



Developing a complex intervention to improve prescribing safety in primary care: mixed methods feasibility and optimisation pilot study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-004153
Article Type:	Research
Date Submitted by the Author:	30-Sep-2013
Complete List of Authors:	Grant, Aileen; University of Dundee, Population Health Sciences Guthrie, Bruce; University of Dundee, Population Health Sciences Dreischulte, Tobias; University of Dundee, Population Health Sciences
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Pharmacology and therapeutics, Health services research, Health informatics, Medical management
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, CLINICAL PHARMACOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adverse events < THERAPEUTICS

SCHOLARONE™
Manuscripts

Developing a complex intervention to improve prescribing safety in primary care: mixed methods feasibility and optimisation pilot study

Authors

Aileen M Grant (a.m.grant@dundee.ac.uk)*

Quality, Safety and Informatics Group, Population Health Sciences, Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383733

Bruce Guthrie (b.guthrie@dundee.ac.uk)

Quality, Safety and Informatics Group, Population Health Sciences, Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383740

Tobias Dreischulte (t.dreischulte@dundee.ac.uk)

Medicines Management Unit, NHS Tayside c/o, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383769

*Corresponding author

Abstract:

Objectives

1. To measure the extent to which candidate outcome measures (for the DQIP trial) can identify high-risk prescribing that is potentially changeable by the DQIP intervention
2. To explore the value of reviewing identified high-risk prescribing to clinicians
3. To optimise the components of the DQIP intervention.

Design: Mixed method study

Setting: General practices in two Scottish health boards.

Participants: Four purposively sampled general practices of varying size and socioeconomic deprivation.

Outcome measures: Prescribing measures targeting (1) 'High-risk use of NSAIDs and antiplatelets'; (2) 'Asthma control'; and (3) 'Antithrombotics in AF' (AF).

Intervention: The prescribing measures above were used to identify patients for review by general practices. The ability of the measures to identify potentially changeable high-risk prescribing was measured as the proportion of patients reviewed where practices identified a need for action. Field notes were recorded from meetings between researchers and staff and key staff participated in semi-structured interviews exploring their experience of piloted intervention processes.

Results: Practices identified a need for action in 68%, 25%, 18% of patients reviewed for prescribing measures targeting (1), (2) and (3), respectively. GPs valued being prompted to review patients, and perceived that (1) 'NSAID and antiplatelets' and (2) 'antithrombotics in AF' measures were the most important to act on. Barriers to initial and ongoing engagement, and to sustaining improvements in prescribing were identified.

Conclusion: 'NSAIDs and antiplatelets' measures were selected as the most suitable outcome measures for the DQIP trial, based on evidence of this prescribing being more easily changeable. In response to the barriers identified the intervention was designed to include a financial incentive, additional on-going feedback on progress, and re-prompting review of patients, whose high-risk prescribing was restarted after a decision to stop.

Trial registration number: Clinicaltrials.gov NCT01425502

Article summary:

Article focus: This study aimed to evaluate the extent to which different candidate outcome measures identified high-risk prescribing that is potentially changeable, explore the perceived value of these measures to clinicians, and to optimise intervention components for evaluation in a cluster-randomised trial.

Key Messages:

- Prescribing measures prioritised for improvement were validated for use in a complex prescribing quality improvement intervention.
- The ability of these measures to identify potentially changeable high-risk prescribing and the perceived value of the measures varied.

- In response to the barriers identified, the intervention to be tested in a trial was designed to include a financial incentive to facilitate initial engagement, to provide additional on-going feedback on overall progress, and to highlight patients whose high-risk prescribing was restarted after a decision to stop.

Strengths and limitations:

- The strength of this study was the use of quantitative and qualitative methods to give a greater understanding of how changeable the identified high risk prescribing was, what the barriers to changing prescribing were and how GPs valued this work, which enabled informed choice of outcome measures and optimisation of the intervention.
- The limitation of this study is that changeability of potential outcome measures was tested by measuring GPs intention to change prescribing or conduct further investigation ('action'), rather than quantifying actual changes in prescribing and their clinical implications (although this is being evaluated in an ongoing cluster-randomised controlled trial).

Background

The safety of medication use in primary care is a major concern for health systems internationally.¹⁻⁴ An estimated 3-4% of unplanned hospital admissions are due to preventable adverse drug events and approximately one third of these have been attributed to prescribing of drugs to people with risk factors for adverse drug effects and under-prescribing of prophylactic treatments (high-risk prescribing).⁴

In the UK, medications may be initiated in primary and secondary care, but general practitioners (GPs) prescribe almost all drugs in the community and have responsibility for reviewing all medications. Previous research has shown that high-risk prescribing in primary care is common and its prevalence varies substantially between practices (after adjusting for case-mix), which indicates scope for improvement.⁵⁻⁸ Given the current UK policy focus on improving patient safety, there is a need to develop and test interventions to reduce high-risk prescribing.^{9,10}

In the UK, the virtually ubiquitous use of electronic medical records (EMRs) in primary care offers opportunities to support quality and safety improvement initiatives. For example, the PINCER (Pharmacist-led Information Technology Intervention for Medication Errors) trial has demonstrated the effectiveness of an intervention, where pharmacists identified patients with high-risk prescribing using data extracted from EMRs, reviewed their records, and recommended changes.¹¹ Similarly, the 'Data-driven quality improvement in primary care' (DQIP) research programme aims to identify patients with high-risk prescribing from EMRs, but in contrast to PINCER, practices are provided with continuous feedback using a web-based informatics tool, and financial incentives to motivate practice staff to review patients identified.¹²

The Medical Research Council (MRC) Framework recommends that complex interventions be modelled before evaluation in a randomised controlled trial in order to optimise both the intervention design and its evaluation by defining outcomes and ensuring feasibility.^{13, 14} In terms of intervention design, the broad shape of the DQIP intervention was defined by the intention that there should be evidence for the effectiveness of its components, that it should be built on existing NHS information technology and be implementable as an 'enhanced service' (a UK National Health Service mechanism for commissioning general practice care). The intention was therefore to combine an educational intervention^{15, 16}, audit and feedback¹⁷, and a financial incentive to review. As a result a priority was to pilot and optimise these elements in a small number of practices. For evaluating the impact of the intervention, a set of potential prescribing outcome measures had previously been validated using consensus methods⁵, but a key question to be clarified was which of these measures could plausibly be improved by the intervention, and therefore used as trial outcome measures.

The specific objectives of this study were to optimise the DQIP intervention and trial evaluation by: (1) identifying which potential outcome measures best identified patients with high-risk prescribing that could potentially be changed; (2) establishing which measures were most valued by practices in terms of improving quality and safety; (3) exploring how best to design and deliver the educational, informatics and financial components of the DQIP intervention to maximise practice engagement.

Methods

The study used mixed qualitative and quantitative methods, and was approved by NHS Tayside Committee on Medical Research Ethics A (09/S1401/54).

Settings

We purposively sampled and recruited four general practices, two from each NHS Scotland Health Board where the intervention was to be trialled, aiming to include larger and smaller practices serving populations that varied in socioeconomic deprivation.

Data collection

Data collection was between March 2010 and August 2011.

Quantitative data

In each practice, thematically related prescribing measures ('prescribing topics') that had previously been identified as priorities for quality improvement⁵ were implemented in EMRs to identify patients with high-risk prescribing for review. These prescribing topics were: (1) High-risk use of NSAIDs and antiplatelets in patients with gastro-intestinal, renal or cardiac risk factors ('NSAIDs and antiplatelets'); (2) Under-use of inhaled corticosteroids and high-risk use of beta-blockers in asthma ('asthma control'); and (3) Over-and under-use of anti-thrombotic drugs in atrial fibrillation ('antithrombotics in AF').

Practices received a feedback report for each topic, which summarised the total numbers of patients identified by each measure of high-risk prescribing, listed the patients affected, and provided supporting educational material (rationale, current evidence and prescribing guidance).¹⁸ Practices were asked to conduct a record review of all identified patients with face-to-face review if necessary, and to document all decision-making on a structured template (tick boxes for a decision to 'change prescribing', conduct 'further investigation' or 'no action' and free text space to specify the rationale for 'no action').

Qualitative data

An initial meeting to explain the study and describe the topics was held in each practice. Practices then worked on one topic at a time, with further meetings held six to eight weeks after practices had received and acted on the feedback report. The meetings were facilitated by the pharmacist (TD), and observed by AG who took ethnographic field notes of 18 hours of meetings. The whole practice was invited but the meetings were generally attended by the GP(s) most involved and the practice manager and lasted between 30 and 60 minutes. At these meetings, practices were asked to describe the practice processes to conduct the review work, to report on the complexities of reviewing or changing prescribing, and to expand on reasons for 'no action'.

The GPs most involved in the review work and practice managers were invited for individual semi-structured interviews in order to explore their perceptions of the value of each prescribing topic and the specific components of the intervention (education, informatics and financial), their experiences of adopting and implementing the intervention in routine practice and to changing prescribing. Eleven interviews were conducted with 8 GPs (one GP was interviewed twice) and 2 practice managers. These interviews were held in the practices, lasted approximately one hour, were audio-recorded and transcribed verbatim.

Data Analysis

Quantitative analysis (research question (RQ) 1: performance of prescribing measures)

The ability of each measure to identify potentially changeable high-risk prescribing was measured as the proportion of patients reviewed whose prescribing was judged to require action ('change prescribing' or 'further investigation'). Reasons why the measures failed to identify potentially changeable high-risk prescribing in patients were classified into three categories: 'clinical' (prescribing changes were deemed inappropriate or unnecessary given the clinical circumstances), 'technical' (the measure mis-identified patients when implemented in live clinical data) and 'other'.

Qualitative analysis (RQ2 perceived value of each prescribing topic and RQ3 optimising intervention components)

Interview transcripts and fieldnotes were merged and analysed by emerging themes to identify a coding frame. Data was imported into Nvivo-8 and the coding frame was systematically applied. Subsequent analysis was by the Framework technique.¹⁹ Thematic charting facilitated comparing the data by theme, practice and prescribing topic. The data was explored for negative cases.

Results

Practice list-sizes ranged from 3,200 to over 10,000, with the percentage of patients living in the most deprived quintile of postcodes ranging from 4% to 46%. All four practices completed the 'NSAID and antiplatelet' and 'asthma control' topics, but only three completed the 'antithrombotics in AF' topic.

Ability of measures to identify patients with potentially changeable high-risk prescribing

Table 1 shows that for the 'NSAID and antiplatelet' topic, practices recorded a need for action in 68% of patients reviewed (change prescribing 35%; further investigation 33%) compared to only 25% of patients reviewed for the 'asthma control' topic (change prescribing 7%; further investigation 18%) and 18% of those reviewed for 'antithrombotics in AF' (change prescribing 1%; further investigation 17%).

Insert table 1 and 2 about here

Table 2 shows the rationales for no action reported by GPs on templates for each patient reviewed. *Clinical reasons* were most commonly reported for the 'NSAIDs and antiplatelets' topic (67%), but less so for the 'antithrombotics in AF' (36%) and much less for the 'asthma control' (4%) topic. The reasons provided reflected that high-risk prescribing was a trade-off between effectiveness and safety. For 'NSAIDs and antiplatelets', the main reported reason for not changing prescribing was that NSAID use was only 'short term'. For 'antithrombotics in AF', clinical reasons reported were mainly 'unfitness for warfarin' (examples reported in interview included fragility and dementia, heavy alcohol use and previous gastrointestinal bleeding), but also included 'paroxysmal AF' (reflecting a misconception that stroke risk is lower than for patients with chronic AF).²⁰

'*Technical reasons*' accounted for one third of rationales for no action for the 'NSAID and antiplatelet' topic, and for 47% 'asthma control' and 48% of the 'antithrombotics in AF' topics. For all three topics, technical reasons related to patients no longer being on practice registers and to situations where identified high-risk prescribing was no longer present at the point of review ('time window of assessment'). For example, for the 'antithrombotics in AF' topic, all practices highlighted in interviews that anticoagulant prescribing intervals often exceeded the 12 week timeframe used by the measures, causing patients to be incorrectly identified as lacking antithrombotic prophylaxis.

Inaccurate disease registers were reported as reasons why 'antithrombotics in AF' and 'asthma control' measures misidentified prescribing as high-risk. One practice reported in interview that many patients on their asthma disease register had chronic obstructive pulmonary disease (COPD) and therefore did not have a clear indication for treatment with inhaled corticosteroids. The deprived practices reported that high numbers of short-acting beta-agonist prescriptions did not necessarily identify patients with uncontrolled asthma, because patients stockpiled inhalers in multiple locations (e.g. home, school, or work).

'Other' reasons were not commonly identified for 'NSAIDs and antiplatelets', but accounted for 16% of 'antithrombotics in AF' and for 48% of 'asthma control' reviews where no action was taken. For the latter, GPs reported that patients had recently received an annual Quality and Outcomes framework (QOF) review, usually from a nurse, and they therefore assumed them to be on optimised asthma treatment. GPs generally

1 felt that changes in prescribing for asthma usually required face-to-face review but patients often did not
2 respond to invitations for review.

3 **Perceived value of each prescribing topic as a target for the DQIP intervention**

4 GPs perceived the pilot intervention raised awareness of targeted high-risk prescribing, improved prescribing
5 practices and the recording of decision-making rationales, but they did not value each topic equally.

6
7
8
9 *"...improving prescribing practice, improving our record keeping, improving our knowledge base and if
10 people are on unsafe meds getting them off them and if there are on them carefully considering why and
11 it is not accidental."* (GP interview 1)

12
13 All GPs interviewed highly valued the process of reviewing patients identified as receiving *high-risk NSAID or
14 antiplatelet* prescriptions.

15
16
17 *"The topic is, I would go so far as to say, essential. I don't even think you can say it's urgent. It's essential
18 that practices are doing this. They could be killing patients totally unnecessarily and it's not as if it's
19 difficult, because in a lot of circumstances, the vast majority of them are non-steroidals in elderly people."*
20 (Interview 7)

21
22 The GP's interviewed perceived that NSAIDs are sometimes initiated with the intention the prescription was
23 a one-off or without full consideration of all risk factors.

24
25
26 *"..I've always thought I've been quite cautious with NSAIDs but then again possibly some of these
27 patients were mine. You know they have been started on NSAID despite them being on ACE inhibitor and
28 a diuretic and you think oh god, that's incredibly embarrassing."* (GP interview 6).

29
30 Where risk factors were missed or NSAIDs were prescribed for longer than intended, GPs valued a prompt to
31 review. In the interviews GPs reported changes to the NSAID and antiplatelet prescribing were the least
32 complex decision-making of the topics, although all but one GP (who felt NSAIDs had 'no place' in pain
33 control and patients should have no choice in whether to use these drugs) highlighted that it is sometimes
34 complicated by patient choice.

35
36
37 *"You know it is a compromise - patients like them [NSAIDs] because they're effective, whatever anybody
38 says without a shadow of doubt people with osteoarthritis find them very effective drugs and often find
39 them far more effective ... for pain relief and symptom relief in total ... than any other medication we've
40 got to give them."* (GP Interview 9).

41
42
43 Although the '*antithrombotics in AF*' measures led to limited changes in prescribing (3 changes from 201
44 reviews) two practices perceived the work to be worthwhile and for one it was their most valued prescribing
45 topic, because two patients and the practice were relieved from the burden of unnecessary warfarin
46 therapy. Two practices felt AF decision-making was often in the hands of consultants, and all GPs reported
47 seeking advice from secondary care regarding the need to initiate or continue warfarin in specific patients.
48 Although GPs reported the notes review work for AF was the most complex, they found validating warfarin
49 prescribing a reassuring process.

50
51
52
53 *"...the non-steroidal one was great. The atrial fibrillation one was great for a different matter, because
54 [although] you identified quite a lot of patients, at the end of the day, when we looked through
55 them,[we] only identified one that we wanted to chase up"* (GP interview 7).

56
57 The '*asthma control*' topic was perceived as the least important by all GPs, mainly because of overlap with
58 measures in QOF,²¹ and because they shared responsibility with practice nurses and were content to leave
59 the decision-making to them.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

"I think sometimes we could use the nurses to do some of it...in the future when we do that we would ask our nurse that does the asthma clinic to do that because that would, you know she's the one that's doing the prescribing so that would've been better for her to take control of that." (GP interview 9)

Optimising the intervention

Practice experiences identified some barriers which facilitated optimising the intervention beyond suggestions in the current literature on changing prescribing.

Facilitating engagement

GPs felt prescribing safety was important but that improvement was always in the context of busy workloads. A financial incentive to review was perceived as important to facilitate engagement and to entice practices to participate in the trial. GPs were asked about how any financial incentive should be structured, and different balances between up-front payments and payment-per-review were discussed. Of the options offered, all GPs and practice managers interviewed were in agreement that £350 (€411, \$538) upfront and £15 (€18, \$23) per review best struck the balance between gaining attention and incentivising payment-per-review.

"I think £350 up front and £15 per review. The reason for this is that the work is very much about the review and if you pay up-front too much, there is a danger the reviews won't get done as the incentive is small. In fact up-front payment could be less, with more per review, provided you have a mechanism for checking the review has been done properly." (GP Interview 7)

Maintaining engagement

Two practices struggled to embed the work within practice routines and expressed the concern that DQIP work could be sidelined by competing work pressures. In addition to the pay-per-review financial incentive, it was therefore decided that practices should receive regular updates on their progress (or lack of progress) via DQIP newsletters. It was anticipated that to maintain engagement, unnecessary reviews had to be minimised. This led to a change in how patients were identified so that patients whose high-risk prescribing had been reviewed and deemed appropriate would not be reflagged for review for the same type of high-risk prescribing in the next year.

Sustaining improved prescribing

All GPs interviewed valued the data but felt high-risk NSAID prescribing required regular review. GPs perceived this was the prescribing topic where prescribing was likely to be restarted because of continuing patient demand for analgesia and restarting by other doctors.

"I think, it will always be very difficult, you will always get colleagues that will go back to prescribing it again and what was interesting was when you were re-running the searches, what was actually happening with that. Looking at what we were doing, because sometimes Dr X would say, 'Crikey look at that!'" (Practice manager interview 2).

It was decided the DQIP informatics tool would need to reflag patients for review where high-risk prescribing was *restarted* after a decision to stop and run charts should be provided to allow practices to monitor high-risk prescribing trends over time.

Discussion

Summary of main findings

All topics examined in this study had previously been identified as priorities for improvement in primary care.

⁵ GP review of the targeted prescribing revealed that measures for each topic varied in their ability to

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1 identify changeable high-risk prescribing and in their perceived importance. The NSAID and antiplatelet
2 measures performed best in identifying potentially changeable high-risk prescribing (68% of patients
3 required action versus 25% for the 'asthma control' and 18% of 'antithrombotics in AF') and were the most
4 valued. Although the 'antithrombotics in AF' topic generated considerable work for little change, it was
5 highly valued by two practices because it identified a small number of patients who could stop warfarin,
6 which mattered given the treatment and monitoring burden this drug imposes on patients and practices. The
7 asthma topic was the least valued due to overlaps with QOF reviews and technical problems in accurately
8 identifying patients with poor asthma control from EMRs. These findings demonstrate the importance of
9 testing potential outcome measures prior to trialling complex interventions in order to ensure they are
10 changeable by the intervention to be evaluated.²²⁻²⁴ Although practices said improving prescribing safety
11 was important, a number of barriers to engagement, maintenance of effort and sustaining improved
12 prescribing were identified which informed the intervention design^{23 25} and ensured sensitivity to practices'
13 needs.²⁴ These barriers were addressed through financial incentives per patient reviewed, and the
14 informatics component would provide continuous measurement and feedback, supplemented by monthly
15 update newsletters.
16
17
18
19

20 *Strengths and limitations*

21 A strength of this study was the use of quantitative and qualitative methods to give a broader understanding
22 of how changeable this high risk prescribing was, what the barriers to changing prescribing were and how
23 GPs valued this work, which enabled informed choice of outcome measures and optimisation of the
24 intervention.^{23 25 26} Additionally, the findings supported the design of the trial process evaluation^{27 28} in
25 addition to the main trial design. The main limitation of this study is that changeability of potential outcome
26 measures was tested by measuring GPs intention to change prescribing or conduct further investigation
27 ('action'), rather than quantifying actual changes in prescribing and their clinical implications. However, this
28 did allow the identification of plausible high-risk prescribing to use as an outcome measure in the trial which
29 will evaluate the ability of the intervention to actually change prescribing will be evaluated in the main trial.
30 A second limitation of this study was the small number of volunteering general practices and reviewing
31 clinicians included, although we sampled for heterogeneity in terms of practice characteristics to minimise
32 the impact of this.
33
34
35
36

37 *Comparison with existing literature*

38 Although there are many examples of studies developing prescribing measures and establishing their face
39 and content validity,^{5 29-32} few have reported the extent to which such measures can identify actual
40 opportunities for improvement.^{33 34} A Dutch study found that patients identified by a measure targeting
41 underuse of inhaled corticosteroids in asthma (using prescriptions of short-acting beta agonists as a proxy for
42 uncontrolled asthma), 46% were candidates for inhaled steroids after a face-to-face review by a clinician,
43 compared to only 25% at most (assuming all 'further investigations' would confirm the need for inhaled
44 steroids) in this study. The much lower proportion found here suggests that estimates of changeability are
45 likely to be context specific (e.g. depending on the accuracy of data sources used) and may also depend on
46 the gold standard against which the performance of prescribing measures is compared. When selecting
47 outcome measures for a trial, findings from previous studies conducted in different health care settings may
48 therefore be of limited value.
49
50
51
52

53 Some of the prescribing measures evaluated here targeted prescribing patterns similar to those used as
54 primary outcome measures in the PINCER trial.¹¹ At six months follow-up, the PINCER trial found a significant
55 reduction in both beta-blocker prescribing in asthma and NSAID prescribing (without use of gastro-
56 protection in patients with a history of peptic ulcer) at 6 months (although sensitivity analyses have not
57 confirmed this finding³⁵). However, part of the improvement in high-risk NSAID prescribing was lost by 12
58 months follow-up, which is consistent with concerns expressed by GPs' in this study that NSAIDs may be
59 restarted due to patient demand or lack of communication between GPs. The DQIP trial and parallel process
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

evaluations will establish to which extent the strategies used in the DQIP intervention to avoid such relapse (continuous feedback, paying per review and regular letters highlighting progress) are successful.

Our finding that changing prescribing of antithrombotics in AF is difficult to change is consistent with large surveys conducted over the last 10 to 15 years demonstrating little improvement in the uptake of anticoagulants in AF patients at high-risk of stroke.³⁶⁻³⁸ Similar to our study, a systematic review exploring barriers to prescribing anticoagulants for AF found that the main reasons not to prescribe anticoagulants were advanced patient age and perceived risk of bleeding events.³⁹ A lower uptake of anticoagulants in paroxysmal AF has also previously been reported, consistent with GPs reporting paroxysmal AF as a reason not to prescribe AF in this study, although stroke risk is as high as in chronic AF.³⁶ This does not mean that such prescribing could not be improved per se, but may indicate that in addition to prompting review, such improvements may require more attention to persuading GPs of the benefits and risks of antithrombotic use in people with AF.

Conclusion

The study had direct relevance to choice of outcome measures and intervention design, but highlights the 'right' intervention to improve primary care prescribing safety is likely to vary by targeted prescribing. Although several RAND studies have identified large sets of 'valid' indicators of prescribing safety, their value and feasibility for change has not been assessed, in terms of the extent to which they identify patients with actual inappropriate prescribing^{32 40}. This study shows their perceived value and feasibility are likely to vary by prescribing topic,^{33 41} and any research or NHS use of prescribing indicators for improvement therefore requires piloting and evaluation. Some prescribing topics, such as NSAIDs will be suitable for low intensity interventions based on repeated feedback using existing electronic data, simple education and possibly small financial incentives but other prescribing topics, such as 'asthma control' and 'antithrombotics in AF' are likely to require prior work to clean electronic data and refine measures, or more intensive educational work to persuade practices what is being measured is important, or more intensive facilitation of change. Safer prescribing is an important aim for policy and commissioners, but there is unlikely to be a one size fits all intervention to deliver it.

1
2 **Authors contributions:** BG was responsible for the initial conceptualisation and design. TD and AG reviewed
3 the literature, carried out the data collection, analysis and interpretation of the data and contributed to the
4 design of the study. AG prepared the first manuscript and is responsible for this article. All authors iteratively
5 commented on successive drafts of the manuscript. All authors read and approved the final manuscript.
6
7

8 **Funding statement:** AG and TD are funded by the Scottish Government Health Directorates Chief Scientist
9 Office Applied Programme Research Grant 07/02 for the Data Driven Quality Improvement in Primary Care
10 programme. This funding body have had no direct role in the design and conduct of, or decision to publish
11 this work.
12

13
14 **Competing Interests:** The authors declare no competing interests
15
16

17
18 **Data Sharing Statement:** No further information available
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Gandhi TK, Weingarten SN, Borus J, Seger AC, Peterson J, Burdick E, et al. Adverse drug events in ambulatory care. *New England Journal of Medicine* 2003;348:1556 - 64.
2. Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, et al. Incidence and preventability of adverse events among older persons in the ambulatory setting. *Journal of American Medical Association* 2003;289:1107-16.
3. Pirmohamed MJ, Meakin S, Green C, Scott AK, Walley T, Farrar K, et al. Adverse drug reactions as a cause of admission to hospital: prospective analysis of 18 820 patients. *British Medical Journal* 2004;329:15-19.
4. Howard RL, Avery AJ, Slavenburg S, Royal S, Pipe G, Lucassen P, et al. Which drugs cause preventable admissions to hospital? A systematic review. *British Journal of Clinical Pharmacology* 2007;63(2):136-47.
5. Dreischulte T, Grant A, McCowan C, McAnaw J, Guthrie B. Quality and safety of medication use in primary care: Consensus validation of a new set of explicit medication assessment criteria and prioritisation of topics for improvement. *BMC Clinical Pharmacology* 2012;12(1):5.
6. Guthrie B, McCowan C, Davey P, Simpson CR, Dreischulte T, Barnett K. High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice. *British Medical Journal* 2011;342.
7. Howard RL, Avery AJ, Howard PD, Partridge M. Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study. *Qual Saf Health Care* 2003;12:280 - 85.
8. Thomsen LA, Winterstein AG, Sondergaard B, Haugbolle LS, Melander A. Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care. *The Annals of Pharmacotherapy* 2007;41:1411-26.
9. Department of Health. An organisation with a memory: report of an expert group on learning from adverse events in the NHS, 2000.
10. Smith J. Building a safer NHS for patients: improving medication safety. London: Department of Health, 2004.
11. Avery AJ, Rodgers S, Cantrill JA, Armstrong S, Cresswell K, Eden M, et al. A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis. *The Lancet* 2012.
12. Dreischulte T, Grant A, Donnan P, McCowan C, Davey P, Petrie D, et al. A cluster randomised stepped wedge trial to evaluate the effectiveness of a multifaceted information technology-based intervention in reducing high-risk prescribing of non-steroidal anti-inflammatory drugs and antiplatelets in primary care: the DQIP study protocol. *Implementation Science* 2012;7:24.
13. Medical Research Council. A framework for the development and evaluation of RCTs for complex interventions to improve health. London: Medical Research Council, 2000.
14. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. *British Medical Journal* 2000 321 694-6.
15. O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, et al. Educational outreach visits: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2009;4.
16. Farmer AP, Legare F, Turcot L, Grimshaw J, Harvey E, McGowan J, et al. Printed Educational Materials: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2008(3):CD004398.
17. Jamtvedt G, Young JM, Kristoffersen DT, O'Brien MA, Oxman AD. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2009;4.

18. Gage BF, Waterman AD, Shannon W, Boehler M, Rich MW, Radford MJ. Validation of a clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *Journal of American Medical Association* 2001;285:2864-70.
19. Ritchie J, Spencer L, O'Connor W. Carrying out Qualitative Analysis. In: Ritchie J, Lewis J, editors. *Qualitative Research Practice, A guide for Social Science Students and Researchers*. London: Sage Publications Ltd, 2003.
20. Camm AJ KP, Lip GYH, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation. *Europace* 2010;12(10):1360-420.
21. Department of Health. Investing in General Practice - the New General Medical Services Contract, 2003.
22. Campbell S, Chauhan U, Lester H. Primary Medical Care Provider Accreditation (PMCPA): pilot evaluation. *Br J Gen Pract* 2010 e295-301.
23. Bradley F, Wiles R, Kinmonth A-L, Mant D, Gantley M. Development and evaluation of complex interventions in health services research: case study of the Southampton heart integrated care project (SHIP). *British Medical Journal* 1999;318(7185):711-15.
24. Van Hecke A, Verhaeghe S, Grypdonck M, Beele H, Flour M, Defloor T. Systematic development and validation of a nursing intervention: the case of lifestyle adherence promotion in patients with leg ulcers. *Journal of Advanced Nursing* 2011;67(3):662-76.
25. Corrigan M, Cupples ME, Smith SM, Byrne M, Leathem CS, Clerkin P, et al. The contribution of qualitative research in designing a complex intervention for secondary prevention of coronary heart disease in two different healthcare systems. *BMC Health Services Research* 2006;6:90.
26. Cresswell K, Sadler S, Rodgers S, Avery A, Cantrill J, Murray S, et al. An embedded longitudinal multi-faceted qualitative evaluation of a complex cluster randomized controlled trial aiming to reduce clinically important errors in medicines management in general practice. *Trials* 2012;13(1):78.
27. Grant A, Dreischulte T, Treweek S, Guthrie B. Study protocol of a mixed-methods evaluation of a cluster randomised trial to improve the safety of NSAID and antiplatelet prescribing: data-driven quality improvement in primary care. *Trials* 2012;13:154.
28. Grant A, Treweek S, Dreischulte T, Foy R, Guthrie B. Process evaluations for cluster-randomised trials of complex interventions: a proposed framework for design and reporting. *Trials* 2013;14(1):15.
29. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *International Journal of Clinical Pharmacology & Therapeutics* 2008;46(2):72-83.
30. Naugler CT, Brymer C, Stolee P, Arcese ZA. Development and validation of an improving prescribing in the elderly tool. . *Canadian Journal of Clinical Pharmacology* 2000;7(2):103-7.
31. Fick DM, Copper JW, Wade WE, Waller JL, Maclean R, Beers MH. Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, resulting of a US consensus panel of experts. *Archives of Internal Medicine* 2003;163:2716-24.
32. Avery A, Dex G, Mulvaney C, Serumaga B, Spencer R, Lester H, et al. Development of prescribing-safety indicators for GPs using the RAND Appropriateness Method. *Br J Gen Pract* 2011;61(589):e526-e36.
33. Pont LG, Denig P, van der Molen T. Validity of performance indicators for assessing prescribing quality: the case of asthma. *European Journal of Clinical Pharmacology* 2004;59:833-40.
34. Dreischulte T, Johnson J, McAnaw J, Geurts M, de Gier H, Hudson S. Medication assessment tool to detect care issues from routine data: a pilot study in primary care. *International Journal of Clinical Pharmacy* 2013.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
35. Hemming K, Chilton PJ, Lilford RJ, Avery A, Sheikh A. Bayesian cohort and cross-sectional analyses of the PINCER trial: a pharmacist-led intervention to reduce medication errors in primary care. *PLoS ONE [Electronic Resource]* 2012;7(6):e38306.
 36. Nieuwlaat R, Capucci A, Lip GY, Olsson SB, Prins MH, Nieman FH, et al. Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation. *European Heart Journal* 2006;27(24):3018-26.
 37. Holt TA, Hunter TD, Gunnarsson C, Khan N, Cload P, Lip GYH. Risk of stroke and oral anticoagulant use in atrial fibrillation: a cross-sectional survey. *British Journal of General Practice* 2012;DOI: 10.3399/bjgp12X656856.
 38. Ogilvie IM, Newton N, Welner S. Underuse of oral anticoagulants in atrial fibrillation: a systematic review. *American Journal of Medicine* 2010(123):638-45.
 39. Pugh D, Pugh J, Mead GE. Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review. *Age and ageing* 2011;40:675-83.
 40. Campbell SM, Cantrill JA, Roberts D. Prescribing indicators for UK general practice: Delphi consultation study. *British Medical Journal* 2000;321(7258):425-28.
 41. Campbell S, Hann M, Hacker J, Roland M. Quality assessment for three common conditions in primary care: validity and reliability of review criteria developed by expert panels for angina, asthma and type 2 diabetes. *Quality and Safety in Health Care* 2002;11:125 - 30.

Table 1: Review decisions made by topic. The data reported on topics 1 (NSAID and antiplatelet) and 2 (asthma) measures is from all four practices and the topic 3 (atrial fibrillation) data is from three of the pilot practices.

Topic /Individual measures implemented (No. of reviews)	No. of times the following decisions were made at point of review:		
	Change medication	Further investigation	No action
1. NSAIDs and antiplatelets (n=290)	101 (35%)	97 (33%)	92 (32%)
1.1 High risk use in patients with GI risk factors (n=120) ^{A,B}	54 (45%)	21 (18%)	45 (38%)
1.2 High risk use of NSAIDs in patients with renal risk factors (n=161) ^C	44 (27%)	72 (45%)	45 (28%)
1.3 High risk use of NSAIDs in heart failure (n= 9)	3 (33%)	4 (44%)	2 (22%)
2. Asthma (n=148)	10 (7%)	26 (18%)	112 (76%)
2.1 Underuse of inhaled corticosteroids (n=130) ^D	7 (5%)	23 (18%)	100 (77%)
2.2 High-risk use of beta blockers (n=18) ^E	3 (17%)	3 (17%)	12 (67%)
3. Atrial fibrillation (n=201)	3 (1%)	34 (17%)	164 (82%)
3.1 Underuse/ low intensity of thromboembolic prophylaxis (n=178)	1 (1%)	34 (19%)	143 (80%)
3.2 High-risk use of oral anticoagulants (n=23)	2 (9%)	0 (0%)	21 (91%)

A – NSAID prescription (in previous 12 weeks) without GI protection to people with at least one of the following risk factors:

(i) history of peptic ulcer, (ii) aged ≥ 75 , (iii) aged ≥ 65 and on aspirin, (iv) aged ≥ 65 and on warfarin

B – Aspirin prescription (in previous 12 weeks) without GI protection to people with at least one of the following risk factors:

(i) history of peptic ulcer, (ii) aged ≥ 65 and on clopidogrel, (iii) aged ≥ 65 and on warfarin

C – NSAID prescription to people with at least one of the following risk factors:

(i) CKD stage 3 to 5, (ii) on ACEI/ARB, (iii) on diuretic, (iv) on combination of ACEI/ARB and diuretic

D - No prescription of inhaled corticosteroid (in previous 12 weeks) in patient with asthma and at least one of the following risk factors: (i) prescription for 3 or more SABA inhalers in previous 12 weeks, (ii) prescription of LABAs, leukotriene receptor antagonist, theophylline or oral prednisolone in previous 12 weeks

E – Prescription of any beta blocker if ‘active asthma’ (prescription of a SABA inhaler in previous 48 weeks) or prescription of a non-cardio-selective beta blocker if ‘previous asthma’ (no prescription of a SABA inhaler in the previous 48 weeks).

Table 2: Reasons stated by clinicians as to why 'no action' was required for patients identified with drug therapy risk(s) by the DQIP measures

Topic (No. of reviews)	No. of reviews where stated reason for 'no action' was ^A :		
	'Technical' (count, %) <i>Specific reasons(count)</i>	'Clinical' <i>Specific reasons(count)</i>	'Other' <i>Specific reasons(count)</i>
1. NSAIDs and antiplatelets (n=92)	30 (33%)	62 (67%)	0
1.1 High risk use in patients with GI risk factors (n=45)	10 (22%) <i>Patient no longer on practice register (5); time window of assessment (3^C); Disease coding error (2)</i>	35 (78%) <i>Short term use (21); Risk adequately mitigated by low dose misoprostol (5); High-risk drug 'well tolerated' (9); No effective alternative (5)</i>	0
1.2 High risk use of NSAIDs in patients with renal risk factors (n=45)	20 (44%) <i>Time window of assessment (15^C); Patient no longer on practice register (5)</i>	20 (44%) <i>Short term use (19); No effective alternative (1);</i>	5 (11%) <i>Unspecified (5^B)</i>
1.3 High risk use of NSAIDs in heart failure (n=2)	0	2 (100%) <i>Short term use (2)</i>	0
2. Asthma (n=112)	53 (47%)	5 (4%)	54 (48%)
2.1 Underuse of inhaled corticosteroids (n=100)	46 (46%) <i>Time window of assessment (21^C); proxies for moderate/severe asthma failed (13^D); disease coding error (10); patient no longer on practice register (2)</i>	0	54 (54%) <i>Needs review but does not attend clinic (29); recently reviewed for QOF (22); patient choice (3)</i>
2.2 High-risk use of beta blockers (n=12)	7 (58%) <i>Disease coding error (7)</i>	5 (42%) <i>Beta blocker 'well tolerated' (5)</i>	0
3. Atrial fibrillation (n=166)	80 (48%)	59 (36%)	27 (16%)
3.1 Underuse/ low intensity of thromboembolic prophylaxis (n=143)	78 (55%) <i>Disease coding error (31); Time window of assessment (29^C); patient no longer on practice register (18);</i>	42 (29%) <i>Not 'fit' for warfarin (30); Paroxysmal AF (7); Satisfactory rate control (5)</i>	23 (16%) <i>Patient choice (16); secondary care decision (3); unspecified (4);</i>
3.2 High risk use of oral anticoagulants (n=21)	2 (10%) <i>Disease coding error (2)</i>	17 (81%) <i>CHADS₂ score judged to underestimate risk (17)</i>	2 (10%) <i>Secondary care decision (2);</i>

A - The number of specific reasons may exceed the number of reviews when more than one reason was provided per review.

B - The reasons provided referred to co-existing gastrointestinal risk factors

C - Refers to situations where a drug that was identified by the searches as 'high-risk' was stopped or a drug identified as 'beneficial' was prescribed between the search date and the review date

D - The proxies for moderate to severe asthma (> 3 prescriptions of short-acting beta agonists issued over last 12 weeks; prescription of step 3 drugs) failed in these cases, because patients had mild asthma but were stock-piling inhalers (eg getting them to have available in multiple locations) or using step 3 drugs for indications other than asthma.



Developing a complex intervention to improve prescribing safety in primary care: mixed methods feasibility and optimisation pilot study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-004153.R1
Article Type:	Research
Date Submitted by the Author:	29-Nov-2013
Complete List of Authors:	Grant, Aileen; University of Dundee, Population Health Sciences Guthrie, Bruce; University of Dundee, Population Health Sciences Dreischulte, Tobias; University of Dundee, Population Health Sciences
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Pharmacology and therapeutics, Health services research, Health informatics, Medical management
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, CLINICAL PHARMACOLOGY, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adverse events < THERAPEUTICS

SCHOLARONE™
Manuscripts

Developing a complex intervention to improve prescribing safety in primary care: mixed methods feasibility and optimisation pilot study

Authors

Aileen M Grant (a.m.grant@dundee.ac.uk)*

Quality, Safety and Informatics Group, Population Health Sciences, Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383733

Bruce Guthrie (b.guthrie@dundee.ac.uk)

Quality, Safety and Informatics Group, Population Health Sciences, Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383740

Tobias Dreischulte (t.dreischulte@dundee.ac.uk)

Medicines Management Unit, NHS Tayside c/o, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383769

*Corresponding author

Abstract:**Objectives**

1. To measure the extent to which different candidate outcome measures identified high-risk prescribing that is potentially changeable by the DQIP intervention
2. To explore the value of reviewing identified high-risk prescribing to clinicians
3. To optimise the components of the DQIP intervention

Design: Mixed method study

Setting: General practices in two Scottish Health boards

Participants: Four purposively sampled general practices of varying size and socioeconomic deprivation.

Outcome measures: Prescribing measures targeting (1) High-risk use of NSAIDs and antiplatelets; (2) 'Asthma control'; and (3) 'Antithrombotics in AF'

Intervention: The prescribing measures above were used to identify patients for review by general practices. The ability of the measures to identify potentially changeable high-risk prescribing was measured as the proportion of patients reviewed where practices identified a need for action. Field notes were recorded from meetings between researchers and staff and key staff participated in semi-structured interviews exploring their experience of the piloted intervention processes.

Results: Practices identified a need for action in 68%, 25%, 18% of patients reviewed for prescribing measures (1), (2) and (3), respectively. GPs valued being prompted to review patients, and perceived that (1)'NSAID and antiplatelet' and (2) 'antithrombotics in AF' were the most important to act on. Barriers to initial and on-going engagement and to sustaining improvements in prescribing were identified.

Conclusion:

'NSAIDs and antiplatelets' measures were selected as the most suitable outcome measures for the DQIP trial, based on evidence of this prescribing being more easily changeable. In response to the barriers identified the intervention was designed to include a financial incentive, additional on-going feedback on progress, and re-prompting review of patients, whose high-risk prescribing was restarted after a decision to stop.

Trial registration number: Clinicaltrials.gov NCT01425502

Article summary:

Article focus: This study aimed to evaluate the extent to which different candidate outcome measures identified high-risk prescribing that is potentially changeable, explore the perceived value of these measures to clinicians, and to optimise intervention components for evaluation in a cluster-randomised trial.

Key Messages:

- Prescribing measures prioritised for improvement were validated for use in a complex prescribing quality improvement intervention.

- The ability of these measures to identify potentially changeable high-risk prescribing and the perceived value of the measures varied.
- In response to the barriers and facilitators identified, the intervention to be tested in a trial was designed to include a financial incentive to facilitate initial engagement, to provide additional on-going feedback on overall progress, and to highlight patients whose high-risk prescribing was restarted after a decision to stop.

Strengths and limitations:

- The strength of this study was the use of quantitative and qualitative methods to give a greater understanding of how changeable the identified high-risk prescribing was, what the barriers to changing prescribing were and how GPs valued this work, which enabled informed choice of outcome measures and optimisation of the intervention.
- The limitation of this study is that changeability of potential outcome measures was tested by measuring GPs intention to change prescribing or conduct further investigation ('action'), rather than quantifying actual changes in prescribing and their clinical implications (although this is being evaluated in an on-going cluster-randomised controlled trial).

Background

The safety of medication use in primary care is a major concern for health care systems internationally.[1-4] An estimated 3-4% of unplanned hospital admissions are due to preventable adverse drug events and approximately one third of these have been attributed to prescribing of drugs to people with risk factors for adverse drug effects and under-prescribing of prophylactic treatments (high-risk prescribing).[4]

In the UK, medications may be initiated in primary and secondary care, but general practitioners (GPs) prescribe almost all drugs in the community and have responsibility for reviewing all medications. Previous research has shown that high-risk prescribing in primary care is common and its prevalence varies substantially between practices (after adjusting for case-mix), which indicates scope for improvement.[5-8] Given the current UK policy focus on improving patient safety, there is a need to develop and test interventions to reduce high-risk prescribing.[9, 10]

In the UK, the virtually ubiquitous use of electronic medical records (EMRs) in primary care offers opportunities to support quality and safety improvement initiatives. For example, the PINCER (Pharmacist-led Information Technology Intervention for Medication Errors) trial has demonstrated the effectiveness of an intervention, where pharmacists identified patients with high-risk prescribing using data extracted from EMRs, reviewed their records, and recommended changes.[11] Similarly, the 'Data-driven quality improvement in primary care' (DQIP) research programme aims to identify patients with high-risk prescribing from EMRs, but in contrast to PINCER, practices are provided with continuous feedback using a web-based informatics tool, and financial incentives to motivate practice staff to review patients identified.[12]

The Medical Research Council (MRC) Framework recommends that complex interventions be modelled before evaluation in a randomised controlled trial in order to optimise both the intervention design and its evaluation by defining outcomes and ensuring feasibility.[13] [14] In terms of intervention design, the broad shape of the DQIP intervention was defined by the intention that there should be evidence for the effectiveness of its components, that it should be built on existing NHS information technology and be implementable as an 'enhanced service' (a UK National Health Service mechanism for commissioning general practice care). The intention was therefore to combine an educational intervention[15, 16], audit and feedback[17], and a financial incentive to review. As a result a priority was to pilot and optimise these elements in a small number of practices. For evaluating the impact of the intervention, a set of potential prescribing outcome measures had previously been validated using consensus methods[5] but an outstanding question was which of these measures could plausibly be improved by this intervention and therefore used as trial outcome measures.

The specific objectives of this study were to optimise the DQIP intervention and trial evaluation by: (1) identifying which potential outcome measures best identified patients with high-risk prescribing that could potentially be changed; (2) establishing which measures were most valued by practices in terms of improving quality and safety; (3) exploring how best to design and deliver the educational, informatics and financial components of the DQIP intervention to maximise practice engagement.

Methods

The study used mixed qualitative and quantitative methods, and study was approved by NHS Tayside Committee on Medical Research Ethics A (09/S1401/54).

Settings

We purposively sampled and recruited four general practices, two from each NHS Scotland Health Board where the intervention was to be trialled, aiming to include larger and smaller practices serving populations that varied in socioeconomic deprivation.

Data collection

Data collection was between March 2010 and August 2011.

Quantitative data

In each practice, thematically related prescribing measures ('prescribing topics') that had been identified as priorities for quality and safety improvement[5] were implemented in EMRs to identify patients with potentially suboptimal prescribing for review. These prescribing topics were: (1) High-risk use of NSAIDs and antiplatelets in patients with gastro-intestinal, renal or cardiac risk factors ('NSAIDs and antiplatelets'); (2) Under-use of inhaled corticosteroids and high-risk use of beta-blockers in asthma ('asthma control'); and (3) Over-and under-use of anti-thrombotic drugs in atrial fibrillation ('antithrombotics in AF').

Practices received a feedback report for each topic, which summarised the total numbers of patients identified by each measure of high-risk prescribing, listed the patients affected, and provided supporting educational material (rationale, current evidence and prescribing guidance).[18] Practices were asked to conduct a record review of all identified patients with face-to-face review if necessary, and to document all decision-making on a structured template (tick boxes for a decision to 'change prescribing', conduct 'further investigation' or 'no action' and free text space to specify the rationale for 'no action'). Our expectation was that clinicians would judge some high-risk prescribing to be appropriate but would identify other patients in whom the prescribing should be stopped. An important aim of the pilot was to estimate how appropriateness and stopping varied across topics, to allow the trial to target prescribing that was more likely to be inappropriate and changeable.

Qualitative data

An initial meeting to explain the study and describe the topics was held in each practice. Practices then worked on one topic at a time, with further meetings held six to eight weeks after practices had received and acted on the feedback report. The meetings were facilitated by the pharmacist (TD), and observed by AG who took ethnographic field notes of 18 hours of meetings. The whole practice was invited but the meetings were generally attended by the GP(s) most involved and the practice manager and lasted between 30 and 60 minutes. At these meetings, practices were asked to describe the practice processes to conduct the review work, to report on the complexities of reviewing or changing prescribing, and to expand on reasons for 'no action'.

The GPs most involved in the review work and practice managers were invited for individual semi-structured interviews in order to explore their perceptions of the value of each prescribing topic and the specific components of the intervention (education, informatics and financial), their experiences of adopting and implementing the intervention in routine practice and to changing prescribing. Eleven interviews were conducted with 8 GPs (one GP was interviewed twice) and 2 practice managers. These interviews were held in the practices, lasted approximately one hour, were audio-recorded and transcribed verbatim.

Data Analysis

Quantitative analysis (research question (RQ) 1: performance of prescribing measures)

The ability of each measure to identify potentially changeable high-risk prescribing was measured as the proportion of patients reviewed whose prescribing was judged to require action ('change prescribing' or 'further investigation'). Reasons why the measures failed to identify potentially changeable high-risk prescribing in patients were classified into three categories: 'clinical' (prescribing changes were deemed

1 inappropriate or unnecessary given the clinical circumstances), 'technical' (the measure misidentified
2 patients when implemented in live clinical data) and 'other'.

3
4 *Qualitative analysis (RQ2 perceived value of each prescribing topic and RQ3 optimising intervention*
5 *components)*

6
7 Interview transcripts and fieldnotes were merged and analysed by emerging themes to identify a coding
8 frame. Data was imported into Nvivo-8 and the coding frame was systematically applied. Subsequent
9 analysis was by the Framework technique.[19] Thematic charting facilitated comparing the data by theme,
10 practice and prescribing topic. The data was explored for negative cases.

11 **Results**

12
13 Practice list-sizes ranged from 3,200 to over 10,000, with the percentage of patients living in the most
14 deprived quintile of postcodes ranging from 4% to 46%. All four practices completed the 'NSAID and
15 antiplatelet' and 'asthma control' topics, but only three completed the 'antithrombotics in AF' topic.

16 **Ability of measures to identify patients with potentially changeable high-risk prescribing**

17
18 Table 1 shows that for the 'NSAID and antiplatelet' topic, practices recorded a need for action in 68% of
19 patients reviewed (change prescribing 35%; further investigation 33%) compared to only 25% of patients
20 reviewed for the 'asthma control' topic (change prescribing 7%; further investigation 18%) and 18% of those
21 reviewed for 'antithrombotics in AF' (change prescribing 1%; further investigation 17%).

22
23 *Insert table 1 and 2 about here*

24
25 Table 2 shows the rationales for no action reported by GPs on templates for each patient reviewed. *Clinical*
26 *reasons* were most commonly reported for the 'NSAIDs and antiplatelets' topic (67%), but less so for the
27 'antithrombotics in AF' (36%) and much less for the 'asthma control' (4%) topic. The reasons provided
28 reflected that high-risk prescribing was a trade-off between effectiveness and safety. For 'NSAIDs and
29 antiplatelets', the main reported reason for not changing prescribing was that NSAID use was only 'short
30 term'. For 'antithrombotics in AF', clinical reasons reported were mainly 'unfitness for warfarin' (examples
31 reported in interview included fragility and dementia, heavy alcohol use and previous gastrointestinal
32 bleeding), but also included 'paroxysmal AF' (reflecting a misconception that stroke risk is lower than for
33 patients with chronic AF). [20]

34
35 '*Technical reasons*' accounted for one third of rationales for no action for the 'NSAID and antiplatelet' topic,
36 and for 47% 'asthma control' and 48% of the 'antithrombotics in AF' topics. For all three topics, technical
37 reasons related to patients no longer being on practice registers and to situations where identified high-risk
38 prescribing was no longer present at the point of review ('time window of assessment'). For example, for the
39 'antithrombotics in AF' topic, all practices highlighted in interviews that anticoagulant prescribing intervals
40 often exceeded the 12 week timeframe used by the measures, causing patients to be incorrectly identified as
41 lacking antithrombotic prophylaxis.

42
43 Inaccurate disease registers were reported as reasons why 'antithrombotics in AF' and 'asthma control'
44 measures misidentified prescribing as high-risk. One practice reported in interview that many patients on
45 their asthma disease register had chronic obstructive pulmonary disease (COPD) and therefore did not have
46 a clear indication for treatment with inhaled corticosteroids. The deprived practices reported that high
47 numbers of short-acting beta-agonist prescriptions did not necessarily identify patients with uncontrolled
48 asthma, because patients stockpiled inhalers in multiple locations (e.g. home, school, or work).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

'Other' reasons were not commonly identified for 'NSAIDs and antiplatelets', but accounted for 16% of 'antithrombotics in AF' and for 48% of 'asthma control' reviews where no action was taken. For the latter, GPs reported that patients had recently received an annual Quality and Outcomes framework (QOF) review, usually from a nurse, and they therefore assumed them to be on optimised asthma treatment. GPs generally felt that changes in prescribing for asthma usually required face-to-face review but patients often did not respond to invitations for review.

Perceived value of each prescribing topic as a target for the DQIP intervention

GPs perceived the pilot intervention raised awareness of targeted high-risk prescribing, improved prescribing practices and the recording of decision-making rationales, but they did not value each topic equally.

"...improving prescribing practice, improving our record keeping, improving our knowledge base and if people are on unsafe meds getting them off them and if there are on them carefully considering why and it is not accidental." (GP interview 1)

All GPs interviewed highly valued the process of reviewing patients identified as receiving *high-risk NSAID or antiplatelet* prescriptions.

"The topic is, I would go so far as to say, essential. I don't even think you can say it's urgent. It's essential that practices are doing this. They could be killing patients totally unnecessarily and it's not as if it's difficult, because in a lot of circumstances, the vast majority of them are non-steroidals in elderly people." (GP interview 7)

The GP's interviewed perceived that NSAIDs are sometimes initiated with the intention the prescription was a one-off or without full consideration of all risk factors.

"..I've always thought I've been quite cautious with NSAIDs but then again possibly some of these patients were mine. You know they have been started on NSAID despite them being on ACE inhibitor and a diuretic and you think oh god, that's incredibly embarrassing." (GP interview 6).

Where risk factors were missed or NSAIDs were prescribed for longer than intended, GPs valued a prompt to review. In the interviews GPs reported changes to the NSAID and antiplatelet prescribing were the least complex decision-making of the topics, although all but one GP (who felt NSAIDs had 'no place' in pain control and patients should have no choice in whether to use these drugs) highlighted that it is sometimes complicated by patient choice.

"You know it is a compromise - patients like them [NSAIDs] because they're effective, whatever anybody says without a shadow of doubt people with osteoarthritis find them very effective drugs and often find them far more effective ... for pain relief and symptom relief in total ... than any other medication we've got to give them." (GP Interview 9).

Although the '*antithrombotics in AF*' measures led to limited changes in prescribing (3 changes from 201 reviews) two practices perceived the work to be worthwhile and for one it was their most valued prescribing topic, because two patients and the practice were relieved from the burden of unnecessary warfarin therapy. Two practices felt AF decision-making was often in the hands of consultants, and all GPs reported seeking advice from secondary care regarding the need to initiate or continue warfarin in specific patients. Although GPs reported the notes review work for AF was the most complex, they found validating warfarin prescribing a reassuring process.

"...the non-steroidal one was great. The atrial fibrillation one was great for a different matter, because [although] you identified quite a lot of patients, at the end of the day, when we looked through them,[we] only identified one that we wanted to chase up" (GP interview 7).

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The 'asthma control' topic was perceived as the least important by all GPs, mainly because of overlap with measures in QOF,[21] and because they shared responsibility with practice nurses and were content to leave the decision-making to them.

"I think sometimes we could use the nurses to do some of it...in the future when we do that we would ask our nurse that does the asthma clinic to do that because that would, you know she's the one that's doing the prescribing so that would've been better for her to take control of that." (GP interview 9)

Optimising the intervention

Practice experiences identified some barriers which facilitated optimising the intervention beyond suggestions in the current literature on changing prescribing.

Facilitating engagement

GPs felt prescribing safety was important but that improvement was always in the context of busy workloads. A financial incentive to review was perceived as important to facilitate engagement and to encourage practices to participate in the trial. GPs were asked about how any financial incentive should be structured, and different balances between up-front payments and payment-per-review were discussed. Of the options offered, all GPs and practice managers interviewed were in agreement that £350 (€411, \$538) upfront and £15 (€18, \$23) per review best struck the balance between gaining attention and incentivising payment-per-review.

"I think £350 up front and £15 per review. The reason for this is that the work is very much about the review and if you pay up-front too much, there is a danger the reviews won't get done as the incentive is small. In fact up-front payment could be less, with more per review, provided you have a mechanism for checking the review has been done properly." (GP Interview 7)

This payment structure mirrors existing financial incentives for quality in use in UK general practice, either in the Quality and Outcomes Framework (an explicit pay for performance system) and in Enhanced Service contracts for work not covered by capitation. [22]

Maintaining engagement

Two practices struggled to embed the work within practice routines and expressed the concern that DQIP work could be side-lined by competing work pressures. In addition to the pay-per-review financial incentive, it was therefore decided that practices should receive regular updates on their progress (or lack of progress) via DQIP newsletters. It was anticipated that to maintain engagement, unnecessary reviews had to be minimised. This led to a change in how patients were identified so that patients whose high-risk prescribing had been reviewed and deemed appropriate would not be reflagged for review for the same type of high-risk prescribing in the next year.

Sustaining improved prescribing

All GPs interviewed valued the data but felt high-risk NSAID prescribing required regular review. GPs perceived this was the prescribing topic where prescribing was likely to be restarted because of continuing patient demand for analgesia and restarting by other doctors.

"I think, it will always be very difficult, you will always get colleagues that will go back to prescribing it again and what was interesting was when you were re-running the searches, what was actually happening with that. Looking at what we were doing, because sometimes Dr X would say, 'Crikey look at that!'" (Practice manager interview 2).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

It was decided the DQIP informatics tool would need to reflag patients for review where high-risk prescribing was *restarted* after a decision to stop and run charts should be provided to allow practices to monitor high-risk prescribing trends over time.

Discussion

Summary of main findings

All topics examined in this study had previously been identified as priorities for improvement in primary care.[5] GP review of the targeted prescribing revealed that measures for each topic varied in their ability to identify changeable high-risk prescribing and in their perceived importance. The NSAID and antiplatelet measures performed best in identifying potentially changeable high-risk prescribing (68% of patients required action versus 25% for the 'asthma control' and 18% of 'antithrombotics in AF') and were the most valued. Although the 'antithrombotics in AF' topic generated considerable work for little change, it was highly valued by two practices because it identified a small number of patients who could stop warfarin, which mattered given the treatment and monitoring burden this drug imposes on patients and practices. The asthma topic was the least valued due to overlaps with QOF reviews and technical problems in accurately identifying patients with poor asthma control from EMRs. These findings demonstrate the importance of testing potential outcome measures prior to trialling complex interventions in order to ensure they are changeable by the intervention to be evaluated.[23-25] Although practices said improving prescribing safety was important, a number of barriers to engagement, maintenance of effort and sustaining improved prescribing were identified which informed the intervention design[24, 26] and ensured sensitivity to practices' needs.[25] These barriers were addressed through financial incentives per patient reviewed, and the informatics component would provide continuous measurement and feedback, supplemented by monthly update newsletters.

Strengths and limitations

A strength of this study was the use of quantitative and qualitative methods to give a broader understanding of how changeable this high risk prescribing was, what the barriers to changing prescribing were and how GPs valued this work, which enabled informed choice of outcome measures and optimisation of the intervention.[24, 26, 27] Additionally, the findings supported the design of the trial process evaluation [28, 29] in addition to the main trial design. The main limitation of this study is that changeability of potential outcome measures was tested by measuring GPs intention to change prescribing or conduct further investigation ('action'), rather than quantifying actual changes in prescribing and their clinical implications. This did, however, allow the identification of plausible high-risk prescribing to use as an outcome measure in the trial which will evaluate the ability of the intervention to actually change prescribing. It is worth noting that although the AF and asthma measures examined were found to be less suitable, this was partly because of technical problems of operationalising them in routine data, and optimising the technical properties of the measures (e.g. by extending the time window for warfarin prescriptions in order to reduce the number of patients falsely identified as lacking antithrombotic prophylaxis) may improve their performance. A second limitation of this study was the small number of general practices and reviewing clinicians included, and the four practices involved were of course all volunteers, who may not be representative of all practices. This is inevitable in small pilot studies though, and the main trial will evaluate effectiveness in wider range of practices with a parallel process evaluation to examine whether and how practices implement the intervention.

Comparison with existing literature

Although there are many examples of studies developing prescribing measures and establishing their face and content validity,[5, 30-33] few have reported the extent to which such measures can identify actual opportunities for improvement.[34, 35] A Dutch study found that patients identified by a measure targeting underuse of inhaled corticosteroids in asthma (using prescriptions of short-acting beta agonists as a proxy for uncontrolled asthma), 46% were candidates for inhaled steroids after a face-to-face review by a clinician, compared to 25% at best (assuming all 'further investigations' would confirm the need for inhaled steroids). The much lower proportion found here suggests that estimates of changeability are likely to be context specific (e.g. depending on the accuracy of data sources used) and may also depend on the gold standard against which the performance of prescribing measures is compared. When selecting outcome measures for a trial, findings from previous studies conducted in different health care settings may therefore be of limited value.

Some of the prescribing measures evaluated here targeted prescribing patterns similar to those used as primary outcome measures in the PINCER trial.[11] At six months follow-up, the PINCER trial found a significant reduction in both beta-blocker prescribing in asthma and NSAID prescribing (without use of gastro-protection in patients with a history of peptic ulcer [36]). However, part of the improvement in high-risk NSAID prescribing was lost by 12 months follow-up, which is consistent with concerns expressed by GPs' in this study that NSAIDs may be restarted due to patient demand or lack of communication between GPs. The DQIP trial and parallel process evaluations will establish to which extent the strategies used in the DQIP intervention to avoid such relapse (continuous feedback, paying per review and regular letters highlighting progress) are successful.

Our finding that changing prescribing of antithrombotics in AF is difficult to change is consistent with large surveys conducted over the last 10 to 15 years demonstrating little improvement in the uptake of anticoagulants in AF patients at high-risk of stroke [37-39]. Similar to our study, a systematic review exploring barriers to prescribing anticoagulants for AF found that the main reasons not to prescribe anticoagulants were advanced patient age and perceived risk of bleeding events.[40] A lower uptake of anticoagulants in paroxysmal AF has also previously been reported, consistent with GPs reporting paroxysmal AF as a reason not to prescribe AF in this study, although stroke risk is as high as in chronic AF.[37] This does not mean that such prescribing could not be improved, but may indicate that more attention would need to be paid to persuading GPs of the benefits and risks of antithrombotic use in people with AF, before interventions like this one which prompt review. For the 'Asthma control' topic, some of the interviewed GPs appeared to show complacency (e.g. the assumption that if patients have had a QOF asthma review they would be on optimal treatment) and it is possible that where this is the case, then more intensive educational or change facilitating interventions may be required.

Conclusion

Although several RAND studies have identified large sets of 'valid' indicators of prescribing safety, their value and feasibility for change has not been assessed, in terms of the extent to which they identify patients with actual inappropriate prescribing.[33, 41] This study shows their perceived value and feasibility may vary by prescribing topic,[34, 42] and any research or NHS use of prescribing indicators for improvement would therefore benefit from piloting and evaluation. Some prescribing topics, such as NSAIDs may be suitable for low intensity interventions based on repeated feedback using existing electronic data, simple education and possibly small financial incentives but other prescribing topics, such as 'asthma control' and 'antithrombotics in AF' may require prior work to clean electronic data and refine measures, or more intensive educational

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1 work to persuade practices what is being measured is important, or more intensive facilitation of change.
2 Safer prescribing is an important aim for policy and commissioners, but there may not be a one size fits all
3 intervention to deliver it.
4
5
6
7
8

9 **Authors contributions:** BG was responsible for the initial conceptualisation and design. TD and AG reviewed
10 the literature, carried out the data collection, analysis and interpretation of the data and contributed to the
11 design of the study. AG prepared the first manuscript and is responsible for this article. All authors iteratively
12 commented on successive drafts of the manuscript. All authors read and approved the final manuscript.
13

14 **Funding statement:** AG and TD are funded by the Scottish Government Health Directorates Chief Scientist
15 Office Applied Programme Research Grant 07/02 for the Data Driven Quality Improvement in Primary Care
16 programme. This funding body have had no direct role in the design and conduct of, or decision to publish
17 this work.
18

19 **Competing Interests:** The authors declare no competing interests.
20

21 **Data sharing:** No further information available
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Gandhi TK, Weingarten SN, Borus J, *et al*: **Adverse drug events in ambulatory care.** *New England Journal of Medicine* 2003, **348**:1556 - 1564.
2. Gurwitz JH, Field TS, Harrold LR, *et al*: **Incidence and preventability of adverse events among older persons in the ambulatory setting.** *Journal of American Medical Association* 2003, **289**:1107-1116.
3. Pirmohamed MJ, Meakin S, Green C, *et al*: **Adverse drug reactions as a cause of admission to hospital: prospective analysis of 18 820 patients.** *British Medical Journal* 2004, **329**:15-19.
4. Howard RL, Avery AJ, Slavenburg S, *et al*. **Which drugs cause preventable admissions to hospital? A systematic review.** *British Journal of Clinical Pharmacology* 2007, **63**(2):136-147.
5. Dreischulte T, Grant A, McCowan C, *et al*. **Quality and safety of medication use in primary care: Consensus validation of a new set of explicit medication assessment criteria and prioritisation of topics for improvement.** *BMC Clinical Pharmacology* 2012, **12**(1):5.
6. Guthrie B, McCowan C, Davey P, *et al*. **High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice.** *British Medical Journal* 2011, **342**.
7. Howard RL, Avery AJ, Howard PD, *et al*. **Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study.** *Qual Saf Health Care* 2003, **12**:280 - 285.
8. Thomsen LA, Winterstein AG, Sondergaard B, *et al*. **Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care.** *The Annals of Pharmacotherapy* 2007, **41**:1411-1426.
9. Department of Health: **An organisation with a memory: report of an expert group on learning from adverse events in the NHS.** In.; 2000.
10. Smith J: **Building a safer NHS for patients: improving medication safety.** In. London: Department of Health; 2004.
11. Avery AJ, Rodgers S, Cantrill JA, *et al*. **A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis.** *The Lancet* 2012.
12. Dreischulte T, Grant A, Donnan P, *et al*. **A cluster randomised stepped wedge trial to evaluate the effectiveness of a multifaceted information technology-based intervention in reducing high-risk prescribing of non-steroidal anti-inflammatory drugs and antiplatelets in primary care: the DQIP study protocol.** *Implementation Science* 2012, **7**:24.
13. Medical Research Council: **A framework for the development and evaluation of RCTs for complex interventions to improve health.** In. London: Medical Research Council; 2000.
14. Campbell M, Fitzpatrick R, Haines A, *et al*. **Framework for design and evaluation of complex interventions to improve health.** *British Medical Journal* 2000 **321** 694-696.
15. O'Brien MA, Rogers S, Jamtvedt G, *et al*. **Educational outreach visits: effects on professional practice and health care outcomes.** *Cochrane Database of Systematic Reviews* 2009, **4**.
16. Farmer AP, Legare F, Turcot L, *et al*. **Printed Educational Materials: effects on professional practice and health care outcomes.** *Cochrane Database of Systematic Reviews* 2008(3):CD004398.
17. Jamtvedt G, Young JM, Kristoffersen DT, *et al*. **Audit and feedback: effects on professional practice and health care outcomes.** *Cochrane Database of Systematic Reviews* 2009, **4**.

18. Gage BF, Waterman AD, Shannon W, et al. **Validation of a clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation.** *Journal of American Medical Association* 2001, **285**:2864-2870.
19. Ritchie J, Spencer L, O'Connor W: **Carrying out Qualitative Analysis.** In: *Qualitative Research Practice, A guide for Social Science Students and Researchers.* edn. Edited by Ritchie J, Lewis J. London: Sage Publications Ltd; 2003.
20. Camm AJ KP, Lip GYH, Schotten U, et al. **Guidelines for the management of atrial fibrillation.** *Europace* 2010, **12**(10):1360-1420.
21. Department of Health: **Investing in General Practice - the New General Medical Services Contract.** In.; 2003.
22. British Medical Association: **Focus on QOF payments.** Available at <http://bma.org.uk/practical-support-at-work/contracts/independent-contractors/qof-guidance/focus-qof-payments> [accessed 25/11/2013].
23. Campbell S, Chauhan U, Lester H: **Primary Medical Care Provider Accreditation (PMCPA): pilot evaluation.** *Br J Gen Pract* 2010 e295-301.
24. Bradley F, Wiles R, Kinmonth A-L, et al. **Development and evaluation of complex interventions in health services research: case study of the Southampton heart integrated care project (SHIP).** *British Medical Journal* 1999, **318**(7185):711-715.
25. Van Hecke A, Verhaeghe S, Grypdonck M, et al. **Systematic development and validation of a nursing intervention: the case of lifestyle adherence promotion in patients with leg ulcers.** *Journal of Advanced Nursing* 2011, **67**(3):662-676.
26. Corrrigan M, Cupples ME, Smith SM, et al. **The contribution of qualitative research in designing a complex intervention for secondary prevention of coronary heart disease in two different healthcare systems.** *BMC Health Services Research* 2006, **6**:90.
27. Cresswell K, Sadler S, Rodgers S, et al. **An embedded longitudinal multi-faceted qualitative evaluation of a complex cluster randomized controlled trial aiming to reduce clinically important errors in medicines management in general practice.** *Trials* 2012, **13**(1):78.
28. Grant A, Dreischulte T, Treweek S, et al. **Study protocol of a mixed-methods evaluation of a cluster randomised trial to improve the safety of NSAID and antiplatelet prescribing: data-driven quality improvement in primary care.** *Trials* 2012, **13**:154.
29. Grant A, Treweek S, Dreischulte T, et al. **Process evaluations for cluster-randomised trials of complex interventions: a proposed framework for design and reporting.** *Trials* 2013, **14**(1):15.
30. Gallagher P, Ryan C, Byrne S, et al. **STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation.** *International Journal of Clinical Pharmacology & Therapeutics* 2008, **46**(2):72-83.
31. Naugler CT, Brymer C, Stolee P, et al. **Development and validation of an improving prescribing in the elderly tool.** *Canadian Journal of Clinical Pharmacology* 2000, **7**(2):103-107.
32. Fick DM, Copper JW, Wade WE, et al. **Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, resulting of a US consensus panel of experts.** *Archives of Internal Medicine* 2003, **163**:2716-2724.
33. Avery A, Dex G, Mulvaney C, et al. **Development of prescribing-safety indicators for GPs using the RAND Appropriateness Method.** *Br J Gen Pract* 2011, **61**(589):e526-e536.
34. Pont LG, Denig P, van der Molen T: **Validity of performance indicators for assessing prescribing quality: the case of asthma.** *European Journal of Clinical Pharmacology* 2004, **59**:833-840.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
35. Dreischulte T, Johnson J, McAnaw J, et al. **Medication assessment tool to detect care issues from routine data: a pilot study in primary care.** *International Journal of Clinical Pharmacy* 2013.
36. Hemming K, Chilton PJ, Lilford RJ, et al. **Bayesian cohort and cross-sectional analyses of the PINCER trial: a pharmacist-led intervention to reduce medication errors in primary care.** *PLoS ONE [Electronic Resource]* 2012, **7**(6):e38306.
37. Nieuwlaat R, Capucci A, Lip GY, et al. **Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation.** *European Heart Journal* 2006, **27**(24):3018-3026.
38. Holt TA, Hunter TD, Gunnarsson C, Khan N, Cload P, Lip GYH: **Risk of stroke and oral anticoagulant use in atrial fibrillation: a cross-sectional survey.** *British Journal of General Practice* 2012, DOI: **10.3399/bjgp12X656856.**
39. Ogilvie IM, Newton N, Welner S: **Underuse of oral anticoagulants in atrial fibrillation: a systematic review.** *American Journal of Medicine* 2010(123):638-645.
40. Pugh D, Pugh J, Mead GE: **Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review.** *Age and ageing* 2011, **40**:675-683.
41. Campbell SM, Cantrill JA, Roberts D: **Prescribing indicators for UK general practice: Delphi consultation study.** *British Medical Journal* 2000, **321**(7258):425-428.
42. Campbell S, Hann M, Hacker J, et al. **Quality assessment for three common conditions in primary care: validity and reliability of review criteria developed by expert panels for angina, asthma and type 2 diabetes.** *Quality and Safety in Health Care* 2002, **11**:125 - 130.

Table 1: Review decisions made by topic. The data reported on topics 1 (NSAID and antiplatelet) and 2 (asthma) measures is from all four practices and the topic 3 (atrial fibrillation) data is from three of the pilot practices.

Topic /Individual measures implemented (No. of reviews)	No. of times the following decisions were made at point of review:		
	Change medication	Further investigation	No action
1. NSAIDs and antiplatelets (n=290)	101 (35%)	97 (33%)	92 (32%)
1.1 High risk use in patients with GI risk factors (n=120) ^{A,B}	54 (45%)	21 (18%)	45 (38%)
1.2 High risk use of NSAIDs in patients with renal risk factors (n=161) ^C	44 (27%)	72 (45%)	45 (28%)
1.3 High risk use of NSAIDs in heart failure (n= 9)	3 (33%)	4 (44%)	2 (22%)
2. Asthma (n=148)	10 (7%)	26 (18%)	112 (76%)
2.1 Underuse of inhaled corticosteroids (n=130) ^D	7 (5%)	23 (18%)	100 (77%)
2.2 High-risk use of beta blockers (n=18) ^E	3 (17%)	3 (17%)	12 (67%)
3. Atrial fibrillation (n=201)	3 (1%)	34 (17%)	164 (82%)
3.1 Underuse/ low intensity of thromboembolic prophylaxis (n=178)	1 (1%)	34 (19%)	143 (80%)
3.2 High-risk use of oral anticoagulants (n=23)	2 (9%)	0 (0%)	21 (91%)

A – NSAID prescription (in previous 12 weeks) without GI protection to people with at least one of the following risk factors:

(i) history of peptic ulcer, (ii) aged ≥ 75 , (iii) aged ≥ 65 and on aspirin, (iv) aged ≥ 65 and on warfarin

B – Aspirin prescription (in previous 12 weeks) without GI protection to people with at least one of the following risk factors:

(i) history of peptic ulcer, (ii) aged ≥ 65 and on clopidogrel, (iii) aged ≥ 65 and on warfarin

C – NSAID prescription to people with at least one of the following risk factors:

(i) CKD stage 3 to 5, (ii) on ACEI/ARB, (iii) on diuretic, (iv) on combination of ACEI/ARB and diuretic

D- No prescription of inhaled corticosteroid (in previous 12 weeks) in patient with asthma and at least one of the following risk factors: (i) prescription for 3 or more SABA inhalers in previous 12 weeks, (ii) prescription of LABAs, leukotriene receptor antagonist, theophylline or oral prednisolone in previous 12 weeks

E – Prescription of any beta blocker if ‘active asthma’ (prescription of a SABA inhaler in previous 48 weeks) or prescription of a non-cardio-selective beta blocker if ‘previous asthma’ (no prescription of a SABA inhaler in the previous 48 weeks).

Table 2: Reasons stated by clinicians as to why 'no action' was required for patients identified with drug therapy risk(s) by the DQIP measures

Topic (No. of reviews)	No. of reviews where stated reason for 'no action' was ^A :		
	'Technical' (count, %) <i>Specific reasons(count)</i>	'Clinical' <i>Specific reasons(count)</i>	'Other' <i>Specific reasons(count)</i>
1. NSAIDs and antiplatelets (n=92)	30 (33%)	62 (67%)	0
1.1 High risk use in patients with GI risk factors (n=45)	10 (22%) <i>Patient no longer on practice register (5); time window of assessment (3^c); Disease coding error (2)</i>	35 (78%) <i>Short term use (21); Risk adequately mitigated by low dose misoprostol (5); High-risk drug 'well tolerated' (9); No effective alternative (5)</i>	0
1.2 High risk use of NSAIDs in patients with renal risk factors (n=45)	20 (44%) <i>Time window of assessment (15^c); Patient no longer on practice register (5)</i>	20 (44%) <i>Short term use (19); No effective alternative (1);</i>	5 (11%) <i>Unspecified (5^b)</i>
1.3 High risk use of NSAIDs in heart failure (n=2)	0	2 (100%) <i>Short term use (2)</i>	0
2. Asthma (n=112)	53 (47%)	5 (4%)	54 (48%)
2.1 Underuse of inhaled corticosteroids (n=100)	46 (46%) <i>Time window of assessment (21^c); proxies for moderate/severe asthma failed (13^d); disease coding error (10); patient no longer on practice register (2)</i>	0	54 (54%) <i>Needs review but does not attend clinic (29); recently reviewed for QOF (22); patient choice (3)</i>
2.2 High-risk use of beta blockers (n=12)	7 (58%) <i>Disease coding error (7)</i>	5 (42%) <i>Beta blocker 'well tolerated' (5)</i>	0
3. Atrial fibrillation (n=166)	80 (48%)	59 (36%)	27 (16%)
3.1 Underuse/ low intensity of thromboembolic prophylaxis (n=143)	78 (55%) <i>Disease coding error (31); Time window of assessment (29^c); patient no longer on practice register (18);</i>	42 (29%) <i>Not 'fit' for warfarin (30); Paroxysmal AF (7); Satisfactory rate control (5)</i>	23 (16%) <i>Patient choice (16); secondary care decision (3); unspecified (4);</i>
3.2 High risk use of oral anticoagulants (n=21)	2 (10%) <i>Disease coding error (2)</i>	17 (81%) <i>CHADS₂ score judged to underestimate risk (17)</i>	2 (10%) <i>Secondary care decision (2);</i>

1 A - The number of specific reasons may exceed the number of reviews when more than one reason was provided per review.
2 B - The reasons provided referred to co-existing gastrointestinal risk factors
3 C - Refers to situations where a drug that was identified by the searches as 'high-risk' was stopped or a drug identified as 'beneficial'
4 was prescribed between the search date and the review date
5 D - The proxies for moderate to severe asthma (> 3 prescriptions of short-acting beta agonists issued over last 12 weeks;
6 prescription of step 3 drugs) failed in these cases, because patients had mild asthma but were stock-piling inhalers (eg getting them
7 to have available in multiple locations) or using step 3 drugs for indications other than asthma.
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Developing a complex intervention to improve prescribing safety in primary care: mixed methods feasibility and optimisation pilot study

Authors

Aileen M Grant (a.m.grant@dundee.ac.uk)*

Quality, Safety and Informatics Group, Population Health Sciences, Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383733

Bruce Guthrie (b.guthrie@dundee.ac.uk)

Quality, Safety and Informatics Group, Population Health Sciences, Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383740

Tobias Dreischulte (t.dreischulte@dundee.ac.uk)

Medicines Management Unit, NHS Tayside c/o, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee. DD2 4BF. Tel. 01382 383769

*Corresponding author

Abstract:**Objectives**

1. To measure the extent to which different candidate outcome measures identified high-risk prescribing that is potentially changeable by the DQIP intervention
2. To explore the value of reviewing identified high-risk prescribing to clinicians
3. To optimise the components of the DQIP intervention

Design: Mixed method study

Setting: General practices in two Scottish Health boards

Participants: Four purposively sampled general practices of varying size and socioeconomic deprivation.

Outcome measures: Prescribing measures targeting (1) High-risk use of NSAIDs and antiplatelets; (2) 'Asthma control'; and (3) 'Antithrombotics in AF'

Intervention: The prescribing measures above were used to identify patients for review by general practices. The ability of the measures to identify potentially changeable high-risk prescribing was measured as the proportion of patients reviewed where practices identified a need for action. Field notes were recorded from meetings between researchers and staff and key staff participated in semi-structured interviews exploring their experience of the piloted intervention processes.

Results: Practices identified a need for action in 68%, 25%, 18% of patients reviewed for prescribing measures (1), (2) and (3), respectively. GPs valued being prompted to review patients, and perceived that (1)'NSAID and antiplatelet' and (2) 'antithrombotics in AF' were the most important to act on. Barriers to initial and on-going engagement and to sustaining improvements in prescribing were identified.

Conclusion:

'NSAIDs and antiplatelets' measures were selected as the most suitable outcome measures for the DQIP trial, based on evidence of this prescribing being more easily changeable. In response to the barriers identified the intervention was designed to include a financial incentive, additional on-going feedback on progress, and re-prompting review of patients, whose high-risk prescribing was restarted after a decision to stop.

Trial registration number: Clinicaltrials.gov NCT01425502

Article summary:

Article focus: This study aimed to evaluate the extent to which different candidate outcome measures identified high-risk prescribing that is potentially changeable, explore the perceived value of these measures to clinicians, and to optimise intervention components for evaluation in a cluster-randomised trial.

Key Messages:

- Prescribing measures prioritised for improvement were validated for use in a complex prescribing quality improvement intervention.

- The ability of these measures to identify potentially changeable high-risk prescribing and the perceived value of the measures varied.
- In response to the barriers and facilitators identified, the intervention to be tested in a trial was designed to include a financial incentive to facilitate initial engagement, to provide additional on-going feedback on overall progress, and to highlight patients whose high-risk prescribing was restarted after a decision to stop.

Strengths and limitations:

- The strength of this study was the use of quantitative and qualitative methods to give a greater understanding of how changeable the identified high-risk prescribing was, what the barriers to changing prescribing were and how GPs valued this work, which enabled informed choice of outcome measures and optimisation of the intervention.
- The limitation of this study is that changeability of potential outcome measures was tested by measuring GPs intention to change prescribing or conduct further investigation ('action'), rather than quantifying actual changes in prescribing and their clinical implications (although this is being evaluated in an on-going cluster-randomised controlled trial).

Funding statement: AG and TD are funded by the Scottish Government Health Directorates Chief Scientist Office Applied Programme Research Grant 07/02 for the Data Driven Quality Improvement in Primary Care programme. This funding body have had no direct role in the design and conduct of, or decision to publish this work.

Competing Interests: The authors declare no competing interests.

Background

The safety of medication use in primary care is a major concern for health care systems internationally.[1-4] An estimated 3-4% of unplanned hospital admissions are due to preventable adverse drug events and approximately one third of these have been attributed to prescribing of drugs to people with risk factors for adverse drug effects and under-prescribing of prophylactic treatments (high-risk prescribing).[4]

In the UK, medications may be initiated in primary and secondary care, but general practitioners (GPs) prescribe almost all drugs in the community and have responsibility for reviewing all medications. Previous research has shown that high-risk prescribing in primary care is common and its prevalence varies substantially between practices (after adjusting for case-mix), which indicates scope for improvement.[5-8] Given the current UK policy focus on improving patient safety, there is a need to develop and test interventions to reduce high-risk prescribing.[9, 10]

In the UK, the virtually ubiquitous use of electronic medical records (EMRs) in primary care offers opportunities to support quality and safety improvement initiatives. For example, the PINCER (Pharmacist-led Information Technology Intervention for Medication Errors) trial has demonstrated the effectiveness of an intervention, where pharmacists identified patients with high-risk prescribing using data extracted from EMRs, reviewed their records, and recommended changes.[11] Similarly, the 'Data-driven quality improvement in primary care' (DQIP) research programme aims to identify patients with high-risk prescribing from EMRs, but in contrast to PINCER, practices are provided with continuous feedback using a web-based informatics tool, and financial incentives to motivate practice staff to review patients identified.[12]

The Medical Research Council (MRC) Framework recommends that complex interventions be modelled before evaluation in a randomised controlled trial in order to optimise both the intervention design and its evaluation by defining outcomes and ensuring feasibility.[13] [14] In terms of intervention design, the broad shape of the DQIP intervention was defined by the intention that there should be evidence for the effectiveness of its components, that it should be built on existing NHS information technology and be implementable as an 'enhanced service' (a UK National Health Service mechanism for commissioning general practice care). The intention was therefore to combine an educational intervention[15, 16], audit and feedback[17], and a financial incentive to review. As a result a priority was to pilot and optimise these elements in a small number of practices. For evaluating the impact of the intervention, a set of potential prescribing outcome measures had previously been validated using consensus methods[5] but an outstanding question was which of these measures could plausibly be improved by this intervention and therefore used as trial outcome measures.

The specific objectives of this study were to optimise the DQIP intervention and trial evaluation by: (1) identifying which potential outcome measures best identified patients with high-risk prescribing that could potentially be changed; (2) establishing which measures were most valued by practices in terms of improving quality and safety; (3) exploring how best to design and deliver the educational, informatics and financial components of the DQIP intervention to maximise practice engagement.

Methods

The study used mixed qualitative and quantitative methods, and study was approved by NHS Tayside Committee on Medical Research Ethics A (09/S1401/54).

Settings

We purposively sampled and recruited four general practices, two from each NHS Scotland Health Board where the intervention was to be trialled, aiming to include larger and smaller practices serving populations that varied in socioeconomic deprivation.

Data collection

Data collection was between March 2010 and August 2011.

Quantitative data

In each practice, thematically related prescribing measures ('prescribing topics') that had been identified as priorities for quality and safety improvement[5] were implemented in EMRs to identify patients with potentially suboptimal prescribing for review. These prescribing topics were: (1) High-risk use of NSAIDs and antiplatelets in patients with gastro-intestinal, renal or cardiac risk factors ('NSAIDs and antiplatelets'); (2) Under-use of inhaled corticosteroids and high-risk use of beta-blockers in asthma ('asthma control'); and (3) Over-and under-use of anti-thrombotic drugs in atrial fibrillation ('antithrombotics in AF').

Practices received a feedback report for each topic, which summarised the total numbers of patients identified by each measure of high-risk prescribing, listed the patients affected, and provided supporting educational material (rationale, current evidence and prescribing guidance).[18] Practices were asked to conduct a record review of all identified patients with face-to-face review if necessary, and to document all decision-making on a structured template (tick boxes for a decision to 'change prescribing', conduct 'further investigation' or 'no action' and free text space to specify the rationale for 'no action'). Our expectation was that clinicians would judge some high-risk prescribing to be appropriate but would identify other patients in whom the prescribing should be stopped. An important aim of the pilot was to estimate how appropriateness and stopping varied across topics, to allow the trial to target prescribing that was more likely to be inappropriate and changeable.

Qualitative data

An initial meeting to explain the study and describe the topics was held in each practice. Practices then worked on one topic at a time, with further meetings held six to eight weeks after practices had received and acted on the feedback report. The meetings were facilitated by the pharmacist (TD), and observed by AG who took ethnographic field notes of 18 hours of meetings. The whole practice was invited but the meetings were generally attended by the GP(s) most involved and the practice manager and lasted between 30 and 60 minutes. At these meetings, practices were asked to describe the practice processes to conduct the review work, to report on the complexities of reviewing or changing prescribing, and to expand on reasons for 'no action'.

The GPs most involved in the review work and practice managers were invited for individual semi-structured interviews in order to explore their perceptions of the value of each prescribing topic and the specific components of the intervention (education, informatics and financial), their experiences of adopting and implementing the intervention in routine practice and to changing prescribing. Eleven interviews were conducted with 8 GPs (one GP was interviewed twice) and 2 practice managers. These interviews were held in the practices, lasted approximately one hour, were audio-recorded and transcribed verbatim.

Data Analysis

Quantitative analysis (research question (RQ) 1: performance of prescribing measures)

The ability of each measure to identify potentially changeable high-risk prescribing was measured as the proportion of patients reviewed whose prescribing was judged to require action ('change prescribing' or 'further investigation'). Reasons why the measures failed to identify potentially changeable high-risk prescribing in patients were classified into three categories: 'clinical' (prescribing changes were deemed

1 inappropriate or unnecessary given the clinical circumstances), 'technical' (the measure misidentified
2 patients when implemented in live clinical data) and 'other'.

3
4 *Qualitative analysis (RQ2 perceived value of each prescribing topic and RQ3 optimising intervention*
5 *components)*

6
7 Interview transcripts and fieldnotes were merged and analysed by emerging themes to identify a coding
8 frame. Data was imported into Nvivo-8 and the coding frame was systematically applied. Subsequent
9 analysis was by the Framework technique.[19] Thematic charting facilitated comparing the data by theme,
10 practice and prescribing topic. The data was explored for negative cases.

11 **Results**

12
13 Practice list-sizes ranged from 3,200 to over 10,000, with the percentage of patients living in the most
14 deprived quintile of postcodes ranging from 4% to 46%. All four practices completed the 'NSAID and
15 antiplatelet' and 'asthma control' topics, but only three completed the 'antithrombotics in AF' topic.

16 **Ability of measures to identify patients with potentially changeable high-risk prescribing**

17
18 Table 1 shows that for the 'NSAID and antiplatelet' topic, practices recorded a need for action in 68% of
19 patients reviewed (change prescribing 35%; further investigation 33%) compared to only 25% of patients
20 reviewed for the 'asthma control' topic (change prescribing 7%; further investigation 18%) and 18% of those
21 reviewed for 'antithrombotics in AF' (change prescribing 1%; further investigation 17%).

22
23 *Insert table 1 and 2 about here*

24
25 Table 2 shows the rationales for no action reported by GPs on templates for each patient reviewed. *Clinical*
26 *reasons* were most commonly reported for the 'NSAIDs and antiplatelets' topic (67%), but less so for the
27 'antithrombotics in AF' (36%) and much less for the 'asthma control' (4%) topic. The reasons provided
28 reflected that high-risk prescribing was a trade-off between effectiveness and safety. For 'NSAIDs and
29 antiplatelets', the main reported reason for not changing prescribing was that NSAID use was only 'short
30 term'. For 'antithrombotics in AF', clinical reasons reported were mainly 'unfitness for warfarin' (examples
31 reported in interview included fragility and dementia, heavy alcohol use and previous gastrointestinal
32 bleeding), but also included 'paroxysmal AF' (reflecting a misconception that stroke risk is lower than for
33 patients with chronic AF). [20]

34
35 '*Technical reasons*' accounted for one third of rationales for no action for the 'NSAID and antiplatelet' topic,
36 and for 47% 'asthma control' and 48% of the 'antithrombotics in AF' topics. For all three topics, technical
37 reasons related to patients no longer being on practice registers and to situations where identified high-risk
38 prescribing was no longer present at the point of review ('time window of assessment'). For example, for the
39 'antithrombotics in AF' topic, all practices highlighted in interviews that anticoagulant prescribing intervals
40 often exceeded the 12 week timeframe used by the measures, causing patients to be incorrectly identified as
41 lacking antithrombotic prophylaxis.

42
43 Inaccurate disease registers were reported as reasons why 'antithrombotics in AF' and 'asthma control'
44 measures misidentified prescribing as high-risk. One practice reported in interview that many patients on
45 their asthma disease register had chronic obstructive pulmonary disease (COPD) and therefore did not have
46 a clear indication for treatment with inhaled corticosteroids. The deprived practices reported that high
47 numbers of short-acting beta-agonist prescriptions did not necessarily identify patients with uncontrolled
48 asthma, because patients stockpiled inhalers in multiple locations (e.g. home, school, or work).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

'Other' reasons were not commonly identified for 'NSAIDs and antiplatelets', but accounted for 16% of 'antithrombotics in AF' and for 48% of 'asthma control' reviews where no action was taken. For the latter, GPs reported that patients had recently received an annual Quality and Outcomes framework (QOF) review, usually from a nurse, and they therefore assumed them to be on optimised asthma treatment. GPs generally felt that changes in prescribing for asthma usually required face-to-face review but patients often did not respond to invitations for review.

Perceived value of each prescribing topic as a target for the DQIP intervention

GPs perceived the pilot intervention raised awareness of targeted high-risk prescribing, improved prescribing practices and the recording of decision-making rationales, but they did not value each topic equally.

"...improving prescribing practice, improving our record keeping, improving our knowledge base and if people are on unsafe meds getting them off them and if there are on them carefully considering why and it is not accidental." (GP interview 1)

All GPs interviewed highly valued the process of reviewing patients identified as receiving *high-risk NSAID or antiplatelet* prescriptions.

"The topic is, I would go so far as to say, essential. I don't even think you can say it's urgent. It's essential that practices are doing this. They could be killing patients totally unnecessarily and it's not as if it's difficult, because in a lot of circumstances, the vast majority of them are non-steroidals in elderly people." (GP interview 7)

The GP's interviewed perceived that NSAIDs are sometimes initiated with the intention the prescription was a one-off or without full consideration of all risk factors.

"..I've always thought I've been quite cautious with NSAIDs but then again possibly some of these patients were mine. You know they have been started on NSAID despite them being on ACE inhibitor and a diuretic and you think oh god, that's incredibly embarrassing." (GP interview 6).

Where risk factors were missed or NSAIDs were prescribed for longer than intended, GPs valued a prompt to review. In the interviews GPs reported changes to the NSAID and antiplatelet prescribing were the least complex decision-making of the topics, although all but one GP (who felt NSAIDs had 'no place' in pain control and patients should have no choice in whether to use these drugs) highlighted that it is sometimes complicated by patient choice.

"You know it is a compromise - patients like them [NSAIDs] because they're effective, whatever anybody says without a shadow of doubt people with osteoarthritis find them very effective drugs and often find them far more effective ... for pain relief and symptom relief in total ... than any other medication we've got to give them." (GP Interview 9).

Although the 'antithrombotics in AF' measures led to limited changes in prescribing (3 changes from 201 reviews) two practices perceived the work to be worthwhile and for one it was their most valued prescribing topic, because two patients and the practice were relieved from the burden of unnecessary warfarin therapy. Two practices felt AF decision-making was often in the hands of consultants, and all GPs reported seeking advice from secondary care regarding the need to initiate or continue warfarin in specific patients. Although GPs reported the notes review work for AF was the most complex, they found validating warfarin prescribing a reassuring process.

"...the non-steroidal one was great. The atrial fibrillation one was great for a different matter, because [although] you identified quite a lot of patients, at the end of the day, when we looked through them,[we] only identified one that we wanted to chase up" (GP interview 7).

1 The 'asthma control' topic was perceived as the least important by all GPs, mainly because of overlap with
2 measures in QOF,[21] and because they shared responsibility with practice nurses and were content to leave
3 the decision-making to them.

4 *"I think sometimes we could use the nurses to do some of it...in the future when we do that we would ask*
5 *our nurse that does the asthma clinic to do that because that would, you know she's the one that's doing*
6 *the prescribing so that would've been better for her to take control of that."* (GP interview 9)
7
8

9 **Optimising the intervention**

10 Practice experiences identified some barriers which facilitated optimising the intervention beyond
11 suggestions in the current literature on changing prescribing.

12 *Facilitating engagement*

13 GPs felt prescribing safety was important but that improvement was always in the context of busy
14 workloads. A financial incentive to review was perceived as important to facilitate engagement and to
15 encourage practices to participate in the trial. GPs were asked about how any financial incentive should be
16 structured, and different balances between up-front payments and payment-per-review were discussed. Of
17 the options offered, all GPs and practice managers interviewed were in agreement that £350 (£411, \$538)
18 upfront and £15 (£18, \$23) per review best struck the balance between gaining attention and incentivising
19 payment-per-review.
20

21 *"I think £350 up front and £15 per review. The reason for this is that the work is very much about the*
22 *review and if you pay up-front too much, there is a danger the reviews won't get done as the incentive is*
23 *small. In fact up-front payment could be less, with more per review, provided you have a mechanism for*
24 *checking the review has been done properly."* (GP Interview 7)
25

26 This payment structure mirrors existing financial incentives for quality in use in UK general practice, either in
27 the Quality and Outcomes Framework (an explicit pay for performance system) and in Enhanced Service
28 contracts for work not covered by capitation. [22]
29

30 *Maintaining engagement*

31 Two practices struggled to embed the work within practice routines and expressed the concern that DQIP
32 work could be side-lined by competing work pressures. In addition to the pay-per-review financial incentive,
33 it was therefore decided that practices should receive regular updates on their progress (or lack of progress)
34 via DQIP newsletters. It was anticipated that to maintain engagement, unnecessary reviews had to be
35 minimised. This led to a change in how patients were identified so that patients whose high-risk prescribing
36 had been reviewed and deemed appropriate would not be reflagged for review for the same type of high-risk
37 prescribing in the next year.
38

39 *Sustaining improved prescribing*

40 All GPs interviewed valued the data but felt high-risk NSAID prescribing required regular review. GPs
41 perceived this was the prescribing topic where prescribing was likely to be restarted because of continuing
42 patient demand for analgesia and restarting by other doctors.
43

44 *"I think, it will always be very difficult, you will always get colleagues that will go back to prescribing it*
45 *again and what was interesting was when you were re-running the searches, what was actually*
46 *happening with that. Looking at what we were doing, because sometimes Dr X would say, 'Crikey look at*
47 *that!'"* (Practice manager interview 2).
48
49

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

It was decided the DQIP informatics tool would need to reflag patients for review where high-risk prescribing was *restarted* after a decision to stop and run charts should be provided to allow practices to monitor high-risk prescribing trends over time.

Discussion

Summary of main findings

All topics examined in this study had previously been identified as priorities for improvement in primary care.[5] GP review of the targeted prescribing revealed that measures for each topic varied in their ability to identify changeable high-risk prescribing and in their perceived importance. The NSAID and antiplatelet measures performed best in identifying potentially changeable high-risk prescribing (68% of patients required action versus 25% for the 'asthma control' and 18% of 'antithrombotics in AF') and were the most valued. Although the 'antithrombotics in AF' topic generated considerable work for little change, it was highly valued by two practices because it identified a small number of patients who could stop warfarin, which mattered given the treatment and monitoring burden this drug imposes on patients and practices. The asthma topic was the least valued due to overlaps with QOF reviews and technical problems in accurately identifying patients with poor asthma control from EMRs. These findings demonstrate the importance of testing potential outcome measures prior to trialling complex interventions in order to ensure they are changeable by the intervention to be evaluated.[23-25] Although practices said improving prescribing safety was important, a number of barriers to engagement, maintenance of effort and sustaining improved prescribing were identified which informed the intervention design[24, 26] and ensured sensitivity to practices' needs.[25] These barriers were addressed through financial incentives per patient reviewed, and the informatics component would provide continuous measurement and feedback, supplemented by monthly update newsletters.

Strengths and limitations

A strength of this study was the use of quantitative and qualitative methods to give a broader understanding of how changeable this high risk prescribing was, what the barriers to changing prescribing were and how GPs valued this work, which enabled informed choice of outcome measures and optimisation of the intervention.[24, 26, 27] Additionally, the findings supported the design of the trial process evaluation [28, 29] in addition to the main trial design. The main limitation of this study is that changeability of potential outcome measures was tested by measuring GPs intention to change prescribing or conduct further investigation ('action'), rather than quantifying actual changes in prescribing and their clinical implications. This did, however, allow the identification of plausible high-risk prescribing to use as an outcome measure in the trial which will evaluate the ability of the intervention to actually change prescribing. It is worth noting that although the AF and asthma measures examined were found to be less suitable, this was partly because of technical problems of operationalising them in routine data, and optimising the technical properties of the measures (e.g. by extending the time window for warfarin prescriptions in order to reduce the number of patients falsely identified as lacking antithrombotic prophylaxis) may improve their performance. A second limitation of this study was the small number of general practices and reviewing clinicians included, and the four practices involved were of course all volunteers, who may not be representative of all practices. This is inevitable in small pilot studies though, and the main trial will evaluate effectiveness in wider range of practices with a parallel process evaluation to examine whether and how practices implement the intervention.

Comparison with existing literature

Although there are many examples of studies developing prescribing measures and establishing their face and content validity,[5, 30-33] few have reported the extent to which such measures can identify actual opportunities for improvement.[34, 35] A Dutch study found that patients identified by a measure targeting underuse of inhaled corticosteroids in asthma (using prescriptions of short-acting beta agonists as a proxy for uncontrolled asthma), 46% were candidates for inhaled steroids after a face-to-face review by a clinician, compared to 25% at best (assuming all 'further investigations' would confirm the need for inhaled steroids). The much lower proportion found here suggests that estimates of changeability are likely to be context specific (e.g. depending on the accuracy of data sources used) and may also depend on the gold standard against which the performance of prescribing measures is compared. When selecting outcome measures for a trial, findings from previous studies conducted in different health care settings may therefore be of limited value.

Some of the prescribing measures evaluated here targeted prescribing patterns similar to those used as primary outcome measures in the PINCER trial.[11] At six months follow-up, the PINCER trial found a significant reduction in both beta-blocker prescribing in asthma and NSAID prescribing (without use of gastro-protection in patients with a history of peptic ulcer ~~(although sensitivity analyses have not confirmed this finding)~~[36]. However, part of the improvement in high-risk NSAID prescribing was lost by 12 months follow-up, which is consistent with concerns expressed by GPs' in this study that NSAIDs may be restarted due to patient demand or lack of communication between GPs. The DQIP trial and parallel process evaluations will establish to which extent the strategies used in the DQIP intervention to avoid such relapse (continuous feedback, paying per review and regular letters highlighting progress) are successful.

Our finding that changing prescribing of antithrombotics in AF is difficult to change is consistent with large surveys conducted over the last 10 to 15 years demonstrating little improvement in the uptake of anticoagulants in AF patients at high-risk of stroke [37-39]. Similar to our study, a systematic review exploring barriers to prescribing anticoagulants for AF found that the main reasons not to prescribe anticoagulants were advanced patient age and perceived risk of bleeding events.[40] A lower uptake of anticoagulants in paroxysmal AF has also previously been reported, consistent with GPs reporting paroxysmal AF as a reason not to prescribe AF in this study, although stroke risk is as high as in chronic AF.[37] This does not mean that such prescribing could not be improved, but may indicate that more attention would need to be paid to persuading GPs of the benefits and risks of antithrombotic use in people with AF, before interventions like this one which prompt review. For the 'Asthma control' topic, some of the interviewed GPs appeared to show complacency (e.g. the assumption that if patients have had a QOF asthma review they would be on optimal treatment) and it is possible that where this is the case, then more intensive educational or change facilitating interventions may be required.

Conclusion

~~The study had direct relevance to choice of outcome measures and intervention design, but highlights the 'right' intervention to improve primary care prescribing safety is likely to vary by targeted prescribing.~~ Although several RAND studies have identified large sets of 'valid' indicators of prescribing safety, their value and feasibility for change has not been assessed, in terms of the extent to which they identify patients with actual inappropriate prescribing.[33, 41] This study shows their perceived value and feasibility ~~are likely to~~ may vary by prescribing topic,[34, 42] and any research or NHS use of prescribing indicators for improvement would therefore benefit from piloting and evaluation. Some prescribing topics, such as NSAIDs ~~will~~ may be suitable for low intensity interventions based on repeated feedback using existing electronic

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1 data, simple education and possibly small financial incentives but other prescribing topics, such as 'asthma
2 control' and 'antithrombotics in AF' ~~are likely to~~ may require prior work to clean electronic data and refine
3 measures, or more intensive educational work to persuade practices what is being measured is important, or
4 more intensive facilitation of change. Safer prescribing is an important aim for policy and commissioners, but
5 there ~~is unlikely~~ may not ~~to~~ be a one size fits all intervention to deliver it.
6

7 **Authors contributions:** BG was responsible for the initial conceptualisation and design. TD and AG reviewed
8 the literature, carried out the data collection, analysis and interpretation of the data and contributed to the
9 design of the study. AG prepared the first manuscript and is responsible for this article. All authors iteratively
10 commented on successive drafts of the manuscript. All authors read and approved the final manuscript.
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

References

1. Gandhi TK, Weingarten SN, Borus J, Seger AC, Peterson J, Burdick E, Seger DL, Shu K, Federico F, Leape LL *et al*: **Adverse drug events in ambulatory care.** *New England Journal of Medicine* 2003, **348**:1556 - 1564.
2. Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, Cadoret C, Fish LS, Garber L, Kelleher M *et al*: **Incidence and preventability of adverse events among older persons in the ambulatory setting.** *Journal of American Medical Association* 2003, **289**:1107-1116.
3. Pirmohamed MJ, Meakin S, Green C, Scott AK, Walley T, Farrar K, Park BK, Breckenridge AM: **Adverse drug reactions as a cause of admission to hospital: prospective analysis of 18 820 patients.** *British Medical Journal* 2004, **329**:15-19.
4. Howard RL, Avery AJ, Slavenburg S, Royal S, Pipe G, Lucassen P, Pirmohamed M: **Which drugs cause preventable admissions to hospital? A systematic review.** *British Journal of Clinical Pharmacology* 2007, **63**(2):136-147.
5. Dreischulte T, Grant A, McCowan C, McAnaw J, Guthrie B: **Quality and safety of medication use in primary care: Consensus validation of a new set of explicit medication assessment criteria and prioritisation of topics for improvement.** *BMC Clinical Pharmacology* 2012, **12**(1):5.
6. Guthrie B, McCowan C, Davey P, Simpson CR, Dreischulte T, Barnett K: **High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice.** *British Medical Journal* 2011, **342**.
7. Howard RL, Avery AJ, Howard PD, Partridge M: **Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study.** *Qual Saf Health Care* 2003, **12**:280 - 285.
8. Thomsen LA, Winterstein AG, Sondergaard B, Haugbolle LS, Melander A: **Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care.** *The Annals of Pharmacotherapy* 2007, **41**:1411-1426.
9. Department of Health: **An organisation with a memory: report of an expert group on learning from adverse events in the NHS.** In.; 2000.
10. Smith J: **Building a safer NHS for patients: improving medication safety.** In. London: Department of Health; 2004.
11. Avery AJ, Rodgers S, Cantrill JA, Armstrong S, Cresswell K, Eden M, Elliott RA, Howard R, Kendrick D, Morris CJ *et al*: **A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis.** *The Lancet* 2012.
12. Dreischulte T, Grant A, Donnan P, McCowan C, Davey P, Petrie D, Treweek S, Guthrie B: **A cluster randomised stepped wedge trial to evaluate the effectiveness of a multifaceted information technology-based intervention in reducing high-risk prescribing of non-steroidal anti-inflammatory drugs and antiplatelets in primary care: the DQIP study protocol.** *Implementation Science* 2012, **7**:24.
13. Medical Research Council: **A framework for the development and evaluation of RCTs for complex interventions to improve health.** In. London: Medical Research Council; 2000.
14. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, Tyrer P: **Framework for design and evaluation of complex interventions to improve health.** *British Medical Journal* 2000 **321** 694-696.
15. O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, Forsetlund L, Bainbridge D, Freemantle N, Davis D *et al*: **Educational outreach visits: effects on professional practice and health care outcomes.** *Cochrane Database of Systematic Reviews* 2009, **4**.

16. Farmer AP, Legare F, Turcot L, Grimshaw J, Harvey E, McGowan J, Wolf F: **Printed Educational Materials: effects on professional practice and health care outcomes.** *Cochrane Database of Systematic Reviews* 2008(3):CD004398.
17. Jamtvedt G, Young JM, Kristoffersen DT, O'Brien MA, Oxman AD: **Audit and feedback: effects on professional practice and health care outcomes.** *Cochrane Database of Systematic Reviews* 2009, 4.
18. Gage BF, Waterman AD, Shannon W, Boehler M, Rich MW, Radford MJ: **Validation of a clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation.** *Journal of American Medical Association* 2001, **285**:2864-2870.
19. Ritchie J, Spencer L, O'Connor W: **Carrying out Qualitative Analysis.** In: *Qualitative Research Practice, A guide for Social Science Students and Researchers.* edn. Edited by Ritchie J, Lewis J. London: Sage Publications Ltd; 2003.
20. Camm AJ KP, Lip GYH, Schotten U, Savelieva I, Ernst S, et al: **Guidelines for the management of atrial fibrillation.** *Europace* 2010, **12**(10):1360-1420.
21. Department of Health: **Investing in General Practice - the New General Medical Services Contract.** In.; 2003.
22. British Medical Association: **Focus on QOF payments.** Available at <http://bma.org.uk/practical-support-at-work/contracts/independent-contractors/qof-guidance/focus-qof-payments> [accessed 25/11/2013].
23. Campbell S, Chauhan U, Lester H: **Primary Medical Care Provider Accreditation (PMCPA): pilot evaluation.** *Br J Gen Pract* 2010 e295-301.
24. Bradley F, Wiles R, Kinmonth A-L, Mant D, Gantley M: **Development and evaluation of complex interventions in health services research: case study of the Southampton heart integrated care project (SHIP).** *British Medical Journal* 1999, **318**(7185):711-715.
25. Van Hecke A, Verhaeghe S, Grypdonck M, Beele H, Flour M, Defloor T: **Systematic development and validation of a nursing intervention: the case of lifestyle adherence promotion in patients with leg ulcers.** *Journal of Advanced Nursing* 2011, **67**(3):662-676.
26. Corrrigan M, Cupples ME, Smith SM, Byrne M, Leathem CS, Clerkin P, Murphy AW: **The contribution of qualitative research in designing a complex intervention for secondary prevention of coronary heart disease in two different healthcare systems.** *BMC Health Services Research* 2006, **6**:90.
27. Cresswell K, Sadler S, Rodgers S, Avery A, Cantrill J, Murray S, Sheikh A: **An embedded longitudinal multi-faceted qualitative evaluation of a complex cluster randomized controlled trial aiming to reduce clinically important errors in medicines management in general practice.** *Trials* 2012, **13**(1):78.
28. Grant A, Dreischulte T, Treweek S, Guthrie B: **Study protocol of a mixed-methods evaluation of a cluster randomised trial to improve the safety of NSAID and antiplatelet prescribing: data-driven quality improvement in primary care.** *Trials* 2012, **13**:154.
29. Grant A, Treweek S, Dreischulte T, Foy R, Guthrie B: **Process evaluations for cluster-randomised trials of complex interventions: a proposed framework for design and reporting.** *Trials* 2013, **14**(1):15.
30. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D: **STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment).** Consensus validation. *International Journal of Clinical Pharmacology & Therapeutics* 2008, **46**(2):72-83.
31. Naugler CT, Brymer C, Stolee P, Arcese ZA: **Development and validation of an improving prescribing in the elderly tool.** . *Canadian Journal of Clinical Pharmacology* 2000, **7**(2):103-107.
32. Fick DM, Copper JW, Wade WE, Waller JL, Maclean R, Beers MH: **Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, resulting of a US consensus panel of experts.** *Archives of Internal Medicine* 2003, **163**:2716-2724.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
33. Avery A, Dex G, Mulvaney C, Serumaga B, Spencer R, Lester H, Campbell S: **Development of prescribing-safety indicators for GPs using the RAND Appropriateness Method.** *Br J Gen Pract* 2011, **61**(589):e526-e536.
34. Pont LG, Denig P, van der Molen T: **Validity of performance indicators for assessing prescribing quality: the case of asthma.** *European Journal of Clinical Pharmacology* 2004, **59**:833-840.
35. Dreischulte T, Johnson J, McAnaw J, Geurts M, de Gier H, Hudson S: **Medication assessment tool to detect care issues from routine data: a pilot study in primary care.** *International Journal of Clinical Pharmacy* 2013.
36. Hemming K, Chilton PJ, Lilford RJ, Avery A, Sheikh A: **Bayesian cohort and cross-sectional analyses of the PINCER trial: a pharmacist-led intervention to reduce medication errors in primary care.** *PLoS ONE [Electronic Resource]* 2012, **7**(6):e38306.
37. Nieuwlaat R, Capucci A, Lip GY, Olsson SB, Prins MH, Nieman FH, Lopez-Sendon J, Vardas PE, Aliot E, Santini M *et al*: **Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation.** *European Heart Journal* 2006, **27**(24):3018-3026.
38. Holt TA, Hunter TD, Gunnarsson C, Khan N, Cload P, Lip GYH: **Risk of stroke and oral anticoagulant use in atrial fibrillation: a cross-sectional survey.** *British Journal of General Practice* 2012, DOI: **10.3399/bjgp12X656856**.
39. Ogilvie IM, Newton N, Welner S: **Underuse of oral anticoagulants in atrial fibrillation: a systematic review.** *American Journal of Medicine* 2010(123):638-645.
40. Pugh D, Pugh J, Mead GE: **Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review.** *Age and ageing* 2011, **40**:675-683.
41. Campbell SM, Cantrill JA, Roberts D: **Prescribing indicators for UK general practice: Delphi consultation study.** *British Medical Journal* 2000, **321**(7258):425-428.
42. Campbell S, Hann M, Hacker J, Roland M: **Quality assessment for three common conditions in primary care: validity and reliability of review criteria developed by expert panels for angina, asthma and type 2 diabetes.** *Quality and Safety in Health Care* 2002, **11**:125 - 130.