# Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

**ScriptSwitch™ Rapid Update 3 – April 2017**

## Statin prescribing for people with severe mental illnesses: a staggered cohort study of 'real-world' impacts.

A recently published UK study of more than 45,000 people with severe mental illnesses (SMI) found that while statins improved lipid modification, there was no evidence of reduced cardiovascular disease (CVD) events. The lack of positive CVD outcomes is probably due to the low power of the study. Medication adherence in people with SMI would appear to be sufficient to support effective lipid modification as per NICE guidance.

**Reference:** Blackburn R, Osborn D, Walters K et al. Statin prescribing for people with severe mental illnesses: a staggered cohort study of 'real-world' impacts. BMJ Open 2017;7e013154. doi:10.1136/ bmjopen-2016-013154

### What do we know already?

- The NICE Clinical Guideline on lipid modification (CG181, 2014) states atorvastatin 20 mg a day should be offered for the primary prevention of CVD to people who have a 10% or greater 10 year risk of developing CVD. Atorvastatin 80 mg a day is the preferred option in secondary prevention (N.B. Lower doses are recommended if there are potential drug interactions, a high risk of adverse effects, or where there is a patient preference for this.).
- The guideline cautions that some people, including people with SMI, will have an underestimated risk when using standard CVD risk scoring tools due to the additional underlying medical conditions or treatment risks.
- Antipsychotic medicines can cause dyslipidaemia, potentially further increasing the CVD risk of people with SMI.

### What does this evidence add?

- This UK study utilised anonymised data within electronic health records of 45,830 participants in a pooled data set of staggered cohorts. Of the 2,944 statin users identified, there was no significant reduction in CVD events or all- cause mortality. The authors state that the non-significant reduction in CVD events may reflect an insufficient study power for detecting a smaller effect than observed in randomised controlled trials of statins in people without SMI.
- However, statin prescribing was associated with significant reductions in total cholesterol of 1.2 mmol/L for up to two years after adjusting for differences in baseline characteristics. These decreased total cholesterol concentrations may translate into long-term clinically meaningful reductions in CVD.
- Based on the results of this study, the potential impact of statin prescribing on intermediate outcomes in people with SMI has a magnitude that is similar to the general population. Hence, medication adherence in people with SMI is sufficient to support effective lipid modification, justifying the widespread prescribing of statins in this population.
- Several limitations are acknowledged within this study. It is possible that residual confounding may remain due to unmeasured confounders, such as diet or severity of mental illness within the participants. Also, the ascertainment of cholesterol data for statin users ranged from 73% to 82%. The authors recognise that it is possible that this is an overestimation of statin treatment, given that those individuals that have a greater adherence to medicines may also be more likely to have a blood test.

## Study details

**Participants:**

- Retrospective analysis of electronic health records of 45,830 participants, aged 40 to 84 years between 2002 and 2012 who had a diagnosis of SMI. Data were obtained from The Health Improvement Network (THIN), which covers approximately six percent of the UK population.
- Median age of participants was 54 years and 59 years in the statin non-user and statin user groups respectively. 51 % of statin non-users and 50% of statin users were diagnosed with bipolar disorder.

**Intervention and comparison:**

- A staggered cohort study design was used to reduce the impact of confounding by indication. Five 'staggered' cohort studies were created within two-year follow-up periods between 1st January 2002 and 1st January 2010. The effectiveness of statin prescribing was assessed using pooled data from these cohorts.
- The primary outcome investigated was first myocardial infarction (MI) or stroke. Secondary outcomes were all-cause mortality, MI, stroke, and change in total cholesterol level/concentration.
- All analyses were undertaken using an intention to treat approach, with exposure defined by statin prescribing at the index date.
- Incident rate ratios (IRR) for the association between statin prescribing and combined MI and stroke were estimated using a Poisson regression model. Changes in total cholesterol concentration were analysed using linear regression models at one or two years after the index date.

**Outcomes and results:**

- A total of 45,830 participants were included within the study, with 42,886 assigned as statin non-users and 2,944 as statin users.
- The IRR for the association between statin prescribing and MI and stroke events after adjustment for all additional covariates was 0.89 (95% confidence interval [CI] 0.68 to 1.15).
- The IRR for the association between statin prescribing and all-cause mortality after adjustment for all additional covariates was 0.89 (95% CI 0.78 to 1.02).
- The IRRs after adjustment for all additional covariates for first MI and first stroke were 0.75 (95% CI 0.48 to 1.15) and 0.96 (95% CI 0.68 to 1.15) respectively.
- All of these results as indicated by the confidence intervals failed to show statistical significance.
- However, statistically significant reductions were shown in total cholesterol of 1.2 mmol/L (95% CI 1.1 to 1.3) for up to two years after adjusting for differences in baseline characteristics.

**Level of evidence:**
Level 2 (limited quality patient-oriented evidence) according to the SORT criteria.

**Study funding:**
National Institute for Health Research (NIHR).