

Report

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If you have any queries please contact us on the email address above or on 020 7772 6211.

Part 1: Project Details			
Principal grant holder's name	Alexander Heazell		
Contact email	alexander.heazell@manchester.ac.uk		
Contact telephone number	07891 123475		
Organisation where grant is held	University of Manchester		
Project title	Evaluating Risk Antenatally in Twin Pregnancies – A Pilot Study		
Project start date	01/04/2018	Project end date	31/12/2021
Type of project (project, studentship fellowship)	Project		
Date report due	April 2021		

Part 2: Progress report
<p>Please provide a detailed report describing the progress of the research, the extent to which the original aims and objectives of the research have been achieved and the scientific and/or technological achievements of the research. This should be not more than two pages of A4.</p> <p>Aims and Objectives - This project initially aimed to address the current paucity of data linking risk factors for adverse outcome which can be detected or identified in the antenatal period in twin pregnancy. The project was undertaken as a pilot study to provide preliminary data to determine the frequency of certain exposures e.g. supine sleep position and to determine the completeness of data and adherence to the study protocol. Together this information would enable authors to assess whether a larger scale study would be achievable.</p> <p>Methods: Approval was obtained from the Health Research Authority (Ref IRAS 264625) and Greater Manchester West Research Ethics Committee (Ref 19/NW/0522).</p> <p>We had initially planned to approach all women with twin pregnancies attending St Mary's Hospital, Manchester and Birmingham Women's & Children's Foundation Trust (BWC) for one calendar year (estimated to be n=70 at each site). During study set-up it was clear that other sites with specialist twin clinics were interested in participation in the study. The study ran at six sites St Mary's Hospital, Manchester, BWC, University Hospital of Wales, Cardiff, Royal Preston Hospital, University Hospitals Coventry and Warwickshire, United Lincolnshire Hospitals. The study opened to recruitment in December 2019 with the intention of remaining open for the duration of 2020. The study was adopted on to the NIHR CRN portfolio. Study sites were kept informed about the study regularly and study meetings were held regularly throughout 2020 to support recruiting sites.</p> <p>The study was affected by the cessation of research activity between March and June 2020 due to the COVID-19 pandemic. Therefore, the study recruitment period was extended by three months to end in March 2021. In total 188 women agreed to participate in the study (see Figure 1).</p>

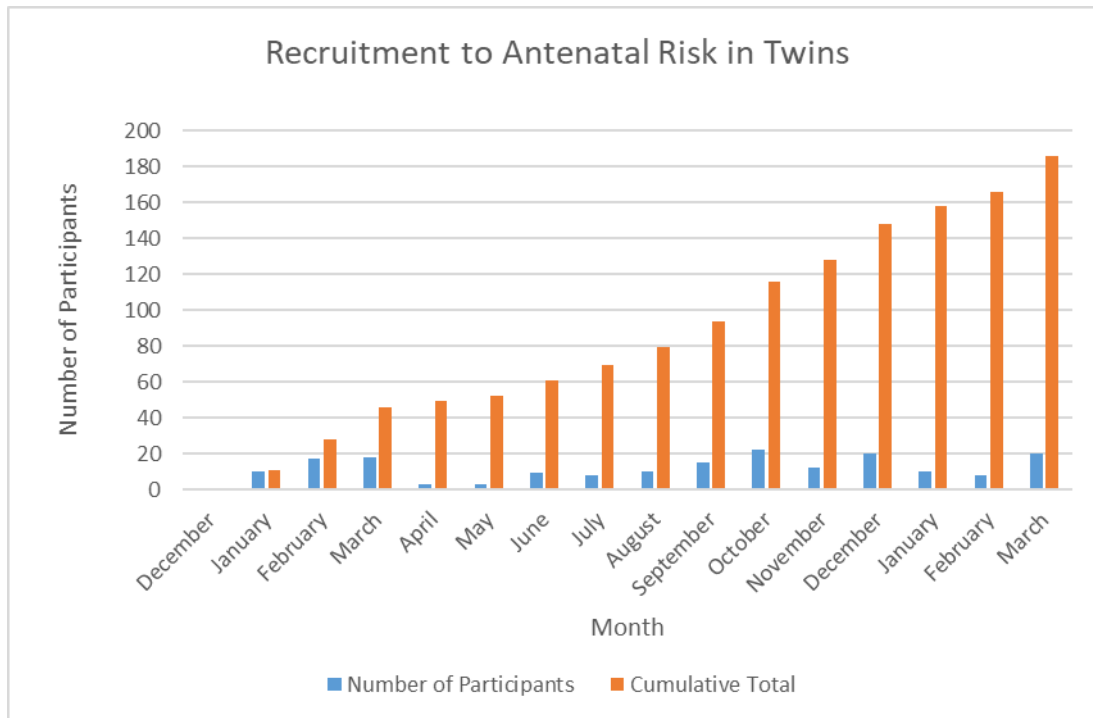


Figure 1 - Recruitment to Evaluating Antenatal Risk in Twins Study. NB Recruitment to the study was halted in late March and recommenced in early June 2020 due to COVID pandemic. Recruitment averaged 15 participants per month when all sites were open to recruitment.

Participants were asked to complete a researcher-administered questionnaire at three time points in their pregnancy (20 weeks', 28 weeks' and 36 weeks' gestation). The questionnaire was based on that used for the Midland and North of England Stillbirth Study which successfully employed similar methodology. Some data was also extracted from medical records e.g. data from ultrasound scans, maternal blood pressure. The final study dataset will include: demographic and socio-economic factors, maternal health, medications, smoking, drug intake, exercise patterns, BMI, fetal movements, sleep habits and fetal growth indices during pregnancy. The research midwife extracted relevant clinical information from medical records. Fetal growth was assessed by ultrasound and selective growth restriction defined as a difference in EFW of >25% (with one twin being <10th centile). To date 121 participants have had outcome data recorded (64%) of all women recruited, but women recruited after November 2020 have yet to have given birth. We anticipate that the dataset will be complete by September 2021 (to allow the women recruited in March 2021 to have given birth). The dataset will be checked for accuracy against the paper data collection forms.

Once the dataset is locked the profile of risk factors will be compared between women who had a normal and adverse pregnancy outcome. Normal outcome will be defined as live births after the recommended gestation for delivery for that type of twin pregnancy and adverse outcome as perinatal death of one or more babies, hypoxic ischaemic encephalopathy and unexpected admission to neonatal intensive care. We will perform a retrospective case-control analysis using standard Mantel-Haenszel odds ratio analysis. All data will be subdivided based upon 'chorionicity'. If there are sufficient numbers of women in exposed vs. non-exposed groups logistic regression will be used to adjust for potential confounders (including gestation).

It is anticipated that this analysis will be completed by Spring 2022 in order that the initial findings can be presented at the BMFMS Annual Meeting in that year.

Please describe the main conclusions you have reached from the research.

Presently, we cannot draw any conclusions from the research project as the dataset is not yet complete. However, we have demonstrated that a study to evaluate antenatal risk factors in twins is ethnically permissible and feasible as we can determine that recruitment of participants to a prospective observational study is achievable and the majority of women recruited can be retained to the completion of the study. It will also be important to delineate (and correct for) the effects of chorionicity. Furthermore, we were approached by more sites via the NHS Clinical Research Network than we could accommodate in this study which suggests that other units would be interested in participating in a larger-scale study. Contact details for these units have been detained.

Have there been any deviations from the original research plan? If yes, please give details.

The duration of the study has been significantly extended due to delays in obtaining requisite ethical and HRA approvals and in study set-up. The COVID-19 pandemic has led to a three-month extension of the recruitment period which was generously supported by additional funding from the Twins Trust.

Please describe any problems you have encountered during the project.

Please see above answer.

Part 3: Lay language progress report

Please describe the progress of the research in lay language.

We know that twin pregnancies have higher rates of complications than pregnancies with a single baby. This project aimed to carry out a study of women with twin pregnancies to find out whether risk factors for poor outcomes for babies can be discovered. This project will not be sufficiently large to give a definite answer, but it will tell us how often women who have twin pregnancies do certain things (e.g. go to sleep laid flat) which are risk factors for poor outcomes in pregnancies with one baby. We ran the study in 6 hospitals in England and Wales and 188 women participated between December 2019 and April 2021. We are now waiting to see the outcomes of all these pregnancies, we expect the last baby to be born in September 2021. We will then analyse the data recorded from the mothers to find out how often there were poor outcomes for babies and mothers, how often mothers had risk factors and whether any of these are related to poor outcomes. The results of the study will be completed by April 2022.

Part 4: Future Research

Please describe your future plans based on the outcomes of this research.

If this study shows that recruiting women to a study of antenatal risk factors in twin pregnancy and retaining them to observe pregnancy outcome is possible, we will apply for further project funding to perform an adequately powered larger-scale study to identify risk factors for adverse outcome in twin pregnancies. We will continue to work with the Twins Trust as the lead stakeholder organisation for mothers with multiple pregnancies.

Has the research led (or do you expect the research to lead) to other successful or pending grant applications? If yes, please provide details below.

We expect that this study will provide evidence that a larger-scale study of antenatal risk factors for adverse outcome in twin pregnancies will be feasible. If that is the case we will submit applications for project grant funding to complete the study.

Has the research led to other academic or industrial collaborations? If yes, please provide details below.

This research has produced a collaboration between Prof Alex Heazell and Prof Mark Kilby's team to investigate and test the Cause of Death in Twins (CoDiT) classification system for perinatal deaths in twin pregnancies. This has been published in BJOG 2020 Nov;127(12):1507-1515.

Part 5: Outputs and outcomes

Please list all publications that have arisen from this grant to date, including any that are currently in press. If possible, please send a copy of publications with this report.

There have been no publications arising from this study to date. Given the sample size recruited to the study we anticipate that there will be at least two papers arising from this study.

Please list all oral and poster presentations that have arisen from this grant to date, including any that are currently submitted. If possible, please send a copy of the abstracts with this report.

There have not been any oral and poster presentations from this grant to date as analysis has not yet commenced. It is anticipated that key initial findings will be presented at the BMFMS meeting in Spring 2022.

Has the research led to any commercial or potential commercial exploitations to date? If yes, please describe the nature of this and if patents have been filed please give details.

No

Please provide a full financial summary of this project. If additional rows for staff are required please insert these. Please provide a breakdown of materials and consumables cost.

	Year 1	Year 2	Total
Staff costs			
Research Midwife (Band 6) 0.2 FTE at two sites	16,038	3,155	19,193
Materials and Consumables			
Travel	105	200	305
Study materials (Pens, Mugs, Printing)	492		492
Open Access Journal Fees		1500	1500
Total	16,635	4,855	21,490

Are there any variations between the original awarded costs and the full financial summary of this project? Please provide an explanation below.

Less resource has been needed for travel between sites (because of the travel ban during COVID pandemic). The Twins Trust agreed to provide an additional £1,612 to support research midwifery salary during the extended recruitment period and to vire funds between headings to allow underspend from travel and consumables to be directed towards salary payments. Funds have been retained for open-access publication fees for one journal publication.

Part 6: Signature of principal grant holder and financial authority of your institute

Print Name	Signature	Date	Position
Alexander Heazell		14 th April 2021	Principal Investigator
Mark Kilby		15 th April 2021	Co-PI

Thank you for taking the time to complete this final report and informing us of your progress