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Prevention of knee Osteoarthritis in Overweight Females

Submission date	Recruitment status	[X] Prospectively registered
29/06/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/06/2006	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
15/07/2019	Musculoskeletal Diseases	

Plain English summary of protocol

Background and study aims
Osteoarthritis is a condition that causes the joints to become painful and stiff. In the past few decades, research has identified the major risk factors for developing osteoarthritis of the knee. The next important step is to test preventive strategies in groups that are at high risk. Being overweight is the major modifiable risk factor for knee osteoarthritis. It is most often caused by unbalanced food intake in relation to physical activity, a way of life which is hard to change. To accomplish any change in such behaviour, a 'tailor made' diet and physical activity intervention is the most successful. However, an intervention with oral crystalline glucosamine sulphate, a chemical with growing scientific evidence for its joint-protective actions, is probably much easier and more feasible. In this study we will test the preventive effect of both interventions.

Who can participate?
Overweight women aged 50-60 (a high-risk group for knee osteoarthritis)

What does the study involve?
Participants are randomly allocated to either receive the tailor made weight loss intervention or to not receive this intervention. Secondly, in both groups half of the participants are randomly allocated to receive oral crystalline glucosamine sulphate while the other half receive a placebo (dummy drug). Both groups are followed for two and a half years. After two and a half years the occurrence of knee osteoarthritis is measured in both groups. After an additional 4-year observational period (i.e., 6.5 years after the start of the study), all available participants are re-evaluated.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Afdeling Huisartsgeneeskunde (Netherlands)

When is the study starting and how long is it expected to run for?
December 2005 to April 2012

Who is funding the study?
Netherlands Organisation for Health Research and Development

Who is the main contact?
Jos Runhaar
j.runhaar@erasmusmc.nl

Contact information

Type(s)
Scientific

Contact name
Mr Jos Runhaar

Contact details
Department of General Practice, Room NA1906
PO Box 2040
Rotterdam
Netherlands
3000 CA
+31 (0)10 704 4192
j.runhaar@erasmusmc.nl

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR679

Study information

Scientific Title
Prevention of knee Osteoarthritis in Overweight Females

Acronym
PROOF

Study objectives
Amended as of 03/12/2008:
In the present study we will test the preventive effect of a tailor made intervention for reducing weight as well as of an intervention with oral crystalline glucosamine sulphate in a factorial design in a high-risk group of overweight middle aged women who have not yet consulted for

knee osteoarthritis. The positive outcomes with respect to feasibility of recruitement, compliance to the interventions, and low percentage of drop-out in the preceding feasibility trial led to the continuation of the study in this full-scale trial.

This trial was preceded by a feasibility trial with recruitment dates December 2005 – April 2007.

Initial information at time of registration:
The present study is a feasibility study. In this study, we will test the feasibility of the procedures used, the compliance to the interventions, and the usefulness of intermediate outcome measures in a specific high-risk group. If the results of this feasibility study are satisfactory, the project will be upgraded into a full scale preventive trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Erasmus MC Medical Ethical Approval Commission, ref: 2005-231

Study design
Placebo-controlled 2 x 2 randomised factorial trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Prevention

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
Osteoarthritis in overweight females

Interventions
Patients are randomised for one of the following two interventions:
Intervention group A: a tailor-made intervention to reduce weight under the direction of dieticians of homecare, Rotterdam for one year
Control group A: the control group will not receive this active intervention to reduce weight

Intervention group B: daily supplementation with glucosamine sulphate (1500 mg per day) for one year
Control group B: the control group will receive a placebo

Intervention Type

Mixed

Primary outcome measure
Amended as of 03/12/2008:
Difference between intervention and control group in:
1. Occurrence of radiological knee OA (Kellgren and Lawrence index two or more), or
2. Joint space narrowing of 1 mm or more in one of the knees during follow-up time, or
3. Occurrence of knee OA according to the American College of Rheumatology (ACR) criteria

Initial information at time of registration:
1. Percentage of participants per group showing a reduction of 5 kg and/or 5% decrease at one year follow-up compared to baseline weight
2. Percentage of women compliant to the interventions in the study
3. Percentage lost to follow-up after one year
4. Percentage of eligible persons

Secondary outcome measures
Amended as of 03/12/2008:
Difference between intervention and control group in:
1. Quality of life (Euroqol)
2. Knee pain and knee function (WOMAC)
3. Actual weight loss
4. Occurrence of knee osteoarthritis seen on MRI (scoring according to the KOSS protocol for the presence of cartilaginous lesions, osteophytes, subchondral cysts, bone marrow oedema, for meniscal abnormalities, presence and size of effusion, synovitis and Baker's cysts)
5. Increase of bone and cartilage degradation markers

Initial information at time of registration:
1. Differences in intermediate outcomes between the intervention group A and control group A at one year follow-up
2. Differences in intermediate outcomes between intervention group B and control group B at one year follow-up
3. Change and variation in change in intermediate outcomes between baseline and one year follow-up.

Overall study start date
01/12/2005

Completion date
01/04/2012

Eligibility

Key inclusion criteria
Women aged 50 - 60 years who are overweight (body mass index [BMI] of 27 kg/m^2 or more)

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
400

Total final enrolment
407

Key exclusion criteria
Amended as of 03/12/2008: point six of the exclusion criteria has been amended as follows:
6. Contraindication for magnetic resonance (MR) imaging

Initial information at time of registration:
1. Knee osteoarthritis (OA)
2. Knee pain indicating knee OA
3. Radiological signs indicating knee OA (Kellgren-Lawrence index of 2 or more)
4. Positive for knee OA according to the American College of Rheumatology (ACR) criteria for knee OA
5. Presence of severe co-morbidity
6. Pacemaker
7. Current use of glucosamine sulphate
8. Not being able to communicate in the Dutch language

Date of first enrolment
01/06/2008

Date of final enrolment
01/05/2009

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus University Medical Center
Department of General Practice
PO Box 2040
Rotterdam
Netherlands
3000 CA

Sponsor information

Organisation
Erasmus Medical Centre (Netherlands)

Sponsor details
Department of General Practice
PO Box 2040
Rotterdam
Netherlands
3000 CA

Sponsor type
Hospital/treatment centre

Website
www.erasmusmc.nl/huisartsgeneeskunde/research/

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Research organisation

Funder Name
Netherlands Organisation for Health Research and Development

Alternative Name(s)
Netherlands Organisation for Health Research and Development

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Netherlands

Results and Publications

Publication and dissemination plan
Results of the first 2.5 years of the PROOF Study will be published from 2012 – 2015
Results of MRI data will be published from 2015 – 2017
Results of the complete follow-up time will be published from 2016 – 2017

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2014		Yes	No
Results article	results	01/08/2014		Yes	No
Results article	results	01/09/2014		Yes	No
Results article	results	01/10/2014		Yes	No
Results article	results	01/08/2015		Yes	No
Results article	results	01/08/2015		Yes	No
Results article	results	01/02/2016		Yes	No
Results article	results	01/04/2016		Yes	No
Results article	results	01/06/2016		Yes	No
Results article	results	01/07/2016		Yes	No
Results article	results	01/10/2016		Yes	No
Results article	results	01/08/2017		Yes	No
Results article	results	01/07/2019	15/07/2019	Yes	No