INTRODUCTION

Reproductive health permeates every aspect of human society. Disorders of reproductive health and pregnancy are some of the most common with up to 10% of couples experiencing subfertility, 25% of pregnancies ending in miscarriage and pregnancy-related complications being the most common reason for hospital admission worldwide.1 Despite the prevalence, large knowledge gaps remain pervasive and common conditions are poorly understood. Research in the area has been hampered by tissue collection on the basis of retrospective reproductive outcome rather than prospective. The Tommy’s National Reproductive Health Biobank (TNHRB) was formed in 2018 to try and bridge this gap.

THEMIS STRUCTURE

The TNHRB is a virtual biobank combining a prospective reproductive outcomes registry with six existing biobanks across Tommy’s funded research centres. These operate under a single governance structure, with material and data sharing agreements and a single-consent model. This allows collection of samples from mother, father, and baby, using expert-designed standard operating procedures, ensuring collection of high-quality samples. Research samples are held at each site and linked by bespoke tissue tracking software developed by Warwick University’s Institute for Digital Health (iDiH).

AIMS AND OBJECTIVES

• Accelerate research in reproductive health by providing high-quality samples and data efficiently
• To link samples to metadata, clinical data, pregnancy outcome data and neonatal outcome data
• To review sample access applications within 2 weeks of receipt
• To work closely with industry partners

SAMPLES AND DATA

<table>
<thead>
<tr>
<th>Funded Investigators</th>
<th>Sample Type</th>
<th>Sample Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brook, 20-24 weeks</td>
<td>Blood, DNA</td>
<td>500 µL of heparinised venous blood</td>
</tr>
<tr>
<td>Brook, 24-26 weeks</td>
<td>Blood, DNA</td>
<td>500 µL of heparinised venous blood</td>
</tr>
<tr>
<td>Brook, 26-30 weeks</td>
<td>Blood, DNA</td>
<td>500 µL of heparinised venous blood</td>
</tr>
<tr>
<td>Other</td>
<td>Fluid, DNA</td>
<td>500 µL of heparinised venous blood</td>
</tr>
</tbody>
</table>

The biobank is providing endometrial tissue for this study.

ENDOMETRIAL TISSUE

Endometrial tissue

Types of Projects Supported to date

<table>
<thead>
<tr>
<th>Type of Project Supported</th>
<th>Number of Projects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigating new treatments for infertility and premature birth</td>
<td>3</td>
</tr>
<tr>
<td>Defining the role of the microbiome in miscarriage</td>
<td>1</td>
</tr>
<tr>
<td>Understanding the role of immune cells in miscarriage</td>
<td>2</td>
</tr>
<tr>
<td>Developing new diagnostic tools for recurrent miscarriage</td>
<td>1</td>
</tr>
</tbody>
</table>

INDUSTRY COLLABORATION

The biobank is proud to be working with the pharmaceutical industry.

Innovating in an international pharmaceutical company to enable reproductive medicine and maternal health. The company is working with researchers at Warwick University to develop a new drug to inhibit uterine contractions as a tocolytic treatment for preterm birth.

CASE STUDY: THE CHROMOSOME ABNORMALITIES AND RECURRENT MISCARRIAGE (CERM) TRIAL

INTRODUCTION

Recurrent miscarriage affects 5% of couples trying to conceive. It carries significant morbidity. In the majority of couples, no clear cause is identified making treatment difficult. One purported cause is chromosomal abnormalities (CAs). However, to date no randomized controlled trial has assessed this and the mechanism remains poorly understood.

OBJECTIVE

To assess the effect of diagnostic line on abortion rates in women suffering from CA and CM. Secondly to assess the mechanism by which CA causes miscarriage.

METHODS

Prospective double-blind placebo randomised adaptive designed trial.

BIOBANK COLLABORATION

Biobank tie-in has allowed the generation of a combined mechanism/critical trial. Diagnostic endometrial samples are collected under the auspices of the biobank allowing researchers application to support a diverse range of mechanistic studies across a range of centre collaborations. Tying in with the RCT allows samples tied to the appropriate clinical phenotype, treatment group and clinical outcome whilst also allowing mechanistic work to build upon new discoveries across fields. To our knowledge this is a novel integration of a biobank within a clinical RCT. To facilitate this integration novel SOPs were created to facilitate specific trial collection procedures.

RESULTS TO DATE

Despite the impact of Covid-19, the CERM trial has progressed apace and to date generated 374 samples from 86 patients. This has allowed an initial work to understand the constituent pattern of expression of CD138 in samples in the diagnostic of CE. Current work across two sites is assessing the characteristics of the endometrium within CE and that of the endometrial microenvironment associated with CE.

CONCLUSION

The use of the biobank with its overarching material and data sharing agreements has led to the development of new collaborations within the mechanistic work of the trial. The development of a collaboration with Imperial College London facilitated by the biobank has allowed specialist microbiome work to be undertaken. A further collaborative development with the University of Oxford is currently being established. This collaboration will extend the biobank beyond Tommy’s funded research units.

IMPAIRMENT IN THE FIELD

Despite the trial only having 3 months of recruitment to date, mechanistic work within the trial driven by the biobank has been presented in the European Society of Human Reproduction and Embryology. The importance of timing in detection of asymptomatic CSF: claim-based endometrial abnormalities. Additionally, several peer-reviewed publications are now in development including the novel integrative biobank design.

ACKNOWLEDGEMENTS

We are extremely grateful to all the women who have agreed to be part of this project, the investigators for their help in recruiting them, as well as all researchers and collaborators whose impact has been described here.

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REFERENCES