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Biomarkers of wholegrain intake

Submission date	Recruitment status	[ ] Prospectively registered
07/04/2014	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
08/07/2014	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
05/08/2019	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Studies show that those who eat more wholegrain foods have a lower risk for developing long-term diseases including heart disease, stroke, diabetes and some cancers. However, the amount needed to give this beneficial effect is not known. To establish whether such a relationship does exist and to test it, we need to make an accurate assessment of peoples wholegrain food intake. However, using food records for this has been difficult because of poor definitions of wholegrain foods, limited information on portion/serving sizes and lack of detail on the wholegrain content of individual foods. Therefore, there is a need to assess wholegrain intake in individuals using other methods. One method is to look for chemical components that are only obtained from wholegrain foods in biological fluids such as blood or urine; the amount of these chemical components is affected by the amount of wholegrain eaten. Sometimes the component can be identified in the same form as occurs in the food, but sometimes as breakdown products (metabolites) formed from the original component can be identified instead. We believe that these components may be used as biomarkers of wholegrain intake. Therefore, we designed this dietary intervention study in healthy volunteers, consuming known amounts of wholegrain foods based on either wheat or rye, to measure corresponding amounts of three candidate biomarkers of wholegrain intake, called alkylresorcinols, enterolactone and enterodiol, in blood and urine.

Who can participate?
Healthy adult men and women can take part in this study.

What does the study involve?
For the first 4 weeks volunteers should avoid eating any wholegrain foods. The volunteers are then randomly allocated to either the wheat group or the rye group. For the next 4 weeks they will then eat three servings per day (about 48 g per day) of either wheat or rye foods according to their group. After this they will eat six servings per day of the same wholegrain foods for another 4 weeks. The volunteers will provide samples of blood and urine at the end of each 4-week period. Once the amount of these components are determined, we will compare which of the three potential biomarkers is a better indicator of rye or wheat intake. We will use a new method of analysis, the metabolomic approach, to identify and quantify the amount of all small molecules present in the blood and urine samples, in order to get a pattern of these small

molecules (metabolites) which might be indicative of a diet rich either in wheat or rye. This method also has the potential to identify new biomarkers related to wholegrain intake, especially metabolites derived from the two primary biomarkers being tested.

What are the possible benefits and risks of participating?
There will be no immediate benefit to those taking part, other than having a health check as part of the screening. The results will be used to develop better methods to measure how much wholegrain people eat, which will help us quantify the health benefit of eating these foods. There are no risks to people taking part. There is a small risk of bruising when giving a blood sample, but we use experienced nursing staff so this is reduced.

Where is the study run from?
Human Nutrition Research Centre at Newcastle University (UK)

When is the study starting and how long is it expected to run for?
January 2008 to July 2009

Who is funding the study?
Food Standards Agency (UK)

Who is the main contact?
Prof. Chris Seal
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N05075

Study information

Scientific Title
Biomarkers of wholegrain intake: contribution of alkylresorcinols and mammalian lignans to the metabolome

Acronym
GrainMark

Study objectives
This is a dietary intervention study designed to compare three different biomarkers of wholegrain intake in response to changes in wholegrain wheat and wholegrain rye consumption. The specific objectives of the study were:
1. To quantify the impact of increased intake of wholegrain wheat or rye on plasma concentrations of alkylresorcinols.
2. To quantify the impact of increased intake of wholegrain wheat or rye on plasma and urinary concentrations of mammalian lignans.
3. To describe the impact of increased intake of wholegrain wheat or rye on the pattern of metabolites (the metabolome) in plasma and urine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Northumberland Research Ethics Committee (NHS REC), 15/11/2007, ref:07/H0902/53. Since the dietary intervention part of the study was undertaken at the Newcastle NIHR CRF, it required NHS Trust Approval which was obtained on 11/12/2007, ref: 4349

Study design
Randomised diet intervention two-group parallel design

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

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

Health condition(s) or problem(s) studied

Changes in concentrations of biomarkers in response to changing wholegrain intake

Interventions
The study is a randomised dietary intervention based on a two-group parallel design with increasing intake of wholegrain wheat or rye to validate two proposed groups of biomarkers of wholegrain intake, and to determine new potential biomarkers of wholegrain intake and overall changes in metabolite profile resulting from their consumption. The design of the intervention is as follows:

1. Wash-out period, 4 weeks: volunteers avoid all wholegrain foods from their diet.
2. Randomisation to study groups using minimisation procedure based on age, gender and BMI.
3. Period 1: three servings per day (equivalent to about 48 g of WG/d) of either WG wheat or WG rye foods for 4 weeks (Dose 1).
4. Period 2: six servings per day of the same WG foods they had during the Dose 1 period, for another 4 weeks (Dose 2).

During the dietary intervention, all wholegrain foods are provided, volunteers avoid all other wholegrain foods.
Wheat intervention group: 100% wholemeal wheat bread, Shredded Wheat Fruitful, Weetabix and 100% wholegrain wheat pasta.
Rye intervention group: 100% wholemeal rye bread, rye porridge, rye muesli and 20% wholegrain rye pasta.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Dose-response changes in plasma and urine concentrations of alkyresorcinols determined by gas chromatography mass spectroscopy, and mammalian lignans determined by high-performance liquid chromatography with Coularray detection. Samples collected after 4 weeks washout (wholegrain free), then 4 weeks consuming three servings of wholegrain per day and, finally, after a further 4 weeks consuming six servings of wholegrain per day.

Secondary outcome measures
Plasma and urine 'metabolome' profile identified by targeted and untargeted metabolite analysis by comprehensive mass spectroscopy analysis. Samples collected after 4 weeks washout (wholegrain free), then 4 weeks consuming three servings of wholegrain per day and, finally, after a further 4 weeks consuming six servings of wholegrain per day.

Overall study start date
01/01/2008

Completion date
01/07/2009

Eligibility

Key inclusion criteria

Males and females aged over 18 years

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
64 volunteers; 32 male, 32 female

Key exclusion criteria
1. Allergies or intolerances to intervention foods
2. Individuals receiving any form of clinical treatment, and/or taking prescribed medications (clinical treatment will affect metabolic profile and/or bioavailability of nutrients from the intervention diet, potentially masking true dietary effects)
3. Individuals taking any form of dietary supplements (dietary supplements may affect metabolic profile and/or bioavailability of nutrients from the intervention diet, potentially masking true dietary effects)
4. Having dietary restrictions, apart from being a vegetarian (for example being on a detox or slimming diet) (some dietary restrictions could interfere with metabolic profile in response to wholegrain diet)
5. Planning to change dietary habits, increase physical activity, change body weight, move away from the study centre locality or to take a lengthy vacation during the time of the study (approximately 12 weeks)
6. Smokers (may affect metabolic profile through increased oxidative stress)
7. History of alcoholism or substance abuse (may affect compliance to dietary intervention and /or metabolic profile)
8. Body Mass Index < 20 kg/m2 or > 30 kg/m2 (very underweight or overweight individuals are likely to have disturbed metabolic profiles and metabolic response to diet)
9. Currently pregnant, planning pregnancy or having had a baby in the past 12 months

Date of first enrolment
01/01/2008

Date of final enrolment
01/07/2009

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Newcastle University
Newcastle upon Tyne
United Kingdom
NE1 7RU

Sponsor information

Organisation
Food Standards Agency (UK)

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Sponsor type
Government

ROR
https://ror.org/05p20a626

Funder(s)

Funder type
Government

Funder Name
Food Standards Agency (UK), Ref. N05075

Alternative Name(s)
The Food Standards Agency, FSA

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration