

# Neurodevelopment of babies born to mothers with epilepsy study

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<b>Registration date</b> 26/04/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 26/04/2016	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims:

Exposure in the womb to certain medications is associated with an increased risk of both physical and developmental problems. Reductions in developmental functioning can have lifelong implications for the child, including poor educational achievement and lower skilled occupational prospects in adult life. Effects on development are not always apparent at birth and problems may go unnoticed for many years after a medication has received its licence. There are methods of investigating adverse effects of exposure to medications in the womb but typically they only look at the physical development of the child and they cover very large regions. Typically, when measuring development the child is assessed in person. This poses financial and time limitations for assessing large numbers of individuals from a large region or entire country. This study seeks to investigate the reliability of using questionnaires filled in by the parents of children known to have been exposed to medications in the womb. If such measures are reliable then they would offer a cost effective way to assess large numbers of children across large regions and would speed up the information which can be collected on medications which are commonly used during pregnancy.

### Who can participate?

Pregnant women in their first or second trimester, diagnosed with epilepsy and are either taking antiepileptic medications or not.

### What does the study involve?

The study involves interviewing each participant briefly during their pregnancy about their health and background. Once the child is born, details about the child's physical health are taken from hospital records. Each mother is then asked to complete two questionnaires about their child's development when they are a year old and again when they are 2 years old. When the child is 2 years old, they are visited at home by a member of the study team to complete a developmental assessment with their child.

### What are the possible benefits and risks of participating?

There may be no direct benefits to participants. However, following the assessment when the child is 2 years old, each parent is provided with brief feedback regarding their child's assessment. This letter will also be copied to their GP and kept on the child's file. If there are any

concerns about specific areas of a child's development, these are discussed with the parent and their GP and Health Visitor.

Where is the study run from?

The study is run by the University of Manchester in collaboration with Central Manchester University Hospitals NHS Foundation Trust and other collaborating hospitals.

When is the study starting and how long is it expected to run for?

July 2014 to March 2019

Who is funding the study?

National Institute for Health Research (UK)

Who is the main contact?

Dr Rebecca Bromley

name.study@cmft.nhs.uk

## Contact information

**Type(s)**

Public

**Contact name**

Dr Rebecca Bromley

**ORCID ID**

<https://orcid.org/0000-0003-4008-0917>

**Contact details**

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## Additional identifiers

**Protocol serial number**

16727

## Study information

**Scientific Title**

Neurodevelopment of Babies Born to Mothers with Epilepsy (NaME): a observational cohort study

## **Acronym**

NaME

## **Study objectives**

1.1. Question: Is the utilisation of parental reporting for neurodevelopmental outcome feasible in large populations of children exposed to teratogens in utero?

1.2. Hypothesis: The utilisation of parental reporting for neurodevelopmental outcome will be feasible in large populations of children exposed to teratogens in utero.

2.1. Question: Is the Ages and Stages Questionnaire (ASQ) or the Vineland Adaptive Behaviour Scales (VABS) a reliable measure of neurodevelopmental impairment in populations prenatally exposed to known and unknown teratogens? Is one method more reliable than the other when considered against the Bayley Scales of Infant and Toddler Development?

2.2. Hypothesis: Parental ratings of neurodevelopment will be reliable in their detection of infants with impaired neurodevelopment. It is anticipated that the VABS is likely to be more reliable than the ASQ.

3.1. Question: Are the ratings made by parents on either the VABS or the ASQ at 12 months predictive of ratings at 24 months of age?

3.2. Hypothesis: Parental ratings of neurodevelopment will predict outcomes at 24 months of age.

4.1. Question: What is the neurodevelopmental outcome of children prenatally exposed to newer AEDs?

4.2. Hypothesis: Prenatal exposure to newer antiepileptic drugs will demonstrate different safety and risk profiles pertaining to the neurodevelopment of the child.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

North West - Greater Manchester Central Research Ethics Committee, 22/04/2014, ref: 14/NW/0193

## **Study design**

Observational cohort study

## **Primary study design**

Observational

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Specialty: Reproductive health and childbirth, Primary sub-specialty: Reproductive and sexual medicine; UKCRC code/ Disease:

## **Interventions**

Surveillance for neurodevelopmental teratogenic effects of pharmacological treatment during pregnancy is limited, the consequence of which is that treatment is unlikely to be optimised for maternal or fetal safety. This study aims to investigate the feasibility and reliability of parental reporting methods for the screening of neurodevelopmental outcomes following prenatal exposure to medications across large populations. Antiepileptic drugs (AEDs) provide a means through which to investigate such methods due to the documented outcomes for the older

AEDs. Women with epilepsy, who are in their first or second trimester, will be invited to consent into this follow up study. Demographics and health information will be collected during gestation. When the child is 12 months of age the parent will complete the Ages and Stages Questionnaire (ASQ) and the Vineland Adaptive Behavior Scale (VABS). At 24 months of age the child will be assessed using the Bayley Scales of Infant and Toddler Development (Bayley Scales) and reassessed with the ASQ and VABS. Diagnostic efficiency statistics of sensitivity (percentage of children that are impaired and are classified correctly), specificity (percentage of children who are not impaired and who are classified correctly) and false positive/negative predictive values will be calculated for the parental measures in comparison to the Bayley Scales. The kappa statistic will be calculated to determine level of agreement between measures. This investigation will also provide critical information regarding neurodevelopmental outcome following prenatal exposure to newer AEDs, for which safety remains uncertain. Bayley scores at 24 months will be analysed utilising multiple regression, adjusting for confounding variables, to address this issue.

### **Intervention Type**

Other

### **Primary outcome(s)**

1. Sensitivity and specificity of the Ages and Stages Questionnaire for assessing child development (collected at 12 and 24 months of age)
2. Behaviour and cognitive skills, assessed using Vineland Adaptive Behaviour Scale-II (collected at 12 and 24 months of age)
3. Child development, assessed using Bayley Scales of Infant and Toddler Development-III (collected at 24 months of age)

### **Key secondary outcome(s)**

Child development, assessed using the Bayley Scales of Infant and Toddler Development-III (collected at 24 months of age) across individual antiepileptic drugs treatments.

### **Completion date**

30/03/2019

## **Eligibility**

### **Key inclusion criteria**

1. A diagnosis of epilepsy and either:
  - 1.1. On antiepileptic drug treatment (experimental group)
  - 1.2. Not on treatment (control group)
2. Living within the North West, North East of England or Northern Ireland.
3. Able to provide informed consent
4. In their first or second trimester of pregnancy

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

**Sex**

All

**Key exclusion criteria**

1. Significant learning disability (defined as not able to live independently).
2. Taking non-AED medications which are known to be teratogenic (e.g. warfarin)
3. Unable to understand written or verbal English (due to the standardised assessments in use)

**Date of first enrolment**

07/07/2014

**Date of final enrolment**

31/03/2016

## **Locations**

**Countries of recruitment**

United Kingdom

England

Northern Ireland

**Study participating centre**

**Central Manchester University Hospitals NHS Foundation Trust (Lead Centre)**

Oxford Road

Manchester

United Kingdom

M13 9WL

**Study participating centre**

**Belfast Health and Social Care Trust**

Royal Hospitals

Grosvenor Road

Belfast

United Kingdom

BT12 6BA

**Study participating centre**

**Lancashire Teaching Hospitals NHS Foundation Trust**

Royal Preston Hospital

Sharoe Green Lane

Preston

United Kingdom  
PR2 9HT

**Study participating centre**

**Liverpool Women's Hospital NHS Foundation Trust**

Crown Street  
Liverpool  
United Kingdom  
L8 7SS

**Study participating centre**

**Salford Royal NHS Foundation Trust**

Stott Lane  
Salford  
United Kingdom  
M6 8HD

**Study participating centre**

**City Hospitals Sunderland NHS Foundation Trust**

Sunderland Royal Hospital  
Kayll Road  
Sunderland  
United Kingdom  
SR4 7TR

**Study participating centre**

**Newcastle Upon Tyne Hospitals NHS Foundation Trust**

Royal Victoria Hospital  
Queen Victoria Road  
Newcastle Upon Tyne  
United Kingdom  
NE1 4LP

**Study participating centre**

**South Tees Hospitals NHS Foundation Trust**

Marlon Road  
Middlesbrough  
United Kingdom  
TS4 3BW

**Study participating centre**

**Walton Centre for Neurology and Neurosurgery NHS Foundation Trust**

Lower Lane  
Liverpool  
United Kingdom  
L9 7LJ

**Study participating centre**

**South Tyneside NHS Foundation Trust**

South Tyneside District General Hospital  
Harton Lane  
South Shields  
United Kingdom  
NE34 0PL

**Study participating centre**

**Northumbria Healthcare NHS Foundation Trust**

Rake Lake  
North Shields  
Tyne and Wear  
United Kingdom  
NE29 8NH

**Study participating centre**

**University Hospitals of Morecambe Bay NHS Foundation Trust**

Lancaster Royal Infirmary  
Ashton Road  
Lancaster  
United Kingdom  
LA1 4RP

**Study participating centre**

**Warrington and Halton Hospitals NHS Foundation Trust**

Lovely Ln  
Warrington  
Cheshire  
United Kingdom  
WA5 1QG

**Study participating centre**

**Countess of Chester Hospital NHS Foundation Trust**

The Countess Of Chester Health Park  
Liverpool Rd  
Chester  
Cheshire  
United Kingdom  
CH2 1UL

**Study participating centre**

**East Lancashire Hospitals NHS Foundation Trust**

Royal Blackburn Hospital  
Haslingden Rd  
Blackburn  
United Kingdom  
BB2 3HH

**Study participating centre**

**Mid Cheshire Hospitals NHS Foundation Trust**

Leighton Hospital  
Crewe  
Cheshire  
United Kingdom  
CW1 4QJ

**Study participating centre**

**York Teaching Hospitals NHS Foundation Trust**

Wigginton Rd  
York  
North Yorkshire  
United Kingdom  
YO31 8HE

**Study participating centre**

**Leeds Teaching Hospitals NHS Foundation Trust**

St James Hospital  
Beckett Street  
Leeds  
United Kingdom  
LS9 7TF

**Study participating centre**

**Southport and Ormskirk Hospitals NHS Trust**

Wigan Rd  
Ormskirk  
Lancashire  
United Kingdom  
L39 2AZ

**Study participating centre****Harrogate and District Hospitals NHS Trust**

Lancaster Park Rd  
Harrogate  
United Kingdom  
HG2 7SX

**Study participating centre****County Durham and Darlington NHS Foundation Trust**

North Rd  
Durham  
United Kingdom  
DH1 5TW

## **Sponsor information**

**Organisation**

The University of Manchester

**ROR**

<https://ror.org/027m9bs27>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes