

# Study of mirtazapine for agitation in dementia

<b>Submission date</b>	<b>Recruitment status</b>	[X] Prospectively registered
13/07/2016	No longer recruiting	[X] Protocol
<b>Registration date</b>	<b>Overall study status</b>	[ ] Statistical analysis plan
28/07/2016	Completed	[X] Results
<b>Last Edited</b>	<b>Condition category</b>	[ ] Individual participant data
05/08/2025	Mental and Behavioural Disorders	

## Plain English summary of protocol

### Background and study aims

Dementia is a common condition in the aging population. People with dementia have difficulties with mental processes such as memory, language, reasoning and identifying people and objects, which become progressively worst over time. There are a range of different types of dementia, but the most common is Alzheimer's disease (AD). Agitation and aggression are common in people who suffer from dementia and can cause problems for the patients, families and the people caring for them. In many cases, agitation is persistent, with many still showing symptoms after six months. There are medicines available to treat agitation, but it is not clear which treatments work best for people with dementia. Current treatments include antipsychotic medication, but these only have limited positive effects and can cause harm. Non-drug treatments are recommended in the first instance, but there is a need for medicines to be available, if non-drug treatments fail. The aim of this study is to investigate the effectiveness of mirtazapine (a type of antidepressant), in the management of agitation in people with dementia.

### Who can participate?

Adults with dementia who are also displaying agitated behaviours, and their carers (family or paid carer)

### What does the study involve?

Participants are randomly allocated to one of two groups. The study is designed so that the participant, their carer, their doctors and the research team do not know which they are taking until the end. Those in the first group are given mirtazapine, those in the second group are given a placebo (dummy pill). All tablets are made in such a way that they look the same, although it is possible to find out which medicine is being taken, in the event of a medical emergency. In both groups, participants are asked to take one tablet for the first two weeks of treatment in the trial, two tablets in the next two weeks and three tablets for the remaining eight weeks of the treatment period (unless there are concerns about side effects resulting from them taking the medication). A blood and ECG (test to check the heart rhythm) test are taken before medication is given and after treatment stops, at 12 weeks. Participants will continue to receive care from their doctors and other health and social services in the usual way whilst they are taking part in the study, and are carefully monitored throughout. Participants and their carers complete a number of questionnaires at the start of the study and then after 6 and 12 weeks to measure agitation and quality of life. There is a long term follow up phone call, six months and one year after trial medication is first taken.

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

Benefits can't be promised, but participation may lead to improved treatments for people with similar symptoms in future. It is however possible that participants may benefit from lower levels of agitation as a result of taking the medication in this study, and improved quality of life for them and their carers. Disadvantages include that the trial will take up time. Blood tests are being taken for participant safety but may cause some discomfort and/or inconvenience.

Mirtazapine does have side effects but most are mild and resolve on their own. These may include: stomach upset, weight gain, feeling drowsy, dizzy, headaches and more rarely a rash and blood problems. A full summary is provided to participants and side effects are carefully monitored by the trial team.

## Where is the study run from?

NHS trusts across the UK

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

December 2015 to October 2019

## Who is funding the study?

National Institute for Health Research (UK)

## Who is the main contact?

1. Miss Juliet High (public)  
[symbad@uea.ac.uk](mailto:symbad@uea.ac.uk)
2. Prof. Sube Banerjee (scientific)  
[sube.banerjee@plymouth.ac.uk](mailto:sube.banerjee@plymouth.ac.uk)

# Contact information

## Type(s)

Public

## Contact name

Miss Juliet High

## Contact details

Norwich Clinical Trials Unit  
Norwich Medical School  
University of East Anglia  
Norwich Research Park  
Norwich  
United Kingdom  
NR4 7TJ  
+44 1603 591708  
[symbad@uea.ac.uk](mailto:symbad@uea.ac.uk)

## Type(s)

Scientific

## Contact name

Prof Sube Banerjee

## Contact details

Executive Dean & Professor of Dementia  
University of Plymouth  
Faculty of Health  
403 Rolle Building  
Plymouth  
United Kingdom  
PL4 8AA  
+44 01752 586740  
sube.banerjee@plymouth.ac.uk

## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2015-003410-25

**ClinicalTrials.gov (NCT)**  
NCT03031184

**Protocol serial number**  
30474

## Study information

### Scientific Title

A pragmatic, multi-centre, double-blind, placebo controlled randomised trial to assess the safety, clinical and cost effectiveness of mirtazapine in patients with Alzheimer's Disease (AD) and agitated behaviours

### Study objectives

Current study hypothesis:

The aim of this study is to assess the safety, clinical and cost effectiveness of mirtazapine in the management of agitation and/or aggression in people with dementia.

Previous study hypothesis:

The aim of this study is to assess the safety, clinical and cost effectiveness of mirtazapine or carbamazepine in the management of agitation and/or aggression in people with dementia.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Committee: South Central – Hampshire A, 04/11/2015, ref: 15/SC/0606

### Study design

Randomized; Interventional; Design type: Treatment, Drug

### Primary study design

Interventional

**Study type(s)**

Treatment

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

Agitation and/or aggression in people with dementia

**Interventions**

Current interventions as of 28/01/2019:

Patients will be randomised in a 1:1 ratio to mirtazapine or placebo, stratified by study region and independent living using permuted block randomisation via a web-based system.

Mirtazapine is a generic 15mg tablet, over encapsulated. IMP and placebo will be identically encapsulated to produce capsules.

Mirtazapine group: Participants receive 15mg starting dose increasing to 30mg after 2 weeks and up to 45 mg in total.

Placebo group: Participants receive 1 capsule starting dose increasing to 2 capsules after 2 weeks and up to 3 capsules in total.

IMP or placebo will be taken for 12 weeks in total. Patients/their carers will be contacted by phone 4 weeks after they stop taking IMP to ask how they are feeling and record any adverse events (AEs). Long term follow up will be at 26 and 52 weeks.

Previous interventions:

Patients will be randomised in a 1:1:1 ratio to mirtazapine, carbamazepine or placebo, stratified by study region and independent living using permuted block randomisation via a web-based system.

Mirtazapine is a generic 15mg tablet, over encapsulated. Carbamazepine is specifically Tegretol Extended Release 100mg tablet, over encapsulated. IMP and placebo will be identically encapsulated (15mg tablets for mirtazapine and 100mg tablets for carbamazepine) to produce capsules.

Mirtazapine group: Participants receive 15mg starting dose increasing to 30mg after 2 weeks and up to 45 mg in total.

Carbamazepine group: Participants receive 100mg starting dose increasing to 200mg after 2 weeks and up to 300mg in total.

Placebo group: Participants receive 1 capsule starting dose increasing to 2 capsules after 2 weeks and up to 3 capsules in total.

IMP or placebo will be taken for 12 weeks in total. Patients/their carers will be contacted by phone 4 weeks after they stop taking IMP to ask how they are feeling and record any adverse events (AEs). Long term follow up will be at 26 and 52 weeks.

**Intervention Type**

Drug

**Phase**

Phase III

**Drug/device/biological/vaccine name(s)**

Mirtazapine

**Primary outcome(s)**

Agitation is measured using the Cohen Mansfield Agitation Inventory (CMAI) long version, at baseline and 12 weeks.

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

1. Cost effectiveness is assessed using a modified Client Service Receipt Inventory (CSRI), alongside information from DEMQOL and EQ-5D-5L interviews at baseline, 6 and 12 weeks
2. Agitation is measured using the CMAI score at 6 weeks (in addition to the primary outcome measure, as a secondary outcome measure)
3. Patient and carer quality of life is assessed via the Zarit carer burden, GHQ-12 and EQ-5D questionnaires at baseline, 6 and 12 weeks
4. Safety is assessed by looking at adverse events and adherence at 6 and 12 weeks. Adverse events are measured by face to face visits, follow up phone calls, review of medical records, notification by other health care professionals, blood and ECG test results and collection of a diary card which is completed by the patient/carer. Adherence is assessed by tablet counts, follow up phone calls and review of a diary card which is completed by the patient/carer, at week 2, 4, 6 and 12.

Long term follow up takes place at 26 and 52 weeks and is assessed via a phone call:

1. Agitation is measured using CMAI
2. Institutionalisation is assessed using a study specific questionnaire
3. Mortality is measured using a study specific questionnaire
4. Clinical management is assessed using a study specific questionnaire

## **Completion date**

30/06/2020

## **Eligibility**

### **Key inclusion criteria**

1. Aged 18 years and over
2. Clinical diagnosis of probable or possible Alzheimer's Disease using National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria
3. A diagnosis of co-existing agitated behaviours
4. Evidence that the agitated behaviours have not responded to management according to the AS/DH algorithm
5. If receiving cholinesterase inhibitors or memantine, must be on a stable dose (defined as three months on current dose)
6. A Cohen Mansfield Agitation Inventory score of 45 or greater
7. Written informed consent to enter and be randomised into the trial or consultee agreement for those without capacity
8. Availability of a suitable informant (consenting identifiable family carer or paid carer) to provide information on carer-completed outcome measures and who consents to take part in the trial

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

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

247

**Key exclusion criteria**

Current exclusion criteria as of 28/01/2019:

1. Current treatment with antidepressants (including monoamine oxidase inhibitors (MAOIs)), anticonvulsants, antipsychotics. Patients must have completed treatment with these medications at least two weeks before trial drug administration
2. Contraindications to the administration of mirtazapine as per its current SmPCs
3. Patients with atrioventricular block, a history of bone marrow depression or history of hepatic porphyrias
4. Cases too critical for randomisation (ie where there is a suicide risk or where the patient presents a risk of harm to others)
5. Female subjects under the age of 55 of childbearing potential, defined as follows: postmenopausal females who have not had at least 12 months of spontaneous amenorrhea or 6 months of spontaneous amenorrhoea with serum FSH>40mIU/ml or females who have not had a hysterectomy or bilateral oophorectomy at least 6 weeks prior to enrolment

Previous exclusion criteria:

1. Current treatment with antidepressants (including monoamine oxidase inhibitors (MAOIs)), anticonvulsants, antipsychotics. Patients must have completed treatment with these medications at least two weeks before trial drug administration
2. Contraindications to the administration of carbamazepine and mirtazapine as per their current SmPCs
3. Patients with atrioventricular block, a history of bone marrow depression or history of hepatic porphyrias
4. Cases too critical for randomisation (ie where there is a suicide risk or where the patient presents a risk of harm to others)
5. Female subjects under the age of 55 of childbearing potential, defined as follows: postmenopausal females who have not had at least 12 months of spontaneous amenorrhea or 6 months of spontaneous amenorrhoea with serum FSH>40mIU/ml or females who have not had a hysterectomy or bilateral oophorectomy at least 6 weeks prior to enrolment

**Date of first enrolment**

01/09/2016

**Date of final enrolment**

29/02/2020

## Locations

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Sussex Partnership NHS Foundation Trust**  
Grove House  
Southview Road  
Crowborough  
United Kingdom  
TN6 1HB

**Study participating centre**

**Norfolk and Waveney Mental Health NHS Foundation Trust**  
Hellesdon Hospital  
Drayton High Road  
Norwich  
United Kingdom  
NR6 5BE

**Study participating centre**

**Gateshead Health Foundation Trust**  
Clinical Trials Office  
Cheviot View  
Queen Elizabeth Hospital  
Queen Elizabeth Avenue  
Sheriff Hill  
Gateshead  
United Kingdom  
NE9 6SX

**Study participating centre**

**Manchester Mental Health and Social Care Trust**  
Greater Manchester Central Manchester University Hospitals NHS Foundation Trust  
West Road  
Off North Road (Between Children's and Adults A&E Departments)  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**Camden and Islington NHS Foundation Trust and Barnet, Enfield and Haringey Mental Health Trust**  
St. Pancras Hospital

4 St. Pancras Way  
London  
United Kingdom  
NW1 3TH

**Study participating centre**

**Birmingham and Solihull Mental Health NHS Foundation Trust**  
Barberry Centre  
25 Vincent Drive  
Edgbaston  
United Kingdom  
B15 2FG

**Study participating centre**

**Guy's and St Thomas' NHS Foundation Trust**  
Guys and St Thomas Hospital  
Great Maze Pond  
London  
United Kingdom  
SE1 9RT

**Study participating centre**

**Surrey and Borders Partnership NHS Foundation Trust**  
Research and Development Department  
Abraham Cowley Unit  
St Peter's Hospital  
Guildford Road  
Chertsey  
United Kingdom  
KT16 OPZ

**Study participating centre**

**Barnet Enfield & Haringey Mental Health NHS Trust**  
St. Ann's Hospital  
London  
United Kingdom  
N15 3TH

**Study participating centre**

**Bradford District Care Foundation Trust**  
Lynfield Mount Hospital

Bradford  
United Kingdom  
BD9 6DP

**Study participating centre**  
**2gether Gloucestershire NHS Foundation Trust**  
Cheltenham  
United Kingdom  
GL53 9DZ

## Sponsor information

**Organisation**  
University of Sussex

**ROR**  
<https://ror.org/00ayhx656>

## 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

The datasets generated during the current study will be available upon request from Prof Sube Banerjee (sube.banerjee@plymouth.ac.uk) once the trial follow-up and analyses are completed. The likely date for this is October 2022.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		23/10/2021	26/10/2021	Yes	No
<a href="#">Results article</a>		01/10/2023	06/11/2023	Yes	No
<a href="#">Abstract results</a>		03/12/2022	05/08/2025	No	No
<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
<a href="#">Protocol file</a>	version 2.0	01/08/2018	31/03/2023	No	No