Conflicts of Interest

- The project was funded by the Alzheimer’s Society (AS-AG-2013-017).
- Dr Fox and Dr Maidment received travel grants and Dr Fox and Dr Myint received lecture fees from Astellas Pharma UK.
- All other authors report no conflict of interest.

Background

- Dementia prevention is a public health priority.
- Evidence is conflicting as to whether the long-term use of medications with anticholinergic (AC) activity increase dementia risk.
- Many indications for potent ACs are risk factors for or are early symptoms of dementia.

Objectives

- Use data from the Clinical Practice Research Datalink (CPRD) to estimate whether potent anticholinergic use is associated with an increased dementia risk.
- Pre-planned subgroup analyses exploring specific anticholinergic medication classes.

Methods: a nested case-control study using data from the Clinical Practice Research Datalink (CPRD)

Sample selection and study design
Cases: First dementia diagnosis or dementia drug. Index dates from Apr ’06 – Jul ’15
Controls: Up to 7 controls matched per case on sex, age +/- 3 years, index of multiple deprivation quintile, and years of up-to-standard data history (minimum 6 years)

Covariates
- Sociodemographic: age, region, Lifestyle: smoking (current, ex, non), harmful alcohol use, BMI
- Cardiovascular disease: Diabetes, Diabetes complications, hyperglycemia, hypertension, stroke/TIA, congestive heart disease, heart failure, peripheral arterial disease, atrial fibrillation, angina, myocardial infarction, coronary artery operations, deep vein thrombosis
- Dementia risk factors: Depression (severity and duration), Anxiety, Anxiety symptoms, Parkinson’s disease. Severe mental illness, Epilepsy, Drug abuse, Cancer, Insomnia. Sleep problems, Migraine, Headache. Pain, Neuropathy,Meniere’s disease, Restless legs syndrome
- Anticholinergic medication indications: COPD, Asthma, rhinitis, GERD, Ulcer, IBS/IBD, Intestinal surgery, Liver disease, arthritis, dermatitis, oesophagus, proctitis, incontinence, chronic kidney disease, prostatitis
- History in the last 12 months: Falls, fractures, GP visits
- Co-medications: other antidepressants, antipsychotics, urologics, possible (ACB=1) and probable (ACB=2) anticholinergics

Results

- Mean (SD) age = 83 (7) years, 63% women.
- 14,224 (35%) cases and 84,751 (30%) controls were prescribed potent ACs.
- 6,295 (15%) cases and 32,783 (12%) controls were prescribed 90+ DDDs of potent ACs.
- Potent anticholinergic medication use is associated with dementia incidence (OR=1.10)
- A dose response effect is evident.

- There is a robust association between some classes of potent anticholinergic medications and dementia incidence.
- However this association is not specific to anticholinergic medication, and is not seen across all anticholinergic classes.

- Limitations of our study include the potential delayed diagnosis of dementia and omission of non-prescribed medications.
- Previous associations between AC use and dementia may be attributable to confounding, drug properties unrelated to AC action, study design, or dementia symptoms.

Conclusions

- When examined by class, association with dementia is inconsistent.
- Potent anticholinergic antidepressants and urologics are associated with greater dementia risk, but anticholinamides and antipsamidosics are not.
- If an anticholinergic effect was real we would expect it to be seen across all classes.

Exposure

- We extracted prescriptions for up to 20 years before the index date. We excluded prescriptions in the 4 years before diagnosis due to potential protopathic bias.
- Potent ACs: drugs scored 3 on Anticholinergic Cognitive Burden scale (see box)
- Primary exposure: WHO defined daily doses (DDD) of potent ACs during drug exposure period
- Secondary exposure: Prescription of potent ACs by drug class

Statistical analyses

- Conditional logistic regression used to estimate adjusted odds ratios (aOR) and 95% CI for dementia associated with AC use during the drug exposure period
- Model 1: Adjusted for covariates measured at drug exposure period end.
- Model 2: Adjusted for covariates measured at drug exposure period start.
* p<0.01 defines statistical significance

Anticholinergic Cognitive Burden scale (ACB)
www.agingbraincare.org/tools/acb-anticholinergic-cognitive-burden-scale/

Antipsamidosics: Dicycloverine, Hyoscyne
Antidepressants: Amitriptyline, Clomipramine, Docusine, Droxpin, Amipramine, Lisopramine, Noramiprine, Paroactine, Trimipramine
Antipsychotics: Chlorpromazine, Cimacazine, Quinipate, Trifluoperazine
Urologics: Oxybutynin, Solifenacin, Tolterodene, Trosiptum
Parkinsonians: Procyclidine
Antishitamines: Chlorphenamine, Hydroxyzene, Promethazine