

Protocol for the Effective Feedback to Improve Primary Care Prescribing Safety (EFIPPS) study: a cluster randomised controlled trial using ePrescribing data

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ABSTRACT

Introduction: High-risk prescribing in primary care is common and causes considerable harm. Feedback interventions to improve care are attractive because they are relatively cheap to widely implement. There is good evidence that feedback has small to moderate effects, but the most recent Cochrane review called for more high-quality, large trials that explicitly test different forms of feedback.

Methods and analysis: The study is a three-arm cluster-randomised trial with general practices being randomised and outcomes measured at patient level. 262 practices in three Scottish Health Board areas have been randomised (94% of all possible practices). The two active arms receive different forms of prescribing safety data feedback, with rates of high-risk prescribing compared with a 'usual care' arm. Sample size estimation used baseline data from participating practices. With 85 practices randomised to each arm, then there is 93% power to detect a 25% difference in the percentage of high-risk prescribing (from 6.1% to 4.5%) between the usual care arm and each intervention arm. The primary outcome is a composite of six high-risk prescribing measures (antipsychotic prescribing to people aged ≥ 75 years; non-steroidal anti-inflammatory drug (NSAID) prescribing to people aged ≥ 75 without gastroprotection; NSAID prescribing to people prescribed aspirin/clopidogrel without gastroprotection; NSAID prescribing to people prescribed an ACE inhibitor/angiotensin receptor blocker *and* a diuretic; NSAID prescription to people prescribed an oral anticoagulant without gastroprotection; aspirin/clopidogrel prescription to people prescribed an oral anticoagulant without gastroprotection). The primary analysis will use multilevel modelling to account for repeated measurement of outcomes in patients clustered within practices.

Ethics and dissemination: The study was reviewed and approved by the NHS Tayside Committee on Medical Research Ethics B (11/ES/0001). The study will be disseminated via a final report to the funder with a publicly available research summary, and peer reviewed publications.

ARTICLE SUMMARY

Article focus

- This paper describes a protocol for a cluster-randomised trial evaluating the impact on high-risk prescribing of two different designs of feedback compared to a simple educational message.

Key messages

- High-risk prescribing and adverse drug events are common
- Feedback interventions are known to have small to moderate effects on targeted quality, but few trials have examined safety data feedback.

Strengths and limitations of this study

- The study addresses areas identified as needing more research in the 2010 Cochrane review of audit and feedback, including measurement of baseline performance, theory based development of interventions, head to head comparison of different feedback designs, and large scale (262 general practices). The intervention is embedded in real-world data systems and designed to be feasible to implement at scale, but a potential limitation is that it may not be intensive enough to show benefit.

Trial registration: ClinicalTrials.gov, dossier number NCT01602705.

BACKGROUND

Used appropriately, prescription drugs significantly improve patient outcomes, but inappropriate use in both hospital and primary care is a major cause of harm.^{1–3} Adverse drug events (ADEs) account for ~6.5% of all hospital admissions,¹ and at least

half of these are preventable.² The most frequent classes of drug implicated are antiplatelet drugs including aspirin, diuretics, non-steroidal anti-inflammatory drugs (NSAIDs), warfarin, opioids, β -blockers and ACE inhibitors (ACEI)/angiotensin receptor blockers (ARB).² Deaths are most frequently associated with NSAIDs and antiplatelet prescribing.¹ In addition, there have been a number of national safety alerts for less commonly prescribed drugs which have been regularly implicated in preventable deaths. Examples include guidance on methotrexate prescribing and monitoring,⁴ and anti-psychotic use in older people with dementia.⁵

There are a number of existing measures of potentially inappropriate or high-risk prescribing. Examples include relevant indicators from the Assessing Care of Vulnerable Elders (ACOVE) project,⁶ the Screening Tool of Older Persons' Potentially inappropriate Prescriptions (STOPP) and the Beers Criteria.^{7 8} However, ACOVE and STOPP rely on manual record review and are therefore not easily applied on a large scale. Although the Beers Criteria can be relatively easily measured using routine healthcare data, the drugs listed do not include those most commonly implicated in serious harm which makes them less useful in safety improvement.

We have recently defined a new set of indicators of high-risk prescribing which can be measured using routine electronic data,⁹ and have applied a subset of 15 indicators to routine clinical data extracted from 315 (~30%) Scottish practices, focusing on drugs most likely to cause harm.^{1 2 10} The indicators related to NSAIDs (prescription in people at high risk of GI bleeding without gastroprotection, in renal impairment, co-prescription with ACEI/ARB and diuretics), warfarin (co-prescription of NSAIDs, antiplatelets, high-risk antibiotics and oral azole antifungals), methotrexate (co-prescription of both 10 and 2.5 mg tablets), anti-psychotic prescription in older people with dementia and prescription of drugs to avoid in heart failure (NSAIDs, tricyclics, glitazones, verapamil and others). In total, 19 308 (13.9% of patients included in one or more denominators) had received one or more high-risk prescriptions in the previous year. On the basis of these data, 60 000 patients in Scotland will be exposed to this high-risk prescribing annually. After adjustment for patient casemix in terms of age, sex, deprivation and number of prescribed medicines, there remained considerable variation between practices in rates of high-risk prescribing, with patients in some practices being twice as likely to receive a high-risk prescription than average. High-risk prescribing is therefore both common and highly variable between practices.¹⁰ Although not all these prescriptions will be inappropriate, the high prevalence and high variation indicate that this is very likely to be improvable.

Health systems internationally have sought to improve the quality and safety of prescribing while controlling or ideally reducing costs, although primary care 'prescribing

improvement' activity in the UK has predominately focused on costs. This partly reflects that existing National Health Service (NHS) data systems can easily measure the total cost and volume of different drugs used by general practices, but cannot usually assess prescribing quality and safety because this usually needs patient-level data. However, the NHS in all four UK countries are developing centrally held patient-level prescribing datasets that make new kinds of measures possible. NHS Scotland has implemented an ePrescribing programme which has created a Scotland-wide, patient-level prescribing data warehouse (the new Prescribing Information System or newPIS). newPIS is held by the Information Services Division (ISD), and ~95% of prescribed items since April 2009 have a unique patient identifier attached, with data available within 8–12 weeks of a drug being prescribed (the delay being due to the pharmacy payment process). Available data include patient demography, drug prescribed, prescribing date, dispensing date, and practice code and practice characteristics. This study takes advantage of this unique opportunity to develop and rigorously test new forms of prescribing safety feedback for use across an entire healthcare system.

Providing feedback of performance is an attractive approach to improving prescribing safety since it is easily scalable and relatively inexpensive to deploy widely, allowing more expensive interventions to be deployed more selectively. There is evidence that feedback can be effective. At the time of designing the study, the most recent Cochrane review (2006) identified 118 randomised trials of clinical audit and feedback, although many were small and 80% were methodologically flawed or weak.¹¹ The median effect size was of a 5% absolute improvement in binary indicators of guideline compliance, but with a very wide range in individual studies from a 16% absolute worsening to a 70% absolute improvement. Only a very small number of studies examined feedback of safety data, mostly relating to benzodiazepine prescribing in the elderly.¹¹ The authors recommended that more high-quality trials were needed. Such trials require baseline measurement, clearly defined primary outcomes, and have to be large enough to reliably detect the small to moderate effect sizes that are likely. Key gaps in the existing evidence literature relate to feedback design, with a need for more theory-informed design¹² and 'for head to head comparisons of different ways of doing audit and feedback'.¹¹ The Effective Feedback to Improve Primary Care Prescribing Safety (EFIPPS) study therefore developed two theory-informed formats for prescribing safety feedback, with the aim of testing their effectiveness compared to simple 'factual' educational material in a large, cluster randomised trial.

We hypothesise that feedback and feedback plus a health psychology informed intervention delivered to practices will reduce high-risk prescribing to patients compared to a simple educational intervention alone. The specific objectives are:

1. To test the effectiveness of the two EFIPPS feedback arms in reducing the specified primary outcome of a composite measure of high-risk antipsychotic, non-steroidal anti-inflammatory drug and antiplatelet drug prescribing;
2. To test the effectiveness of the two EFIPPS feedback arms in reducing the specified secondary outcomes of the six individual measures constituting the composite;
3. To assess the cost effectiveness of the intervention.

METHODS AND ANALYSIS

Trial design

The outcomes were chosen and the intervention components designed in an initial development phase. The trial is a highly pragmatic, three arm, cluster randomised controlled trial with the practice as the unit of randomisation, and outcomes measured at the individual patient level (figure 1). A cluster randomised design was chosen because the feedback intervention being tested is necessarily targeted at practices or professionals (in this case practices, as the data are not available at the individual professional level).

Participants and settings

The trial will be conducted in all eligible general medical practices in three Scottish Health Boards which provide healthcare for approximately 1.8 million people in both urban and rural settings, and across the range of socioeconomic deprivation. Primary medical care in these three Health Boards is provided by 279 general medical practices, and all Boards already use a variety of means to seek to influence General Practice prescribing, including the use of formularies, guidelines, newsletters, the use of primary care pharmacists to provide prescribing advice and support for implementation and the financial incentives for prescribing improvement in the Quality and Outcomes Framework of the GP contract. In all three Boards, virtually all community prescribing is done by General Practices and by General Practitioners in particular (nurses, health visitors and pharmacists are

increasingly prescribing some medicines under defined protocols, but this is only for a relatively small group of drugs and currently represents only a small proportion of total prescribing). The intervention therefore targets existing teams of professionals working in General Practices in the three Health Boards.

Inclusion and exclusion criteria

Practice inclusion criteria

- ▶ General medical practices in the three participating health boards

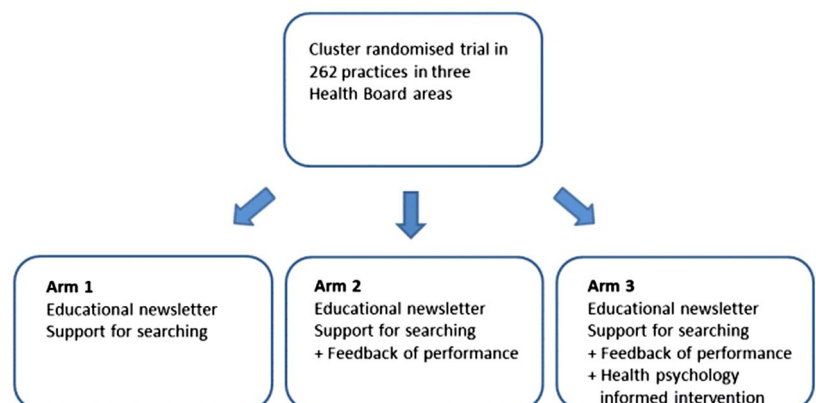
Practice exclusion criteria

- ▶ Practices with registered listsizes <250 patients (all of these are unusual practices in various ways, for example serving the homeless or people with challenging behaviour)
- ▶ Practices with <93% of scripts in the newPIS data warehouse having a unique patient identifier (the Community Health Index (CHI) number)
- ▶ Practices which were formed after 1 January 2011 (since the first round of feedback in 2012 includes historical trend data)
- ▶ Practices which cease to exist during the trial
- ▶ Practices which merge during the trial, where the merging practices were originally in different arms of the trial

Recruitment of practices

The interventions being implemented in each of the three arms are variants of existing 'usual care', in that practices are already routinely sent educational material relating to prescribing safety and feedback about their prescribing of various kinds (usually comparative cost or formulary compliance data). With the consent of the NHS Research Ethics Committee that reviewed the application, practices will not be formally recruited or consented to take part. The trial is therefore a highly pragmatic one, in that all eligible practices will be randomised and followed up.

Figure 1 Effective Feedback to Improve Primary Care Prescribing Safety trial design.



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Recruitment of patients

The intervention is targeted at practices, and it remains at each practice's discretion whether and when to search for patients with the specified high-risk prescribing, to review their records or the patients themselves, and to change prescribing (or not). With the consent of the NHS Research Ethics Committee that reviewed the application, there is therefore no recruitment of patients by the research team.

Intervention components

The intervention was designed to be feasible in real-life practice, in terms of the time spent on its overall design, its implementation in existing IT systems at NHS Scotland Information Services Division, and the frequency and intensity of feedback. For example, feedback delivery was chosen to be by email because this is definitely achievable routinely, whereas resources for face to face facilitation by a primary care pharmacist vary by area, and there are multiple competing demands on pharmacist resource. All components will be delivered at practice (cluster) level only, and [table 1](#) shows the timing of the interventions to be delivered.

1. *Educational intervention for all three arms.* All educational material was created by the research team in conjunction with the study advisory group and where necessary topic-specific experts. A short written educational intervention will be delivered to all practices by email in the month before the first feedback round. This consists of two pages of text which emphasises that high-risk prescribing is common and that good practice is to regularly identify and review patients with it, which lists the indicators and briefly summarises the risk that targeted prescribing poses and advice on what to do, and which directs readers to a website with additional more detailed educational material.

2. *Support for searching for patients in each practice's own electronic record for all three arms.* The website additionally has a set of downloadable searches for the two general practice electronic records in use in Scotland.

3. *Feedback of performance on the targeted indicators.* Practices in the two treatment arms (2 and 3) will be emailed quarterly written feedback of their rate of high-risk prescribing on five occasions. Feedback was designed by the research team working with the study advisory group which included clinical and managerial representatives from the three participating Health Boards and input from the technical team at NHS Scotland Information Services Division who were responsible for implementation. The feedback consists of a cover sheet which lists the indicators, a set of six summary-run charts with a benchmark on one page, and a more detailed one page summary for each indicator consisting of the same run chart, with additional text explanation. The run chart shows the practice percentage of patients receiving a high-risk prescribing, benchmarked¹³ against the lowest quartile for all Scottish practices in the year before feedback started. Two kinds of text are included for each indicator. The first is the same for all practices, and explains why the indicator is important and makes recommendations about what practices should do (eg, to avoid particular combinations of drugs or review patients with particular prescribing) in order to make the feedback more 'actionable'.^{14 15} The second varies by practice and by time, since it describes what the run chart is showing, in terms of how the practice compares to the benchmark and whether the practice only has a small number of patients eligible for the indicator.

Feedback is sent quarterly to practices as an attachment to a personalised email signed by a Health Board primary care clinical manager from the practice's Board

Table 1 Timeline of interventions to practices in each arm of the trial

Trial arm Date	Arm 1 Educational intervention only (control)	Arm 2 Educational intervention plus quarterly feedback	Arm 3 Educational intervention+quarterly feedback plus health psychology informed intervention
June 2012	Sent 2 page educational material Access via web to more detailed educational material and patient searches throughout	Sent 2 page educational material Access via web to more detailed educational material and patient searches throughout	Sent 2 page educational material Access via web to more detailed educational material and patient searches throughout
July 2012	–	Feedback 1	Feedback 1 plus action planning intervention
October 2012	–	Feedback 2	Feedback 2 plus perceived behavioural control intervention
January 2013	–	Feedback 3	Feedback 3 plus attitude intervention
April 2013	–	Feedback 4	Feedback 4 plus social norms intervention
July 2013	–	Feedback 5	Feedback 5 plus action planning intervention

and the Director of the NHS Scotland National Medicines Utilisation Unit. Each practice will receive five rounds of feedback during the trial.

4. *Health psychology informed intervention.* Practices in arm 3 will additionally receive a health psychology informed intervention embedded in the feedback emailed quarterly on five occasions. This was designed by the research team drawing on social cognition models including both the Theory of Planned Behaviour (TPB), a motivational model that focuses on behavioural intention¹⁶ and the Health Action Process Approach (HAPA)¹⁷ that has a similar motivational phase to TPB but also has a volitional phase that focuses on action-controlled strategies. Four focus groups were carried out with general practitioners, primary care pharmacists and prescribing advisers to elicit a broad range of attitudes, subjective norms and perceived behavioural control beliefs (barriers) to reviewing patients with high-risk prescribing and changing their medication.

Using the information obtained in the focus groups a two-stage email Delphi study was then delivered to GPs to prioritise attitudes, norms and barriers to reviewing patients prescribing in order of those, viewed by GPs, to be the most important or influential. The psychology constructs within each of the social cognition models were mapped to behaviour change techniques¹⁸ and then, using the results from the email Delphi study, four one-page interventions were designed targeting each of the four psychology constructs. Participating practices in arm 3 receive interventions targeting (in order of receipt): action planning (HAPA), attitudes (TPB), subjective norms (TPB), perceived behavioural control (TPB) and a repeat of the action planning intervention in the fifth round of feedback. The intervention appears as page 2 in the feedback document.

Outcome measures

The outcome measures were chosen by the EFIPPS steering group which included representatives from each of the three Health Boards participating, NHS Scotland Information Services Division and National Medicines Utilisation Unit and the research team. Measures were drawn from those which had been the subject of a recent formal consensus process to validate them,^{9 19} and were selected for their perceived importance to the participating Health Boards and their feasibility to implement in the newPIS data warehouse.

Primary outcome measure

The primary outcome is a composite of the six individual secondary outcome indicators. At patient level, it is defined as whether or not a patient who is particularly at risk of an adverse event from the specified prescribing (due to age or co-prescribing) is prescribed one or more high-risk prescriptions in each quarter. At practice-level, it is defined as the proportion of patients particularly at risk of an adverse event from the specified

prescribing, who receives one or more high-risk prescriptions. A composite is reasonable as a coherent measure of 'high-risk prescribing' because each of the underlying indicators is based on evidence of harm and has been judged valid in one or more formal consensus studies.^{9 19}

Secondary outcome measures

The six individual high-risk prescribing measures will be measured quarterly

1. Oral antipsychotic prescription to a patient aged 75 years and over (as a proxy of oral antipsychotic prescribing to older people with dementia).^{5 20 21}
2. Oral non-steroidal anti-inflammatory drug (NSAID) prescription to a patient aged 65 years and over who is currently prescribed a diuretic *and* an ACE inhibitor or Angiotensin Receptor Blocker (the 'triple whammy').^{22 23}
3. Oral NSAID prescription to a patient aged 75 years and over who is not currently prescribed a gastroprotective drug.²⁴⁻²⁶
4. Oral NSAID prescription to a patient aged 65 years and over who is currently prescribed either aspirin or clopidogrel, but is not currently prescribed a gastroprotective drug.^{24 27 28}
5. Oral NSAID prescription to a patient currently prescribed an oral anticoagulant but who is not currently prescribed a gastroprotective drug.^{24 27 28}
6. Aspirin or clopidogrel prescription to a patient currently prescribed an oral anticoagulant but who is not currently prescribed a gastroprotective drug.^{24 27 28}

Cost measurement

Data on the resources used to develop the interventions in each of the three arms will be recorded along with the resources needed in responding to queries from GP practices in each arm. In addition the resources used within GP practices as a result of the intervention will be estimated based on a sample of GP practices.

Outcome measurement

Primary and secondary outcomes will be measured using routinely available data from the newPIS data warehouse held by ISD Scotland.

Sample size

The power calculations were based on a cluster randomised trial and were calculated using the `n4prop` function in the `CRTSize` library in R.^{29 30} In the period prior to the study an average of 700 patients per practice were in one of the composite risk groups. Of these 6.1% had a high-risk prescription in the previous quarter, and the intraclass correlation coefficient was 1.26%. There are two primary comparisons in the study, each of the two feedback arms compared to standard practice, and each are to be tested at a significance level of 0.025. With 85 practices randomised to each arm, then there is 93% power to detect a 25% difference in the percentage of

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high-risk prescribing (from 6.1% to 4.5%) between standard arm and the intervention arm at the end of the study. A sensitivity analysis of the power to reductions in the average number of patients in the composite risk group per practice, reductions in the percentage with a high-risk prescription and an increase in the intraclass correlation showed that differences in the range 20–30% will be detected with a power of at least 80% if as few as 70 practices complete the study (table 2).

The intraclass correlations for the secondary outcome 5 measure (NSAID prescribed to a patient prescribed oral anticoagulation without gastroprotection) is 14.5% and there is no power to detect any differences for this single end point. For the other five secondary outcomes,

the intraclass correlation range from 1.3% for those based on all patients aged 75 and over to 4.9% for secondary outcome 6 (antiplatelet prescribed to a patient prescribed oral anticoagulation without gastroprotection). With a sample size of 80 practices per arm, there is a power of at least 90% to detect differences of 40%, or 80% power for differences of 35%, on each of the individual measures.

Randomisation and allocation concealment

The three Health Boards were recruited to be representative of the types of practices in Scotland. In total, 262 (94.3%) practices in the three participating boards satisfied the eligibility criteria and were randomised. There

Table 2 Powers to detect the specified percentage reductions in the percentages of high-risk prescribing associated with a variety of intra class correlations (ICC), average practice size, anticipated percentages of high-risk prescribing in the control arm and numbers of practices randomised

Percentage control (%)	Percentage intervention (%)	Percentage reduction	ICC (%)	Average practice size	Number practices control	Number practices intervention	Power
6.1	4.8	21	1.3	700	85	85	0.80
6.1	4.7	22	1.3	700	79	79	0.81
6.1	4.7	22	1.3	700	75	75	0.79
6.1	4.7	23	1.3	700	70	70	0.80
6.1	4.5	25	1.3	700	85	85	0.93
6.1	4.5	25	1.3	700	79	79	0.91
6.1	4.5	26	1.3	700	75	75	0.92
6.1	4.5	26	1.3	700	70	70	0.90
6.1	4.5	25	1.3	700	85	85	0.93
6.1	4.4	27	1.3	700	79	79	0.95
6.1	4.4	27	1.3	700	75	75	0.94
6.1	4.4	28	1.3	700	70	70	0.94
6.1	4.7	23	1.9	700	70	70	0.80
6.1	4.7	23	1.9	700	75	75	0.83
6.1	4.8	21	1.9	700	85	85	0.80
6.1	4.5	26	1.9	700	70	70	0.90
6.1	4.5	26	1.9	700	75	75	0.92
6.1	4.4	28	1.9	700	70	70	0.94
6.1	4.4	27	1.9	700	75	75	0.94
6.1	4.5	25	1.9	700	85	85	0.93
6.1	4.7	23	1.3	600	70	70	0.79
6.1	4.7	23	1.3	600	75	75	0.82
6.1	4.7	22	1.3	600	80	80	0.81
6.1	4.5	25	1.3	600	75	75	0.89
6.1	4.5	25	1.3	600	80	80	0.91
6.1	4.6	24	1.3	600	85	85	0.90
6.1	4.4	27	1.3	600	80	80	0.95
6.1	4.4	27	1.3	600	85	85	0.96
4.5	3.4	26	1.3	700	70	70	0.78
4.5	3.4	26	1.3	700	75	75	0.81
4.5	3.4	26	1.3	700	80	80	0.84
4.5	3.4	25	1.3	700	85	85	0.83
4.5	3.2	30	1.3	700	70	70	0.90
4.5	3.2	29	1.3	700	75	75	0.90
4.5	3.3	27	1.3	700	80	80	0.90
4.5	3.3	27	1.3	700	85	85	0.89
4.5	2.9	36	1.3	700	70	70	0.98
4.5	3.2	30	1.3	700	85	85	0.95

Table 3 Number of practices randomised to each strata

NHS health board	Tertile of rate of high-risk prescribing	Group A*	Group B*	Group C*
HB1		4	4	4
HB2	1 (lowest rate)	6	6	6
HB3		19	19	19
HB1		3	4	4
HB2	2	11	11	10
HB3		15	15	15
HB1		9	10	10
HB2	3 (highest rate)	14	13	14
HB3		6	6	5

*The research team are blind to which arm is control, treatments 1 or 2 (an independent statistician allocated treatment groups to arms). HB, NHS health board.

were two stratification factors, Health Board and baseline high-risk prescribing, in tertiles, giving nine strata. Stratifying by the Health Board was necessary in case a board-implemented improvement activity designed to influence high-risk prescribing, while stratifying by high-risk prescribing was to achieve balance over the three treatment arms. No further restriction was placed on the randomisation other than ensuring that there were approximately equal numbers in the three treatment groups in each strata—exact equality was not possible as the number of practices in each strata was not a multiple of 3. Rather than randomising fewer practices all eligible practices were included (table 3).

As all practices were included in the study at one time there was no need to balance the allocation sequence. Randomisation to the treatment group was carried out by the statistical team and the Tayside Clinical Trials Unit independently allocated each treatment group to one of the three arms (control arm 1, feedback arm 2, feedback+psychology informed intervention arm 3). Practices cannot be blinded to their treatment allocation, but the statistical team was blinded to this allocation and will analyse the data blind.

Statistical methods

The main analysis will be through the use of a multilevel logistic regression model to take into account both patient-level characteristics and GP practice-level variables. We will test the effect of both experimental arms separately against the control arm (at the 2.5% significance level) to control for an overall 5% significance level.

The first analysis is the comparison of the percentages of patients in the composite risk groups who have a high-risk prescription in the quarter following the end of the study. There are two primary contrasts arm 2 compared to arms 1 and 3 compared to 1. The analysis will be based on a two-stage hierarchical logistic regression model, where the cluster is the GP practice, adjusting

for the strata, health board and high-risk prescribing at baseline. This will be carried out using the lme4 package in R (<http://lme4.r-forge.r-project.org/>). This represents the analysis that the study power is based upon.

The second analysis will take into account the repeated observations over time and will be based on individual data from six quarters pre-randomisation and four quarters postrandomisation. Again a hierarchical logistic regression model will be used with patients clustered within practices. The primary variables in the regression model are strata, treatment group and time. Time will be included as an ordinal factor effect with the linear trend being the most important term. Adjustment will be made for individual-level and practice-level variables in the quarter before randomisation. It is anticipated that an autoregressive covariance matrix will be used for the temporal effects though a general, unconstrained matrix will be investigated. The choice of appropriate covariance matrix will be based on penalised log likelihood methods such as AIC. In this analysis the prime aim is to investigate if the temporal trends in high-risk prescribing in the two feedback arms (arms 2 and 3) are different from the trend in the standard arm (arm 1). This is an interaction test between treatment group and time in the model. By using repeated observations from the practices then an increased precision in the estimated effects is anticipated.

The primary analysis is based on the composite measure and the individual measures will be part of the secondary analysis. The main explanatory variables at the patient level will be gender, age, socioeconomic status measured using postcode assigned Scottish Index of Multiple Deprivation score,³¹ and comorbidity measured using hospital admission data. We will also have information on the main class of prescribing and length of time on prescription and these may be used if the quality of the data is sufficiently high. At the practice level we anticipate having data on practice size, accreditation for postgraduate training and previous levels of high-risk prescribing. The proportion of patients with high-risk prescribing patterns will be used as an explanatory variable in the analysis, through the stratification in the randomisation.

We propose to carry out an interim analysis midway through the intervention. This analysis, as well as the final analysis, will be blinded to the treatment allocation. The interim analysis will serve to check the initial assumptions made in the power calculation and to validate the data extraction from the ISD prescribing database.

Furthermore, as the duration of prescribing will be available we propose to analyse the length of time that high-risk prescribing has occurred and investigate if this is shorter in the two feedback arms compared to the standard control arm. This analysis will be carried out using a cox proportional hazards model with a random effect (frailty term) associated with practice.

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The analysis of the end-of-study data and the time trend data will be based upon an intention-to-treat analysis. Drop-out of practices is not expected and use of imputation methods is not foreseen. Some practices may merge and others may close or split. The numbers likely to be involved are small and no special treatment is required.

Cost-effectiveness methods

The cost-effectiveness analysis will investigate the cost per reduction in the number of person years over which individuals are exposed to high-risk prescribing in the two feedback arms (arms 2 and 3) compared to standard practice (arm 1). The reduction in the number of person years over which individuals are exposed to high-risk prescribing will be based on the composite measure of high-risk prescribing taking into account quarterly variations in the estimated intervention effect, after controlling for baseline levels, until one-quarter after the end of the study. The costs considered in each arm of the intervention will include both the fixed costs associated with developing indicators, feedback templates and also include those variable costs associated with responding to queries from GP practices and the actual GP practice resources involved in changing high-risk prescribing in terms of GPs' time taken to; read materials, undertake searches for high-risk patients, review patients and change prescribing, if needed. The benefits and costs will be modelled around the potential future implementation of such an intervention Scotland-wide given that the fixed costs are unlikely to change; however, the impact on the cost-effectiveness to changes in the scale of the intervention will also be analysed. Uncertainty in terms of costs as well as outcomes will be explored via a multivariate sensitivity analysis.

ETHICS AND DISSEMINATION

The feedback intervention seeks to prompt a review of potentially high-risk prescribing to ensure that it is appropriate, but prescribing decisions and patient care remains entirely the responsibility of the practice that a patient is registered with, with any changes in prescribing being done in the context of normal clinical care. The Tayside Committee for Medical Ethics B committee reviewed the study and gave a favourable ethical opinion. Dissemination will include a final report to the funder with a lay summary for publication, peer-reviewed journal articles and NHS-targeted summaries and implementation support material.

CONCLUSION

High-risk prescribing in primary care is common and varies considerably between practices, and improving the safety of primary care prescribing is important.¹⁰ There is some evidence that relatively intensive intervention involving pharmacist-led review is effective,³² but

such interventions are expensive and may therefore be difficult to scale. Feedback interventions are much less resource intensive, and therefore potentially more scalable and feasible to use in everyday practice, but most reported trials have uncertain or high risk of bias,³³ and there is little evidence for their use in improving safety outcomes.³³ The 2012 Cochrane review update authors echoed the 2006 review¹¹ in recommending that more high-quality trials were needed, with such trials ideally having baseline measurement, clearly defined primary outcomes and being large enough to reliably detect the small-to-moderate effect sizes that are likely. They specifically state that: "To build upon the current evidence base, the field would benefit from more attention to four areas: improved reporting and methods; explicit use of theory, empirical evidence, and logic to develop hypotheses and to design the intervention and comparison arms; a focus on professional practices for which there is compelling evidence of patient benefits with clearly defined primary outcomes; and more head-to-head trials (e.g. comparing different ways of providing feedback)."³³

Although designed before the most recent Cochrane review,³³ the EFIPPS trial fulfils the design requirements cited above (careful design of feedback, clearly defined primary outcome baseline measurement, large scale); drew on existing evidence, theory and NHS professionals' expertise in designing the feedback to be used; focused on high-risk prescribing where there is good evidence of the magnitude of harm caused; and includes a head-to-head comparison of two different forms of feedback with different resource implications. It will therefore significantly add to the existing literature.

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