



Important New Evidence Service In Partnership with The Centre for Medicines Optimisation at Keele University

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Stroke: are stroke prevention therapies under-prescribed?

A recently published UK study that analysed data from more than 29,000 patients who had experienced a stroke or transient ischaemic attack (TIA) found that more than half of those with a clinical indication for the use of lipid-lowering, anticoagulant, or antihypertensive drugs as preventative therapies were not prescribed them prior to first stroke/TIA. The findings suggest that a significant number of strokes and TIAs could be prevented through optimising prescribing in primary care.

Reference: [Turner GM, Calvert M, Feltham MG, et al. Under-prescribing of Prevention Drugs and Primary Prevention of Stroke and Transient Ischaemic Attack in UK General Practice: A Retrospective Analysis. PLOS Med 2016;13\(11\): e1002169. doi:10.1371/journal.pmed.1002169](#)

What do we know already?

- Stroke is the [fourth](#) single largest cause of death in the UK and is a leading cause of adult disability. Dyslipidaemia, atrial fibrillation and hypertension are important modifiable risk factors for stroke, and lipid-lowering drugs, antihypertensive drugs and anticoagulants have been shown to reduce the incidence of stroke associated with these risk factors.
- NICE guidance on lipid modification ([CG181](#), 2014) recommends lipid-lowering drugs for prevention of cardiovascular disease (CVD), with atorvastatin 80 mg daily the preferred initial treatment for secondary prevention (N.B. lower doses are recommended if there is the potential for drug interactions or adverse effects). For primary prevention, atorvastatin 20 mg daily should be offered to people with $\geq 10\%$ ten-year risk of developing CVD.
- NICE ([CG180](#), 2014) recommends that people with atrial fibrillation and at high risk of stroke (assessed using CHA₂DS₂-VASc scoring system), should be offered an anticoagulant (e.g. warfarin, apixaban, dabigatran etexilate, rivaroxaban or edoxaban), taking bleeding risk into account.
- The NICE clinical guideline on hypertension ([CG127](#), 2011) recommends antihypertensive drug treatment for people:
 - aged < 80 years with clinic blood pressure (BP) $\geq 140/90$ mmHg and ambulatory blood pressure monitoring [ABPM] or home blood pressure monitoring [HBPM] average $\geq 135/85$ mmHg who have one or more of: target organ damage, established CVD, renal disease, diabetes, or a 10-year CV risk $\geq 20\%$.
 - of any age with clinic BP $\geq 160/100$ mmHg and ABPM daytime average or HBPM average $\geq 150/95$ mmHg.

What does this evidence add?

- This UK study retrospectively analysed electronic medical records of 29,043 people who had experienced a first-ever stroke or TIA between January 2009 to December 2013. More than half of those (9,579 of 17,680) with a clinical indication for one or more stroke prevention drugs (lipid-lowering, anticoagulant, or antihypertensive drugs) had not been prescribed them in the three or four months before their stroke/TIA. In 83% of cases, one of these drugs was not prescribed, in 16% two of these drugs were not prescribed and in 0.4%, three of these drugs were not prescribed.
- A clinical code indicating that prevention drugs were contraindicated or declined, or that there was an adverse reaction, was recorded for only a small proportion of patients (5%, 7% and 0.7% for lipid-lowering, anticoagulant and antihypertensive drugs respectively).
- Based on the study findings and using estimates of the UK population and stroke incidence, the study authors estimate that improved prescribing of anticoagulant, lipid-lowering and antihypertensive drugs could potentially prevent approximately **12,000 first strokes annually** in the UK.
- A major limitation of this study is that reasons for not prescribing stroke prevention drugs were unclear and, as acknowledged by the study authors, there may have been legitimate reasons in some cases that were not available in the dataset e.g. anticoagulants may not have been prescribed for some patients because of bleeding

risk. Furthermore, prevention of stroke/TIA is complex and the study definition of “under-prescribing” did not address patient’s adherence to medication or medication targets e.g. blood pressure levels.

Study details

Participants:

- Retrospective analysis of electronic primary care medical records of 29,043 adults (age ≥ 18 years) who had experienced a first-ever stroke or TIA during the period January 2009 to December 2013. Data were obtained from The Health Improvement Network (THIN), which covers approximately 6% of the UK population. The median age of included participants was 74 years (interquartile range 64 to 82) and 51% were female.

Intervention and comparison:

- The proportions of strokes or TIAs with prevention drugs (lipid-lowering, anticoagulant, or antihypertensive drugs) under-prescribed when clinically indicated prior to the time of stroke/TIA were calculated.
- Clinical indications for preventative drugs were based on NICE guidance *during the study period* (i.e. guidance from 2009 to 2013):^{1,2,3}
 - Indications for lipid-lowering drugs were defined as coronary heart disease (CHD) chronic kidney disease (CKD), peripheral arterial disease (PAD), TIA, diabetes if aged over 40 years, familial hypercholesterolaemia, or 10-year CVD risk $\geq 20\%$.
 - Indications for anticoagulant drugs were defined as diagnosis of atrial fibrillation and CHADS2 score ≥ 1
 - Indications for antihypertensive drugs were blood pressure $\geq 160/100$ mmHg) or $\geq 140/90$ mmHg and CHD, CKD, PAD, TIA, diabetes if aged over 40 year, or 10 year CVD risk $\geq 20\%$
- Under-prescribing of prevention drugs was recorded when patients in whom a lipid-lowering or antihypertensive drug was clinically indicated had no record of a prescription for up to 90 days before their stroke or TIA and no clinical code to indicate that the patient was on these drugs. If an anticoagulant drug was clinically indicated, under-prescribing was defined as no prescription up to 120 days before the event (to allow for referral to an anticoagulation clinic) and no clinical code to indicate that the patient was on anticoagulant drugs.

Outcomes and results:

- A total of 17,680 patients were considered to have been eligible for at least one prevention drug at the time of their stroke or TIA (9,953 had one prevention drug indicated, 6,904 had two indicated, and 823 had three indicated).
 - 16,028 patients had a clinical indication for lipid-lowering drugs.
 - 7,008 for antihypertensive drugs.
 - 3,194 for an anticoagulant drug.
- At least one prevention drug had not been prescribed when clinically indicated (according to the above criteria) in 54% (9,579/17,680) of patients:
 - 49% (7,836/16,028) people with a clinical indication for lipid-lowering drugs were not prescribed them.
 - 25% (1,740/7,008) of people with hypertension were not prescribed antihypertensive drugs.
 - 52% (1,647/3,194) of those with atrial fibrillation and a high risk of stroke were not prescribed anticoagulants.
- In the majority of cases, one drug was not prescribed (83%), in 16% two drugs were not prescribed and in 0.4%, three drugs were not prescribed.
- A clinical code indicating that prevention drugs were declined or contraindicated, that the patient had white coat hypertension (for those with high blood pressure measurements) or that there was an adverse reaction was recorded in only 5% of people with a clinical indication for lipid-lowering drugs, 7% for anticoagulant drugs and 0.7% for antihypertensive drugs.
- Over half (54%) of the patients not prescribed antihypertensive drugs when considered clinically indicated had previously been prescribed these drugs, but their prescriptions had been stopped, compared with only 14% for anticoagulant drugs and 30% for lipid-lowering drugs.
- There was a decrease in the under-prescribing of anticoagulant drugs between 2009 (58%) and 2013 (45%) but no change was observed for lipid-lowering and antihypertensive drugs.
- Exploratory analysis that assessed the impact of updated NICE guidance found that:
 - lowering the 10-year CVD risk threshold from $\geq 20\%$ to $\geq 10\%$ (as recommended in 2014 updated NICE guidance on lipid modification) increased the number of patients eligible for lipid-lowering drugs to 19,462, of which, 54% were not prescribed them. When QRISK2 rather than the Framingham risk equation was used to calculate CVD risk, the number of eligible patients for lipid-lowering drugs increased to 19,253.
 - Use of the CHA₂DS₂-VASc score rather than the CHADS2 score to calculate stroke risk (as recommended in the 2014 NICE guideline on atrial fibrillation) increased the number of patients eligible for anticoagulant therapy by 280.

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

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