

Miscarriage Matters:

Findings from The Lancet Miscarriage Series and Implications for Policy with Recommendations



Tommy's

Together, for every baby

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EXECUTIVE SUMMARY

"When we lost our third baby, as heartbroken as I was, it was almost a relief that something would get done."

Julie

Miscarriage, defined as the loss of a pregnancy before 24 weeks, is the most common complication of pregnancy. An estimated 1 in 5 women experience the heartbreak of miscarriage, which has an untold emotional and physical impact on the whole family. Early miscarriages occur before 12 weeks, and this is when the majority (98%) of miscarriages happen. The **national rate of miscarriage is not currently recorded in the UK**, and so it is difficult to know the exact number of women experiencing miscarriage every year. Multiple regional studies have been carried out to calculate this, and the **estimated rate ranges from 15% up to 30%**. Recurrent pregnancy loss is currently defined as three or more consecutive miscarriages in the UK.

The grief and psychological impact of miscarriage is often not comprehended, both by society and by healthcare professionals. The loss can often be minimised by the view that a pregnancy before 12 weeks 'isn't a real baby' or that 'it just wasn't meant to be'.

Miscarriage can be isolating. Many women do not share the news of their pregnancy until they reach 12 weeks, and a woman may not tell their family, friends, colleagues or even their partner about an early pregnancy loss. Many women and their partners suffer from this grief in silence, as psychological effects of miscarriage may have little or no outward physical manifestation, and so can go unrecognised by healthcare professionals, family and friends.

In 2016, Tommy's opened the UK's first centre dedicated to miscarriage research to find answers for families suffering from early miscarriage. The centre undertakes innovative research to develop tests and treatments for early pregnancy loss. We want to be able to tell women why their baby died, and help them to increase their chances of having a successful pregnancy.

Researchers at the Tommy's National Centre for Miscarriage Research have been invited to submit a series of review articles on miscarriage to The Lancet journal. There are three papers in total focusing on:

1. **Miscarriage matters: the epidemiological, physical, psychological and economic burden of early pregnancy loss**
2. **Sporadic miscarriage: evidence to provide effective care**
3. **Recurrent miscarriage: evidence to accelerate action**

To write these articles, multiple literature searches were performed for systematic reviews and primary studies on MEDLINE (from the database's inception to May 2020). Systematic reviews and primary studies were searched for risk factors for miscarriage (demographic, lifestyle, clinical and environmental factors). A separate search was conducted for observational studies of obstetric, perinatal and long-term health risks associated with miscarriage. Comprehensive literature searches were performed to define optimal care for women suffering sporadic or recurrent miscarriages. For each systematic review, the raw aggregate data were extracted from every included individual study to estimate unadjusted and adjusted associations. All extracted raw data were meta-analysed with inverse variance weighted method to combine odds ratios (ORs) to produce a pooled OR. Random effects models were used for all analyses to allow for between-study heterogeneity.

KEY FINDINGS

- The short-term national economic costs of miscarriage, associated with immediate costs to hospital and community health and social services, are estimated to be £471 million annually to the UK. Taking a wider view of miscarriage would undoubtedly raise this figure, once GP-associated costs and the costs of caring for couples with psychological conditions brought on by a miscarriage are included. Other factors to consider would be longer-term employment and occupational status, income, and receipt of social welfare benefits.
- Female age is one of the most prominent risk factors for miscarriage, along with the number of previous losses. Miscarriage rate is the lowest in women aged 20 – 29 years at 12%, increasing steeply to 65% in women aged 45 years and over.
- Black women are at a 40% increased relative risk of miscarriage than White women.
- Smoking is an important modifiable risk factor for miscarriage. Women who smoke in the first trimester are 1.2 times more likely to have a miscarriage than non-smokers, and the risk of miscarriage increases with the amount smoked (1% increase in relative risk per cigarette smoked per day).
- A woman's BMI is associated with the risk of miscarriage. The BMI associated with the least risk of miscarriage is 18.5 – 24.9 kg/m², considered to be the healthy weight range, whilst women with a BMI under 18.5 are 1.6 times more likely to miscarry and those with a BMI over 30 were 1.9 times more likely to miscarry.
- Miscarriage, particularly recurrent miscarriage, is a sentinel risk marker for obstetric complications in a future pregnancy. The risk of preterm birth increases stepwise with each previous miscarriage, demonstrating a biological gradient. Women after one miscarriage are 1.2 times more likely to have a preterm birth, after two 1.4 times more likely and after three 1.8 times more likely. Miscarriage is associated with an increased risk of placental dysfunction disorders in later pregnancies. Our review found that after three miscarriages women are 1.7 times more likely to experience placental abruption in a later pregnancy, and 1.6 times more likely to have a stillbirth.

- Recurrent miscarriage is associated with a significantly increased risk of cardiovascular disease and venous thromboembolism. After experiencing three miscarriages, women are 1.4 times more likely to suffer from cardiovascular diseases, and 6.1 times more likely to suffer from venous thromboembolism.
- Anxiety, depression, post-traumatic stress and suicide are strongly associated with miscarriage. It is important to note that it is not only recurrent miscarriage that is associated with these psychological conditions, but also that one miscarriage can have a significant psychological impact. A recent study^[1] from the Tommy's centre found that nine months after a pregnancy loss, 18% of women met the criteria for post-traumatic stress, 17% for moderate to severe anxiety, and 6% for moderate to severe depression. This demonstrates that distress remains at clinically important levels for some months after an early pregnancy loss. One miscarriage also increased the likelihood of suicide, with women who had experienced miscarriage being 3.8 times more likely to die by suicide.

RECOMMENDATIONS

1. Miscarriages must be recorded so that the rate of miscarriage can be measured nationally

Data on the number of miscarriages must be made available along with stillbirth and preterm birth rates. This will allow us to fully understand the scope of the problem and enable the setting of targets for reduction.

Recommendation: A process for recording miscarriage exists, however standardisation of data entry and then centralised data collation is the challenge. Look to the Department of Health to incorporate miscarriage data into a women's reproductive data set to complement the maternity data set.

2. Access to care after sporadic miscarriage must be available with a clear pathway for follow-up mental health support

Women must receive appropriate, standardised care during and after their first miscarriage, including the best management of miscarriage and pre-conceptual support to intervene on modifiable risk factors. Women and partners should have access to follow-up mental health support to help reduce mental illness post-miscarriage.

Recommendation: Healthcare professionals who are involved in the care of a woman who has miscarried and their partner to follow guidance within *The National Bereavement Care Pathway* developed to improve bereavement care and reduce variability in provision for families after miscarriage. This includes providing information about the emotional support available via the hospital Trust, primary care colleagues and via local and national support organisations, as well as standards for follow-up appointments, and a referral for a mental health assessment and, where appropriate, treatment. See also NICE guidance on antenatal/postnatal mental health (<https://www.nice.org.uk/guidance/qs115>).

3. Tests and treatments must be standardised across the UK through a 'graded approach' to recurrent miscarriage

Health services should standardise and structure care using a 'graded model' where women are offered online healthcare advice and support after one miscarriage, care in a nurse or midwife-led clinic after two miscarriages, and care in a medical consultant-led clinic after three miscarriages. This approach balances the need for evidence-based management and supportive care, whilst targeting health care resources appropriately. Where Early Pregnancy Units and miscarriage clinics already exist, these services are well-structured to deliver care within this graded model.

Recommendation: Implementation of a pre-conceptual care package after first miscarriage through the Public Health Outcomes Framework. Nurse-led care after second miscarriage and consultant-led care after third miscarriage through Trust miscarriage services or Early Pregnancy Unit. See model on page 9.

4. Specific, personalised care pathways should be established for high risk women

At-risk groups, including Black women, women over the age of 40 and women with existing medical conditions, must receive personalised care according to their individual risk factors, which may include a closer level of care and monitoring in early pregnancy.

Recommendation: Appropriate care pathways using a modified 'graded approach' to recurrent miscarriage should be established for these groups.

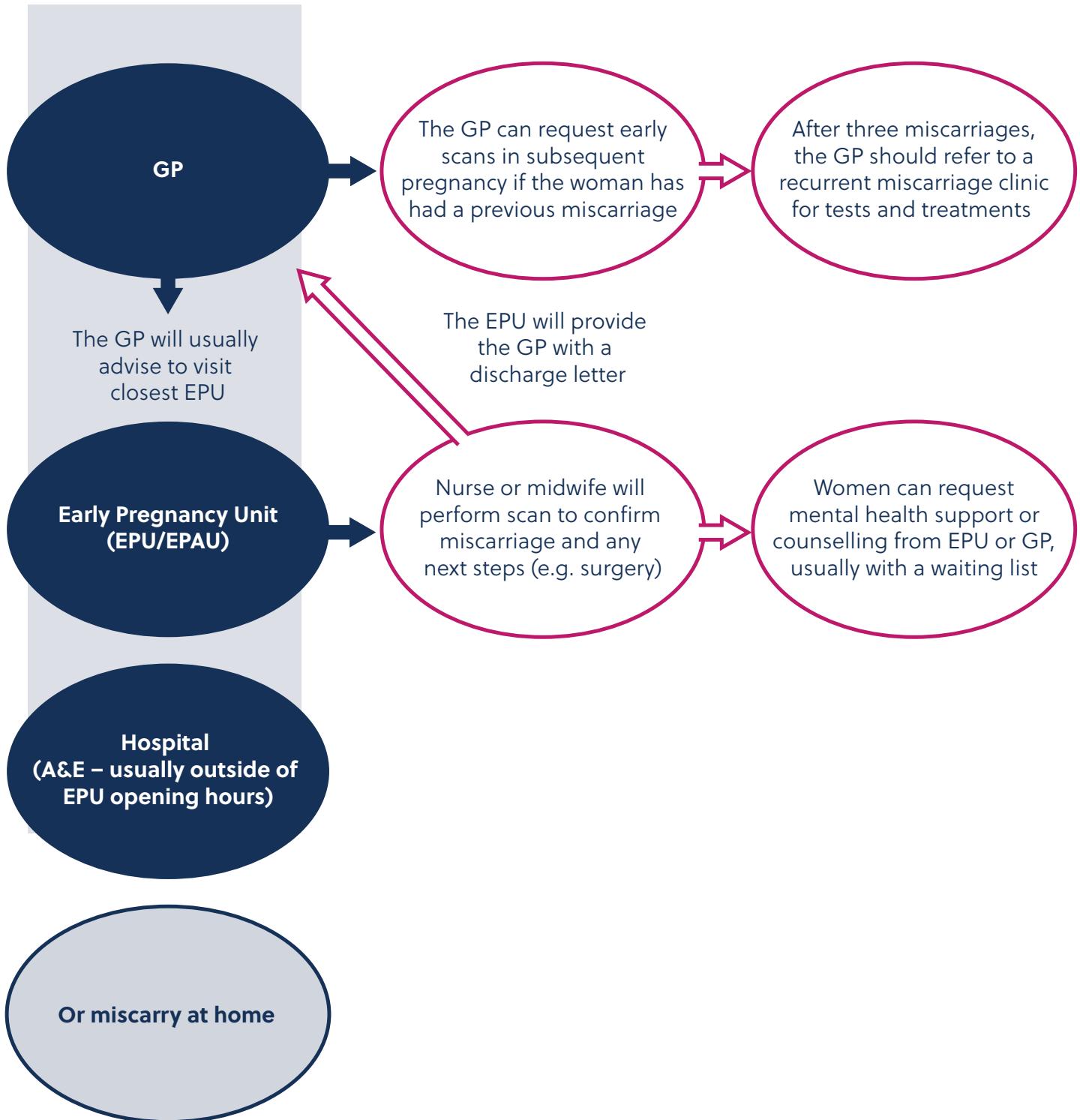
5. A clear pathway for preconception support and guidance must be established

Support and advice to plan and be ready for pregnancy should not only be widely available but also targeted to high-risk groups, including women with long-term conditions and those with multiple vulnerabilities. These groups should receive help early to plan pregnancy and additional support to have a healthy pregnancy.

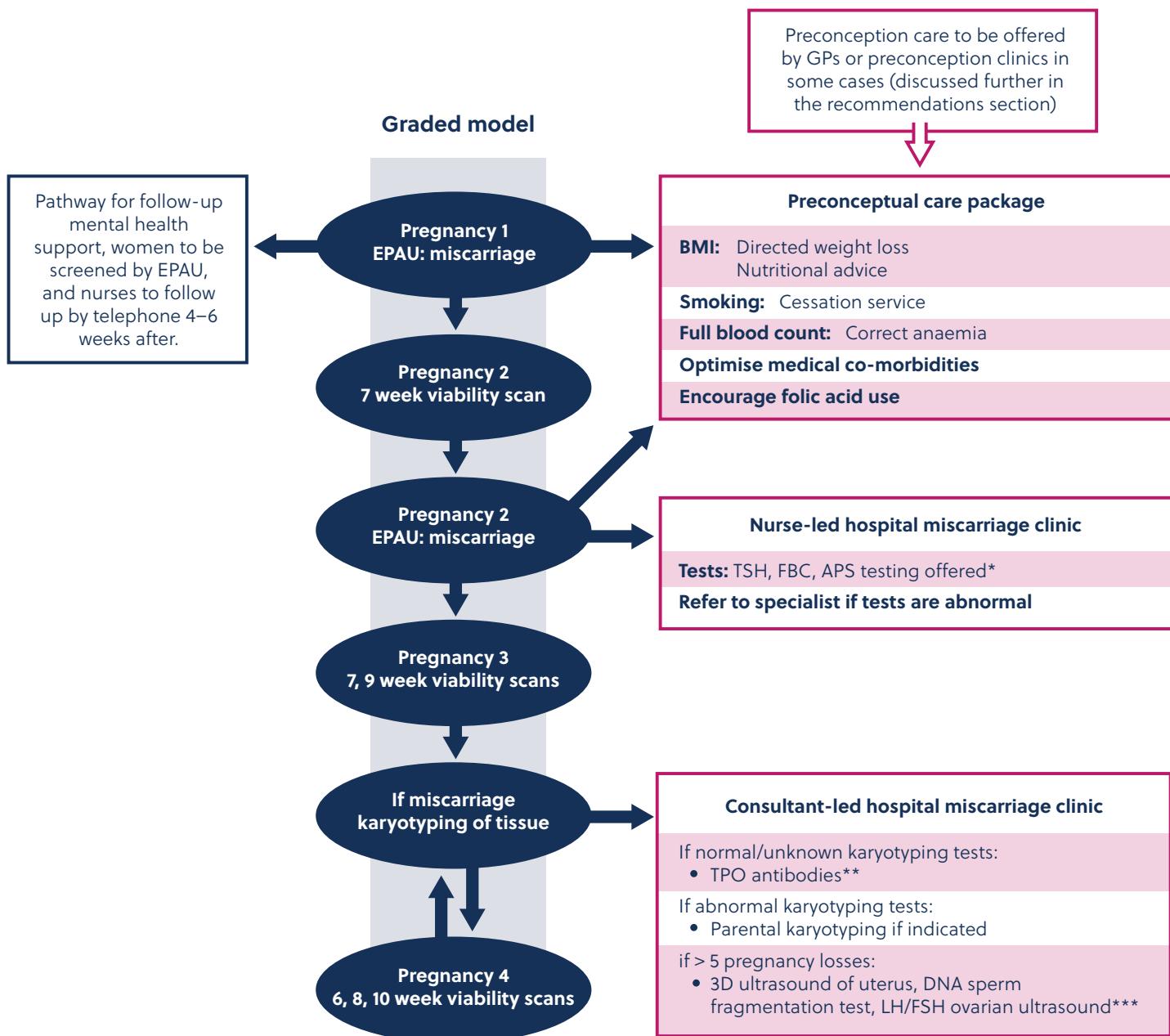
Recommendation: To build on the existing work of Public Health England and NHS England's Maternity Transformation Programme in developing a preconception pathway and preconception indicators. Preconception care to be offered by GPs or preconception clinics in some cases, using existing information and resources including the Tommy's 'Planning for Pregnancy' tool.

Currently, when a woman has symptoms of a miscarriage

She can present to:



Proposed System with graded model of care



Women with additional risk, e.g. Black women and women over 40 to be accelerated along this graded model of care (as discussed in the recommendations section).

* TSH = Thyroid function test; FBC = Full Blood Count test;
APS = Antiphospholipid syndrome test

** TPO antibodies = Thyroid antibodies

*** LH = Luteinizing hormone; FSH = Follicle stimulating hormone

INTRODUCTION

"It stays with you - it's not over. You'll never again have that moment of excitement or joy when you see those two little lines on a pregnancy test; that's no longer guaranteed, you're then worrying about how long until you lose it."

Charlotte

In the UK, miscarriage is defined as the loss of a pregnancy before 24 weeks. Although the most common complication of pregnancy, miscarriage is often misunderstood by women, men and healthcare professionals. Early miscarriages occur before 12 weeks, and this is when the majority of pregnancy losses happen. In 2016, Tommy's opened the UK's first centre dedicated to miscarriage research, focused on four key themes on early pregnancy loss centred around the questions commonly asked by patients suffering: what causes a miscarriage, what is the likelihood of a miscarriage in the next pregnancy, can we prevent a miscarriage from happening again, and how can we support women and their families emotionally to cope with what has happened.

Researchers at the Tommy's National Centre for Miscarriage Research have been invited to submit a series of review articles on miscarriage to The Lancet journal. There are three papers in total focusing on the following areas:

1. **Miscarriage matters: the epidemiological, physical, psychological and economic burden of early pregnancy loss**
2. **Sporadic miscarriage: evidence to provide effective care**
3. **Recurrent miscarriage: evidence to accelerate action**

This report will start with the importance of miscarriage, discussing the prevalence of miscarriage and referencing evidence to support the economic and psychological impact that miscarriage has. The report will then present the key findings from The Lancet Miscarriage Series, focussing on at-risk groups, modifiable risk factors, the effect of miscarriage on outcomes in subsequent pregnancies and the impact of miscarriage on the long-term health of the woman. The report will then outline the implications for policy and make recommendations to improve care, before finally closing with the next steps.

THE IMPORTANCE OF MISCARRIAGE

"We were basically told 'it's quite common, these things happen', and left to deal with it. I felt completely crushed, and kept this loss to myself so it was an incredibly lonely experience."

Anonymous

There are many misconceptions surrounding miscarriage, ranging from the belief that miscarriage is a rare occurrence to the perception that miscarriage grief isn't as real or acute as other forms of bereavement. We know that some miscarriages are a natural response from the body. Up to 50% of miscarriages are caused by chromosomal abnormalities in the embryo, in which case the miscarriage cannot be prevented. However, even when this is the case, the experience of a miscarriage still takes a huge emotional toll on the mother and their partner. This also means that around half of miscarriages have no identifiable cause, highlighting the lack of knowledge around the reasons for early pregnancy loss. This section will discuss why miscarriage must be prioritised in maternal health care and research, focusing on the prevalence, cost and psychological effects of miscarriage.

The prevalence of miscarriage

Miscarriage is the most common complication of pregnancy, affecting thousands of couples in the UK every year. The average risk of miscarriage has been calculated to be 15.3% of all recognised pregnancies^[2], based on a systematic review of nine large cohort studies involving 4,638,974 pregnancies. This statistic is based on recognised pregnancies, and therefore does not include those losses that happen before the woman knows she is pregnant.

In the UK, there were 40-45,000 hospital admissions per year for miscarriage management^[3], but since miscarriages and pre-clinical pregnancy losses are commonly managed through outpatient expectant or medical management, the actual miscarriage rate and volume of women being seen in hospital is considerably higher. Unfortunately, since 2012 the data on hospital admissions for miscarriage are no longer included in the UK maternity statistics report. Inclusion of pre-clinical losses and those defined as the loss of a pregnancy before it could be identified on ultrasound scan, will increase the miscarriage rate.

The average population prevalence of women with one previous miscarriage is 10.8%, two miscarriages is 1.9% and three or more miscarriages is 0.7%^[4].

Miscarriages also have a profound effect on partners, with differences in the level and type of response between partners, which perhaps explains the higher level of relationship breakdown after pregnancy loss. This means that there is a large section of the population living with what is likely to have been a traumatic experience, both physically and emotionally.

"I can't talk too much about this second loss yet, it's too painful. Our experiences have put a lot of strain on our relationship and, for a while, it felt like the magic left our marriage when our baby died."

Markus

The psychological effects of miscarriage

"There's not a day that goes by where I don't wonder, what they'd have looked like, what they would've achieved, who they'd be as they grew."

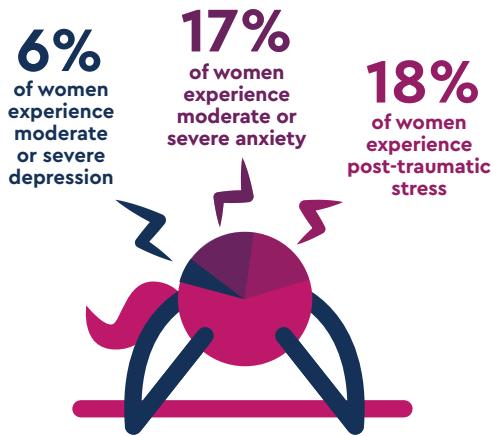
The lasting effects and my continual mental health issues, surrounding the recurrent miscarriages, could've been prevented, had I received proper after care and help following the losses."

Jemma was diagnosed with PTSD after the trauma of experiencing recurrent miscarriage

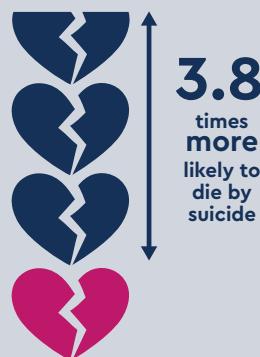
The grief that follows a miscarriage is often not comprehended, both by society and by healthcare professionals. The loss can often be minimised by the view that a pregnancy before 12 weeks 'isn't a real baby' or that 'it just wasn't meant to be'. Miscarriage is a distressing and life-changing event, causing intense pain for both parents. The psychological consequences of miscarriage involve both bereavement, and what may be a traumatic experience. Research shows that miscarriage grief is similar to that following a stillbirth.

Our systematic review identified that anxiety, depression and suicide are strongly associated with miscarriage^[5]. A multicentre prospective cohort study of 537 women following a miscarriage found that nine months after a pregnancy loss, 18% of women met the criteria for post-traumatic stress, 17% for moderate or severe anxiety, and 6% for moderate or severe depression^[6]. One miscarriage also increased the likelihood of suicide, with women who had experienced miscarriage being 3.8 times more likely to die by suicide.

Nine months after a pregnancy loss



A single miscarriage makes someone



Miscarriage can be isolating, as a woman may not tell their family, friends or even their partner about their loss. Many women and their partners are suffering from this grief in silence, as psychological effects of miscarriage may have little or no outward physical manifestation, and so can go unrecognised by healthcare professionals, family and friends.

Although not always visibly evident, it is clear that for many couples, miscarriage is not something that is forgotten about after the event. Rather, the emotional and psychological consequences have a long-term, and sometimes life-long, detrimental effect on their health.

[5] Quenby et al, "Miscarriage Matters"

[6] Farren et al, "Posttraumatic stress, anxiety and depression following miscarriage and ectopic pregnancy: a multicenter, prospective, cohort study" American Journal of Obstetrics and Gynaecology. (2020)

The cost of miscarriage

A systematic review has been undertaken to identify and summarise evidence on the economic cost of miscarriage, cost-effectiveness and preference-based outcomes derived using economic methods.

Published evidence on the economic consequences of miscarriage has largely focused on direct health service costs associated with miscarriage treatment procedures. A few studies have estimated the non-healthcare costs associated with miscarriage or its management, and these have mainly concentrated on the economic value of lost productivity for women experiencing miscarriage. These studies have highlighted both the economic costs of time taken off work and lower productivity after women had returned to work.

The economic studies emerging from our literature review typically adopt a short-term time view focusing on the initial treatment period. They do not cover long lasting effects such as the economic consequences associated with increased risk of psychological ill health.

This review has found that the short-term national economic costs of miscarriage, associated with immediate costs to hospital and community health and social services and estimates of costs associated with lost productivity, are estimated to be £471 million annually to the UK^[7].



Taking a wider view of miscarriage would undoubtedly raise this figure, once GP-associated costs and the costs of caring for couples with psychological conditions brought on by a miscarriage are included. Other factors to consider would be longer-term employment and occupational status, income, and receipt of social welfare benefits.

There is also evidence that a miscarriage is linked to complications in subsequent pregnancies. A previous miscarriage increases the risk of a premature or very premature delivery, and this risk increases with the number of previous miscarriages. In 2009, Tommy's funded a study, which estimated the cost of preterm births to the UK to be an extra £939 million a year^[8]. Reduction of the stillbirth and preterm birth rates is on the UK government agenda and is prominent in the implementation of the Saving Babies' Lives Care Bundle.

The associated costs of a miscarriage are therefore likely to be much higher than the initial estimate of £471 million identified. This demonstrates that the effects of miscarriage transcend the parents who have lost their baby, to have a much broader impact on the healthcare system and wider society, which, until now, had been mostly unacknowledged.

KEY FINDINGS FROM THE SERIES AND IMPLICATIONS FOR POLICY

This section will discuss the key findings from The Lancet Miscarriage Series and the relevant implications for policy and the NHS Long Term Plan where appropriate.

This will focus on:

1. at-risk groups,
2. preconception care for those with modifiable risk factors,
3. the effect of miscarriage on subsequent pregnancies,
4. the effect of miscarriage on the long-term health of the woman.

1. At risk groups

**Black women are
40%
more likely
to have a
miscarriage
than White
women^[9]**



Ethnicity		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>Our review has found that Black women are more likely to have a miscarriage than Caucasian women, with a 40% relative increase in risk^[9].</p> <p>This increase is after other factors have been accounted and adjusted for, making ethnicity a clear risk factor. This is in line with previous research on ethnic differences in pregnancy outcomes, such as the MBRRACE-UK report in 2020 that found that Black women are more than four times more likely to die in childbirth than White women, whilst Asian women were twice as likely^[10]. Black, Asian, and minority ethnic (BAME) women are also at an increased risk of having a preterm birth, stillbirth, neonatal death or a baby born with low birth weight.</p> <p>It is important to note that Asian women were not found to be at a higher risk of miscarriage than White women.</p>	<p>The reasons for this increase in miscarriage risk are not currently evident and this will be a research priority, however it is likely that the reasons for health disparities in general among these groups are complex and multi-dimensional.</p> <p>Action is needed to address these inequalities and to find out why Black women are at such a higher risk.</p> <p>A RCOG report on racial disparities in women's healthcare states that BAME women are less likely to have participated or be included in medical research compared to White people^[11]. Lack of understanding and preconceptions about the incidence, prevalence and presentation of common conditions within certain ethnic groups amongst healthcare professionals leads to delays in diagnosis, resulting in a higher risk of morbidity and mortality^[12].</p> <p>The Covid-19 pandemic and its unequal effects on different ethnic groups has led to NHS trusts rolling out additional support for pregnant BAME women, including initiatives such as more tailored communications and ensuring that BAME women have a lower threshold to clinician-led care. This higher level of support should continue to be available for Black women in early pregnancy.</p> <p>It is also vital that medical research is representative of all women, and there is need for basic science research into ethnic differences in pregnancy outcomes. Tommy's research centres focus on including at risk groups in all studies and trials.</p> <p>The fact that Asian women were not found to be at increased risk highlights the need to personalise care and focus resources on investigating why Black women are at such a higher risk of miscarriage, rather than relying on 'BAME' to categorise risk.</p> <p>Black women must be treated as a higher risk group in early pregnancy and miscarriage care, and should receive personalised care with a closer level of monitoring.</p> <p>While continuity of carer is an NHS priority, the majority of miscarriages occur in early pregnancy before midwife-led begins. This supports the need for access to EPUs. Many women have nowhere to turn to in early pregnancy apart from A&E.</p> <p>An appropriate care pathway should be established for Black women.</p>	<p><i>A systematic approach to reducing health inequalities and addressing unwarranted variation in care.</i></p> <p><i>Support for BAME women in pregnancy through continuity of care. By 2024, 75% of women from BAME communities and a similar percentage of women from the most deprived groups will receive continuity of care from their midwife throughout pregnancy, labour and the postnatal period.</i></p>

[9] Quenby et al, "Miscarriage Matters"

[10] MBRRACE-UK: Saving Lives, Improving Mothers' Care 2020: Lessons to inform maternity care from the UK and Ireland Confidential Enquiries in Maternal Death and Morbidity 2016-18

[11] Royal College of Obstetricians & Gynaecologists, "Racial Disparities in Women's Healthcare" (2020) p.4

[12] Ibid.

Age	
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations
<p>Female age is one of the most prominent risk factors for miscarriage, along with the number of previous losses.</p> <p>There is a strong association between female age and miscarriage risk, with a powerful biological gradient, found consistently in several studies^[13].</p> <p>Miscarriage rate is the lowest in women aged 20 – 29 years at 12%, increasing steeply to 65% in women aged 45 years and over^[14].</p> <p>Male age of over 40 years is associated with an increase in miscarriage risk, even after adjusting for confounders such as female partner age^[15].</p>	<p>The age at which a woman becomes a mother is governed by a number of complex personal, social, professional and life circumstances, but women should be informed of the risks associated with becoming pregnant at a later age.</p> <p>Women over 40 must be recognised as an at-risk group and an appropriate care pathway should be established and care personalised to their individual level of risk.</p> <p>There should be a standardisation of tests and treatments in maternity units, to ensure these women at higher risk receive a closer level of care post-miscarriage.</p> <p>An appropriate care pathway should be established for women over 40.</p>

Underlying health conditions	
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations
<p>Several maternal conditions, including autoimmune disorders such as antiphospholipid antibodies, thyroid autoantibodies, and subclinical hypothyroidism, are associated with miscarriage.</p> <p>Uterine anomalies, in particular canalization defects such as septum, have been associated with both spontaneous and recurrent miscarriage^[16]</p>	<p>A report by Public Health England in 2018 found that women are entering pregnancy with more pre-existing problems, including both significant mental, learning and physical health disorders (including obesity, epilepsy, type 2 diabetes), as well as complex social challenges^[17].</p> <p>There must be better identification of these risk factors and standardisation of tests and treatments in maternity units, to ensure these women at higher risk receive a closer level of care.</p>

[13] Quenby et al, "Miscarriage Matters"

[14] Quenby et al, "Miscarriage Matters"

[15] Quenby et al, "Miscarriage Matters"

[16] Quenby et al, "Miscarriage Matters"

[17] Public Health England "Making The Case For Preconception: Care Planning And Preparation For Pregnancy To Improve Maternal And Child Health Outcomes" (2018) p.22

2. Preconception care for those with modifiable risk factors

Smoking		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>Smoking is an important modifiable risk factor for miscarriage.</p> <p>Women who smoke in the first trimester are 1.2 times more likely to have a miscarriage than non-smokers, and the risk of miscarriage increases with the amount smoked (1% increase in relative risk per cigarette smoked per day)^[18].</p>	<p>According to the NHS, 10.6% of pregnant women were known to be smokers at the time of delivery in 2018/19^[19]. In some areas of the UK, this percentage is much higher, for example in Blackpool where the number increases to 23.4%.</p> <p>Whilst smoking cessation services are available, they are not always equally available to women. All women should be able to easily access services and this should be monitored. We do not currently know if women who have a miscarriage specifically are being offered this service and/or if they are attending sessions.</p> <p>Behaviour change campaigns can also have a significant impact in this area, as they can greatly influence more healthy behaviours in the population. Although smoking can be a difficult subject to discuss with pregnant women, our experience in digital campaigns has shown that if the message is carefully framed without blame, and users are involved throughout the process, we can expect high engagement and reach.</p> <p>It would also be beneficial to promote messaging of cutting down smoking as risk is proportional to the amount smoked.</p> <p>It is important that there is specific targeting of women who may be harder to reach but essential parts of the target audience to inform about the potential risks associated with smoking in pregnancy. These specific audiences at higher risk should be identified, through measures such as location, to narrow down and segment targeting. Audiences can be targeted effectively through digital campaigns on social media using location measures but also through researching likely behaviours of the target audience.</p> <p>Behaviour change initiatives should be prioritised, and support should be given to run wide-reaching behaviour change campaigns with a central message to raise awareness of the importance of a smoke-free pregnancy. These campaigns should also include referrals to local smoking cessation services or resources.</p>	<p><i>There is a 24-32% increased risk of a miscarriage for mothers who smoke and that there is also a possible risk of miscarriage from second-hand smoke.</i></p> <p><i>The tobacco treatment services model will be adapted for expectant mothers, and their partners, with a new smoke-free pregnancy pathway including focused sessions and treatments.</i></p> <p><i>All women who smoke during their pregnancy are to be offered specialist smoking cessation support to help them quit.</i></p>

Alcohol		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	
Alcohol use is also an important modifiable risk factor for miscarriage, as high alcohol consumption during the first trimester is associated with an increase in miscarriage, with those who have a high alcohol intake 1.7 times more likely to miscarry.	<p>The Lancet Global Health report in 2017 found that the UK was one of the five countries with the highest estimated prevalence of alcohol use during pregnancy, at an estimated 41.3%^[20].</p> <p>Similarly to smoking, behaviour change initiatives could be greatly influential in this area.</p> <p>Behaviour change initiatives should be prioritised, and support should be given to run wide-reaching behaviour change campaigns with a central message to raise awareness of the importance of an alcohol-free pregnancy.</p>	
BMI		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>A woman's BMI is associated with an increased risk of miscarriage.</p> <p>The BMI associated with the least risk of miscarriage is 18.5 – 24.9 kg/m²^[21], considered to be the healthy weight range, whilst women with a BMI under 18.5 are 1.2 times more likely to miscarry and those with a BMI over 30 were 1.9 times more likely before adjusting for other factors.</p>	<p>The rate of obesity is increasing nationally. According to the National Maternity and Perinatal Audit 2017 report, fewer than half of pregnant women had a normal BMI at booking. While a low BMI is associated with an increased risk of miscarriage, only 2.9% of women had a booking BMI below 18.5. By contrast, 21.3% of women had a BMI of 30 or over^[22].</p> <p>It is not advised to try and lose weight whilst pregnant in order to mitigate the risks of a high BMI, as this can be harmful to the baby, and is unlikely to have much of an impact after conception. Therefore, preconception care and guidance around planning a pregnancy is crucial.</p> <p>Services should take a forward view to promote healthy behaviours and support early interventions to reduce risks, before a woman's first pregnancy, and then between pregnancies. Support and advice to plan and be ready for pregnancy should not only be widely available but also targeted to particularly high-risk areas and groups.</p> <p>Guidance on maintaining a healthy weight, amongst other factors, should be proactively given to people before they become, or are actively trying to become, pregnant.</p>	<p><i>The NHS will provide a targeted support offer and access to weight management services in primary care for people with a diagnosis of type 2 diabetes or hypertension with a BMI of 30+.</i></p>

[20] Popova et al, "Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis" The Lancet Global Health. (2017)

[21] Quenby et al, "Miscarriage Matters"

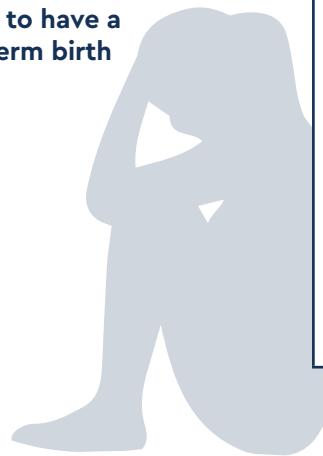
[22] NMPA Project Team, National Maternity And Perinatal Audit: Clinical Report 2017. RCOG London. (2017)

3. The effect of miscarriage on subsequent pregnancies

After 3 miscarriages
women are

1.8

times more
likely to have a
preterm birth

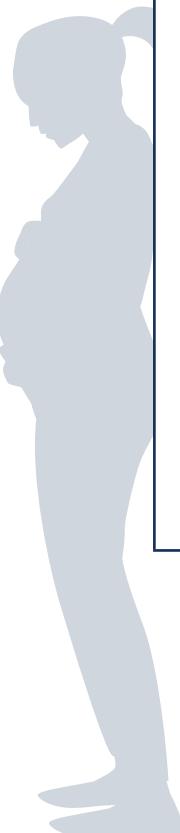


Preterm birth		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>The risk of preterm birth increases stepwise with each previous miscarriage, demonstrating a biological gradient^[23]; this association persists even after adjusting for confounding variables.</p> <p>Women after one miscarriage are 1.2 times more likely to have a preterm birth, after two 1.4 times more likely and after three 1.8 times more likely.</p>	<p>More research is needed to understand the link between miscarriage and preterm birth. It is likely that there is a biological spectrum relating to shared mechanisms, which reinforces the need to understand the underlying science so that outcomes can be modified both for miscarriage but also later pregnancy outcomes.</p> <p>Adverse outcomes after miscarriage could be, in part, due to the management of miscarriage, for example after surgical management which can be performed to clear the uterine lining after a miscarriage. It could also be linked to uterine conditions such as chronic endometritis. This area will continue to be a research focus.</p>	<p><i>A strong start in life for children and young people includes reducing rates of stillbirth and neonatal death, of which preterm labour and birth is a leading cause.</i></p>

After 3 miscarriages women are
1.7
times more likely to experience placental abruption in a later pregnancy

and

1.6
times more likely to have a stillbirth



Placental dysfunction and stillbirth		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>Our review also shows an increased risk of placental dysfunction disorders in later pregnancies.</p> <p>Our review found that after three miscarriages women are 1.7 times more likely to experience placental abruption in a later pregnancy, and 1.6 times more likely to have a stillbirth. These estimates are after adjusting for other factors.</p>	<p>The inadequate decidual response, if it does not lead to miscarriage, may lead to poor formation of the placenta causing placental dysfunction disorders, and therefore increasing the risk of, placental abruption, fetal growth restriction, preterm birth and perinatal death.</p> <p>The increasing risk of perinatal complications with increasing number of previous pregnancy losses suggests a need for closer antenatal surveillance in patients with a history of multiple miscarriages.</p> <p>It also demonstrates that miscarriage history is an important indicator of the need to closely monitor subsequent pregnancies to reduce stillbirth risk and other related adverse outcomes.</p>	<p><i>A strong start in life for children and young people includes reducing rates of stillbirth and neonatal death.</i></p>

4. The effect of miscarriage on the long-term health of the woman

After 3 miscarriages women are
1.4
times more likely to suffer from cardiovascular diseases and

6.1
times more likely to suffer from venous thromboembolism



Cardiovascular disease and venous thromboembolism		
Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>Our systematic review found that recurrent miscarriage is associated with a significantly increased risk of cardiovascular disease and venous thromboembolism.^[24]</p> <p>After experiencing three miscarriages, women are 1.4 times more likely to suffer from cardiovascular diseases, and 6.1 times more likely to suffer from venous thromboembolism. These estimates are after adjusting for other factors.</p>	<p>Both cardiovascular diseases and venous thromboembolism are important causes of death and their prevention and management is a priority for the NHS.</p> <p>These findings are crucial because they add to the concept of a recurrent miscarriage syndrome, and may mean that a history of repeated miscarriage is an opportunity for reducing risks for cardiovascular and thromboembolic disease.</p>	<p><i>Heart and circulatory disease, also known as cardiovascular disease (CVD), causes a quarter of all deaths in the UK and is the largest cause of premature mortality in deprived areas. This is the single biggest area where the NHS can save lives over the next 10 years.</i></p>

Psychological consequences: anxiety, depression, post-traumatic stress disorder and suicide

Key findings from The Lancet Miscarriage Series	Policy implications and recommendations	Link to NHS Long Term Plan
<p>Our systematic review identified that anxiety, depression and suicide are strongly associated with miscarriage.^[25]</p> <p>It is important to note that it is not only recurrent miscarriage that is associated with these psychological conditions, but also that one miscarriage can significantly increase the risk of anxiety and depression in particular.</p> <p>The recent study^[26] that found that nine months after a pregnancy loss, 18% of women met the criteria for post-traumatic stress, 17% for moderate or severe anxiety, and 6% for moderate or severe depression demonstrates that distress remains at clinically important levels at nine months.</p>	<p>Identifying women at risk of psychological distress following sporadic and recurrent miscarriage and the development of optimal treatment strategies would be beneficial in helping to prevent the onset of severe psychological conditions and should be prioritised.</p> <p>Women and partners should have access to follow-up mental health support to help reduce mental illness post-miscarriage and to deal with mental health issues in subsequent pregnancies.</p>	<p><i>Improve access to and the quality of perinatal mental health care for mothers, their partners and children:</i></p> <ul style="list-style-type: none"> • <i>Extending care provided by specialist perinatal mental health services to be available from preconception to 24 months after birth</i> • <i>Offering fathers/partners of women accessing specialist perinatal mental health services and maternity outreach clinics evidence-based assessment for their mental health and signposting to support as required.</i> • <i>Increasing access to evidence-based psychological support and therapy, including digital options, in a maternity setting.</i>

RECOMMENDATIONS FOR POLICY AND SOLUTIONS TO IMPROVE CARE

Using the key findings from The Lancet Miscarriage Series, this section will identify the top priorities for miscarriage care to make recommendations to improve both prevention and management.

Miscarriages must be recorded so that the rate of miscarriage can be measured nationally

"After I'd had 3 miscarriages, I was relieved to get my referral for specialist support. But our appointment at the clinic was very disappointing. The consultant said that I was still young and told us to keep trying. He implied that my losses were 'just one of those things'."

Danielle experienced recurrent miscarriage before being treated at Tommy's National Centre for Miscarriage Research.

Recommendation: A process for recording miscarriage exists, however standardisation of data entry and then centralised data collation is the challenge. Look to the Department of Health to incorporate miscarriage data into a women's reproductive data set to complement the maternity data set.

National miscarriage figures are currently not recorded, and hospital admissions for miscarriage have not been recorded since 2012. This means that we do not know how many women and their partners are suffering with miscarriage each year. It also means that we do not know if miscarriages are increasing or decreasing.

Data on the number of miscarriages must be made available along with stillbirth and preterm birth rates. This will allow us to fully understand the scope of the problem and enable the setting of targets for reduction. The ONS could be one way of measuring and producing this information, however there is a time lag between the collection of data and reporting on it.

A process for recording miscarriage exists, however standardisation of data entry and then centralised data collation is the challenge. A maternal health dataset, that includes miscarriage figures, should be developed. This would involve data linkage from Early Pregnancy Units, GPs and hospitals. We should look to the Department of Health to incorporate miscarriage data into a women's reproductive data set to complement the maternity data set.

Access to care after sporadic miscarriage must be available with a clear pathway for follow-up mental health support

Recommendation: healthcare professionals who are involved in the care of a woman who has miscarried and their partner to follow guidance within *The National Bereavement Care Pathway* developed to improve bereavement care and reduce variability in provision for families after miscarriage. This includes providing information about the emotional support available via the hospital Trust, primary care colleagues and via local and national support organisations, as well as standards for follow-up appointments, and a referral for a mental health assessment and, where appropriate, treatment.

See also NICE guidance on antenatal/postnatal mental health (<https://www.nice.org.uk/guidance/qs115>).

It is important that women receive appropriate care during and after their first miscarriage, including the best management of miscarriage and access to follow-up mental health and pre-conceptual support.

When women experience a miscarriage, they should be presented with the available evidence and be free to choose the miscarriage management approach that suits their needs and preferences. Our systematic review has analysed the most effective treatments for managing a miscarriage based on different choices that the woman has. If a woman with missed miscarriage chooses to have the surgical option, suction aspiration with cervical preparation should be recommended, but if she chooses to have the medical option, a combination therapy with mifepristone and misoprostol should be recommended. Women with incomplete miscarriage have over 90% chance of completing the miscarriage without medical intervention, as the process of expelling pregnancy tissue has already started. Expectant management is therefore recommended as the first-line option for women with incomplete miscarriage, provided there is no evidence of excessive bleeding or intrauterine infection^[27].

In terms of follow-up care, women currently receive minimal or no care until they have had three miscarriages. This results in missed opportunities for preconception counselling and care, including the opportunity to address body weight, smoking, alcohol consumption, and diet, particularly intake of micronutrients such as folate. Couples may not be offered any reasons for the miscarriages, with the only advice being 'try again'. Effects on mental health following miscarriage are not appreciated or addressed, and dissatisfaction with the service is common.

After the first miscarriage women should be signposted to information about miscarriage, resources to address their physical and mental health needs following pregnancy loss and ways to optimise their health for future pregnancy. This could involve patient support-groups,

online self-help strategies for mental health, weight management, smoking and recreational drugs cessation services, information regarding appropriate pre-conceptual folate and Vitamin D supplementation, referral to necessary services for management and optimisation of chronic maternal medical conditions, such as diabetes, hypertension, heart disease and epilepsy, and screening for mental health issues.

Even where an effective treatment is not available, the knowledge of contributory factors for miscarriages, likelihood of outcomes for future pregnancy, and acknowledgement of the trauma and distress experienced and the personal quest for answers, can be very important for women and partners.

We urge health funders and providers to invest in early pregnancy care, with specific focus on training for clinical nurse specialists and doctors to deliver comprehensive miscarriage care within the setting of dedicated Early Pregnancy Units.

Women also need to be signposted to services, as Early Pregnancy Units are not always easily accessible, and many of the ones that are available to women are only open from Monday to Friday, 9am-5pm. There is no clear guidance on what women who are experiencing symptoms of miscarriage should do if the Early Pregnancy Unit is closed, or if there is not one close by. Information needs to be made available for women in these situations.

A clear pathway for follow-up mental health support must also be established to help couples through this very difficult time, and reduce the risks of anxiety, depression, post-traumatic stress disorder (PTSD) and suicide associated with miscarriage. Following up with a patient after they have had a miscarriage would be a responsibility for the Early Pregnancy Unit. Nurses should follow up by telephone 4–6 weeks after a patient has miscarried, asking them how they are feeling and signposting to any mental health support if needed. The information and services that are offered must be accessible to the couple to allow them to benefit from that support. The unit should then correspond with the GP to inform them of the miscarriage and that they have followed up with mental health support.

In the future, women and services would benefit from the development of a robust screening tool to be used for every woman who has had a miscarriage, containing questions from a validated mental health questionnaire. This tool would enable healthcare professionals to see if patients need further mental health support and what type of support would be appropriate. Women and their partners could be suffering from different conditions which would require different levels of support, e.g. treatment for general anxiety would be different to PTSD. This screening tool would most likely need to be implemented by the Early Pregnancy Unit. Alongside the validated mental health questionnaire, staff should check for other factors that may make someone more at risk, e.g. lack of support from friends and family.

Once patients in need of mental health support have been identified, targeted help must be provided. There will need to be research into which type of support is most effective, for example, an online CBT-based approach could be trialled before being offered as a widely available service.

Tests and treatments must be standardised across the UK through a 'graded approach' to recurrent miscarriage

Recommendation: Implementation of a pre-conceptual care package after first miscarriage through the Public Health Outcomes Framework. Nurse-led care after second miscarriage and consultant-led care after third miscarriage through Trust miscarriage services or Early Pregnancy Unit. See model on page 29 below.

Miscarriage services vary greatly in quality and accessibility. Some women receive tests and treatment after two miscarriages, while others must endure the pain of a further loss before being seen. In parts of the UK, there are no miscarriage services at all.

The wide variation in practice is reflected in professional body guidelines that often have varying, and occasionally contradictory recommendations. Tommy's National Centre for Miscarriage Research is developing a National Miscarriage Care Package to standardise tests and treatments nationwide. We propose a set of guidelines based on a model of care that could be implemented by the health service to offer high quality care for couples suffering recurrent miscarriages. We are also developing a patient's charter to empower women to know what service they should be able to expect.

Caregivers should neither normalise nor over-medicalise recurrent miscarriage care, but individualise care according to women's and their partners' needs and preferences. We suggest health services structure care using a 'graded model' where women are offered online healthcare advice and support, care in a nurse or midwife-led clinic, and care in a medical consultant-led clinic, according to clinical needs^[28].

We define a minimum set of investigations and treatments to be offered to couples suffering recurrent miscarriages, and urge healthcare policy-makers and providers to make these universally available. The essential investigations include measurements of lupus anticoagulant, anticardiolipin antibodies, thyroid function, and a transvaginal pelvic ultrasound scan^[29].

The key treatments to consider are first trimester progesterone administration (for women with one or more previous miscarriages and current pregnancy bleeding), levothyroxine for women with subclinical hypothyroidism, and the combination of aspirin and heparin for women with antiphospholipid antibodies. Appropriate screening and care for mental health issues and future obstetric risks, particularly preterm birth, fetal growth restriction and stillbirth, will need to be incorporated into the care pathway for couples with a history of recurrent miscarriage^[30].

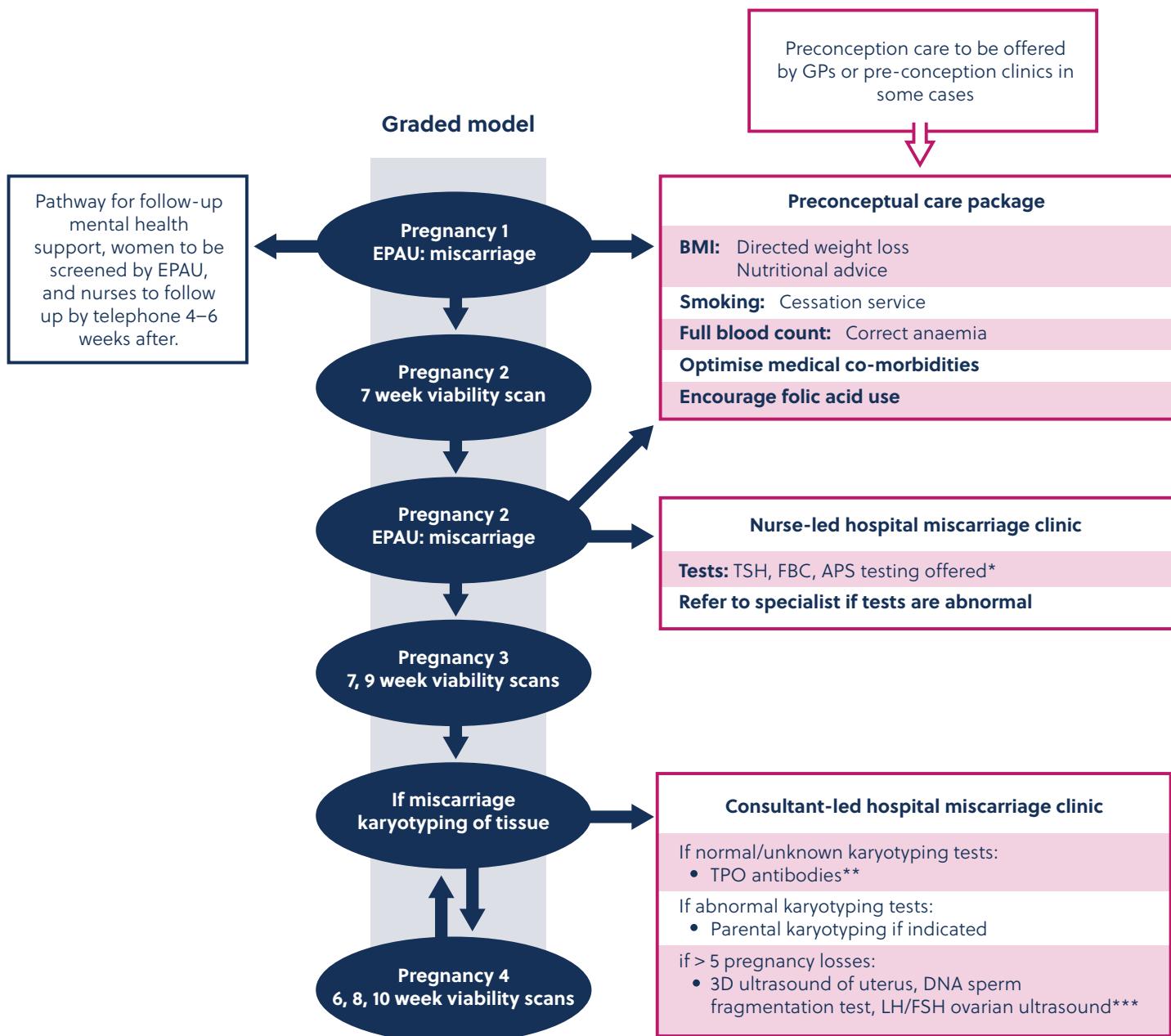
The graded model will comprise the following steps^[31]:

1. After the first miscarriage women will be signposted to information about miscarriage, resources to address their physical and mental health needs following pregnancy loss and ways to optimize their health for future pregnancy, as outlined in the previous recommendation.
2. Following a second miscarriage, women will be offered an appointment at a miscarriage clinic that could be nurse or midwifery led, where tests for full blood count and thyroid function are offered, in addition to addressing lifestyle issues. Referral for specialist care will be arranged if tests are abnormal or if there is a chronic medical or mental health problem. Women will have access to support and early pregnancy reassurance scans in subsequent pregnancies.
3. After a third miscarriage, women will be offered an appointment at a medical consultant-led clinic, where additional tests and a full range of treatments can be offered. Pregnancy tissue from the third and any subsequent miscarriages will be sent for genetic testing. Blood tests for antiphospholipid antibodies and a pelvic ultrasound scan (ideally 3-dimensional transvaginal) will be arranged, and if necessary, parental karyotyping will be offered depending on the clinical history and the results of the genetic analysis of pregnancy tissue from previous losses.

The graded approach balances the need for evidence-based management and supportive care, whilst targeting health care resources appropriately. It takes advantage of online resources, as well as promotion of continuity of care, and could benefit couples who lose pregnancies in different resource and health system settings.

We are calling for support to implement our care package across the UK. We propose to work with local clinicians and midwives to support uptake of these guidelines in maternity sites. It is important that healthcare providers support us in these efforts to standardise tests and treatments, so that women across the UK can benefit from best-practice care.

Proposed system with graded model of care



Women with additional risk, e.g. Black women and women over 40 to be accelerated along this graded model of care (as discussed in the recommendations section).

* TSH = Thyroid function test; FBC = Full Blood Count test;
APS = Antiphospholipid syndrome test

** TPO antibodies = Thyroid antibodies

*** LH = Luteinizing hormone; FSH = Follicle stimulating hormone

Specific, personalised care pathways should be established for high risk women

Recommendation: Appropriate care pathways using a modified 'graded approach' to recurrent miscarriage should be established for these groups.

At-risk groups, including Black women, women over the age of 40 and women with existing medical conditions, must receive personalised care according to their individual risk factors, which may include a closer level of care and monitoring in early pregnancy. Appropriate care pathways using a modified 'graded approach' to recurrent miscarriage should be established for these groups.

There are already established care pathways for women with existing medical conditions. These pathways need to be accessible for women in early pregnancy, and they should continue their care with the right units in the healthcare system. Healthcare professionals must ensure they are signposting these women to the right care.

For women over the age of 40 they should be offered preconception support and care from their GPs. Once they become pregnant, there are multiple issues to consider. Whilst they are likely to suffer from miscarriages due to chromosomal abnormalities, there could still be underlying issues that may need monitoring and treating. They are also more likely to suffer from complications including pre-eclampsia and gestational diabetes. Pregnant women over 40 are considered high-risk in most hospitals and many will be under consultant-led care. This specialist care must be available from early pregnancy to ensure that these women have the highest possible chance of a safer pregnancy.

Black women are at a 40% relative increased risk of miscarriage. Despite also being at increased risk of obstetric complications and maternal death, Black women are not receiving the specialist care that they need. We propose that Black women's care should be upgraded using our graded model of care. As outlined in the previous recommendation, we recommend that women should be signposted to information and resources to address their physical and mental health needs after one miscarriage, and to be seen in a nurse-led miscarriage clinic after two. For Black women, we recommend that they should be seen in a nurse-led miscarriage clinic after one miscarriage, and should access consultant-led care in a specialist clinic where a full range of tests and treatments can be offered after two miscarriages. This would enable them to access specialist care faster in light of their additional risk.

A clear pathway for preconception support and guidance must be established

Recommendation: To build on the existing work of Public Health England and NHS England's Maternity Transformation Programme in developing a preconception pathway and preconception indicators. Preconception care to be offered by GPs or preconception clinics in some cases, using existing information and resources including the Tommy's 'Planning for Pregnancy' tool.

As mentioned in section 3 on both at-risk groups and modifiable risk factors for miscarriage, preconception care would have a major beneficial impact on the risk of miscarriage and should be prioritised. Early Pregnancy Units should be able to refer women into the graded pathway directly so care is streamlined. Currently couples go from emergency care for miscarriage management, to primary care to get a referral to secondary care for miscarriage follow up care - a slow convoluted pathway for a grieving couple to travel.

It is often too late to reduce risk after conception, and therefore increasing access to services and facilitating early intervention for people in their early and reproductive years could help to mitigate and manage preconception risk factors.

It is vital to note that access to and uptake of preconception care interventions may be uneven and those with the greatest need may have the most difficulty accessing care^[32]. Support and advice to plan and be ready for pregnancy should not only be widely available but also targeted to high-risk groups, including women with long-term conditions and those with multiple vulnerabilities. These groups should receive help early to plan pregnancy and additional support to have a healthy pregnancy.

A clear pathway for preconception support must be established before a first pregnancy, and between pregnancies. Guidance on smoking cessation, sensible alcohol consumption and maintaining a healthy weight, amongst other factors, should be pro-actively given to people before they become, or are actively trying to become, pregnant. This responsibility would fall in the first instance under primary care providers, such as GPs, which are designed to equip patients with the preventative care they need. It would also be useful to explore how miscarriage services and preconception clinics can work better together to safeguard women at risk.

As miscarriage affects hundreds of thousands of women in the UK, there needs to be a discussion between recurrent miscarriage services and preconception clinics about how to manage this. Certain women would benefit greatly from having specialist preconception care in a clinic before a next pregnancy, therefore increased dialogue between the two is likely to reduce miscarriage. Similarly, we know that miscarriage, and particularly recurrent miscarriage, increases the risk of obstetric complications including stillbirth and preterm birth, so therefore it may also be beneficial to refer affected women to preterm birth clinics if appropriate.

NEXT STEPS

The Lancet Miscarriage Matters series will be published in late April. At the same time of publication, Tommy's will run a public-facing campaign to raise awareness of the prevalence and impact of miscarriage, and to support women and their partners with the message that every miscarriage counts. This campaign has been launched with an online petition raising awareness of our key recommendations following Miscarriage Matters research findings.

Following publication, we will finalise the guidelines for our National Miscarriage Care Package. These guidelines will be the best-practice care on recurrent pregnancy loss, to inform health practitioners on how best to treat and advise women. Standing with this care package will be example commissioning guidelines, developed in partnership with several local authorities.

Alongside the development of the care package and commissioning guidelines, we will develop a patient's charter. This document will comprise information for the woman and their partner to know what service and care they should be able to expect. This will empower couples to advocate for themselves to access the care that they are entitled to.

Tommy's National Centre for Miscarriage Research will then work with local clinicians and midwives to support uptake of the care package guidelines in maternity sites. It is important that healthcare providers support us in these efforts to standardise tests and treatments, so that women across the UK can benefit from best-practice care.

We must report on the uptake of these guidelines to monitor the standardisation of tests and treatments for miscarriage in maternity units.

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