

Identify adults with Down syndrome aged  $\geq 50$  in GG&C, Lothian, Tayside, via primary care, Down Syndrome Scotland, local services, etc. and send information

Telephone call with adults with Down syndrome aged  $\geq 50$ /carers to answer their questions and check whether they should be invited to participate\*  
N~100

Home visit to recruit, collect baseline data on cognitive function, adaptive behaviour and health. Randomize, stratified by age (<55 years or  $\geq 55$  years), APO E e4, cholesterol (<5 or  $\geq 5$ mmol/l)  
N=60

Meets exclusion criteria\*  
Exclude

Simvastatin 40mg OD  
N=30

Placebo  
N=30

Clinical and blood assessment for ARs after 6-12 weeks of drug.  
AEs assessed every 3 months

Clinical and blood assessment for ARs after 6-12 weeks of placebo.  
AEs assessed every 3 months

Cognitive function and general health assessed after 12 months of drug.  
N~25

Cognitive function and general health assessed after 12 months of placebo.  
N~25

Nested qualitative study  
N~10,  
plus N~10 who are not RCT participants

- \*Exclusion criteria:**
- 1) Failure to gain consent
  - 2) Unable to comply with the protocol
  - 3) Dementia at baseline
  - 4) Diabetes
  - 5) Atherosclerotic disease
  - 6) At risk of cardiovascular disease
  - 7) Liver disease
  - 8) Chronic renal insufficiency
  - 9) Prescribed: statin, fibrates; nicotinic acid; cyclosporine, triazole antifungals, including fluconazole, itraconazole, posaconazole; ketoconazole, voriconazole; miconazole oral gel, macrolide antibiotics, including erythromycin, clarithromycin, telithromycin; danazol; fusidic acid; HIV protease inhibitors, e.g. nelfinavir; nefazodone; verapami; amiodarone; warfarin; diltiazem; amlodipine; moderate CYP3A4 inhibitors if the person lives alone or with only part-time paid support; Hepatitis C protease inhibitors, e.g. boceprvir, telaprevir.
  - 10) Previous statin SAR
  - 11) Unable or unwilling to avoid consumption of grapefruit juice
  - 12) Alcohol use >21 units/week for men or >14 units/week for women.