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Towards Onset Prevention of COGnition decline in adults with Down syndrome (the TOP-COG study)

Submission date
07/10/2011

Recruitment status
No longer recruiting

Registration date
17/11/2011

Overall study status
Completed

Last Edited
01/08/2016

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered

[X] Protocol

[ ] Statistical analysis plan

[X] Results

[ ] Individual participant data

Plain English summary of protocol

Background and study aims
This study is to find out whether it will be feasible to conduct a larger study to test whether a medication called simvastatin can prevent the onset of dementia in adults with Down syndrome. A lot of people with Down syndrome develop memory problems or Alzheimers disease /dementia in middle age. This is disabling, causing loss of skills and abilities. Over time, a naturally occurring product called amyloid-beta builds up in the brain and causes these memory problems. Studies show simvastatin may possibly slow this down, and delay the start of memory problems. Down syndrome is caused by having extra genetic material on chromosome 21. This extra genetic material means people with Down syndrome also have a double dose of the amyloid-beta that causes memory problems, as it is also coded on chromosome 21. There has only been one previous study on simvastatin with people with Down syndrome. It looked at the medications they had taken in the past, and found the people who did not have memory problems were more likely to have taken simvastatin than those who had memory problems. So simvastatin may help prevent the chance of getting memory problems, but we do not know for sure. Doctors do not at present prescribe simvastatin to prevent dementia but do prescribe it for other conditions.

Who can participate?
Everyone with Down syndrome who will be aged 50 or more by Autumn 2012, and stays in Greater Glasgow and Clyde, Lothian, or Tayside can participate, if they do not already have dementia. GPs, learning disabilities services, and Down Syndrome Scotland are writing to people to send out invitations to take part in the study. The plan is that 60 people will take part.

What does the study involve?
A researcher will visit participants at home and ask questions about their health and supports. She/he will ask for a blood test, or a thumb pin-prick sample and saliva collection. Participants are then allocated to one of two groups. This is so we can compare the outcomes of taking simvastatin against taking a placebo (a placebo is a capsule with no medication in it.) To try to make sure the groups are the same to start with, each person is put into a group by chance (a bit like tossing a coin). There is an equal chance of getting into either of the two groups. For the

following year, the doctor will prescribe people in one group a simvastatin capsule every night (40mg), and the other group a placebo capsule every night. Both groups also continue to receive all their health care and supports as per usual. Six to 12 weeks after starting, we will visit to make sure there are no side effects. After a year of taking the medication, the researcher will visit again to ask about health and supports, and request an optional blood test. We can then check the differences between the two groups. The study will assess how many people take part, and factors affecting participation. It will determine the most sensitive tests and puzzles to detect early memory changes. Differences between the two groups in memory changes over a year will be measured, to gauge the number who should be recruited in the future large study. A sub-study will also seek the views of about 10 people regarding taking part in the trial. We will also ask participants if we may store their blood samples for future use, and link to their health records in future.

What are the possible benefits and risks of taking part?
We cannot promise the study will prevent participants from developing memory problems /Alzheimers disease. However the study will provide important information necessary for a much larger study on simvastatin. If simvastatin does reduce the chance of getting Alzheimer disease, then half of the study participants would have benefited, and the other half will benefit from its future use, and this will also be important news for everyone with Down syndrome. We hope that people will enjoy taking part in the study and meeting with the researcher. Participants have to take a simvastatin or placebo capsule every night for a year, and avoid drinking grapefruit juice and excessive alcohol. Placebo has no risks. All medications whether given by a doctor or bought over the counter can cause side-effects in some people, and simvastatin is not an exception. It is however commonly used, so we know its safety profile is good. We have no reason to think this will be any different for people with Down syndrome, but will check. Lots of people take simvastatin to prevent heart attacks and strokes. Most people do not get side-effects. The most common side effect is muscle pain or weakness, which affects about 1 in every 100 people; occasionally people have to stop the simvastatin to get rid of this.

Where is the study run from?
The study is run from the Institute of Health and Wellbeing at the University of Glasgow (UK)

When is the study starting and how long is it expected to run for?
The study is starting at the beginning of 2012 and will run for 24 months. We plan to recruit participants until Autumn 2012.

Who is funding the study
The Chief Scientist Office, Scottish Health Department of the Scottish Government (UK)

Who is the main contact person?
Prof. Sally-Ann Cooper
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Contact information

Type(s)
Scientific

Contact name
Prof Sally-Ann Cooper

Contact details
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Additional identifiers

Protocol serial number
Sponsors protocol number: GN09CP301

Study information

Scientific Title
Towards Onset Prevention of COGnition decline in adults with Down syndrome (the TOP-COG study): a double-blind randomised placebo-controlled trial

Acronym
TOP-COG

Study objectives
It is feasible to study and collect pilot data on whether simvastatin is effective in the primary prevention of dementia in older adults with Down syndrome.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Scotland A REC approved on 05/07/2011, amendment approved on 06/10/2011, Ref: 11/AL/0200

Study design
Double-blind randomised placebo-controlled trial with a nested qualitative study

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Dementia in people with Down syndrome

Interventions

A researcher will visit participants at home and ask questions about their health and supports. She/he will ask for a blood test, or a thumb pin-prick sample and saliva collection. Participants are then allocated to one of two groups. This is so we can compare the outcomes of taking simvastatin against taking a placebo. To try to make sure the groups are the same to start with, each person is put into a group by chance. There is an equal chance of getting into either of the two groups. For the following year, the doctor will prescribe people in one group a simvastatin capsule every night (40mg), and the other group a placebo capsule every night. Both groups also continue to receive all their health care and supports as per usual. 6-12 weeks after starting, we will visit to make sure there are no side effects. After a year of taking the medication, the researcher will visit again to ask about health and supports, and request an optional blood test. We can then check the differences between the two groups.

The study will assess how many people take part, and factors affecting participation. It will determine the most sensitive tests and puzzles to detect early memory changes. Differences between the two groups in memory changes over a year will be measured, to gauge the number who should be recruited in the future large study.

A sub-study will also seek the views of about 10 people regarding taking part in the trial.

We will also ask participants if we may store their blood samples for future use, and link to their health records in future.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Simvastatin

Primary outcome(s)
The numbers screened and recruited each month over a 6-month recruitment period

Key secondary outcome(s))
Current secondary outcome measure(s):
1. Memory for objects from the Neuropsychological Assessment of Dementia In Intellectual Disabilities (NADIID) battery
2. Selective Attention Cancellation Task
3. Pattern Recognition Memory from the Cambridge Neuropsychological Test Automated Battery (CANTAB)
4. The cats and dogs test
5. Tower of London Test
6. Cued Recall Test
7. Category fluency
8. Story recall (adapted from the Rivermead Behavioural Memory Test for Children)
9. Adaptive Behavior Scale (AAID-ABS)
10. Townsend scale
11. EQ-5D

12. Client Services Receipt Inventory (CSRI)
13. Carer General Health Questionnaire-12 (GHQ-12)
14. Blood AB40 / AB42 level

Previous secondary outcome measure(s):
1. Memory for objects from the Neuropsychological Assessment of Dementia In Intellectual Disabilities (NADIID) battery
2. Selective Attention Cancellation Task
3. Pattern Recognition Memory from the Cambridge Neuropsychological Test Automated Battery (CANTAB)
4. Delayed Matching to Sample from the CANTAB
5. Tower of London Test
6. Cued Recall Test
7. Category fluency
8. Story recall (adapted from the Rivermead Behavioural Memory Test for Children)
9. Adaptive Behavior Scale (AAID-ABS)
10. Townsend scale
11. EQ-5D
12. Client Services Receipt Inventory (CSRI)
13. Carer General Health Questionnaire-12 (GHQ-12)
14. Blood AB40/AB42 level

Completion date
31/03/2014

Eligibility

Key inclusion criteria
1. Down syndrome
2. Aged 50 years or over

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. No consent obtained
2. Unable to comply with the protocol, including providing blood or saliva for baseline apolipoprotein E e4 polymorphism (APO E e4) measurement, and venous or capillary blood for cholesterol measurement
3. Dementia at baseline (as the study is investigating primary prevention)
4. Diabetes (as this is an indication for a prescription of a statin)
5. Clinically evident atherosclerotic disease (as this is an indication for a prescription of a statin)

6. Being at risk for cardiovascular disease (as this is an indication for a prescription of a statin)
7. Liver disease
8. Chronic renal insufficiency
9. Being prescribed a statin or medicines that are listed as contraindicated with simvastatin in its summary of product characteristics:
9.1. Statin
9.2. Fibrates
9.3. Nicotinic acid
9.4. Cyclosporine
9.5. Triazole antifungals, including fluconazole, itraconazole, posaconazole
9.6. Ketoconazole
9.7. Macrolide antibiotics, including erythromycin, clarithromycin, telithromycin
9.8. Danazol
9.9. Fusidic acid
9.10. Human immunodeficiency virus (HIV) protease inhibitors, e.g. nelfinavir
9.11. Nefazodone
9.12. Verapamil
9.13. Amiodarone
9.14. Warfarin
10. Having previously had a statin serious adverse reactions (SAR)
11. Unable or unwilling to avoid consumption of grapefruit juice
12. Excessive alcohol use (>21 units/week for men, or >14 units/week for women)

Date of first enrolment
01/04/2012

Date of final enrolment
31/03/2014

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
University of Glasgow
Glasgow
United Kingdom
G12 0XH

Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office (Reference: CZH/4/626)

Alternative Name(s)
CSO

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	29/07/2016		Yes	No
Protocol article	protocol	03/06/2014		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes