

# Effect of exercise on lipid challenged insulin resistance and cardiovascular risk markers in PolyCystic Ovary Syndrome (PCOS)

<b>Submission date</b> 15/07/2013	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 31/07/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 08/03/2022	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Polycystic ovary syndrome (PCOS) is commonly associated with obesity, high levels of free fatty acids and insulin resistance (a condition in which the body produces insulin, but the cells in the body become resistant to it and are unable to use it effectively). Therefore, women with PCOS are at risk of diabetes and heart disease. Over 50 years ago, it was proposed that excessive fat (free fatty acids) interferes with skeletal muscle insulin resistance. Women with PCOS are found to have an insulin signalling defect.

This study aimed to examine the effect of lipid infusion (a mixture of soya oil, glycerol, purified egg phospholipids and phosphate supplement given through a vein) on insulin resistance in PCOS compared to controls. Secondly it aimed to investigate the effect of moderate intensity exercise, which promotes fat utilization, on basal and lipid-induced insulin resistance in PCOS. Then we examine the effect of exercise on cardiovascular risk in women with PCOS and healthy volunteers.

### Who can participate?

We recruit healthy women and women with PCOS aged 19-40 years, both lean participants with body mass index (BMI) 18-25 kg/m<sup>2</sup> and obese participants with BMI 26-40 kg/m<sup>2</sup>.

### What does the study involve?

Participants will be randomly allocated to two day procedures of either saline or intralipid infusion for 5 hours. All participants receive an 8-week program of supervised moderate intensity exercise.

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

Participants would improve their physical fitness and insulin resistance and subsequent cardiovascular risk at the end of the exercise program. The exercise intervention should not harm the participants apart from possible aches and pain in muscles at the beginning. During the insulin sensitivity measurement, there is a slight chance of lowering of blood glucose level (hypoglycaemia) that will be closely monitored and corrected appropriately. Lipid infusion contains soya oil, glycerol, purified egg phospholipids and phosphate. It is licensed to use as

nutritional supplement given through the vein to have a quick effect. Possible adverse effects are occasional febrile (fits) episodes and rarely (i.e. less than 1 in 1000 patients reported) severe allergic reactions. Appropriate safety measures are in place in the department and the whole test will be supervised and monitored by the experienced study doctor and staff. Inserting the cannulas (tubes) and taking blood samples may well cause discomfort and risks of inflammation /infection/bruising at the needle site. The risk will be minimised as the cannulation will be performed by the experienced study doctor in accordance with the local guidelines.

Where is the study run from?

This study is conducted at a single unit, the research diabetes centre, Hull Royal Infirmary.

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

The study started in October 2010 and will run until October 2014.

Who is funding the study?

The funding is provided by diabetes endowment fund and Hull York Medical School.

Who is the main contact?

Prof Stephen Atkin

Stephen.atkin@hyms.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

Prof Stephen Atkin

### Contact details

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## Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

# Study information

## Scientific Title

Testing the hypothesis of metabolic competence in polycystic ovary syndrome

## Acronym

PCOS

## Study objectives

Metabolic incompetence is a progressive condition with chronic elevation of free fatty acids secondary to progressive weight gain and increased central obesity ultimately leading to polycystic ovary syndrome in women with reproductive age. It may be reversible when fat metabolism is modulated by endurance exercise.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Leeds (Central) Research Ethics Committee; Reference:10/H1313/44

## Study design

Case control descriptive hypothesis generating study

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Prevention

## Participant information sheet

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

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

Polycystic ovary syndrome

## Interventions

The participants who fulfil the inclusion and exclusion criteria will be recruited for the study. All the participants will undergo two day procedures of either saline or intralipid infusion for 5 hours with the measurement of insulin sensitivity in the last two hours of infusion by a hyperinsulinaemic euglycaemic clamp. Briefly, following a 12 hour overnight fast, subjects will attend the research centre at 8am for the infusion test. A cannula will be inserted in the elbow for the test infusions as per protocol. Another cannula will be placed into the other forearm vein for blood sampling. This arm will be wrapped with a blanket (60 deg C) in a heating box to be

able to measure the reliable blood glucose. An infusion either saline or intralipid with heparin will be given for first three hours and it will be followed by two hours of glucose/ insulin infusions to measure the rate of glucose disposal by the muscles (insulin sensitivity). A drop of blood will be taken for plasma glucose measurements every 5 minutes throughout 120 minutes. Blood samples will be collected every hour for 5 hours.

The same procedures will be repeated at the end of the exercise program.

Participants will be asked to attend the Department of Sport, Health and Exercise Science at the University of Hull to complete the VO<sub>2</sub>max test and receive 8 week exercise prescription. The VO<sub>2</sub>max test is an exercise test that will be performed on a motorised treadmill. The exercise program is 3 sessions (aiming 60 minutes in each session) per week, moderate intensity for 8 weeks. The performance and attendance will be supervised by the sports specialists from University of Hull. At the end of the program, the repeat measurement of VO<sub>2</sub>max will be conducted on the treadmill.

### **Intervention Type**

Other

### **Phase**

Not Applicable

### **Primary outcome measure**

VO<sub>2</sub> max, HOMA-IR, rate of glucose disposal before or after intralipid, before or after exercise.

### **Secondary outcome measures**

1. Lipid profiles, Blood pressure. BMI, HsCRP, endothelial markers (microparticles)
2. Platelet activation before and after intralipid infusion

All parameters will be measured at baseline and at the end of the exercise program

### **Overall study start date**

17/10/2010

### **Completion date**

01/10/2014

## **Eligibility**

### **Key inclusion criteria**

1. Age 18-40 year premenopausal women
2. For lean participants BMI 18-25 kg/m<sup>2</sup>
3. For obese participants 26-40 kg/m<sup>2</sup>
4. The absence or presence of polycystic ovary syndrome (evidence of anovulation /oligomenorrhoea, clinical or biochemical hyperandrogenism, polycystic ovaries on ultrasound scanning which meets the PCOS diagnostic criteria of Rotterdam consensus statement) for controls and women with PCOS respectively

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

Patient

### **Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

40 Years

**Sex**

Female

**Target number of participants**

48

**Key exclusion criteria**

1. Pregnancy/breastfeeding/trying to conceive
2. History of cardiovascular, renal, hepatic and thyroid disease
3. History of physical disability to exercise
4. History of diabetes mellitus
5. History of allergy to insulin/ soy oil, purified egg (intralipid)
6. Currently on oral anti-diabetic medication that improves insulin sensitivity such as metformin, weight reduction medication (orlistat, sibutramine)
7. Family history of sudden death
8. History of regular exercise three times a week for the last three months
9. Unwilling to be informed to their GP about their participation

**Date of first enrolment**

17/10/2010

**Date of final enrolment**

01/10/2014

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

England

United Kingdom

**Study participating centre**

**Professor of Diabetes, Endocrinology and Metabolism**

Hull

United Kingdom

HU3 2RW

**Sponsor information**

**Organisation**

Hull and East Yorkshire Hospitals NHS Trust (UK)

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.hey.nhs.uk/>

**ROR**

<https://ror.org/01b11x021>

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

University/education

**Funder Name**

Diabetes Endowment Funds/ Hull York Medical School (UK)

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

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan**

Not provided at time of registration

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	28/02/2014		Yes	No
<a href="#">Results article</a>	results	27/02/2019		Yes	No
<a href="#">Results article</a>	results	01/08/2019	02/09/2020	Yes	No
<a href="#">Results article</a>	results	30/09/2020	27/10/2020	Yes	No
<a href="#">Results article</a>		17/02/2022	08/03/2022	Yes	No