

10,000 days of drugs: Effect of Acetylcholinesterase inhibitors in real-world data

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Alzheimer's dementia research

Two types of drugs have been licensed for the treatment of AD symptoms:

AcEIs (donepezil, rivastigmine, and galantimine) and NMDA receptor antagonist (memantine) (*Jindra et al., 2018*)

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Clinical trials have good efficacy and internal validity, but they underperform on measures of external validity

Sources of additional evidence: EHRs

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Data of interest is locked in natural text format

The goal

- 1) NLP models that can extract information of interest from the records
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- 3) Investigate personalised therapies based on the available medical history in UK-CRIS

New Mind 1

Feasibility study:

- diagnosis of dementia

- 3 drugs (Rivastigmine, Donepezil and Galantamine)

- 2 mental health scores (MMSE and MOCA)

Oxford UK-CRIS Health centre

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Epidemiological analysis to investigate deterioration of cognitive performance and effect of the drugs

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Scale: 11298 for 4,521 patients

MMSE	MOCA
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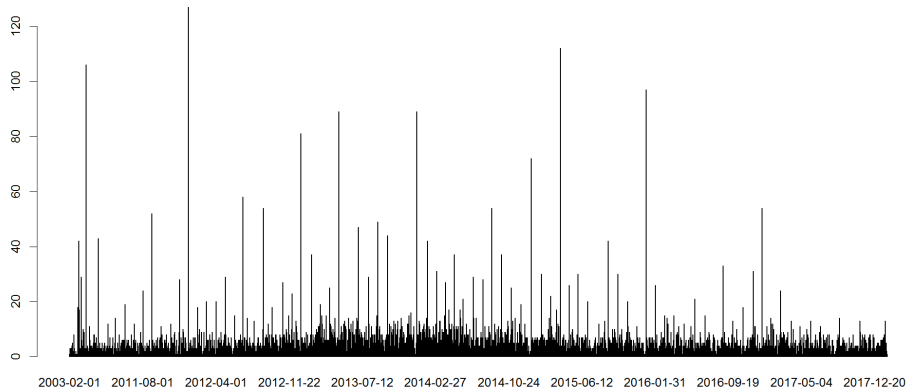
AChEi	Donepezil	Galantamine	Mementine	Rivastigmine
1,981	18,341	1,656	7,068	3,714

Diagnosis: 35,010 for 5,740 patients

AD	DLB	FTD	Mixed	Other	PPD	Unspecified	VaD
10,723	937	479	600	4	120	18,918	3,229

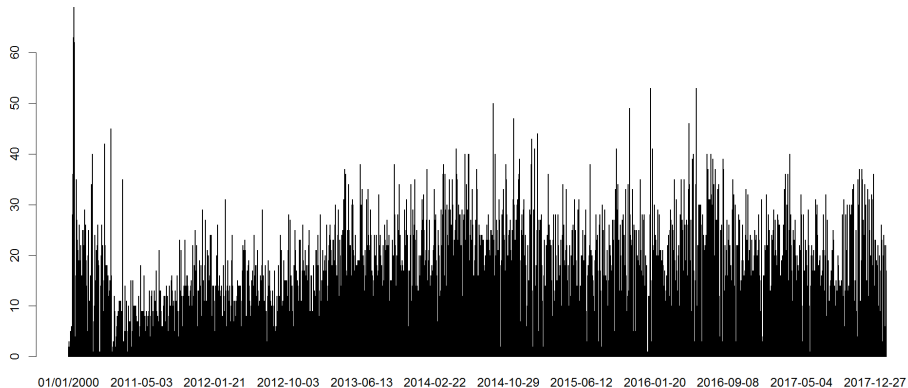
Extraction of the time information

Scale: if date is not extracted take the document date



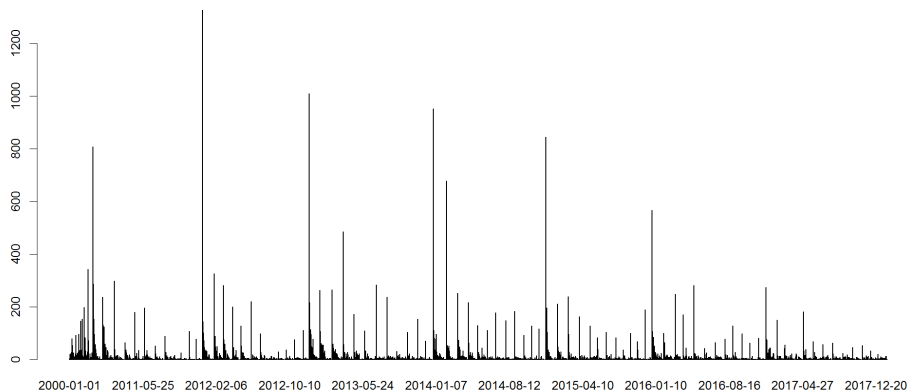
Extraction of the time information

Medication: if date is not extracted, use the earliest document date



Extraction of the time information

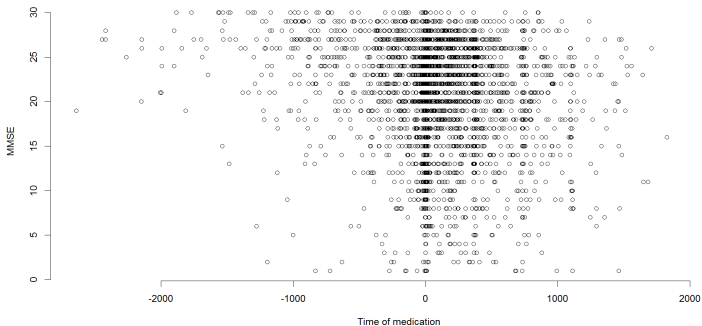
Diagnosis: use the earliest document date



MMSE across the time of medication

1968 patients with information on scale and medication

1312 with MMSE and 1008 with MOCA scores



Patterns of the data

Number of observations where there is change of drug prescriptions:

No Medication -> AChEi: 877

No Medication -> Mementine: 841

AChEi -> Mementine: 1098

AChEi -> AChEi: 6463

Generalized additive mixed-effect modelling

Nonlinear and linear structure

1) Proposes optimal relation between variables: $y = f(x) + e$

The magnitude of cognitive deterioration across time

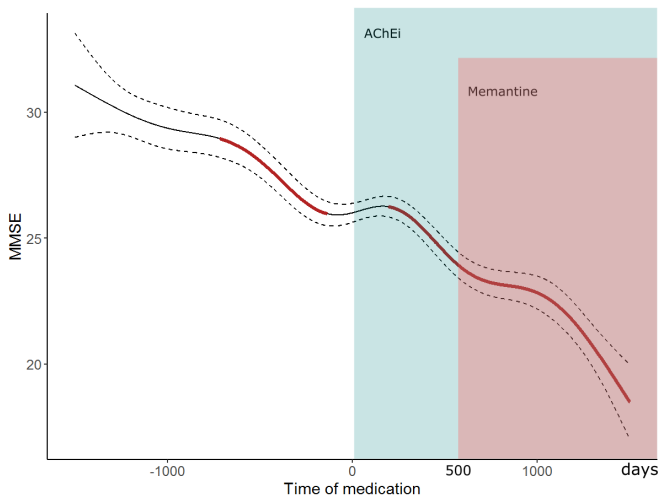
Periods of significant changes in the slope of the nonlinear functions

2) Linear structure has standard general (multilevel) equation

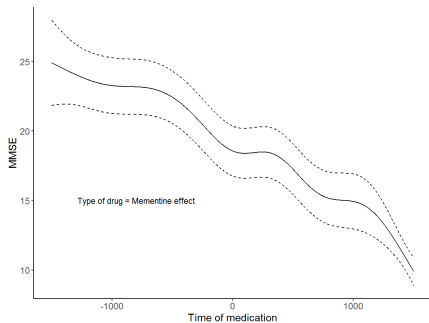
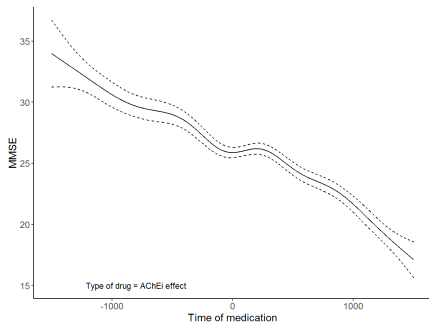
The participants' intercept is adjusted in all models

Effect of medication

Period of changes: - 717 to -136 and 197 to NA (11 months of stabilization)



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Improved precision of the time scale on which we capture effects, however, there is need to improve the extractions of different drugs