Anticholinergics, Benzodiazepines, Cognition and Dementia Study

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Does commonly used medication increase the risk of cognitive decline and dementia?

Background and rationale

There may be a higher rate of dementia among people who use certain commonly used medicines for long periods of time.

Benzodiazepines (BZD) (used for sleeping disorders and anxiety) and medications with anticholinergic activity have been particularly implicated.

Billioti de Gage et al (2012) found an increased risk of dementia in benzodiazepines users, HR=1.59 (1.1-2.3)

Confounding by indication?
- BZD use could also be early risk marker for dementia.
- Studies suggest that poor sleep quality and anxiety may be early signs of dementia.
- Anticholinergic medication may be prescribed for dementia risk factors
- We will carefully control for all of these factors in our analyses

Benzodiazepines (BZD) use could also be an early risk marker for dementia. Does impaired cognition persist, following medication cessation?

Definite anticholinergic medicine:

- www.agingbraincare.org/tools/abc-anticholinergic-cognitive-burden-scale/

Using observational data we will test whether anticholinergic medications (AChl), Benzodiazepines (BZD) or Z-drugs cause irreversible cognitive impairment or increase the risk of dementia.

Specific research questions:
- Do AChl/BZD/Z-drugs increase dementia risk?
- Does this depend on dose and duration of use?
- Does any excess risk persist after cessation?
- Is the risk restricted to a subgroup of AChl medications?
- Do Z-drugs differ from BZD in dementia risk?

Our previous work (Fox et al, 2011) suggests that the use of medications with anticholinergic activity increases cognitive decline over 2 years.

- The anticholinergic burden scale (ACB) measures the total amount of anticholinergic medication being used by an individual
- People with an ACB score of 4 or more had higher cognitive decline
- People using a definite anticholinergic had greater cognitive decline.

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Our findings will contribute to prescribing guidance and management of many common long term conditions.

Ultimately this could help prevent many cases of dementia.

Research plan

Work package 1 - PRIMARY CARE DATA
We are using routine primary care data collected through the CPRD, to estimate the risk of dementia diagnosis associated with prescriptions of each medication class.

DATA SOURCE: Clinical Practice Research Datalink (CPRD):
We are extracting GP records from over 34,000 patients with dementia and over 230,000 patients without dementia aged 65-99 years from over 650 practices, with each patient having at least 6 years of follow-up data.

Work package 2 - COHORT STUDIES
Cohort studies provide more in depth and objectively captured data than primary care datasets.

Data from the MRC CFAS and TILDA cohort studies to examine the cognitive effects of AChl, BZD and Z-drugs.

Using the MRC CFAS neuropathology study we are also able to look at whether neuropathological changes occur for those with long-term exposure to AChl, BZD or Z-drugs.

DATA SOURCE: The Irish Longitudinal Study on Ageing (TILDA):
- 8175 people aged 50+ recruited between 2008-2010; Representative of the population of Ireland.
- Comprehensive health assessment
- Link to medicines dispensing database
- Three waves of data collection

Work package 3 – EVIDENCE SYNTHESIS
Finally we will synthesise the available international evidence with the results from our observational studies.

DATA SOURCE: Medical Research Council Cognitive Function and Ageing Studies (MRC CFAS) I and II:
- 13,004 people aged 65+ recruited in 1991 – 10 year follow-up
- 7796 people aged 65+ recruited in 2010 – 2 year follow-up
- Participants representative of England and Wales
- The MRC CFAS neuropathology study: more than 500 CFAS I participants donated brains for pathological analysis.

REFERENCES
- Fox C, Richardson K, Maidment I, Savva GM, Matthews FE, Smithard D, Coutinol L, Katona C, Boulton MA, Byrne C. Anticholinergic medication use and cognitive impairment in the older population: the Medical Research Council Cognitive Function and Ageing Study. JAGS. 2011; 59:1477-1483