**Impacts of COVID-19 on deprescribing of Antihypertensive Medications in dementia patients: protocol**

Background / Rationale

Many older adults, especially those with dementia, take multiple medications simultaneously (polypharmacy). This has been shown to increase the risk of negative outcomes such as falls, confusion, adverse drug reactions and cognitive impairments [1]. Cardiovascular disease is a significant burden in this population. Consequently, antihypertensive medications are commonly prescribed to manage high blood pressure and reduce the risk of cardiovascular events. However, observational studies have found an association between lower blood pressure and cardiovascular mortality especially in frail patients taking antihypertensive medicines [2]. Some clinical trials have investigated the effects of stopping antihypertensives, but frail individuals and those with dementia are often excluded from these studies, and there is a need for further research [3].

Medication reviews are a good opportunity for clinicians to improve medication safety by considering the range of medications being taken by a patient. Annual medication reviews are a key part of a person with dementia's care. As of December 2024, there were 498,221 patients with a diagnosis of dementia in England. Approximately 41.2% (205,450) of these received a medication review in the preceding 12 months [4]. However, their effectiveness for stopping medicines (deprescribing) remains poorly understood.

The COVID-19 pandemic dramatically altered healthcare delivery, leading to a significant reduction in routine services, including medication reviews. A study in OpenSAFELY investigating changes in the delivery of medication reviews showed monthly rates dropped by as much as 20%, and yearly rates by 10%, during the pandemic, compared to preceding years [5]. It is not clear how reductions in medication reviews during this period impacted management of antihypertensive medications. However, a qualitative study in care homes in Northern Ireland indicated that the suspension of medication reviews during the pandemic hindered medicines optimisation, with primary care services often taking a reactive rather than proactive approach. Communication and relationship challenges stemming from reduced face-to-face contact further exacerbated these issues [6].

Many NHS services remain under strain since the pandemic, but the ongoing impact on medication management of dementia patients remains unclear. Dementia patients are particularly vulnerable to polypharmacy and inappropriate prescribing, so it is possible that they were especially affected by the reduction in medication reviews during the pandemic.

This study will investigate the relationship between medication reviews and subsequent medication discontinuation with a focus on antihypertensive medications, while also assessing the immediate and ongoing impact of COVID-19 on deprescribing.

Aims / Objectives

This study aims to describe trends in stopping antihypertensive medicines among dementia patients following medication reviews from 2015, when the National Institute for Health and Care Excellence (NICE) first issued current guidelines on medication optimisation [7], through to 2024. Specifically, the aims are:

1. **Determine an appropriate definition for stopping medicines in this context.**

We will analyse the distribution of gaps in the prescriptions of antihypertensive medications to determine a definition for “stopping”.

1. **Assess the relationship between medication reviews and changes in antihypertensive medication.**

We will determine if there is an association between medication reviews and deprescribing events. We will also determine the frequency and prevalence that medication reviews are being performed in this population.

1. **Determine the impact of the covid pandemic on the patterns in medication cessation and medication reviews.**

During the Covid 19 pandemic, medication reviews were recommended to be deferred. We will examine the trends in medication stopping rates and medication reviews patterns, before, during and after the pandemic.

Research Questions

1. On average how many antihypertensive medications are dementia patients prescribed in England?
2. How frequently do dementia patients stop antihypertensive medications?
3. What is the likelihood of a dementia patient stopping a drug following a medication review? Does this vary based on region, deprivation, ethnicity etc?
4. Did the pandemic affect the rates of polypharmacy and deprescribing in England?

Data Sources

This research will use routinely collected primary care electronic health records within the OpenSAFELY research platform (OpenSAFELY-TPP) [8]. Additional data will be used from the following linked sources:

* Secondary Uses Services (SUS)
  + Hospital Episode Statistics (HES)
  + Emergence Care Dataset (ECDS)
* Office of National Statistics, Death Registry (ONS)
* Index of Multiple Deprivation (IMD)

Study Population

We will conduct a retrospective cohort study using a dynamic cohort of dementia patients over the 10-year period from 1 January 2015 to 31 December 2024.

Individuals will be included in the cohort when they meet all of the following criteria:

1. Diagnosis of dementia.
2. Patient must be a long-term user of at least one antihypertensive medicine (at least 3 prescriptions in the 12 months preceding the study period).
3. Alive on the study start date.
4. Age greater than 65 years.
5. Are registered at an English GP practice using TPP software during the study period.
6. Known sex.
7. Known deprivation.
8. Known region.

Quality Assurance

We will ensure data quality by applying the following quality assurance rules:

1. Remove individuals who are missing year of birth
2. Remove individuals whose year of birth is after their year of death
3. Remove individuals whose date of death is after today

Exposure

The exposure will be defined as a medication review ([from the NHSD medication review codelist](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/demmedrvw_cod/20250627/)) coded within the electronic health record. In cases where there are multiple medication reviews for an individual patient, we will select a random medication review within the study period. This avoids correlated outcomes within the same patient, which could introduce bias to the regression estimates.

Outcome

The outcome will be defined as the patient stopping an antihypertensive medication following a medication review. To define what constitutes a medication being stopped, we will examine the distribution of time gaps between successive prescriptions. We will be pragmatic and identify a relevant cutoff for future sensitivity analysis. Different classifications of antihypertensive drugs will be considered separately, so that a patient changing from one drug to another within the same class would not be considered stopping.

Histograms will be constructed to visualise these gaps, stratified by antihypertensive type. Based on these distributions, we will identify an appropriate period to follow after the medication review (e.g., ≥30, ≥60, or ≥90 days). If they do not receive a prescription within this period, this will be defined as them having stopped the medication.

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| --- |
| Antihypertensive medicine codelists |
| [OpenCodelists: ACE Inhibitor Medications](https://www.opencodelists.org/codelist/opensafely/ace-inhibitor-medications/2020-05-19/) |
| [OpenCodelists: Alpha-Adrenoceptor Blocking Drugs](https://www.opencodelists.org/codelist/opensafely/alpha-adrenoceptor-blocking-drugs/2020-05-19/) |
| [OpenCodelists: Angiotensin II Receptor Blockers (ARBs)](https://www.opencodelists.org/codelist/opensafely/angiotensin-ii-receptor-blockers-arbs/2020-05-19/) |
| [OpenCodelists: Beta-blocker medications](https://www.opencodelists.org/codelist/opensafely/beta-blocker-medications/2020-05-19/) |
| [OpenCodelists: Calcium Channel Blockers](https://www.opencodelists.org/codelist/opensafely/calcium-channel-blockers/2020-05-19/) |
| [OpenCodelists: Thiazide type diuretic medication](https://www.opencodelists.org/codelist/opensafely/thiazide-type-diuretic-medication/2020-05-19/) |
| [Potassium sparing diuretics](https://openprescribing.net/bnf/020204/) |
| [Centrally-acting antihypertensives](https://openprescribing.net/bnf/020502/) |

Analysis

This analysis will be conducted in two parts. Part 1 will provide descriptive statistics to characterise the population. Part 2 will assess the association between medication reviews and medication cessation. The cohort will be defined using OpenSAFELY’s EHRQL and analysis will be performed in R.

**Part 1: Descriptive Statistics**

We will begin by describing the characteristics of the study population using descriptive statistics. This will include distributions of age, sex, ethnicity, region, and dementia subtype. We will report how many patients died during the study period, how many received medications reviews and how many antihypertensive prescriptions there were and how many were stopped. Additionally, we will perform analysis on subgroups, based on the clinical indications associated with taking antihypertensive medications (e.g. heart failure)

**Part 2: Stopping Rates and Association with Medication Reviews**

We will use the definition of stopping to calculate monthly stopping rates, defined as the number of stopping events per patient per month. These rates will be plotted over time to examine trends, particularly around the COVID-19 pandemic period, to assess any disruption in deprescribing activity.

To evaluate the relationship between medication reviews and medication cessation, we will use logistic regression models. The study period will be divided into three periods, before COVID, during COVID and after COVID. We will fit separate logistic regression models for each time period. We will compare the estimated associations (odds ratios and 95% confidence intervals) in each period to assess the impact of the COVID pandemic on deprescribing.

The study period will be divided into three periods which will be analysed separately to assess the effect of the COVID pandemic:

1. Pre-COVID (Jan 2015 – March 2020),
2. COVID disruption (Mar 2020 – Jun 2021, covering major lockdowns and service restrictions)
3. Recovery/post-COVID (Jun 2021 – Dec 2024).

The primary exposure will be a coded medication review recorded in primary care, and the outcome will be a stopping event within one month of the medication review. Confounders will be measured on the date of intervention. Both unadjusted and adjusted models will be presented. Adjusted models will include covariates listed below. Subgroup analyses will be conducted to explore effect by region, deprivation level, and ethnicity.

We will perform a sensitivity analysis on the chosen interval for defining stopping, repeating the analysis with alternative thresholds for defining stopping (e.g. ≥30, ≥60, ≥90 days). This will allow us to determine whether the association between reviews and deprescribing is sensitive to the operational definition.

Confounders

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| --- | --- | --- | --- | --- |
| **Covariate** | **Type** | **Description** | **Codelist** | **Comment** |
| Age | Continuous | Age in years | N/A |  |
| Sex | Categorical | Male, Female | N/A |  |
| Ethnicity | Categorical | Patient ethnicity | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). | We will use the ethnicity variable available in OpenSAFELY |
| Deprivation | Categorical | 10 categories from Index of Multiple Deprivation 2019 | N/A |  |
| Number of medications | Continuous | Count of medications currently prescribed | N/A | Number of distinct medications prescribed in the last 3 months. |
| Dementia Type | Categorical | Alzheimer’s, Vascular dementia, Other | [OpenCodelists: Vascular dementia codes](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/demvasc_cod/20250627/) , [OpenCodelists: Alzheimer’s disease dementia codes](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/demalz_cod/20250627/) ,  [OpenCodelists: Codes for dementia](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/dem_cod/20250627/) | Codelists taken from NHSD refsets |
| Days since dementia diagnosis | Continuous | Number of days between the intervention and the patient’s dementia diagnosis | N/A | Patient is more likely to have changes to medications immediately following dementia diagnosis. |
| Geographical Region | Categorical | The region of the England that the individual lives in. | N/A |  |
| Chronic Heart Disease | Binary | 1 if diagnosis present; 0 otherwise. | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). |  |
| Acute myocardial infarction | Binary | 1 if diagnosis present; 0 otherwise. | From NHSD [REFSET](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/mi_cod/20250627/) |  |
| Stroke | Binary | 1 if diagnosis present; 0 otherwise. | From NHSD REFSET [OpenCodelists: Stroke diagnosis codes](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/strk_cod/20250627/) |  |
| Cancer | Binary | 1 if diagnosis present; 0 otherwise. | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). |  |
| Multimorbidity score | Continuous |  | TBD | Which conditions are necessary to include on their own if we are using a multimorbidity score? |
| Recent hospital admission | Binary | 1 patient has been admitted in the last 30 days; 0 otherwise | TBD | Hospital admissions often result in lots of changes to a patient’s medication |
| Smoking | Categorical |  | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). |  |
| Obesity | Binary | 1 obesity code present, 0 otherwise | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). |  |
| Care home resident | Binary | 1 if diagnosis present; 0 otherwise. | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). |  |
| Hypertension | Binary | 1 if diagnosis present; 0 otherwise. | From OpenSAFELY [reusable variables repository](https://github.com/opensafely/reusable-variables). |  |
| Consultation rate | Continuous | Number of GP appointment in the preceding 12 months | TBD |  |
| Time since last medication review | Continuous | Number of days since previous medication review | [OpenCodelists: Dementia medication review codes](https://www.opencodelists.org/codelist/nhsd-primary-care-domain-refsets/demmedrvw_cod/20250627/) | Patients who have a medication review more recently are less likely to have changes to their medicines. |
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Tables / Figures

* Table 1: Patient characteristics
* Table 2: Summary of outcomes
* Histogram showing frequencies of the gaps in prescription in months
* Venn Diagram of dementia types
* Table of monthly deprescribing rate based on subgroups.

Must deal with other cardio conditions when thinking about confounding

Separate analysis by wether or not there is hypertension or heart failure diagnosises

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2. Benetos, A., et al., *Reduction of Antihypertensive Treatment in Nursing Home Residents.* New England Journal of Medicine. **0**(0).

3. Hayes, K.N., et al., *Evaluation of real-world evidence to assess health outcomes related to deprescribing medications in older adults: an International Society for Pharmacoepidemiology-endorsed systematic review of methodology.* Am J Epidemiol, 2024.

4. England, N.H.S. *Primary Care Dementia Data, December 2024*. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/primary-care-dementia-data/december-2024>.

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6. Alsulami, N., C.M. Hughes, and H.E. Barry, *A qualitative interview study of care home managers’ experiences of medicines optimisation for residents with dementia during the COVID-19 pandemic.* BMJ Open, 2025. **15**(1): p. e091645.

7. *Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes.* National Institute for Health and Care Excellence, 2015. **03**: p. 03.

8. Nab, L., et al., *OpenSAFELY: A platform for analysing electronic health records designed for reproducible research.* Pharmacoepidemiology & Drug Safety. **33**(6): p. e5815.