Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

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

Researchers
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Aim
To acquire data to design a full-scale multi-centre placebo-controlled randomised controlled trial (RCT) of simvastatin to prevent the onset of dementia in older adults with Down syndrome.

Project Outline/Methodology
Over age 50, 40% of adults with Down syndrome (trisomy 21) have dementia. Trisomy 21 also causes a triple dose of amyloid precursor protein, increasing brain deposition of a protein called amyloid ß, which is implicated in Alzheimer disease. Statins slow brain amyloid ß deposition. Studies suggest they may delay onset/progression of Alzheimer disease, so help populations with amyloid overproduction e.g. Down syndrome. However, there are no RCTs, and only one Down syndrome cohort study which found people on statins had less than half the risk of dementia.

There are few medication RCTs with adults with learning disabilities, so little information to inform likely recruitment rates. Studies provide data on onset of dementia and change in proxy-reported skills and functioning over time, but little on actual cognitive decline, and how best to measure this.

TOP-COG was a small double-blind RCT of simvastatin 40mg/day versus placebo for 12 months, in adults with Down syndrome aged 50 and over, who did not have dementia. It assessed feasibility of recruitment, retention, recruitment sources, safety, and most useful tools to measure early cognitive decline. It included a qualitative study, to determine motivators and barriers to recruitment, and experience of study participation. It considered whether a full-scale RCT should be undertaken, and if so, how many participants it would need.

Key Results
Over 12 months we identified 78% of the likely eligible Down syndrome population (aged 50 and over, without dementia), and recruited 21 (11.6%), from a total population size of 3,135,974. Most were recruited from learning disabilities day centres, health professionals, and via the Scottish Primary Care Research Network. Sixty-two percent completed the full study. Medication was well tolerated. We found the most useful cognitive measure was the Memory for Objects from the NADIID battery, with the Category Fluency Test also having utility. The main reasons people declined to participate were not wanting to take medication, and not knowing if they would receive the active or placebo medication. We identified a need for information/education on the importance of RCTs with this population. Amyloid ß blood tests need further investigation as a potential marker of cognitive problems in this population. The full-scale RCT is feasible, requires 155 participants to demonstrate the effectiveness of simvastatin, and will need to recruit from 36% of the UK population.

Conclusions
The full-scale RCT should be undertaken.

What does this study add to the field?
In addition to designing the full-scale RCT, the study provides useful information for other future research with this population (recruitment, cognitive tests).

Implications for Practice or Policy
Dementia is a highly disabling, progressive disorder culminating in premature death. It has a negative impact on the adult with dementia, their family and friends, leads to increasing health and social care resource consumption, and has a major societal and economic cost. No effective treatments have yet been found for adults with Down syndrome. Hence preventative measures are urgently needed, and it is crucial that trials are undertaken. If statins are effective, there is a case for their routine prescription for all adults with Down syndrome. Simvastatin is a very cheap intervention, at 38p per 28 tablets.

Where to next?
To apply for funds to conduct the full-scale RCT.

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