.340)	0.96 (1.316)	0.109 (-0.335- 0.552)
Internal examinations	0.82 (1.090)	0.86 (1.239)	-0.036 (-0.451-0.380)
Giving birth	2.26 (1.608)	2.26 (1.390)	0.000 (0.411-0.411)
Coping with a new baby	2.28 (1.425)	2.04 (1.318)	0.234 (-0.097-0.565)
Giving up work	1.21 (1.573)	1.15 (1.560)	0.064 (-0.371- 0.498)
Partner will be with you for the birth	0.28 (0.743)	0.34 (0.867)	-0.064 (-0.340- 0.213)
Risk of miscarriage	3.19 (1.409)	2.00 (1.319)	**1.191* (0.801- 1.582)**

* p=<0.001

The risk of miscarriage and the possibility of their being something wrong were the baby were significantly of less worry after the 10 weeks scan than before the 6 week scan in the standard risk group. Housing, money problems, problems with the law, own health, internal examinations and partner being there for the birth all had higher mean scores after the 10 week scan but not significantly so.

Unpaired T- tests were used to compare the mean item scores between the recurrent miscarriage group and standard risk group.

Table 21: Comparison of the mean CWS scores between the recurrent miscarriage and standard risk groups pre 6 week scan

CWS	Pre 6 week		Mean difference & (95% CI)
	Recurrent miscarriage group	Standard risk group	
Your housing	1.03 (1.5)	0.89 (1.4)	0.136 (-0.509-0.780)
Money problems	1.56 (1.4)	1.56 (1.46)	0.112 (-0.530-0.754)
Problems with the law	0.03 (0.17)	0	0.029 (-0.30-0.089)
Your relationship with husband/partner	0.50 (0.75)	0.28 (0.62)	0.223 (-0.079-0.526)
Your relationship with family and friends	0.71 (0.91)	0.47 (0.72)	0.238 (-0.121-0.597)
Your own health	1.41 (1.05)	0.89 (0.92)	**0.518* (0.082-0.954)**
The health of someone close to you	1.53 (1.26)	1.13 (1.36)	0.402 (-0.190-0.993)
Employment problems	0.88 (1.12)	0.91 (1.30)	-0.33 (-0.583-0.518)
The possibility of something being wrong with the baby	3.76 (1.37)	2.79 (1.50)	**0.977** (0.328-1.627)**
Going to hospital	1.21 (1.20)	1.07 (1.34)	0.141 (-0.437-0.718)
Internal examinations	0.91 (1.11)	0.98 (1.29)	-0.067 (-0.614-0.480)
Giving birth	2.44 (1.59)	2.26 (1.608)	0.186 (-0.533-0.905)
Coping with a new baby	1.35 (1.35)	2.28 (1.43)	**-0.924*** (-1.543—0.300)**
Giving up work	0.82 (0.94)	1.21 (1.57)	-0.389 (-0.947-0.169)
Partner will be with you for the birth	0.12 (0.41)	0.28 (0.74)	-0.159 (-0.416-0.098)
Risk of miscarriage	4.35 (1.01)	3.19 (1.41)	**1.161**** (0.626-1.697)**

*p=0.020, **p=0.004, ***p=0.004, ****p=<0.001

The risk of miscarriage, the possibility of something being wrong with the baby and own health were significantly more of a worry in the recurrent miscarriage group before the 6 week scan than in the standard risk group. Participants in the standard risk group significantly worried more about coping with a new baby than the recurrent miscarriage group. Employment problems, internal examinations, giving up work and partner being present at birth were also more of a worry for the standard risk group but not significantly so.

Table 22: Comparison of the mean CWS scores between the recurrent miscarriage and standard risk groups post the 10 week scan

CWS	Post 10 week		Mean Difference & (95% CI)
	Recurrent Miscarriage Group	Standard risk Group	
Your housing	1.09 (1.31)	1.04 (1.53)	0.047 (-0.597-0.690)
Money problems	1.50 (1.42)	1.56 (1.41)	-.063 (-0.694-0.569)
Problems with the law	0.12 (0.54)	0.04 (0.20)	0.076 (-0.093-0.245)
Your relationship with husband/partner	0.29 (0.91)	0.44 (0.80)	-0.143 (-0.519-0.233)
Your relationship with family and friends	0.53 (0.93)	0.40 (0.64)	0.134 (-0.212-0.479)
Your own health	1.29 (1.22)	1.0 (1.05)	0.294 (-0.207-0.795)
The health of someone close to you	1.35 (1.25)	1.13 (1.52)	0.288 (-0.405-0.861)
Employment problems	0.97 (1.17)	0.85 (1.10)	0.116 (-.0385-0.618)
The possibility of something being wrong with the baby	2.85 (1.44)	1.90 (1.13)	0.957* (0.365-1.549)
Going to hospital	1.21 (1.39)	0.94 (1.30)	0.275 (-0.325-0.875)
Internal examinations	0.65 (1.10)	0.52 (1.15)	0.126 (-0.377-0.629)
Giving birth	2.21 (1.56)	2.25 (1.38)	-0.44 (-0.692-0.603)
Coping with a new baby	1.68 (1.32)	2.04 (1.30)	-.0365 (-0.950-0.219)
Giving up work	0.68 (1.17)	1.15 (1.54)	-0.469 (-1.095-0.156)
Partner will be with you for the birth	0.09 (0.29)	0.33 (0.86)	-0.245 (-0.512-0.022)
Risk of miscarriage	3.12 (1.61)	1.98 (1.31)	1.138** (0.469-1.808)

*p=0.002, **p=0.001

The risk of miscarriage and the possibility of something being wrong with the baby were still more of a worry for the recurrent miscarriage participants than the standard risk participants after the 10 week scan. Coping with a new baby, money problems, relationship with husband/partner, giving up

work and partner being present for birth were more of a worry in the standard risk group but not significantly.

3.5.3 Summary of worries in pregnancy

The CWS showed that participants in the recurrent miscarriage group were mainly worried about miscarriage both pre 6 week scan and post 10 week scan. Their levels of worry regarding miscarriage were significantly higher than those of the standard risk group. After the 10 week scan the main worry in the standard risk group was one of giving birth.

3.6 Coping Strategies

Participants from both groups were asked to complete the MBSS prior to the 6 week scan. The monitoring scores were evaluated.

Table 23: Monitoring scores of the MBSS in both groups

	Monitoring Score		**Blunting Score**	
	Recurrent Miscarriage	Standard Risk	Recurrent Miscarriage	Standard Risk
Mean	10.91	9.71	4.24	4.04
Median	11.50	10.0	4.00	4.00
SD	2.48	3.320	2.86	2.76
Range	10	14	13	11
Minimum	5	2	0	0
Maximum	15	16	13	11

There were 17 recurrent miscarriage participants who had median Monitoring scores of 12 or above. This equates to exactly 50% of the recurrent miscarriage group being classed as high monitors, having characteristics of typically associated with monitoring in general and 50% being low monitors, having characteristics associated with blunting.

Within the standard risk group 30 participants (62%) could be classified as being high monitors as opposed to 18 low monitors.

Table 24: Comparsion of the Mean Monitoring scores between the groups

	Recurrent miscarriage mean	Standard Risk Mean	Mean diference & 95% CI
Monitoring Score	10.91	9.71	1.20 (-.135-2.542)
Blunting Score	4.24	4.04	0.94 (-1.06-1.44)

On comparing the means the monitoring scores between the recurrent miscarriage and standard risk groups there were no significant differences.

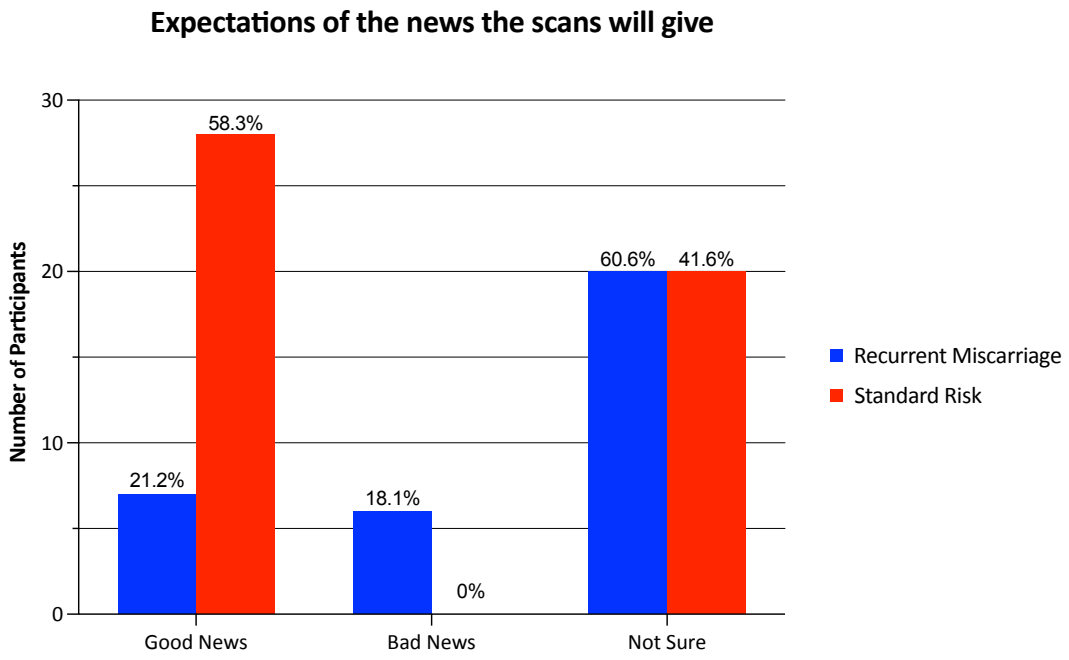
3.6.1 Summary of coping

This study found that there was no difference in the mean monitoring score on completion of the MBSS, however the larger number of participants who could be classed as high monitors was within the standard risk group (62% vs 50%).

3.7 Attitudes to pregnancy

Participants attitudes to the ultrasound scans and to their pregnancies were assessed using semantic differentiation scales prior to the 6 week scan and after the 10 week scan.

Figure 18: The participants expectations of the news that the ultrasound scans will show prior to thier 6 week scan

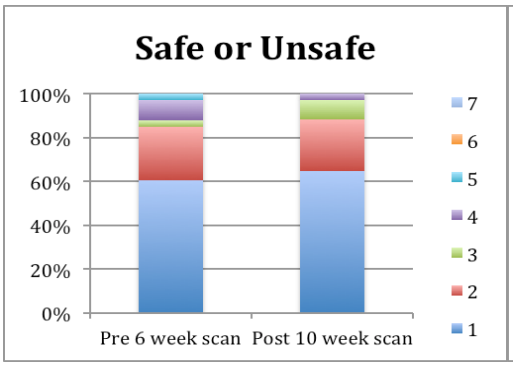


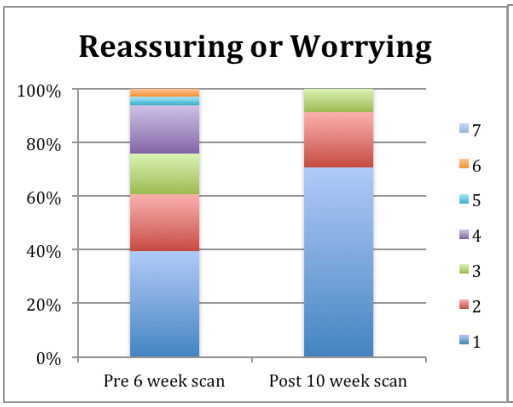
Twenty (60.6%) of the recurrent miscarriage participants were not sure what news the scans would bring, 7 (21.2%) thought it would bring good news and 6 (18.1%) bad news. Twenty eight standard risk participants (58.3%) thought that the scans would bring good news, none believed that they would receive bad news, 20 (41.7%) were unsure what the news would be.

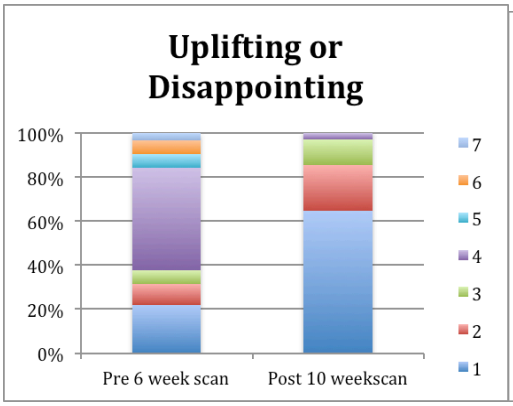
Figure 19: Participants feelings towards their ultrasound scans

The lower the number on the scale the more positive the answer, the higher the number the participant agreed with the more negative adjective.

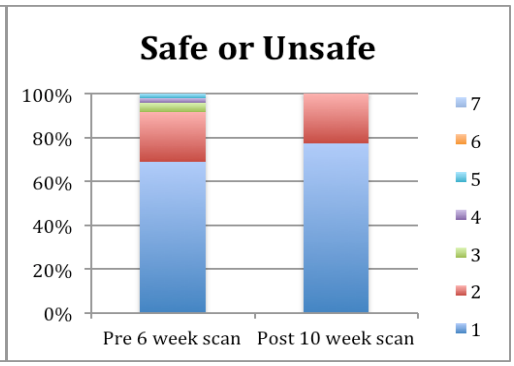
Recurrent Miscarriage

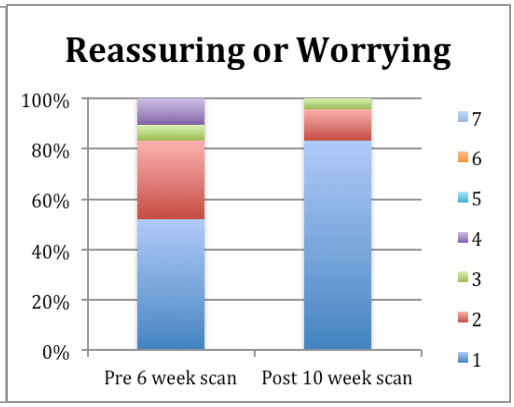


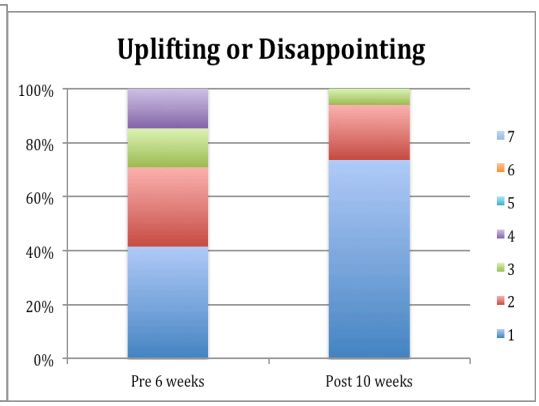




Standard Risk







Prior to the 6 week scan, 20 (60.6%) of recurrent miscarriage participants completely agreed that the scans were safe, scoring 1, collectively (scoring 1-3) 29 (87.9%) of recurrent miscarriage

participants tended to feel that the scans were safe whilst 3 (9.1%) felt neither one way or the other and 1 (3%) gave a rating of 5, i.e indicating a feeling that the scans were more unsafe than safe. After the 10 week scan 33 participants (97%) collectively felt that the scans were safe and 1 (2.9%) felt neither one way or the other. Prior to the 6 week scan 33 (68.8%) of standard risk participants completely agreed that the scans were safe and collectively 46 (95.8%) of standard risk participants viewed the scans to be safe, 1(2.1%) neither rated scans as safe or unsafe and 1 (2.1%) gave a rating of 5, indicating a tendancy that the scans were unsafe. Following the 10 week scan all standard risk participants regarded the scans as safe.

Before the 6 week scan 13 (39.4%) of recurrent miscarriage participants completely felt that the scans would be reassuring, overall 75.8% of recurrent miscarriage participants felt that the scans would be reassuring, 6 (18.2%) were unsure and 2 (6.1%) participants felt the scans would be worrying. After the 10 week scan 24 recurrent miscarriage participants felt the scans had been completely (score of 1) reassuring and all participants overall felt that the scans had been reassuring. Of the standard risk participants, 25 (52.1%) completely felt that the scans would be reassuring and 43 (89.6%) overall felt that the scans would be reassuring. Five (10.4%) of standard risk women felt that the scans would be neither reassuring or worrying. After the 10 week scan 24 (70.6%) of standard risk participants completely felt that the scans had been reassuring and overall all standard risk participants felt reassured by the scans.

Prior to the 6 week scan 15 (45.5%) of recurrent miscarriage participants gave a rating of 4, neither agreeing that the scans were going to be uplifting or diasappointing. Twelve (36.4%) recurrent miscarriage participants felt the scan would be uplifting and 5 (15.2) felt that the scans would be disappointing. After the 10 week scan 22(64.7%) of recurrent miscarriage participants felt uplifted by the scans. All but 1 recurrent miscarriage participant collectively found the scans uplifting. Within the standard risk group 20 (41.7%) of participants felt that the scans would be completely uplifting and all but 7 (14.6%) of them who thought neither one way or the other thought that the scans would overall be uplifting. After the 10 week scan 36 (75%) of standard risk participants found that the scans had completely been uplifting (scoring 1) and overall all of this group found the scans uplifting.

3.7.1 Statistical Comparisons

The Wilcoxan- signed rank test was used to assess whether there was a median difference between the scores for participants attitudes to scan before the 6 week scan compared with after the 10 weeks scan within each group. Of the 34 recurrent miscarriage participants, 33 answered both pre 6 week and post 10 week semantic questions, therefore 33 results were analysed. Of these participants 10 (30.3%) thought the scans were safer after the 10 week scan, 7 (21.2%) were more negative with their feelings and 16 (48.5%) ratings were unchanged. The post 10 week scan showed no significant median difference in feeling as to whether the scan was safe or not, see table 25.

Table 25: The median semantic differentiation scores of the recurrent miscarriage group attitude to the ultrasound scans

	Pre 6 week scan median score	**Post 10 week scan median score**	**z**	**p**
Safe -unsafe	1	1	-0.856	0.392
Reassuring-worrying	2	1	-3.160	**0.002**
Uplifting-disappointing	4	1	-4.05	**<0.001**

Within the recurrent miscarriage group 19 (57.6%) participants thought the scan gave more reassurance after the 10 week scan than before the 6 week, 2 (6.1%) indicated more negative thoughts and 12 (36.4%) scores remained the same. Twenty-four (72.7%) participants felt that the scans were more uplifting after the 10 week scan, 2 (6.1%) were more negative and 6 (18.2%) participants feelings remained unchanged. The Wilcoxan signed –rank test showed a significant increase in feelings of reassurance and uplifting towards the scans in both the reccurent miscarriage and standard risk groups after their 10 week scans compared to before the 6 week scan see table 25.

Of the 48 participants from the standard risk group 10 (20.8%) felt that the scans were safer after the 10 week scan, 5 (10.4%) scored more negatively and 33 (68.8%) participants feelings were unchanged. Within the same group 21 (43.7%) participants felt more reassured, 3 (6.3%) less reassured and 24 (50%) participants feelings were unchanged. Twenty–five (52.1%) of the

standard risk group felt that the scans were more uplifting and 3 (6.3%) were more negative, 20 (41.7%) felt the same after the 10 week scan as they did before the 6 week scan.

Table 26: The median semantic differentiation scores of the standard risk group attitude to the ultrasound scans

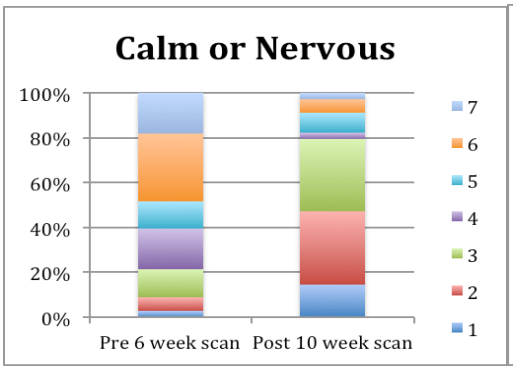
	Pre 6 week scan median score	Post 10 week scan median score	z	p
Safe -unsafe	1	1	-1.79	0.074
Reassuring-worrying	1	1	-3.36	**0.001**
Uplifting-disappointing	2	1	-3.86	**<0.001**

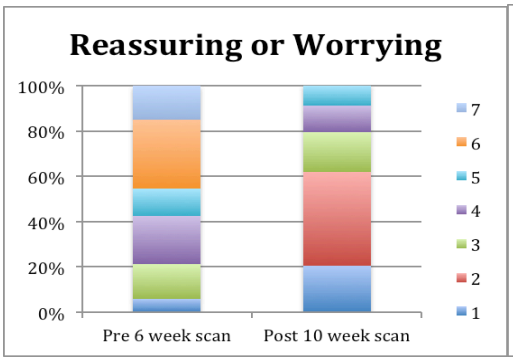
There was statistically significant increase in feelings of reassurance and uplifting towards the scans after the 10 weeks scan when compared with the 6 week within the standard risk group but no significanct difference with feelings of safety. See table 26.

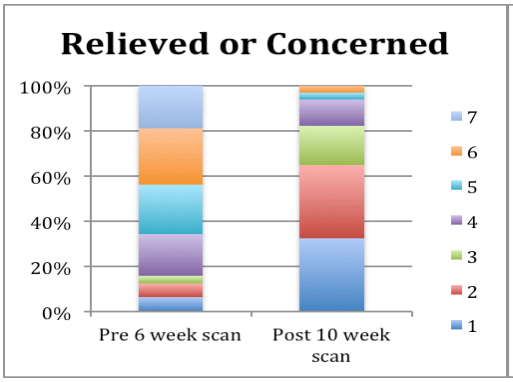
Figure 20: Participants feelings towards their pregnancy

The lower the number on the scale the more positive the answer, the higher the number the participant agreed with the more negative adjective

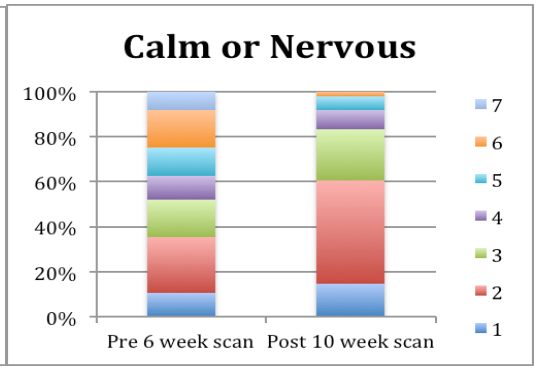
Recurrent Miscarriage

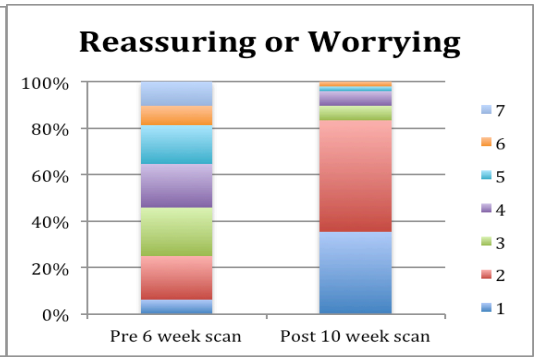


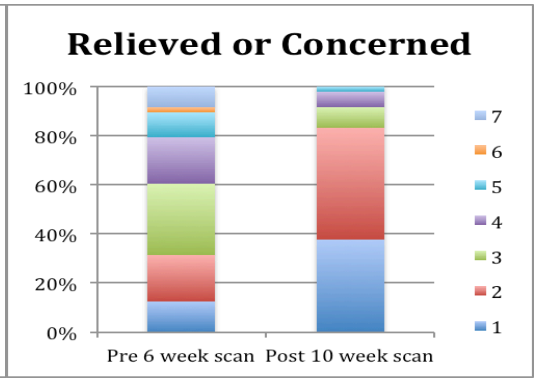




Standard Risk







Before the 6 week scan, 20 recurrent miscarriage participants (60%) scored 5-7 on the scale indicating being more nervous when asked whether they felt calm or nervous towards their pregnancy, 6 (18.2%) felt neither one way nor the other whilst collectively 7 (21.2%) felt calm.

Following the 10 weeks scan 27 (79%) of recurrent miscarriage participants felt calm towards their pregnancy. Of the standard risk participants, 25 (52.1%) felt calm towards their pregnancy prior to the 6 week scan, 5 (10.4%) were neither calm nor nervous and 18 (37.5%) felt more nervous. After the 10 week scan 40 (83.3%) expressed feeling of calm towards their pregnancy whilst 3 (6.25%) still felt nervous.

The majority (54%) of recurrent miscarriage participants felt worried about their pregnancy before the 6 week scan and 7 (21.9%) scored 1-3 indicating that they were reassured. After the 10 week scan 27(79.4%) recurrent miscarriage participants felt reassured towards their pregnancy and 3 (8.8%) still felt nervous. Before the 6 week scan the majority (52.1%) of standard risk participants had feelings of reassured towards their pregnancy, whilst 18 (37.5) had felt worried. On completion of the 10 week scan 43 (89.6%) of standard risk participants felt reassured whilst 2 (4.2%) felt worried.

Five (14.7%) of recurrent miscarriage participants had expressed feelings of relief towards their pregnancy before the 6 week scan, whilst 21 (61.8%) had feelings of concern. After the 10 weeks scan 28 of the same group (82.4%) had feelings of relief, 4 (11.8%) had feelings not one way nor the other and 2 (5.8%) felt concern. Of the standard risk group 29 (60.4%) participants felt relief about their pregnancy, 9 (18.8%) felt neither relief or concern and 10 (20.8%) felt worried. Forty-four (91.7%) standard risk participants felt relief after the 10 week scan and 1 (2.1%) felt concern.

Wilcoxan signed-rank analysis was used to examine the median score of the semantic scales of participant's feelings towards their pregnancy in both groups.

Of the recurrent miscarriage participants 24 (72.7%) felt increasingly calm towards their pregnancy following the 10 week scan, 4 (12.1%) more negatively and 5 (15.2%) were unchanged in their

feelings. Within the same group 28 (84.8%) participants felt reassured towards their pregnancy, 3 (9.1%) less reassured and 2 (6.1%) unchanged. Twenty-eight (84.8%) participants also felt more relieved about their pregnancies and 5 (15.2%) less so. Table 27 shows the median semantic scale scores. There was a statistical significant increase in feelings of calmness, reassurance and relief (p=<0.001) about the pregnancy after the 10 week scan compared with the pre 6 week scan, see table 27.

Table 27: The median semantic differentiation scores of the recurrent miscarriage group attitude to the pregnancy

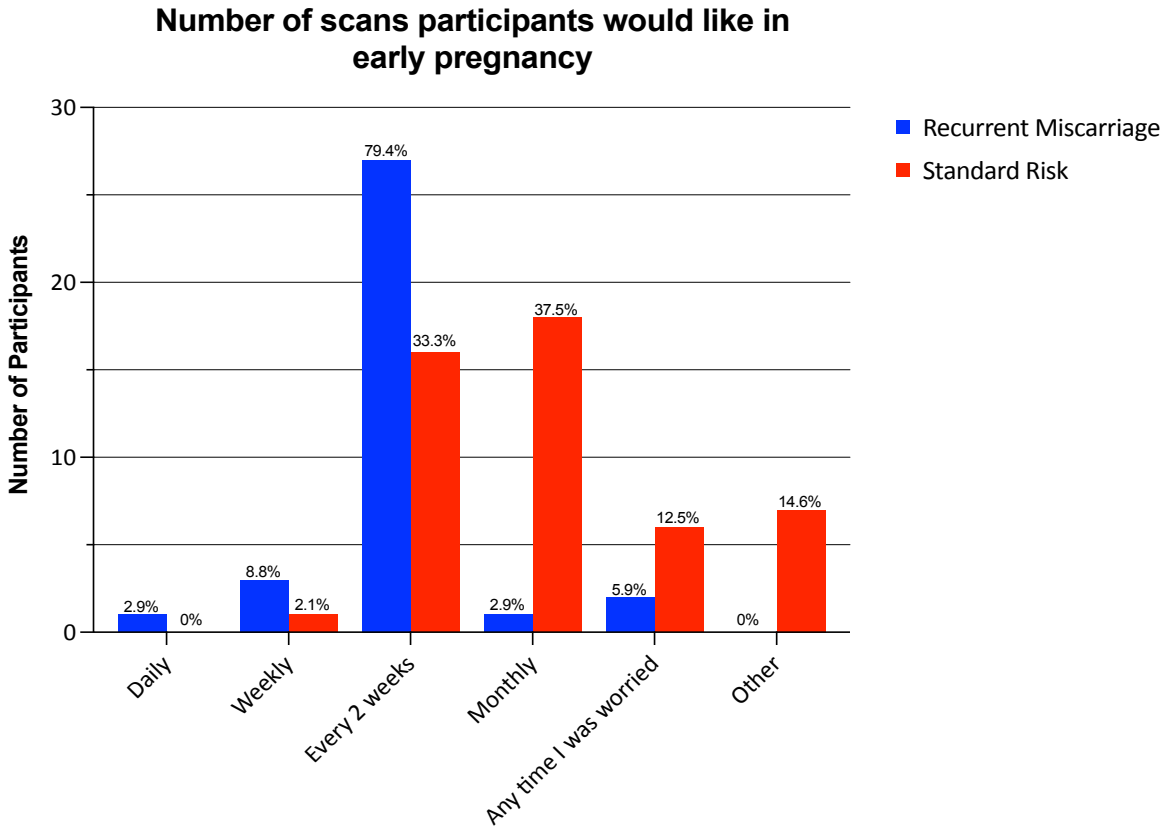
	Pre 6 week scan median score	Post 10 week scan median score	z	p
Calm- nervous	5	3	-3.84	**<0.001**
Relief- Concern	5	2	-4.47	**<0.001**
Reassurance-Worry	5	2	-4.16	**<0.001**

After the 10 week scan 27 (56.3%) participants in the standard risk group felt more calm about their pregnancy, 5 (10.4%) felt less calm and 16 (33.3%) felt the same. Forty (83.3%) standard risk participants felt more reassured toward their pregnancy, 2 (4.2%) less so and 6 (12.5%) the same and 31 (64.6%) of the same group felt more relieved about their pregnancy, 3 (6.2%) less so and 14 (29.2%) were unchanged in their feelings. On comparison of the median scores participants feelings in the standard risk group towards their pregnancy were significantly more, calm, relieved and reassured (p=<0.001) after the 10 week scan than before the 6 week scan, see table 28.

Table 28: The median semantic differentiation scores of the standard risk group attitude to the pregnancy

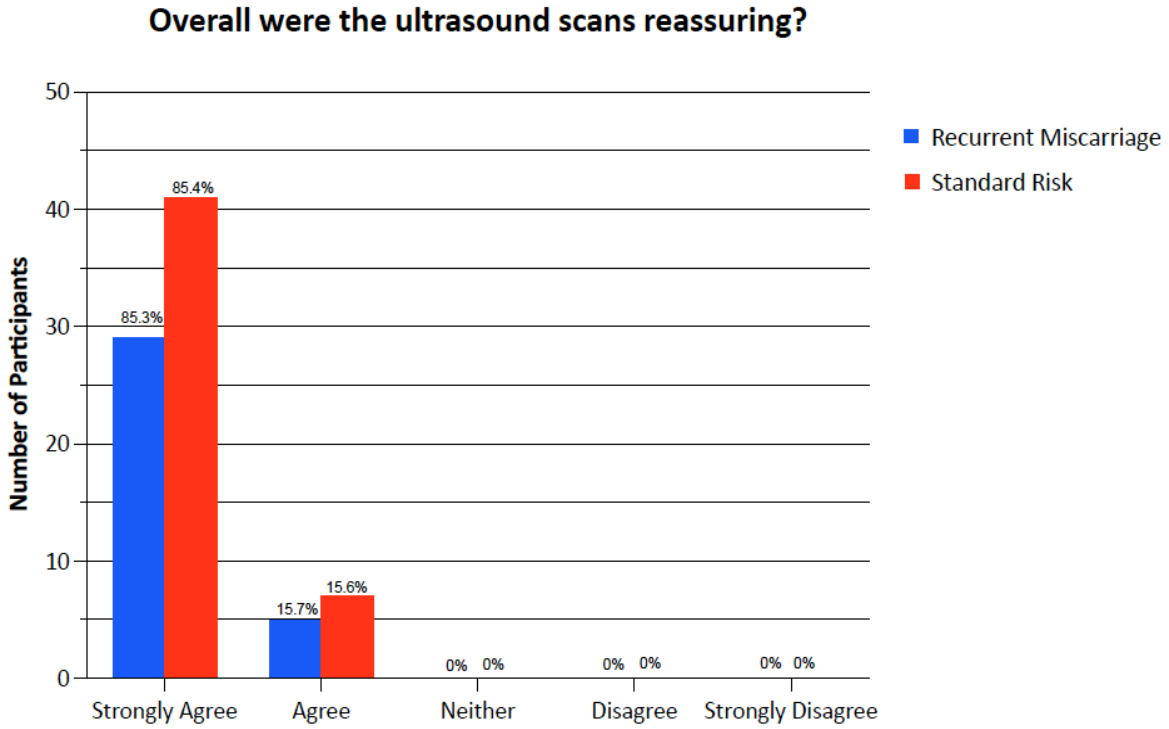
	Pre 6 week scan median score	Post 10 week scan median score	z	p
Calm- nervous	3	2	-3.84	**<0.001**
Relief- Concern	3	2	-5.49	**<0.001**
Reassurance-Worry	4	2	-4.48	**<0.001**

Figure 21: The number of scans participants would like



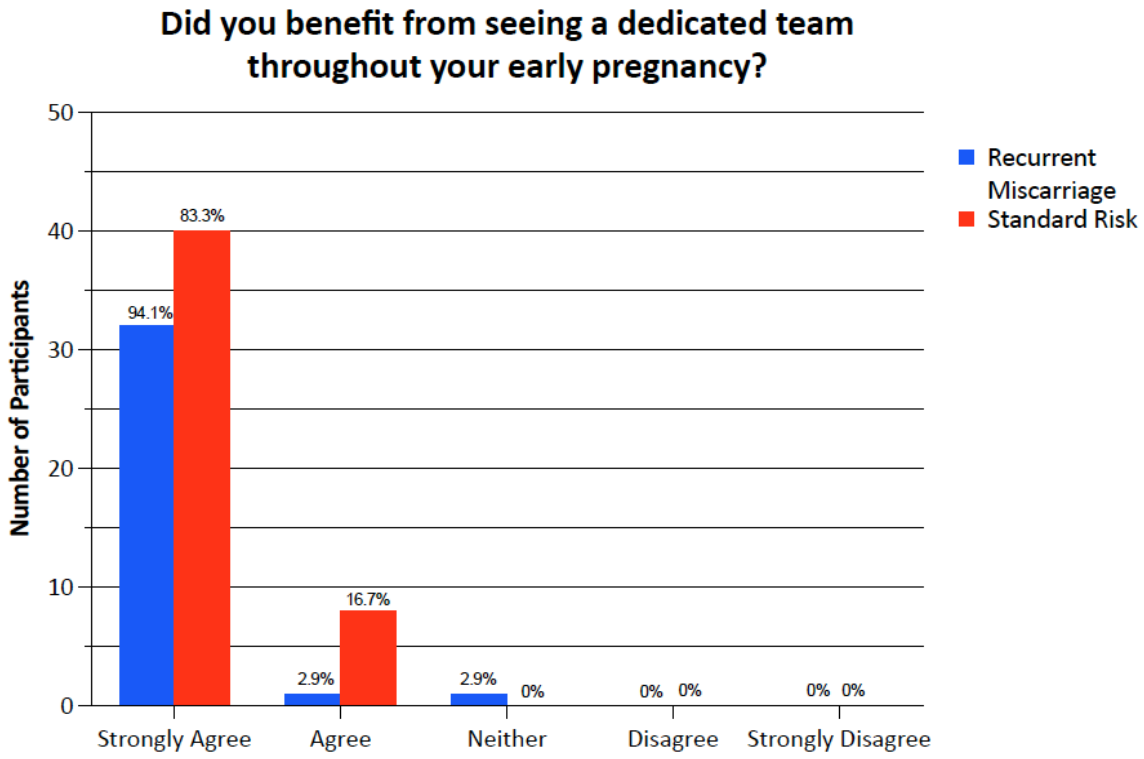
Twenty-seven (79.4%) of the recurrent miscarriage participants wanted a scan every fortnight, 3 (8.8%) wanted weekly scans, 2 (5.9%) any time they were worried and 1 (2.9%) wanted daily scans. Eighteen (37.5%) of the standard risk participants wanted monthly scans, 16 (33.3%) wanted fortnightly scans, 6 (2.1%) anytime they were worried and 1 (2.1%) wanted weekly scans.

Figure 22: The level of agreement that the ultrasound scans were reasurring



All participants from both groups either strongly agreed (85.3% and 85.4% recurent miscarriage and standard risk groups respectively) or agreed that the ultrasound scans were reassuring.

Figure 23: Whether women found seeing a dedicated team in early pregnancy beneficial



Of the recurrent miscarriage group 32 participants (94.1%) strongly agreed that seeing a dedicated team in early pregnancy was of benefit to them, 1 agreed and 1 neither agreed nor disagreed. Forty (83.3%) participants from the standard risk group strongly agreed to the question and 8 (16.7%) agreed.

3.7.2 Summary of attitudes to pregnancy

Participants in both groups felt significantly more uplifted and reassured after the 10 week scan than before the 6 week scan and significantly more calm, relief and reassurance towards their pregnancies after the 10 week scan than before the 6 week scan.

All participants from both groups either strongly agreed (85.3% and 85.4% recurent miscarriage and standard risk groups respectively) or agreed that the ultrasound scans were reassuring.

Chapter 4 Discussion

Serial ultrasound scanning is the most significant feature of supportive care in early pregnancy for women who have previously, repeatedly miscarried. Serial scans are more commonly referred to as “reassurance scans”. This term presumes that the scan result is positive and the patient believes that it means her pregnancy is more likely to continue. Women with repeated early pregnancy loss have often, previously only received bad news at a scan. Some patients with such histories choose to avoid scanning as they realise that even if the result is reassuring on a specific day that does not prevent them from miscarrying at a later date.

There is a lack of randomised controlled trials or studies in a sufficiently large number of patients to endorse supportive care (hinging on serial scanning). Where feasible, early pregnancy units and individual clinicians will seek to provide some level of early pregnancy scanning to unexplained recurrent miscarriage couples, on the basis that this might help. There are significant service implications in attempting to deliver this level of care, resulting in “post code” disparities in what is available to individual couples. Studies have not addressed the alternative hypothesis that serial scanning in early pregnancy may provoke and/or increase anxiety.

The impact of miscarriage on the future mental health of those involved is better recognised than when this study was designed and undertaken (18) (72) (106) There has been a rethink of the belief that supportive care is justified as it reduces the risk of further miscarriage (for which the evidence is poor) to an acknowledgement of the impact of miscarriage, its aftermath and stress of future pregnancies on a patient’s mental wellbeing. This study provides needed data on the effects of serial scanning in early pregnancy on the latter.

To our knowledge it is the first study to quantitatively assess background anxiety levels prior to a first pregnancy scan at six weeks’ gestation and after the last “reassurance scan” at 10 weeks, in

women with recurrent miscarriage and those with a “standard risk” early pregnancy. Anxiety levels are also quantitatively assessed (through questionnaires previously validated in pregnancy) before and after each two weekly scan and at the mid time point between.

A stipulation of the study ethical approval was that the data of any participant, from either group, who miscarried, was excluded from analysis. Pregnancy outcome was not part of this study but if all of the pregnancies in recurrent miscarriage women which progressed to 10 weeks resulted in a live birth, the success rate would be 77.3%. This is in keeping with published data for unexplained recurrent miscarriage and supportive care (11). The miscarriage rate of the standard risk group in early pregnancy was 14.3%, again in keeping with the sporadic miscarriage rate of the general population (13).

Women with recurrent miscarriage tended to be older than women without a previous adverse pregnancy outcome, perhaps reflecting the length of time taken trying to achieve an ongoing pregnancy**.** Age, ethnicity, marital status, qualifications, being a smoker, history of depression or of fertility treatment did not differ between the two groups. The ethnicity within both groups was not diverse and not a reflection of the immediate surrounding area. 88% of the recurrent miscarriage and 83% of the standard risk groups were Caucasian. There was a single black participant in each group. The two boroughs immediately served by GSTT are Lambeth and Southwark. Within Southwark 52.2% of the population describe themselves as White British which is lower than in London generally and in England and Wales. Of the population of Southwark, 25.9% is black, compared to 10.9% in London and 2.3% in England and Wales. (107). Miscarriage is still a taboo subject within many cultures, with associated stigma and perceived judgement by society. Cultural differences could influence the likelihood of women with recurrent miscarriage seeking help, as could a language barrier or lack of awareness of local services (61)**.** The deprivation scores were higher in participants within the recurrent miscarriage group, which is reflective of the surrounding population served by GSTT. In 2010 Southwark ranked as 25th most deprived borough out of 326 local authorities in England, whilst Lambeth ranked the 14th most deprived. The domains of

deprivation by which scores and ranks are given are: Income; employment; health, deprivation and disability; education, skills and training; crime, barriers to housing and service; living environment.

Income and employment carry the most weight in deprivation scores. Southwark scored 25th in income and 33rd in employment, whilst Lambeth scored 21st in income and 23rd in employment, where 1 is the most deprived and 326 the least deprived (105). The participants from the standard risk group lived further afield, with 22 travelling from outside of a London borough including; Essex, Cambridge, Kent, Guildford, Hertfordshire and Devon. All of these areas (with the exception of two boroughs in Essex) rank in the 50% of least deprived quintiles.

A problem in many studies is that volunteers in the control arms are often the "worried well" which may in itself influence outcome. Our study findings are strengthened by the fact that the miscarriage rates in each arm are consistent with those published. The lack of diversity and equivalent highest level of qualifications in both groups emphasises that the reassurance scanning service in our Trust is not being accessed equitably by all women in our catchment area.

The STAI is validated for use within pregnancy as a self assessment of anxiety, both examining the situational (state) anxiety [S] and the participant's baseline or predisposition to anxiety (trait) [T]. The STAI was not primarily designed to diagnose anxiety disorders and therefore agreement on cut off levels for STAI scores to indicate a low or high anxiety state or traits vary in different populations. Although a score of 40 in the State anxiety is commonly used to define probable levels of clinical anxiety (108) (109). In pregnancy the cut off can vary for different gestations and the postpartum (110, 111) and has not been clearly established in early pregnancy and recurrent miscarriage populations. Comparison of the scores within and between groups and over time was helpful in our work.

We found that participants with a history of recurrent miscarriage had significantly higher "baseline" or trait anxiety scores than standard risk women prior to the 6 week scan. Their "acute" or situational anxiety scores were also higher before each of the three scans. This confirms the subjective impression that recurrent miscarriage patients have higher background anxiety levels

which are further amplified before each “reassurance” scan, than participants with no previous pregnancy loss. Post scan situational anxiety scores were significantly lower than pre scan levels in both groups, for each of the 6,8 and 10 week scans. The effect of a reassuring scan result in reducing anxiety is short lived. Levels were found to have increased again in both groups (although not to the pre 6 week level) at 7 and 9 weeks, the midway points between scheduled scans. Both these effects were more pronounced in the recurrent miscarriage compared to the standard risk group. All women had a lower level of baseline anxiety after the 10 week scan than when starting the study. We would have expected that this trait/ T- anxiety would remain unchanged throughout the study as it is thought to be a stable characteristic, unaffected by changing situational variables. Other studies (44) have shown stable T-anxiety scores when assessed pre and post scans, with a minimal intervening time delay between completing the questionnaires. Our T- anxiety was examined 4 weeks apart, after a series of intervening scans. Participants may not have been able to recall their previous answers, which can influence the test if questionnaires are completed close together. All women’s S-anxiety after the 10 week scan was at such a reduced level compared to prior to the 6 week scan that we can speculate that this may have affected participants’ responses to the trait (T) assessment. Our data questions the robustness of this test in these circumstances but further work in larger numbers of women is needed to investigate this.

State (S) anxiety was found to be significantly higher in the recurrent miscarriage than the standard risk group before each of the three scans, at 7 and 9 weeks’ gestation and after the 8 week scan. The immediate effect of any of the scans is to reduce S-anxiety levels in both groups. This reduction in acute anxiety was greater in the recurrent miscarriage group. This suggests that the difference between the anxiety induced by an imminent early pregnancy scan and the modulation of this anxiety by a reassuring result does not vary between six and ten weeks’ gestation or with a previous good scan outcome, whether or not there has been a previous poor obstetric outcome. Women with recurrent miscarriage have higher S- anxiety levels than those who have not miscarried both prior to and during pregnancy (39) (112) (38). Women who have not miscarried but who are at high risk for potential fetal abnormalities, as a result of an elevated AFP level at routine screening have high S-anxiety levels compared to normal AFP level controls. This S-anxiety was found to reduce by a greater amount in the high risk groups to levels similar to those found in the

control groups after an ultrasound scan where no abnormality was found (42). Our findings mirrored this pattern.

The decrease in S-anxiety in our study is short lived as state anxiety increases again in all women when assessed between the scans, at 7 and 9 weeks' gestation. These "between scan" questionnaires were completed at home. We do not know when anxiety levels begin to increase again after a reassuring scan and before a further scan, in the absence of any pain or bleeding. Despite this increase in anxiety, not related to an imminent scan it is of note that none of the women who completed the study presented to an EPU between their scheduled appointments.

Of equal importance is that after the 10 week scan, S-anxiety levels in both groups were similar and at their lowest levels within the study. Previous studies have shown that a reduction in anxiety after an ultrasound scan is related to increased positivity towards the pregnancy, reaffirming the reassuring effects (95) (42). Our data supports the case for offering serial scanning (across the gestation range when they had previously miscarried) to women with a history of repeated early pregnancy loss. We have also shown that standard risk participants have lower levels of background anxiety but become more anxious at the prospect of a scan, even if they have had a previous reassuring result. Although these levels will return to normal after the scan, this serves as a cautionary note to the increasing demands for early pregnancy scans for "souvenir scans and photographs" and not medically indicated reasons.

Miscarriage was the biggest worry for everyone before the 6 week scan and this was, as would be expected, at a higher level in those with recurrent miscarriage. After the last scan in the study, at 10 weeks', the main worry in the standard risk group was of giving birth whereas the women with recurrent miscarriage were still most anxious about miscarrying, although the percentage feeling this way had almost halved to 44% and despite the majority of women having previously miscarried before 10 weeks. Whereas the possibility of miscarriage and something being wrong with the baby

were still the top two worries in the recurrent miscarriage group after the 10 week scan, the standard risk group had replaced these two worries with concerns more directed at the birth; giving birth and coping with a new baby. This could reflect that the standard risk group have the capacity to look ahead without thoughts of previous pregnancy losses and think not only about reaching the stage of giving birth but also to worry about their ability to be a parent and cope with a baby. The recurrent miscarriage group are less likely to think that far ahead and may not question their ability to be able to cope with being a parent but are focused on being a parent in the first place. The mean score of coping with a new baby significantly increased from the 6 week scan to the 10 week scan in the standard risk group and although the mean worry of coping with a new baby did increase from 6 to 10 weeks in the recurrent miscarriage group, this was not significant.

We used the Cambridge Worry Scale (CWS), which was developed, initially for use in early pregnancy, to examine women's concerns regarding the health of their baby within the context of other worries in and outside of pregnancy. Green et al (46) used the CWS on a unselected antenatal population of women at three different time points, the earliest being at less than 16 weeks' gestation. The mean score for worry about the possibility of miscarriage at the early gestation was 2.54, which is considerably less than that of our recurrent miscarriage and standard risk women. Many of the women at the "early gestation" stage in the published study had completed the first trimester (when most miscarriages happen) and all participants were recruited from an unselected, low risk antenatal population with an unknown background rate of miscarriage. Our standard risk participants knew the study aim and that their eligibility depended on them not having had a previous miscarriage. Miscarriage may, therefore have been pushed more to the forefront of their minds. Problems with the law, whether their partner would be at the birth and relationship with family and friends consistently scored low at both pre the 6 and post the 10 week scan. Money problems were the highest scoring worry after concerns about the baby in both the recurrent miscarriage and standard risk groups which is consistent with other studies from the UK, Spain and Sweden (48). These findings are particularly interesting in light of the national guidelines introduced secondary to the Covid-19 pandemic in 2020-21, restricting the access of partners and accompanying persons to antenatal appointments, including scans and delivery.

The corona virus pandemic impacted on every aspect of life including maternity and early pregnancy care. In March 2020 many hospitals were preparing for a potential onslaught of providing care for highly infectious and seriously ill patients with Covid-19, a virus not fully understood in its pathogenesis or management. Many elective procedures were postponed, freeing operating theatres, theatre recovery and anaesthetic machines to become extensions of Intensive Care, freeing anaesthetists to manage and intubate the seriously unwell and freeing surgical beds to become medical ones. Care was rationalised to try to minimise the spread and exposure of coronavirus for health care professionals and patients and to account for staff shortages.

Pregnant women were deemed to be at high risk of contracting coronavirus (113) and measures were put into place to minimise the number of women who needed to come to hospital and all partners were banned from routine scans and appointments. Due to pregnant women being deemed higher risk, many hospitals world wide noticed a downward trend of emergencies including in early pregnancy and gynaecology leading to concerns by health care professionals that patients were “risking life threatening complications by avoiding the emergency department” (114). A further retrospective study showed a statistically increased rate of ruptured ectopic during the pandemic (115) compared with pre pandemic numbers. One group recorded a 60% decrease in OB-GYN ED consults during the pandemic (116).

The RCOG issued guidance to support early pregnancy services during the pandemic (117), outlining what elements of care should be prioritised. All women were triaged over the phone by an experienced healthcare professional allowing prioritization of those women deemed to be at high risk of complications (mainly ectopic pregnancy), where hospital visits were essential to ensure patient safety rather than phone or video consultations with advice. A traffic light system was put into place: red meant women needed a scan or clinical assessment without delay e.g. signs and symptoms of an ectopic pregnancy, heavy bleeding for over 24 hours, septic miscarriage or a combination of risk factors and symptoms for ectopic pregnancy; amber meant scans or visits that can be delayed without affecting clinical care e.g. moderate bleeding or heavy bleeding that’s

resolved and green, scans or visits that can be avoided for the duration of the pandemic e.g. reassurance scans, previous miscarriage and light bleeding. The traffic light system and postponing of elective work meant that those women with recurrent miscarriage eligible for reassurance scans were unable to attend and missed out on scans during the first 10 weeks of pregnancy.

This thesis showed that women with recurrent miscarriage have higher anxiety levels than women who have not had a previous pregnancy loss and that scanning lowers these levels over time. Without the scans these women would potentially be running high levels of anxiety impacting on their mental health and well being until their 12 week scan. We showed that anxiety levels in women with recurrent miscarriage were reduced to the same low levels as those of women without a previous pregnancy loss by 10 weeks, after receiving reassurance scans. The pandemic prevented these women and their partners from having this supportive care. Although it is understandable why these restrictions had to be put in place it was also difficult for staff used to providing this care to have to explain to patients why it was not allowed. Due to the number of miscarriages many of these women have experienced, they are well know to staff who have either given them bad news or helped guide them through the early stages of pregnancy. The restrictions went against everything staff knew helped women and against the main elements of supportive care, namely scans and face to face open access and reassurance. The pandemic has given the opportunity to show how important scans are by the volume of women calling on a daily or weekly basis requesting scans and making verbal and written complaints when these were not available. In a local District General Hospital Early Pregnancy Unit, feedback from staff reflected the disappointment of women with recurrent miscarriage: “Our recurrent miscarriage ladies were very, very disappointed as we had promised reassurance scans could happen in a subsequent pregnancy when the women had been reviewed in recurrent miscarriage clinic and now they were told they could not be seen unless they were clinically unwell”. Staff found they were ‘treating anxiety symptoms over the phone rather than any physical symptoms”. It was also observed that “many women booked private reassurance scans in clinics who were continuing to scan”.

There is no current evidence that Covid-19 increases the miscarriage rate in women who contract the virus in the first trimester (118) (119). Studies and commentaries over the last year have, however expressed grave concern about the mental health of pregnant women throughout the pandemic and in those with previous loss (120) (121) (122). The longer impact on mental health in women with previous recurrent loss, unable to access supportive care remains to be seen.

We did not demonstrate that having more children or a longer period of time since the last miscarriage decreased anxiety levels or that a history of larger numbers of miscarriages increased them, on initial regression analysis. Anecdotal thinking might expect anxiety levels to be proportionately related to previous poor pregnancy experience and that living children would be a protective factor. Previous studies have also shown that the number of children and the number of miscarriages are not predictive of anxiety scores (38) (39). Craig et al (39) postulated that perhaps the pressures of having children "may provide as much stress as they provide protection againgst the psychological sequelae of recurrent miscarriage". Mevorach et al (76) devised a formula to examine the relationship between number of children and anxiety levels. They found that the higher the number of children, the greater the anxiety. The corollary of this anxiety and responsibility is joy at the reality of having a child and wanting to replicate that and desire for a sibling. Bagchi et al (59) suggested that a woman with recurrent miscarriage and no children is more likely to respond to miscarriage with a depressive reaction and that having children may be a protective factor.

We used linear mixed models to examine whether the same variables, used in the multiple and simple linear regression, can predict the anxiety score pre scan, post scan and the change score in each group. Our sample size was small. To increase the power of the analysis the pre scan s-anxiety scores from the 6, 8 and 10 week scans were combined, as were the s-anxiety scores post the 6,8 and 10 week scans and the change scores (difference in anxiety levels pre and post scan)

were also combined from each of the scans for all the participants in each group. On this further analysis, women with an increasing number of children had significantly lower pre scan S-anxiety levels in both the recurrent miscarriage and standard risk groups, suggesting that having children was a protective factor. Having children reduced the change score (comparison of anxiety levels pre and post each scan) in the standard risk but not recurrent miscarriage women; those in the standard risk group who already had children had less of a drop in anxiety levels pre and post scan. Pre scan s-anxiety levels are significantly lower in the standard risk group overall and, in particular in those with children. A smaller drop in anxiety levels would return them to a baseline level, hence the change scores will be less in these participants. Post scan S-anxiety levels are lower and closer to a potential "normal" in all women so it is unsurprising that there is no effect of already having children on this.

The Miller Behavioural Style Scale is a self reported written questionnaire designed to identify whether participants would actively seek out information about an uncontrollable stressful situation (Monitor) or avoid and distract from any information gathering (Blunter). We chose this to analyse women's background tendency to seek information as its predictive value is proven in pregnancy (104). The range of monitoring score is 0-16; the maximum score was recorded once, by one of the standard risk group. Women were divided into high and low monitors by the median monitoring score. There was an equal split between high and low monitors, in the recurrent miscarriage group. This may initially seem surprising as participants with a history of recurrent miscarriage would potentially want to seek out more information due to their previous pregnancy losses. Serial reassurance scans are offered as part of the recurrent miscarriage service and are optional. The fact that these women with recurrent miscarriage had chosen to attend for reassurance scans increases the likelihood that they would be monitors. Women with recurrent miscarriage are focused on being a parent and find it difficult to think of anything else. When asked, most would like to have scans as part of their subsequent care (36). We propose that in an often vulnerable state when offered a scan, women may feel that they have no choice but to accept it. The act of having a scan is seen as proactively "doing something" in the pregnancy that they are so desperate to be successful; especially when they have been advised that no intervention is of proven value. Some first time mothers in the UK feel that the antenatal scans offered at 12 and 20 weeks, as part of

routine antenatal care, are part of the “treatment of pregnancy” and that they have to have these scans (1). We know that there is a subset of women with a history of recurrent miscarriage who opt not to have additional pregnancy scans whilst asymptomatic. Although ethically and logistically difficult to obtain, further information on this group with regard to background anxiety levels and monitoring scores and acute anxiety over the first trimester would be extremely helpful in understanding the role of serial scanning and for whom it is most of benefit. As all of our women were recruited when they rang to request serial scanning, it was not ethical to randomise them to scanning or review appointments without scanning.

The standard risk group had a non significant tendency to contain a greater percentage of high monitors (62% *vs* 50% in the recurrent miscarriage group). This group was composed entirely of volunteers; no-one was directly approached, all were recruited via advertisements. These participants often travelled from out of the area for scans. This could be interpreted as wanting to seek out more information regarding their pregnancy. Early pregnancy can sometimes be accompanied by symptoms such as nasuea and tiredness but not always. There is no visible increase in uterine size and no fetal movements to be felt by the mother. The only indication of a pregnancy can sometimes be a postive pregnancy test. An ultrasound scan offers a method of seeing the baby and women describe the experience of having a scan as making their pregnancy more “real”. Visual confirmation by a professional endorses the reality of their pregnancy and allows them to take back some control of what is happening (1) (2) (94).

In our study, the recurrent miscarriage group did not think that a scan was most likely to bring bad news but very few thought it would bear good news; opting for a more cautious approach of being unsure what news the scans would bring (51.5%). This provides supporting evidence for the subjective impression that women with recurrent early pregnancy loss dare not allow themselves to believe that the next pregnancy might be successful but they cannot have written off all hope otherwise they would not have continued to try. By contrast, none of the standard risk group thought that the scans would bring bad news which is consistent with them having had no previous

pregnancy losses and them being asymptomatic with regards to miscarriage. Evidence from first trimester screening scans suggests that most women attend routine pregnancy scans expecting confirmation of normality and have not considered that the scan could show a problem (2) (94). In keeping with this, the majority (58.3%) of our standard risk participants expected the scans to give good news.

Semanitc scales have been used in pregnancy to ascertain women's attitudes to scans and the pregnancy (42) (43) . We used three sets of opposing adjectives to elicit these attitudes before the 6 and after the 10 week scan. The majority of participants in both groups thought that scans were safe prior to the 6 week scan and this was unchanged when re- assessed after the 10 week scan. This should be expected as participants are opting to go through an intervention that could have implications for themselves and their pregnancy, if unsafe. Ultrasound is proven to be safe when used correctly, as discussed in chaper 1. Women with recurrent miscarriage were more likely to consider the scans to be extremely reassuring after the 10 week scan (60%) than when asked before the six week scan (39.4% of this group), reflected in the median score showing an increase in positivity towards the scan being reassuring (p=0.002). Similar results were found when the recurrent miscarriage group was asked if they felt the scans would be uplifting or disappointing. Before the 6 week scan, 45.5% of participants chose the middle value on the scale neither agreeing or disagreeing with either adjective, indicating more uncertainty. After the 10 week scan, 64.7% of this group felt that the scan was uplifting, reflected in a drop in the median score (p=<0.001). Feelings of reassurance and being uplifted are to be expected immediately after a scan which brings good news in this group of women. Of note, approximately 40% of women who have previously miscarried, often by 10 weeks still do not feel reassured after this scan gives positive news. The median scores for feeling uplifted in the standard risk group also significantly moved towards increasing positivity after the 10 week scan, although the majoirty of this group also rated scans as uplifting before the 6 week assessment.

Prior to the first scan, women with recurrent miscarriage were more likely to describe their feelings as nervous (60%), worried (54%) and concerned (61.8%) which after the last scan had changed to calm (79%), reassured (79.4%) and relieved (82.4%). The median scores became more significantly positive across all three questions. As with feelings of reassurance and being uplifted, a small proportion of participants persisted in having more negative than positive feelings even after three reassuring scans. The standard risk group were overall more positive in their feelings prior to the 6 week scan; calm (52.1%), reassured (52.1%) and relieved (60.4%). Post 10 week scan feelings became significantly even more calm, reassurred and relieved. This shift of all descriptors in a more positive direction will be influenced by the fact that only those with an ongoing pregnancy were allowed to continue in the study. Future work is needed to examine if women diagnosed with miscarriage at reassurance scanning would choose to have such scanning in a future pregnancy as ethical considerations precluded us from gathering such information.

Our findings are consistent with other studies showing more positive attitudes towards the pregnancy and fetus immdeiately after a scan (42). This could reflect a transfer of the positivity of the findings of the scan towards the pregnancy. The same authors followed up their participants 4-5 weeks after the scan and observed that womens' attitudes to the pregnancy return towards pre scan levels indicating that positivity is short lived (43) . We found a similar pattern for state anxiety which had increased by one week after the last reassuring scan.

Participants were directly asked how many scans they would like in early pregnancy. The recurrent miscarriage group largely opted for fortnightly scans (79.4%), wheras the majority of the standard risk group were split between preferring fortnightly (33.3%) and monthly (37.5%) scans. All of the recurrent miscarriage patients were recruited from the recurrent miscarriage service at GSTFT which offers fortnightly scans from 6 until 10 weeks' gestation. This is important feedback that when patients have been advised by clinicians to expect this frequency they are happy with it and comply, not attending between appointments even though they had again become more anxious. The two week interval was selected as a compromise between perceived patient demand and service

constraints but appears to be the appropriate interval. Other institutions have described differing approaches from twice weekly (100), to weekly (22) (23) (33) (101) to fortnightly scans. When asked, women with recurrent miscarriage stated they would prefer to be scanned when they had symptoms, directly after a postitive pregnancy test and every two weeks (36).

There was overwhelming support from the recurrent miscarriage group, 94.1% of whom strongly agreed that they felt they benefitted from seeing a dedicated team throughout their early pregnancy, as did 83.3% of women with no previous poor pregnancy outcome. It is recommended that women with a history of recurrent miscarriage are seen by a specialist team (11) which will usually involve the same group of clinicians. This allows women to have confidence and familiarity with their care giver. Women prefer to be seen by a clinician specialising in recurrent miscarriage (36). Not all hospitals have the resources, skill mix or training to provide this level of service but the importance of aiming for minimum and consistent standards of care in all centres has again been highlighted recently (123).

This thesis examined women's attitudes and expectations and did not address anxiety and attitudes of their partners who have also experienced pregnancy loss. Partners may witness the woman go through pain and heavy bleeding, powerless to stop or control what is happening. They are also losing their unborn child. Nearly all studies examining the impact of miscarriage on mental health only involve the partner carrying the pregnancy. Those studies that address a male partner suggest that men feel neglected, with little opportunity to voice their emotions, many feel they play a supportive or secondary role and that there is often a lack of understanding from friends and family of their grief (124) (125) (126). Gender and societal expectations for them to be "strong and silent" often still prevail. One in twelve male partners experience post traumatic stress after miscarriage or ectopic pregnancy (73). The "Miscarriage Association" ran an awareness campaign and produced a leaflet "Partners Too" (127) due to the demand for this support on their help lines. There is little published evidence on the experience of same sex or transgender partners where the impact of miscarriage may be compounded by the additional planning that needed to go into the pregnancy.

National guidelines recommending partners do not attend pregnancy scans and other antenatal appointments during the Covid-19 pandemic only serve to re-enforce all of the above.

In their review of the psychological impact of early pregnancy loss Farren et al (72) reviewed 27 articles from study groups in the UK, Europe, the USA and Asia where participants were assessed for depression, anxiety or Post Traumatic Stress Disorder (PTSD). They found women with early pregnancy loss (miscarriage or ectopic pregnancy) had significant depression and anxiety in the first month following the loss. They also observed that partners had depression and anxiety, but at a lower level. The same group studied the differences between PTS, anxiety and depression following miscarriage or ectopic pregnancy between women and their partners. From three early pregnancy units, 192 couples were recruited and followed up at 1, 3 and 9 months. Although the response rates decreased with time, partners also experienced PTS, anxiety and depression to clinically relevant levels although this was to a lesser extent than the woman (106). The reviews and this study demonstrate that not only are women undergoing significant psychological suffering so are their partners which can have immediate and longer term effects on their mental health.

Although this last study was open to same sex couples, none were recruited. It may be that LGBTQ and transgender partners of women who physically miscarry have more difficulty in being acknowledged even as the partner and parent of the pregnancy loss. Usually a form of assisted conception has been used which may have taken a long time to conceive at physical and financial cost which may increase the feelings of grief and sense of loss. Negative views of their sexuality and relationship can impact access to support leading to isolation and may exacerbate levels of anxiety, depression and PTS (127). Further research is needed to evaluate this.

This study has shown raised anxiety levels in women with recurrent miscarriage in a subsequent pregnancy and that reassurance scans lowers these levels. What was not explored was the impact of anxiety levels on mental health outside a subsequent pregnancy. Tavoli et al 2018 (128) compared non pregnant women with and without a history of recurrent miscarriage attending a

gynaecology clinic, using a quality of life questionnaire and the Hospital Anxiety and Depression scale (HADS) to measure anxiety and depression. They found that women with a history of recurrent miscarriage have significantly higher levels of anxiety and depression than those without. Within the recurrent miscarriage group women with at least one child had lower levels of anxiety and depression than those without children. When quality of life was compared between women with recurrent miscarriage and those without recurrent miscarriage, they found that those with a history of recurrent miscarriage had significantly lower levels of general health, vitality, social functioning and mental health and than those without recurrent miscarriage. The detrimental effect on mental health in the recurrent miscarriage group could be explained by the impact of anxiety and depression. Within this study we did not consider gestation at which the miscarriage occurred, and time since last miscarriage was not powered strongly enough so we cannot speculate on anxiety levels outside a subsequent pregnancy.

Women with a history of recurrent miscarriage were assessed for the prevalence of depression and emotional stress by Kolte et al (129), the majority of whom had miscarried within the last 6 months and compared to a group who were trying to conceive naturally. All completed the Major Depression Index (MDI) to measure depression and the Cohen's Perceived stress scale, measuring stress. They found that there were significantly higher levels of self reported stress amongst the recurrent miscarriage group than those women trying to conceive naturally and the group with recurrent miscarriage had over 5 times higher levels of moderate to severe depression then the control group. There was no correlation of scores on the MDI or PSS and time since last pregnancy loss in the recurrent miscarriage group. This suggests that level of anxiety and depression remain unaltered despite the passage of time. It is worth noting that the control group in this study were women taken from the Soon Parents Study, volunteers in heterosexual relationships actively trying to conceive, of whom a large number had had either a previous single miscarriage or stillbirth. These control participants would therefore be expected to have a history of psychological distress. Again these findings reiterate that women with recurrent miscarriage have higher levels of anxiety and depression than women with a single pregnancy loss at any gestation. Similar findings were observed by Adib-Rad et al (130) on another comparison between women with unexplained

recurrent miscarriage and women without a history of recurrent miscarriage and no previous pregnancy loss and at least one living child. Participants had to complete the Symptom Checklist-90 (SCL-90-R) and the Intolerance of Uncertainty Scale (IUS). Women in the recurrent miscarriage groups showed higher levels of psychological symptoms including anxiety and depression. They also found that levels of psychological distress remained the same at 1-6 months, 7-12 months and >12 months after a loss. Those women without recurrent miscarriage were found to have significantly reducing levels of anxiety and depression with increasing time after a successful birth.

Campillo et al (131) attempted to systematically review the effect of non medical interventions, such as counselling and support, to reduce stress in pregnant women with a history of miscarriage. Of 4140 papers initially screened, only 7 potential RCTs were identified all of which failed to meet the inclusion criteria for review, either because miscarriage could not be separated from other forms of pregnancy loss or women were not pregnant at the time of the study. This highlights the poor quality and lack of evidence for supportive care in women with a history of miscarriage (sporadic and recurrent) when not pregnant and in a subsequent conception.

One example of non pharmacological intervention is a happiness training program which aims to allow recipients to adopt a more positive attitude towards life events. Women with a history of recurrent miscarriage were randomly assigned to the intervention group who received happiness counselling sessions and those who did not (132). There were 30 women in each group who all were asked to complete the 21-item Depression, Anxiety and Stress Scale (DASS-21). Whilst no difference in stress, anxiety and depression between the two groups was observed prior to the counselling sessions, all participants who subsequently received happiness counselling in a series of 8 sessions, had significantly lower depression, anxiety and stress levels than those who did not. There is no long term data on the impact of happiness counselling and the practicalities of training and cost implications need to be considered but these results support further research into this and similar interventions .

All of these studies highlight the impact of the anxiety of recurrent miscarriage on mental health and the importance of recognition of this (both inside and outside of pregnancy) by health care professionals. Our data supports the conclusion of these recent studies that the care of women with repeated early pregnancy loss must include psychological support.

Chapter 5 Conclusion

Publically funded early pregnancy (less than 12 weeks' gestation) scanning in the United Kingdom is reserved for those with symptoms, such as pain or bleeding. In women with repeated early pregnancy loss, a practice has arisen where scans are offered to asymptomatic women, on the presumption that these will reduce anxiety levels and increase the likelihood of a successful pregnancy outcome. The evidence base for this practice is weak and the service implications are significant. It also ignores prescribing something for the patient which has often, previously only delivered "bad news".

This study has shown that baseline anxiety levels are higher in women with recurrent miscarriage when compared to women with no previous adverse pregnancy outcome. It demonstrates that scanning immediately lowers anxiety levels in recurrent miscarriage and standard risk women.

It indicates that anxiety levels will rise one week following the six or eight week scan, when reassuring. A subsequent scan will then again reduce the anxiety levels.

The anxiety levels of women with recurrent miscarriage reduce to a similar level to that found in the standard risk group after the 10 week scan. This suggests that reassurance scanning is reassuring.

During the study, women had increased positive thoughts and feelings towards their pregnancy and the scan itself. No woman in the recurrent miscarriage group presented requesting additional unscheduled review and scan. Women with recurrent miscarriage stated that they felt fortnightly scanning was an appropriate interval.

This study suggests that women with recurrent miscarriage want to have a specialist team providing consistency of care and expert knowledge to support them during the early stages of a subsequent pregnancy. These women should have access to a specialist team as standard and serial / reassurance scanning is a gold standard part of this supportive care.

5.1 Limitations

There are several limitations of the work presented in this thesis. This was a preliminary study with small patient numbers, ideally a larger sample in multiple centres would provide larger numbers for analysis and ensure that the results were generalisable. It was not possible to assess whether the variables of ethnicity, a history of depression or whether the heart beat was seen at the first scan had a significant effect on anxiety levels as there were too few numbers to perform statistical analysis.

The recurrent miscarriage participants were not randomised into those who had scans and those who did not, so it was not possible to say what the level of anxiety was when women with recurrent miscarriage did not have an ultrasound scan. It would not have been ethical to have withheld the scans.

The pre six week scan anxiety level was distorted by the imminent scan. In retrospect, we should have assessed this at five weeks' gestation although it may have been difficult to capture all of the women this early, particularly the standard risk group.

5.2 Future Research

The study demonstrates the changing anxiety levels in the recurrent miscarriage population within the early pregnancy period. Further research is needed, with a larger sample size, reflecting all patient demographics and in multiple settings.

It is equally important in future to capture the attitude of women who were removed from analysis becuase they miscarried during the study. Would these women want serial scanning in a subsequent pregnancy?

The anxiety levels of standard risk women pre scan were higher than may have been predicted and future work should focus on what ultrasound scanning in early pregnancy means for each individual.

The financial and service provision implications of serial scanning in women with recurrent miscarriage need to be pursued. The suggested psychological implications of scanning standard risk, asymptomatic women also appear to be of interest.

APPENDIX 1 Pre 6 week questionnaire bundle

Participant number:

Date:

Gestation:

Early Pregnancy Ultrasound Scanning

Thank you for taking you time to complete this questionnaire, we hope you find it interesting.

The questions are easy to answer.

For most questions, just tick the box beside the answer that applies to you.

There will be an instruction at the top of each section telling you to either tick one box only, or all that apply.

If there is a small number beside the box please ignore it, this is for office use.

Other questions require you to either circle a single number or a word, which applies best to you

There may also be a long box for you to write your answer in

APPENDIX 1 s- anxiety **A: SELF-EVALUATION Y1**

A1 A number of statements which people have used to describe themselves are given below. Read each statement and then tick the box to the right of the statement to indicate how you feel right at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feeling best.

	Not at all	Somewhat	Moderately	Very much
I feel calm	☐ 1	☐ 2	☐ 3	☐ 4
I feel secure	☐ 1	☐ 2	☐ 3	☐ 4
I am tense	☐ 1	☐ 2	☐ 3	☐ 4
I feel strained	☐ 1	☐ 2	☐ 3	☐ 4
I feel at ease	☐ 1	☐ 2	☐ 3	☐ 4
I feel upset	☐ 1	☐ 2	☐ 3	☐ 4
I am presently worrying over possible misfortune	☐ 1	☐ 2	☐ 3	☐ 4
I feel satisfied	☐ 1	☐ 2	☐ 3	☐ 4
I feel frightened	☐ 1	☐ 2	☐ 3	☐ 4
I feel comfortable	☐ 1	☐ 2	☐ 3	☐ 4
I feel self-confident	☐ 1	☐ 2	☐ 3	☐ 4
I feel nervous	☐ 1	☐ 2	☐ 3	☐ 4
I am jittery	☐ 1	☐ 2	☐ 3	☐ 4
I feel indecisive	☐ 1	☐ 2	☐ 3	☐ 4
I am relaxed	☐ 1	☐ 2	☐ 3	☐ 4
I feel content	☐ 1	☐ 2	☐ 3	☐ 4
I am worried	☐ 1	☐ 2	☐ 3	☐ 4
I feel confused	☐ 1	☐ 2	☐ 3	☐ 4
I feel steady	☐ 1	☐ 2	☐ 3	☐ 4
I feel pleasant	☐ 1	☐ 2	☐ 3	

APPENDIX 1 T- anxiety **A: SELF-EVALUATION Y2**

A2 A number of statements which people have used to describe themselves are given below. Read each statement and then tick the box to the right of the statement which indicates how you generally feel.

	Almost Never	Sometimes	Often	Almost Always
I feel pleasant	☐ 1	☐ 2	☐ 3	☐ 4
I feel nervous and restless	☐ 1	☐ 2	☐ 3	☐ 4
I feel satisfied with myself	☐ 1	☐ 2	☐ 3	☐ 4
I wish I could be as happy as others seem to be	☐ 1	☐ 2	☐ 3	☐ 4
I feel like a failure	☐ 1	☐ 2	☐ 3	☐ 4
I feel rested	☐ 1	☐ 2	☐ 3	☐ 4
I am “calm, cool and collected”	☐ 1	☐ 2	☐ 3	☐ 4
I feel that difficulties are piling up so that I cannot overcome them	☐ 1	☐ 2	☐ 3	☐ 4
I worry too much over something that really doesn’t matter	☐ 1	☐ 2	☐ 3	☐ 4
I am happy	☐ 1	☐ 2	☐ 3	☐ 4
I have disturbing thoughts	☐ 1	☐ 2	☐ 3	☐ 4
I lack self-confidence	☐ 1	☐ 2	☐ 3	☐ 4
I feel secure	☐ 1	☐ 2	☐ 3	☐ 4
I make decisions easily	☐ 1	☐ 2	☐ 3	☐ 4
I feel inadequate	☐ 1	☐ 2	☐ 3	☐ 4
I am content	☐ 1	☐ 2	☐ 3	☐ 4
Some unimportant though runs through my mind and bothers me	☐ 1	☐ 2	☐ 3	☐ 4
I take disappointments so keenly that I can’t put them out of my mind	☐ 1	☐ 2	☐ 3	☐ 4
I am a steady person	☐ 1	☐ 2	☐ 3	☐ 4
I get in a state of tension or turmoil as I think over my recent concerns and interests	☐ 1	☐ 2	☐ 3	☐ 4

APPENDIX 1 - CWS B: PRESENT CONCERNS

B1 Most of us worry about something. This list is not meant to give you more things to worry about, but we would just like to know if any of these things are worrying you at all right now. Please tick a box for each item to show how much of a worry it is to you at the moment; from the left hand side if it is not a worry to the right hand side if it is something that you are extremely worried about.

Tick one on each line

	Not a worry					Major Worry
Your Housing	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Money Problems	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Problems with the law	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Your relationship with your husband/partner	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Your relationship with your family and friends	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Your own health	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
The health of someone close to you	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Employment problems	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
The possibility of something being wrong with the baby	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Going to hospital	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Internal examinations	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Giving birth	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Coping with the new baby	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Giving up work	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Whether your partner will be with you for the birth	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
The possibility of miscarriage	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

APPENDIX 1 MBSS C: COPING MECHANISMS

Most of us cope with situations in different ways. We would like to know how you would deal these different events

C1 Vividly imagine that you are **afraid** of the dentist and have to get some dental work done. Which of the following would you do? Tick **all** of the statements that might apply to you.

I would ask the dentist exactly what work was going to be done ☐ 1

I would take a tranquilizer or have a drink before going ☐ 2

I would try to think about pleasant memories ☐ 3

I would want the dentist to tell me when I would feel pain ☐ 4

I would try to sleep ☐ 5

I would watch all the dentist's movements and listen for the sound of the drill ☐ 6

I would watch the flow of water from my mouth to see if it contained blood ☐ 7

I would do mental puzzles in my mind ☐ 8

C2 Vividly imagine that you are being held hostage by a group of armed terrorists in a public building. Which of the following would you do? Tick **all** of the statements that might apply to you.

I would sit by myself and have as many daydreams and fantasies as I could ☐ 1

I would stay alert and try to keep myself from falling asleep ☐ 2

I would exchange life stories with the other hostages ☐ 3

If there was a radio present, I would stay near it and listen to the bulletins about what the police were doing ☐ 4

I would watch every movement of my captors and keep an eye on their weapons ☐ 5

I would try to sleep as much as possible ☐ 6

I would think about how nice it's going to be when I get home ☐ 7

I would make sure I knew where every possible exit was ☐ 8

C3 Vividly imagine that, due to a large drop in sales, it is rumored that several people in your department at work will be laid off. Your supervisor has turned in an evaluation of your work for the past year. The decision about lay-offs has been made and will be announced in several days. Tick **all** of the statements that might apply to you.

I would talk to my fellow workers to see if they knew anything about what the supervisor evaluation of me said ☐ 1

I would review the list of duties for my present job and try to figure out if I had fulfilled them all ☐ 2

I would go to the movies to take my mind off things ☐ 3

I would try to remember any arguments or disagreements I might have had that would have resulted in the supervisor having a lower opinion of me ☐ 4

I would push all thoughts of being laid off out of my mind ☐ 5

I would tell my spouse that I'd rather not discuss my chances of being laid off ☐ 6

I would try to think which employees in my department the supervisor might have thought had done the worst job ☐ 7

I would continue doing my work as if nothing special was happening ☐ 8

C4 Vividly imagine that you are on an airplane, thirty minutes from your destination, when the plane unexpectedly goes into a deep dive and then suddenly levels off. After a short time, the pilot announces that nothing is wrong, although the rest of the ride may be rough. You, however, are not convinced that all is well. Tick **all** of the statements that might apply to you.

I would carefully read the information provided about safety features in the plane and make sure I knew where the emergency exits were ☐ 1

I would make small talk with the passenger beside me ☐ 2

I would watch the end of the movie, even if I had seen it before ☐ 3

I would call for the flight attendant and ask what exactly the problem was ☐ 4

I would order a drink from the flight attendant or take a tranquilizer ☐ 5

I would listen carefully to the engines for unusual noises and would watch the crew to see if their behaviour was out of the ordinary ☐ 6

I would talk to the passenger beside me about what might be wrong ☐ 7

I would settle down and read a book or magazine or write a letter ☐ 8

APPENDIX 1 Demographics D: ABOUT YOU

We would like to find out more about you and your circumstances.

D1 Please write in the month and year of your birth ☐☐ 19 ☐☐

Month Year

D2 Please indicate your marital status (Tick one only)

Single ☐ 1

Married ☐ 2

Civil Partnership ☐ 3

Partner ☐ 4

Other ☐ 5

Please write in marital status if not listed ☐

D3 What is your ethnic group? (Tick one only)

White ☐ 1

Mixed ☐ 2

Asian ☐ 3

Black ☐ 4

Far Eastern ☐ 5

Other ethnic group ☐ 6

Please write in ethnic group if not listed ☐

D4 Which of these qualifications do you have? (Tick one only)

GCSE level (CSE or O level) ☐ 1

A- level or equivalent ☐ 2

Degree or equivalent ☐ 3

None of these ☐ 4

Please write in qualification if not listed

D5 What is your postcode?

D6 What is the title of your main job?

D7 Do you smoke? Yes ☐ 1 No ☐ 2

D8 How many cigarettes per day?

D9 Do you drink alcohol? Yes ☐ 1 No ☐ 2

D10 How many units of alcohol do you drink per week?

(A unit is a standard wine glass or a measure of spirits)

D11 Please list any medical problems you have e.g. asthma, diabetes, high blood pressure;

D12 Please list any psychiatric problems you have;

D13 Have you ever suffered from depression? Yes ☐ 1 No ☐ 2

D14 If yes are you currently being treated? Yes ☐ 1 No ☐ 2

D15 What medications are you taking?

D16 Do you give your permission for us to take additional information from your medical records? Yes ☐ 1 No ☐ 2

E: PREVIOUS PREGNANCIES

These are just a few questions about your previous pregnancies. We are asking these as past experiences can affect the way women feel in later pregnancies.

E1 How many times have you been pregnant?
(Including this pregnancy) ☐

E2 How many children do you have? ☐

E3 How many miscarriages have you had? ☐

E4 Have all of these been with your current partner? Yes ☐ 1 No ☐ 2

E5 If no, which of the pregnancies in the table below e.g. (P1 or P2) were with a different partner? ☐

E6 How many years have you been trying to conceive? ☐

E7 Please include all pregnancies in the following table:

Pregnancy						
	P1	P2	P3	P4	P5	P6
Year						
Number of weeks						
Outcome						
Miscarriage						
Still birth						
Ectopic						
Termination						
Vaginal delivery						
Caesarean section						
Ventouse						
Forceps						

E8 How long has it been since your last miscarriage?

E9 Did you have fertility treatment prior to conception? Yes ☐ 1 No ☐ 2

If "Yes" please give details.

APPENDIX 1 Semantic Differentiation Scale F: ABOUT THE SCANS

This section is about your views of the ultrasound scans, which you are going to have and are increasingly used in early pregnancy and antenatal care

F1 Do you expect that the scans are going to give you? Please circle the answer closest to how you feel

Good News Bad News Neither good nor bad Not Sure

F2 For each of the following pairs of words with opposite meaning, please circle the number along the scale, which you think says what you feel about ultrasound scanning. There are no right or wrong answers; just let us know what you think.

Safe	1	2	3	4	5	6	7	Unsafe
Reassuring	1	2	3	4	5	6	7	Worrying
Uplifting	1	2	3	4	5	6	7	Disappointing

F3 For each of the following pairs of words with opposite meaning, please circle the number along the scale, which you think, says what you feel about your pregnancy. There are no right or wrong answers; just let us know what you think.

Calm	1	2	3	4	5	6	7	Nervous
Reassured	1	2	3	4	5	6	7	Worried
Relieved	1	2	3	4	5	6	7	Concerned

APPENDIX 2 post 6 &8 week scan and 7&9 week questionnaire S-anxiety

Participant number:

Date:

Gestation:

Early Pregnancy Ultrasound Scanning

Thank you for taking you time to complete this questionnaire, we hope you find it interesting. The questions are easy to answer.

If there is a small number beside the box please ignore it, this is for office use.

APPENDIX 2 s- anxiety **A: SELF-EVALUATION Y1**

A1 A number of statements which people have used to describe themselves are given below. Read each statement and then tick the box to the right of the statement to indicate how you feel right at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feeling best.

	Not at all	Somewhat	Moderately	Very much
I feel calm	☐ 1	☐ 2	☐ 3	☐ 4
I feel secure	☐ 1	☐ 2	☐ 3	☐ 4
I am tense	☐ 1	☐ 2	☐ 3	☐ 4
I feel strained	☐ 1	☐ 2	☐ 3	☐ 4
I feel at ease	☐ 1	☐ 2	☐ 3	☐ 4
I feel upset	☐ 1	☐ 2	☐ 3	☐ 4
I am presently worrying over possible misfortune	☐ 1	☐ 2	☐ 3	☐ 4
I feel satisfied	☐ 1	☐ 2	☐ 3	☐ 4
I feel frightened	☐ 1	☐ 2	☐ 3	☐ 4
I feel comfortable	☐ 1	☐ 2	☐ 3	☐ 4
I feel self-confident	☐ 1	☐ 2	☐ 3	☐ 4
I feel nervous	☐ 1	☐ 2	☐ 3	☐ 4
I am jittery	☐ 1	☐ 2	☐ 3	☐ 4
I feel indecisive	☐ 1	☐ 2	☐ 3	☐ 4
I am relaxed	☐ 1	☐ 2	☐ 3	☐ 4
I feel content	☐ 1	☐ 2	☐ 3	☐ 4
I am worried	☐ 1	☐ 2	☐ 3	☐ 4
I feel confused	☐ 1	☐ 2	☐ 3	☐ 4
I feel steady	☐ 1	☐ 2	☐ 3	☐ 4
I feel pleasant	☐ 1	☐ 2	☐ 3	☐ 4

APPENDIX 3 Post 10 week questionnaire

Participant number: ☐

Date: ☐

Gestation: ☐

Early Pregnancy Ultrasound Scanning

Thank you for taking you time to complete this questionnaire, we hope you find it interesting.

The questions are easy to answer.

For most questions, just tick the box beside the answer that applies to you.

There will be an instruction at the top of each section telling you to either tick one box only, or all that apply.

If there is a small number beside the box please ignore it, this is for office use.

Other questions require you to either circle a single number or a word, which applies best to you

There may also be a long box for you to write your answer in.

APPENDIX 3 s- anxiety A: SELF-EVALUATION Y1

A1 A number of statements which people have used to describe themselves are given below. Read each statement and then tick the box to the right of the statement to indicate how you feel right at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feeling best.

	Not at all	Somewhat	Moderately	Very much
I feel calm	☐ 1	☐ 2	☐ 3	☐ 4
I feel secure	☐ 1	☐ 2	☐ 3	☐ 4
I am tense	☐ 1	☐ 2	☐ 3	☐ 4
I feel strained	☐ 1	☐ 2	☐ 3	☐ 4
I feel at ease	☐ 1	☐ 2	☐ 3	☐ 4
I feel upset	☐ 1	☐ 2	☐ 3	☐ 4
I am presently worrying over possible misfortune	☐ 1	☐ 2	☐ 3	☐ 4
I feel satisfied	☐ 1	☐ 2	☐ 3	☐ 4
I feel frightened	☐ 1	☐ 2	☐ 3	☐ 4
I feel comfortable	☐ 1	☐ 2	☐ 3	☐ 4
I feel self-confident	☐ 1	☐ 2	☐ 3	☐ 4
I feel nervous	☐ 1	☐ 2	☐ 3	☐ 4
I am jittery	☐ 1	☐ 2	☐ 3	☐ 4
I feel indecisive	☐ 1	☐ 2	☐ 3	☐ 4
I am relaxed	☐ 1	☐ 2	☐ 3	☐ 4
I feel content	☐ 1	☐ 2	☐ 3	☐ 4
I am worried	☐ 1	☐ 2	☐ 3	☐ 4
I feel confused	☐ 1	☐ 2	☐ 3	☐ 4
I feel steady	☐ 1	☐ 2	☐ 3	☐ 4
I feel pleasant	☐ 1	☐ 2	☐ 3	☐ 4

APPENDIX 3 T- anxiety A: SELF-EVALUATION Y2

A2 A number of statements which people have used to describe themselves are given below. Read each statement and then tick the box to the right of the statement which indicates how you generally feel.

	Almost Never	Sometimes	Often	Almost Always
I feel pleasant	☐ 1	☐ 2	☐ 3	☐ 4
I feel nervous and restless	☐ 1	☐ 2	☐ 3	☐ 4
I feel satisfied with myself	☐ 1	☐ 2	☐ 3	☐ 4
I wish I could be as happy as others seem to be	☐ 1	☐ 2	☐ 3	☐ 4
I feel like a failure	☐ 1	☐ 2	☐ 3	☐ 4
I feel rested	☐ 1	☐ 2	☐ 3	☐ 4
I am “calm, cool and collected”	☐ 1	☐ 2	☐ 3	☐ 4
I feel that difficulties are piling up so that I cannot overcome them	☐ 1	☐ 2	☐ 3	☐ 4
I worry too much over something that really doesn't matter	☐ 1	☐ 2	☐ 3	☐ 4
I am happy	☐ 1	☐ 2	☐ 3	☐ 4
I have disturbing thoughts	☐ 1	☐ 2	☐ 3	☐ 4
I lack self-confidence	☐ 1	☐ 2	☐ 3	☐ 4
I feel secure	☐ 1	☐ 2	☐ 3	☐ 4
I make decisions easily	☐ 1	☐ 2	☐ 3	☐ 4
I feel inadequate	☐ 1	☐ 2	☐ 3	☐ 4
I am content	☐ 1	☐ 2	☐ 3	☐ 4
Some unimportant though runs through my mind and bothers me	☐ 1	☐ 2	☐ 3	☐ 4
I take disappointments so keenly that I can't put them out of my mind	☐ 1	☐ 2	☐ 3	☐ 4
I am a steady person	☐ 1	☐ 2	☐ 3	☐ 4
I get in a state of tension or turmoil as I think over my recent concerns and interests	☐ 1	☐ 2	☐ 3	☐ 4

APPENDIX 3 CWS B: PRESENT CONCERNS

B1 Most of us worry about something. This list is not meant to give you more things to worry about, but we would just like to know if any of these things are worrying you at all right now. Please tick a box for each item to show how much of a worry it is to you at the moment; from the left hand side if it is not a worry to the right hand side if it is something that you are extremely worried about.

	Not a worry					Major Worry
Your Housing	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Money Problems	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Problems with the law	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Your relationship with your husband/partner	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Your relationship with your family and friends	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Your own health	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
The health of someone close to you	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Employment problems	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
The possibility of something being wrong with the baby	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Going to hospital	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Internal examinations	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Giving birth	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Coping with the new baby	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Giving up work	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Whether your partner will be with you for the birth	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
The possibility of miscarriage	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Tick one on each line

APPENDIX 3 -Semantic Differentiation Scale C: ABOUT THE SCANS

This section is about your views of the ultrasound scans that you had in early pregnancy.

C1 How many scans ideally would you have wanted?

Daily ☐ 1

Weekly ☐ 2

Every two weeks ☐ 3

Monthly ☐ 4

Any time I was worried ☐ 5

None ☐ 6

Other- please specify ☐

C2 For each of the following pairs of words with opposite meaning, please circle the number along the scale which you think says what you feel about ultrasound scanning. There are no right or wrong answers, just let us know what you think

Safe	1	2	3	4	5	6	7	Unsafe
Reassuring	1	2	3	4	5	6	7	Worrying
Uplifting	1	2	3	4	5	6	7	Disappointing

C3 For each of the following pairs of words with opposite meaning, please circle the number along the scale, which you think, says what you feel about your pregnancy. There are no right or wrong answers; just let us know what you think.

Calm	1	2	3	4	5	6	7	Nervous
Reassured	1	2	3	4	5	6	7	Worried
Relieved	1	2	3	4	5	6	7	Concerned

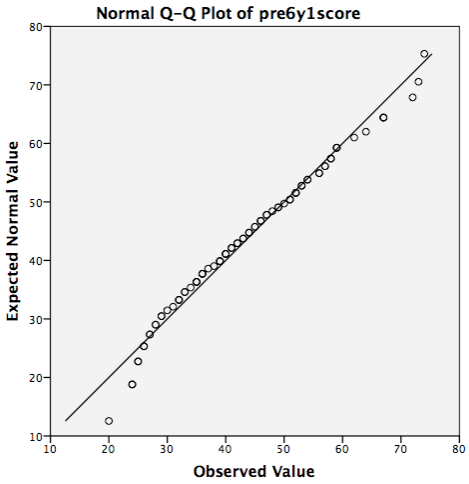
C4 Over all were the ultrasound scans reassuring? Please circle the most appropriate answer.

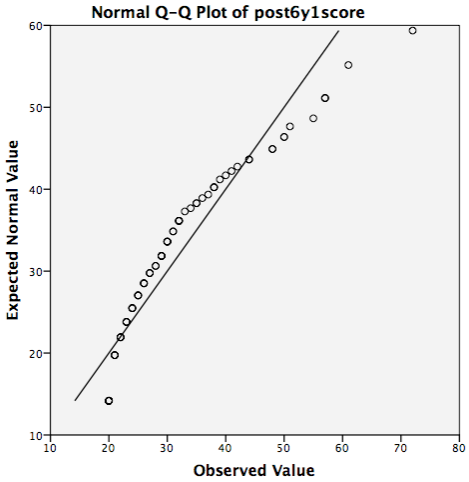
Strongly agree agree neither disagree strongly disagree

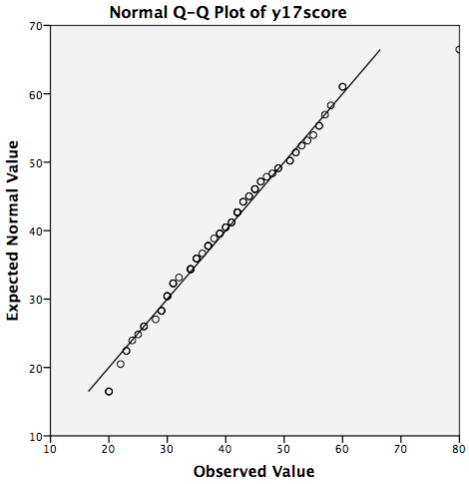
C5 Do you think you benefited from seeing a dedicated team throughout your early pregnancy?

Strongly agree agree neither disagree strongly disagree

APPENDIX 4 q-q plots to show the distribution of results of each of the STAI scores



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Observed Value
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60
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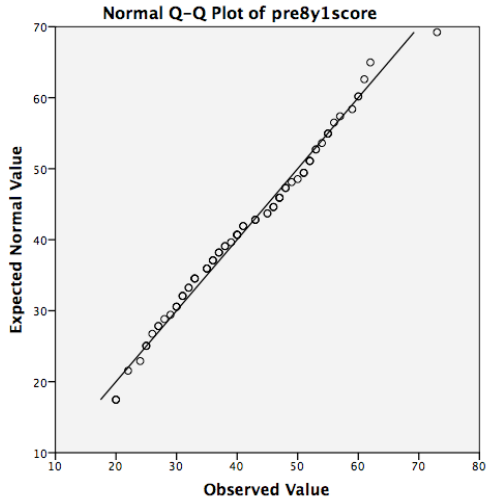
80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50
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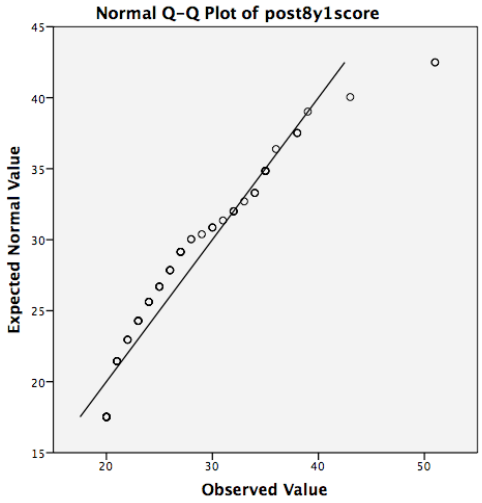
80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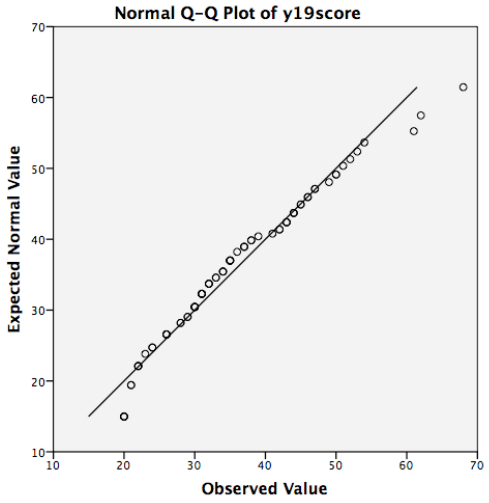
30
25
20
15
20
30
40
50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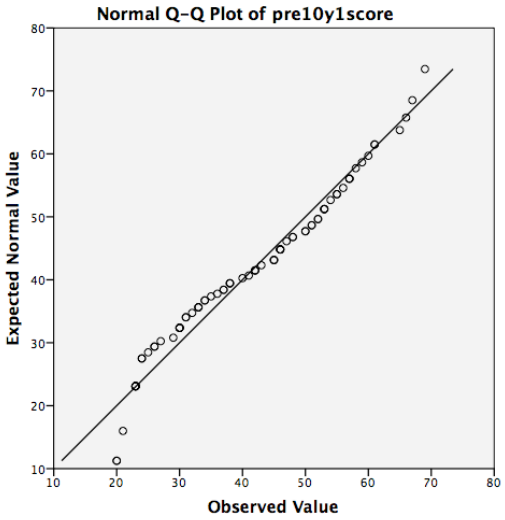
20
30
40
50
60
70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Observed Value
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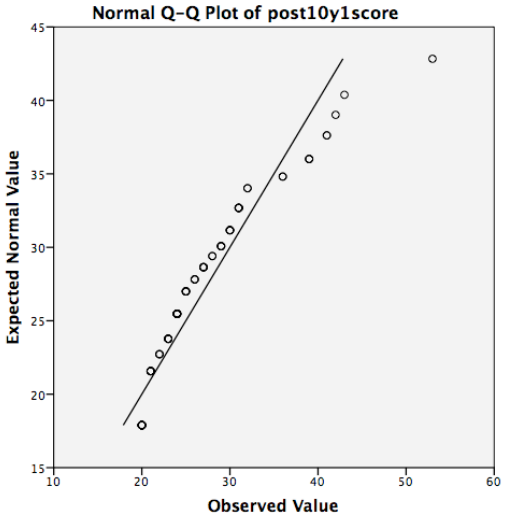
70
80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Observed Value
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20
30
40
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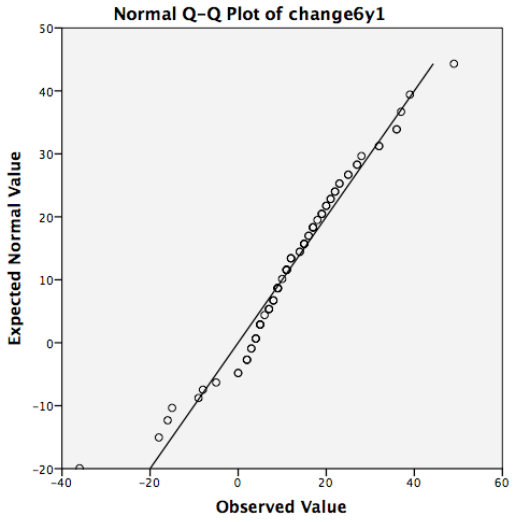
60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20
40
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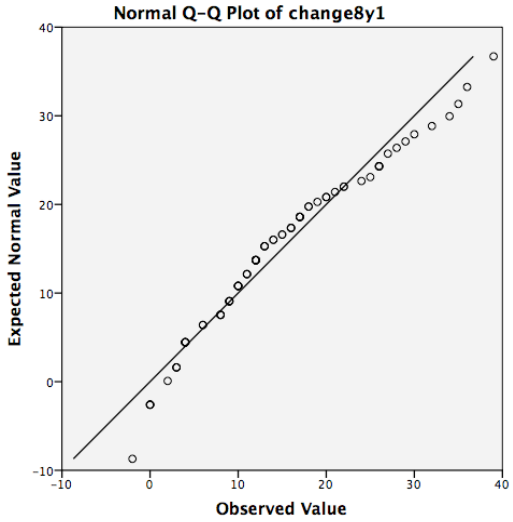
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Observed Value
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-10
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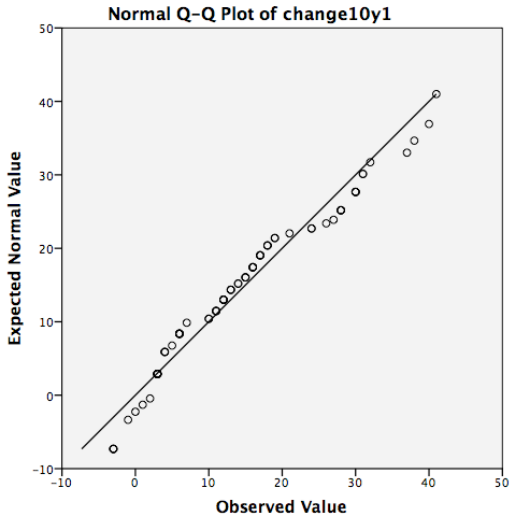
40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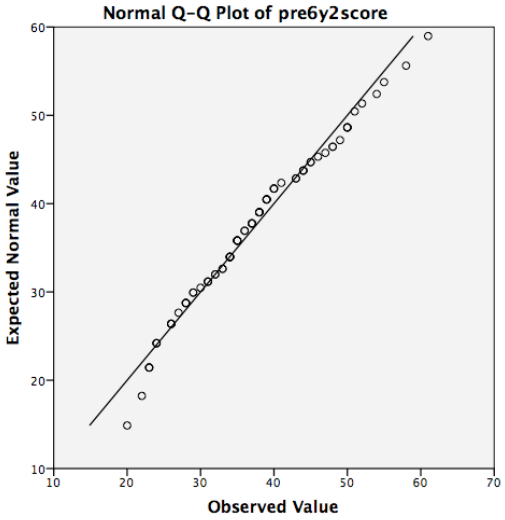
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Expected Normal Value
Observed Value
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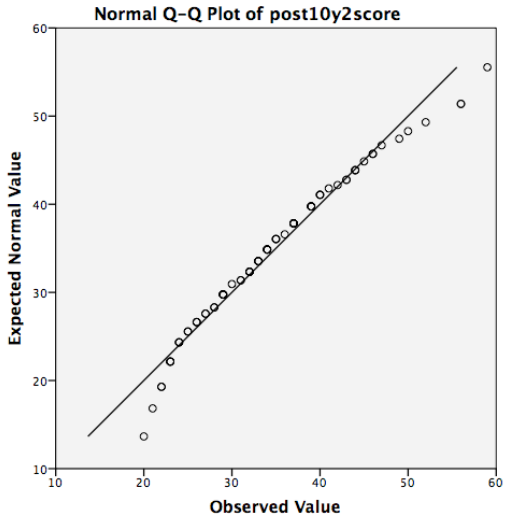
70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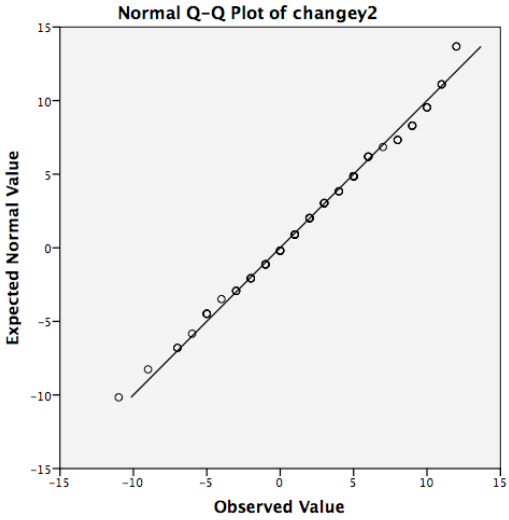
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Expected Normal Value
Observed Value
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15

Appendix 5 Ethical Approval Letter

NHS
National Research Ethics Service

NRES Committee London - Bentham
Research Ethics Committee Offices
South House
Block A, Rooms 7-12
Royal Free Hospital
Pond Street
London
NW3 2QG

Tel: 020 7794 0500 x34836

13 June 2011

Dr Judith Hamilton
Consultant Gynaecologist and Clinical Lead Early Pregnancy Unit
Guy's and St Thomas' NHS Foundation Trust
Emergency Gynaecology Unit
8th Floor, North Wing, St Thomas'
Westminster Bridge Road
SE1 7EH

Dear Dr Hamilton

Study title: **Attitudes of women with recurrent miscarriage to serial ultrasound scanning in a new pregnancy and subsequent outcome of that pregnancy.**
REC reference: **10/H0715/69**
Amendment number: 1

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Advertisement	4	05 April 2011
Questionnaire	2	01 April 2011
Questionnaire: Early Pregnancy Ultrasound Scanning		
GP/Consultant Information Sheets	2	05 April 2011
Participant Information Sheet	5	05 April 2011
Participant Information Sheet	6	05 April 2011
Notice of Substantial Amendment (non-CTIMPs)		

Appendix 5 Ethical Approval Letter

Covering Letter		

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

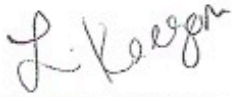
All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

10/H0715/69:	**Please quote this number on all correspondence**

Yours sincerely



Professor David Katz
Chair

E-mail: laura.keegan@nhs.net

Enclosures: List of names and professions of members who took part in the review

Copy to: Ms Karen Ignatian

Appendix 6 R&D Approval

Guy's and St Thomas' NHS
NHS Foundation Trust

Research & Development
16th Floor Tower Wing
Guy's Hospital
Great Maze Pond
London SE1 9RT
Tel: 020 7188 7188

Date: 20th April 2011

Dear Sarah

Title: Attitudes of women with recurrent miscarriage to serial ultrasound scanning in a new pregnancy and subsequent outcome of that pregnancy.

In accordance with the Department of Health's Research Governance Framework for Health and Social Care, all research projects taking place within the Trust must receive a favourable opinion from an ethics committee and approval from the Department of Research and Development (R&D) prior to commencement.

- **Ethics Number:** 10/H0715/069
- **Sponsor:** GSTT
- **Funder:** pending
- **End Date:** 03/04/2012
- **Protocol:** version 5
- **Site:** GSTT
- **R&D Approval Date:** 20th April 2011

NHS permission for the above research has been granted on the basis described in the application form, protocol and supporting documentation as listed in the ethics letter of favourable opinion letter dated 17th January. I am pleased to inform you that we are approving the work to proceed within Guy's and St Thomas' NHS Foundation Trust and that the study has been allocated the Trust R&D registration number RJ111/N120. Please quote the R&D registration number in any communications with the R&D Department regarding your project.

Conditions of Approval:

- The principal investigator must ensure that the recruitment figures are reported.
- The principal investigator must notify R&D of the actual end date of the project.
- R&D must be notified of any changes to the protocol prior to implementation.
- The project must follow the agreed protocol and be conducted in accordance with all Trust Policies and Procedures especially those relating to research and data management.
- Members of the research team must have appropriate substantive or honorary contracts with the Trust prior to the study commencing. Any additional researchers who join the study at a later stage must also hold a suitable contract.

Appendix 6 R&D Approval

Data Protection:
Please ensure that you are aware of your responsibilities in relation to The Data Protection Act 1998, NHS Confidentiality Code of Practice, NHS Caldicott Report and Caldicott Guardians, the Human Tissue Act 2004, Good Clinical Practice, the NHS Research Governance Framework for Health and Social Care, Second Edition April 2005 and any further legislation released during the time of this study.

The Principal Investigator is responsible for ensuring that Data Protection procedures are observed throughout the course of the project.

If the project is a clinical trial under the European Union Clinical Trials Directive the following must also be complied with:

1. The EU Directive on Clinical Trials (Directive 2001/20/EC) and UK's implementation of the Directive: The Medicines for Human Use (Clinical Trials) Regulations 2004;
2. The EU Directive on Principles and Guidelines for Good Clinical Practice (EU Commission Directive 2005/28/EC); and UK's implementation of the Directive: The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006;

If appropriate it is recommended that you register with the Current Controlled Trials website; http://isrctn.org/

Amendments:
Please ensure that you submit a copy of any amendments made to this study to the R&D Department.

Annual Progress Report:
It is obligatory that an annual report is submitted by the Chief Investigator to the research ethics committee, and we ask that a copy is sent to the R&D Department. The yearly period commences from the date of receiving a favourable opinion from the ethics committee.

Please submit a copy of the progress report on the anniversary of the Ethics favourable opinion **(17 January)**

Should you require any further information please do not hesitate to contact us.

In line with the Research Governance Framework, your project may be randomly selected for monitoring for compliance against the standards set out in the Framework. For information, the Trust's process for the monitoring of projects and the associated guidance is available from the Trust's intranet or on request from the R&D Department. You will be notified by the R&D Department if and when your project has been selected as part of the monitoring process. No action is needed until that time.

Thank you for registering your research project.

Yours sincerely

Ignatian

Karen Ignatian
R&D Governance Manager

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