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The effect of intermittent ketogenic diets on weight loss and markers of breast cancer risk

Submission date	Recruitment status	[_] Prospectively registered
21/06/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
31/07/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
11/09/2023	Cancer	

Plain English summary of protocol

Background and study aims

Breast cancer is unfortunately very common; approximately 1 in 9 women in the UK develops breast cancer at some point in her lifetime. We know that being overweight increases the chances of developing breast cancer, whilst research has shown that losing weight reduces risk. Researchers at the Genesis Prevention Centre are trying to find the best weight loss diet to reduce risk of breast cancer. This research will be testing two new diets to see whether very low calorie and low carbohydrate ketogenic diets for just two days per week are easier to follow and are better for reducing weight and levels of hormones linked to breast cancer than the usual daily calorie controlled diets. Changes in weight and blood levels of hormones with the diets will show their potential for reducing risk of breast cancer.

Who can participate?

To join the study, women must have a family history of breast cancer (lifetime risk >1 in 6), be any age, have gained greater than 7kg weight since age 20, have a body mass index (BMI) of 24 45 kg/m2 and / or body fat > 30%, be able to record diet diaries. Women must not already be losing weight, be pregnant or planning pregnancy over next few months, have an eating disorder, depression or alcoholism, have a co-morbidity which affects weight or ability to exercise (i.e. diabetes, cardiovascular, respiratory, musculoskeletal, or thyroid disease), or have a previous history of cancer.

What does the study involve?

You will be asked to follow one of the test diets for 4 months. The first 3 months are designed to help you lose weight and the fourth month is designed to help you maintain this weight loss.

After successfully trying the restricted ketogenic diet for two days you will attend an assessment appointment that includes measurement of weight and body fat (using a special pair of scales), blood pressure, fasting blood and urine samples, completion of some simple questionnaires, and your diet (and exercise) advice.

You will be asked to attend monthly appointments with the study dietician during the study that will check your progress and your weight, and discuss any problems (20 - 30 minute appointment). We also aim to repeat all assessments, including fasting bloods, diet diaries and activity monitoring after 1, 3 and 4 months (1 hour appointment).

There are two smaller studies within this study, and women on the study will be able to choose whether to take part. Thirty women (10 from each group) will be asked to provide 2 additional fasting blood samples during week 12, and 30 women (10 from each group) will be asked if they are able to provide 4 additional fasting blood and urine samples (2 during week 12, and 2 during week 16 of the study). These samples will be used to test the short term effect of the diets on markers in the blood that indicate cancer risk, and also the relative effects of the diets on the pattern of genes (the instructions in all of the cells in our bodies) that are active or 'expressed' in our blood cells. This will indicate the direct effects of the diets on our body cells and their potential benefits to health and cancer risk.

What are the possible benefits and risks of taking part?
The diets are very safe and will meet all your nutritional needs except that it is low in calories. However, if you are pregnant, planning a pregnancy or breast feeding, you would not be able to take part in the study.
You will almost certainly lose some weight whilst participating in this diet study. This may reduce your risk of developing breast cancer and other weight related health problems such as diabetes and heart disease, providing that you manage to maintain the weight loss. We will give you advice on how to do this. You will be contributing to our knowledge about the effects of weight loss on breast cancer risk

At the end of the study once the analysis has been done we will let you know your own blood results. Some of the substances we analyse are well-known markers of health, such as insulin and blood sugar, and blood fats such as cholesterol. If these are out of the recommended range we will be able to advise you or refer you on to your GP for further tests or advice.

Where is the study run from?
The Nightingale Centre and Genesis Prevention Centre at Wythenshawe Hospital, Manchester, UK

When is the study starting and how long is it expected to run for?
The study started in June 2009 and finished recruiting in December 2010.

Who is funding the study?
The Genesis Appeal, UK

Who is the main contact?
Dr Michelle Harvie

Contact information

Type(s)
Scientific

Contact name
Dr Michelle Harvie

Contact details
The Nightingale Centre and Genesis Prevention Centre
Wythenshawe Hospital
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United Kingdom
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
09/H1006/34

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
2009BR001

Study information

Scientific Title
The acceptability and efficacy of intermittent ketogenic diets for weight loss and their effects on biomarkers of breast cancer risk

Study objectives
We hypothesise that intermittent ketogenic (very low carbohydrate) diets either as a restricted ketogenic (600 kcal) (RK) or ad lib ketogenic (ALK) diet for 12 days/week only along with exercise will be as or more effective than continuous energy restriction (CER) (a daily modest restriction) and exercise for prevention, and be more acceptable to women on a long term basis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West 10 Research Ethics Committee - Greater Manchester North, 07/05/09, REC ref: 09 /H1006/34

Study design
Single-centre randomised trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied

Breast cancer

Interventions
114 subjects will be randomised to one of three diet groups for 3 months weight loss followed by 1 month weight loss maintenance:

Group 1: Restricted ketogenic diet (RK) (<40g carbohydrate, ~600kcal/day) for 2 days week and ad lib Mediterranean diet for 5 days/week for 3 months, followed by RK 1 day and ad lib Mediterranean diet 6 days/week for 1 month.

Group 2: Ad libitum ketogenic diet (ALK) diet (<40g carbohydrate day, ~ 1200kcal/day) for 2 days /week and ad lib Mediterranean diet for 5 days/week followed by ALK 1 day and ad lib Mediterranean diet 6 days/week for 1 month.

Group 3. Continuous Energy Restriction (CER) Mediterranean diet (~1500kcal/day) 7 days/week for 3 months, followed by ~1900 kcal Mediterranean diet 7 days/week for 1 month.

Women will receive comprehensive written instructions of how to follow the diets at home, including recommended portion sizes, recipes, and behavioural techniques for promoting adherence to diets. The 600 kcal ketogenic diet includes ~ 10oz of protein foods e.g. meat, fish, eggs, tofu, quorn, textured vegetable protein, limited monounsaturated and polyunsaturated fats [Mono-unsaturated Fatty Acid (MUFA), Polyunsaturated fatty acids (PUFA)] and dairy foods, 4 portions of vegetables, 1 portion of fruit. The ad lib ketogenic diet includes unlimited meat, fish, eggs, tofu, quorn, textured vegetable protein , and unlimited MUFA and PUFA fats, limited dairy foods, 4 portions of vegetables, 1 portion of fruit. Both intermittent diets include 2 pints of other low energy fluids, a multivitamin and mineral supplement and are limited in saturated fat, which has possible links with breast cancer. The Mediterranean diet provides 30% energy from fat (15% MUFA, 8% PUFA, 7% saturated) 25% energy from protein and 45% from low glycaemic load carbohydrate.

All participants will also be advised to become more active and will each receive a booklet providing a programme of walking, strengthening, toning and flexibility exercises which can be undertaken at home. They are advised to gradually increase the frequency and intensity of exercise according to current activity levels, to aim to undertake 5 x 45 minutes of moderate activity/week.

All participants will have monthly review with the study dietitian to check their progress. Adherence to the diet and exercise regimens will be assessed from weight change, 7 day food and activity diaries.The intermittent diet groups will also be asked to record adherence/ non adherence to the 2 day diets each week in a study diary.

Intervention Type
Behavioural

Primary outcome(s)
1. Insulin sensitivity from fasting insulin (electrochemiluminescence immunoassay), and glucose (hexokinase/G6PD method) using homeostasis model assessment (HOMA) and Glycosylated hemoglobin (HbA1C) (baseline and 3 months only)
2. Body mass and composition: fat free mass and total fat mass (Bioelectrical impedance: Tanita MC-180) waist and hip and bust circumferences
3. Retention to the energy restriction programmes

Key secondary outcome(s))
1. Plasma leptin (enzyme immunoassay)
2. Serum IGF-1, adiponectin, triglycerides, high density lipoprotein (HDL), and low density lipoprotein (LDL) cholesterol
3. Ketones in serum and urine
4. Inflammatory markers: Tumor necrosis factor (TNF), Interlukin (IL)-6
5. Markers of oxidative stress; advanced oxidation protein products (AOPP)
6. Intake of energy, fat, protein and carbohydrate (7-day food diary) (Dietplan)
7. Activity - 7 day activity diary
8. Profile of mood states questionnaire
9. Hunger and appetite visual analogue scales
10. Any adverse effects associated with the programmes e.g. headaches, constipation, fatigue, cramp, sleep pattern disturbance
11. Resting systolic and diastolic blood pressure
12. Menstrual cycle length for premenopausal women not taking contraceptives

Completion date
28/04/2011

Eligibility

Key inclusion criteria
1. Women
2. Family history of breast cancer (lifetime risk >1 in 6)
3. Pre, post or perimenopausal any age
4. Weight gain since age of 20 > 7 kg
5. Body mass index 2445 kg/ m2 and / or body fat > 30%
6. Able to record diet diaries

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
115

Key exclusion criteria
1. Already successfully losing weight
2. Pregnant or planning pregnancy over next few months
3. Eating disorder, depression or alcoholism

4. Co-morbidity which affects weight or ability to exercise (i.e. diabetes, CV, respiratory, musculoskeletal, or thyroid disease)
5. Previous history of cancer

Date of first enrolment
14/09/2009

Date of final enrolment
28/04/2011

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Nightingale Centre and Genesis Prevention Centre
Manchester
United Kingdom
M23 9LT

Sponsor information

Organisation
University Hospital of South Manchester (UHSM) NHS Foundation Trust (UK)

ROR
https://ror.org/00he80998

Funder(s)

Funder type
Charity

Funder Name
The Genesis Appeal Company Ltd (UK) Grant Ref: GA 10-005

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2013	27/11/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes