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

### Background and rationale

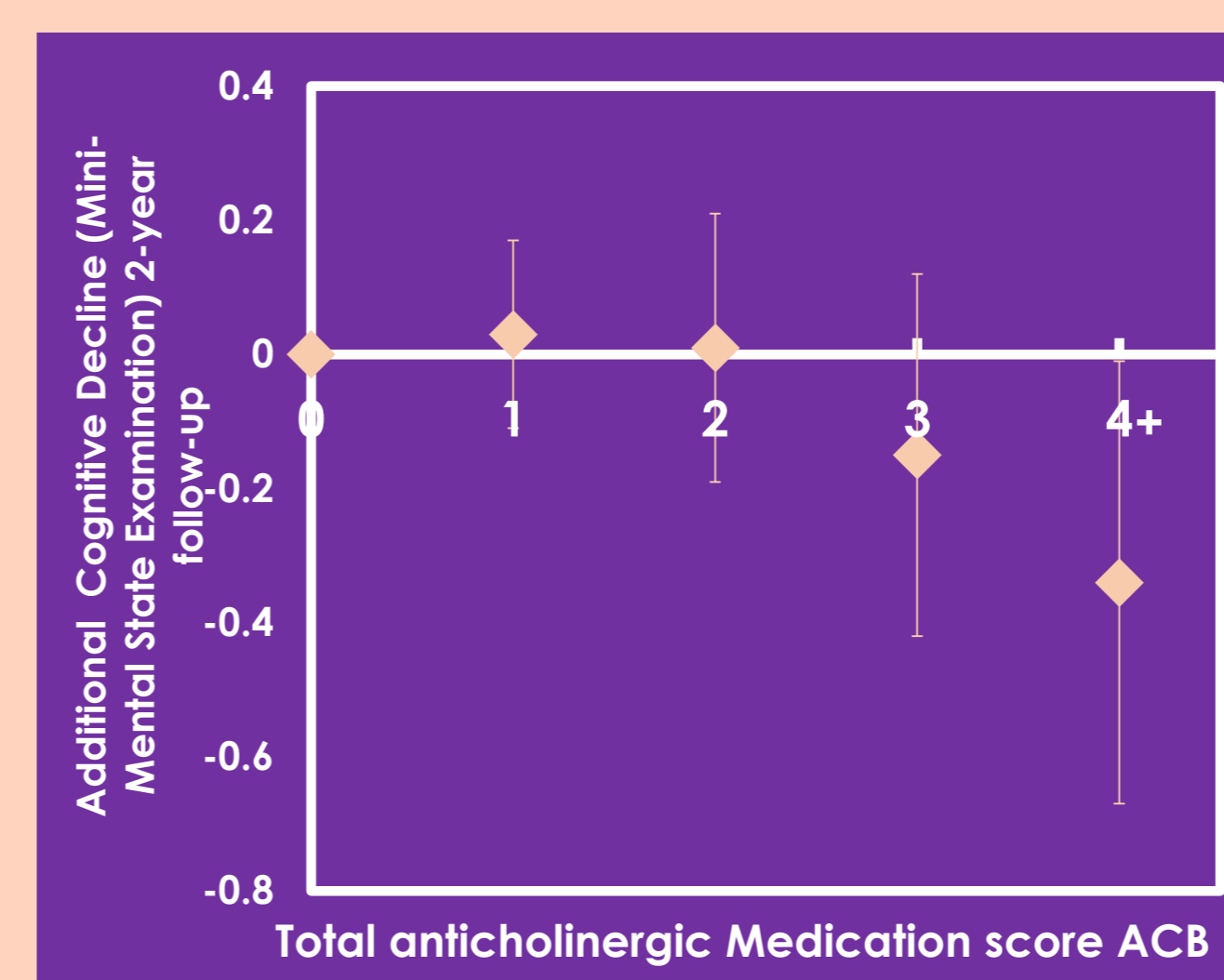
There may be a higher rate of dementia among people who use certain commonly used medicines for long periods of time.

**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)**

15 year follow-up	Incident Dementia	No dementia
No BZ use	88%	92.4%
BZD use	12%	7.6%

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



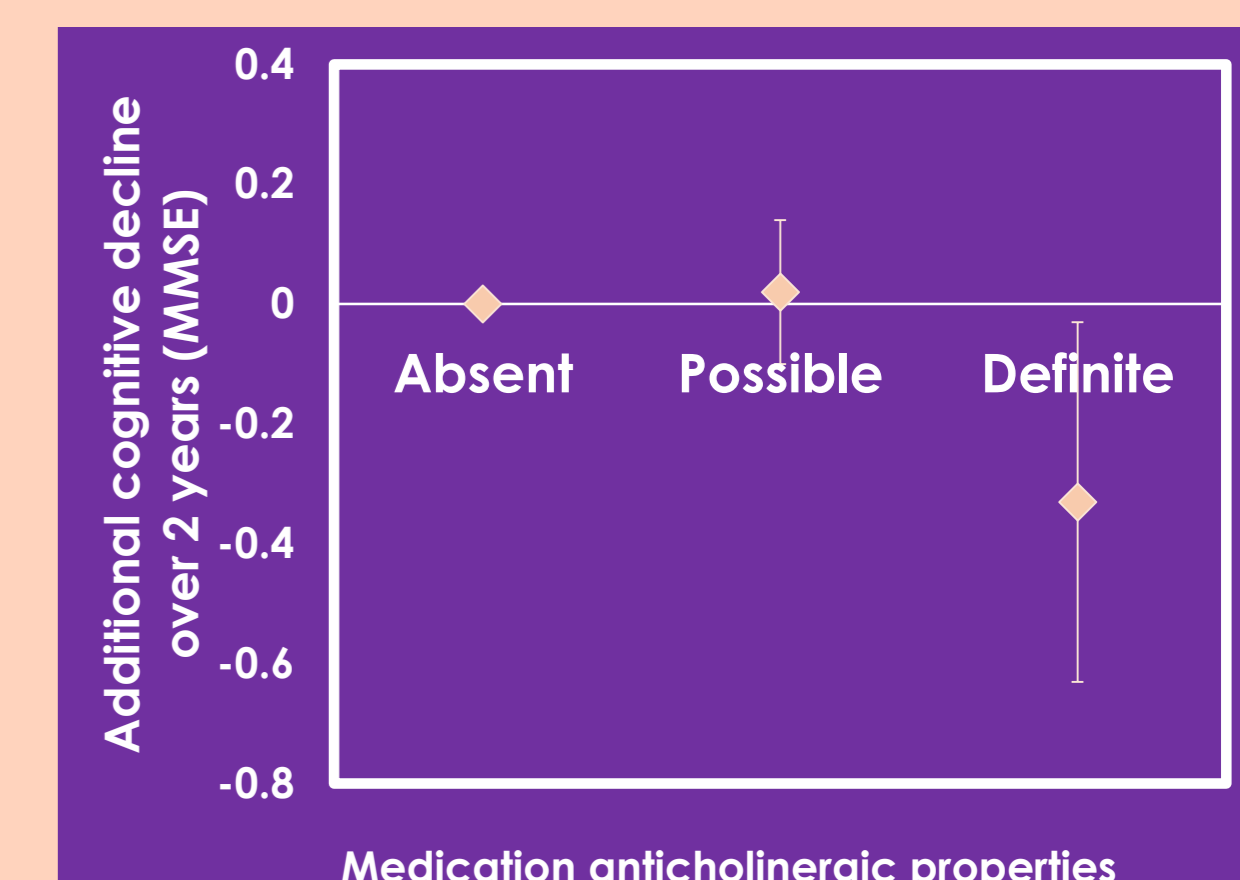
- The anticholinergic burden scale (ACB) measures the total amount of anticholinergic medication being used by an individual
- People with an ACB score of 4 or more had higher cognitive decline
- People using a definite anticholinergic had greater cognitive decline.

#### 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

#### Definite anticholinergic medicine:

- [www.agingbraincare.org/tools/abc-anticholinergic-cognitive-burden-scale/](http://www.agingbraincare.org/tools/abc-anticholinergic-cognitive-burden-scale/)



### Aim and research questions

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

Specific research questions:

- Do AChI/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 AChI medications**?
- Do **Z-drugs differ from BZD** in dementia risk?
- How are **memory and non-memory cognitive domains** affected
- Does impaired cognition persist, returns to pre-medication levels or **continue to decline** following medication cessation?
- What are the **neuropathological correlates** of AChI/BZD/Z-drugs?

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 AChI, 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 AChI, BZD or Z-drugs.

#### 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

#### DATA SOURCE: The Irish Longitudinal Study on Ageing (TILDA)

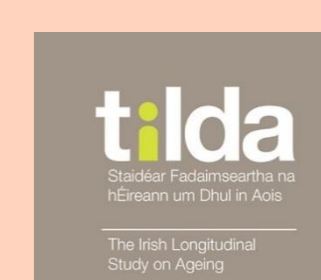
- 8175 people aged 50+ recruited between 2008-2010**; Representative of the population of Ireland.
- Comprehensive health assessment**
- Link to medicines dispensing database**
- Three waves of data collection**

#### Work package 3 – EVIDENCE SYNTHESIS

Finally we will synthesis the available international evidence with the results from our observational studies.



[www.cfes.ac.uk](http://www.cfes.ac.uk)  
[www.tilda.ie](http://www.tilda.ie)



#### REFERENCES

- Billioti de Gage S, Begaud B, Bazin F, Verdoux H, Dartigues JF, Peres K, Kurth T, Pariente A. Benzodiazepine use and risk of dementia: prospective population based study. *BMJ*, 2012; 345
- Fox C, Richardson K, Maidment I, Savva GM, Matthews FE, Smithard D, Coulton S, Katona C, Boustani MA, Brayne 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