This protocol is an extract from a programme of work as approved by our ethics board and HRA. ***Med IDREC Ref:*** *R55595/RE001.* ***Date and Version No:*** *22/2/2019 v2.1. Full protocol needs to be made available somewhere.*

Script to ID practices eligible to contact is here:
https://github.com/ebmdatalab/jupyter-notebooks/tree/master/nimodipine

The Effect of Audit & Feedback on Prescribing Behaviour and Engagement with Data on OpenPrescribing.net - A Programme of Randomised Controlled Trials and Cohort Studies

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Conflict of Interest Statement

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare the following: BG has received research funding from the Laura and John Arnold Foundation, the Wellcome Trust, the Biomedical Research Centre, Oxford, the NHS National Institute for Health Research School of Primary Care Research, the Health Foundation, and the World Health Organisation; he also receives personal income from speaking and writing for lay audiences on the misuse of science. HC, AW, RC and SB are employed on BG's grants for the OpenPrescribing project. RC is employed by a CCG to optimise prescribing (this CCG will be excluded from the trial), and has received income as a paid member of advisory boards for Martindale Pharma, Menarini Farmaceutica Internazionale SRL and Stirling Anglian Pharmaceuticals Ltd. BMK works for NHS England as a pharmacist adviser and all other declarations can be read here. MR and RP declare no competing interests.

3.1. BACKGROUND AND RATIONALE

Nimodipine is a drug with a single indication. It is prescribed for 21 days immediately after aneurysmal subarachnoid haemorrhage, a relatively rare type of stroke with incidence 9 per 100,000 person-years (de Rooij et al. 2007), i.e. approximately 4,500 per year in England (equivalent to just over

once for every two practices). If the 21-day course is not completed during the inpatient stay, the remaining tablets will usually be dispensed with the patient on discharge, leaving little requirement for prescribing in primary care. However, from anecdotal clinical experience, and from examining the publicly available prescribing data (https://openprescribing.net/chemical/0206020M0/), it is clear that some GPs are prescribing nimodipine more frequently than expected, sometimes for long periods of time. It is likely that this will often be an error, which could be due to a failure in communication between secondary/tertiary and primary care, or perhaps through confusion with similarly named drug amlodipine (Medicines and Healthcare products Regulatory Agency 2018).

As part of our programme of work on "audit and feedback" using our OpenPrescribing.net tools, we will identify the practices with the highest nimodipine prescribing and send them tailored information on their recent prescribing levels compared to their peers, in an attempt to both engage participants with their data and impact their behaviour. Within this process we intend to determine whether or not this is a behaviour which is amenable to change with such an intervention, and why.

There have been a variety of attempts to change prescribing behaviour for other treatments such as antibiotics, but none for nimodipine. Our study will be similar in scope to a recent trial which provided feedback on total antibiotics to the 20% of GP prescribers with the highest baseline levels and made a small but significant impact (Hallsworth et al. 2016). We will contact practices where at least 2 items of nimodipine have been prescribed, totalling more than 56 tablets, i.e. at least two weeks' supply. This will be approximately 75 of 7,000 active practices in England, all of which will be sent the intervention.

The reasons that nimodipine is prescribed in primary care have not been well studied, so within our intervention we will invite participants to contact us with any reasons that nimodipine may be prescribed in their practice. With this information we will increase understanding of why nimodipine prescribing behaviour may or may not be amenable to change via audit and feedback. For example, if prescriptions are continued in primary care due to miscommunication or confusion with amlodipine, this could be amenable to change. Conversely, if, for example, clinicians prescribe nimodipine off-label for other indications, change may be less likely.

Within every intervention, practices will be supplied with a link to their practice dashboard on OpenPrescribing.net, with a slight difference according to the method of sending (email, fax, letter), to allow us to track interactions with each method.

Objectives

P1. Our overall objective is to determine whether receipt of data feedback highlighting unusual nimodipine prescribing prompts practices to improve performance in prescribing and increase their engagement with prescribing data.

S2. Our secondary objective is to identify which method of communication is most effective (email, letter, fax) at prompting practices to engage and improve performance.

Our null hypothesis is that feedback on current prescribing performance has no impact on information-seeking or prescribing behaviour.

3.2. OBJECTIVES AND OUTCOME MEASURES

3.2.1. Core Outcomes

Objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure (if applicable)
Primary Objective P1. Our overall objective is to determine whether receipt of data feedback highlighting unusual nimodipine prescribing prompts practices to improve performance in prescribing and increase their engagement with prescribing data.	ENGAGEMENT: Change from baseline in the proportion of practices having their dashboard viewed during the 5 week follow-up period. PRESCRIBING: Change from baseline in the rate of nimodipine prescribing per 1,000 registered patients compared to the change in an earlier control period.	ENGAGEMENT: Follow-up period: 5 weeks following the intervention. Baseline period: 5 weeks prior to intervention. PRESCRIBING: Follow-up period: Three months following intervention, **not** including month of sending. Baseline period: latest available three months of data at start of study. Control period: baseline period minus one year, follow-up period minus one year.
S1. Our secondary objective is to identify which method of communication is most effective (email, letter, fax).	ENGAGEMENT: ● Proportion of practices accessing at least one link sent in the intervention (Objective P1). ● Change from baseline in the proportion of practices having their dashboard viewed during the follow-up period (Objective P1). ● Number of links accessed at least once as a proportion of all links delivered by each method of contact (email, fax, letter) (Objective S1). PRESCRIBING:	See above.

	● Change from baseline in overall rate of nimodipine prescribing per 1,000 population, across all practices in England (Objective P1).	

3.2.2. Other Analyses

Sub-group analyses:

Outcome measures will also be compared between the sub-groups interacting with the link supplied, versus those not interacting; and for the sub-groups providing any reason for their prescribing pattern versus those not responding, and between sub-groups giving different reasons (grouped into predefined categories).

Qualitative measures:

We will collect any information supplied by participants explaining why nimodipine is prescribed. When recording these data in trial documents we will remove any details that could allow any specific clinicians or patients to be identified. For publication, we will summarise key themes, for example giving the percentage of respondents who mentioned: following instructions from secondary care to complete the course post-discharge, mistakenly extending the required prescribing period, off-label prescribing, overestimation/lack of awareness of practice performance, or any other broadly categorised reasons. The responses to the feedback question asked upon following the link in any of the interventions will be analysed against prior and post usage of the site. Any other feedback supplied by participants will also be collected (anonymously) and key themes compiled.

Detection of contamination:

Contamination may occur between practices. By tracking links and web page access, we will be able to measure the extent of contamination by some routes:

- Link sharing (links and pages accessed by multiple IP addresses)
- Number of non-intervention practices having their OpenPrescribing.net pages viewed during sessions arising from links being clicked. This could either arise from participants observing other practices' behaviour after their own, or sharing the links with others who then look for their own practice.

3.3. STUDY DESIGN

Cohort study. Recruitment, screening and consent will all follow that specified by the programme above. All practices will receive the intervention. We will assess outcomes before versus after. For the primary prescribing outcome, we will compare this with an earlier control period, as a natural reduction would be expected in the initial cohort. A follow-up letter will be sent to intervention practices 6-12 months after the end of the trial, to summarise any improvements in prescribing behaviour and also to serve as a reminder of how to use the OpenPrescribing site to monitor other prescribing behaviours.

Engagement data will be accessed via Google Analytics as per standard practice for any website. Practice-level prescribing data will be obtained from national datasets published monthly by NHS Digital, with approximately two months' lag time (NHS Digital 2017). This is generated from claims for items dispensed from pharmacies so cannot be altered by practices except by changes in prescribing behaviour. It is routinely compiled and loaded into our database. We will also collect responses to a

simple feedback question. The first time each link is ever accessed (by any IP address), a single (anonymous) feedback question will be asked: “Did the message we sent give you new information about your prescribing?” to which an answer (“Yes” or “No”) should be selected.

3.4. PARTICIPANT IDENTIFICATION AND RECRUITMENT

3.4.1. Study Participants

Participants will be GP Practices in England (and any staff involved in prescribing therein). Using the latest available 3-12 months of prescribing data at study commencement, we will select practices with the highest rates of nimodipine which, based on clinical judgement, may be indicative of problematic prescribing. We expect this will include approximately 75 practices.

3.4.2. Inclusion and Exclusion Criteria

The eligibility criteria are set out in Table 1.

Table 1. Eligibility criteria for practices.

GP Practice Eligibility Criteria	**Rationale**	**Data source / timepoint**
Standard GP practices (Setting type 4) in England	Exclude non-standard settings such a walk-in centres, prisons etc.	Latest release of NHS Digital organisation data
At least one method of contact (postal address, fax number and/or email address)	Required for intervention to be sent.	At time of randomisation
Active status	Exclude dormant and closed practices.	Latest release of NHS Digital organisation data
>= 1000 registered patients (with 10-85% aged 25-64)	Exclude non-standard practices. Limit noise in data. Exclude practices in process of closing.	Latest release of NHS Digital organisation data
More than one item of nimodipine prescribed OR more than 56 tablets prescribed in the latest 12 months	It would be unlikely for a single practice to need to prescribe more than one occasional week’s supply.	Latest 12 months of prescribing data
Individual practices and whole CCGs not involved in preliminary testing	Prior exposure to intervention. This will exclude from the study the CCG in which RC is employed.	Prior to intervention
Any nimodipine prescribed during the latest three months	Target current prescribers.	Latest three months of prescribing data

3.5. STUDY PROCEDURES

3.5.1. Baseline Assessments

We will identify practices, apply eligibility criteria and measure the baseline nimodipine prescribing rate together in software (Appendix A). All other baseline measurements will be carried out in the data analysis process, in code (Appendix B).

3.5.2. Follow-Up Data collection

Follow-up data for prescribing outcomes will be collected from the publicly available prescribing data, when published by NHS Digital approximately two months after the end of the prescribing follow-up period. For engagement outcomes, follow-up data will be extracted from Google Analysis services immediately after completion of the engagement follow-up period. Data extraction and follow-up measurements will be carried out in code (Appendix B). Any feedback received from participants will be recorded (anonymously and with any potentially identifiable details redacted) in a spreadsheet.

3.5.3. Discontinuation/Withdrawal of Participants from Study

A record will be kept of practices opting out. Interventions will be forwarded to new contact details if provided. Any practices which are found to have changed status (from being a standard practice) or become dormant/closure during the intervention will be excluded from analysis. Our intervention is not expected to influence overall items prescribed, number of patients, change of status or closure/dormancy of practices. Withdrawn participants will not be replaced.

3.6. INTERVENTIONS / INVESTIGATIONS

The 'intervention' will be the delivery of tailored written feedback to each practice, which details their recent performance on the selected measure in a graphical form and invites recipients to access the other services available at OpenPrescribing.net via a unique link for their practice. Research group contact details will be provided and recipients invited to contact us about reasons for the prescribing patterns observed.

Interventions will be delivered to practices by all available routes concurrently (email, letter and fax).

Within every intervention, practices will be supplied with a link to their practice dashboard on OpenPrescribing.net. The first time each link is ever accessed (by any IP address), a single (anonymous) feedback question will be asked: "Did the message we sent give you new information about your prescribing?" After an answer ("Yes" or "No") is selected, the dashboard will appear, with the selected measure highlighted. On the dashboard, practices can find more detail on this measure and others, along with interactive charts. Users will also be able to see how other practices/CCGs perform and access all the usual features of the website such as custom analyses.

3.7. STATISTICS AND ANALYSIS

3.7.1. Description of Statistical Methods

Data analysis will be carried out in code (Appendix B).

For our primary prescribing outcome, we will compare the nimodipine prescribed by practices we contacted before versus after the intervention using a paired t-test. For comparison, we will calculate the change occurring for the equivalent cohort one year earlier, over the equivalent baseline and follow-up

periods. For our secondary prescribing outcome we will assess the national change in rate of nimodipine prescribing across all practices using interrupted time series analysis.

Engagement outcomes:

- We will extract data on “Unique Pageviews” (separate browsing sessions) for practice dashboards from Google Analytics, for all practices eligible for the study. Aggregated measure values for each baseline and follow-up period will be calculated by summing the relevant outcomes for all practices.
- Before versus after outcomes will be assessed using paired t-tests, except:
    - For the proportion of links accessed by each method of contact, a McNemar paired-sample test will be used, because these measurements are not independent, e.g. a practice using the link supplied by email may be less likely to access the link in the letter. We will also perform a sensitivity analysis where we restrict analysis to only practices contacted by all three methods, to assess bias, e.g. practices with a discoverable fax number may be less responsive to email.
    - Analysis of browsing sessions, which will be discussed by distribution and basic descriptive statistics.
- Missing data: engagement data will be gathered from Google Analytics, therefore is expected to be complete except where users of the website have installed tools to prevent their activity being collected. This is likely to be uncommon, and equally distributed between intervention and control groups.

Qualitative analysis:

- Once summarised into key themes we will describe feedback supplied by participants using descriptive statistics.

3.7.2. The Number of Participants

All practices in England meeting eligibility criteria will be included. This is the complete set of all available participants. Our inclusion criteria will give approximately 75 practices. This is the full set of practices prescribing nimodipine in an unusual way. For our primary prescribing outcome, based on current prescribing levels we have 80% power to detect a decrease in quantity of 23% (alpha = 0.05).

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APPENDIX A: ENROLMENT AND ALLOCATION SCRIPTS

To follow.

APPENDIX B: DATA ANALYSIS SCRIPTS

To follow.