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Lithium versus quetiapine in treatment resistant depression

Submission date	Recruitment status	[X] Prospectively registered
28/02/2016	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/02/2016	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
12/05/2025	Mental and Behavioural Disorders	

Plain English summary of protocol

Background and study aims
Major depressive disorder (MDD), often referred to as depression, is one of the most common mental health conditions in the world. The symptoms of MDD can vary greatly from person to person, but they generally include low mood, problems with sleeping and/or eating, and a general loss of interest in life. Treatment often relies heavily on antidepressant medications, which work by increasing the activity and levels of a group of chemicals in the brain (neurotransmitters). However, around 30-50% of patients fail to respond adequately to the first or second antidepressant they take (treatment resistant depression). Sufferers of treatment resistant depression have been found to take longer to recover and are often hit harder by the depressive symptoms. A possible option for treating treatment resistant depression is by adding an additional antidepressant medication to those they already take. Lithium and quetiapine are drugs usually used for treating conditions such as bipolar disorder, however there is evidence that they can be effective in the treatment of treatment resistant depression, however little is known about whether this is effective in the long-term. The aim of this study is to find out whether lithium or quetiapine is more effective and cost-effective at treating patients with treatment resistant depression over one year.

Who can participate?
Adults with treatment resistant depression who have been taking the same antidepressant for at least six weeks.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are prescribed lithium to take as well as any antidepressant medication they are already taking. At the start of the study, it is recommended that participants are started on 400mg to take every night, which can be increased or decreased to find the optimum dose for each patient. Those in the second group are prescribed quetiapine to take as well as any antidepressant medication that they are already taking. It is recommended that participants are started on a dose of 50mg per day for the first two days, increasing to 150mg per day on the third day, and up to 300mg per day by week two. It is recommended that the dosage can be adjusted within the range of 150mg-300mg per day as required. Throughout the 52 weeks of the study, participants in both groups complete three short weekly questionnaires about their depression severity, social functioning,

and medication via an online system. They also have assessment visits with a member of the research team at the start of the study and after 8, 26 and 52 weeks, which includes a number of self-report and clinician rated questionnaires, as well as optional blood, hair and saliva samples.

What are the possible benefits and risks of participating?
Participants may benefit from an improvement to their depressive symptoms in the long term from the drug treatment they are assigned to. The risks of taking part are small, although some patients may experience side effects from the medication.

Where is the study run from?
1. King's College London (UK)
2. University of Oxford (UK)
3. Newcastle University (UK)

When is the study starting and how long is it expected to run for?
May 2016 to July 2022

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Prof. Anthony Cleare
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2016-001637-27

ClinicalTrials.gov (NCT)
NCT03004521

Protocol serial number
N/A

Study information

Scientific Title
A randomised pragmatic trial comparing the clinical and cost effectiveness of Lithium and Quetiapine augmentation in treatment resistant Depression

Acronym
LQD

Study objectives
The aim of this study is to assess whether it is more clinically and cost-effective to augment an antidepressant with lithium or quetiapine for patients with treatment resistant depression.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England - Cambridge South Research Ethics Committee, 20/09/2016, ref: 16/EE/0318

Study design
Multi-centre randomized pragmatic randomised parallel trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Major depressive disorder (MDD)

Interventions
Interventions as of 22/11/2016:
Each participant will be randomised 1:1 to lithium or quetiapine add on therapy, after their eligibility has been confirmed. Randomisation will be stratified by recruiting centre and TRD severity (failure of two or failure of three or more antidepressant treatments) with the block size randomly varying. Randomisation will not be blinded.

The trial is designed to be pragmatic, reflecting real world UK clinical practice, in which add-on therapy for treatment resistant depression is given at the dosage and duration deemed most appropriate by the patient's treating clinician. The following dosing regimens will be provided as recommendations only.

Quetiapine arm: Quetiapine (IR or XR) added on to the current antidepressant, typically taken once daily, before bedtime for the XR formulation, twice daily for the IR formulation. Dosing recommendations as per the BNF are as follows: Dose titrated upwards from 50mg on days 1 and 2 and 150mg on day 3, aiming for a dose of 300 mg/day by week 2 if tolerated. Thereafter, flexible dosing is recommended in the range 150-300 mg/day according to tolerance. In elderly patients (>65 years old), the dose titration recommendation will be modified according to the SmPC and best practice as follows: 50 mg/day on Days 1-3, increasing to 100 mg/day on Day 4, 150 mg/day on Day 8 and 300 mg/day not before Day 22 of treatment if required. Patients may remain on the mediation for the full 12 months of the trial (and thereafter) if deemed appropriate by their clinician.

Lithium arm: Lithium carbonate or citrate added on to the current antidepressant. Dosing recommendations are as follows: Dose titration as per standard BNF protocol typically taken orally at night and flexible dose adjustment thereafter aiming for an optimal therapeutic plasma level of 0.6-1.0 mmol/l. Essential pre lithium blood tests will be conducted as per the Maudsley Prescribing Guidelines. Recommended monitoring thereafter will include standard lithium plasma level testing frequency in the acute phase (1 week, 3 weeks and 8 weeks). Recommendations for the continuation phase are to aim for a plasma level of 0.6-1.0 mmol/l with 3 monthly plasma level testing. Patients may remain on the mediation for the full 12 months of the trial (and thereafter) if deemed appropriate by their clinician.

Original interventions:
Each Participant will be randomised 1:1 to lithium or quetiapine add on, after their eligibility has been confirmed. Randomisation will be stratified by recruiting centre and TRD severity (failure of two or failure of three or more antidepressant treatments) with the block size randomly varying. Randomisation will not be blinded.

In both arms, the guidance will be to trial at least 8 weeks of treatment, and to keep the dose of existing antidepressant treatment unchanged and above minimal therapeutic dosage during that time. We propose a pragmatic trial that reflects real world UK clinical practice, in which add-on therapy for TRD is given initially for an acute phase of treatment, leading to a decision point regarding continuation of the therapy and/or the addition of other therapies, depending on response. The two treatment arms for both acute and continuation phases of treatment will be as follows:

Lithium arm: Lithium carbonate, added on the current antidepressant. Acute phase treatment includes dose titration as per standard BNF protocol starting at 400 mg/day taken at night and flexible dose adjustment thereafter aiming for an optimal therapeutic plasma level of 0.6-1.0 mmol/l (Bauer, Pfennig, et al., 2013; Taylor et al., 2015). Blood monitoring will be performed as per Maudsley Prescribing Guidelines, including standard lithium plasma level testing frequency during the acute phase (1 week, 3 weeks and 8 weeks). Continuation phase will continue to aim for a plasma level of 0.6-1.0 mmol/l with 3 monthly plasma level testing.

Quetiapine arm: quetiapine fumarate (quetiapine XR), taken once daily before bedtime. Dose titrated upwards using a standard BNF dose titration protocol of 50 mg on days 1 and 2 and 150 mg on day 3, aiming for a dose of 300 mg/day by week 2 if tolerated. Thereafter, flexible dosing will be followed in the range 150-300 mg/day according to tolerance during the acute phase (as per Bauer et al 2013). Fully flexible dosing during the continuation phase (manufacturer guidance suggests lowest dose to control symptoms should be used in 50-300 mg/day range). In elderly patients (>65 years old), the dose titration protocol will be modified according to the SmPC and best practice as follows: 50 mg/day on Days 1-3, increasing to 100 mg/day on Day 4, 150 mg/day on Day 8 and 300 mg/day on Day 22 of treatment if required during the acute phase.

Continuation phase will be as per younger adults (lowest dose to control symptoms in 50-300 mg /day range).

Participants in both groups are followed up at 8, 26 and 52 weeks.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Lithium (carbonate or citrate), Quetiapine (IR or XR)

Primary outcome(s)
Primary outcome measures as of 22/11/2016:
1. Depression severity is measured weekly using the self-rated Quick-Inventory of Depressive Symptomatology (QIDS-SR), over 52 weeks.
2. Time to all cause discontinuation is measured using patient medical notes and patient self-report to determine the time between first prescription and discontinuation over 52 weeks

Original primary outcome measure:
Longitudinal depressive symptom severity, as measured using the Quick Inventory of Depressive Symptoms self rated (QIDS-SR) questionnaire, assessed weekly via the True Colours system (www.truecolours.nhs.uk) over 52 weeks.

Key secondary outcome(s))
Secondary outcome measures as of 14/11/2018:
1. Change in depression severity measured using the clinician rated Montgomery-Åsberg Depression Rating Scale, MADRS, at baseline, week 8 and week 52
2. Response rates measured by the MADRS at 8 and 52 weeks
3. Remission rates measured using the MADRS at 8 and 52 weeks
4. Health-related quality of life measured using the EuroQol-5D at 8 and 52 weeks
5. Social functioning measured using the Work & Social Adjustment Scale score at baseline, 8 and 52 weeks
6. Adherence to treatment measured using the MARS-5 at weeks 8 and 52
7. Change in weight measured in kilograms by a researcher at baseline, 8 and 52 weeks
8. Change in diastolic blood pressure measured in mmHg by the researcher at baseline, 8 and 52 weeks
9. Change in systolic blood pressure measured in mmHg by the researcher at baseline, 8 and 52 weeks
10. Time to uptake of a new intervention for depression (pharmacological or non-pharmacological) measured by patient self-report up to 52 weeks
11. Time to initiation of treatment measured by patient self-report up to 52 weeks
12. Global improvement measured using the CGI at 8 and 52 weeks
13. Side Effects, measured using the PRISE at 8 and 52 weeks
14. Serious Adverse Events – the number of SAEs measured by reviewing medical notes, patient self-report and patient interview up to 52 weeks

Tertiary outcomes
1. Global severity measured using the CGI at 8, 26 and 52 weeks

2. Global efficacy measured using the CGI at 8, 26 and 52 weeks
3. Side effects measured using the PRISE at 8, 26, and 52 weeks
4. Side Effects measured using the three FIBSER subscales: Frequency, Intensity, and Burden at 8 and 52 weeks
5. Physical health changes measured using continuous blood parameters measured in appropriate units and waist circumference in cm measured at baseline, 8, 26 and 52 weeks (these measures will not be completed for all participants; and will be reported if they are completed for a sufficient number)
6. Satisfaction with lithium / quetiapine treatment measured using the TSQM at 8, 26 and 52 weeks
7. Change in self-report manic symptoms measured using the Altman Mania Self Rating Scale at baseline, 8, 26 and 52 weeks
8. Change in anxiety symptoms measured using the GAD-7 at baseline, 8, 26 and 52 weeks
9. Time to prescription measured by reviewing patient medical records and patient interview up to 52 weeks
10. Baseline adherence to antidepressant treatment measured using the MARS-5 at baseline
11. Change in cognition measured using the DSCT at baseline, 8, 26 and 52 weeks
12. Adherence of clinicians to prescribing and monitoring guidelines for clinical practice as published and recommended measured by reviewing patient medical records up to 52 weeks
13. Proportion of participants having an adequate treatment trial in the acute phase measured by reviewing patient medical records and patient self report
14. Number of hospital admissions for depressive episode measured by reviewing medical records and patient self-report up to 52 weeks
15. Change in personality measure measured using the SAPAS at baseline, 8, 26 and 52 weeks
16. Social functioning measured using the Work & Social Adjustment Scale score weekly over 52 weeks
17. Patient rated experience of the True Colours weekly monitoring system, measured using qualitative interview at a follow up appointment (either 8, 26, or 52 week visit).
18. Patient views and experiences of lithium and quetiapine, measured using qualitative interview (at, or after, 52 week visit).

Ancillary analyses
The following analyses will not be reported in separate publications and not reported in the primary trial paper:
1. Costs over 12 months Measured using the CSRI, modified for TRD, at baseline, 8, 26, and 52 weeks
2. Predictors of treatment response measured using the Maudsley Staging Model, the HAM-D, the MINI 7.0, the IDS-C, the SAPAS, the Maudsley Treatment Inventory, the HCL-16 and medical records up to 52 weeks
3. Change in longitudinal depression severity until treatment discontinuation between lithium and quetiapine measured using the QIDS-SR weekly for up to 52 weeks
4. Collection of biological samples measured using participants who consented to provide blood, hair and saliva samples to the BRC Bioresource collaboration
5. Reliability and validity of the Maudsley VAS current and change measures. Measured using the Mausley VAS current and change, the QIDS-SR and MADRS measured at baseline, 8, 26, and 52 weeks
6. Discrepancy between the self-rated and clinician-rated version of the 16 item IDS measured using the QIDS-SR and the IDS-C at baseline and 8 weeks
7. Relationship between quetiapine and lithium serum levels, prescribed dose and depressive symptom severity measured using blood tests, reviewing medical records, patient interview and the MADRS at baseline to 8 and 52 weeks
8. New interventions and amount of concomitant psychological treatment for depression

(psychotropic medication and/or non-pharmacological) measured using the concomitant medication and concomitant therapy questionnaires at baseline, 8, 26, and 52 weeks

Secondary outcome measures as of 22/11/2016:
1. Change in depression severity measured using the clinician rated Montgomery-Åsberg Depression Rating Scale, MADRS, at baseline, week 8 and week 52
2. Response rates measured by the MADRS at 8 and 52 weeks
3. Remission rates measured using the MADRS at 8 and 52 weeks
4. Health-related quality of life measured using the EuroQol-5D at 8 and 52 weeks
5. Social functioning measured using the Work & Social Adjustment Scale score at baseline, 8 and 52 weeks
6. Adherence to treatment measured using the MARS-5 at weeks 8 and 52
7. Change in weight measured in kilograms by a researcher at baseline, 8 and 52 weeks
8. Change in diastolic blood pressure measured in mmHg by the researcher at baseline, 8 and 52 weeks
9. Change in systolic blood pressure measured in mmHg by the researcher at baseline, 8 and 52 weeks
10. Time to uptake of a new intervention for depression (pharmacological or non-pharmacological) measured by patient self-report up to 52 weeks
11. Time to initiation of treatment measured by patient self-report up to 52 weeks
12. Global improvement measured using the CGI at 8 and 52 weeks
13. Side Effects, measured using the PRISE at 8 and 52 weeks
14. Serious Adverse Events – the number of SAEs measured by reviewing medical notes, patient self-report and patient interview up to 52 weeks

Tertiary outcomes
1. Global severity measured using the CGI at 8, 26 and 52 weeks
2. Global efficacy measured using the CGI at 8, 26 and 52 weeks
3. Side effects measured using the PRISE at 8, 26, and 52 weeks
4. Side Effects measured using the three FIBSER subscales: Frequency, Intensity, and Burden at 8 and 52 weeks
5. Physical health changes measured using continuous blood parameters measured in appropriate units and waist circumference in cm measured at baseline, 8, 26 and 52 weeks (these measures will not be completed for all participants; and will be reported if they are completed for a sufficient number)
6. Satisfaction with lithium / quetiapine treatment measured using the TSQM at 8, 26 and 52 weeks
7. Change in self-report manic symptoms measured using the Altman Mania Self Rating Scale at baseline, 8, 26 and 52 weeks
8. Change in anxiety symptoms measured using the GAD-7 at baseline, 8, 26 and 52 weeks
9. Time to prescription measured by reviewing patient medical records and patient interview up to 52 weeks
10. Baseline adherence to antidepressant treatment measured using the MARS-5 at baseline
11. Change in cognition measured using the DSCT at baseline, 8, 26 and 52 weeks
12. Adherence of clinicians to prescribing and monitoring guidelines for clinical practice as published and recommended measured by reviewing patient medical records up to 52 weeks
13. Proportion of participants having an adequate treatment trial in the acute phase measured by reviewing patient medical records and patient self report
14. Number of hospital admissions for depressive episode measured by reviewing medical records and patient self-report up to 52 weeks

15. Change in personality measure measured using the SAPAS at baseline, 8, 26 and 52 weeks
16. Social functioning measured using the Work & Social Adjustment Scale score weekly over 52 weeks

Ancillary analyses
The following analyses will not be reported in separate publications and not reported in the primary trial paper:
1. Costs over 12 months Measured using the CSRI, modified for TRD, at baseline, 8, 26, and 52 weeks
2. Predictors of treatment response measured using the Maudsley Staging Model, the HAM-D, the MINI 7.0, the IDS-C, the SAPAS, the Maudsley Treatment Inventory, the HCL-16 and medical records up to 52 weeks
3. Change in longitudinal depression severity until treatment discontinuation between lithium and quetiapine measured using the QIDS-SR weekly for up to 52 weeks
4. Collection of biological samples measured using participants who consented to provide blood, hair and saliva samples to the BRC Bioresource collaboration
5. Reliability and validity of the Maudsley VAS current and change measures. Measured using the Mausley VAS current and change, the QIDS-SR and MADRS measured at baseline, 8, 26, and 52 weeks
6. Discrepancy between the self-rated and clinician-rated version of the 16 item IDS measured using the QIDS-SR and the IDS-C at baseline and 8 weeks
7. Relationship between quetiapine and lithium serum levels, prescribed dose and depressive symptom severity measured using blood tests, reviewing medical records, patient interview and the MADRS at baseline to 8 and 52 weeks
8. New interventions and amount of concomitant psychological treatment for depression (psychotropic medication and/or non-pharmacological) measured using the concomitant medication and concomitant therapy questionnaires at baseline, 8, 26, and 52 weeks

Original secondary outcome measure:
1. Costs of each treatment arm, measured using the Client Service Receipt Inventory (modified for treatment resistant depression) at baseline, 8, 26, and 52 weeks
2. Observer-rated depressive symptoms measured at baseline, 8, 26, and 52 weeks using the Hamilton Depression Rating Scale (HAM-D), Montgomery-Asberg Depression Rating Scale (MADRS) and Clinician rated Quick-Inventory of Depressive Symptomatology (QIDS-CR). Outcomes including, proportion of time over 12 months when patients were free from depressive symptoms (QIDS-SR≤5), response rates (≥50% reduction in HAM-D) and remission rates (HAM-D ≤7).
3. Time before other medication added for depression
4. Amount of concomitant treatment (medication and/or non-pharmacological) over 12 months
5. Withdrawal from quetiapine or lithium due to adverse effects
6. Social functioning, measured weekly via the True Colours system using the Work and Social Adjustment Schedule)
7. Health-related quality of life measured using the EuroQol-5D health index completed weekly via the True Colours system
8. Adherence to treatment, using weekly True Colours self report and a modified version of the Medical Adherence Report Scale for treatment resistant depression.
9. Side effects and acceptability of treatment, measured at baseline, 8, 26, and 52 weeks using the UKU Side Effect Rating Scale.
10. Serious Adverse Events including deliberate self-harm and suicidal behaviour
11. Death (all cause and cause-specific including suicide)
12. Physical health (weight, ECG, blood pressure and blood parameters) at baseline, 8, 26, and 52 weeks

13. Global outcome, measured using the Clinical Global Impressions scale (CGI) at 0, 8, 26, and 52 weeks
14. Manic symptoms, assessed using the Altman Mania Self Rating Scale at baseline, 8, 26, and 52 weeks
15. Anxiety symptoms, assessed using the Zung Anxiety Scale at baseline, 8, 26, and 52 weeks
16 New intervention (admission, psychological or drug treatment) for depressive episode by 52 weeks

Completion date
22/07/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 15/12/2017:
1. Under the care of a GP and/or adult mental health services
2. Current episode of depression meeting DSM-5 criteria for major depressive disorder (MDD) – single or recurrent episode
3. 17-item HAM-D score ≥ 14 – this cut-off reflects a pragmatic minimum severity of depression as also chosen in comparable studies such as STAR*D (Rush et al 2006, Trivedi et al 2006)
4. Any gender and aged 18 years or over
5. Meet criteria for treatment resistant depression (Fekadu et al., 2009a; Cleare et al., 2015): current episode has not responded to at least two antidepressants given for at least 6 weeks at minimum therapeutic dose defined as fluoxetine ≥20mg/day, paroxetine ≥20mg/day, sertraline ≥50mg/day, citalopram ≥20mg/day, escitalopram ≥10mg/day, venlafaxine ≥75mg/day, duloxetine ≥60 mg/day, mirtazapine ≥15mg/day, tricyclic antidepressant ≥125mg/day, and dosage as guided by the national Maudsley Prescribing Guidelines or BNF for any other antidepressant. Please note, relapse whilst on an antidepressant also counts as a failed treatment trial
6. Current antidepressant treatment has remained unchanged and at, or above, a therapeutic dose for ≥6 weeks
7. Provision of written, informed consent.

Inclusion criteria as of 22/11/2016:
1. Under the care of a GP and/or adult mental health services
2. Current episode of depression meeting DSM-5 criteria for major depressive disorder (MDD) – single or recurrent episode
3. 17-item HAM-D score ≥ 14 – this cut-off reflects a pragmatic minimum severity of depression as also chosen in comparable studies such as STAR*D (Rush et al 2006, Trivedi et al 2006)
4. Any gender and aged 18 years or over
5. Meet criteria for treatment resistant depression (Fekadu et al., 2009a; Cleare et al., 2015): current episode has not responded to at least two antidepressants given for at least 6 weeks at minimum therapeutic dose defined as fluoxetine ≥20mg/day, paroxetine ≥20mg/day, sertraline ≥50mg/day, citalopram ≥20mg/day, escitalopram ≥10mg/day, venlafaxine ≥75mg/day, duloxetine ≥60 mg/day, mirtazapine ≥30mg/day, tricyclic antidepressant ≥125mg/day, and dosage as guided by the national Maudsley Prescribing Guidelines or BNF for any other antidepressant. Please note, relapse whilst on an antidepressant also counts as a failed treatment trial
6. Current antidepressant treatment has remained unchanged for ≥6 weeks
7. Provision of written, informed consent.

Original inclusion criteria:
1. Under the care of a GP and/or adult mental health services
2. Current episode of depression meeting DSM-V criteria for major depressive disorder (MDD) – single or recurrent episode
3. Score 14 or over on the 17-item Hamilton Depression Rating Scale (HAMD)
4. Aged 18 years or older
5. Meet criteria for treatment resistant depression: current episode has not responded to at least two antidepressants given for at least 6 weeks at minimum therapeutic dose defined as fluoxetine ≥20mg/day, paroxetine ≥20mg/day, sertraline ≥50mg/day, citalopram ≥20mg/day, escitalopram ≥10mg/day, venlafaxine ≥75mg/day, duloxetine ≥60 mg/day, mirtazapine ≥30mg /day, tricyclic antidepressant ≥125mg/day, and as guided by the Maudsley Prescribing Guidelines or BNF for any other antidepressant
6. Current antidepressant treatment has remained unchanged for ≥4 weeks
7. Provision of written, informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
261

Key exclusion criteria
Exclusion criteria as of 15/12/2017:
1. Diagnosis of bipolar disorder (defined as meeting DSM-5 criteria bipolar 1 or bipolar 2) on the MINI 7.0 (as recommended treatments are different for bipolar depression)
2. Diagnosis of current psychosis (as recommended treatments are different for current psychosis – antidepressants plus antipsychotics is the first-line treatment recommendation (NICE, 2009; Cleare et al., 2015)
3. Adequate use of lithium or quetiapine during the current episode. An adequate dose of lithium is defined as the patient taking lithium for at least 4 weeks at an adequate dose (leading to a documented plasma concentration of >0.4mmol/L) and for quetiapine, prescription in the range of 150-300mg/d for 4 weeks or longer. Or, if the patient has taken an inadequate dose of lithium or quetiapine in the current episode, the patient and clinician are not willing to re-prescribe/take the medication.
4. Ongoing use of another atypical antipsychotic (discontinuation will be required before study entry i.e. any time prior to randomisation)
5. Known contraindication to use of either lithium or quetiapine: known hypersensitivity of lithium or quetiapine or any of their excipients; severe renal insufficiency / impairment; untreated hypothyroidism; severe cardiac disease / insufficiency; low sodium levels e.g.

dehydrated patients or those on low sodium diets; Addison's disease; Brugada syndrome or family history of Brugada syndrome; the rare hereditary inborn errors of metabolism galactosaemia, the Lapp lactase deficiency or glucose-galactose malabsorption, concomitant administration of cytochrome P450 3A4 inhibitors; or congenital QT prolongation.
6. We will not recruit any individual who is currently participating in a clinical trial of an investigational medical product (CTIMP).
7. Insufficient degree of comprehension or attention to be able to engage in trial procedures.
8. We will exclude women who are pregnant, actively trying for pregnancy, or currently breastfeeding. This will be based on verbal report of the subject. Otherwise the management will be as appropriate according to standard clinical practice within the context of a pragmatic, open trial, for example adequate contraceptive precautions decided on the clinical judgement of the prescriber.

Exclusion criteria as of 22/11/2016:
1. Diagnosis of bipolar disorder (defined as meeting DSM-5 criteria bipolar 1 or bipolar 2) on the MINI 7.0 (as recommended treatments are different for bipolar depression)
2. Diagnosis of current psychosis (as recommended treatments are different for current psychosis – antidepressants plus antipsychotics is the first-line treatment recommendation (NICE, 2009; Cleare et al., 2015)
3. Use of lithium or quetiapine during current episode
4. Ongoing use of another atypical antipsychotic (discontinuation will be required before study entry i.e. any time prior to randomisation)
5. Known contraindication to use of either lithium or quetiapine: known hypersensitivity of lithium or quetiapine or any of their excipients; severe renal insufficiency / impairment; untreated hypothyroidism; severe cardiac disease / insufficiency; low sodium levels e.g. dehydrated patients or those on low sodium diets; Addison's disease; Brugada syndrome or family history of Brugada syndrome; the rare hereditary inborn errors of metabolism galactosaemia, the Lapp lactase deficiency or glucose-galactose malabsorption, concomitant administration of cytochrome P450 3A4 inhibitors; or previously diagnosed QT prolongation.
6. We will not recruit any individual who is currently participating in a clinical trial of an investigational medical product (CTIMP).
7. Insufficient degree of comprehension or attention to be able to engage in trial procedures.
8. We will exclude women who are pregnant, actively trying for pregnancy, or currently breastfeeding. This will be based on verbal report of the subject. Otherwise the management will be as appropriate according to standard clinical practice within the context of a pragmatic, open trial, for example adequate contraceptive precautions decided on the clinical judgement of the prescriber.

Original exclusion criteria:
1. Diagnosis of bipolar disorder
2. Diagnosis of current psychosis
3. Below age of 18
4. Use of lithium or quetiapine during current episode
5. Ongoing use of another atypical antipsychotic (discontinuation will be required before study entry)
6. Contraindication to use of either lithium or quetiapine. To this end, all patients will have a physical examination, ECG and blood test assessments as per the standard lithium workup. In addition, clinical concerns about the risk of overdose being sufficient to contra-indicate the prescription of lithium in the judgement of the treating clinician would be an exclusion
7. Being in another treatment trial
8. Insufficient degree of comprehension or attention to be able to engage in trial procedures.
9. Pregnant women, those actively trying for pregnancy and those who are breastfeeding

Date of first enrolment
25/11/2016

Date of final enrolment
31/05/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College London
Centre for Affective Disorders
Institute of Psychiatry, Psychology and Neuroscience
103 Denmark Hill
London
United Kingdom
SE5 8AF

Study participating centre
University of Oxford
Department of Psychiatry
Warneford Hospital
Warneford Lane
Oxford
United Kingdom
OX3 7JX

Study participating centre
Newcastle University
Institute of Neuroscience,
Wolfson Research Centre
Campus for Ageing and Vitality
Newcastle upon Tyne
United Kingdom
NE4 5PL

Study participating centre

The South London and Maudsley NHS Foundation Trust
Beckenham
United Kingdom
BR3 3BX

Study participating centre
Oxford Health NHS Foundation Trust
Oxford
United Kingdom
OX3 7JX

Study participating centre
Northumberland, Tyne and Wear Valleys NHS Foundation Trust
Newcastle upon Tyne
United Kingdom
NE3 3XT

Study participating centre
Tees, Esk and Wear Valleys NHS Foundation Trust
West Park Hospital
Edward Pease Way
Darlington
United Kingdom
DL2 2TS

Study participating centre
Sussex Partnership NHS Foundation Trust
Swandean
Arundel Road
Worthing
United Kingdom
BN13 3EP

Study participating centre
Avon and Wiltshire Mental Health NHS Trust
Bath NHS House
Newbridge Hill
Bath
United Kingdom
BA1 3QE

Sponsor information

Organisation
King’s College London, and South London and Maudsley NHS Foundation Trust

ROR
https://ror.org/015803449

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
Access to participant-level data will be judged by the Chief Investigator on a case by case basis. All trial data will be stored in line with the Medicines for Human Use (Clinical Trials) Amended Regulations 2006 and the Data Protection Act and archived in line with the Medicines for Human Use (Clinical Trials) Amended Regulations 2006 as defined in the Kings Health Partners Clinical Trials Office Archiving SOP.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/04/2025	21/03/2025	Yes	No
Results article		01/05/2025	12/05/2025	Yes	No
Protocol article	protocol	26/06/2017		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet		14/11/2018	14/11/2018	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes