

The MAMA Study: Looking at the effects of stopping or continuing biologics for the treatment of inflammatory arthritis in pregnancy

Submission date	Recruitment status	<input checked="" type="checkbox"/> Prospectively registered
01/08/2024	Recruiting	<input type="checkbox"/> Protocol
Registration date	Overall study status	<input type="checkbox"/> Statistical analysis plan
23/10/2024	Ongoing	<input type="checkbox"/> Results
Last Edited	Condition category	<input type="checkbox"/> Individual participant data
04/02/2026	Pregnancy and Childbirth	<input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

1-2% of women are affected by inflammatory arthritis. Many are treated with bDMARD medications known as 'biologics'. More women with inflammatory arthritis are considering starting a family, because biologics mean they are more able to manage their arthritis. They may face difficult decisions around treatments during pregnancy. Uncontrolled arthritis can lead to worse outcomes in pregnancy, so managing arthritis well is important. Biologics are often avoided during pregnancy because of limited understanding of how these drugs impact pregnancy or arthritis activity. There are concerns about the possible effects of these drugs on babies' immune systems, and some baby vaccinations are routinely delayed. Until recently, most women were advised to stop their biologics during pregnancy; however, due to mounting evidence of their safety, national guidance now states that women can stay on biologics throughout pregnancy. It is unknown whether there is any benefit to this in terms of arthritis control. Certain other medicines used to treat arthritis flares in pregnancy can pose potential harm. We are inviting pregnant women with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) who are prescribed a regularly dosed biologic to join the MAMA. MAMA aims to find out the effects of stopping or continuing biologics during pregnancy. It will compare whether women who continue their biologics have better arthritis control than those who stop, and assess the impact on their pregnancy, their baby, and the costs associated with this decision.

Who can participate?

Pregnant women at less than 28 completed weeks' gestation, aged 16 years old and over with a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) and prescribed a regularly dosed biologic. You do not need to be receiving care at one of the MAMA Participant Sites in order to take part in MAMA. If you would like more information or are interested in taking part in the MAMA Study, please get in touch with the team at the MAMA Co-ordinating Centre.

What does the study involve?

Participants will have an equal (random) chance to continue their biologics throughout pregnancy or to stop by the 28 weeks of pregnancy. During pregnancy, women will be asked to complete a simple arthritis symptom severity questionnaire, monthly via an app (or in writing), and at 3, 6, and 12 months after the baby is born. The woman will be asked if they would be happy for their baby to have blood tests to check their immune response to vaccinations. Mums and babies will be followed up until 24 months after the end of pregnancy, their general health, and their baby's development.

This is a trial of two treatment strategies relating to continuing or stopping prescribed biologics. Biologics are a broad group of drugs which includes many classes and within each class, many marketed products are largely similar in safety profile. The classes of biologics included in this study are detailed in the inclusion criteria and the MAMA trial Reference Safety Information. All drugs are licensed for use in inflammatory arthritis and are already prescribed in pregnancy. Additionally, their use in pregnancy is outlined in the 2022 BSR guidelines on the use of medications in pregnancy.

What are the possible benefits and risks of participating?

Whilst there are no direct benefits to taking part, your contribution may help answer an important question, which could benefit women and their babies in the future.

Both continuing and stopping using biologics beyond 28 weeks of pregnancy are routine practices in the UK, so there are no additional risks to being involved in the trial. Stopping biologic medications can increase the risk of disease activity and flares during pregnancy. Continuing biologic medication in pregnancy may have possible effects on babies' immune systems, and some baby vaccinations may be delayed. This will be discussed with women as part of their clinical care they will also be encouraged to discuss any concerns with their rheumatologist or clinical team.

Optional Infant Immunology part of the Trial

Blood sampling can cause bruising or pain, minimised with local anaesthetic cream.

Where is the study run from?

National Perinatal Epidemiology Unit (NPEU), University of Oxford, UK

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

July 2024 to February 2030

Who is funding the study?

NIHR Health Technology Assessment Programme, HTA

Who is the main contact?

mama@npeu.ox.ac.uk

Contact information

Type(s)

Public, Scientific

Contact name

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Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

1009876

ClinicalTrials.gov (NCT)

Nil known

Central Portfolio Management System (CPMS)

65203

Study information

Scientific Title

The Monoclonal Antibody Medications in inflammatory Arthritis: stopping or continuing in pregnancy (MAMA) trial

Acronym

MAMA

Study objectives

Primary objectives:

To compare the peak of disease activity up to 6 months after the end of pregnancy in pregnant women with AIA randomised to continue bDMARDs versus those randomised to stopping bDMARDs before the third trimester of pregnancy.

Secondary objectives:

In pregnant women with AIA randomised to continue bDMARDs versus those randomised to stopping bDMARDs before the third trimester of pregnancy:

To compare the peak of disease activity up to 12 months after the end of pregnancy

To compare other features of arthritis disease activity

To investigate pregnancy outcomes

In infants born to women with AIA randomised to continue bDMARDs versus those randomised to stop bDMARDs

To compare neonatal outcomes

To investigate infant and child outcomes including global development at 24 months of age, infection up to 24 months of age, and immune function at 2, 5 and 13 months (in a subset of infants where consent has been obtained with an address within geographical reach of Oxford)

Economic evaluation:

To examine using an economic evaluation, whether any additional benefits associated with continuing bDMARDs are justified by any additional health care resources needed

Ethics approval required

Ethics approval required

Ethics approval(s)

approved 30/09/2024, London - Central Research Ethics Committee (3rd Floor 3 Piccadilly Place, London Road, Manchester, M1 3BN, United Kingdom; +44 (0)207 104 8061; londoncentral.rec@hra.nhs.uk), ref: 24/LO/0678

Study design

Interventional randomized controlled trial

Primary study design

Interventional

Study type(s)

Efficacy

Health condition(s) or problem(s) studied

Pregnant women with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), or axial spondyloarthritis (axSpA)

Interventions

This trial will compare two existing pathways of care for bDMARD use in pregnancy that are already being used in the UK, albeit with wide variation. MAMA is a pragmatic, comparative effectiveness trial of these two pathways of care.

The two pathways of care being assessed are:

1. Intervention: continuing bDMARDs throughout pregnancy. The woman's current bDMARD, dose and frequency of administration will continue.
2. Comparator: stopping bDMARDs before the third trimester (week 28) of pregnancy and restarting no earlier than 2 weeks after the end of pregnancy.

For both groups, all other aspects of clinical care are determined by the treating clinical team.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Humira [adalimumab], Enbrel [etanercept], Remicade [infliximab], Simponi [golimumab], Cimzia [certolizumab pegol], ORENCIA [abatacept], RoActemra [tocilizumab], Kevzara [sarilumab], Kineret [anakinra], Ilaris [canakinumab], Cosentyx [secukinumab], Taltz [ixekizumab], Bimzelx [bimekizumab], Tremfya [guselkumab], Skyrizi [risankizumab], Stelara [ustekinumab]

Primary outcome(s)

Peak disease activity measured by the highest RAPID3 total score [self-report] from randomisation up to 6 months after the end of pregnancy

Key secondary outcome(s)

Measured at variable time points up to 24 months after the end of pregnancy:

1. Peak disease activity measured by the highest RAPID3 total score [self-report]
2. Peak pain level measured by the highest RAPID3 pain score [self-report]
3. Peak overall wellbeing measured by the highest RAPID3 patient global estimate score [self-report]
4. Any occurrence of arthritis flare [self-report]
5. Need for escalation of therapy due to inflammatory disease activity [self-report], defined as:
 - New or increased dose of any DMARD for arthritis;
 - New or increased dose of systemic glucocorticoid (GC) for arthritis (oral or intramuscular injection);
 - Received intra-articular GC joint injection
6. Any use of NSAIDs and frequency of use for treatment of joint pain [self-report] (described only using summary statistics)
7. Any occurrence of arthritis flare [maternal self-report] (described only using summary statistics)
8. Health-related quality of life measured using the EQ-5D-5L
9. Anxiety and depression measured using the EQ-5D-5L
10. Livebirth
11. Stillbirth (fetal loss greater than or equal to 24 weeks' gestation)(described using summary statistics)
12. Pregnancy loss less than 24 weeks' gestation (described using summary statistics)

13. Termination of pregnancy (with or without known congenital anomaly)
14. Mode of birth (described only using summary statistics)
15. Preterm prelabour rupture of membranes (described only using summary statistics)
16. New diagnosis of pre-eclampsia (described only using summary statistics)
17. New diagnosis of gestational diabetes (described only using summary statistics)
18. Venous thromboembolism (described only using summary statistics)
19. Confirmed or suspected maternal infection (defined as positive culture from a usually sterile site and/or maternal treatment with antibiotics) (described only using summary statistics)
20. Gestational age (continuous) and preterm birth at:
 - <28
 - 28 to <32 and
 - 32 to 37 gestational weeks
21. Birth weight z-score
22. Early-onset neonatal infection: (<72 hours after birth), microbiologically-confirmed or clinically suspected infection
23. Late-onset infection (>72 hours after birth): microbiologically-confirmed or clinically suspected infection
24. Neonatal death (up to 24 months)
25. Neonatal unit admission
26. Received intensive care (described only using summary statistics)
27. Necrotising enterocolitis (NEC). [defined as babies born <32+0 gestational weeks where NEC is diagnosed at surgery, post-mortem or based on the following clinical and radiographic signs:
 - 27.1. At least one clinical feature from:
 - Bilious gastric aspirate or emesis
 - Abdominal distension
 - Occult or gross blood in the stool (no fissure)
 - 27.2. And at least one radiographic feature from:
 - Pneumatosis
 - Hepato-biliary gas
 - Pneumoperitoneum] (described only using summary statistics)
28. Brain injury [defined as any of neonatal seizures, intracranial haemorrhage (including intraventricular/periventricular haemorrhage grade 3 or 4), perinatal/neonatal stroke, hypoxic-ischaemic encephalopathy, central nervous system infection, bilirubin encephalopathy and among preterm infants only, cystic periventricular leukomalacia] (described only using summary statistics)
29. Chronic lung disease [defined as babies born <32+0 gestational weeks who are alive and receiving any respiratory support at 36+0 corrected gestational weeks] (described only using summary statistics)
30. Retinopathy of prematurity requiring treatment [defined as babies born <32+0 gestational weeks who received treatment with laser, cryotherapy or intravitreal injection for retinopathy of prematurity] (described only using summary statistics)
31. Any congenital anomaly [classified according to Eurocat] and to include congenital heart block as recommended by EULAR (described only using summary statistics)

Key long-term outcome:

32. Child development (measured using the parent-completed Ages and Stages Questionnaire-3 (ASQ-3) 24-month questionnaire total score)
33. ASQ-3 score below the cut-off for risk of developmental delay in the following domains:
 - Communication skills
 - Gross motor skills
 - Fine motor skills
 - Problem-solving skills

- Personal social skills

(described only using summary statistics)

34. Number of infections (defined by admission to hospital for infection or prescribed antibiotic treatment for infection)

35. Duration of breastfeeding

36. Infant death up to 24 months of age

37. Healthcare utilisation and costs

Including neonatal unit admission level of care: intensive care, high dependency, special care, transitional care, including length of stay at different care levels

38. Quality-adjusted life years (QALYs)

39. Cost-consequence analysis

40. Cost-utility analysis

41. Child Quality of Life (measured using the parent-completed PedsQL)

Infant Immunology subset infants:

42. Child vaccine/immunological response:-

- Total IgG/A/M immunoglobulin levels

- Detailed lymphocyte phenotyping

- Vaccine-specific antibodies (diphtheria, tetanus, pertussis antigens, Hib and measles antibody, and PCV13 at 13 months only)

Completion date

28/02/2030

Eligibility

Key inclusion criteria

Current inclusion criteria as of 20/12/2024:

Pregnant women with Autoimmune Inflammatory Arthritis (AIA), satisfying the following criteria:

1. Have a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA)

2. Pregnant at less than 28 completed weeks' gestation

3. Prescribed a regularly dosed bDMARD (including biologic originators and biosimilars) for RA, JIA, PsA or axSpA.

4. Aged 16 years or over

5. Has provided informed consent

For Infant Immunology (optional element):

6. Address "within geographical reach" from the Oxford Vaccine Group

7. Ongoing consent from parents for infant immunological follow-up

Previous inclusion criteria:

Pregnant women with Autoimmune Inflammatory Arthritis (AIA), satisfying the following criteria:

1. Have a diagnosis of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA)

2. Pregnant at less than 28 completed weeks' gestation

3. Prescribed a regularly dosed bDMARD (including biologic originators and biosimilars) for RA, JIA, PsA or axSpA. This includes all current bDMARDs in the following classes and any future

bDMARD licensed under these same classes:

- 3.1. Biologic drugs which block Tumour necrosis factor (TNF)
- 3.2. Biologic drugs which block CD80/86
- 3.3. Biologic drugs which block Interleukin 6
- 3.4. Biologics which block interleukin 1
- 3.5. Biologics which block interleukin 17
- 3.6. Biologics which block interleukin 23
- 3.7. Biologics which block interleukin 12/23
4. Aged 16 years or over
5. Has provided informed consent

For Infant Immunology (optional element):

6. Address "within geographical reach" from the Oxford Vaccine Group
7. Ongoing consent from parents for infant immunological follow-up

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

16 years

Upper age limit

99 years

Sex

Female

Total final enrolment

0

Key exclusion criteria

1. Prescribed rituximab either during pregnancy or in the 6 months prior to conception
2. Prescribed JAK inhibitors
3. Contraindication to cessation of bDMARDs (e.g. active, sight-threatening uveitis)
4. Current, active tuberculosis in the immediate or close family or household members
5. Plans to move in the first 6 months after birth with their infant to live in a country with a high rate of tuberculosis (incidence >40 per 100,000 population)

For Infant Immunology (optional element):

6. Temporary exclusion criteria for taking immunology samples from the babies - fever in previous 72 hours (or felt to be systemically unwell)

Date of first enrolment

10/02/2025

Date of final enrolment

31/08/2028

Locations

Countries of recruitment

United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre

Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust

Doncaster Royal Infirmary

Armthorpe Road

Doncaster

England

DN2 5LT

Study participating centre

Oxford University Hospitals

John Radcliffe Hospital

Headley Way

Headington

Oxford

England

OX3 9DU

Study participating centre

Liverpool Women's NHS Foundation Trust

Liverpool Womens Hospital

Crown Street

Liverpool

England

L8 7SS

Study participating centre

University Hospitals of Leicester NHS Trust

Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre

Manchester University NHS Foundation Trust

Cobbett House
Oxford Road
Manchester
England
M13 9WL

Study participating centre

Kettering General Hospital NHS Foundation Trust

Rothwell Road
Kettering
England
NN16 8UZ

Study participating centre

Great Western Hospitals NHS Foundation Trust

Great Western Hospital
Marlborough Road
Swindon
England
SN3 6BB

Study participating centre

The Royal Wolverhampton NHS Trust

New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
England
WV10 0QP

Study participating centre

Chelsea and Westminster Hospital NHS Foundation Trust

Chelsea & Westminster Hospital
369 Fulham Road
London
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SW10 9NH

Study participating centre

St George's University Hospitals NHS Foundation Trust

St George's Hospital
Blackshaw Road
Tooting
London
England
SW17 0QT

Study participating centre

University Hospital Southampton NHS Foundation Trust

Southampton General Hospital
Tremona Road
Southampton
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SO16 6YD

Study participating centre

Imperial College Healthcare NHS Trust

The Bays
St Marys Hospital
South Wharf Road
London
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W2 1BL

Study participating centre

University Hospitals Birmingham NHS Foundation Trust

Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
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B15 2GW

Study participating centre
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
London
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SE1 7EH

Study participating centre
Tunbridge Wells Hospital
The Tunbridge Wells Hospital
Tonbridge Road
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TN2 4QJ

Sponsor information

Organisation
University of Oxford

ROR
<https://ror.org/052gg0110>

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

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?
Participant information sheet		11/11/2025	11/11/2025	No	Yes
Participant information sheet	version 1.0	18/09/2025	27/01/2026	No	Yes
Study website		11/11/2025	11/11/2025	No	Yes