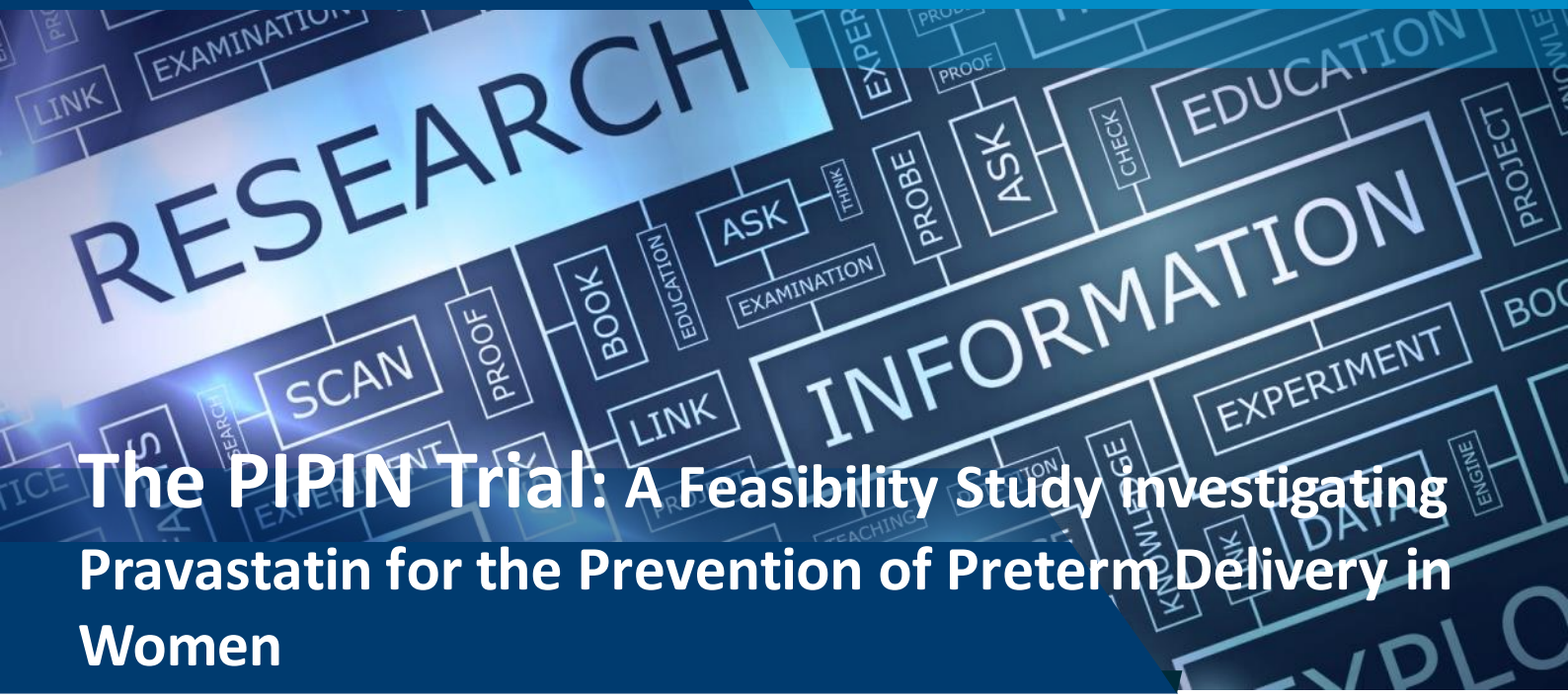
CHIEF SCIENTIST OFFICE

CODE: TCS/18/30

RESEARCH PROJECT BRIEFING



The PIPIN Trial: A Feasibility Study investigating Pravastatin for the Prevention of Preterm Delivery in Women

AIMS

The PIPIN Trial is a phase II feasibility study investigating whether women with signs and symptoms of preterm labour would be willing to take pravastatin (a "statin" tablet) as a part of a placebo-controlled, double masked trial (neither participants nor the study team knew who was taking pravastatin until the end of the study).

The main aims were to investigate recruitment of eligible women to the study, the feasibility of the study protocol, and the clinical outcomes of recruited women.

KEY FINDINGS

Some women with evidence of preterm labour are willing to take part in a placebo – controlled, randomised trial of pravastatin for the prevention of preterm delivery. Of all eligible women who were invited to take part in PIPN, 39% consented to take part.

The study design would be challenging to scale up to investigate whether pravastatin prevents preterm delivery, due to the to intensive nature of recruitment arising from the specific narrow inclusion criteria applied. Indeed, the study was terminated early due to poor recruitment, with 7 participants recruited over a period of 15 months despite screening of 214 patients.

There were no reported side effects in any patients taking pravastatin, and no pravastatin found in the umbilical cord.

WHAT DID THE STUDY INVOLVE?

PIPIN was a feasibility study. This means that rather on primarily focussing on the clinical outcomes of participants recruited, we were investigating whether this type of trial is acceptable to patients and their families. This would tell us whether it would be possible to deliver this as a large scale trial which could be used to test whether pravastatin could prevent preterm delivery.

We aimed to recruit 40 women over 2 years from in one hospital in Scotland, with around 9,000 deliveries per year.

When a woman came to hospital with signs or symptoms of preterm labour, we (the study team), we would provide them and (where possible), their partners with information about PIPIN. Once they had time to consider this information, we would recruit them to the study if they were willing and eligible.

As part of the trial, participants took one study tablet (either pravastatin or an identical placebo tablet) per day for up to a week or until delivery – whichever occurred sooner. Neither the participants nor the researchers knew whether the participants were taking active or placebo tablets (double-masked study). During this time we collected blood tests to look at levels of inflammation. We also collected samples both from mothers, and from the umbilical cord, at delivery. A few weeks after they were due to deliver their babies, we also asked our participants what their experience of the trial was, and how they thought we could improve it.

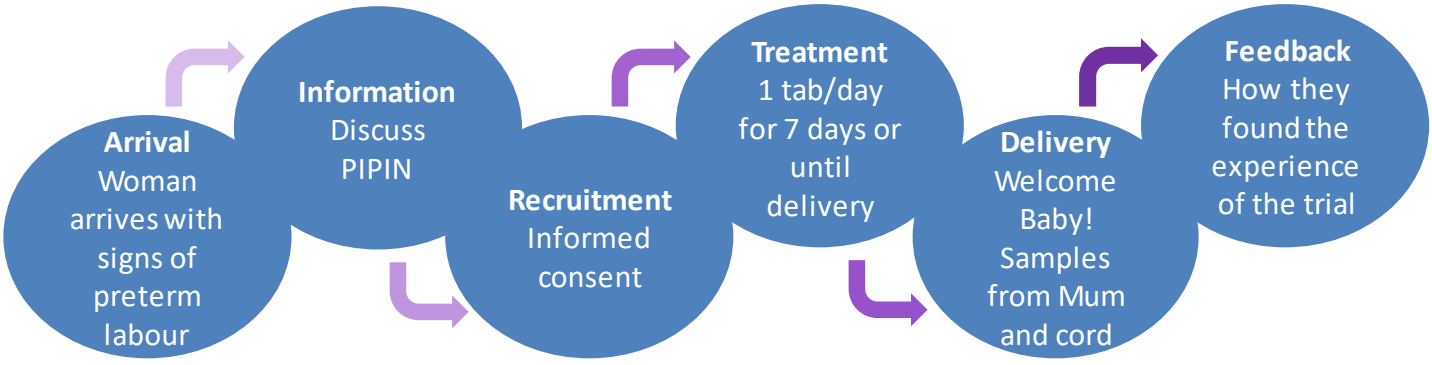


Figure 1 - A Participant's Journey Through PIPIN

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

- Pregnant women at risk of having a preterm delivery are willing to take part in a clinical trial of pravastatin.

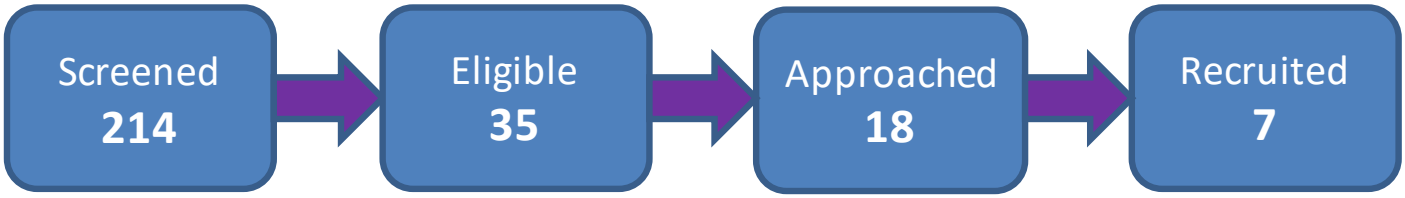


Figure 2 – progress through the PIPIN trial

- PIPIN had a recruitment rate of 39% of patients who were eligible AND received information from the research team about PIPIN. This shows that some pregnant women who are at risk of having a premature baby due to preterm labour are willing to take part in a trial where they would take pravastatin or placebo without knowing which (double masked). This agrees with other trials of pravastatin in pregnancy.

- The design of PIPIN is not feasible for a larger trial which would answer whether pravastatin in pregnancy can prevent preterm delivery.

- Over 15 months, just 7 participants were recruited. Of 35 that could have been, we couldn't discuss the trial with nearly half of these (17), often because they had their baby or went home or to another hospital before we were able to meet them.

- There were no reported side effects in the pravastatin treatment group of PIPIN, and no pravastatin found in the cord blood. This adds to the safety profile of pravastatin in pregnancy.

WHAT IMPACT COULD THE FINDINGS HAVE?

- Some (but less than 50%) of regnant women at risk of preterm delivery are willing to take pravastatin in a trial setting for the prevention of preterm delivery.
- Recruiting women in established preterm labour is difficult.
- Further studies of statins for the prevention of preterm birth should recruit women at high risk of preterm birth, prior to the onset of labour.

HOW WILL THE OUTCOMES BE DISSEMINATED?

These outcomes (and protocol) will be published as part of the PhD thesis of Dr. Eleanor Whitaker. We also aim to publish the results in an open access journal format.

An abstract of these results will be submitted for presentation at the European Spontaneous Preterm Birth Conference, which is attended by many of the world leading experts in preterm birth research.

The public will be informed through this website.

CONCLUSION

Pravastatin is an acceptable intervention and should tested for the prevention of preterm delivery in pregnant women. Recruitment of women already in preterm labour is very challenging, and may not be feasible. We recommend evaluating pravastatin for treatment of women at high risk of preterm birth.

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Additional Information

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