



# USING PROGESTERONE TO INCREASE LIVE BIRTHS

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## EXECUTIVE SUMMARY

- The PRISM trial, led by the University of Birmingham and funded by the NIHR, suggests that giving the hormone progesterone to pregnant women with early pregnancy bleeding and a history of miscarriage could increase their chances of having a baby.
- NICE clinical guidelines do not currently recommend the use of progesterone under these circumstances. We recommend that the guidance should be updated in the light of the new findings.

### Introduction

Research led by the University of Birmingham suggests that giving progesterone to pregnant women with early pregnancy bleeding and a history of miscarriage could increase their chances of having a baby.

The role of progesterone in women with early pregnancy bleeding has been studied and debated for the last 60 years, however what we have previously lacked is high quality evidence. The largest study before the PRISM trial involved fewer than 200 participants. More than 4,000 people took part in the PRISM trial.

### PRISM trial

The PRISM trial, funded by the National Institute for Health Research (NIHR) and co-ordinated by Birmingham Clinical Trials Unit in collaboration with Tommy's National Centre for Miscarriage Research, is the largest ever trial of its kind and involved 4,153 pregnant women who presented with early pregnancy bleeding.

The women, being treated at 48 hospitals across the UK and with the average age of 31, were randomly assigned by computer into one of two

groups – one group of 2,079 women were given progesterone, while the other group of 2,074 women were given a placebo.

While there was not enough statistically strong evidence to suggest that progesterone could help all women who suffer early pregnancy bleeding to go on and have a baby, the results showed that it benefited women who had early pregnancy bleeding and had previously suffered a miscarriage.

Researchers found a 4% increase in the number of babies born to women in the study who were given progesterone and had previously had one or two miscarriages, compared to those who were given a placebo.

Of the 777 women given progesterone who had previously had one or two miscarriages, 591 (76%) went on to have a live birth, compared with 534 women out of 738 in the placebo group (72%).

The benefit was even greater for the women who had previous 'recurrent miscarriages' (i.e., three or more miscarriages) – with a 15% increase in the live birth rate in the progesterone group compared to the placebo group.

Of the 137 women taking part in the trial who had previously had three or more miscarriages, 98 (72%) went on to have a live birth, compared to 57% (85 out of 148) women in the placebo group who went on to have a baby.

### Case study: Samantha Allen

Samantha Allen, aged 31, of Bradford, is married to 36-year-old Stephen. Samantha, who suffered a miscarriage in December 2015, was recruited to the PRISM trial in June 2017 when she was

nine weeks pregnant and she was in the group of participants that were given progesterone. The couple's son, Noah, was born in February 2018 weighing 9lbs 6oz.

She said: "It was on my birthday in November 2015 when I found out that I was pregnant; it was the best birthday gift I could have hoped for.

"However, my joy soon started to turn to concern when I began having some bleeding when I was around seven weeks pregnant and I ended up in A&E. I had a scan and was told to come back on Christmas Eve for another scan.

"But then on December 23rd I started bleeding quite heavily and had to call an ambulance. I was taken to A&E where I was told the baby had died when I was eight weeks pregnant and I was miscarrying. The following day, on Christmas Eve, I had to also go through the trauma of miscarriage surgery.

"Words can't describe our devastation. I think people can often be dismissive of miscarriage when it happens in early pregnancy, you are treated as a statistic and told it's common. But I am not a statistic, we lost our child and it is a loss we will always grieve.

"Around 15 months after I miscarried I found out I was pregnant again and I was delighted. However, when I was around seven weeks pregnant I started having spotting and, given my previous loss, I decided to go to the early pregnancy unit.

"I had a scan and they said they thought they could detect a heartbeat but weren't certain, so booked me in for another scan two weeks later.

"The spotting continued during those two weeks, so I was relieved when the second scan showed I was pregnant.

"That's when they told me about the PRISM trial and I decided to take part.

"I was prescribed progesterone pessaries which I self-administered until I was 16 weeks pregnant.

"The bleeding stopped within a week of starting the trial, and apart from having some issues with a condition called symphysis pubis dysfunction, which causes pelvic pain in pregnancy, my pregnancy went really well.

"I opted for a water birth and Noah was born weighing a very healthy 9lbs 6oz in February last year. He's now 14 months old and he's such a lively and incredibly bright little boy who brings us so much joy, I can't imagine life without him.

"Of course, we'll never know whether or not I would have miscarried if I had not taken part in the trial, or if I had been part of the group that received the placebo, either way I feel fortunate and happy that I did participate. I hope the results of the trial will make a difference to the way women receive treatment moving forwards, and that I had a small part to play in that."

## About the study

The research was supported by the United Kingdom NIHR Health Technology Assessment Programme (project number HTA 12/167/26).

The women in the group who received progesterone were given 400mg twice daily as vaginal pessaries. The women in the placebo group received a placebo with an identical appearance. They were given the progesterone or placebo from presentation with bleeding and confirmation of a pregnancy seen on ultrasound scan no later than 12 weeks of gestation, until 16 completed weeks of gestation or earlier if the pregnancy ended before 16 weeks. Recruitment to the trial took place from May 19, 2015, through to July 27, 2017. Follow-up of patients was completed by June 2018.

## Research team

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12. Nottingham University Hospitals NHS Trust: Shilpa Deb
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28. Surrey and Sussex Healthcare NHS Trust: Catherine Wykes

## Read the study

Coomarasamy et al (2019). 'A Randomized Trial of Progesterone in Women with Early Pregnancy Bleeding'. *New England Journal of Medicine*; available at <https://www.nejm.org/doi/full/10.1056/NEJMoa1813730>

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