







# Prednisolone in adrenal insufficiency disease

<b>Submission date</b> 28/01/2019	<b>Recruitment status</b> No longer recruiting	 Prospectively registered
<b>Registration date</b> 29/01/2019	<b>Overall study status</b> Completed	 Protocol not yet added
<b>Last Edited</b> 04/11/2019	<b>Condition category</b> Nutritional, Metabolic, Endocrine	 SAP not yet added
		 Results not yet added and study completed for less than 1 year
		 Raw data not yet added
		 Study completed

## Plain English Summary

### Background and study aims

In adrenal Insufficiency (AI), the body is unable to produce vital steroid hormones, the chief of these being cortisol. There are about 27,000 individuals in the UK with AI, with up to 3140 new cases per year. The main treatment is replacement of the absent hormone with tablets. This is commonly done using hydrocortisone, taken 3 times daily. Correctly replacing the hormones is a significant challenge. If an individual is given too much hydrocortisone, they risk long term complications including diabetes, osteoporosis (weakened bones) and cardiovascular disease (heart attacks). If, however, they are given too little, patients can feel tired, unwell and may collapse as there is insufficient steroid hormone to cope with stress. As hydrocortisone is eliminated by the body very quickly, it must be taken three times a day to maintain adequate levels, and omitting a dose can be dangerous. This study will look at hydrocortisone as well as an alternative steroid hormone for replacement called prednisolone. Prednisolone is similar to hydrocortisone but is eliminated more slowly, requiring only once daily administration. For the purposes of hormone replacement, prednisolone should be used in much smaller doses than typically used for conditions like rheumatoid arthritis. In the past, prednisolone was used in one-size-fits-all doses of 7.5 mg daily but this caused side effects such as weakening of the bones (osteoporosis) and high blood sugar (diabetes). It is now known that we can prevent these problems by the following plan: (1) we can reduce the dose required for replacement to 3-5 mg a day; (2) by using a blood test to measure the amount of prednisolone remaining in the blood 8 hours after a given dose of prednisolone, we can confirm the right dose of prednisolone for each patient: 3, 4 or 5 mg. Using this plan, we can ensure that patients get the right dose of prednisolone, and minimise any side effects. The aim of this study is to compare low-dose prednisolone with standard hydrocortisone replacement to ensure that low-dose prednisolone is equivalent to standard hydrocortisone treatment in terms of replacing the steroid hormone needs of patients with AI, and in terms of maintaining their overall health.

### Who can participate?

Patients aged 18 – 70 with AI

### What does the study involve?

The participants are randomly allocated to treatment with either (a) 4 months of once daily prednisolone (at the determined dose with placebo at midday and the afternoon) followed by a

2-week washout period followed by 4 months of standard thrice daily hydrocortisone, or (b) 4 months of standard thrice daily hydrocortisone followed by the same washout period and then 4 months of prednisolone. Patients and doctors do not know whether they are taking prednisolone in the first 4 months or the second 4 months as the prednisolone and the hydrocortisone have been specifically made for this study. During each of these 4 month periods, participants are asked to attend the study centre 3 times on Day 1, Day 30 and Day 120 for study visits. This means there is a total of 6 study visits (two 4-month study periods). During each study visit, participants attend having fasted from the night before and having taken their morning steroid tablet at an individualised fixed time. The visit involves: having measurements such as weight, heart rate, and blood pressure taken; providing a urine sample; providing a blood sample; and completing questionnaires. In all, the study visits should take no longer than 3 hours. In between the three study visits, there are also telephone consultations to follow each participant up and to ensure that they are safe.

What are the possible benefits and risks of participating?

The information from this study may help us to understand better how to treat future patients who do not produce enough steroid naturally. Participants will not benefit directly from participating in the study. We will not take any more than 450 ml of blood over a 3-month period. This is about the same amount of blood taken in a single blood donation. Furthermore, on any single visit day we will not take more than 50 ml (about 10 teaspoons). This is a safe amount of blood loss. Participants will be monitored to ensure that they do not become anaemic. As blood is being drawn in this study, there is a risk of slight pain when this is done, and a bruise may remain for a short period after blood is taken. As participants will be changing their steroid treatment as part of this study, there is a risk of undertreatment. This risk will be minimised as patients will be trialled on the new regimen if they have not previously received it before. Possible symptoms will include tiredness, dizziness, pre-syncope, syncope, palpitations, and abdominal pain. These will be detected through symptom reporting, which will take place during all visits and telephone consultations. Participants will also have a 24-hour emergency contact number for a study clinician which they will be instructed to call if they feel unwell.

Where is the study run from?

Imperial College Healthcare NHS Trust (UK)

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

January 2018 to August 2023

Who is funding the study?

National Institute for Health Research (NIHR) (UK)

Who is the main contact?

Dr Sirazum Choudhury  
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## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Sirazum Choudhury

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**Additional identifiers****EudraCT/CTIS number**

2018-001502-28

**IRAS number****ClinicalTrials.gov number**

NCT03936517

**Protocol/serial number**

40936

**Study information****Scientific Title**

Safety and efficacy of Prednisolone in Adrenal Insufficiency Disease (PRED-AID study)

**Acronym**

PRED-AID

**Study hypothesis**

Low dose prednisolone and hydrocortisone as glucocorticoid replacement therapy are equivalent in efficacy and safety

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Current ethics approval as of 04/11/2019:

Approved 15/02/2019, London-South East Research Ethics Committee (Health Research Authority, Skipton House, 80 London Road, London SE1 6LH; +44 (0)207 104 8340; NRESCommittee.London-SouthEast@nhs.net), ref: 19/LO/0083

Previous ethics approval:

London-South East Research Ethics Committee, Health Research Authority, Skipton House, 80 London Road, London SE1 6LH, ref: 19/LO/0083, approval pending

### **Study design**

Randomised; Both; Design type: Treatment, Drug, Cohort study

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

### **Condition**

Adrenocortical insufficiency

### **Interventions**

The method of randomisation is blocked randomisation according to type of adrenal insufficiency (primary versus secondary).

1. Four months of prednisolone once daily followed by 4 months of hydrocortisone thrice daily or
2. Four months of hydrocortisone thrice daily followed by 4 months of prednisolone once daily

The dose of the participant's usual regimen will be unchanged from their pre-study dose. The dose of the alternative medication to be used will be elucidated prior to each participant's enrolment on the study.

There is no follow up period in this study. The study duration of each participant is 9 months.

### **Intervention Type**

Other

### **Phase**

Phase III

### **Primary outcome measure**

Bone health assessed by Osteocalcin concentration at Day 1, Day 30 and Day 120 of each study period

### **Secondary outcome measures**

1. Bone health assessed by urinary NTX concentration at Day 1, Day 30 and Day 120 of each study period
2. Cardiovascular risk assessed by heart rate at Day 1, Day 30 and Day 120 of each study period
3. Cardiovascular risk assessed by blood pressure at Day 1, Day 30 and Day 120 of each study period
4. Cardiovascular risk assessed by waist-hip circumference at Day 1, Day 30 and Day 120 of each study period
5. Cardiovascular risk assessed by lipid profile (total cholesterol, HDL, LDL and triglycerides) at Day 1, Day 30 and Day 120 of each study period
6. Cardiovascular risk assessed by high sensitivity CRP at Day 1, Day 30 and Day 120 of each study period
7. Glycaemic handling assessed by Glucose at Day 1, Day 30 and Day 120 of each study period
8. Glycaemic handling assessed by HbA1c Day 1, Day 30 and Day 120 of each study period
9. Infection rates and severity assessed by completion of the German National Cohort Questionnaire (GNCQ) at Day 1, Day 30 and Day 120 of each study period
10. Wellbeing assessed by completion of the short form health survey-36 (SF-36) at Day 1, Day 30 and Day 120 of each study period
11. Wellbeing assessed by completion of Addisons Quality of Life questionnaire (AddiQoL) at Day 1, Day 30 and Day 120 of each study period

**Overall study start date**

01/01/2018

**Overall study end date**

01/08/2023

## Eligibility

**Participant inclusion criteria**

1. Aged 18 – 70 years
2. Male or female
3. Diagnosed with AI for over 6 months according to standard diagnostic criteria
4. Established on stable HC replacement or prednisolone replacement, dose not altered for at least 3 months
5. Established on a stable dose of Fludrocortisone, if taking, dose not altered for at least 3 months
6. Participants taking other hormone replacements (e.g. levothyroxine, testosterone or growth hormone in secondary adrenal insufficiency) are accepted providing that their replacement doses have not altered for at least 3 months
7. Participants who are otherwise healthy enough to participate, as determined by pre-study medical history and physical examination
8. Participants who are able and willing to give written informed consent to participate in the study

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

Planned Sample Size: 55; UK Sample Size: 55

**Participant exclusion criteria**

1. Participants with a diagnosis of Type 1 or Type 2 diabetes mellitus
2. Unable to give informed consent
3. Taking supplements or herbal medications that the participant is unwilling or unable to stop prior to and during the study period e.g. St John's Wort (may decrease prednisolone levels), Cat's claw, Echinacea (immunomodulatory properties)
4. Currently taking medications that alter CYP3A4 metabolism of glucocorticoids that the participant is unwilling or unable to stop prior to and during the study period e.g. phenytoin, phenobarbital, rifampicin, rifabutin, carbamazepine, primidone, aminogluethimide, itraconazole, ketoconazole, ciclosporin or ritonavir
5. Pregnancy, taking the oral contraceptive pill, or oral oestrogen replacement therapy due to the effects on cortisol binding globulin levels and determination of prednisolone levels. Transdermal oestrogen replacement is permitted
6. Diagnosis of congenital adrenal hyperplasia, untreated

**Recruitment start date**

01/02/2019

**Recruitment end date**

01/02/2023

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Imperial College Healthcare NHS Trust**

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**Sponsor information**

**Organisation**

Imperial College of Science, Technology and Medicine

**Sponsor details**

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**Sponsor type**

University/education

**ROR**

<https://ror.org/041kmwe10>

**Funder(s)****Funder type**

Government

**Funder Name**

NIHR Academy; Grant Codes: DRF-2017-10-115

**Results and Publications****Publication and dissemination plan**

Currently, additional documentation are not available. The trialists are considering publishing the protocol, but this has yet to be confirmed. Publication of the results from this study are expected to be in a high-impact peer reviewed journal around one year after the trial ends.

**Intention to publish date**

01/08/2024

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

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. The data from this study will be published in an anonymised format only. No patient identifiable data (raw data), will be available to anyone other than the researchers and the sponsor (for monitoring purposes only).

## IPD sharing plan summary

Other

## Study outputs

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