PINCER trial: a cluster randomised trial comparing the effectiveness and cost-effectiveness of a pharmacist-led IT-based intervention with simple feedback in reducing rates of clinically important errors in medicines management in general practices

A report for the Department of Health Patient Safety Research Portfolio
February 2010

Anthony J Avery¹, Sarah Rodgers², Judith A Cantrill³, Sarah Armstrong⁴, Matthew Boyd⁵, Kathrin Cresswell⁶, Martin Eden³, Rachel Elliott⁶, Matthew Franklin⁶, Julia Hippsley-Cox¹, Rachel Howard⁷, Denise Kendrick³, Caroline J Morris⁸, Scott A Murray⁷, Robin J Prescott⁵, Koen Putman⁹, Glen Swanwick¹⁰, Lorna Tuersley³, Tom Turner¹⁰, Yana Vinogradova¹, Aziz Sheikh⁵

¹Division of Primary Care, University of Nottingham Medical School, Queen's Medical Centre, Nottingham, NG7 2UH, UK.
²Research and Evaluation Team, Quality and Governance Directorate, NHS Nottinghamshire County, Birch House, Southwell Road West, Mansfield, Nottinghamshire NG21 0HJ
³Drug Usage & Pharmacy Practice Group, School of Pharmacy & Pharmaceutical Sciences, University of Manchester, Oxford Road, Manchester, M13 9PL, UK
⁴Trent Research Design Service, Division of Primary Care, Tower Building, University Park, Nottingham, NG7 2RD, UK
⁵Centre for Population Health Sciences, University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG, UK
⁶Division for Social Research in Medicines and Health, The School of Pharmacy, University of Nottingham, University Park, Nottingham, NG7 2RD, UK
⁷School of Pharmacy, University of Reading, PO Box 226, Whiteknights, Reading, RG6 6AP, UK
⁸Department of Primary Health Care and General Practice, Wellington School of Medicine and Health Sciences, University of Otago, Mein Street, Wellington South, New Zealand
⁹Department of Medical Sociology and Health Sciences, Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel, Laarbeeklaan 103 B-1090 Brussel, Belgium
¹⁰Consumers in Research Advisory Group, c/o: Research and Evaluation Team, Quality and Governance Directorate, NHS Nottinghamshire County, Birch House, Southwell Road West, Mansfield, Nottinghamshire NG21 0HJ

Corresponding author:

Professor Anthony J Avery
Division of Primary Care,
University of Nottingham Medical School,
Queen’s Medical Centre,
Nottingham NG7 2UH

Email address: tony.avery@nottingham.ac.uk
Telephone: 0115 8230207 or 8230209
Fax: 0115 8230214

Competing interests: none
Foreword

Medication related errors are now recognised internationally as an important – potentially avoidable – source of morbidity and mortality. Although we have over recent years developed a good understanding of the frequency of and causes underpinning such errors, there is much less known about how effectively to reduce the risk of harm from such errors.

This report, summarising findings from the PINCER trial and related studies, is unique in that it provides a detailed account of how medication related errors can be reduced in an acceptable, effective and efficient manner. Its implications will, we hope, be profound for improving the safety of medicines management both in England, and beyond.

We have many people to thank who have contributed to the developments that have allowed us to arrive at this juncture and these individuals and organisations are duly acknowledged in the report. We would however in particular like to underscore our appreciation to the Patient Safety Research Portfolio, led by Professor Richard Lilford, for entrusting us with the resources to undertake this work, which we hope will aid clinicians in realising the truth in that enduring maxim ‘Primum non nocere’.

Tony Avery, Judith Cantrill and Aziz Sheikh on behalf of the PINCER Team
Nottingham, Manchester and Edinburgh
February 2010
Abstract

Title
PINCER trial: a cluster randomised trial comparing the effectiveness and cost-effectiveness of a pharmacist-led IT-based intervention with simple feedback in reducing rates of clinically important errors in medicines management in general practices

Authors

Background
Medication errors in general practice are an important source of potentially preventable morbidity and mortality. Building on previous descriptive, qualitative and pilot work, we sought to investigate the effectiveness, cost-effectiveness and likely generalisability of a complex pharmacist-led IT-based intervention aiming to improve prescribing safety in general practice.

Objectives
We sought to:

- Test the hypothesis that a pharmacist-led IT-based complex intervention using educational outreach and practical support is more effective than simple feedback in reducing the proportion of patients at risk from errors in prescribing and medicines management in general practice.
- Conduct an economic evaluation of the cost per error avoided, from the perspective of the National Health Service (NHS).
- Analyse data recorded by pharmacists, summarising the proportions of patients judged to be at clinical risk, the actions recommended by pharmacists, and actions completed in the practices.
- Explore the views and experiences of healthcare professionals and NHS managers concerning the intervention; investigate potential explanations for the observed effects, and inform decisions on the future roll-out of the pharmacist-led intervention
- Examine secular trends in the outcome measures of interest allowing for informal comparison between trial practices and practices that did not participate in the trial contributing to the QRESEARCH database.
Methods
Two-arm cluster randomised controlled trial of 72 English general practices with embedded economic analysis and longitudinal descriptive and qualitative analysis. Informal comparison of the trial findings with a national descriptive study investigating secular trends undertaken using data from practices contributing to the QRESEARCH database. The main outcomes of interest were prescribing errors and medication monitoring errors at six- and 12-months following the intervention.

Results
Participants in the pharmacist intervention arm practices were significantly less likely to have been prescribed a non-selective NSAID without a proton pump inhibitor (PPI) if they had a history of peptic ulcer (OR 0.58, 95%CI 0.38, 0.89), to have been prescribed a beta-blocker if they had asthma (OR 0.73, 95% CI 0.58, 0.91) or (in those aged 75 years and older) to have been prescribed an ACE inhibitor or diuretic without a measurement of urea and electrolytes in the last 15 months (OR 0.51, 95% CI 0.34, 0.78).

The economic analysis suggests that the PINCER pharmacist intervention has 95% probability of being cost effective if the decision-maker’s ceiling willingness to pay reaches £75 (6 months) or £85 (12 months) per error avoided.

The intervention addressed an issue that was important to professionals and their teams and was delivered in a way that was acceptable to practices with minimum disruption of normal work processes.

Comparison of the trial findings with changes seen in QRESEARCH practices indicated that any reductions achieved in the simple feedback arm were likely, in the main, to have been related to secular trends rather than the intervention.

Conclusions
Compared with simple feedback, the pharmacist-led intervention resulted in reductions in proportions of patients at risk of prescribing and monitoring errors for the primary outcome measures and the composite secondary outcome measures at six-months and (with the exception of the NSAID/peptic ulcer outcome measure) 12-months post-intervention. The intervention is acceptable to pharmacists and practices, and is likely to be seen as cost-effective by decision makers.
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<td>CHD</td>
<td>Coronary heart disease</td>
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<td>CTU</td>
<td>Clinical Trials Unit</td>
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<td>DMEC</td>
<td>Data Monitoring and Ethics Committee</td>
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<td>EMIS</td>
<td>Egton Medical Information Systems (the name of a GP computer system)</td>
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<tr>
<td>GP</td>
<td>General practitioner (or family practitioner)</td>
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<td>ICC</td>
<td>Intraclass correlation coefficient</td>
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<td>ICER</td>
<td>Incremental cost effectiveness ratio</td>
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<td>IMD</td>
<td>Index of Multiple Deprivation</td>
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<td>INR</td>
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<td>IT</td>
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<td>NHS</td>
<td>The UK National Health Service</td>
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<td>NPSA</td>
<td>National Patient Safety Agency</td>
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<td>NSAIDs</td>
<td>non-steroidal anti-inflammatory drugs</td>
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<td>ONS</td>
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<tr>
<td>OR</td>
<td>odds ratio</td>
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<td>Primary Care Trust</td>
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<td>PPI</td>
<td>proton pump inhibitor</td>
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<tr>
<td>SPSS</td>
<td>Statistical Package for the Social Sciences</td>
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<td>TFT</td>
<td>Thyroid Function test</td>
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<td>TPP</td>
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<td>TSC</td>
<td>Trial Steering Committee</td>
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<td>U&amp;E</td>
<td>Urea and electrolytes</td>
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Executive summary

Background

Medication errors occurring in general practice are an important cause of morbidity and mortality. UK Government reports have suggested that while there may still be a need to understand more about medication errors, the burden they pose and the reasons for their occurrence, the priority is now to find cost-effective, acceptable and sustainable ways of preventing patients from being harmed from such errors.

Aims

To determine the effectiveness, cost-effectiveness and acceptability of a complex pharmacist-led information technology (IT)-based intervention compared with simple feedback in reducing the proportion of patients at risk from hazardous prescribing and inadequate medication monitoring in general practice.

Objectives

We sought to:

1. Test the hypothesis that a pharmacist-led IT-based complex intervention using educational outreach and practical support is more effective than simple feedback in reducing the proportion of patients at risk from errors in prescribing and medicines management in general practice.

2. Conduct an economic evaluation of the cost per error avoided, from the perspective of the National Health Service (NHS), of the pharmacist-led intervention compared with simple feedback.

3. Explore the views and experiences of health care professionals and NHS managers concerning the intervention; investigate potential explanations for the observed effects, and inform the development of a model for future roll-out of the pharmacist-led intervention depending on whether or not it proved to be effective.

4. Analyse data recorded by pharmacists, summarising the proportions of patients judged to be at clinical risk, the actions recommended by pharmacists, which actions were undertaken and the time taken to: review cases, make recommendations, and implement actions.
5. Examine secular trends in the outcome measures of interest, allowing for informal comparison between trial practices and practices contributing to the QRESEARCH database that did not participate in the trial.

Methods

Main trial

**Research subject group:** Patients, aged 18 or over, registered with computerised general practices in two geographical regions in England.

**Design:** Parallel group, pragmatic, cluster randomised trial.

**Interventions:** Practices were randomised to either: (i) Computer-generated feedback (henceforth referred to as 'simple feedback'); or (ii) the pharmacist-led intervention comprising of computer-generated feedback, educational outreach and dedicated support.

**Primary outcome measures:** The proportion of patients in each practice at six- and 12-months post-intervention:
- With a computer-recorded history of peptic ulcer being prescribed non-selective non-steroidal anti-inflammatory drugs (NSAIDs) without also being prescribed a proton pump inhibitor (PPI)
- With a computer-recorded diagnosis of asthma being prescribed beta-blockers
- Aged 75 years and older receiving long-term prescriptions for angiotensin converting enzyme (ACE) inhibitors or loop diuretics without a recorded renal function and/or electrolytes result in the preceding 15 months.

The main analysis for the clinical outcomes used in the trial was undertaken using the six-month follow-up data.

**Secondary outcome measures:** These related to a number of other examples of errors in prescribing and medicines management and composite outcome measures for prescribing-related errors and monitoring-related errors.

**Sample size:** We estimated that 34 practices in each of the two treatment arms would provide at least 80% power (two-tailed alpha of 0.05) to demonstrate a 50%
reduction in error rates for each of the three primary outcome measures in the pharmacist-led intervention arm compared with a 11% reduction in the simple feedback arm.

**Economic analysis**

An economic evaluation was undertaken of the cost per error avoided, from the perspective of the English NHS, comparing the pharmacist-led intervention with simple feedback. Costs of delivering the interventions only were included in this analysis.

**Qualitative analysis**

Participants were key stakeholders involved in either the delivery or the reception of the intervention. They included trial pharmacists, practice staff, researchers and primary care trust (PCT) prescribing leads. Data were collected through a combination of one-to-one, digitally recorded, semi-structured telephone interviews, documents (including diaries and meeting notes) and focus groups. Analysis was thematic and was facilitated by the computer software NVivo7. Diffusion of innovation theory provided the theoretical framework.

**Analysis of data recorded by trial pharmacists**

Data were collected on the characteristics of patients and pharmacists. Pharmacists provided the following information for each of the cases identified to be at risk of medication error: i) whether, in their view, the patient was at clinical risk; ii) the actions they recommended, and iii) whether recommended actions were accepted by the practice. Data were analysed using descriptive statistics.

**QRESEARCH analysis of secular trends in outcome measures**

We conducted a cohort study utilising the patients registered with practices contributing to the UK-wide QRESEARCH database.

The study period was the three years between 01 January 2006 and 31 December 2008 and quarterly data were collected during this time period for the outcome
measures used in the main trial. Informal comparisons were made with data were collected in the PINCER trial.

Findings

Main trial

We deliberately over-recruited and 36 practices were randomly assigned to the simple feedback arm and 36 to the pharmacist intervention arm. The median list size of the practices was 6,438 and 6,295 respectively. The groups were reasonably well matched at baseline in terms of the proportion of patients at risk for primary and secondary outcome measures. Analysis of primary and secondary outcome measures at six- and 12-months post-intervention were adjusted for randomisation stratum, baseline medication-related problems, practice deprivation and training status.

Six-month follow-up data. Patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed a non-selective NSAID without a proton pump inhibitor (PPI) if they had a history of peptic ulcer (OR 0.58, 95% CI 0.38, 0.89), to have been prescribed a beta-blocker if they had asthma (OR 0.73, 95% CI 0.58, 0.91) or (in those aged 75 years and older) to have been prescribed an ACE inhibitor or diuretic without a measurement of urea and electrolytes (U&E) in the last 15 months (OR 0.51, 95% CI 0.34, 0.78). In terms of the a priori specified composite secondary outcome measures (one relating to prescribing problems; the other to monitoring problems), patients in the pharmacist intervention arm practices were significantly less likely to have a prescribing error (OR 0.71, 95% CI 0.59, 0.86) or a monitoring error (OR 0.56, 95% CI 0.44, 0.70). In terms of the other secondary outcome measures, patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed warfarin without an INR in the previous three months (OR 0.53, 95% CI 0.29, 0.95) or to have been prescribed amiodarone without a thyroid function test (TFT) in the last six-months (OR 0.57, 95% CI 0.36, 0.92). There were no significant differences between treatment arms for other secondary outcome measures.

12-month follow-up data. Patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed a beta-blocker if they had asthma (OR 0.78, 95% CI 0.63, 0.97) or (in those aged 75 years and older) to have
been prescribed an ACE inhibitor or diuretic without a U&E in the last 15 months (OR 0.63, 95% CI 0.41, 0.95). However, there was no longer a significant difference in terms of being prescribed a non-selective NSAID without a PPI for patients with a history of peptic ulcer (OR 0.91, 95% CI 0.59, 1.39).

In terms of the composite secondary outcome measures, patients in the pharmacist intervention arm practices were significantly less likely to have a prescribing error (OR 0.78, 95% CI 0.64, 0.94) or monitoring error (OR 0.64, 95% CI 0.51, 0.82). In terms of the other secondary outcome measures, patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed methotrexate without a full blood count (FBC) (OR 0.51, 95% CI 0.27, 0.99) or liver function tests (LFTs) in the last three months (OR 0.50, 95% CI 0.28, 0.91), or to have been prescribed lithium without a lithium level in the last three months (OR 0.50, 95% CI 0.29, 0.85). There were no significant differences between treatment arms in other secondary outcome measures.

Economic analysis

The cost per practice in the simple feedback arm was £93 at six months and £139 at 12 months (no range available). The median cost per practice in the pharmacist intervention arm was £968 (range: £329 - 2087) at six months and £1014 (range: £376 - £2133) at 12 months. The errors were combined into one composite outcome (total errors per practice) for the economic analysis. This analysis suggests that the PINCER pharmacist intervention has 95% probability of being cost effective if the decision-maker's ceiling willingness to pay reaches £75 (6 months) or £85 (12 months) per error avoided.

Analysis of data recorded by trial pharmacists

Pharmacists recorded their activities in relation to 2,038 potential errors in prescribing and medication monitoring for 1,946 patients (92 patients were identified by two outcome measures). 1465/2026 (72.2%) of these cases were judged to be at clinical risk of harm by the pharmacists. The percentage of cases judged to be at risk varied markedly between outcome measures (from 23.5% to 93.8%), but was over 80% for each of the primary outcome measures.
Pharmacists recommended 2,118 actions in 1518/2038 (74.5%) of cases identified by the electronic searches. Pharmacists’ recommendations were tailored to the outcome measures and individual patients. General practitioners (GPs) accepted 1,388 (65.5%) of pharmacists’ recommendations. The percentage of accepted recommendations varied markedly between outcome measures (from 35.8% to 88.1%). General practitioners also recommended alternative actions to those recommended by the pharmacists, therefore, 1,675 actions were completed in 1253/2038 (61.5%) of cases. The percentage of cases where actions were completed varied markedly between outcome measures (from 50% to 100%).

Pharmacists spent a median of 20 minutes (IQR 10, 30) reviewing and making recommendations, and implementing changes in each case.

**Qualitative analysis**

The qualitative study indicated that the intervention (or alternative models) might be enhanced if certain facilitating or inhibiting circumstances were addressed. In both intervention arms, these included motivational issues, attitudes, the extent of involvement of key individuals (e.g. practice manager, GPs), macro issues (especially local arrangements with secondary care) and organisational and planning issues. Additional aspects specific to the pharmacist intervention included the effective integration of the pharmacist in the practice, ongoing face-to-face contact and pharmacist job satisfaction. The involvement and support of PCTs was seen to be important both in terms of implementation and roll-out.

**QRESEARCH analysis of secular trends in clinical outcome measures**

Data from 438 QRESEARCH practices were available for analysis for all outcomes, except that for warfarin monitoring, where data were available from 233 practices.

QRESEARCH practices had a higher median list size than PINCER trial practices (7,711 versus 6,680), but both samples had similar age structures to the Office for National Statistics’ (ONS) figures for the UK for 2007.

Baseline figures for the PINCER trial practices and those from QRESEARCH practices at 1 April 2007 were similar for most of the outcome measures in terms of the proportions of patients at risk, and the proportions of at risk patients with an error.
For the outcome measures involving the monitoring of methotrexate and lithium, PINCER trial practices appeared to have higher proportions of at risk patients not receiving monitoring at baseline.

Examining changes in outcome measures in QRESEARCH practices over the time that the trial took place (median time points for data collection in PINCER trial practices at baseline versus six-months and 12-months follow-up), there were statistically significant reductions in the proportion of patients at risk of monitoring errors for all of the monitoring outcome measures. In contrast, there was a statistically significant increase in the proportion of patients with asthma receiving beta-blockers, even when patients with coronary heart disease (CHD) were excluded from the denominator. There were no statistically significant changes for the other prescribing error outcome measures.

Conclusions

Compared with simple feedback, the pharmacist led intervention resulted in reductions in proportions of patients at risk of prescribing and monitoring errors for the primary outcome measures and the composite secondary outcome measures at six-months and (with the exception of the NSAID/peptic ulcer outcome measure) also at 12-months post-intervention.

The PINCER pharmacist intervention has 95% probability of being cost effective if the decision-maker’s ceiling willingness to pay reaches £75 (6 months) or £85 (12 months).

Analysis of data recorded by trial pharmacists indicated that over 70% of cases identified by the outcome measures were considered at clinical risk (over 80% for each of the primary outcome measures). Pharmacists recommended actions in three quarters of cases identified by the electronic searches and these recommendations were tailored to the outcome measures and individual patients. General practitioners were reported to have accepted around two-thirds of pharmacists’ recommendations.

The qualitative analysis identified a number of factors that might have contributed to the success of the pharmacist-led intervention. These factors, which included
involvement of key individuals the practice, support for pharmacists in their roles and support from PCTs need to be considered in any roll-out of the intervention.

Baseline estimates of the frequency of errors were similar in PINCER trial practices and practices contributing to the national QRESEARCH database. Examining changes in outcome measures in QRESEARCH practices over the time that the trial took place showed statistically significant reductions in the proportion of patients at risk of monitoring errors for all of the monitoring outcome measures. Informal comparison with PINCER trial practices at six- and 12-months post-intervention suggest that any apparent improvements in monitoring outcome measures in the simple intervention arm practices may have been associated more with secular trends than the intervention itself.

Overall, the main trial and associated studies have shown the PINCER trial pharmacist intervention to be effective and cost-effective at reducing medication errors whilst also being acceptable to general practices.

**Trial registration:** Current controlled trials ISRCTN21785299
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Chapter 1: Introduction
1.1 Background

Medication errors in primary and secondary care are an important cause of morbidity and mortality, and a number of reports from the UK, USA and other countries have highlighted the need to reduce error rates to prevent patients suffering from avoidable harm\(^1\).\(^2\).

In England, publication by the Government of An organisation with a memory\(^1\) and Building a safer NHS for patients\(^3\) illustrates a strong commitment to reducing errors; the establishment of the National Patient Safety Agency (NPSA) was a clear further example of this commitment.

Recent UK Government reports have suggested that while there may still be a need to understand more about medication errors and the reasons for their occurrence\(^3\),\(^4\), the priority now must be to find effective, acceptable and sustainable ways of preventing patients from being harmed as a result of such errors.

1.1.1 Definition of error

In this study we have taken the definition of “medication error” used by the US National Co-ordinating Council for Medication Error Reporting and Prevention\(^5\) and the NPSA i.e.:

“A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professional, patient or consumer”.

This definition thus covers the whole of the medicines management process, from prescribing through to medication monitoring\(^4\).

1.1.2 Human error theory

To understand the causes of errors it is helpful to have an underlying theoretical framework. Reason's work in this field has had a major influence on our
understanding of the causes of medication errors. We have, in developing our interventions, taken account of human error theory in considering the causes of medication errors in general practice and the approaches that are most likely to reduce error rates.

1.1.3 Medication errors in general practice

This trial builds on our narrative and systematic reviews of the international literature on medication errors in primary care and on our own related empirical work. We have drawn on these experiences to identify and select outcome measures that are clinically important. This work has shown that the following groups of drugs are both commonly and consistently associated with medication errors that result in serious morbidity and, in some cases, mortality:

- Cardiovascular drugs (including angiotensin converting enzyme (ACE) inhibitors, beta-adrenoceptor blocking drugs and diuretics).
- Non-steroidal anti-inflammatory drugs (NSAIDs).
- Oral anticoagulants (i.e. warfarin).

We have also taken account of errors associated with the use of methotrexate, in view of warnings about this drug from the Chief Pharmaceutical Officer for England, and lithium and amiodarone because of their narrow therapeutic indices and nationally accepted guidance for regular blood test monitoring.

1.1.4 Underlying causes of medication errors

There have been a number of studies that have investigated the underlying causes of medication errors in hospitals. Leape et al, for example, identified 16 major systems failures from an analysis of 334 errors. The most common underlying problem was “failure of drug knowledge dissemination” (i.e. the doctor not knowing enough about the drug) and this accounted for 29% of errors. In contrast, Dean et al investigated the causes of 44 prescribing errors and found that slips in attention or failure to apply relevant rules were the commonest underlying causes.
There have been relatively few detailed analyses of the causes of medication errors in primary care although several studies have identified the points in the medicines management process where most errors occur\textsuperscript{10, 16}.

Gurwitz \textit{et al} found that the majority of preventable adverse drug events associated with community-based prescribing were due to errors in the prescribing and monitoring phases of pharmaceutical care\textsuperscript{16}. These findings were mirrored in the study of drug-related hospital admissions that was undertaken in Nottingham, UK\textsuperscript{10}, where 35\% of admissions were thought to be due to unsafe prescribing decisions and 26\% due to inadequate monitoring.

Our analysis of these studies suggest that in aiming to reduce rates of medication error in general practice the key factors that need to be addressed are:

- Ensuring that general practitioners (GPs) are aware of the risks of the drugs most commonly associated with adverse events.
- Ensuring that GPs recognise the hazards of rule violation, e.g. prescribing drugs that are contraindicated.
- Developing robust systems for monitoring patients on high-risk medications (including call and recall for blood tests) so that patients are not exposed to correctable hazards.

We have taken account of these issues in the design of the complex pharmacist-led information-technology (IT) based intervention for our trial.

1.1.5 The development of methods for identifying medication errors using GP computer systems

The use of clinical computer systems to identify patients with medication errors is a potentially powerful method for “error trapping” that may allow general practices to correct errors before patients are harmed.

We used MIQUEST\textsuperscript{17} software successfully in our pilot work to identify preventable drug-related morbidity in general practice\textsuperscript{18, 19}. This process involved writing precise computer queries that are capable of extracting the information required.
In our pilot work\textsuperscript{18, 19}, we found the processing of MIQUEST data very time-consuming. This is because it usually involves visiting general practices to extract data and then a considerable amount of work in processing and checking the data. Also, it does not produce user-friendly output for practices on individual patients who are deemed to be “at risk”.

We resolved these problems through the use of an additional type of software called Quest Browser (\texttt{www.tcr.i12.com}). This well-established software uses MIQUEST queries of GP computer systems, but has several advantages over using MIQUEST alone. Firstly, it can produce user-friendly feedback at the practice-level on patients with medication errors (or any other clinical problem). Secondly, output from Quest Browser can be imported straight into a database without the need for additional manipulation. Thirdly, Quest Browser has a facility (called Quest Browser Central) whereby, with agreement from the practices and research ethics committees, linked-anonymised data can be sent to researchers in an encrypted form via the Internet. This reduces the number of visits that researchers need to make to practices and helps with the timely collection of large volumes of data.

### 1.1.6 Development of the complex pharmacist-led IT-based intervention

Informed by the Medical Research Council’s (MRC) framework for complex interventions\textsuperscript{20}, we took account of the theoretical considerations outlined above, along with pilot work, to develop the pharmacist-led IT-based intervention. This is described in more detail below (see “pharmacist-led intervention” section).

### 1.2 Aims of the study

To determine the effectiveness, cost-effectiveness and acceptability of a complex pharmacist-led information technology (IT)-based intervention compared with simple feedback in reducing the proportion of patients at risk from hazardous prescribing and inadequate medication monitoring in general practice.
1.3 Specific objectives

We sought to:

1. Test the hypothesis that a pharmacist-led IT-based complex intervention using educational outreach and practical support is more effective than simple feedback in reducing the proportion of patients at risk from errors in prescribing and medicines management in general practice.

2. Conduct an economic evaluation of the cost per error avoided, from the perspective of the National Health Service (NHS), of the pharmacist-led intervention compared with simple feedback.

3. Examine secular trends in the outcome measures of interest allowing for informal comparison between trial practices and practices contributing to the QRESEARCH database that did not participate in the trial.

4. Analyse data recorded by pharmacists, summarising the proportions of patients judged to be at clinical risk, the actions recommended by pharmacists, which actions were undertaken and the time taken to: review cases, make recommendations, and implement actions.

5. Explore the views and experiences of health care professionals and NHS managers concerning the intervention; investigate potential explanations for the observed effects, and inform decisions on the future roll-out of the pharmacist-led intervention depending on whether or not it proved to be effective.
Chapter 2: Main trial
2.1 Introduction

In this chapter we present the methods, results and discussion for the main trial.

2.2 Methods

2.2.1 Trial design

We conducted a two-arm pragmatic cluster randomised trial. Trial practices received either i) computerised feedback on patients identified to be at risk from potentially hazardous prescribing and medicines management (simple feedback') or ii) a complex pharmacist-led IT-based intervention in addition to computerised feedback.

2.2.2 Eligibility of general practices for entering the trial

2.2.2.1 Inclusion criteria:

- English NHS general practices within a 50 mile radius of Manchester and Nottingham.
- Practices within NHS primary care trusts (PCTs) that agreed to be involved in the study.
- Practices that were laboratory-linked (or had other reliable systems for recording blood test results on the practice computer system) for at least 15 months prior to the time of baseline data collection (being laboratory-linked means having all blood test results relayed electronically to the practice so that these can be downloaded into patients’ computerised records).

2.2.2.2 Exclusion criteria:

- Practices that stated they did not routinely record morbidities such as asthma or peptic ulcer on patients’ computerised records.
- Practices not routinely using their computers to record prescriptions issued.
• Practices that were intending to change their GP computer systems to that of a different supplier which was not Quest Browser compatible during the course of the study.

• Practices in PCTs that were undertaking interventions that might overlap with our intervention.

• Practices that were involved in the pilot study for the trial.

• Practices that already had a dedicated practice pharmacist (over and above that provided by their PCT).

• Practices that expected major changes in list size (numbers of registered patients) during the course of the study, either because of the splitting up of the practice, merger with other practices or any other reason for a large influx or loss of patients.

### 2.2.3 Recruitment of general practices

We wrote to 240 general practices in PCTs in Nottinghamshire, Staffordshire and Central and Eastern Cheshire, England informing them of the study. Where practices expressed an interest in participating we arranged a face-to-face meeting at which the study was explained in more detail. A member of the practice team then signed a consent form, on behalf of the practice, if the practice decided to participate. Copies of letters to general practices, information leaflets and consent forms are provided in Appendix 1.

#### 2.2.3.1 Patients

For the main trial it was not necessary to recruit individual patients because data were extracted electronically and no patient-identifiable data left practices or was accessible to research staff. Nevertheless, practices were provided with lists of patients identified by the computer searches used in the trial. In addition, patients were recruited for the economic analysis and details of this are provided in Chapter 3: Pincer economic analysis.
2.2.4 Interventions

We did not feel it would be appropriate to randomise practices to a no intervention control arm. This is because it would have meant identifying patients at risk from medication errors with there being no prospect of these being rectified.

We decided on a two arm study with one receiving simple feedback and the other receiving a complex pharmacist-led intervention.

2.2.4.1 Simple feedback

Those practices randomly allocated to this arm received computerised feedback on patients identified to be at risk from potentially hazardous prescribing and medicines management along with brief written educational materials explaining the importance of each type of error (in terms of the evidence-base and risks associated with each error (see Appendix 2). This information was given to a nominated member of the general practice (usually the practice manager) after baseline data had been collected from the practice computer system, using Quest Browser software.

Practices in the simple feedback arm were asked to try to make any changes to patients' medications within a 12 week (intervention) period following the baseline data collection.

2.2.4.2 Pharmacist intervention

Those practices randomly allocated to this arm received simple feedback and in addition, had a complex pharmacist-led IT-based intervention.

First, the trial pharmacists arranged to meet with members of the practice team to discuss the computer-generated feedback on patients with medication errors. All doctors were encouraged to attend this meeting along with at least one member of the nursing staff, the practice manager and at least one member of the reception staff.
Before the meeting, wherever possible, all relevant members of staff were provided with a brief summary of the objectives of the pharmacist-led intervention and a summary of the findings from the computer search.

At the meeting the pharmacists were asked to use the following approach derived from the principles of educational outreach\textsuperscript{21} while also taking account of human error theory\textsuperscript{6}:

- Establish professional credibility by explaining their own background in clinical pharmacy and their affiliation with either the University of Manchester or University of Nottingham (depending on the site they are working from).
- Take a non-judgemental approach in all discussions with members of the practice team.
- Outline the findings from the computer search.
- Explore the views of team members about the findings.
- Investigate the baseline knowledge of team members regarding the importance of each of the errors.
- Provide clear, concise, evidence-based materials on each of the errors, encouraging active participation by team members.
- Explore the views of team members on the underlying causes of the medication errors (using root-cause analysis techniques\textsuperscript{22} where appropriate).
- Explain their availability to work part-time with the practice over the following 12 weeks to:
  - Help take corrective action in individual patients with medication errors.
  - Help improve the systems operating in the practice in order to prevent future errors.
- Encourage the team to agree on an action plan with clear objectives.
- Ask for a member of the practice team to volunteer to liaise with the pharmacist over arrangements for making changes to individual patients’ medication and introducing changes to systems within the practice.
- Ask the practice to agree to a follow-up meeting within four to six weeks of the initial meeting.

Following this initial meeting, the pharmacists used a range of techniques to help correct the medication errors that had been identified and prevent future medication
errors. They were asked to work closely with the practice team member assigned to provide liaison with other members of the practice.

We envisaged that the pharmacists would be taking any, or all, of the following approaches to deal with patients identified to be at risk from hazardous prescribing and medicines management:

- Inviting patients into the surgery for a prescription review with the pharmacist, or a member of the general practice team, with the aim of correcting medication errors, e.g.
  - For patients with a past history of peptic ulcer who were being prescribed a non-selective NSAID to either:
    - Stop the NSAID.
    - Add a proton pump inhibitor (PPI).
    - Consider using a selective inhibitor of cyclo-oxygenase-2 (COX-2 inhibitor), while recognising concerns about these drugs in relation to cardiovascular risk.
  - For patients with asthma who were being prescribed a beta-blocker:
    - In those taking beta-blocker eye drops for glaucoma, to change to an alternative preparation.
    - In those taking oral beta-blockers, to carefully consider the risks and benefits of the medication and, where appropriate, slowly withdraw the drug and replace it with an alternative preparation.
  - For patients who were being prescribed methotrexate without instructions that it should be taken weekly:
    - Carefully check the dosage instructions.
    - Convey this information to the patient verbally and in writing.
    - Ensure that accurate dosage instructions were entered onto the computer system so that these would be printed out when the prescription was next issued.
- Inviting the following groups of patients to have a blood test:
  - Those aged 75 years and older being prescribed ACE inhibitors or loop diuretics who had not had a blood test to check renal function and electrolytes within the previous 15 months.
Those being prescribed methotrexate who had not had a full blood count or liver function test within the previous three months.

Those being prescribed warfarin who had not had an INR test within the previous 12 weeks (this is the maximum interval recommended by the British National Formulary (BNF)\textsuperscript{13}).

Those being prescribed lithium who had not had a lithium level recorded within the previous 3 months.

We envisaged the pharmacists taking the following approaches to try to prevent future instances of hazardous prescribing and medicines management, having agreed these approaches with the practice teams:

- **In relation to hazardous prescribing:**
  - Meeting up with any doctors unable to attend the initial meeting in order to provide educational outreach.
  - Reinforcement of educational messages provided at the initial meeting by repeating these messages at future meetings.
  - Encouraging doctors to take heed of contraindication messages on their computer systems.

- **In relation to inadequate blood-test monitoring:**
  - Encouraging practices to use their computer systems to automatically recall patients for a blood test if they had gone beyond a pre-specified time.
  - To use routine prescription reviews as the trigger for ensuring that if patients needed blood tests, these were arranged.

Throughout the intervention period the pharmacists were asked to maintain regular contact with the practice liaison member of staff to facilitate changes and discuss, and resolve, any difficulties encountered. The pharmacists were asked to keep a written log of changes made in relation to patients with medication errors, and changes made to practice systems.

Towards the end of the intervention period, the pharmacists were asked to undertake a further check of patients’ computer records to provide feedback to practices on progress made in correcting medication errors. They were asked to arrange a final meeting with members of the practice team to:
• Provide feedback on progress made in dealing with patients identified to be at risk from potentially hazardous prescribing and medicines management.
• Provide feedback on changes made to safety systems.
• Reinforce key educational messages.
• Agree on an action plan for the practice to continue to work towards reducing instances of hazardous prescribing and medicines management.

2.2.5 Allocation of trial interventions

The practice was the unit of allocation. Consenting practices were stratified by centre (two strata: Manchester and Nottingham) and the size of the practice population (three strata: <2500, 2500-6000, >6000) and randomly allocated within strata (1:1 ratio) to one of the two intervention arms.

The reason for stratifying by centre was to help ensure an even distribution of practices allocated to each of the intervention groups within each centre. The reason for stratifying by size of the patient population in each general practice was because a trial of educational outreach suggested that the larger the practice the more difficult it is to make changes to practice\(^{23}\).

Block randomisation, using non-predictable block sizes of either two or four, was used to ensure a similar number of practices in each arm. Practices were centrally randomised using the independent Internet-based randomisation service provided by the Clinical Trials Unit (CTU) at the University of Nottingham. Access to the sequence was confined to the CTU Data Manager (who was independent from the study team). The sequence of treatment allocations was concealed until all data analyses had been completed.

2.2.6 Outcome measures

In identifying outcome measures for our proposed trial we took account of a number of factors. We decided that the outcome measures needed to be:
Examples of hazardous prescribing or inadequate medication monitoring that are important in terms of morbidity.

Detectable by interrogation of GP computer systems.

Limited in number so that it would be feasible for general practices and pharmacists to make potentially major changes in error rates.

In deciding on examples of hazardous prescribing or inadequate medication monitoring that are important in terms of morbidity we took into account:

- A number of studies on preventable drug-related morbidity.7-9
- Literature in relation to specific examples of hazardous prescribing or inadequate medication monitoring (see Appendix 2).
- Our own work on the development of indicators of preventable drug-related morbidity.10-12
- Warnings from the Committee on Safety of Medicines (CSM) in the UK (http://medicines.mhra.gov.uk/home).

A key factor in deciding on our primary outcome measures was that the prevalence rate of the relevant medication errors needed to be great enough that a clinically important change could be detected using a number of practices that is feasible within the funding allocated to the study.

Outcome measures were measured at the following two time points:

- Six-months after the end of the intervention period.
- 12-months after the end of the intervention period.

A summary of the main outcome measures is given in Table 1. The measures are described in more detail in section 2.2.6.
Table 1. Summary of main outcome measures used in the trial

<table>
<thead>
<tr>
<th>Outcome measure number</th>
<th>Brief description of outcome measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Patients with a history of peptic ulcer who have been prescribed a non-selective NSAID</td>
</tr>
<tr>
<td>2</td>
<td>Patients with asthma who have been prescribed a beta-blocker</td>
</tr>
<tr>
<td>3</td>
<td>Patients aged 75 years and older who have been prescribed an ACE inhibitor or a loop diuretic long-term who have not had a computer-recorded check of their renal function and electrolytes in the previous 15 months</td>
</tr>
<tr>
<td>4</td>
<td>Proportions of women with a past medical history of venous or arterial thrombosis who have been prescribed the combined oral contraceptive pill</td>
</tr>
<tr>
<td>5</td>
<td>Patients receiving methotrexate for at least three months who have not had a recorded full blood count (Outcome 5a) and/or liver function test (Outcome 5b) within the previous three months</td>
</tr>
<tr>
<td>6</td>
<td>Patients receiving warfarin for at least three months who have not had a recorded check of their INR within the previous 12 weeks</td>
</tr>
<tr>
<td>7</td>
<td>Patients receiving lithium for at least three months who have not had a recorded check of their lithium levels within the previous three months</td>
</tr>
<tr>
<td>8</td>
<td>Patients receiving amiodarone for at least six-months who have not had a thyroid function test within the previous six-months</td>
</tr>
<tr>
<td>9</td>
<td>Patients receiving prescriptions of methotrexate without instructions that the drug should be taken weekly</td>
</tr>
<tr>
<td>10</td>
<td>Patients receiving prescriptions of amiodarone for at least one month who are receiving a dose of more than 200mg per day</td>
</tr>
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</table>
2.2.6.1 Primary outcome measures

We used the following primary outcome measures based on proportions of:

1. Patients with a history of peptic ulcer who had been prescribed a non-selective NSAID:
   - More specifically, those with a computer-coded diagnosis of peptic ulcer disease, at least six-months prior to data collection, who had a computer record for one or more prescriptions for a non-selective NSAID in the six-months prior to data collection who have not also had a prescription for a PPI within that six-month period.
   - The denominator for this outcome measure was patients with a computer-coded diagnosis of peptic ulcer disease, at least six-months prior to data collection, who had not also had a prescription for a PPI in the six-months prior to data collection.

2. Patients with asthma who had been prescribed a beta-blocker:
   - More specifically those with a computer-coded diagnosis of asthma, at least six-months prior to data collection, who had a computer record of one or more prescriptions for a beta-blocker (oral preparations or eye drops) in the six-months prior to data collection.
   - The denominator for this outcome measure was patients with a computer-coded diagnosis of asthma, at least six-months prior to data collection.

3. Patients aged 75 years and older who had been prescribed an ACE inhibitor or a loop diuretic long-term (see below) who had not had a computer-recorded check of their renal function and electrolytes in the previous 15 months:
   - More specifically, long-term prescribing implies a first prescription for an ACE inhibitor or a loop diuretic at least 15 months before the time of data collection and at least one prescription in the six-months beforehand.
   - The denominator for this outcome measure was patients aged 75 years and older who had been prescribed an ACE inhibitor or a loop diuretic long-term according to the above definition.
2.2.6.2 Secondary outcome measures

We collected data on a number of secondary outcome measures relating to contraindicated prescribing, inadequate monitoring and dosing problems. We also created composite outcome measures (see below) for prescribing problems and for monitoring problems.

Contraindicated prescribing:

4. Proportions of women with a past medical history of venous or arterial thrombosis who had been prescribed the combined oral contraceptive pill:
   - More specifically, women with a history of venous or arterial thrombosis recorded at least six-months prior to data collection who had a computer-recorded prescription for the combined oral contraceptive pill in the six-months prior to data collection.

Inadequate monitoring:

These outcomes were based on proportions of:

5. Patients receiving methotrexate for at least three months who had not had a recorded full blood count (FBC) and/or liver function tests (LFTs) within the previous three months:
   - More specifically
     - 5a: patients with one or more prescriptions for methotrexate recorded on computer three to six-months prior to data collection and in the three months prior to data collection who had not had a computer-recorded FBC within the previous three months.
     - 5b: patients with one or more prescriptions for methotrexate recorded on computer three to six-months prior to data collection and in the three months prior to data collection who had not had a computer-recorded LFT within the previous three months.

6. Patients receiving warfarin for at least three months who had not had a recorded check of their INR within the previous 12 weeks:
• More specifically, patients with one or more prescriptions for warfarin recorded on computer three to six-months prior to data collection and in the three months prior to data collection who had not had a computer-recorded INR within the previous three months.

7. Patients receiving lithium for at least three months who had not had a recorded check of their lithium levels within the previous three months:
   • More specifically, patients with one or more prescriptions for lithium recorded on computer three to six-months prior to data collection and in the three months prior to data collection who had not had a computer-recorded lithium level within the previous three months.

8. Patients receiving amiodarone for at least six-months who had not had a thyroid function test (TFT) within the previous six-months:
   • More specifically, patients with one or more prescriptions for amiodarone recorded on computer six to 12-months prior to data collection and in the three months prior to data collection who had not had a computer-recorded TFT within the previous six-months.

*Dosing problems:*

These outcomes were based on proportions of:

9. Patients receiving prescriptions of methotrexate without instructions that the drug should be taken weekly:
   • More specifically, patients with one or more prescriptions for methotrexate recorded on computer within the three months prior to data collection who did not have the term “weekly” or “week” in the dosage instructions field of the latest prescription for the drug.

10. Patients receiving prescriptions of amiodarone for at least one month who were receiving a dose of more than 200mg per day:
    • More specifically, patients with evidence of being prescribed amiodarone 200mg tablets for more than one month in the three months prior to data collection, who do not have the term “once daily” (or similar) in the dosage instructions field for the drug.
Additional outcome measure relating to prescription of beta-blockers to patients with asthma

This secondary outcome measure was based on proportions of patients with asthma who did not have coronary heart disease (CHD) and had been prescribed a beta-blocker:

- More specifically those with a computer-coded diagnosis of asthma and no record of CHD, at least six-months prior to data collection, who had a computer record of one or more prescriptions for a beta-blocker (oral preparations or eye drops) in the six-months prior to data collection.
- The denominator for this outcome measure was patients with a computer-coded diagnosis of asthma and no computer-coded record of CHD, at least six-months prior to data collection.

Composite outcome measures

As outlined in our published trial protocol, we also used data from the above outcome measures to create a series of composite outcome measures for prescribing- and monitoring-related problems.

The composite prescribing outcome is based on proportions of patients at risk of at least one prescribing problem who had at least one prescribing problem:

- More specifically, patients appearing in the numerator for one or more of Outcomes 1, 2 and 4 (as shown in Table 1) were counted as numerators for this composite outcome measure.
- The denominator was patients who were identified to be at risk of one or more of Outcomes 1, 2 and 4 (as shown in Table 1).

The composite monitoring outcome was based on proportions of patients at risk of at least one monitoring problem who had at least one monitoring problem:

- More specifically, patients appearing in the numerator for one or more of Outcomes 3, 5a and/or 5b, 6, 7 and 8 (as shown in Table 1).
- The denominator was patients who were identified to be at risk of one or more of Outcomes 3, 5, 6, 7 and 8 (as shown in Table 1).
It should be noted that patients appeared only once in the denominator in relation to Outcome 5, but they appeared in the numerator if either FBC or LFT had not been recorded.

2.2.7 Ascertainment of outcomes

During the first three months of the study, we worked with TCR Nottingham, the company that produce Quest Browser software (www.tcrnottingham.com). We developed computerised queries that would produce precisely the same types of data as we used in our pilot study of primary outcome measures that used QRESEARCH practices (www.qresearch.org). We also worked with the company to produce the outputs needed for the secondary outcome measures.

For each practice agreeing to be involved in the trial, Quest Browser software had to be installed on their clinical computer system. At the time of installation of the software, a search of the GP computer system, using Quest Browser was undertaken to provide anonymised baseline data and details of individual patients at risk from hazardous prescribing and medicines management.

Anonymised and encrypted data pertaining to the computerised primary and secondary outcomes measures were sent via the Internet to secure computers at the University of Nottingham and at TCR Nottingham. Using Quest Browser Central software the pseudo-anonymised data were automatically imported into an Access database along with a unique code identifying the practice and a unique code for each patient.

Further data were collected at six- and 12-months after the completion of the 12-week intervention period in practices in each arm of the trial.

2.2.7.1 Issues concerning ascertainment of secondary outcome measures

Over the course of the study we identified issues concerning three of our secondary outcome measures.
As already noted, for Outcome 6, we identified seven practices that kept records of INR results separate from their main practice computer system and thus appeared to have very high proportions of patients not having INRs checked according to the computer searches we have used in our study. As stated in our published trial protocol\textsuperscript{24}, we have excluded these practices from the analysis of this outcome measure.

For Outcome 9, during the course of our study, the NPSA required all GP computer systems to introduce methods of ensuring that electronic prescriptions for methotrexate gave instructions that the medication should be taken weekly\textsuperscript{25}. Since this change was introduced our computer searches were unable, for all patients, to capture the text used to confirm the dosage instructions. Having obtained the data, however, we judged that there were sufficient numbers of patients with dosage instructions present to allow for an analysis to be undertaken.

For Outcomes 9 and 10, we found that for the 11 practices that used The Phoenix Partnership (TPP) computer system, we were unable to extract information on dosage instructions. This meant that we were not able to report on these outcome measures for the practices that use this software system.

\subsection*{2.2.8 Adverse events}

The protocol for dealing with serious adverse events that might occur in study practices in patients identified by the PINCER trial outcome measures is shown in Appendix 3.

\subsection*{2.2.9 Sample size}

Our sample size calculations were based on the assumption that for the proportion of patients fulfilling the criteria for any one of our primary outcome measures, there would be a maximum 11\% reduction in the simple feedback arm and a 50\% reduction in the pharmacist intervention arm.
The suggested 11% reduction in the simple feedback arm is the equivalent to the 75% centile for changes observed as a result of audit and feedback in a Cochrane systematic review available at the time that we did our sample size calculations\textsuperscript{26}.

The suggested 50% reduction in the pharmacist intervention arm of the trial is based on extrapolation from our pilot studies\textsuperscript{18, 19} and findings from systematic reviews and other studies that, at the time of applying for funding for our study, showed that:

- Pharmacist-led interventions can lead to resolution of medication-related problems in 55-93% of patients\textsuperscript{27-31}.
- Educational outreach is a moderately powerful tool for changing professional behaviour\textsuperscript{32}.
- Multifaceted interventions aimed at different barriers to change are more effective than single interventions\textsuperscript{33}.

Separate sample size calculations were performed for each of three primary outcome measures (see Table 2). Sample sizes unadjusted for clustering were calculated using the software package nQuery Advisor\textsuperscript{®} version 6.0\textsuperscript{34}. Sample sizes were inflated to adjust for clustering using ICCs and average cluster sizes estimated from QRESEARCH practices, as described below and shown in Table 2.

Data from 43 general practices contributing anonymous clinical data to the QRESEARCH research database (www.qresearch.org) were used to describe prevalence rates of asthma and peptic ulcer disease and to estimate the median proportions for each of our primary outcome measures. The intracluster correlation coefficients (ICCs) used in the calculation of the design effect (to inflate the sample sizes to adjust for the cluster design)\textsuperscript{35} were as follows:

- 0.01082 for patients with a history of peptic ulcer who had been prescribed a non-selective NSAID (excluding those that were also in receipt of PPIs, which would protect against the risks from NSAIDs);
- 0.010657 for patients with asthma who had been prescribed a beta-blocker;
- 0.00952 for patients aged 75 years and older who have been prescribed an ACE inhibitor or a loop diuretic long-term who had not had a computer-recorded check of their renal function and electrolytes in the previous 15 months.
The calculation shown in Table 2 indicates that we needed at least 66 practices to detect a difference between an 11% reduction in error rate in the simple feedback arm and a 50% reduction in the intervention arm for each of our three primary outcome measures.

On the basis of these calculations, we decided to aim to recruit at least 68 practices. With 34 practices in each of the two intervention arms, we would have at least 80% power (two-tailed alpha of 0.05) to demonstrate a 50% reduction in rates of hazardous prescribing and medicines management in the pharmacist-led arm compared with 11% in the simple feedback arm.

Table 2. Sample size calculations for the three primary outcome measures assuming an 11% reduction in error rates for the simple feedback group and a 50% reduction in error rates for the intervention group

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Patients with a history of peptic ulcer who have been prescribed a non-selective NSAID</th>
<th>Patients with asthma who have been prescribed a beta-blocker</th>
<th>Patients aged 75 years and older prescribed an ACE inhibitor or a loop diuretic long-term without a check of their renal function and electrolytes in the previous 15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median error rate* (Interquartile range)</td>
<td>5.76% (3.76% - 7.85%)</td>
<td>1.90% (1.27% - 3.08%)</td>
<td>19.80% (15.13% - 32.69%)</td>
</tr>
<tr>
<td>Error rate in control group (assuming 11% reduction)</td>
<td>5.13%</td>
<td>1.69%</td>
<td>17.62%</td>
</tr>
<tr>
<td>Error rate in intervention group (assuming 50% reduction)</td>
<td>2.88%</td>
<td>0.95%</td>
<td>9.90%</td>
</tr>
<tr>
<td>Intraclass Correlation Coefficient (ICC)*</td>
<td>0.01082</td>
<td>0.00657</td>
<td>0.00952</td>
</tr>
<tr>
<td>Cluster size</td>
<td>63</td>
<td>439</td>
<td>105</td>
</tr>
<tr>
<td>Inflation factor</td>
<td>1.7</td>
<td>3.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Total number of practices required</td>
<td>64</td>
<td>66</td>
<td>12</td>
</tr>
</tbody>
</table>

*Estimated using data obtained from 43 general practices contributing to the QRESEARCH database (www.qresearch.org)

No adjustments were made for multiple endpoints. Instead, as described in our published trial protocol24 we decided that findings would be interpreted with caution in view of the number of statistical tests undertaken.
2.2.10 Compliance

We recognised that it can be a challenge to encourage general practices to engage in trials. However, as the intervention involved either simple feedback or feedback and the provision of a pharmacist to work with the practices, we did not expect non-compliance with the intervention to be a large problem. In addition, from our experience of the pilot study and of conducting previous trials, we believed that the risks of non-compliance would be minimised by providing practices with clear information on what the study involved, providing access to members of the research team to answer queries and address problems experienced by the practices, and support from the PCTs.

2.2.11 Loss to follow-up

We did not envisage practices dropping out of the study once they had agreed to take part. Nevertheless, at the outset we stressed to the practices the importance of allowing us to collect follow-up data, even if the practice had not engaged fully in one of the interventions. As outcome data collection required minimal input from practices, we did not foresee major problems.

Some patients were likely to have moved practices and some will have died within the intervention period. However, we were of the opinion that this was unlikely to have had a large impact on the proportion of patients with errors at follow-up, unless leaving the practice or death was differentially related to medication error. This was considered unlikely because the number of deaths attributable to the medication errors we were studying was likely to have been small during the course of the study. Nevertheless, where patient consent was given, we followed up patients who died by viewing their electronic medical records up until the time of death, and supplemented this by viewing paper-based records containing details of contacts with secondary care. In addition, at the end of the study, we asked general practices to inform us of the number of patients identified in the baseline searches that had left the practice or died within 12-months of these baseline searches (see Appendix 4).
### 2.2.12 Withdrawal of patients from the study

Informed consent of patients was requested to allow the research team to access medical records for the purposes of the economic study (see section 3.2.1). Informed consent was not required for the analysis of the main outcomes as these were obtained from anonymised computer searches of all “at risk” patients in the general practices recruited to the study. Therefore, withdrawal of patients was not an issue for the analysis of the main outcome data.

### 2.2.13 Examining potential differences in mortality between the treatment arms

In July 2009 we sent a letter to participating practices asking them to tell us how many of the patients identified to be at risk from their medicine from the computer searches had, in the 15 months following the start of the intervention, either left the practice or died. An example of the letter sent is shown in Appendix 4.

Data from practices responding to the letter were entered into SPSS and proportions of patients dying in each of arm of the trial were described. Potential differences were examined using non-parametric statistics after adjusting for patients that had left the practices within 15 months following the start of the intervention.

### 2.2.14 Data processing and data cleaning for the trial outcome measures

Data from the general practices for each data collection time point were collated into separate Access databases by TCR Nottingham for each of the primary and secondary outcome measures. These databases contained no information about which arm of the trial the practices belonged to. This meant that any further data processing and data cleaning was done blind to the intervention arm.

We held separate copies of the anonymised data for each time point, outcome measure and practice at the University of Nottingham in order to cross-check anomalies.

For each of the outcome measures we ran a number of data-checks to help ensure that:
Data from all the practices were present for all time points (or, if data were not present, a cross-check against the original data revealed no cases).

Patients included in the outcome measures were all registered with the general practices for sufficient time to fulfill the criteria for being included.

The ages of patients included in the outcome measures fulfilled the criteria for being included in the relevant outcome measure.

The morbidity Read codes, and dates for these codes, fulfilled the criteria for the relevant outcome measure.

The drug codes, and dates for these codes, fulfilled the criteria for the relevant outcome measure.

Cases labelled as numerators fulfilled the criteria for being numerators.

Cases labelled as non-numerators were correctly labelled as non-numerators, whilst also fulfilling the criteria for being denominators.

For the monitoring outcome measures we ran data checks to help ensure that:

- The monitoring Read codes fulfilled the criteria for the relevant monitoring outcome measures.
- The dates of the latest relevant monitoring codes (where available) were used correctly to assign the patient to being either a numerator or denominator.

In relation to the combined hormonal contraceptive outcome measure (Outcome 4, see Table 1), we checked that all patients were female.

In relation to the methotrexate dosing instructions outcome measure (Outcome 9, see Table 1) we included only those patients that had dosing instructions recorded (i.e. records with blank dosage instructions fields were excluded – see section 2.2.7.1).

For the prescribing composite outcome measures we combined data from Outcomes 1, 2 and 4 (see Table 1 and section 2.2.6.2) ensuring that, by using patients’ unique pseudo-anonymised codes, they were not double counted. We then identified patients who appeared one or more times as numerators in order to calculate the proportion of patients with one or more prescribing problems from those at risk of one or more prescribing problems. For example, if a patient appeared as a numerator in any of Outcomes 1, 2 and 4 they would appear as a numerator in the composite outcome measure.
For the monitoring composite outcome measures we combined data from Outcomes 3, 5, 6, 7 and 8 (see Table 1 and section 2.2.6.2) ensuring that, by using patients' unique pseudo-anonymised codes, they were not double counted. We then identified patients who appeared one or more times as numerators in order to calculate the proportion of patients with one or more monitoring problems from those at risk of one or more monitoring problems.

2.2.15 Statistical analysis

Data analysis, using the following analysis plan, was undertaken blind to treatment arm allocation (i.e. the treatments were identified only as X and Y until analysis was complete). The main analysis for the clinical outcomes used in the trial was undertaken using the six-month follow-up data.

2.2.15.1 Descriptive analyses

Characteristics of practices and patients were described using frequencies and percentages for categorical variables, and means and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous variables, dependent on the normality of their distribution. Practice and patient characteristics at baseline were compared informally between treatment arms.

Describing baseline characteristics of patients and practices

The following characteristics are described by treatment arm:

- Patient age and gender.
- Practice list size (median and IQR, or mean and SD if normally distributed).
- Practice population by age group (number and %).
- Practice deprivation using the Index of Multiple Deprivation (IMD) 200436 (median and IQR, or mean and SD if normally distributed) Note this was calculated by multiplying the proportion of the total list size living in each Lower Layer Super Output Area (LSOA) by IMD 2004 LSOA level score and then summing these across all LSOAs in which patients registered at the practice live.
- Practice training status (%).
- Practice Quality and Outcomes Framework (QOF) medicines management. indicator points and total QOF points\(^{37}\) if available (Mean (SD) or median (IQR) dependent on distributions).

*Describing baseline prevalence of medication-related problems*

The following are described using the numerator, denominator and percentage by treatment arm, at patient level:

- **Primary outcome measures:**

  1. Patients with a history of peptic ulcer prescribed an NSAID without a PPI (numerator) / Patients with a history of peptic ulcer without a PPI (denominator).

  2. Patients with asthma prescribed a beta-blocker (numerator) / Patients with asthma (denominator).

  3. Patients aged ≥75 on long term ACE inhibitors or diuretics without urea and electrolyte monitoring in the previous 15 months (numerator) / Patients aged ≥75 on long term ACE inhibitors or diuretics (denominator).

- **Secondary outcome measures:**

  2a. Patients with asthma and not CHD prescribed a beta-blocker (numerator) / Patients with asthma and not CHD (denominator).

  4. Female patients with a history of venous or arterial thromboembolism and arterial thrombosis prescribed combined oral contraceptives (numerator) / Female patients with a history of venous or arterial thromboembolism and arterial thrombosis (denominator).

  5a. Patients prescribed methotrexate for ≥3 months without a FBC in the last three months (numerator) / Patients prescribed methotrexate for ≥3 months (denominator).
5b. Patients prescribed methotrexate for ≥3 months without a LFT test in last three months (numerator) / Patients prescribed methotrexate for ≥3 months (denominator).

6. Patients prescribed warfarin for ≥3 months without an INR in last three months (numerator) / Patients prescribed warfarin for ≥3 months (denominator).

7. Patients prescribed lithium for ≥3 months without a lithium level in last three months (numerator) / Patients prescribed lithium for ≥3 months (denominator).

8. Patients prescribed amiodarone for ≥6 months without a thyroid function test in the last six-months (numerator) / Patients prescribed amiodarone for ≥6 months (denominator).

9. Patients prescribed methotrexate without instructions to take weekly (numerator) /Patients prescribed methotrexate (denominator).

10. Patients prescribed amiodarone for ≥1 month a dose >200mg/day (numerator) / Patients prescribed amiodarone for ≥1 month (denominator).

Two composite outcome measures were also used:

- Number of patients with at least one prescribing problem (numerator) / Number of patients at risk of at least one prescribing problem (denominator).

- Number of patients with at least one monitoring problem (numerator) / Number of patients at risk of at least one monitoring problem (denominator).

As detailed in our published trial protocol\(^{24}\), we also planned to report the following composite outcome measures:

- Number of patients with at least two prescribing problems (numerator) / Number of patients at risk of at least two prescribing problems (denominator).
• Number of patients with at least two monitoring problems / Number of patients at risk of at least two monitoring problems (denominator).

When we completed our data collection, however, we found that the numbers of numerators for these composite outcome measures were very small and so we have not reported these. Data are available, however, from our analysis of QRESEARCH practices.

Describing outcome data

The prevalence of each primary and secondary outcome measure listed above are described using numerators, denominators and percentage by treatment arm separately at six- and 12-months follow-up.

2.2.15.2 Comparing baseline characteristics between treatment arms

Baseline characteristics were compared informally between treatment arms\textsuperscript{38}.

2.2.15.3 Comparisons between treatment arms

All outcome measures were binary in nature. They were compared between treatment arms using random effects logistic regression with patient at level one and practice at level two. Odds ratios and 95% confidence intervals (CI) were estimated using two-level random intercepts logistic models, with patients at level one and practices at level two. Models include randomisation stratum as a fixed effect\textsuperscript{39}. Three separate analyses were undertaken\textsuperscript{40-42}:

i) Adjusting only for stratum (practice level).
ii) Adjusting for stratum (practice level) and for the presence of medication-related problems at baseline (patient level).
iii) Adjusting for stratum (practice level), baseline medication-related problems (patient level), and deprivation and training status (practice level).

In the results section we present this latter analysis as the main analysis.
Sub-group analyses for primary outcome measures assessed whether the intervention effect varied by practice size or practice deprivation by incorporating a term for the interaction between treatment arm and the (continuous) covariate of interest into regression models. Where there was evidence of non-linearity, the covariate was categorised at the median value.

An intention-to-treat (ITT) analysis was used such that practices were analysed in the arms they were allocated to regardless of whether they received the intervention or not. Significance was assessed based on likelihood ratio tests with a p value of <0.05 taken as significant. All analyses were undertaken using Stata version 10. ICCs were estimated from regression models adjusted for stratum, baseline medication problem rates, practice deprivation and training status.

Outcome data were obtained for all participating practices at both follow-up time points, hence there were no missing data. No adjustments were made for multiple endpoints. Models were checked by examining plots of standardised empirical Bayes estimates for the random effects and sensitivity analyses undertaken excluding practices with estimates above or below two SDs.

**Primary outcomes**

The proportions of “at risk” patients in each treatment arm with the errors of interest were compared between treatment arms at six- and 12-months after the end of the intervention period in each practice.

The ICC and 95%CI were estimated for each of the primary outcome measures from the regression models adjusted for stratum, baseline medication errors, practice deprivation and training status.

If any practices had been lost to follow-up, we had planned to do a sensitivity analysis replacing the missing follow-up data with the baseline data for that practice.

It should be noted that some patients (for both primary and secondary outcome measures) will have become “at risk” between the time of the baseline data collection and the follow-up data collections. For the primary outcome measures this may have occurred because:
• They had diagnosis of asthma or peptic ulcer added to their computer record after the baseline data collection.
• They reached the age of 75 years following the time of the baseline data collection.
• At time of the baseline data collection, they did not fall within our definition of being prescribed an ACE inhibitor or a loop diuretic long-term, but they did so at the six and/or 12-month follow-up data collection points.
• They joined the practice after the time of baseline data collection and fell within one of the “at risk” groups.

We judged that it was important to include these patients in the analysis because the intervention is aimed not only at correcting hazardous prescribing, but also at introducing systems to prevent future errors. Nevertheless, for the primary outcome measures, a sensitivity analysis will be undertaken excluding patients that (for the reasons outlined above) became “at risk” between the baseline data collection and the follow-up data collections. At the time of writing this report, this analysis had not been completed.

Secondary outcome measures

The proportion of “at risk” patients in each treatment arm with the error of interest were compared between treatment arms at six- and 12-months after the end of the intervention period.

We recognised the potential for Type 1 errors associated with significance testing for multiple end points. We therefore considered our analyses of secondary outcome measures to be partly exploratory in nature, and partly confirmatory of our findings for the primary outcome measures.

2.2.15.4 Missing data

This was not relevant as a complete case analysis was undertaken at six- and 12-months. No practices were lost to follow-up.
2.2.15.5 Comparing characteristics of participating and non-participating practices

The following characteristics were compared between participating and non-participating practices:

- List size (Mann Whitney U test).
- Number of GPs (Mann Whitney U test).
- % of practice population aged ≥75 years (Mann Whitney U test).
- Training status ($\chi^2$ test).
- Deprivation using IMD2004 Mann Whitney U test).
- QoF medicines management points (Mann Whitney U test).
- QoF total points (Mann Whitney U test).

2.3 Results

2.3.1 Description of general practices and patients

Two hundred and forty practices were approached and 72 (30%) agreed to participate. We did not formally collect information on reasons for non-participation, but when asked, the most common reason given was that practices were too busy.

The first practice was recruited 13 July 2006 and the final practice was recruited 18 September 2007. Thirty-six practices were randomly assigned to the simple feedback arm and 36 to the pharmacist intervention arm.

The flow of practices and patients through the trial is shown in Figure 1. Baseline characteristics of practices are reported in Table 3.
Patient Safety Research Portfolio: PINCER Trial

Analysis

36 practices included in analysis of primary outcome measures at baseline, six month follow-up and twelve month follow-up

Six Month Follow-up
Patients per practice by primary outcome measure:
Outcome 1 – mean 51 (range 11 to 120)
Outcome 2 – mean 66 (range 29 to 482)
Outcome 3 – mean 148 (range 29 to 482)

Twelve Month Follow-up
Patients per practice by primary outcome measure:
Outcome 1 – mean 55 (range 11 to 115)
Outcome 2 – mean 592 (range 111 to 1371)
Outcome 3 – mean 161 (range 30 to 452)

Excluded from analysis
Exclusions from Outcome 3 analysis due to data quality issues:
2 patients at baseline
16 patients at six month follow-up
8 patients at twelve month follow-up
See main report for details of excluded data from the secondary outcome measures

Enrolment

Invited to participate (240 practices)

Agreed to face-to-face consent visit meeting (98 practices)

Randomised (72 practices)

Excluded
1 practice with pharmacist employed
1 practice with student population
1 practice not lab-linked

Allocation

Allocated to Simple Feedback Arm (32 practices)
Site A: 22 practices
Site B: 14 practices
List size strata:
Small: 3 practices
Medium: 14 practices
Large: 18 practices

Patients per practice by primary outcome measure:
Outcome 1 – mean 53 (range 7 to 129)
Outcome 2 – mean 73 (range 93 to 1219)
Outcome 3 – mean 131 (range 22 to 379)

Instances of “at-risk” patients at baseline: 32308
(For all outcomes)

Allocated to Pharmacist Intervention (58 practices)
Site A: 21 practices
Site B: 17 practices
List size strata:
Small: 4 practices
Medium: 13 practices
Large: 18 practices

Patients per practice by primary outcome measure:
Outcome 1 – mean 51 (range 8 to 124)
Outcome 2 – mean 523 (range 94 to 1396)
Outcome 3 – mean 121 (range 18 to 287)

Instances of “at-risk” patients at baseline: 30399
(For all outcomes)

Lost to follow-up

Lost to follow-up: 0 practices, 0 patients
Instances of “at-risk” patients at six month follow-up: 35470
(For all outcomes)

Lost to follow-up: 0 practices, 0 patients
Instances of “at-risk” patients at twelve month follow-up: 34413
(For all outcomes)

Declined
1 practice declined after consent visit

Excluded
1 practice with pharmacist employed
1 practice with student population
1 practice not lab-linked

*Repeated cross-sectional design accounts for no loss to follow-up at the patient level
Table 3. Characteristics of practices at baseline by treatment arm

<table>
<thead>
<tr>
<th>Practice characteristics</th>
<th>Simple feedback arm (%)</th>
<th>Pharmacist intervention arm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of practices</td>
<td>36 (50.0)</td>
<td>36 (50.0)</td>
</tr>
<tr>
<td>Study centre</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nottingham</td>
<td>22 (61.1)</td>
<td>21 (58.3)</td>
</tr>
<tr>
<td>Manchester</td>
<td>14 (38.9)</td>
<td>15 (41.7)</td>
</tr>
<tr>
<td>Median list size (IQR)</td>
<td>6438 (3834, 9707)</td>
<td>6295 (2911, 9390)</td>
</tr>
<tr>
<td>Age of practice population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-14</td>
<td>38804 (16.3)</td>
<td>39818 (17.4)</td>
</tr>
<tr>
<td>15-64</td>
<td>159277 (67.1)</td>
<td>152156 (66.5)</td>
</tr>
<tr>
<td>65-74</td>
<td>20683 (8.7)</td>
<td>19151 (8.4)</td>
</tr>
<tr>
<td>&gt;=75</td>
<td>18648 (7.9)</td>
<td>17623 (7.7)</td>
</tr>
<tr>
<td>Total</td>
<td>237412 (100.0)</td>
<td>228748 (100.0)</td>
</tr>
<tr>
<td>Sex of practice population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>118469 (49.9)</td>
<td>113284 (49.5)</td>
</tr>
<tr>
<td>Female</td>
<td>118943 (50.1)</td>
<td>115464 (50.5)</td>
</tr>
<tr>
<td>Median Index of Multiple Deprivation 2004 score (IQR)</td>
<td>26.3 (18.8, 36.5)</td>
<td>30.3 (18.2, 39.6)</td>
</tr>
<tr>
<td>GP training practices (%)</td>
<td>10 (27.8)</td>
<td>13 (36.1)</td>
</tr>
<tr>
<td>Median Quality and Outcomes Framework medicines management points (IQR)</td>
<td>42 (38,42)</td>
<td>42 (38,42)</td>
</tr>
<tr>
<td>Median total Quality and Outcomes Framework points (IQR)</td>
<td>1041 (1004, 1049)</td>
<td>1036 (993, 1048)</td>
</tr>
</tbody>
</table>
Practices in the pharmacist intervention arm had a slightly higher Index of Multiple Deprivation (2004) score and were slightly more likely to be GP training practices. Otherwise treatment arms were well balanced in terms of practice characteristics at baseline.

In our original grant application (but not our published trial protocol)\textsuperscript{24} we said that we would report rurality scores. We had intended to obtain a measure of rurality from the Rural and Urban Area Classification of 2004. However a sample of 17 PINCER practices drawn from three PCTs showed that the vast majority (n=16) practices fell within one category: “Urban – Less Sparse”, so we did not report rurality scores. Over 80\% of Super Output Areas in England are classified as “Urban – Less Sparse”\textsuperscript{46}.

Table 4 reports baseline characteristics of patients. Patients in the simple feedback arm were slightly more likely to have had methotrexate prescribed without a FBC or LFT in the previous three months and amiodarone prescribed without a TFT in the last six-months. Patients in the pharmacist intervention arm were slightly more likely to have had an ACE inhibitor or diuretic prescribed without a U&E in the previous 15 months and to have had lithium prescribed without a lithium level in the previous three months. Otherwise treatment arms were well balanced in terms of patient characteristics at baseline.
Table 4. Characteristics of patients at baseline by treatment arm

<table>
<thead>
<tr>
<th>OM</th>
<th>Patient characteristics</th>
<th>Simple feedback arm (%)</th>
<th>Pharmacist intervention arm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Primary outcome measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Patients with a history of peptic ulcer prescribed an NSAID without a PPI / Patients with a history of peptic ulcer without a PPI</td>
<td>93/1970 (4.7)</td>
<td>87/1828 (4.8)</td>
</tr>
<tr>
<td>2</td>
<td>Patients with asthma prescribed a beta-blocker / Patients with asthma</td>
<td>628/20634 (3.0)</td>
<td>537/18906 (2.8)</td>
</tr>
<tr>
<td>3</td>
<td>Patients aged ≥75 on long term ACE inhibitors or diuretics without urea and electrolyte monitoring in the previous 15 months / Patients aged ≥75 on long term ACE inhibitors or diuretics</td>
<td>483/4722 (10.2)</td>
<td>549/4349 (12.6)</td>
</tr>
<tr>
<td></td>
<td><strong>Secondary outcome measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>Patients with asthma and not CHD prescribed a beta-blocker / Patients with asthma and not CHD</td>
<td>375/19528 (1.9)</td>
<td>337/17968 (1.9)</td>
</tr>
<tr>
<td>4</td>
<td>Female patients with a history of venous or arterial thromboembolism and arterial thrombosis prescribed combined oral contraceptives / Female patients with a history of venous or arterial thromboembolism and arterial thrombosis</td>
<td>16/2588 (0.6)</td>
<td>5/2284 (0.2)</td>
</tr>
<tr>
<td>5a</td>
<td>Patients prescribed methotrexate for ≥3 months without a full blood count in last three months / Patients prescribed methotrexate for ≥3 months</td>
<td>202/483 (41.8)</td>
<td>170/480 (35.4)</td>
</tr>
<tr>
<td>5b</td>
<td>Patients prescribed methotrexate for ≥3 months without a liver function test in last three months / Patients prescribed methotrexate for ≥3 months</td>
<td>184/483 (38.1)</td>
<td>172/480 (35.8)</td>
</tr>
<tr>
<td>6</td>
<td>Patients prescribed warfarin for ≥3 months without an INR in last three months / Patients prescribed warfarin for ≥3 months</td>
<td>99/1496 (6.6)</td>
<td>92/1591 (5.8)</td>
</tr>
<tr>
<td>7</td>
<td>Patients prescribed lithium for ≥3 months without a lithium level in last three months / Patients prescribed lithium for ≥3 months</td>
<td>101/224 (45.1)</td>
<td>97/194 (50.0)</td>
</tr>
<tr>
<td>8</td>
<td>Patients prescribed amiodarone for ≥6 months without a thyroid function test in the last six months / Patients prescribed amiodarone for ≥6 months</td>
<td>130/253 (51.4)</td>
<td>111/240 (46.3)</td>
</tr>
<tr>
<td>9</td>
<td>Patients prescribed methotrexate without instructions to take weekly / Patients prescribed methotrexate</td>
<td>12/345 (3.5)</td>
<td>7/305 (2.3)</td>
</tr>
<tr>
<td>10</td>
<td>Patients prescribed amiodarone for ≥ one month a dose &gt;200mg/day / Patients prescribed amiodarone for ≥ one month</td>
<td>1/223 (0.5)</td>
<td>1/222 (0.5)</td>
</tr>
<tr>
<td></td>
<td>Patients with at least one prescribing problem/patients at risk of at least one prescribing problem</td>
<td>736/24550 (3.0)</td>
<td>629/22473 (2.8)</td>
</tr>
<tr>
<td></td>
<td>Patients with at least one monitoring problem/patients at risk of at least one monitoring problem</td>
<td>1015/6756 (15.0)</td>
<td>1018/6371 (16.0)</td>
</tr>
</tbody>
</table>
Table 5 shows the characteristics of participating and non-participating practices. It can be seen that the practices that agreed to participate were larger than those that were approached but did not agree to participate. In addition, participating practices had higher Quality and Outcomes Framework scores and were more likely to be GP training practices.

Table 5. Characteristics of participating and non-participating practices

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participating practices n=72</th>
<th>Non-participating practices n=168</th>
<th>Test statistic, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median list size (IQR)</td>
<td>6332.5 (3566.0, 9389.5)</td>
<td>4557.5 (3040.0, 7777.5)</td>
<td>Z=2.03, p=0.04</td>
</tr>
<tr>
<td>Median number of GPs (IQR)</td>
<td>3 (2, 5)</td>
<td>3 (1, 4) [9]</td>
<td>Z=1.97, p=0.05</td>
</tr>
<tr>
<td>Median percentage of practice population aged 75 years and over (IQR)</td>
<td>7.8 (6.0, 9.0) [3]*</td>
<td>7.4 (6.1, 8.9) [3]*</td>
<td>Z=0.72, p=0.47</td>
</tr>
<tr>
<td>Training practice (%)</td>
<td>23 (31.9)</td>
<td>29 (17.3)</td>
<td>$X^2=6.40, 1$ df, p=0.01</td>
</tr>
<tr>
<td>Median IMD score (IQR)</td>
<td>28.4 (18.5, 39.0)</td>
<td>27.2 (17.5, 36.6)</td>
<td>Z=0.77, p=0.44</td>
</tr>
<tr>
<td>Median QoF medicines management points (10th, 90th centile)</td>
<td>42 (38, 42)</td>
<td>42 (34, 42)</td>
<td>Z=2.45, p=0.01</td>
</tr>
<tr>
<td>Median QoF total points (IQR)</td>
<td>99.0 (95.5, 99.9)</td>
<td>98.0 (94.7, 99.5)</td>
<td>Z=2.14, p=0.03</td>
</tr>
</tbody>
</table>

*Figures in square brackets are missing values

2.3.2 Findings for trial outcome measures at six-months follow-up

Table 6 reports primary and secondary outcome measures at six-months follow-up. In view of the imbalance between treatment arms in practice deprivation and training status we present analyses adjusted for randomisation stratum, baseline medication-related problems, practice deprivation and training status. Intra-cluster correlation coefficients are also shown. Analyses adjusted only for stratum and for stratum and baseline medication-related problems are shown in Appendix 5, as are sub-group analyses. There was no evidence of statistically significant interactions between treatment arm and either practice size or practice deprivation for any of the primary outcome measures.

Patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed a non-selective NSAID without a PPI if they had a history of
peptic ulcer (OR 0.58, 95%CI 0.38, 0.89), to have been prescribed a beta-blocker if they had asthma (OR 0.73, 95% CI 0.58, 0.91) or to have been prescribed an ACE inhibitor or diuretic without a U&E in the last 15 months (OR 0.51, 95% CI 0.34, 0.78).

In terms of the composite secondary outcome measures, patients in the pharmacist intervention arm practices were significantly less likely to have a prescribing problem (OR 0.71, 95% CI 0.59, 0.86) or monitoring problem (OR 0.56, 95% CI 0.44, 0.70). In terms of the other secondary outcome measures, patients in the pharmacist intervention arm practices were less likely to have been prescribed warfarin without an INR in the previous three months (OR 0.53, 95% CI 0.29, 0.95), to have been prescribed amiodarone without a TFT in the last six-months (OR 0.57, 95% CI 0.36, 0.92). There were no significant differences between treatment arms for other secondary outcome measures.
Table 6. Prevalence of prescribing and monitoring problems at six-months follow-up by treatment arm

<table>
<thead>
<tr>
<th>OM</th>
<th>Outcome</th>
<th>Simple feedback arm (%)</th>
<th>Pharmacist intervention arm (%)</th>
<th>Adjusted odds ratio (95% CI)*</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary outcome measures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Patients with a history of peptic ulcer prescribed an NSAID without a PPI / Patients with a history of peptic ulcer without a PPI</td>
<td>86/2014 (4.3)</td>
<td>51/1852 (2.8)</td>
<td>0.58 (0.38, 0.89)</td>
<td>4.68x10^-7</td>
</tr>
<tr>
<td>2</td>
<td>Patients with asthma prescribed a beta-blocker / Patients with asthma</td>
<td>658/22224 (3.0)</td>
<td>499/20312 (2.5)</td>
<td>0.73 (0.58, 0.91)</td>
<td>3.50x10^-7</td>
</tr>
<tr>
<td>3</td>
<td>Patiens aged ≥75 on long term ACE inhibitors or diuretics without urea and electrolyte monitoring in the previous 15 months / Patients aged ≥75 on long term ACE inhibitors or diuretics</td>
<td>436/5329 (8.2)</td>
<td>255/4851 (5.3)</td>
<td>0.51 (0.34, 0.78)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Secondary outcome measures**

| 2a | Patients with asthma and not CHD prescribed a beta-blocker / Patients with asthma and not CHD | 387/21048 (1.8) | 299/19286 (1.6) | 0.81 (0.63, 1.04), p=0.10, n=37159 | 4.94x10^-6 |
| 4 | Female patients with a history of venous or arterial thromboembolism and arterial thrombosis prescribed combined oral contraceptives / Female patients with a history of venous or arterial thromboembolism and arterial thrombosis | 8/2783 (0.3) | 3/2490 (0.1) | 0.39 (0.07, 2.15), p=0.26, n=4835 | 0.05 |
| 5a | Patients prescribed methotrexate for ≥3 months without a full blood count in last three months / Patients prescribed methotrexate for ≥3 months | 162/518 (31.3) | 122/494 (24.7) | 0.80 (0.45, 1.43), p=0.45, n=817 | 0.15 |
| 5b | Patients prescribed methotrexate for ≥3 months without a liver function test in last three months / Patients prescribed methotrexate for ≥3 months | 154/518 (29.7) | 121/494 (24.5) | 0.79 (0.43, 1.45), p=0.44, n=817 | 0.17 |
| 6 | Patients prescribed warfarin for ≥3 months without an INR in last three months / Patients prescribed warfarin for ≥3 months | 78/1618 (4.8) | 52/1720 (3.0) | 0.53 (0.29, 0.95), p=0.03, n=2519 | 1.11x10^-6 |
| 7 | Patients prescribed lithium for ≥3 months without a lithium level in last three months / Patients prescribed lithium for ≥ three months | 84/211 (39.8) | 67/190 (35.3) | 0.53 (0.24, 1.19), p=0.12, n=350 | 0.24 |
| 8 | Patients prescribed amiodarone for ≥6 months without a thyroid function test in the last six-months / Patients prescribed amiodarone for ≥6 months | 106/235 (45.1) | 81/242 (33.5) | 0.57 (0.36, 0.92), p=0.02, n=404 | 4.86x10^-7 |
| 9 | Patients prescribed methotrexate without instructions to take weekly / Patients prescribed methotrexate | 16/310 (5.2) | 2/268 (0.8) | 0.72 (0.06, 9.25), p=0.80, n=482 | 5.20x10^-7 |
| 10 | Patients prescribed amiodarone for ≥ one month a dose >200mg/day / Patients prescribed amiodarone for ≥ one month | 1/228 (0.4) | 1/228 (0.4) | 0.96 (0.06, 15.55), p=0.97, n=456 (adjusted for stratum only†) | 2.1x10^-3 |
| | Patients with at least one prescribing problem/patients at risk of at least one prescribing problem | 752/26329 (2.9) | 553/24073 (2.3) | 0.71 (0.59, 0.86), p=0.0003, n=46378 | 9.16x10^-7 |
| | Patients with at least one monitoring problem/patients at risk of at least one monitoring problem | 868/7409 (11.7) | 584/6963 (8.4) | 0.56 (0.44, 0.70), p<0.001, n=11584 | 0.04 |

* adjusted for randomisation stratum, baseline prevalence of errors, deprivation and training status unless otherwise stated. Number does not equal the sum of the denominators in each arm, as this only includes those with baseline and follow-up data.
† adjustment for other variables not calculable
2.3.3 Findings for trial outcome measures at 12-months follow-up

Table 7 reports primary and secondary outcome measures at 12-months follow-up adjusted for randomisation stratum, baseline medication-related problems, practice deprivation and training status. Intra-cluster correlation coefficients are also shown. Analyses adjusted only for stratum and for stratum and baseline medication-related problems are shown in Appendix 5, as are sub-group analyses. There was no evidence of statistically significant interactions between treatment arm and either practice size or practice deprivation for any of the primary outcome measures.

Patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed a beta-blocker if they had asthma (OR 0.78, 95% CI 0.63, 0.97) or to have been prescribed an ACE inhibitor or diuretic without a U&E in the last 15 months (OR 0.63, 95% CI 0.41, 0.95). However there was no significant difference in terms of being prescribed a non-selective NSAID without a PPI for patients with a history of peptic ulcer (OR 0.91, 95% CI 0.59, 1.39).

In terms of the composite secondary outcome measures, patients in the pharmacist intervention arm practices were significantly less likely to have a prescribing problem (OR 0.78, 95% CI 0.64, 0.94) or monitoring problem (OR 0.64, 95% CI 0.51, 0.82). In terms of the other secondary outcome measures, patients in the pharmacist intervention arm practices were significantly less likely to have been prescribed methotrexate without a FBC (OR 0.51, 95% CI 0.27, 0.99) or LFT in the last 3 months (OR 0.50, 95% CI 0.28, 0.91), or to have been prescribed lithium without a lithium level in the last 3 months (OR 0.50, 95% CI 0.29, 0.85). There were no significant differences between treatment arms in other secondary outcome measures.
<table>
<thead>
<tr>
<th>OM</th>
<th>Outcome</th>
<th>Simple feedback arm (%)</th>
<th>Pharmacist intervention arm (%)</th>
<th>Adjusted odds ratio* (95% CI)</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Patients with a history of peptic ulcer prescribed an NSAID without a PPI / Patients with a history of peptic ulcer without a PPI</td>
<td>78/2035 (3.8)</td>
<td>61/1852 (3.3)</td>
<td>0.91 (0.59, 1.39), p=0.65, n=3331</td>
<td>6.54x10⁻⁷</td>
</tr>
<tr>
<td>2</td>
<td>Patients with asthma prescribed a beta-blocker / Patients with asthma</td>
<td>692/23520 (2.9)</td>
<td>545/21359 (2.6)</td>
<td>0.78 (0.63, 0.97), p=0.02, n=39221</td>
<td>0.008</td>
</tr>
<tr>
<td>3</td>
<td>Patients aged ≥75 on long term ACE inhibitors or diuretics without urea and electrolyte monitoring in the previous 15 months / Patients aged ≥75 on long term ACE inhibitors or diuretics</td>
<td>452/5813 (7.8)</td>
<td>306/5242 (5.8)</td>
<td>0.63 (0.41, 0.95), p=0.03, n=7848</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td><strong>Secondary outcome measures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>Patients with asthma and not CHD prescribed a beta-blocker / Patients with asthma and not CHD</td>
<td>414/22294 (1.9)</td>
<td>326/20283 (1.6)</td>
<td>0.79 (0.62, 1.02), p=0.06, n=37108</td>
<td>0.009</td>
</tr>
<tr>
<td>4</td>
<td>Female patients with a history of venous or arterial thromboembolism and arterial thrombosis prescribed combined oral contraceptives / Female patients with a history of venous or arterial thromboembolism</td>
<td>15/2987 (0.5)</td>
<td>4/2640 (0.2)</td>
<td>0.57 (0.05, 6.17), p=0.64, n=4840</td>
<td>0.24</td>
</tr>
<tr>
<td>5a</td>
<td>Patients prescribed methotrexate for ≥3 months without a full blood count in last three months / Patients prescribed methotrexate for ≥3 months</td>
<td>194/552 (35.1)</td>
<td>130/531 (24.5)</td>
<td>0.51 (0.27, 0.99), p=0.05, n=787</td>
<td>0.22</td>
</tr>
<tr>
<td>5b</td>
<td>Patients prescribed methotrexate for ≥3 months without a liver function test in last three months / Patients prescribed methotrexate for ≥3 months</td>
<td>186/552 (33.7)</td>
<td>134/531 (25.2)</td>
<td>0.50 (0.28, 0.91), p=0.02, n=787†</td>
<td>0.16</td>
</tr>
<tr>
<td>6</td>
<td>Patients prescribed warfarin for ≥3 months without an INR in last three months / Patients prescribed warfarin for ≥3 months</td>
<td>69/1752 (3.9)</td>
<td>76/1877 (4.1)</td>
<td>0.98 (0.52, 1.85), p=0.94, n=2487</td>
<td>0.10</td>
</tr>
<tr>
<td>7</td>
<td>Patients prescribed lithium for ≥3 months without a lithium level in last three months / Patients prescribed lithium for ≥3 months</td>
<td>88/213 (41.3)</td>
<td>56/176 (31.8)</td>
<td>0.50 (0.29, 0.85), p=0.01, n=329</td>
<td>0.02</td>
</tr>
<tr>
<td>8</td>
<td>Patients prescribed amiodarone for ≥6 months without a thyroid function test in the last six-months / Patients prescribed amiodarone for ≥6 months</td>
<td>92/247 (37.3)</td>
<td>80/233 (34.3)</td>
<td>0.77 (0.41, 1.43), p=0.41, n=376</td>
<td>0.11</td>
</tr>
<tr>
<td>9</td>
<td>Patients prescribed methotrexate without instructions to take weekly / Patients prescribed methotrexate</td>
<td>13/309 (4.2)</td>
<td>0/271 (0.0)</td>
<td>Not calculable</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Patients prescribed amiodarone for ≥1 month a dose &gt;200mg/day / Patients prescribed amiodarone for ≥1 month</td>
<td>1/231 (0.4)</td>
<td>1/232 (0.4)</td>
<td>0.95 (0.06, 15.45), p=0.97, n=463 (adjusted for stratum only$)</td>
<td>1.07x10⁻³</td>
</tr>
<tr>
<td></td>
<td>Patients with at least one prescribing problem / Patients at risk of at least one prescribing problem</td>
<td>785/27808 (2.8)</td>
<td>610/25246 (2.4)</td>
<td>0.78 (0.64, 0.94), p=0.01, n=46287</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Patients with at least one monitoring problem / Patients at risk of at least one monitoring problem</td>
<td>901/8011 (11.3)</td>
<td>652/7449 (8.8)</td>
<td>0.64 (0.51, 0.82), p=0.0006, n=11193†</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* * adjusted for randomisation stratum, baseline prevalence of errors, deprivation and training status unless otherwise stated. Number does not equal the sum of the denominators in each arm, as this only includes those with baseline and follow-up data. † includes interaction between treatment arm and covariate dichotomised at the median value (≤ median vs. > median) $‡$ adjustment for other variables not calculable
2.3.4 Model checking

All except three models were robust to excluding practices, with standardised empirical Bayes estimates of random effects above or below 2 SDs. The six-month follow-up model for methotrexate prescription without an LFT in the last three months became significant after excluding three practices with standardised empirical Bayes estimates of random effects above or below 2 SDs (OR including all practices 0.79 (95% CI 0.43, 1.45) and OR excluding three practices 0.53 (95% CI 0.30, 0.93)).

The 12-month follow-up model for methotrexate prescription without a FBC in the last three months became non-significant when three practices with standardised empirical Bayes estimates of random effects above or below 2 SDs were excluded from the analysis (OR including all practices 0.51 (95% CI 0.27, 0.99) and OR excluding three practices 0.62 (95% CI 0.35, 1.10). The 12-month follow-up model for the prescribing composite secondary outcome measure became non significant when 3 practices with standardised empirical Bayes estimates of random effects above or below 2 SDs were excluded from the analysis (OR including all practices 0.78 (95% CI 0.64, 0.94) and OR excluding 3 practices 0.83 (95% CI 0.68, 1.00).

In addition, model checking was not possible for some models. Firstly where the intra-cluster correlation coefficient was very small, model checking became unreliable. In these cases the standardised empirical Bayes estimates for some practices could not be estimated because the standard deviation of the empirical Bayes estimates was zero. Therefore, testing for the removal of outliers was not possible (Outcome 1 at six- and 12-months, Outcome 2a (for patients with asthma but not coronary heart disease) at six-months, Outcome 6 at six-months, Outcome 8 at six-months and the prescribing composite secondary outcome measure at six-months). Secondly where the number of patients with an outcome was very small, models excluding practices would not converge (Outcome 4 at 12-months, Outcome 9 at six- and 12-months and Outcome 10 at six- and 12-months).

Further information on subgroup analyses is shown in Appendix 5.
2.3.5 Examining potential differences in mortality between the treatment arms

Forty-four practices provided data (response rate = 61%). Two practices were excluded from the analysis because we were not confident in the validity of the data: they reported no deaths or patients leaving the practice. Therefore the analysis was done on 42 practices.

Simple feedback practices accounted for 54.8% (n=23) of the sample with pharmacist intervention practices making up 45.2% (n=19).

The total number of patients identified at baseline in the 42 practices was 2266 (mean: 53.9 patients per practice; range: 12 - 191).

The total number of patients identified at baseline minus those who subsequently left the practice was 2169 (mean: 51.6 patients per practice; range: 11 to 183). This is the sample on which we did statistical analysis because we felt that it would not be valid to include patients who had left the practice (where we had no information on whether they had died or not).

Table 8 below shows the proportions of patients who died during the 15 months following baseline data collection by intervention group. The unadjusted mortality refers to all patients identified at baseline, whereas the adjusted mortality excludes patients that had left the practice within the 15 months following baseline data collection.

A non-parametric two-independent-samples test was used to examine differences in mortality data between the two intervention arms for the adjusted mortality data. There was no statistically significant difference between the two groups (p=0.85).

Table 8. Proportions of patients who died during the 15 months following baseline data collection by intervention group

<table>
<thead>
<tr>
<th></th>
<th>Simple Feedback</th>
<th>Pharmacist intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Inter-quartile range</td>
</tr>
<tr>
<td><strong>Unadjusted mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients who</td>
<td>4.58</td>
<td>[3.03, 10.53]</td>
</tr>
<tr>
<td>died</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adjusted mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients who</td>
<td>5.0</td>
<td>[3.03, 10.64]</td>
</tr>
<tr>
<td>died</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.4 Discussion

2.4.1 Summary of main findings

This trial has shown that a pharmacist-led IT-based complex intervention using educational outreach and practical support is more effective than simple feedback in reducing the proportions of patients at risk from hazardous prescribing and inadequate medication monitoring in general practice. Statistically significant differences were noted for each of the three primary outcome measures at six-months follow-up and for two of the three primary outcome measures at 12-months follow-up. Statistically significant differences were noted for both the prescribing and monitoring composite outcome measures at both six- and 12-months follow-up. Given the high risk of serious iatrogenic harm associated with these errors, reductions of the magnitude observed in this trial are likely to be clinically important.

2.4.2 Strengths and limitations of the trial

2.4.2.1 Recruitment of general practices

Our recruitment of general practices was moderately successful give that 30% of those approached agreed to participate. It is likely that our success in recruitment relates to the attention to detail we put into developing a feasible intervention that was seen to be relevant to general practices. This view is backed up by the findings of our qualitative study.

In addition, we put considerable effort into our recruitment strategy including pre-publicising the trial, sending documentation to general practices about the trial and following up on this to arrange visits to practices where the study was explained in more detail.

2.4.2.2 Allocation to intervention groups

We avoided any risk of bias in allocation to intervention groups by using an independent web-based randomisation service, and the sequence of treatment allocations was concealed until all data analyses had been completed. The groups were reasonably well matched in terms of list size, age-sex structure of the practice population and Quality and Outcomes.
Framework scores, although the pharmacist intervention practices were slightly more deprived and were slightly more likely to be GP training practices (see Table 3). We took account of the latter two factors in our analysis. Nevertheless, one could argue that we should have collected comparative data on other factors such as the proportion of UK graduate doctors, doctors with postgraduate qualifications, and measures of prescribing practice outside Quality and Outcomes Framework.

2.4.2.3 Sample size calculations

Our sample size calculations were based on the assumption that for the proportion of patients fulfilling the criteria for any one of our primary outcome measures, there would be a maximum 11% reduction in the simple feedback arm and a 50% reduction in the pharmacist intervention arm.

Our findings at six-months follow-up show that for the primary Outcomes 1-3 (see Table 1), the reductions in proportions of patients with potentially hazardous patterns of prescribing and medication monitoring were 41.6%, 10.7% and 57.9% in the pharmacist intervention group and 8.5%, 0 and 19.6% in the simple feedback group respectively (these figures were calculated from data in Table 4 and Table 6). The reductions in the pharmacist intervention arm were large for Outcomes 1 and 3, but only just over 10% for Outcome 2. The reductions in the simple feedback arm were less than our estimated 11% for Outcomes 1 and 2, but twice this amount for Outcome 3.

2.4.2.4 Ascertainment of outcome measures

Baseline data extraction was undertaken smoothly and successfully and provided the information needed for practices to consider acting on patients with potentially hazardous prescribing and medicines management. In particular, data extraction for our pre-specified primary outcome measures appears to have worked successfully in all general practices recruited to the study. Nevertheless, we encountered some difficulties with the secondary outcome measures, as described above (see section 2.2.7.1). Some of these problems could have been avoided with better foresight on behalf of the research team. For example, had we been aware that some general practices kept a separate record of INR results and did not keep these on their main clinical computer systems, we could have excluded such practices from our recruitment. Similarly, if we had realised that it would not be possible to
extract dosage instructions for general practices using the TPP computer system, we could have excluded practices using this computer system (we did pilot our outcome measures using the TPP computer system and went ahead with recruiting practices because we erroneously believed that there was a solution to the problem). For Outcome 9, which focused on dosage instructions for methotrexate (see Table 1), a national policy change that occurred during the course of our study\(^\text{25}\) may have reduced the proportion of analysable cases. This is because the introduction of a forcing function to GP computer systems, which does not allow for anything, but weekly dosing, does not always appear as a line of dosing text that can be picked up by MIQUEST software. Nevertheless, we did find sufficient numbers of patients with dosage instructions in order to do this analysis.

### 2.4.2.5 Compliance

All practices recruited to the study complied to the extent that they allowed data to be extracted from their clinical computer systems. All practices in the pharmacist intervention arm of the trial allowed the pharmacists into the practice. In both arms of the trial there was a lack of engagement in some practices as indicated by our qualitative analysis (see Chapter 5: Qualitative evaluation of the PINCER trial)

### 2.4.2.6 Losses to follow-up

None of the practices were lost to follow-up. As noted in our qualitative analysis, this may in part be due to the fact that the study was seen to be relevant to GPs and that it did not involve them in running computer searches themselves or recruiting patients.

### 2.4.2.7 Missing data

No data were missing for any of the outcome measures for any practice for any time point. It was a major undertaking to obtain complete data and this was partly due to the organisation and hard work of the research team, with support from TCR Nottingham, and partly due to the willingness of practices to allow the research team in to run computer searches at baseline as well as six-months and 12-months follow-up.
2.4.2.8 Analysis

The analysis was undertaken independently by two statisticians both producing similar findings. Where minor differences were found, the reasons for these were explored and in all cases discrepancies were resolved.

2.4.2.9 Generalisability

Practices that took part in the study were larger than those that were approached but did not take part. Also, the participating practices had higher scores in the Quality and Outcomes Framework and were more likely to be GP training practices. This means that the practices recruited to the PINCER trial were not representative of all practices approached.

In addition, comparison of outcome measures at baseline for trial practices with a similar time point for the practices used in the analysis from the QRESEARCH database shows reasonably similar findings (see Table 50 in Chapter 6: QRESEARCH analysis of secular trends in outcome measures). The PINCER trial practices had relatively low proportions (29% vs. 35%) of patients aged 75 years and older on ACE inhibitors or loop diuretics with no U&E monitoring in the previous 15 months. The PINCER trial practices had relatively high proportions of patients on methotrexate that had not had FBC and LFT checked within the previous three months (10.5% and 10.0% respectively vs. 6.0% and 6.2%).

Practices taking part in the PINCER trial and QRESEARCH practices appeared to be quite similar in terms of list size and demographic characteristics (see Table 46 in section 6.3.1). Compared with UK data from 1st April 2007 practices participating in the PINCER trial had slightly higher median (interquartile range) list sizes: simple feedback arm 6438 (3834, 9707); pharmacist intervention arm 6295 (2911, 9390); UK practices 5582 (3235 to 8781).

Both the PINCER and QRESEARCH samples had similar age distribution to the UK population according to figures from the Office for National Statistics.

The prevalence of asthma in both practice samples (11.4% in QRESEARCH and 10.9% in PINCER) was similar. These figures are lower than the prevalence quoted in the Health Survey for England 2001 where 15% of those aged 16 and older were reported to have ever had “doctor diagnosed asthma” (as recalled by the respondents).
The prevalence is however higher than the UK prevalence of 5.7% from the national Quality and Outcomes Framework (2007-08)\textsuperscript{20}. This is probably because the QoF data exclude “patients who were prescribed no asthma related drugs in the previous 12-months”. The prevalence of peptic ulcer in both samples was close to UK national prevalence (1.6% in PINCER and QRESEARCH vs. 1.4%)\textsuperscript{51}. 
Chapter 3: Pincer economic analysis
3.1 Introduction

We have undertaken a two-stage economic analysis from the perspective of a payer within the English NHS: a within-trial analysis of cost per error avoided and a modelling analysis of economic impact of error reduction.

The principal objective of the within-trial analysis was to identify and value the resource use associated with the interventions used in the trial, in relation to changes in error rates between intervention and control practices.

The principal objectives of the modelling analysis were to:
- Identify and value the impact on patients’ health status of the interventions;
- Identify and value the resource use associated with reduced prescribing errors in general practice;
- Assess the relative value for money of the interventions.

We report the methods and results for the within trial analysis here; the results of the modelling analysis will be reported separately, although we do outline our approach to the modelling analysis in this chapter.

3.2 Methods

3.2.1 Recruitment of patients

For the purposes of the economic analysis, the general practices recruited to the study were asked to write to all patients identified through baseline data collection who appeared in the numerator of one of our outcome measures (i.e. they had potentially been subjected to errors in prescribing or medication monitoring). In the accompanying patient information leaflet, patients were given information about the study and were asked to give consent for the research team to access their medical records. Patients were asked to sign a consent form and to return this to the study team. Copies of letters sent to patients along with information leaflet and consent forms are provided in Appendix 1.
For Outcome 6 (prescribing warfarin with no record of INR in the previous 12 weeks), we identified some practices that keep their records of international normalised ratio (INR) results for monitoring anticoagulation therapy separate from their main practice computer system and thus appeared to have very high proportions of patients not having INRs checked according to the computer searches we undertook. In these cases, we did not write to patients to seek consent to access their records because it is likely that the majority were not at risk.

3.2.2 Perspective

We undertook the economic analysis from the perspective of the funder of the pharmacist intervention or simple feedback intervention (such as the English NHS) in terms of the direct costs of providing an intervention to reduce prescribing errors in general practice.

3.2.3 Comparators and key parameters under investigation

The evaluation compared the pharmacist-led intervention with simple feedback. Figure 2 illustrates the comparators and the probabilistic events that are associated with each strategy in the within-trial analysis.
For the purposes of the within trial analysis of cost per error avoided, we examined the differences in costs of the pharmacist intervention compared with simple feedback, in the context of error rate reduction.

3.2.4 Outcomes

The primary outcome was the number of errors detected by the report generation process in both the pharmacist intervention and simple feedback arms. The outcome associated with the intervention and control arms is the probability of error detected by the practice at six-months and 12-months after the intervention.

We incorporated data on Outcomes 1, 2, 3, 5, 7 and 8 (see Table 1). We decided not to incorporate data for the economic analysis for Outcomes 6, 9 and 10, because of the problems we had with data ascertainment (see section 2.2.7.1); in addition, the numbers of patients identified for Outcome 4 were too low to allow for meaningful within-trial economic analysis and so this outcome measure was also not included.
3.2.5 Costs

Costs were obtained from the perspective of the NHS in terms of the direct costs of providing an intervention to reduce prescribing errors in general practice.

In this cluster trial, costs could have been incurred at both the patient and cluster (practice) level. Randomising by cluster can lead to imbalances between treatment arms in practice or patient level factors, including resource use. The costs measured at practice level were the costs of setting-up and delivering the intervention. The costs measured at the patient level were any costs of delivering the intervention that can be linked to individual patients. In the within-trial analysis, all costs were incurred at practice level, so correction for clustering was not required.

3.2.6 Simple feedback arm resource use

The simple feedback arm required the researchers to go back into the practices at set time periods and extract patient data from the GP systems; this is the only cost that is associated with the simple feedback arm of the PINCER trial.

These report generation costs were also incurred by the pharmacist intervention arm.

If practices put some effort into correcting patients’ problems then this would have been a cost in the simple feedback arm and the pharmacist intervention arm, but these data were not collected in either arm.

3.2.6.1 Pharmacist intervention resource use

The pharmacist intervention comprised the following stages: a training session; facilitated meetings; monthly meetings and practice feedback meetings; plus time spent in each practice outside meetings following up errors. We discuss the cost implications of these components of the intervention in turn below:
• Training session
The initial training session costs included stationery, food and drink, room and equipment hire/use, trainers’ time, pharmacists’ time, travel and accommodation. These costs can be seen as the set up costs of the intervention and would be incurred if the intervention were rolled out into clinical practice. Training costs were allocated to intervention practices according to list size. This was calculated by deriving the total training cost for the 36 practices, and then allocating a portion of that training cost to a practice based on the list size.

• Facilitated meetings
The aim of the facilitated meeting was to provide a strategic overview of the initiative and to maximise homogeneity of the pharmacist intervention. In clinical practice, a facilitated meeting would equate to a strategic practice meeting. Facilitated meeting costs were allocated to intervention practices according to list size. This was calculated by deriving the total facilitated meeting cost for the 36 practices, and then allocating a portion of that cost to a practice based on the list size.

• Monthly meetings
The aim of the monthly meeting between practice pharmacists and the study co-ordinator was to deal with operational issues within individual practices. Monthly meetings between the project co-ordinator and the pharmacists would equate to operational practice meetings, and, in practice, would be added onto other PCT team pharmacist meetings. Monthly meeting costs were allocated to pharmacist intervention practices according to list size.

• Practice feedback sessions
The aim of the feedback session was to provide each practice with feedback and support on management of errors, using root cause analysis to look at systems. Practice feedback sessions were usually 15-60 minutes, with up to three feedback sessions per practice. Practice feedback session costs were allocated to the pharmacist intervention practices according to how many were carried out.

• Other time spent by PINCER pharmacists on intervention
PINCER pharmacists also spent time working on the intervention outside the meetings listed above. Costs of time spent per error detected were calculated and added to the cost for each practice.
3.2.6.2 Unit costs

- Costs of consumables and room hire
  Actual local unit costs were used (2008 costs, written communication), and are assumed to reflect unit costs of items that would be consumed in practice.

- Staff costs
  Hourly wage was calculated using average annual gross salary plus employers on costs. Annual wages were obtained from the individual people involved. The annual wage is presumed to be based on working 37.5 hours per week, for 44 weeks a year. Therefore the annual gross wage, plus employers' on costs, was divided by 1500 (2008 costs).

- Construction of total costs associated with intervention delivery
  The following costs were allocated to each practice on a per practice (weighted by list size) basis: training; facilitated meetings; and monthly meetings.
  The following costs were allocated to each practice using individual practice data:
  - Practice feedback session costs: combination of pharmacist costs
  - Other time spent by PINCER pharmacists on the intervention.

  The cost of generating the reports was added to the pharmacist intervention practice’s costs. This generated a total intervention cost per practice.

3.2.7 Economic analysis

An economic evaluation was carried out to generate the cost per detected error avoided, from the perspective of the English NHS, comparing the pharmacist-led intervention with simple feedback.

The study was not powered to detect differences in costs because there is no prior study upon which to base a power calculation. Error rates in practices in both groups were followed up for six- and 12-months following the completion of the intervention in each practice. The time horizon for the within-trial analysis was the length of the intervention i.e. 12 weeks in the pharmacist intervention practices. The costs measured at practice level were the costs of setting up and delivering the intervention.
Incremental cost-effectiveness ratios (ICERs) were calculated for differences in error rates between the simple feedback and pharmacist-led interventions. If the lower cost intervention was also associated with better outcomes than the more costly comparator, this was treated as the dominant intervention. In this scenario, incremental ratios would not be calculated for this intervention, since its use would lead to both net savings and greater benefits. ICERs were calculated if the higher cost intervention was associated with better outcomes. The incremental ratios were calculated as:

\[
\frac{\text{Cost pharmacist intervention} - \text{Cost simple feedback}}{\text{Outcome pharmacist intervention} - \text{Outcome simple feedback}}
\]

Statistical analysis is not appropriate to test the robustness of ICERs. It is not possible to generate 95% confidence intervals around ICERs because the ratio of two distributions does not necessarily have a finite mean, or therefore, a finite variance. Therefore, generation of a bootstrap estimate of the ICER sampling distribution to identify the magnitude of uncertainty around the ICERs is required. Bootstrapping with replacement was employed, utilising Microsoft Excel, using a minimum of 1000 iterations to obtain 2.5% and 97.5% percentiles of the ICER distribution. The within trial analysis generated cost per detected error avoided.

Prior to incremental economic analysis, costs and outcomes were adjusted for specific characteristics. Regression analysis was planned to assess the effect of base list-size and at-risk list-size, as well as number of GPs, in order to capture scale effects (this included the square of base list-size and at-risk list-size to also capture non-linear economies of scale); QOF and medicine-related QOF-score (both were tested but QOF score was more informative), in order to capture efficiency; SHA, in order to capture any potential regional fixed effects; and finally demographic information on area-level deprivation, average ages and gender proportions.

The negative binomial model was used for regression analysis of errors. The negative binomial model is used to estimate count data when overdispersion means that the Poisson regression model would be inappropriate. Variance is greater than the mean for errors per practice in both groups, and the relative variation differs between groups. As a result Poisson regression would underestimate the standard errors of the coefficients. Costs were estimated via GLM assuming a gamma distribution.
A cost effectiveness acceptability curve was constructed to express the probability that the cost per extra unit of outcome (error avoided in this study) gained from within the trial (y-axis) is cost-effective as a function of the decision-maker’s ceiling cost effectiveness ratio (\( \lambda \)) (x-axis)\(^5\). Net benefit was not determined for the within trial analysis as a value could not be assigned to the outcome.

### 3.2.8 Modelling analysis

To assess the full economic impact of an intervention to reduce errors, we are in the process of carrying out a more extensive modelling-based economic analysis. This analysis supplements the within-trial analysis and is still ongoing. It will be completed in 2010.

For the modelling analysis of cost per quality adjusted life year (QALY) gained, we intend to examine the differences in overall NHS costs, in the context of QALYs gained, and to generate a net benefit statistic.

Outcomes used in the modelling analysis will be derived from published evidence on the link between specific category of error reduction and impact on health. The PINCER study was not designed to calculate the impact of the intervention on patient health outcomes, either in terms of sample size or length of follow-up. Use of proxy measures such as number of primary and secondary care contacts (hospital admissions, accident and emergency visits and outpatient visits) may be subject to difficulties if considered as patient outcomes. This is because the intervention may lead to increased NHS contact in the short term. We will model the long-term benefit associated with avoidance of errors, using standard Markov modelling techniques.

A literature review is being undertaken to obtain published utility weights to allow QALY generation and cost utility analysis.

### 3.2.9 Cost data

For the purposes of the economic analysis, the general practices recruited to the study were asked to write to all patients identified through baseline data collection who appeared in the numerator of one of our outcome measures (i.e. they had potentially been subjected to errors in prescribing or medication monitoring). In the accompanying patient information
leaflet, patients were given information about the study and were asked to give consent for the research team to access their medical records. Patients were asked to sign a consent form and to return this to the study team. Copies of letters sent to patients along with information leaflet and consent forms are provided in Appendix 1.

For outcome measure six (prescribing warfarin with no record of INR in the previous 12 weeks), we identified some practices that keep their records of international normalised ratio (INR) results for monitoring anticoagulation therapy separate from their main practice computer system and thus appeared to have very high proportions of patients not having INRs checked according to the computer searches we undertook. In these cases, we did not write to patients to seek consent to access their records because it is likely that the majority were not at risk.

Patients identified from the baseline computer system searches as being at risk of hazardous prescribing and inadequate medication monitoring were included in the economic modelling analysis provided that they gave informed consent for researchers to view their records.

Wherever possible, data were extracted electronically, although in the case of correspondence regarding hospital contacts it was usually necessary to anonymise and photocopy relevant information. Anonymised data were sent to the University of Nottingham where data processing and analysis took place.

Patients in both arms of the study were followed up for 12-months following the completion of the intervention in each practice. Error-related resource use data were collected from these patients. NHS resource use data were collected retrospectively for the 12-month period before the intervention (baseline) and for 12-months after the intervention (follow-up). This allows us to adjust our analyses for baseline cost\textsuperscript{55}.

Error-related resource use data have been collected from the GP records of 962 patients who had consented to access to their medical records ("consented numerator").

UK standard costs will be used for unit costs. This may somewhat over- or under-estimate local unit costs, but allows explicit comparison of costs and local adjustments can be made. Unit costs associated with the intervention will be obtained from the PSSRU\textsuperscript{56} and other publicly available sources as required.
3.2.10 Modelling analysis of costs

The practice level cost of the intervention will be combined with patient-level costs of error management. The cost per patient was estimated over the study period. The costs for each event (GP surgery visit, investigations, out of hours, accident and emergency, outpatient and hospital admission costs) will be estimated for each patient in the trial for both treatment arms. The costs are calculated as resource use multiplied by unit cost and are reported descriptively, both as resource use and cost data, for each error.

These data will be used to populate the modelling economic analysis. Where there are gaps, these data are supplemented with data from the literature. Distributional forms of secondary data follow modelling convention. A literature review is being undertaken to validate the primary error-related resource use data and to assess any long term resource use consequences not detected during the study period.

3.3 Results for within-trial analysis

3.3.1 Outcomes

3.3.1.1 Probability of error
Table 9 provides a summary of sum of errors from PINCER at six-months. The three primary Outcomes i.e. 1, 2 and 3 and three of the secondary Outcomes i.e. 5, 7 and 8 are included in this analysis.
Table 9. Summary of errors for each error type by intervention at six and 12 months post-intervention

<table>
<thead>
<tr>
<th>Error type</th>
<th>Number of errors/population at risk post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 months</td>
</tr>
<tr>
<td></td>
<td>Simple feedback</td>
</tr>
<tr>
<td>1</td>
<td>86/2014</td>
</tr>
<tr>
<td>2</td>
<td>658/22224</td>
</tr>
<tr>
<td>3</td>
<td>436/5329</td>
</tr>
<tr>
<td>5 a and b</td>
<td>316/1036</td>
</tr>
<tr>
<td>7</td>
<td>84/211</td>
</tr>
<tr>
<td>8</td>
<td>106/235</td>
</tr>
<tr>
<td>Total</td>
<td>1686/31049</td>
</tr>
<tr>
<td></td>
<td>(0.054%)</td>
</tr>
</tbody>
</table>

Negative binomial regression determined that only intervention and list size were important predictors of error rates (see Table 10). An interaction term was also included between intervention and scale variables, however it was not significant and was subsequently removed based upon information criteria performance.

The model was estimated using the robust sandwich-estimator of the variance-covariance matrix\textsuperscript{57}. Marginal effects from the final model are in Table 10.
Table 10. Coefficients (standard errors) from negative binomial regression of errors per practice

<table>
<thead>
<tr>
<th>Variable</th>
<th>6 months coefficient (s.e.)</th>
<th>12 months coefficient (s.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>-11.2520*** (4.0502)</td>
<td>-10.0475*** (3.7493)</td>
</tr>
<tr>
<td>Base list-size/100</td>
<td>1.3031*** (0.4406)</td>
<td>1.8265*** (0.5146)</td>
</tr>
<tr>
<td>Base list-size squared/100</td>
<td>-0.0043* (0.0025)</td>
<td>-0.0068* (0.0029)</td>
</tr>
<tr>
<td>At-risk list-size</td>
<td>-0.0092 (0.0157)</td>
<td>-0.0069 (0.0194)</td>
</tr>
<tr>
<td>At-risk list-size squared</td>
<td>0.0000 (0.0000)</td>
<td>0.0000 (0.0000)</td>
</tr>
<tr>
<td>No. GPs</td>
<td>-4.7186 (5.7827)</td>
<td>-11.0905 (6.6207)</td>
</tr>
<tr>
<td>No. GPs squared</td>
<td>0.3857 (0.5549)</td>
<td>0.9626 (0.6664)</td>
</tr>
<tr>
<td>IMD score</td>
<td>0.0528 (0.1607)</td>
<td>-0.1744 (0.1384)</td>
</tr>
<tr>
<td>QOF score 05/06</td>
<td>-0.1452 (0.3566)</td>
<td>-0.2679 (0.3859)</td>
</tr>
</tbody>
</table>

*** Significant at 1%
** Significant at 5%
*Significant at 10%

Base list-size was scaled downwards for regression; the coefficient therefore reflects the marginal increase in errors from, a predicted mean of 33.69 per practice, of an additional 100 patients. The variables for number of GPs and at-risk list-size are not statistically significant when base list-size is included, suggesting that they are all representing the overall catchment of the practice. Neither area-level deprivation nor QOF scores were statistically significant, nor particularly large.

Besides using information criteria to select specifications and to choose between Poisson and negative binomial regression models, standard approaches to testing for independence in the errors were used, including fitting covariates to the residuals and fitting residuals to the fitted values. This supported the models above as appropriate approaches.
3.3.2 Costs

3.3.2.1 Simple feedback arm resource use

In total, three reports were run in each practice (baseline, six-months and 12-months) costing a total of £92.84 per practice at six-months follow-up, and £139.26 per practice at 12-months follow-up (see Table 11 below for details).

Table 11. Resource use and cost associated with generating reports

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Cost/£</th>
<th>Source of unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running the query</td>
<td>5.16</td>
<td>Assistants hourly wage*</td>
</tr>
<tr>
<td>Printing the report</td>
<td>41.26</td>
<td>Assistants hourly wage*</td>
</tr>
<tr>
<td><strong>Total cost per report</strong></td>
<td><strong>46.42</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Hourly wage was calculated based on working 37.5 hours a week, for 44 weeks a year. The amount of weeks worked per year is based on 8 weeks off a year due to holiday and sick leave.

From discussions with researchers, we estimated running queries took two hours and report printing took 15 minutes. These times varied greatly for a number of different reasons. The time it took to print the report depended purely on the speed of the printer. The time to run the query however varied greatly between practices, and this was not based on the size of the practices. Key reasons included the speed of the system in the practice, how many people were using the system at the time the query was run and whether the system crashed before completion. If the system crashed before finishing the query, then the query would have to be run again from the start. For this reason, a flat rate was assumed for the time taken to run the computer queries based on the time it should take without any problems occurring.

3.3.2.2 Training session costs

Training sessions were held for the pharmacists running the interventions across the 36 intervention practices. Training session costs are summarised in Table 12.
Table 12. Training costs

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Cost/£</th>
<th>Source of unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparation time</td>
<td>1851.30</td>
<td>Participants hourly wage*</td>
</tr>
<tr>
<td>Stationery costs</td>
<td>278.06</td>
<td>Stationery order forms</td>
</tr>
<tr>
<td>Food and drink</td>
<td>736.70</td>
<td>Hospitality service statement</td>
</tr>
<tr>
<td>Room hire</td>
<td>650.00</td>
<td>Primary Care Information Services (PRIMIS+)</td>
</tr>
<tr>
<td>Equipment hire</td>
<td>450.00</td>
<td>PRIMIS+</td>
</tr>
<tr>
<td>Assistants’ time</td>
<td>1751.46</td>
<td>Assistants hourly wage</td>
</tr>
<tr>
<td>Pharmacist time</td>
<td>3420.33</td>
<td>Pharmacists hourly wage</td>
</tr>
<tr>
<td>Travel costs</td>
<td>795.41</td>
<td>Mileage rate as of Oct 2009 (Manchester University rate)</td>
</tr>
<tr>
<td>Accommodation</td>
<td>195.00</td>
<td>University rates</td>
</tr>
<tr>
<td><strong>Total costs</strong></td>
<td><strong>9933.26</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Hourly wage was calculated based on working 37.5 hours a week, for 44 weeks a year. The amount of weeks worked per year is based on eight weeks off a year due to holiday and sick leave.

3.3.2.3 Preparation for monthly meetings and quarterly facilitated meetings

The set up costs for both monthly meetings and quarterly facilitated meetings included preparation time and stationery costs. These costs are summarised in Table 13, and were allocated to practice by list size.

Table 13. Preparation costs

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Cost/£</th>
<th>Source of unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparation time</td>
<td>82.52</td>
<td>Participants hourly wage*</td>
</tr>
<tr>
<td>Stationery</td>
<td>20.37</td>
<td>University costs</td>
</tr>
<tr>
<td><strong>Total costs</strong></td>
<td><strong>102.89</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Hourly wage was calculated based on working 37.5 hours a week, for 44 weeks a year. The amount of weeks worked per year is based on eight weeks off a year due to holiday and sick leave.

3.3.2.3.1 Facilitated meeting costs

Five quarterly facilitated meetings were held for the pharmacists running the interventions across the 36 intervention practices. The costs for running these ‘facilitated meetings’ are summarised in Table 14.
Table 14. Facilitated meeting costs

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Cost/£</th>
<th>Source of unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room hire and catering</td>
<td>753.05</td>
<td>PRIMIS+ room hire</td>
</tr>
<tr>
<td>Assistants’ time</td>
<td>531.22</td>
<td>Assistants hourly wage</td>
</tr>
<tr>
<td>Pharmacist time</td>
<td>3335.89</td>
<td>Pharmacists hourly wage</td>
</tr>
<tr>
<td>Pharmacist travel costs**</td>
<td>2278.65</td>
<td>Mileage rate, Oct 2009 (Manchester University)</td>
</tr>
<tr>
<td>Accommodation</td>
<td>78.00</td>
<td>Staff expenses claim form</td>
</tr>
<tr>
<td><strong>Total costs</strong></td>
<td>6976.81</td>
<td></td>
</tr>
</tbody>
</table>

*Hourly wage was calculated based on working 37.5 hours a week, for 44 weeks a year. The amount of weeks worked per year is based on eight weeks off a year due to holiday and sick leave.

**Pharmacists travel costs includes the mileage that was claimed for travelling, but also how much they were paid during their travel time to the meeting.

3.3.2.3.2 Monthly meeting costs

Twelve monthly meetings were held for the pharmacists running the interventions across the 36 intervention practices. Monthly meeting costs are summarised in Table 15.

Table 15. Monthly meeting costs

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Cost/£</th>
<th>Source of unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room hire and catering</td>
<td>75.00</td>
<td>Invoice/Price list from venue</td>
</tr>
<tr>
<td>Assistants’ time</td>
<td>186.72</td>
<td>Assistants hourly wage</td>
</tr>
<tr>
<td>Pharmacist time</td>
<td>687.68</td>
<td>Pharmacists hourly wage</td>
</tr>
<tr>
<td>Pharmacist travel costs**</td>
<td>1046.90</td>
<td>Mileage rate Oct 2009 (Manchester University)</td>
</tr>
<tr>
<td><strong>Total costs</strong></td>
<td>1996.30</td>
<td></td>
</tr>
</tbody>
</table>

*Hourly wage was calculated based on working 37.5 hours a week, for 44 weeks a year. The amount of weeks worked per year is based on 8 weeks off a year due to holiday and sick leave.

**Pharmacists travel costs includes the mileage that was claimed for travelling, but also how much they were paid during their travel time to the meeting.

3.3.2.3.3 Practice feedback session costs

Between one and three practice feedback sessions were held for each of the 36 intervention practices. The length of time spent per practice was not recorded, but was estimated by the pharmacists to be about one hour. Therefore, each practice was allocated the costs for a practice feedback session costs as summarised in Table 16.
Table 16. Practice feedback session costs

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Cost/£</th>
<th>Source of unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacist time</td>
<td>22.07</td>
<td>Pharmacist hourly wage</td>
</tr>
<tr>
<td>Total costs per practice</td>
<td>794.52</td>
<td></td>
</tr>
</tbody>
</table>

3.3.2.3.4 Time spent by pharmacists dealing with errors

Of 2037 detected errors, the time spent dealing with these was recorded for 1889 (see Table 17. The mean time spent dealing with each error was 23.3 minutes (median 18.4 minutes, range 0-180 minutes) as shown in Table 17.

Table 17. Details of time spent dealing with errors

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall number of errors/number of errors with time recorded</th>
<th>Mean (median) time per error/min</th>
<th>Minimum-maximum/min</th>
<th>Missing values</th>
<th>Total time recorded/min</th>
<th>Estimated total time taken/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>88/88</td>
<td>26.2 (20)</td>
<td>5-120</td>
<td>0</td>
<td>2306</td>
<td>2306</td>
</tr>
<tr>
<td>2</td>
<td>535/520</td>
<td>31.5 (30)</td>
<td>0-180</td>
<td>15</td>
<td>16393</td>
<td>16865.9</td>
</tr>
<tr>
<td>3</td>
<td>561/552</td>
<td>21.6 (15)</td>
<td>5-150</td>
<td>9</td>
<td>11914</td>
<td>12108.3</td>
</tr>
<tr>
<td>4</td>
<td>5/5</td>
<td>22 (10)</td>
<td>10-60</td>
<td>0</td>
<td>110</td>
<td>110</td>
</tr>
<tr>
<td>5</td>
<td>181/180</td>
<td>19.5 (19.5)</td>
<td>5-75</td>
<td>1</td>
<td>3516</td>
<td>3535.5</td>
</tr>
<tr>
<td>6</td>
<td>213/93</td>
<td>18.4 (18.4)</td>
<td>5-120</td>
<td>120</td>
<td>1707</td>
<td>3909.6</td>
</tr>
<tr>
<td>7</td>
<td>99/98</td>
<td>20.6 (15)</td>
<td>5-75</td>
<td>1</td>
<td>2015</td>
<td>2035.6</td>
</tr>
<tr>
<td>8</td>
<td>118/117</td>
<td>25.9 (20)</td>
<td>5-105</td>
<td>1</td>
<td>3024</td>
<td>3049.9</td>
</tr>
<tr>
<td>9</td>
<td>228/227</td>
<td>12.1 (10)</td>
<td>2-60</td>
<td>1</td>
<td>2739</td>
<td>2751.1</td>
</tr>
<tr>
<td>10</td>
<td>9/9</td>
<td>25 (20)</td>
<td>5-60</td>
<td>0</td>
<td>225</td>
<td>225</td>
</tr>
<tr>
<td>Total</td>
<td>2037/1889</td>
<td>23.3 (18.4)</td>
<td>0-180</td>
<td>148</td>
<td>43949</td>
<td>47392.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Hours</th>
<th>Working days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>732.5</td>
<td>97.7</td>
</tr>
<tr>
<td></td>
<td>789.9</td>
<td>105.3</td>
</tr>
</tbody>
</table>

The time spent on dealing with these errors was calculated for each practice. Where data were missing for time spent dealing with an error, it was assumed that time taken equated to the mean time taken for that error. The mean time spent in a pharmacist intervention practice was 1300 minutes (median 1004 minutes, range 205.0-4818.4 minutes). The mean cost per practice was £478.2 (median £369.3, range £75.4 – £1772.4). Although the
distribution of costs is clearly right skewed, means are reported as well as medians because, when calculating costs, it is necessary to take account of all costs. This requires the use of means, rather than medians, in calculations.

The time spent dealing with errors included in the economic analysis was then calculated as shown in Table 18.

Table 18. Details of time spent dealing with errors included in economic analysis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall number of errors/number of errors with time recorded</th>
<th>Mean (median) time per error/min</th>
<th>Minimum-maximum/ min</th>
<th>Missing values</th>
<th>Total time recorded/min</th>
<th>Estimated total time taken/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>88/88</td>
<td>26.2 (20)</td>
<td>5-120</td>
<td>0</td>
<td>2306</td>
<td>2306</td>
</tr>
<tr>
<td>2</td>
<td>535/520</td>
<td>31.5 (30)</td>
<td>0-180</td>
<td>15</td>
<td>16393</td>
<td>16865.9</td>
</tr>
<tr>
<td>3</td>
<td>561/552</td>
<td>21.6 (15)</td>
<td>5-150</td>
<td>9</td>
<td>11914</td>
<td>12108.3</td>
</tr>
<tr>
<td>5</td>
<td>181/180</td>
<td>19.5 (19.5)</td>
<td>5-75</td>
<td>1</td>
<td>3516</td>
<td>3535.5</td>
</tr>
<tr>
<td>7</td>
<td>99/98</td>
<td>20.6 (15)</td>
<td>5-75</td>
<td>1</td>
<td>2015</td>
<td>2035.6</td>
</tr>
<tr>
<td>8</td>
<td>118/117</td>
<td>25.9 (20)</td>
<td>5-105</td>
<td>1</td>
<td>3024</td>
<td>3049.9</td>
</tr>
<tr>
<td>Total</td>
<td>1582/1555</td>
<td>25.2 (20)</td>
<td>0-180</td>
<td>27</td>
<td>39168</td>
<td>39901.07</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Hours</th>
<th>Working days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>652.80</td>
<td>90.04</td>
</tr>
<tr>
<td></td>
<td>665.02</td>
<td>91.73</td>
</tr>
</tbody>
</table>

The mean time spent in a pharmacist intervention practice on the errors included in the economic analysis was 1106 minutes (median 873 minutes, range 155-3585 minutes). The mean cost per practice was £406.7 (median £320.9, range £57.0 – £1318.8).

3.3.2.3.5 Construction of total costs associated with pharmacist intervention delivery

The cost components were summed together to give a total cost per pharmacist intervention practice. This is summarised in
Table 19.
Table 19. Summary of total costs associated with pharmacist intervention

<table>
<thead>
<tr>
<th>Cost parameter per practice</th>
<th>Mean cost/£</th>
<th>Median, range/£</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report generation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months:</td>
<td>92.84</td>
<td>n/a</td>
</tr>
<tr>
<td>12 months:</td>
<td>139.26</td>
<td>n/a</td>
</tr>
<tr>
<td>Training costs</td>
<td>275.92</td>
<td>267.76, 79.54 – 591.23</td>
</tr>
<tr>
<td>Facilitated meetings</td>
<td>195.23</td>
<td>189.45, 56.28 – 418.33</td>
</tr>
<tr>
<td>Monthly meetings</td>
<td>56.88</td>
<td>55.20, 16.40 – 121.88</td>
</tr>
<tr>
<td>Practice feedback</td>
<td>22.07</td>
<td>21.42, 6.36 – 47.29</td>
</tr>
<tr>
<td>Managing errors</td>
<td>406.70</td>
<td>320.93, 57.04 – 1318.68</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months:</td>
<td>1049.67</td>
<td>967.86, (329.22-2086.78)</td>
</tr>
<tr>
<td>12 months:</td>
<td>1096.09</td>
<td>1014.28, (375.64-2133.20)</td>
</tr>
</tbody>
</table>

Adjusted costs were estimated via GLM assuming a gamma distribution. Only the intervention group was used in this analysis, since intervention costs in the control group were constant. Results are in Table 20.

Table 20. Coefficients (standard errors) from regression of intervention cost per practice

<table>
<thead>
<tr>
<th>Variable</th>
<th>6 months coefficient (s.e.)</th>
<th>12 months coefficient (s.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base list-size/100</td>
<td>39.5040* (20.4400)</td>
<td>-0.0179 (16.8212)</td>
</tr>
<tr>
<td>Base list-size squared/100</td>
<td>-0.1855 (0.1388)</td>
<td>-0.0066 (0.0982)</td>
</tr>
<tr>
<td>At-risk list-size</td>
<td>-0.3738 (0.6852)</td>
<td>-0.1374 (0.5488)</td>
</tr>
<tr>
<td>At-risk list-size squared</td>
<td>0.0003 (0.0004)</td>
<td>0.0001 (0.0003)</td>
</tr>
<tr>
<td>No. GPs</td>
<td>-63.5842 (227.5400)</td>
<td>64.9077 (211.6131)</td>
</tr>
<tr>
<td>No. GPs squared</td>
<td>6.9328 (27.0750)</td>
<td>-4.6072 (19.0732)</td>
</tr>
<tr>
<td>IMD score</td>
<td>0.6389 (5.4158)</td>
<td>0.0729 (5.3311)</td>
</tr>
<tr>
<td>QOF score 05/06</td>
<td>2.6424 (9.9520)</td>
<td>-3.1226 (10.1581)</td>
</tr>
</tbody>
</table>

*** Significant at 1%
** Significant at 5%
* Significant at 10%
Only base list-size was significantly correlated with intervention cost, which is a sensible result when the nature of the intervention is considered.

### 3.3.3 Probabilistic incremental economic analysis

A probabilistic incremental economic analysis was completed using the adjusted cost and outcome data outlined above. The predicted errors and costs following the negative binomial regression for errors and the GLM regression for cost were used to characterise the distributions of incremental cost and effect. This allowed for bootstrapping with broader probabilistic sensitivity analysis since the values of the covariates were allowed to vary in the sample.

Results are summarised in Table 21.
Figure 3. Cost effectiveness plane (cost per error avoided at six and 12 months) illustrates the ICER distribution at six and 12 months, and Figure 4 illustrates the cost effectiveness acceptability curves at six and 12 months. This analysis suggests that the PINCER pharmacist intervention has 95% probability of being cost effective if the decision-maker’s ceiling willingness to pay reaches £75 (6 months) or £85 (12 months) per error avoided.

Table 21. Summary statistics of bootstrapped incremental cost effectiveness ratios

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean incremental cost (SD, 95% CI)/£</td>
<td>871.88 (54.04, 765.96-977.79)</td>
<td>870.63 (53.60, 858.42-1068.52)</td>
</tr>
<tr>
<td>Mean incremental errors (SD, 95% CI)</td>
<td>-12.90 (0.26, -13.42-12.39)</td>
<td>-12.71 (0.29, -13.27-12.14)</td>
</tr>
<tr>
<td>Mean ICER (2.5-97.5th percentile)/£ per error avoided</td>
<td>65.60 (58.2-73.0)</td>
<td>66.53 (66.8-81.5)</td>
</tr>
</tbody>
</table>
Figure 3. Cost effectiveness plane (cost per error avoided at six and 12 months)

Figure 4. Cost-effectiveness acceptability curve (cost per error avoided at six and 12 months)
3.4 Discussion

3.4.1 Main findings
The pharmacist-led intervention reduced error rates, with increased cost, at six and 12 months post-intervention, and if the decision-maker attaches a value of £75, at 6 months and £85 at 12 months, or more to the avoidance of one error, the intervention has a 95% probability of being cost effective.

3.4.2 Limitations

The costs of the simple feedback and pharmacist intervention arms were assumed to reflect how the interventions would be implemented in practice. It is possible that, once the trial environment is not present, the interventions may consume resources differently, although the qualitative work (see Chapter 5: Qualitative evaluation of the PINCER trial) does not suggest that this would be the case. There are also many models of this type of service provision, which may affect costs.

This economic analysis did not include any costs other than those incurred as a direct result of the intervention. These costs assume no time spent by the practice dealing with errors in both the simple feedback and pharmacist intervention arm. It is not clear which arm this would favour. However, this means that the costs presented are an underestimate of the real cost to the practice.

This analysis did not include any costs or outcomes that may have been incurred as a result of the error. Therefore, the true clinical and economic impact of the intervention cannot be assessed on the basis of this analysis. This is reflected in the lack of a net benefit statistic.
3.4.3 Comparison with other studies

Cost per error avoided has not been widely generated by other studies. There has been no systematic review of economic evaluations of interventions to reduce medication errors in primary or secondary care. A review of economic effects of clinical pharmacy interventions demonstrated that studies had serious limitations in their methodological quality and applicability to current practice, did not use a comparative study design or include incremental cost-effectiveness analysis\(^58\). This review found 17 studies, of which only three were RCTs, and none were based in primary care or reported cost per error avoided.

One modelling study was found that aimed to detect the economic impact of a pharmacy-based intervention to reduce medication errors\(^59\). No cost per error was reported. However, using a range of assumptions, this UK study estimated from the error rate, what was the potential to cause harm. Probability of harm from undetected errors was divided into harm associated with errors of omission and errors of commission\(^59\). Probability of harm was divided into significant (resulted in temporary harm to the patient and required intervention without (increase in) hospital stay); serious (resulted in temporary harm and required hospitalisation) and severe, life-threatening or fatal (resulted in permanent patient harm, required intervention to sustain life, or contributed to a patient’s death). Utility weights were attached to harm from undetected errors divided into significant, serious, severe, life-threatening or fatal. These were hypothetical estimates as there are no relevant data available to describe the utility effects of the broadly defined severity categories. This approach has not been used in this study, as knowledge of the types of errors affected by the PINCER intervention means that we can use a more data-driven approach.

Due to the use of the cost per error avoided statistics, it is not possible to assess whether the ICER generated for this intervention would be considered cost effective according to current policy decision rules in England, such as a £20,000 to £30,000 per QALY threshold, as used by NICE. Again, this is reflected in the lack of a net benefit statistic.
Chapter 4: Analysis of data recorded by PINCER trial pharmacists
4.1 Introduction

In this chapter we provide details of an analysis for data recorded by the trial pharmacists.

4.1.1 Aim

To assess whether patients identified by the outcome measures were considered to be at clinical risk, and to record the actions taken by pharmacists.

4.1.2 Objectives

To record the following:

1. Demographic characteristics of pharmacists.
2. Number of cases and patients identified by outcome measures and percentage of cases deemed to be at clinical risk.
3. Number of actions recommended by pharmacists and number (percentage) of actions which were completed.
4. Types of actions recommended and completed for each outcome measure.
5. Median (IQR) time taken for pharmacists to assess cases, make recommendations and complete the agreed actions.

4.2 Methods

4.2.1 Data collection

Pharmacists completed record forms recording their activity for each case they reviewed whilst working in PINCER practices. Three record forms were completed:

1. A summary record of whether the patient was clinically at risk, action recommended, action taken, and time spent working on that case.
2. A case specific record detailing the medication problem, recommendations made, actions taken as a result, and contact with patients.
3. A general record of actions to be taken following the feedback meeting with members of the practice team.

This analysis includes data from forms 1 and 2 (see Appendix 6).

4.2.2 Data entry

Data from the summary record (form 1) were entered into SPSS v15 (by Sadaf Qureshi) and data entry was double checked for accuracy (by Caroline Mulvaney and Sherie Smith). Discrepancies were noted and corrected by referring to the summary record in 553 (27.0%) cases.

The summary record form allowed pharmacists to code up to 9 types of actions recommended and actions completed, all remaining actions were coded as “other” (this accounted for 523 (21.7%) of actions recommended and 416 (19.0%) of actions completed). As a result, case specific records were reviewed for 597/2038 (29.3%) cases and actions coded as “other” were re-coded as one of an additional 53 types of actions recommended or completed. These data were single entered into SPSS v15 (by Rachel Howard). Data were validated by checking that actions recommended or completed were appropriate for the outcome measure (discrepancies were noted in 15 (1.6%) entries and corrected by referring back to the case specific record). Duplicate data were noted for 8 cases and duplicate entries were removed.

4.2.3 Data analysis

Data were summarised using percentages, mean (SD) (for normally distributed data) and median (IQR) (for non-normally distributed data).
4.3 Results

4.3.1 Characteristics of pharmacists

Six pharmacists were recruited to work on the PINCER trial. Three pharmacists had a primary care pharmacy background and three had a community pharmacy background (and no other experience of working in a primary care setting). The pharmacists had a wide range of years of experience, and five had at least one postgraduate qualification. The demographic characteristics of the pharmacists are summarised in Table 22.

Table 22. Characteristics of pharmacists recruited to work on the PINCER trial

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of pharmacists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
</tr>
<tr>
<td>Age range (years)*</td>
<td></td>
</tr>
<tr>
<td>26-30</td>
<td>1</td>
</tr>
<tr>
<td>31-35</td>
<td>4</td>
</tr>
<tr>
<td>41-45</td>
<td>1</td>
</tr>
<tr>
<td>Years since registration as a pharmacist*</td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>1</td>
</tr>
<tr>
<td>10-14</td>
<td>3</td>
</tr>
<tr>
<td>20-24</td>
<td>2</td>
</tr>
<tr>
<td>Pharmacy background*</td>
<td></td>
</tr>
<tr>
<td>Primary care pharmacy</td>
<td>3</td>
</tr>
<tr>
<td>Community pharmacy</td>
<td>3</td>
</tr>
<tr>
<td>Post graduate qualifications achieved*</td>
<td></td>
</tr>
<tr>
<td>Diploma in community pharmacy</td>
<td>2</td>
</tr>
<tr>
<td>Diploma/MSc in clinical pharmacy</td>
<td>2</td>
</tr>
<tr>
<td>Diploma in management studies</td>
<td>1</td>
</tr>
<tr>
<td>PhD</td>
<td>1</td>
</tr>
</tbody>
</table>

* At start of PINCER trial training (July 2006)

4.3.2 Clinical computer systems used by the practices

General practices used 5 different electronic clinical systems (see Table 23); EMIS LV was the most commonly used system in both areas.
Table 23. Clinical computer systems used in general practices

<table>
<thead>
<tr>
<th>Clinical computer systems</th>
<th>Number (%) of general practices using each computer system</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All practices (n=36)</td>
</tr>
<tr>
<td>EMIS LV</td>
<td>20 (55.6)</td>
</tr>
<tr>
<td>EMIS PCS</td>
<td>2 (5.6)</td>
</tr>
<tr>
<td>Torex synergy</td>
<td>7 (19.5)</td>
</tr>
<tr>
<td>TPP</td>
<td>5 (13.9)</td>
</tr>
<tr>
<td>Vision</td>
<td>2 (5.6)</td>
</tr>
</tbody>
</table>

4.3.3 Patients

1946 patients were identified as at risk from potentially hazardous medicines management. Ninety-two (4.7%) patients were identified by two outcome measures, resulting in 2038 cases of potentially hazardous medicines management. No patients were identified by more than two outcome measures.

4.3.4 Number of cases identified by searches

Pharmacists judged that 1463/2026 (72.2%) cases were clinically at risk (data missing for 12 cases which pharmacists did not have time to review); the remainder had been identified by the searches because the necessary information was available but not coded on the computer, or because the information had been coded incorrectly on the computer. A higher proportion of cases identified in Manchester were described by the pharmacists as clinically at risk ($\chi^2$ 17.1, df 1, p<0.001) (see Table 24).

Table 24. Number (%) of cases identified as at risk from hazardous prescribing

<table>
<thead>
<tr>
<th>Number (%) of “at clinical risk” cases</th>
<th>All practices</th>
<th>Small practices (&lt;2500) (n=80)*</th>
<th>Medium practices (2500-6000) (n=396)*</th>
<th>Large practices (&gt;6000) (n=1550)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both centres (n=2026) †</td>
<td>1463 (72.2)</td>
<td>63 (78.8)</td>
<td>305 (77.0)</td>
<td>1095 (70.6)</td>
</tr>
<tr>
<td>Nottingham (n=1243) †</td>
<td>857 (68.9)</td>
<td>7 (8.8)</td>
<td>165 (41.7)</td>
<td>685 (44.2)</td>
</tr>
<tr>
<td>Manchester (n=783) †</td>
<td>606 (77.4)</td>
<td>56 (70.0)</td>
<td>140 (35.4)</td>
<td>410 (26.5)</td>
</tr>
</tbody>
</table>

†n=number of valid cases identified by searches for each centre

* †n=number of valid cases identified by searches for each practice size
The percentage of at risk cases varied markedly between outcome measures, with more than 90% of cases considered at risk for Outcomes 3 and 8, whilst less than 40% of cases were considered to be at risk for Outcomes 6 and 9 (see Table 25). In Outcome 6, one practice had a parallel recording system for patients' INRs which was not identified by the electronic search. Therefore, 114 patients from this practice were considered not to be at clinical risk. If these data are excluded then pharmacists considered 50 (50.5%) of 99 patients to be at clinical risk in Outcome 6.

**Table 25. Number (%) of cases judged to be at clinical risk by outcome measure**

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number (%) cases identified (n=2038)</th>
<th>Number cases at clinical risk (% of cases identified for each outcome measure)</th>
<th>Number of cases not at clinical risk (% of cases identified for each outcome measure)</th>
<th>Coding error</th>
<th>Information available but not coded</th>
<th>Other reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 NSAID &amp; Peptic Ulcer</td>
<td>89 (4.4)</td>
<td>80 (89.9)</td>
<td>7 (7.9)</td>
<td>1 (1.1)</td>
<td>2 (2.2)</td>
<td></td>
</tr>
<tr>
<td>2 Asthma &amp; Beta-blocker</td>
<td>535 (26.3)</td>
<td>433 (80.9)</td>
<td>55 (10.3)</td>
<td>0</td>
<td>57 (10.7)</td>
<td></td>
</tr>
<tr>
<td>3 ACEI/diuretic &amp; lab test</td>
<td>561 (27.5)</td>
<td>526 (93.8)</td>
<td>0</td>
<td>7 (1.2)</td>
<td>23 (4.1)</td>
<td></td>
</tr>
<tr>
<td>4 AT/VT &amp; Combined Oral Contraceptive</td>
<td>5 (0.2)</td>
<td>4 (80)</td>
<td>1 (20)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5 Methotrexate &amp; FBC/LFT</td>
<td>181 (8.9)</td>
<td>105 (58.0)</td>
<td>0</td>
<td>21 (11.6)</td>
<td>57 (31.5)</td>
<td></td>
</tr>
<tr>
<td>6 Warfarin &amp; INR</td>
<td>213 (10.5)</td>
<td>50 (23.5)</td>
<td>2 (0.9)</td>
<td>7 (3.3)</td>
<td>152 (71.4)</td>
<td></td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels</td>
<td>99 (4.9)</td>
<td>74 (74.7)</td>
<td>0</td>
<td>5 (5.1)</td>
<td>18 (18.2)</td>
<td></td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT</td>
<td>118 (5.8)</td>
<td>112 (94.9)</td>
<td>1 (0.9)</td>
<td>0</td>
<td>3 (2.5)</td>
<td></td>
</tr>
<tr>
<td>9 Methotrexate &amp; weekly dosage</td>
<td>228 (11.2)</td>
<td>73 (32.0)</td>
<td>0</td>
<td>2 (0.9)</td>
<td>146 (64.0)</td>
<td></td>
</tr>
<tr>
<td>10 Amiodarone &amp; daily dosage</td>
<td>9 (0.4)</td>
<td>6 (66.7)</td>
<td>0</td>
<td>0</td>
<td>3 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2038 (100)</td>
<td>1463 (71.8)</td>
<td>66 (3.3)</td>
<td>43 (2.1)</td>
<td>461 (22.1)</td>
<td></td>
</tr>
</tbody>
</table>

4.3.5 Actions recommended by and completed by pharmacists

Pharmacists recommended 2118 actions in 1518/2038 (74.5%) cases identified by the computer searches. In 1064/2038 (52.2%) cases one action was recommended, in 345/2038 (16.9%) cases two actions were recommended, in 72/2038 (3.5%) cases three actions were recommended, and in 37/2038 (1.8%) cases four actions were recommended. 1794 actions
were recommended in 1284/1463 (87.8%) cases classed “at clinical risk” (see Table 26 and Table 27 below).
Table 26. Number of actions recommended and completed (%) in all cases, by outcome measure

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number (%) of cases where actions recommended and completed</th>
<th>Total no. of actions (% completed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rec†</td>
<td>Comp‡</td>
</tr>
<tr>
<td>Number of actions</td>
<td>No action recommended or taken</td>
<td>1 action</td>
</tr>
<tr>
<td>1</td>
<td>NSAID &amp; PU (n=89)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>Asthma &amp; beta-blocker (n=535)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>102</td>
<td>229</td>
</tr>
<tr>
<td>3</td>
<td>ACEI/diuretic &amp; lab test (n=561)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>52</td>
<td>450</td>
</tr>
<tr>
<td>4</td>
<td>AT/VT &amp; COC (n=5)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>Methotrexate &amp; FBC/LFT (n=181)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>74</td>
</tr>
<tr>
<td>6</td>
<td>Warfarin &amp; INR (n=213)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>143</td>
<td>29</td>
</tr>
<tr>
<td>7</td>
<td>Lithium &amp; Li levels (n=99)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>Amiodarone &amp;TFT (n=118)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>72</td>
</tr>
<tr>
<td>9</td>
<td>Methotrexate &amp; weekly dosage (n=228)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>109</td>
<td>73</td>
</tr>
<tr>
<td>10</td>
<td>Amiodarone &amp; daily dosage (n=9)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Total (n=2038)*</td>
<td>520</td>
<td>1064</td>
</tr>
</tbody>
</table>

*N=number of cases  
†Percentage of cases identified for outcome measure where recommendations made  
‡Percentage of cases identified for outcome measure where actions completed  
**Percentage of recommended actions where an action was completed (including alternatives to the recommended actions)
### Table 27. Number of actions recommended and completed (%) in “at clinical risk” cases, by outcome measure

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number of at risk cases where actions recommended and completed</th>
<th>Total no. of actions (% completed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recommended (Rec) or Completed (Comp) Number of actions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No action taken</td>
<td>1 action</td>
</tr>
<tr>
<td>1 NSAID &amp; PU (n=80)*</td>
<td>7 (8.8)</td>
<td>12 (15.0)</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blocker (n=433)*</td>
<td>67 (15.5)</td>
<td>194 (44.8)</td>
</tr>
<tr>
<td>3 ACEI/diuretic &amp; lab test (n=526)</td>
<td>31 (5.9)</td>
<td>83 (15.8)</td>
</tr>
<tr>
<td>4 AT/VT &amp; COC (n=4)*</td>
<td>1 (25)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>5 Methotrexate &amp; FBC/LFT (n=105)*</td>
<td>17 (16.2)</td>
<td>28 (26.7)</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR (n=50)*</td>
<td>8 (16.0)</td>
<td>11 (22.0)</td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels (n=74)*</td>
<td>15 (20.3)</td>
<td>22 (29.7)</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT (n=112)*</td>
<td>14 (12.5)</td>
<td>15 (13.4)</td>
</tr>
<tr>
<td>9 Methotrexate &amp; weekly dosage (n=73)*</td>
<td>17 (23.3)</td>
<td>22 (30.1)</td>
</tr>
<tr>
<td>10 Amiodarone &amp; daily dosage (n=6)*</td>
<td>2 (33.3)</td>
<td>4 (66.7)</td>
</tr>
<tr>
<td>Total (n=1463)*</td>
<td>179 (12.2)</td>
<td>392 (26.8)</td>
</tr>
</tbody>
</table>

*n=number of at risk cases
1675 actions were completed in 1253/2038 (61.5%) cases. In 949 (46.6%) cases one action was completed, in 216 (10.6%) cases two actions were completed, in 58 (2.8%) cases three actions were completed and in 30 (1.5%) cases four actions were completed. 1411 actions were completed in 1071/1463 (73.2%) cases classed “at clinical risk” (see Table 26 and Table 27 above).

Overall, 1388 (65.5%) of 2118 recommended actions were completed. The percentage of recommended actions which were completed varied between outcome measures from 85.3% (Outcome 7) to 35.8% (Outcome 2) (see Table 28). In 154 cases, it was unknown whether 169 (8.0%) recommended actions had been completed (see Table 29).

Table 28. Number (%) of recommended actions completed by outcome measure

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number of cases where recommended actions were completed</th>
<th>Total no. of recommended actions completed (% of recommended actions)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1 NSAID &amp; PU (n=110)*</td>
<td>62</td>
<td>7</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blocker (n=698)*</td>
<td>183</td>
<td>27</td>
</tr>
<tr>
<td>3 ACEI/diuretic &amp; lab test (n=568)*</td>
<td>393</td>
<td>42</td>
</tr>
<tr>
<td>4 AT/VT &amp; COC (n=5)*</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>5 Methotrexate &amp; FBC/LFT (n=236)*</td>
<td>69</td>
<td>7</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR (n=127)*</td>
<td>32</td>
<td>21</td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels (n=109)*</td>
<td>40</td>
<td>9</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT (n=135)*</td>
<td>75</td>
<td>19</td>
</tr>
<tr>
<td>9 Methotrexone &amp; weekly dosage (n=126)*</td>
<td>73</td>
<td>5</td>
</tr>
<tr>
<td>10 Amiodarone &amp; daily dosage (n=4)*</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total (n=2118)*</td>
<td>933</td>
<td>137</td>
</tr>
</tbody>
</table>

*n=number of recommended actions
Table 29. Number (%) of recommended actions where it is unknown whether the action was completed

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number of cases where it is unknown if the recommended actions were completed</th>
<th>Total no. of recommended actions where it is unknown if completed (% of recommended actions)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1 NSAID &amp; PU (n=110)*</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>2 Asthma &amp; B-blocker (n=698)*</td>
<td>65</td>
<td>12</td>
</tr>
<tr>
<td>3 ACEI/diuretic &amp; lab test (n=568)*</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>4 AT/VT &amp; COC (n=5)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5 MTX &amp; FBC/LFT (n=236)*</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR (n=127)*</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>7 Li &amp; Li levels (n=109)*</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT (n=135)*</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>9 MTX &amp; weekly dosage (n=126)*</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>10 Amiodarone &amp; daily dosage (n=4)*</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total (n=2118)</strong></td>
<td><strong>140</strong></td>
<td><strong>13</strong></td>
</tr>
</tbody>
</table>

*N=number of recommended actions

In 100 cases, 108 (5.1%) actions were completed which were different to the recommended actions (see Table 30). In 75 cases, 90 (4.2%) recommended actions had been accepted by the GP, but had yet to be completed (see Table 31).
Table 30. Number (%) of recommended actions where an alternative action was completed, by outcome measure

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number of cases where alternatives to the recommended actions were completed</th>
<th>Total no. of alternative actions completed (% of recommended actions)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of actions completed</td>
<td>1</td>
</tr>
<tr>
<td>1 NSAID &amp; PU (n=110)*</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blocker (n=698)*</td>
<td>52</td>
<td>4</td>
</tr>
<tr>
<td>3 ACEI diuretic &amp; lab test (n=568)*</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>4 AT/VT &amp; COC (n=5)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5 Methotrexate &amp; FBC/LFT (n=236)*</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR (n=127)*</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels (n=109)*</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT (n=135)*</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>9 Methotrexate &amp; weekly dosage (n=126)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10 Amiodarone &amp; daily dosage (n=4)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total (n=2118)</strong></td>
<td><strong>92</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>

*N=number of recommended actions

NB: More than one alternative action may have been taken for a recommended action.
Table 31. Number (%) of recommended actions which have been accepted but not yet completed, by outcome measure

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Number of cases where recommended actions were to be completed in the future</th>
<th>Total no. of recommended actions to be completed in the future (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of actions completed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1 NSAID &amp; PU (n=110)*</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>2 Asthma &amp; B-blocker (n=698)*</td>
<td>48</td>
<td>12</td>
</tr>
<tr>
<td>3 ACEI/diuretic &amp; lab test (n=568)*</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>4 AT/VT &amp; COC (n=5)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5 MTX &amp; FBC/LFT (n=236)*</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR (n=127)*</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>7 Li &amp; Li levels (n=109)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT (n=135)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9 MTX &amp; weekly dosage (n=126)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10 Amiodarone &amp; daily dosage (n=4)*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total (n=2118)*</td>
<td>61</td>
<td>13</td>
</tr>
</tbody>
</table>

*n=number of recommended actions

4.3.6 Types of action recommended or completed for each outcome measure

4.3.6.1 Outcome 1: Prescribing NSAIDs to patients with a past history of peptic ulceration

Pharmacists recommended nine different types of action in 79/89 (88.8%) patients identified and that no action be taken for 10 (11.2%) of the 89 patients. Actions were completed in 76/89 (85.4%) patients. Details of all actions recommended and completed are summarised in Table 32 below.
### Table 32. Actions recommended and completed by pharmacists for patients identified by Outcome 1

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=89 patients)</th>
<th>Number (%) completed (n=89 patients)</th>
<th>Percentage of recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop NSAID</td>
<td>37 (41.6)</td>
<td>27 (30.3)</td>
<td>73.0</td>
</tr>
<tr>
<td>Add proton pump inhibitor</td>
<td>29 (32.6)</td>
<td>14 (12.4)</td>
<td>48.3</td>
</tr>
<tr>
<td>Add screen message to avoid NSAIDs and add previous ulcer to significant history</td>
<td>25 (28.1)</td>
<td>29 (32.6)</td>
<td>116.0*</td>
</tr>
<tr>
<td>Correct coding error e.g. remove peptic ulceration related diagnosis code</td>
<td>7 (7.9)</td>
<td>9 (10.1)</td>
<td>128.6*</td>
</tr>
<tr>
<td>Add screen message to prescribe PPI with future NSAIDs</td>
<td>6 (6.7)</td>
<td>7 (7.9)</td>
<td>116.7*</td>
</tr>
<tr>
<td>Add diagnosis detail to problem screen</td>
<td>1 (1.1)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Add read codes</td>
<td>1 (1.1)</td>
<td>1 (1.1)</td>
<td>100</td>
</tr>
<tr>
<td>Review H2-blocker</td>
<td>1 (1.1)</td>
<td>1 (1.1)</td>
<td>100</td>
</tr>
<tr>
<td>Review non-NSAID analgesia</td>
<td>1 (1.1)</td>
<td>1 (1.1)</td>
<td>100</td>
</tr>
<tr>
<td>Patient contacted about presence or absence of symptoms</td>
<td>0</td>
<td>2 (2.2)</td>
<td>-</td>
</tr>
<tr>
<td>Medication review booked/completed</td>
<td>0</td>
<td>2 (2.2)</td>
<td>-</td>
</tr>
<tr>
<td>other action</td>
<td>2 (2.2)</td>
<td>2 (2.2)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>10 (11.2)</td>
<td>5 (5.6)</td>
<td>-</td>
</tr>
<tr>
<td>No action completed</td>
<td>-</td>
<td>8 (9.0)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>1 (1.1)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total number of actions</strong></td>
<td><strong>110</strong></td>
<td><strong>95</strong></td>
<td><strong>77.6</strong></td>
</tr>
</tbody>
</table>

*Action was completed in more cases than it was recommended

Pharmacists most commonly recommended:

- NSAIDs be stopped in 37 (41.6%) of the 89 patients. This recommendation was completed in 73% of these patients. Where pharmacists felt that stopping an NSAID might be unacceptable, they recommended:
  - Adding a proton pump inhibitor to current therapy in 29 (32.6%) of cases. This recommendation was completed in 48.3% of these patients.
  - Adding a screen message to the patient’s record advising prescribers to avoid using NSAIDs in the future and adding the previous peptic ulcer to the patients significant history (so that it was more visible to prescribers). These were the most commonly completed actions in 29 (32.6%) of the 89 patients.
• In 7 (7.9%) patients the history of peptic ulceration was unclear and pharmacists recommended that the coding for peptic ulceration be removed (if appropriate). This action was completed in 9 (10.1%) of cases (in some cases, GPs completed actions which the pharmacists had not recommended).

4.3.6.2 Outcome 2: Prescribing beta-blockers to patients with a history of asthma

Pharmacists recommended 17 different types of action in 433/535 (80.9%) patients. Pharmacists often made multiple recommendations for patients identified for Outcome 2, where if the first recommendation was unsuitable, an alternative recommendation was immediately available to the prescriber e.g. review beta-blocker, or if not suitable then increase frequency of asthma monitoring. Pharmacists recommended that no action be taken for 85 (15.9%) of the 535 patients. Actions were completed in 296 (55.3%) patients. Details of all actions recommended and completed are summarised in Table 33 below.
Table 33. Actions recommended and completed by pharmacists for patients identified by Outcome 2

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=535 patients)</th>
<th>Number (%) completed (n=535 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review beta-blocker</td>
<td>280 (52.3)</td>
<td>127 (23.7)</td>
<td>45.4</td>
</tr>
<tr>
<td><strong>Outcome following review</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blocker stopped</td>
<td>-</td>
<td>60 (11.2)</td>
<td>21.4</td>
</tr>
<tr>
<td>Beta-blocker to be reviewed in the future</td>
<td>-</td>
<td>36 (6.7)</td>
<td>12.9</td>
</tr>
<tr>
<td>Beta-blocker changed to bisoprolol</td>
<td>-</td>
<td>23 (4.3)</td>
<td>8.2</td>
</tr>
<tr>
<td>Weaning off beta-blocker</td>
<td>-</td>
<td>8 (1.5)</td>
<td>2.9</td>
</tr>
<tr>
<td>Recommend asthma review/monitoring</td>
<td>179 (33.5)</td>
<td>68 (12.7)</td>
<td>38.0</td>
</tr>
<tr>
<td>Counsel patient about risks of continuing medication</td>
<td>54 (10.1)</td>
<td>18 (3.4)</td>
<td>33.3</td>
</tr>
<tr>
<td>Correct coding error e.g. recode diagnosis as asthma resolved</td>
<td>52 (9.7)</td>
<td>50 (9.4)</td>
<td>96.2</td>
</tr>
<tr>
<td>Add message to screen re. monitoring asthma with beta-blocker/reason for beta-blocker</td>
<td>23 (4.3)</td>
<td>46 (8.6)</td>
<td>200</td>
</tr>
<tr>
<td>Request confirmation of diagnosis</td>
<td>20 (3.7)</td>
<td>13 (2.4)</td>
<td>65.0</td>
</tr>
<tr>
<td>Contact consultant to query beta-blocker</td>
<td>19 (3.6)</td>
<td>15 (2.9)</td>
<td>78.9</td>
</tr>
<tr>
<td>Add read codes</td>
<td>13 (2.5)</td>
<td>13 (2.5)</td>
<td>86.7</td>
</tr>
<tr>
<td>Recommend BP check</td>
<td>6 (1.1)</td>
<td>5 (1.0)</td>
<td>83.3</td>
</tr>
<tr>
<td>Add diagnosis detail to problem/summary screen</td>
<td>5 (0.9)</td>
<td>4 (0.8)</td>
<td>80.0</td>
</tr>
<tr>
<td>Add “asthma resolved” to notes</td>
<td>4 (0.7)</td>
<td>7 (1.4)</td>
<td>175*</td>
</tr>
<tr>
<td>Recommend medication review</td>
<td>3 (0.6)</td>
<td>19 (3.7)</td>
<td>633.3*</td>
</tr>
<tr>
<td>Add salbutamol inhaler</td>
<td>3 (0.6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Add screen message to avoid beta-blockers with asthma</td>
<td>3 (0.6)</td>
<td>11 (2.1)</td>
<td>366.7*</td>
</tr>
<tr>
<td>Add screen reminder to review beta-blocker</td>
<td>2 (0.4)</td>
<td>12 (2.3)</td>
<td>600.0*</td>
</tr>
<tr>
<td>Implement changes recommended in hospital letter (not related to indicator)</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>100</td>
</tr>
<tr>
<td>Change inhaler devices</td>
<td>1 (0.2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Screen reminder for asthma review added</td>
<td>-</td>
<td>2 (0.4)</td>
<td>-</td>
</tr>
<tr>
<td>Beta-blocker restarted at patient request</td>
<td>-</td>
<td>2 (0.4)</td>
<td>-</td>
</tr>
<tr>
<td>Reduce repeat authorisation to 0 to prompt monitoring</td>
<td>-</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td>Other action</td>
<td>22 (4.1)</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td>Beta-blocker already stopped</td>
<td>1 (0.2)</td>
<td>8 (1.5)</td>
<td>-</td>
</tr>
<tr>
<td>Insufficient time to review</td>
<td>16 (3.0)</td>
<td>16 (3.0)</td>
<td>-</td>
</tr>
<tr>
<td>no action recommended</td>
<td>85 (15.9)</td>
<td>77 (14.8)</td>
<td>-</td>
</tr>
<tr>
<td>no action completed</td>
<td>-</td>
<td>219 (42.0)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>56 (10.8)</td>
<td>-</td>
</tr>
<tr>
<td>Form lost</td>
<td>-</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total no. actions</strong></td>
<td><strong>800</strong></td>
<td><strong>794</strong></td>
<td><strong>46.0</strong></td>
</tr>
</tbody>
</table>

*Action was completed in more cases than it was recommended*
Pharmacists most commonly recommended:

- Reviewing beta-blocker prescribing in 280 (52.3%) patients; this recommendation was accepted in 45.4% of these patients. These actions included stopping betablockers (60 (11.2%) patients), changing non-selective beta-blockers to bisoprolol (23 (4.3%) patients), weaning patients off betablockers (8 (1.5%) patients) and agreeing to review the betablockers at the patient’s next routine appointment (36 (6.7%) patients).
- That patients either have an asthma review (if overdue) or more frequent asthma monitoring in 179 (33.5%) patients; this action was completed in 38% of these patients.
- Counselling about the potential risks of continuing the beta-blocker, and what action to take if problems occurred, in 54 (10.1%) patients; this action was completed in 33.3% of these patients.
- Removing the diagnosis code for asthma (or recoding as asthma resolved) in 52 (9.7%) patients where the history of asthma was unconvincing; this action was completed in 96.2% of these patients.

4.3.6.3 Outcome 3: Monitoring renal function and electrolytes in patients aged 75 years and older prescribed an angiotensin converting enzyme inhibitor or a loop diuretic long-term

Pharmacists recommended 9 different types of action for 509/561 (90.7%) patients and that no action be taken for 47 (8.5%) patients. Actions were completed in 458 (81.6%) patients. Details of all actions recommended and completed are summarised in Table 34 below.
### Table 34. Actions recommended and completed by pharmacists for patients identified by Outcome 3

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=561 patients)</th>
<th>Number (%) completed (n=561 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrange blood test</td>
<td>492 (88.5)</td>
<td>434 (78.2)</td>
<td>88.4</td>
</tr>
<tr>
<td>Add read codes (e.g., blood test)</td>
<td>58 (10.4)</td>
<td>54 (9.7)</td>
<td>87.7</td>
</tr>
<tr>
<td>Screen message to monitor blood tests at an appropriate interval</td>
<td>8 (1.4)</td>
<td>10 (1.8)</td>
<td>93.1</td>
</tr>
<tr>
<td>Recommend medication review</td>
<td>2 (0.4)</td>
<td>1 (0.2)</td>
<td>50.0</td>
</tr>
<tr>
<td>Review diuretic prescription</td>
<td>2 (0.4)</td>
<td>3 (0.6)</td>
<td>150.0*</td>
</tr>
<tr>
<td>Review monitoring arrangements</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>100.0</td>
</tr>
<tr>
<td>Obtain blood result from secondary care and read code</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>100.0</td>
</tr>
<tr>
<td>Discuss blood results with GP</td>
<td>1 (0.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Contact clinic and request regular results via lablink</td>
<td>1 (0.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diuretic stopped</td>
<td>-</td>
<td>2 (0.4)</td>
<td>-</td>
</tr>
<tr>
<td>Letter sent to patient reminding them of need for regular blood results</td>
<td>-</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td>Other action</td>
<td>-</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>47 (8.5)</td>
<td>46 (8.3)</td>
<td>97.8</td>
</tr>
<tr>
<td>No action completed</td>
<td>-</td>
<td>46 (8.3)</td>
<td>-</td>
</tr>
<tr>
<td>Patient declined bloods</td>
<td>-</td>
<td>7 (1.3)</td>
<td>-</td>
</tr>
<tr>
<td>Patient not contactable</td>
<td>-</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td>Unable to bleed and decided not to pursue further</td>
<td>-</td>
<td>1 (0.2)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>4 (0.7)</td>
<td>-</td>
</tr>
<tr>
<td>Form lost</td>
<td>-</td>
<td>2 (0.4)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total number of actions</strong></td>
<td><strong>566</strong></td>
<td><strong>508</strong></td>
<td><strong>89.8</strong></td>
</tr>
</tbody>
</table>

*Action was completed in more cases than it was recommended*

Pharmacists most commonly recommended that:

- A blood test be arranged in 492 (88.5%) patients; this was completed in 88.4% of these patients.
- Existing blood test results be Read coded in the electronic record in 58 (10.4%) patients; this was completed in 87.7% of these patients.
4.3.6.4 Outcome 4: Prescribing combined hormonal contraceptive preparations in women with a past medical history of venous or arterial thrombosis

Pharmacists recommended two different types of action for four patients and that no action be taken for one of the five patients. Actions were completed in four patients. Details of all actions recommended and completed are summarised in Table 35 below.

Table 35. Actions recommended and completed by pharmacists for patients identified by Outcome 4

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n = 5 patients)</th>
<th>Number (%) completed (n = 5 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct coding error</td>
<td>3 (60)</td>
<td>3 (60.0)</td>
<td>100.0</td>
</tr>
<tr>
<td>Stop COC</td>
<td>2 (40)</td>
<td>2 (40.0)</td>
<td>100.0</td>
</tr>
<tr>
<td>No action</td>
<td>1 (20)</td>
<td>1 (20.0)</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Total number of actions</strong></td>
<td><strong>5</strong></td>
<td><strong>5</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

Pharmacists recommended that:

- The diagnosis of thrombosis be removed from 3 (60%) patients’ electronic records where the diagnosis was unclear or had subsequently been found to be incorrect; this action was completed in all these patients.
- The combined oral contraceptive be stopped in 2 (40%) patients; this action was completed in both these patients.

4.3.6.5 Outcome 5: Monitoring full blood count and/or liver function tests in patients receiving methotrexate

Pharmacists recommended 13 different types of action for 131/181 (72.4%) patients and that no action be taken for 50/181 (27.6%) patients. Actions were completed in 112 (61.9%) patients. Details of all actions recommended and completed are summarised in Table 36 below.
Table 36. Actions recommended and completed by pharmacists for patients identified by Outcome 5

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=181 patients)</th>
<th>Number (%) completed (n=181 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrange blood test</td>
<td>56 (30.9)</td>
<td>41 (22.7)</td>
<td>73.2</td>
</tr>
<tr>
<td>Add read codes e.g. blood test result</td>
<td>41 (22.7)</td>
<td>32 (17.7)</td>
<td>78.0</td>
</tr>
<tr>
<td>Obtain blood result from secondary care and read code</td>
<td>39 (21.5)</td>
<td>38 (21.0)</td>
<td>97.4</td>
</tr>
<tr>
<td>Contact clinic and request regular results via lablink or letter (correct GP code to allow lab linking)</td>
<td>28 (15.5)</td>
<td>22 (12.2)</td>
<td>78.6</td>
</tr>
<tr>
<td>Monitor exceptions with search template</td>
<td>25 (13.8)</td>
<td>25 (13.8)</td>
<td>100.0</td>
</tr>
<tr>
<td>Add screen message to monitor bloods at appropriate interval</td>
<td>19 (10.5)</td>
<td>21 (11.6)</td>
<td>110.5*</td>
</tr>
<tr>
<td>Review monitoring arrangements</td>
<td>11 (6.1)</td>
<td>12 (6.6)</td>
<td>109.1*</td>
</tr>
<tr>
<td>Prescribe folic acid</td>
<td>4 (2.2)</td>
<td>4 (2.2)</td>
<td>100.0</td>
</tr>
<tr>
<td>Send letter to patient reminding of need for regular blood test</td>
<td>3 (1.7)</td>
<td>2 (1.1)</td>
<td>66.6</td>
</tr>
<tr>
<td>Stop methotrexate</td>
<td>2 (1.1)</td>
<td>3 (1.6)</td>
<td>150.0*</td>
</tr>
<tr>
<td>Alter dose instructions for methotrexate</td>
<td>1 (0.6)</td>
<td>1 (0.6)</td>
<td>100.0</td>
</tr>
<tr>
<td>Recommend medication review</td>
<td>1 (0.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Discuss blood results with GP</td>
<td>1 (0.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Patient removed from practice list</td>
<td>-</td>
<td>1 (0.6)</td>
<td>-</td>
</tr>
<tr>
<td>other action</td>
<td>3 (1.7)</td>
<td>1 (0.6)</td>
<td>33.3</td>
</tr>
<tr>
<td>Form lost</td>
<td>1 (0.6)</td>
<td>1 (0.6)</td>
<td>-</td>
</tr>
<tr>
<td>no action completed</td>
<td>-</td>
<td>26 (14.4)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>50 (27.6)</td>
<td>50 (27.6)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>5 (2.8)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total number of actions</strong></td>
<td><strong>234</strong></td>
<td><strong>203</strong></td>
<td><strong>86.8</strong></td>
</tr>
</tbody>
</table>

*Action was completed in more cases than it was recommended

Pharmacists most commonly recommended that:

- Blood tests be arranged in 56 (31.3%) patients; this action was completed in 73.2% of these patients.
- Existing blood test results be Read coded on the electronic record in 41 (22.9%) patients; this action was completed in 78.0% of these patients.
- Blood test results be obtained from the specialist clinic monitoring 39 (21.8%) of patients and read coded on their electronic record; this action was completed in 97.4% of these patients.
• The clinic responsible for laboratory monitoring of 28 (15.6%) patients be requested to send the results via lab link or letter on a regular basis to the practice; this recommendation was accepted in 78.6% of these patients.

• A search template be set up to identify patients who have not had their bloods monitored within an appropriate interval in 25 (14%) patients; this action was completed in all patients.

• A screen message be added to the electronic record of 19 (10.6) patients reminding prescribers to monitor bloods at an appropriate interval; this action was completed in all these patients, and an additional 2 patients.

4.3.6.6 **Outcome 6: Monitoring INR in patients receiving warfarin**

Pharmacists recommended 11 different types of action for 70/213 (32.9%) patients and that no action be taken for 141 (66.5%) of 213 patients, and actions were completed in 66 (31.0%) patients. Details of all actions recommended and completed are summarised in Table 37 below.
Table 37. Actions recommended and completed by pharmacists for patients identified by Outcome 6

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=213 patients)</th>
<th>Number (%) completed (n=213 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtain blood result from secondary care and read code</td>
<td>28 (13.1)</td>
<td>29 (13.6)</td>
<td>103.6*</td>
</tr>
<tr>
<td>add read codes (e.g. blood test)</td>
<td>24 (11.3)</td>
<td>25 (11.7)</td>
<td>104.2*</td>
</tr>
<tr>
<td>Review monitoring arrangements</td>
<td>22 (10.3)</td>
<td>23 (10.8)</td>
<td>104.5*</td>
</tr>
<tr>
<td>Contact clinic and request regular blood results via lablink</td>
<td>20 (9.4)</td>
<td>15 (7.1)</td>
<td>75.0</td>
</tr>
<tr>
<td>Arrange blood test</td>
<td>13 (6.1)</td>
<td>10 (4.7)</td>
<td>76.9</td>
</tr>
<tr>
<td>correct coding error</td>
<td>4 (1.9)</td>
<td>1 (0.5)</td>
<td>25.0</td>
</tr>
<tr>
<td>Monitor exceptions with search template</td>
<td>10 (4.7)</td>
<td>10 (4.7)</td>
<td>100.0</td>
</tr>
<tr>
<td>Add screen message to monitor bloods at an appropriate interval</td>
<td>1 (0.5)</td>
<td>2 (0.9)</td>
<td>200.0*</td>
</tr>
<tr>
<td>Record monitoring arrangements on medical record</td>
<td>1 (0.5)</td>
<td>6 (2.8)</td>
<td>600.0*</td>
</tr>
<tr>
<td>Ask patient to contact practice with INR result (Self monitoring)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>100.0</td>
</tr>
<tr>
<td>Recommend medication review</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>100.0</td>
</tr>
<tr>
<td>other action</td>
<td>1 (0.5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Warfarin already stopped</td>
<td>1 (0.5)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>no action completed</td>
<td>-</td>
<td>8 (3.8)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>143 (67.1)</td>
<td>141 (66.2)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>6 (2.8)</td>
<td>-</td>
</tr>
<tr>
<td>Total number of actions</td>
<td><strong>126</strong></td>
<td><strong>123</strong></td>
<td><strong>97.6</strong></td>
</tr>
</tbody>
</table>

*Action was completed in more cases than it was recommended

Pharmacists most commonly recommended that:

- Blood test results be obtained from the specialist clinic monitoring 28 (13.2%) of patients and Read coded on their electronic record; this action was completed in all these patients and one additional patient.
- Existing blood test results be Read coded on the electronic record in 24 (11.3%) patients this action was completed in all these patients and one additional patient.
- The arrangements for monitoring 22 (10.4%) patients INR be confirmed and recorded on the electronic record; this action was completed in all these patients and one additional patient.
- The clinic responsible for monitoring 20 (9.4%) patients’ INR be requested to send the results via lab link; this recommendation was accepted in 15 (75.0%) of these patients.
• Blood tests be arranged in 13 (6.1%) patients; this action was completed in 76.9% of these patients.

4.3.6.7 Outcome 7: Monitoring lithium levels in patients receiving lithium

Pharmacists recommended 8 different types of action for 70/99 (70.7%) patients and that no action be taken for 29 (29.3%) patients. Actions were completed in 63 (63.6%) patients. Details of all actions recommended and completed are summarised in Table 38 below.

Table 38. Actions recommended and completed by pharmacists for patients identified by Outcome 7

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=99 patients)</th>
<th>Number (%) completed (n=98 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrange blood test</td>
<td>46 (46.5)</td>
<td>40 (40.4)</td>
<td>87.0</td>
</tr>
<tr>
<td>Add read codes (e.g. blood test)</td>
<td>16 (16.2)</td>
<td>12 (12.1)</td>
<td>75.0</td>
</tr>
<tr>
<td>Obtain blood result from secondary care and read code</td>
<td>15 (15.2)</td>
<td>13 (13.1)</td>
<td>86.7</td>
</tr>
<tr>
<td>Review monitoring arrangements</td>
<td>12 (12.1)</td>
<td>12 (12.1)</td>
<td>100.0</td>
</tr>
<tr>
<td>Monitor exceptions with search template</td>
<td>11 (11.1)</td>
<td>13 (13.1)</td>
<td>118.2</td>
</tr>
<tr>
<td>Contact clinic and request regular results via lablink (correct GP code to allow lab linking)</td>
<td>6 (6.1)</td>
<td>6 (6.1)</td>
<td>100.0</td>
</tr>
<tr>
<td>Add screen message to monitor bloods at appropriate intervals</td>
<td>3 (3.0)</td>
<td>4 (4.0)</td>
<td>133.3</td>
</tr>
<tr>
<td>Record monitoring arrangements on medical record</td>
<td>-</td>
<td>2 (2.0)</td>
<td>-</td>
</tr>
<tr>
<td>Stop lithium</td>
<td>1 (1.0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>1 (1.0)</td>
<td>-</td>
</tr>
<tr>
<td>No action completed</td>
<td>-</td>
<td>10 (10.1)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>29 (29.3)</td>
<td>28 (28.3)</td>
<td>-</td>
</tr>
<tr>
<td>Patient declined bloods</td>
<td>-</td>
<td>1 (1.0)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>1 (1.0)</td>
<td>-</td>
</tr>
<tr>
<td>Total number of actions</td>
<td>110</td>
<td>89</td>
<td>80.9</td>
</tr>
</tbody>
</table>

Pharmacists most commonly recommended that:

• Blood tests be arranged in 46 (46.9%) patients; this action was completed in 87.0% of these patients
• Existing blood test results be Read coded on the electronic record in 16 (16.3%) patients this action was completed in all these patients and one additional patient.

• Blood test results be obtained from the specialist clinic monitoring 28 (13.2%) of patients and read coded on their electronic record; this action was completed in 75.0% of these patients.

• The arrangements for monitoring 12 (12.2%) patients lithium levels be confirmed and recorded on the electronic record; this action was completed in all these patients.

• A search template be set up to identify patients who have not had their bloods monitored within an appropriate interval in 11 (11.2%) patients; this action was completed in all patients and two additional patients.

4.3.6.8 Outcome 8: Monitoring thyroid function tests in patients receiving amiodarone

Pharmacists recommended 7 different types of action for 99/118 (83.9%) patients and that no action be taken for 19 (16.1%) of 118 patients. Actions were completed in 98 (83.1%) patients. Details of all actions recommended and completed are summarised in Table 39 below.
Table 39. Actions recommended and completed by pharmacists for patients identified by Outcome 8

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=118 patients)</th>
<th>Number (%) completed (n=118 patients)</th>
<th>% Recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrange blood test</td>
<td>96 (82.1)</td>
<td>92 (78.6)</td>
<td>95.8</td>
</tr>
<tr>
<td>Add screen message to monitor bloods at appropriate intervals</td>
<td>15 (12.8)</td>
<td>15 (12.8)</td>
<td>100.0</td>
</tr>
<tr>
<td>Add read codes (eg blood test)</td>
<td>9 (7.7)</td>
<td>9 (7.7)</td>
<td>66.7</td>
</tr>
<tr>
<td>Monitor exceptions with search template</td>
<td>9 (7.7)</td>
<td>3 (2.6)</td>
<td>33.3</td>
</tr>
<tr>
<td>Alter dose instructions for amiodarone</td>
<td>3 (2.6)</td>
<td>3 (2.6)</td>
<td>100.0</td>
</tr>
<tr>
<td>Review monitoring arrangements</td>
<td>2 (1.7)</td>
<td>1 (0.9)</td>
<td>50.0</td>
</tr>
<tr>
<td>Implement changes recommended in hospital letter (unrelated to indicator)</td>
<td>1 (0.9)</td>
<td>1 (0.9)</td>
<td>100.0</td>
</tr>
<tr>
<td>Obtain blood result from secondary care and read code</td>
<td>-</td>
<td>2 (1.7)</td>
<td>-</td>
</tr>
<tr>
<td>Medication review booked/completed</td>
<td>-</td>
<td>2 (1.7)</td>
<td>-</td>
</tr>
<tr>
<td>Letter sent to patient reminding of need for regular blood tests</td>
<td>-</td>
<td>1 (0.9)</td>
<td>-</td>
</tr>
<tr>
<td>No action completed</td>
<td>-</td>
<td>4 (3.4)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>19 (16.1)</td>
<td>17 (14.5)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>5 (4.3)</td>
<td>-</td>
</tr>
<tr>
<td>Patient declined bloods</td>
<td>-</td>
<td>1 (0.9)</td>
<td>-</td>
</tr>
<tr>
<td>Patient not contactable</td>
<td>-</td>
<td>1 (0.9)</td>
<td>-</td>
</tr>
<tr>
<td>Total number of actions</td>
<td>135</td>
<td>129</td>
<td>95.6</td>
</tr>
</tbody>
</table>

Pharmacists most commonly recommended that:

- Blood tests be arranged in 96 (82.1%) patients; this action was completed in 95.8% of these patients
- A screen message be added to the electronic record of 15 (12.8%) patients reminding prescribers to monitor bloods at an appropriate interval; this action was completed in all these patients

4.3.6.9 **Outcome 9: Prescribing methotrexate without instructions that methotrexate should be taken weekly**

Pharmacists recommended 10 different types of action for 119/228 (52.2%) patients and that no action be taken for 109 (47.8%) patients. Actions were completed in 78
(34.2%) patients. Details of all actions recommended and completed are summarised in Table 40 below.

Table 40. Actions recommended and completed by pharmacists for patients identified by Outcome 9

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=228 patients)</th>
<th>Number (%) completed (n=228 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alter dose instructions for methotrexate</td>
<td>100 (44.1)</td>
<td>65 (28.6)</td>
<td>65.0</td>
</tr>
<tr>
<td>Prescribe folic acid</td>
<td>5 (2.2)</td>
<td>5 (2.2)</td>
<td>100.0</td>
</tr>
<tr>
<td>Change methotrexate to 2.5mg tablets</td>
<td>4 (1.8)</td>
<td>4 (1.8)</td>
<td>100.0</td>
</tr>
<tr>
<td>arrange blood test</td>
<td>4 (1.8)</td>
<td>2 (0.9)</td>
<td>50.0</td>
</tr>
<tr>
<td>Alter folic acid dose</td>
<td>3 (1.3)</td>
<td>1 (0.4)</td>
<td>33.3</td>
</tr>
<tr>
<td>Obtain blood result from secondary care and read code</td>
<td>2 (0.9)</td>
<td>1 (0.4)</td>
<td>50.0</td>
</tr>
<tr>
<td>Recommend alter quantity supplied</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td>100.0</td>
</tr>
<tr>
<td>Screen message to monitor bloods at appropriate intervals</td>
<td>1 (0.4)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Stop methotrexate</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td>100.0</td>
</tr>
<tr>
<td>Contact secondary care re. methotrexate dose</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
<td>100.0</td>
</tr>
<tr>
<td>other action</td>
<td>4 (1.8)</td>
<td>3 (1.3)</td>
<td>75.0</td>
</tr>
<tr>
<td>No action recommended</td>
<td>108 (47.6)</td>
<td>105 (46.3)</td>
<td>-</td>
</tr>
<tr>
<td>Form lost</td>
<td>-</td>
<td>3 (1.3)</td>
<td>-</td>
</tr>
<tr>
<td>No action completed</td>
<td>-</td>
<td>39 (17.2)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown outcome</td>
<td>-</td>
<td>2 (0.9)</td>
<td>-</td>
</tr>
<tr>
<td>Total number of actions</td>
<td>126</td>
<td>84</td>
<td>66.7</td>
</tr>
</tbody>
</table>

Pharmacists most commonly recommended that:

- The dosage instructions for 100 (44.1%) patients prescribed methotrexate be amended in line with NPSA recommendations e.g. prescribed weekly and/or dose given in milligrams and number of tablets; this action was completed in 65% of these patients
- Folic acid be prescribed to 5 (2.2%) patients in line with local recommendations for patients taking regular methotrexate; this action was completed in all these patients
- The strength of methotrexate tablet prescribed for 4 (1.8%) patients be changed to 2.5mg in line with NPSA recommendations; this action was completed for all patients.
4.3.6.10 Outcome 10: Prescribing long term amiodarone at total daily doses greater than 200mg

Pharmacists recommended that the dose instructions for 4/9 (44.4%) patients be altered to 200mg daily; this action was completed in two of these patients. Pharmacists recommended that no action be taken for 5 (55.6%) patients and no action was completed in 7 (77.8%) patients. Details of all actions recommended and completed are summarised in Table 41 below.

Table 41. Actions recommended and completed by pharmacists for patients identified by Outcome 10

<table>
<thead>
<tr>
<th>Actions</th>
<th>Number (%) recommended (n=9 patients)</th>
<th>Number (%) completed (n=9 patients)</th>
<th>% recommended actions completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alter dose instructions for amiodarone</td>
<td>4 (44.4)</td>
<td>2 (22.2)</td>
<td>50.0</td>
</tr>
<tr>
<td>No action completed</td>
<td>-</td>
<td>2 (22.2)</td>
<td>-</td>
</tr>
<tr>
<td>No action recommended</td>
<td>5 (55.6)</td>
<td>5 (55.6)</td>
<td>-</td>
</tr>
<tr>
<td>Total number of actions</td>
<td>4</td>
<td>2</td>
<td>50.0</td>
</tr>
</tbody>
</table>

4.3.7 Time taken for pharmacists to make recommendations and complete agreed actions

Information on the time taken for pharmacists to review cases, make recommendations and complete agreed actions was available for 1890/2038 (92.7%) cases. Median time taken for each intervention was 20 minutes (IQR 10, 30) (range from 0 to 180 minutes). The median time taken for each outcome measure is shown in Table 42 below.
Table 42. Median time taken by pharmacists to review cases, make recommendations, and complete agreed actions for each outcome measure

<table>
<thead>
<tr>
<th>Outcome measure (number patients identified)</th>
<th>Median time taken (minutes)</th>
<th>IQR</th>
<th>Min, Max</th>
<th>Total intervention time for all patients (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (89)</td>
<td>20</td>
<td>15, 30</td>
<td>5, 120</td>
<td>38.5</td>
</tr>
<tr>
<td>2 (520)</td>
<td>30</td>
<td>15, 45</td>
<td>0, 180</td>
<td>273.2</td>
</tr>
<tr>
<td>3 (552)</td>
<td>15</td>
<td>10, 30</td>
<td>5, 150</td>
<td>198.6</td>
</tr>
<tr>
<td>4 (5)</td>
<td>10</td>
<td>10, 40</td>
<td>10, 60</td>
<td>1.8</td>
</tr>
<tr>
<td>5 (180)</td>
<td>17.5</td>
<td>10, 25</td>
<td>5, 75</td>
<td>58.6</td>
</tr>
<tr>
<td>6 (93)</td>
<td>15</td>
<td>10, 20</td>
<td>5, 120</td>
<td>28.5</td>
</tr>
<tr>
<td>7 (98)</td>
<td>15</td>
<td>10, 30</td>
<td>5, 75</td>
<td>33.6</td>
</tr>
<tr>
<td>8 (117)</td>
<td>20</td>
<td>15, 30</td>
<td>5, 105</td>
<td>50.4</td>
</tr>
<tr>
<td>9 (227)</td>
<td>10</td>
<td>5, 15</td>
<td>2, 60</td>
<td>45.7</td>
</tr>
<tr>
<td>10 (9)</td>
<td>20</td>
<td>10, 40</td>
<td>5, 60</td>
<td>3.8</td>
</tr>
</tbody>
</table>

The total time spent assessing cases, making recommendations and changes was 732.6 hours (97.7 working days); equivalent to 2.7 working days per practice (based on a standard NHS pharmacist contract of 7.5 hour days).

Pharmacists working in small practices (list size <2500) spent a median of 30 minutes on each case (IQR 15, 30) (max 120). The total time they spent assessing cases, making recommendations and changes was 34.6 hrs (4.6 working days or 1.2 days per practice).

Pharmacists working in medium-sized practices (list size 2500-6000) spent a median of 15 minutes on each case (IQR 10, 30) (max 180). The total time they spent assessing cases, making recommendations and changes was 153.5 hrs (20.5 working days or 1.6 days per practice).

Pharmacists working in large practices (list size >6000) spent a median of 20 mins on each case (IQR 10, 30) (max 150). The total time they spent assessing cases, making recommendations and changes was 544.5 hrs (72.6 working days or 3.8 days per practice).
4.4 Discussion

The summary data have shown that pharmacists made a broad range of recommendations in order to reduce the risk of harm to individual patients. Many of these recommendations would have implications for the future management of these patients, and in some cases, other patients within the practices.

4.4.1 Strengths and limitations

The summary data recorded by the pharmacists give us a broad overview of the types of recommendations made by pharmacists for individual patients, the outcomes of these recommendations and the time pharmacists spent on each case. This allows us to assess how many of the recommendations made by pharmacists were implemented in the practices at the individual patient level, and how much pharmacist time was devoted to individual patient interventions. In addition, from this data it is possible to predict which interventions are most likely to be accepted by general practice staff.

The summary data do not, however, give us detail about the pharmacists’ recommendations and why they were made, or help us understand why some recommendations were not accepted. Also, the data do not help us to understand what role the pharmacists played in the practices when they were not working on individual patient interventions. Given that the vast majority of pharmacist time appears to have been spent in other duties, this is a significant limitation of the summary data in terms of understanding the role of the pharmacist in the trial. A detailed analysis of the pharmacist case record forms and general action forms should provide greater understanding of the role of the pharmacist within the practice and why some recommendations were not accepted.

It should be noted that there are small differences in numbers of patients identified in the pharmacist reports and those included in the main trial analysis. This is partly due to pharmacists not recording information on all patients identified by the computer searches, and partly due to them sometimes including additional patients that they had identified. In addition, in the main trial, the process of data cleaning removed
small numbers of patients (identified by the practice-level computer searches) because they did not fit the outcome measure criteria.

4.4.2 Specificity of outcome measures for identifying patients at clinical risk of harm

Pharmacists judged that nearly three-quarters of the cases identified by the electronic searches were at clinical risk of harm, suggesting that the outcome measures may be a useful way of targeting pharmacists work to patients at a high risk of harm from medicines management problems. However, the proportion of patients considered at clinical risk of harm varied greatly between outcome measures with 90% or more patients identified by Outcomes 1, 3, and 8 judged to be at clinical risk, whilst less than a quarter of patients identified by Outcome 6 were judged to be at clinical risk. However, the majority of these patients (114) were registered in one practice which had a parallel recording system for patients' INRs which was not identified in the electronic searches. Therefore, excluding these data, 50 (50.5%) of 99 patients were considered to be at clinical risk by the pharmacists. Problems with the compatibility of Outcome 9 with changes to clinical computer systems meant that only one-third of patients identified were judged to be at clinical risk.

4.4.3 Pharmacists’ recommendations

Pharmacists made recommendations to improve medicines management in three-quarters of the cases identified, and actions were completed in almost two-thirds of the cases identified. The number of recommendations made per case varied, with half of cases receiving only one recommendation. Where multiple recommendations were made, these were often of the form “I recommend action A, but if this is not suitable/accepted, then please consider action B”. This could be why the level of acceptance for the pharmacists’ recommendations was comparatively low for Outcome 2 (around one-third of recommendations were accepted).

Pharmacists recommended actions in more cases where they considered the patient to be at clinical risk (87.8% of “at clinical risk cases” compared to 74.5% of all cases). In addition, actions were completed in more cases where patients were considered to be at clinical risk (73% of “at clinical risk cases” compared to 61.5% of all cases).
Pharmacists’ recommendations were targeted to the outcome measure being addressed, although there were recommendations which overlapped and would be applicable to a wide range of clinical situations. These include:

- Using screen alerts to highlight risky clinical situations such as a history of peptic ulcer, or diagnosis of asthma.
- Ensuring important diagnoses are Read coded in the patients’ significant history (these are then readily available to prescribers in the patients’ summary screen).
- Stopping high risk medications such as NSAIDs or betablockers. Or, where this was not deemed clinically feasible, adding a prophylactic medication, increasing the frequency of monitoring for adverse effects, or counselling patients about the risks of continuing the medication and warning signs of adverse effects to monitor for e.g. shortness of breath.
- Altering dose instructions for high risk medications.
- Removing incorrect diagnosis codes to avoid medications being inappropriately withheld.
- Arranging blood tests for patients where tests are overdue.
- Read coding existing test results so they can be readily viewed on the electronic clinical system.
- Setting up systems to ensure regular reporting of blood test results from specialist monitoring clinics to GP practices (important where shared care arrangements are in place). This could be via letter (requiring manual Read coding) or by ensuring that results were sent via lab link (requiring specialist clinics and laboratories to have the correct GP practice code recorded).
- Setting up monthly search templates to highlight patients where monitoring is overdue, or using screen alerts to highlight appropriate monitoring intervals for high risk medications.
- Confirming monitoring arrangements (and recording these on the electronic clinical system) for patients managed under shared care agreements.

Many of these interventions were not predicted before the start of the study. Instead, they developed from pharmacists’ experience of working with the GPs and learning from each other. This highlights the importance of providing a forum where pharmacists can learn from each other when engaging in new roles.
As might be predicted from the broad range of different recommendations made, the time spent resolving problems in each case varied widely (from 0 to 180 minutes). However, pharmacists reported spending a median of 20 minutes on each case. This included the time needed to assess each case, make recommendations, and implement any agreed changes. The median time spent on each case varied depending on the outcome measure (from 10 minutes to 30 minutes) and practice list size (30 minutes in small practices, 15 minutes in medium practices, and 20 minutes in large practices).

The comparatively short duration of time required to assess and resolve medicines management problems suggests that the PINCER trial pharmacist role could be incorporated into existing primary care and general practice pharmacists’ roles. It is important to remember, however, that in addition to the time spent working directly on individual cases, pharmacists duties included organising and attending meetings, liaising with practice staff, and reviewing systems of work. Therefore, the total commitment of time required by a pharmacist to implement the intervention will be greater than 3 days per practice.

Although Outcome 2 (beta-blockers in asthma) had the lowest percentage of completed actions, it was the most time consuming of the outcome measures. Pharmacists spent over 36 days reviewing 520 patients (median of 30 minutes per patient), and made recommendations in four-fifths of these patients. In contrast, for Outcome 3 (monitoring of renal function and electrolytes in patients prescribed ACE inhibitors or diuretics) pharmacists spent 27 days reviewing 552 patients (median 15 minutes per patient) and recommended actions in nine-tenths of patients. In Outcome 2, actions were completed in two fifths of patients, compared to four-fifths of patients for Outcome 3. Numerically, in Outcome 2, these actions were equivalent to two-thirds of the recommended actions, but only one-third of the recommended actions were completed (the remainder included alternative actions or actions which were accepted and would be completed in the future). In Outcome 3, over four-fifths of the recommended actions were completed.

Before the study began, we predicted that Outcome 2 would be the most difficult for pharmacists to address because of the complexity of assessing the cases and lack of clear guidelines on how to manage patients (which reflects the inadequate information available on the relative risks and benefits or using beta-blockers in
patients with a history of cardiovascular disease). This is reflected in the time taken to review the cases and percentage of cases where actions were completed.

4.4.4 Further research

The summary data have given a broad overview of the pharmacists’ interventions in the general practices. In order to fully understand the role of the pharmacist within the practice, however, a further analysis of the detailed information recorded on individual cases and on general action plans within practices is needed. In addition, further information on the pharmacists’ role may be gleaned from the pharmacists’ diaries and interviews. A qualitative analysis of these data sources is likely to be helpful in understanding why the pharmacist intervention has been successful in reducing the numbers of patients at risk of medication errors.
Chapter 5: Qualitative evaluation of the PINCER trial
5.1 Introduction

A qualitative evaluation study was running parallel to the main RCT. The aim here was to obtain a more detailed understanding of the trial interventions by focusing on the experiences of key stakeholders. It is hoped that this will complement quantitative findings and contribute to a more in-depth appreciation of the social and organisational context in which the interventions are delivered.

5.1.1 Why qualitative evaluation?

Several contextual factors can influence effectiveness of complex RCTs which might be neglected in examining numbers alone. Here, social and organisational aspects in trial practices have to be considered in particular as they might be crucial in affecting outcomes and in addressing issues of generalisability\textsuperscript{60}.

The value of qualitative methods investigating experiences of key players, effects on individuals and perceived feasibility are increasingly recognised in complementing RCTs\textsuperscript{20, 61-67}.

A central component of qualitative evaluation of complex interventions is a focus on the experiences of key stakeholders in aiding the interpretation of quantitative data. These experiences also formed the basis for exploration in the current study exploring issues of generalisability, acceptability and the trial's potential for widespread implementation.

Both positive and negative views of key stakeholders were actively sought in order to gain a comprehensive insight into the trial interventions. Two waves of telephone interviews (brief and in-depth) and multidisciplinary focus groups formed the core of the study. These were conducted throughout the delivery period of the trial.

In outlining both method and results of the qualitative evaluation of the PINCER trial, it is hoped that the potential of embedding longitudinal qualitative evaluations within complex RCTs will become apparent to the reader. Several issues relating to both the practicalities of conducting such studies (especially with regards to sampling and data collection) as well as emerging issues from the viewpoints of those involved will
be discussed in detail. Furthermore, an attempt will be made to outline possible solutions for refinement of the trial interventions and concrete recommendations for a potential roll-out. The research will then be applied to the wider innovation literature.

5.1.2 The organisational context

The present study draws on principles from diffusion of innovations literature, which provides a valuable conceptual framework of how innovations are adopted by individuals over time and how they spread through organisations\cite{68,69}.

Research into the diffusion of innovations in healthcare is increasing but most evidence is coming from industry or other service organisations. In particular, primary care has received little attention, although it was identified as one of the key areas in the NHS improvement plan\cite{70}. Most existing research has focussed on adoption behaviours of individual healthcare professionals (mostly General Practitioners).\cite{71} However, it has been argued that “implementation efforts focusing on the individual physician with a single strategy are unlikely to be successful. Rather, implementation efforts must use multiple strategies that take into account of multiple characteristics of the guideline, practice organisation, and external environment” (p. 172)\cite{72}.

Pharmacists’ routine employment in general practice as well as the utilisation of the full potential of information technology in the healthcare setting is yet to be established. Therefore, the delivery of the PINCER trial interventions is likely to be perceived as innovations by key stakeholders. Diffusion of innovation theory can provide a theoretical background of how specific aspects of the interventions can either facilitate or inhibit the success of the project, and how the results obtained from the qualitative component of the trial can contribute to its widespread implementation (if found to be successful). In particular, characteristics of the primary care environment that make it more receptive to change can be examined in more detail. Conversely, areas that need extra attention for diffusion to occur can be identified. If the interventions are found to be ineffective, the results from the current study can be used to design possible alternatives. Finally, the results may point towards more general characteristics that facilitate the adoption of innovations within the primary care context. The findings can then be utilised to help inform facilitators/barriers of change in other innovations within the primary care context, which have yet to be implemented.
The main components of the current study consisted of a combination of telephone interviews and focus groups. The initial brief interviews aimed at identifying possible early facilitators and/or barriers that may be important to take into account during the future roll-out of the interventions. The in-depth telephone interviews were conducted in order to generate an in-depth appreciation of the acceptability and effectiveness of the interventions under study (especially from the views of trial pharmacists). The focus groups explored potential roll-out, the refinement of the trial interventions, alternative interventions and their acceptability.

5.2 Methods

In order to develop a suitably rounded understanding of the pertinent issues, at the levels of individuals, processes and underlying theory, both negative and positive views from all key stakeholders were sought.

Qualitative data was collected through one-to-one, audio-taped, semi-structured telephone interviews and focus groups. Additional data was collected from four pharmacist meetings facilitated by the research team, notes of practices meetings made by pharmacists during the delivery of the intervention, and six pharmacist diaries.

The initial phase of brief telephone interviews took place at the early stages of the interventions, the in-depth interviews were conducted when the interventions were well underway and the focus groups were conducted when the interventions had been delivered.

Altogether, 20 interviews were conducted in the initial phase and 32 in the second phase.

Interviews lasted between 7 and 60 minutes. Issues addressed in interviews included general perceptions of prescribing safety in general practice, experiences and opinions of the PINCER trial, expectations for the project, sustainability of the interventions, and opinions on the potential roll-out of the intervention.

Six focus groups were conducted altogether lasting between 22 and 68 minutes. The emphasis here was on the wider usability and the potential roll-out of the PINCER
trial exploring possible alternative interventions and associated models (including a discussion of the strengths and limitations of each alternative approach).

Detailed interview schedules and focus group topic guides can be found in Appendix 7.

5.2.1 Participants

In order to obtain a sufficiently rounded understanding of the trial interventions and possible early facilitators and barriers, a variety of key stakeholders was purposively sampled from both intervention sites (Nottingham and Manchester). These included trial pharmacists (interviewed at three different time-points during the delivery of the interventions), GPs, practice managers, nurses, administrative staff, PCT prescribing leads, community pharmacists, and members of the research team* involved in delivering the interventions.

Detailed participant information for each qualitative data collection phase can be found in Table 43-Table 45.

* Please note: these consisted of researchers running the searches and liaising with practices
Table 43. Participant information brief interviews

<table>
<thead>
<tr>
<th>Gender</th>
<th>Intervention Arm</th>
<th>Location</th>
<th>Occupation</th>
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<td>Nottingham</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>ManBi2</td>
<td>F</td>
<td>Pharmacist Intervention</td>
<td>Manchester Practice Manager</td>
</tr>
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<td>Pharmacist Intervention</td>
<td>Manchester GP</td>
</tr>
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<td>Pharmacist</td>
</tr>
<tr>
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<td>F</td>
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<td>M</td>
<td>Simple Feedback</td>
<td>Manchester GP</td>
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<td>Nottingham Practice Manager</td>
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<td>Nottingham Practice Manager</td>
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Table 44. Participant information in-depth interviews

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<td>Pharmacist</td>
</tr>
<tr>
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<td>M</td>
<td>Manchester</td>
<td>Pharmacist</td>
</tr>
<tr>
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<td>Nottingham</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>PharNottDI4</td>
<td>F</td>
<td>Nottingham</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>PharNottDI5</td>
<td>F</td>
<td>Nottingham</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>PharManDI6</td>
<td>F</td>
<td>Manchester</td>
<td>Pharmacist</td>
</tr>
<tr>
<td>CommPharmManPIDI7</td>
<td>M</td>
<td>Manchester</td>
<td>Community Pharmacist</td>
</tr>
<tr>
<td>PracManNottPIDI8</td>
<td>M</td>
<td>Nottingham</td>
<td>Practice Manager</td>
</tr>
<tr>
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<td>Practice Manager</td>
</tr>
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<td>Practice Nurse</td>
</tr>
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</tr>
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<td>Manchester</td>
<td>Practice Manager</td>
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<td>Nottingham</td>
<td>Practice Manager</td>
</tr>
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<td>Practice Manager</td>
</tr>
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<td>PharManEIDI16 (Exit Interview)</td>
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<td>Manchester</td>
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<td>M</td>
<td>Manchester</td>
<td>GP</td>
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<td>GP</td>
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</tr>
<tr>
<td>NurManSFDI21</td>
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<td>Practice Nurse</td>
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<td>GPManSFDI22</td>
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<td>GP</td>
</tr>
<tr>
<td>GPNottSFDI23</td>
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<td>Nottingham</td>
<td>GP</td>
</tr>
<tr>
<td>PCTNottDI24</td>
<td>F</td>
<td>Nottingham</td>
<td>Prescribing lead</td>
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<tr>
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<td>Nottingham</td>
<td>Community Pharmacist</td>
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<td>Prescribing lead</td>
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</tr>
<tr>
<td>PharManEIDI28 (Exit Interview)</td>
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Table 45. Participant information focus groups

<table>
<thead>
<tr>
<th>Participants</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacist Focus Group (3 from Nottingham, 1 from Manchester)</strong></td>
<td>4 PINCER Trial pharmacists, 3 female and one male</td>
<td></td>
</tr>
<tr>
<td><strong>Focus Group pharmacist intervention practice 1, Nottingham</strong></td>
<td>7 participants: practice manager (f), assistant practice manager (f), 4 GPs (3m, 1f), 1 practice nurse (f)</td>
<td></td>
</tr>
<tr>
<td><strong>Focus Group pharmacist intervention practice 2, Nottingham</strong></td>
<td>6 participants: practice manager (f), 1 administrative staff (f), 1 practice nurse (f), 3 GPs (1m, 2f)</td>
<td></td>
</tr>
<tr>
<td><strong>Focus Group simple feedback practice 1, Nottingham</strong></td>
<td>6 participants: practice manager (f), F2 doctor (f), 2 GPs (1m, 1f), medical student (m), PINCER pharmacist (f)</td>
<td></td>
</tr>
<tr>
<td><strong>Focus Group simple feedback practice 2, Nottingham</strong></td>
<td>4 participants: practice manager (f), Deputy Medical Director/GP Nottinghamshire County Teaching PCT (m), 2 Data quality officers (f)</td>
<td></td>
</tr>
<tr>
<td><strong>PCT focus group, Manchester</strong></td>
<td>4 participants: Community Medical Advisor, Senior Medicines Management Individual, GP tutor, Member of the Local Pharmaceutical Committee/Community Pharmacist (all m)</td>
<td></td>
</tr>
<tr>
<td><strong>PCT interview, Nottingham</strong></td>
<td>Senior Member of PCT (f)</td>
<td></td>
</tr>
</tbody>
</table>

5.2.2 Data analysis

Interviews and focus groups were transcribed verbatim. Broad themes and sub-themes were identified employing thematic analysis using NVivo7 software to aid the coding process. Transcripts and notes were analysed one by one, creating themes and sub-themes until no new themes emerged. This resulted in a general framework capturing the essence of the data collected for each stage of data collection. Careful attention was paid to the comparison and integration of different professional groups and intervention arms. This was accomplished through outlining negative cases in particular (i.e. those that do not fit well within the structure).

Credibility of the data and the analysis was enhanced by close involvement of the extended research team, and the local principal investigator in particular. Results of the brief interviews were fed back to pharmacists at a meeting and a second qualitative researcher re-coded brief and in-depth interview transcripts and gave thorough feedback on the report. This resulted in minor amendments.
Data obtained from different sources was triangulated in the analysis by paying particular attention to comparing themes identified across different sources, participants and geographical locations.

5.3 Findings and discussion

Diagrams of emerging results from different phases can be viewed in the Appendix 7. In line with the aims of the qualitative evaluation, the main findings relate to facilitators and barriers to the successful implementation of the interventions. The second part of the results relates to the potential roll-out and possible alternatives. The results are framed in a generally positive view of the trial amongst participants.

5.3.1 Facilitators, barriers and associated conditions

Altogether, a greater number of facilitators than barriers were identified, which may be due to extensive development and piloting work on the intervention and preparation by the research team.

5.3.1.1 Practice attitude

5.3.1.1.1 Willingness to learn

Practice staffs' willingness to listen, learn and to accept change was identified as a facilitator for the successful implementation of the trial.

“Oh yes, I don’t think it will make me feel, well it will make me feel good that somebody’s pointing out to me that what am I doing is not right and I should be really looking at, to ways and things so that we don’t commit the same mistakes again.”

(GP, Simple feedback, Manchester, ManBi6)
GPs from both pharmacist intervention and simple feedback practices appeared grateful that their mistakes were picked up on and expressed positive views towards learning how to improve their practice as opposed to being defensive or threatened.

Willingness to learn as an individual facilitator for the adoption of innovations has been identified in previous studies. However, QOF might to a certain degree contribute to developing this as there are significant financial incentives. Willingness to learn may also be explained in terms of what has been referred to as receptive context. Receptive context can be divided into individual receptivity and organisational receptivity, whereby the willingness to consider change contributes to a higher degree of receptivity.

5.3.1.1.2 Perceived value of the interventions, pharmacists and research in general

The trial was generally positively received by all involved. Participants referred most frequently to the educational value of pharmacist intervention/simple feedback and the trial’s potential to improve patient safety in this context.

“(…) you find out something and we are doing it and know intentionally it will be a good thing to know that, why we shouldn’t be doing that. (…) Yeah, well it will be effective because you are flagging the patients out who’ve been prescribed perhaps inappropriately or unintentionally the things they shouldn’t prescribe where they can cause more complications to them. (…) What will I, will be actually alert, you know, next time we prescribe other things (…)”

(GP, Simple feedback, Manchester, ManBi6)

The perceived value of research in general further reinforced this positive attitude in practices.

This can be viewed in terms of what Rogers refers to as relative advantage and compatibility. Relative advantage, is the extent to which the innovation is seen as better than current practice, fitting in well with interviewees’ perceived educational value of the interventions. Compatibility, on the other hand, is the extent of agreement between the innovation and individual (or organisational) values and
beliefs. Patient safety is clearly an organisational priority, making the PINCER trial interventions compatible.

In the healthcare setting, studies investigating the predictive power of these two innovation attributes and adoption behaviour have been mixed. Although some studies have suggested that diffusion of innovations in healthcare is slow if it involves acquiring new skills, the PINCER trial clearly supports the view that adoption is more influenced by the perceived benefits for patients (i.e. safety).

### 5.3.1.1.3 Perceived appropriateness of the trial’s design and outcome measures

Participants viewed the design of the trial and its outcome measures as appropriate. Typical statements from interviews would include:

> “I think that’s, then obviously [name of the principal investigator] has done his homework and we realize that those areas you know, the nine most current ones but there are different issues in terms of erm, prescribing safety that we see.”

(Pharmacist, Nottingham, NottBi14)

However, participants frequently mentioned issues with outcome number 2 (patients with a computer recorded history of asthma receiving beta blockers). It was felt that here risk assessments had to be made based on individual patient cases and that in some instances GPs decided to continue the beta-blocker.
Similar issues were found with outcome number 1 (patients with a history of peptic ulcer being prescribed NSAIDS).

The group of researchers implementing the PINCER trial may be viewed as what Rogers describes as the change agency. It is the change agency’s aim to implement the innovation into the organisation with a focus on the collective goals of the social system (here to improve prescribing safety). Few studies have investigated the role of the change agency in healthcare innovation and the current study adds to the sparse evidence base in this area by pointing to the important role of individual adopters’ trust in the change agency’s abilities in successful implementation of healthcare innovation\textsuperscript{83, 84}. There are also some implications surrounding the issue of the potential roll-out of the interventions – if the change agency changes then so might an individual’s perceptions of competency, possibly leading to reduced adoption rates (assuming that the perceived competency of the change agency is a strong facilitator).

5.3.1.1.4 Perceived value of pharmacists in primary care

It also became evident from participants’ accounts that the practice’s attitude towards and appreciation of pharmacists’ was important.
This also involved taking an interest in the trial and the pharmacist’s work. A lack of thereof was often expressed in terms of “not being bothered”.

A lack of engagement often resulted in pharmacists chasing practice staff to get things done such as filling in action plans. Pharmacist sometimes concluded that practices were relatively happy for them to do the work, whilst wanting to have as little as possible work.

"In my last few weeks in the practice the senior Practice Nurse has on several occasions expressed her gratitude for the changes she feels I have made in the practice. For her personally she feels she has learnt an enormous amount about monitoring and I can sense that she knows “where the patients are at” in terms of their monitoring.” (Pharmacist diary, Pharmacist 2)

Versus

“The Practice Manager is really rude, has made it quite clear that it is an inconvenience to have me there.” (Pharmacist diary, Pharmacist 1)

Trial pharmacists may be viewed as change agents. According to Rogers, these are individuals “who influence clients’ innovation decisions in a direction deemed desirable by a change agency (p. 335)”79. The change agent (the pharmacist) is typically enlisted by the change agency (the research team) to bring about the desired changes. However, the role of the change agent in healthcare innovations has been poorly researched. Our study supports Roger’s notion of the importance of the change agent’s credibility, the importance of the approach and the extent to which the change agent works through opinion leaders (discussed below). We have
found that the perceived value of the change agent’s role and the perceived competencies can be an important facilitator for adoption. This is in line with the increasing recognition that pharmacists can make a valuable contribution to the healthcare team. Having made these points, it could be argued that the effectiveness of the pharmacist intervention in our study had relatively little to do with their role as change agents, and more to do with the practical support they provided.

5.3.1.5 GPs’ attitudes

Although most pharmacists reported that GPs had been receptive, some pharmacists had experienced issues with GPs, which resulted in increased feelings of frustration and isolation.

Attitudes of GPs were referred to by participants relatively regularly, as a barrier to the success of the interventions. For example, in some instances there appeared to be a certain reluctance to change old practices and defensiveness to pharmacists’ suggestions. There was also often a lack of interest by the GPs for the trial.

“Erm, one GP was a bit defensive in the feedback meeting, you know, he sort of had quite a lot of excuses for things that didn’t really sound very plausible and when I actually looked into patient records, you know, it wasn’t the reasons he was giving at all. I think he was just, you know, saying the first thing that came into his mind in a sort of defensive way, you know, rather than thinking about the real reasons. Or, you know, just accepting that there were other reasons.” (Pharmacist, Manchester, PharManDi1)

However, the biggest and most frequently mentioned issue for pharmacists appeared to be that it was extremely difficult to get GPs to action and return forms issued by the pharmacist. This was in line with the often generally sparse contact between GPs and pharmacists due to GPs’ extremely busy work schedule.

“I think the biggest concern from my point of view (...) is that it’s difficult to manage your time always because you’re constantly dependent on other people’s actions really. You’re constantly waiting for GPs to review them, you know, people go on holiday, forget etc.” (Pharmacist, Manchester, PharManDi2)
GPs, in line with previous studies, may be viewed as opinion leaders\textsuperscript{86}. According to innovation theory, the role of opinion leaders is crucial for the adoption of innovations locally as their apprehensiveness to change this is likely to influence other potential adopters\textsuperscript{86-88}.

Although Rogers has argued that ideally the change agent should harness the influence of opinion leaders, the nature of this relationship remains under-researched\textsuperscript{79}. In the current study, the pharmacist as the change agent has the potential to influence opinion leaders, which makes a good relationship between the two essential for change to occur. If this is not the case and this relationship is characterised by infrequent contact, power struggles, or the opinion leader’s resistance to the change agent’s efforts to implement what has been initiated by the change agency, then the diffusion of the innovation can be inhibited.

5.3.1.2 Other practice context issues/characteristics important in pharmacist intervention practices

5.3.1.2.1 Practice’s previous involvement with pharmacists

Practices’ previous involvement with pharmacists was important for the successful implementation of pharmacist intervention. This often led to a realisation of how helpful pharmacists could be in improving prescribing safety.

“Yes we’ve, with, our PCT has provided some pharmacy support and we’ve found that very helpful, they do educational meetings, erm, I think three a year, erm, and we had a pharmacist coming in and looking at one or two aspects of our prescribing. And that’s always been very helpful, particularly if they’re highlighting patients where they’ve come across potential difficult to find interactions or whatever.” (GP, Pharmacist intervention, Nottingham, NottBi5)

In line with this, the amount of information individual adopters have about the innovation has been found to be crucial in facilitating adoption, especially during Roger’s pre-adoption and early use stage\textsuperscript{89, 90}.
5.3.1.2.2 Accommodation of pharmacists in the practice

In the innovation literature, the degree of integration of the change agent has received little attention. However, as the current study indicates, this integration and move away from being an outsider into becoming a more integral part of the team might play a crucial role for the adoption and diffusion of innovations. In this context, the way the change agent is accommodated appears to be particularly important.

Pharmacists reported that their place in the practice was often not ideal, resulting in feelings of isolation. Repeatedly, pharmacists had to work in busy areas of the reception room, to move desks several times a day not having a stable work station or they had to work in a room remote from the main practice.

“Some days there has been nowhere at all for me to work and I have had to work in the tearoom – difficult as people are coming in and out and there is no computer access.” (Pharmacist diary, Pharmacist 2)

“I had very little to do with GPs/nurses. Was given a room in the attic, so did not see anyone during the day, unless I came out of my room to make tea/coffee etc.” (Pharmacist diary, Pharmacist 6)

As can be seen, increased visual exposure to change agents may be a facilitating factor in getting individuals to adopt.

5.3.1.2.3 Integration of the pharmacist into the practice team

An issue that arose from interviews with trial pharmacists was the isolating nature of their work for the PINCER trial and the lack of opportunities to form good relationships with the practices. The reason for this appeared to be the short amount of time spent in GP practices:
Pharmacists and PCT staff felt that some of these issues could be addressed through having more contact with practice staff through constant pharmacist input over a longer period of time. Practice staff, however, preferred periodical rather than constant pharmacist input.

Nevertheless, it also became apparent from the interviews that, whilst pharmacists did not always feel integrated into the practice, they were in general treated well by the practices and this had been a motivation to get involved in the trial the opportunity to be more proactive than reactive with GPs.

Although this issue has not been investigated in relation to the integration of the change agent, recent studies indicate that multi-professional team working is critical for the spread and sustainability of change. Our findings support the importance of team climate in organisational innovation and suggest that investing in teambuilding activities can maximise the impact of pharmacist intervention.
5.3.1.2.4 Practice meetings with the pharmacist throughout course of the project

Pharmacists further highlighted the importance of regular practice meetings throughout the course of the intervention. These were thought to facilitate contact with practice staff and increased awareness of the trial. It was therefore seen as important that as many members of the practice staff as possible attended these meetings and for the pharmacist to be flexible whilst still planning these meetings well in order to get everyone involved.

“Erm, if they know what you’re there for they’re a little bit happier to help you but if they haven’t been at the meeting they’re not quite sure what you’re doing and all they can see is you at a computer all the time. I think they’re sort of like, you know, ‘Well what are you here doing? What are you doing and why do you need these notes and what are you doing here?’”

(Pharmacist, Nottingham, PharNottD15)

Pharmacists also gave examples of practice meetings that did not go well. These were often characterised by difficulties engaging practice staff, irregular and short timings, cancellations, interruptions small number of practice staff turning up.

5.3.1.2.5 Priorities in practices

Some participants also had the perception that pharmacists’ work for the PINCER trial was not a priority for practices due to busy schedules.

“I think they’ve got so many priorities and in that particular case they were a single-handed practice erm, so many priorities that erm, some of the issues that, you know, with Pincer such as monitoring erm, are possibly not top of the list.”

(Pharmacist, Manchester, PharManBi9)

For some pharmacists, this made it hard to get appointments with practice staff (especially GPs).
In line with this, the importance of aligned priorities in facilitating the successful adoption and implementation of innovations has also been supported in other studies\cite{88, 91, 93-96}. According to Greenhalgh and colleagues, this may be viewed in terms of what Rogers refers to as “mandate for adoption”\cite{97}. Here the individual’s decision to adopt is thought to be influenced by external forces/priorities. This also supports the important role of PCT support in the context of the current study.

5.3.1.3 Pharmacist approach in pharmacist intervention practices

5.3.1.3.1 Non-threatening approach

A non-threatening, constructive and positive approach by the pharmacist was identified as a facilitator for successful adoption by preventing GPs feeling threatened.

“I guess we potentially felt threatened at the outset. You know, here’s somebody coming in who’s going to tell us how we should be doing our job. (...) I suppose a lot of it has to do with the manner in which the Pharmacist approaches it, you know, in other words it needs to be seen as a non-threatening.”

(GP, Pharmacist intervention, Nottingham, NottBi19)

It is relatively well established that under some circumstances GPs can feel threatened by pharmacists’ expanding clinical role. E.g.\cite{98} Studies from (mainly) educational contexts point to a similar direction\cite{99-101}.

5.3.1.3.2 Involving everyone in the practice

It became apparent from pharmacists’ accounts that in their approach of delivering the intervention, involving every member in the practice was considered important. The diffusion of innovation literature in the healthcare context supports these findings, indicating that staff involvement can facilitate the implementation and diffusion of innovations\cite{86, 91, 102, 103}.
5.3.1.3.3 A good personal relationship between the pharmacist and the practice

GPs, pharmacists and practice managers found that a friendly pharmacist was important and a good personal relationship between pharmacist and practice staff was valued.

“… and I guess it depends in part on the personalities, having pharmacists who fit, fit well into the team makes quite a big difference, obviously you can’t predict who’s going to fit where, and you can’t pick and choose.”

(GP, pharmacist intervention, Nottingham, NottBi5)

In line with this, according to Rogers, a strong interpersonal relationship between change agents and clients can facilitate adoption79. Recent critical reviews have reached similar conclusions97, 104.

5.3.1.3.4 Pharmacist competencies important for carrying out PINCER work

Pharmacists were also asked about characteristics and competencies needed for working as a PINCER pharmacist. Among those most frequently mentioned were assertiveness, people, organisational and problem solving skills.

“It’s knowing, it’s kind of, sort of erm, I suppose not making too many waves but being forceful enough to get your own way.”

(Pharmacist, Nottingham, PharNottDi3)

Moreover, the importance of existing clinical skills and experience was viewed as important. Experience was often mentioned in terms of not only clinical experience but also relating to experience of working in the general practice environment in order to gain an insight into the practice dynamics and to identify key players that could then be systematically targeted. This may have taken the form of previous PCT work.
5.3.1.4 Other key individuals

5.3.1.4.1 Practice managers

Practice managers were frequently responsible for organising the trial in the practice. Other roles of practice managers ranged from helping with admin work, such as sending out monitoring letters to patients, to arranging desks and meetings, helping with running the searches on the computer, to providing computer and organisational support. In some cases practice managers also acted as a link between PINCER team and practice staff.

However, the most crucial role of the practice manager in pharmacist intervention practices was that of a change aide in working with the PINCER pharmacist to achieving the objectives of the trial. This was often expressed in terms of providing a link between the pharmacist and GPs and helping the pharmacist to “hassle” GPs so that they would complete actions forms.

“Well if it’s something related to the surgery or practice or my working then I ask the practice manager, he like, some of the doctors, what happened was I left some of them envelopes with some action plans in them. When I went back the next week they were still there, the doctors hadn’t picked them up or some of them were a bit lazy picking their work out of the pigeon holes and so basically the practice manager said, ‘I’ll sort it out, don’t worry’. Then he’s going to go and nag them now with the envelopes.”

(Pharmacist, Manchester, PharManDI6)

Managerial support and facilitation have previously been shown to be essential for the adoption and diffusion of innovations in the healthcare context. However,
the present results provide us with insights into how this managerial facilitation is construed. In this context, it seems that the practical and organisational aspects are particularly important. Systematically harnessing the practice manager’s influence might contribute to maximizing the impact of the trial interventions.

5.3.1.4.2 Nurses and administrative staff

Practice nurses also played an important role in the trial as nurses were routinely responsible for monitoring bloods within practices and also involved completing action plans issued by the pharmacist.

Nurses also often did most of the changes to do with the trial but consulted the GPs if in doubt. This was especially evident in simple feedback practices.

“I think they [referring to GPs] would just take an overview of, from a clinical point of view erm, if I’m honest it’s probably one of the note summarises or the nurses that tend to take, tend to do the work.”
(Practice Manager, Simple feedback, Nottingham, PractManNottSFDI13)

Administrative staff was usually involved in calling patients in for monitoring, helping researchers to sort out administrative issues and putting systems into place for future recalls.

“I also in that practice as well the reception staff also helped me a lot by, by running some of the computer programmes that needed to be run before we could go in there. So they saved me trips down to Stoke, you know, because they was there so they just erm, offered to help. (…) Yeah, very, like they saved me like a lot of travelling time so it was like really helpful.”
(Researcher, ManBi17)

Ideally, practice nurses and administrative staff should therefore be targeted specifically through educational outreach.
5.3.1.4.3 **Regular pharmacist meetings and exchanges with colleagues**

Pharmacists valued contact with other colleagues from the PINCER trial as it allowed sharing of experiences and reduced feelings of isolation.

> “And we got lots of meetings which was really helpful. The meetings were one of the most valuable things because it’s good to share experiences with the other Pharmacists. To see what they think and what they’ve been doing because you pick up ideas from that as well. You know, how to approach your doctors and this, that and the other, so. And they were one, I think they were one of the most valuable things we had. All the meetings, they were very valuable, yes.”

(Pharmacist. Manchester. PharManEIDI16)

This could be seen in terms of what Yetton and colleagues refer to as ‘informal support’ from social networks, which can be an organisational facilitator for the sustainability of innovations in healthcare\textsuperscript{107-111}.

5.3.1.4.4 **Need for patient cooperation**

Patients also played an important role in contributing to the success of the interventions. However, this some patients did not cooperate and refused to get their medication changed, or have their bloods taken.

> “Erm, there’s a few patients that have fallen through monitoring, the repeat senders where you can see they’ve sent letters out to them, repeatedly they’ve sent letters to them but these patients haven’t turned up. And where I have sent a letter to a patient who’s never had any monitoring, which is really surprising, she sort of rang back quite angry to the practice saying, ‘Why have you sent me a letter. I don’t want to have any bloods taken’: So they’ve obviously got problems with a few patients.”

(Pharmacist facilitated meeting 9 October 2007)

A further problem was that non-attenders were often not followed up by practice staff and that patients often lived abroad, which complicated monitoring. Others had
issues with understanding in the elderly and some had problems with patients not filling in forms correctly.

Patient consent and cooperation is crucial for interventions like the PINCER trial to be successful. Issues of this kind are inevitable to public health research and it has to be acknowledged that this may have an effect on outcomes as these patients, although identified to be potentially at-risk by the searches, could in some instances not get their medication changed.

### 5.3.1.5 Macro issues

The wider social, economic and political context can both facilitate and inhibit diffusion and adoption of innovations in healthcare.\(^{97}\)

#### 5.3.1.5.1 Support and cooperation of the PCT

Persuading managers and other influential leaders within the PCT of the PINCER trial's benefits was viewed as crucial in getting practices motivated to participate, and in facilitating the potential spread of the interventions throughout the primary care environment.

Participants also believed that effective communication between the PINCER team and the PCT was important to ensure cooperation.

“\textit{I actually didn't receive anything. So I didn't really know, you know, once we'd signed up to the Trial, you know, I didn't get any regular feedback about how, you know, practices were doing and how Pharmacists were getting on. So that would really be like my only kind of little gripe really.}”

(PCT, Nottingham, PCTNottDI26)

In some instances, the PCT was also looking at similar issues in practices as the PINCER trial potentially resulting in a lack of impact of the interventions.
Management support is important in facilitating the successful implementation of innovations. However, the PCT might not necessarily be equivalent to management. An alternative viewpoint would be to see the PCT’s role in a similar light to what was discussed earlier under compatibility and the QOF (if the innovation fits with organisational values, it is more likely to be adopted).

5.3.1.5.2 Cooperation and communication between primary and secondary care and between primary care and nursing homes

Issues with communication between primary and secondary care are recognised as an important problem in the UK and beyond. This is often characterised by issues surrounding monitoring. In line with this, participants pointed to issues surrounding shared care protocols and a lack of communication between primary and secondary care.

“I think what we really should be taking forward is this shared care which is quite a worry, you know, the hospital are doing one thing and we’re doing another and we’re supposed to be sharing the care. We’re prescribing the medication but we’re not getting to know the results from the hospital.”
(Nurse, Pharmacist intervention, Nottingham, NurNottPIDI10)

Similar issues were evident in relation to nursing homes and housebound patients.

5.3.1.5.3 Other macro issues

Participants also mentioned a range of other broader issues that they felt impacted on the trial and prescribing safety in general. These included the need for setting up a more structured system for repeat prescriptions, for addressing issues surrounding data quality and for addressing issues surrounding monitoring requirements.

“I think a lot of it depends to some extent on the quality of your data I feel. Er, because it was attaching drugs with diagnoses erm, and that again is an area where I know that we’re being encouraged to look at the quality of data.”
(GP, Pharmacist intervention, Nottingham, Focus Group PlpracticeNott1)
5.3.1.6 Design, organisation and planning

5.3.1.6.1 Outcome measures

Similarly to GPs, pharmacists and PCT staff also felt that stopping the administration of a beta-blocker in patients with heart disease had to be carefully thought through, carrying out individual risk assessments.

“I think some of them [referring to outcome measures] aren’t so simple. Like eye drops I think, was that, is that right? Eye drops in asthma patients? I think some of that may well be down to the severity of the asthma patient and then you have to that’s what GPs do every day, you make that risk assessment about is there heart failure or whatever they’re taking the beta blockers for, does it benefit more than and then some of it’s about communication with patients and saying to the patients erm, you know, ‘I’m going to put you on this drug to benefit your heart failure, it may make you feel lousy for the first couple of weeks and also, you know, it could affect your asthma. If that does happen I want you to stop taking the drug and come back and, back and see me’. ‘But I’m willing to take that risk of giving you this drug because I think the benefits of it far outweigh that risk’.” (Prescribing lead, Nottingham, NottBi14)

Gustafson and colleagues have identified what they call “radicalness of design” as one of the main success factors of organisational change initiatives. This relates to the finding that individuals are more likely to adopt an innovation if they perceive it to be reasonable. If, for instance, a GP or pharmacist believed that replacing the beta-blocker could increase the risk of a heart attack in individual patient with asthma, then the medication would not be stopped. Nevertheless, even if the individual GP did not agree with changing a particular patients’ medication, the trial still holds some value in raising awareness of potential future changes in other patients.

5.3.1.6.2 Timing

It appeared to be important for pharmacists to know in advance when and which practice they were going into with as little wait as possible in between practices. It
was felt that this would allow a better planning of their time and reduce the frustration of waiting for practices to be allocated. Ideally, extra time should also be allocated for the first practice pharmacists go into as it takes time for pharmacists to get used to systems and the organisational environment.

Conversely, in some practices, pharmacists believed that there was not enough work for them to do. This often resulted in frustration and boredom.

“I think it’s, I think it’s very difficult to be seen as, you’re only there for twelve weeks anyway and at the moment because we’re trying to catch up on practices and also because there isn’t, in all fairness, you know, if you’ve only got 3,000 population practice there isn’t enough work for twelve weeks.”

(Pharmacist, Nottingham, PharNottDI3)

This was especially prominent in small practices and could to some extent be overcome by pharmacists working in more than one practice at the same time. However, in some instances the 12 week intervention period did not account sufficiently for delays resulting in actions not being completed by GPs.

Practice staff stated that the start of the intervention should avoid busy periods such as Christmas and QOF, and believed that ideally the intervention would start in practices in quick succession after recruitment.

“Well we saw it, the letter from [name] and [name] many, many months ago, May 2006. (...) But the reports on System 1 were not ready until about 2 months ago. (...) So there was a big gap between, between us saying we’d participate and them coming along and saying, ‘Right here’s the computer reports now let’s run them’.” (Practice Manager, Simple feedback, Nottingham, PractManNottSFDI11)

These issues will be important when considering the roll-out of the trial.

5.3.1.6.3 Feedback of performance

Participants also stated that it was best to give both practices and pharmacists feedback of their performance. For practices, this was perceived to be important for
knowing where they stood in relation to other practices and how they were improving over the course of the project. Pharmacists wanted to know how practices had improved over the course of the intervention in order to see whether their work had made a difference.

Pharm 1: *I feel that once you’ve gone from the practice, whether these systems that you’ve set in place are still actually operating 12-months later.*

Pharm 3: *Yeah. I would kind of love it to be employed almost to go back and do, you know, in 12-months time and to actually go into those practices again and see what’s going on because I think I kind of from a slightly egotistical point of view think when the 6-month data comes out and the 12-month data, if my GPs haven’t got those numbers down, I’m going to be really cross with them. (Laughs). In fact I may go back (laughs) because I kind of think, you know, I damn well expect you to do these.*

Pharm 1: *Well I feel the same.*

(Pharmacist facilitated meeting 9 October 2007)

Feedback of performance and the impact of the innovation has been found to be important in facilitating the adoption of innovations in the healthcare environment, fitting in well with the current results\textsuperscript{97, 116}. Although audit and feedback of previous performance was incorporated in the present interventions, the trial did not include feedback of the impact and progress of the interventions. This may have impacted on individual perceptions of relative advantage and could have acted as an additional incentive for practices.

5.3.1.6.4 Incentives

Practices repeatedly expressed that they wanted to be reimbursed for their time and effort of taking part in the trial.

“I mean, you know, my role is, you know, is if you send me lots of money then that’s great. If you don’t then, you know, it’s not so important. Unfortunately that’s the way I have to look at it…I mean unfortunately that’s the name of the game, yeah. Erm, it’s no good giving us free pens anymore. We want cash.”

(Practice Manager, Simple feedback, Nottingham, PractManNottSFDI13)
Financial incentives may be viewed in terms of Roger's notion of relative advantage\textsuperscript{117}. Providing financial incentives has been found to facilitate adoption of healthcare technologies\textsuperscript{88, 118-121}.

5.3.1.6.5 Computer systems and training

Technical issues were apparent in researchers’, practice staffs’ and pharmacists’ accounts. As a consequence of technical problems, the running of the queries was sometimes delayed due to the time taken to rectify this. In other instances, technical issues would slow down the practice systems.

“I think one of the first problems we had was the fact that he must have come about 5 times to try and get the thing to run on the computer system. (…) Erm, it doesn’t go easily erm, so that was a problem. (…) And trying to get that sorted. Trying to find time to get him [referring to pharmacist] a computer when there was nobody on it and then it wasn't working and then somebody from IT had to be here at the same time and then that didn't work and they went away and they had to take the bottom of the system, bring it back with something else on and then they had to come back again. It must have been about, oh trying to get everything up and running and together took ages, absolutely ages.”

(Nurse, Simple feedback, Manchester, NurManSFDi21)

Although pharmacists valued the overall training “package”, all referred to a lack of training on different GP computer systems as areas for improvement. Interviewees suggested that practical training on these systems would have been particularly beneficial as it would have given pharmacists time to practice in a safe space and an idea of what they were likely to encounter.

“And I think maybe the only other thing that I would quite like, erm, a little bit more hands on training on the different types of GP systems. The computer systems because we had quite a lot of theory behind it but I think, erm, I’m only really au fait with one computer system.”

(Pharmacist, Nottingham, PharNottBi1)
Other technical issues experienced by pharmacists emerged from the second pharmacist facilitated meeting. In some instances MIQUEST inappropriately picked up patients and in other instances it missed patients, which was directly connected to the way certain events were coded in the practice system.

Technical barriers were anticipated by the research team and were difficult to prevent in interventions that rely on information technology. Pharmacists’ perceived lack of training on practice computer systems in this context is important but can be easily addressed.

5.3.1.6.6 Workload implications for practices

Only a small number of participants identified workloads as a barrier, but this is worth discussing. Simply the pressure of having another thing to consider seemed to contribute to increased stress in GPs participating in the trial.

“Well simply because it’s something else to do in addition to everything else that we do, it’s the same old story isn’t it? You know, our time is pretty much taken up. Erm, and all of us in General Practice and elsewhere balk at any additional work. But, you know, in truth it, we haven’t found it as much extra work as, as I suppose it could have been. We could have feared.”

(GP, Pharmacist intervention, Nottingham, NottBi19)

Increased workloads as a potential barrier to the adoption of innovations in primary care is relatively well established\textsuperscript{122-125}. Within Roger’s framework, workload implications of an innovation are thought to be most apparent in the pre-adoption stage when potential adopters consider whether to adopt an innovation or whether to reject it\textsuperscript{69}. This highlights that, during the recruitment of practices, researchers should ideally focus on diffusing possible concerns about additional workloads generated by the trial.
5.3.1.6.7 Job construction of the pharmacist role

There were some issues with the way the pharmacist role in delivering the intervention was constructed, which might have impacted negatively on job satisfaction.

The qualitative investigation indicated that pharmacist job satisfaction may be adversely influenced by several factors. Firstly, pharmacists commented that they missed patient contact in their work as a PINCER pharmacist.

“Professional concern re one patient who had ‘daily’ methotrexate dose specified instead of ‘weekly’. GP did not wish for the patient to be contacted to ensure correct dose being taken. I, however, felt that contact would be a sensible extra precaution and should be logged in the records. I did, however, feel that it is unnecessary to pursue this matter further. I do, however, question the safety of internal dispensing practices with no pharmacist input. Such errors would be highlighted at an external pharmacy. This also highlighted the issue of lack of patient contact during the trial. The ability to discuss medication with a patient is, I feel, a fundamental role for a pharmacist and has not been utilised in the trial. It is greatly missed.”

(Pharmacist diary, Pharmacist 4)

Secondly, pharmacists commented that their work for the trial was frustrating at times, as some of the problems encountered in practices were beyond the scope of their work.
Pharmacists further mentioned that their work for the trial was monotonous and repetitive at times and that the temporary contract did not provide the desired job security.

These issues are important to consider should this model be rolled out in the future in order to achieve a more stable working relationship between pharmacist and practices as well as offering job stability through a permanent contract.

5.3.2 The roll-out and potential alternatives

5.3.2.1 Facilitators for the potential roll-out of the trial interventions

In terms of the diffusion of innovation literature this section deals with issues surrounding the sustainability and spread of the innovation throughout the NHS as a whole. Participants recognised the trial’s potential to improve prescribing safety. They argued that financial incentives, seeing others get involved, sharing positive experiences, PCT support and practice motivation were important for an eventual roll-out.
Within the innovation literature this is best understood in terms of peer influence and interpersonal professional networks. These play an important role for diffusion to spread\textsuperscript{79, 86, 105, 126, 127}.

Disseminating the results of the trial and documenting its benefits was also viewed as important in this context. This is in line with evidence documenting that demonstrating the benefits of the innovation is be positively associated with sustainability and spread\textsuperscript{91} and that research evidence plays an important role in healthcare professionals’ decisions to adopt new behaviours\textsuperscript{87, 88}.

5.3.2.2 Outcome measures

Some interviewees suggested that some monitoring outcome measures could be dropped due to various reasons, which included the fact that they were not very common, not clinical enough for pharmacists, and due to issues surrounding secondary care. Some interviewees also suggested that other outcome measures could be included (Box 1). Alternative suggestions of areas to focus on could provide a starting point for future interventions.
Box 1. Other suggested outcome measures

- Digoxin and Theophylline as they have low therapeutic margin
- Epilepsy treatments
- Glitazones and side effects
- Non-steroidal anti-inflammatories and renal disease
- Non-steroidal anti-inflammatories and cardiovascular risk
- Low-dose aspirin
- Black triangle drugs
- Fluticasone
- High dose steroids (including high dose steroid inhalers for children)
- Minocycline monitoring
- Thyroxine

When deciding which outcome measures to include, participants argued that it was important that these are up-to-date, evidence based and tailored to individual practices. External input in relation to outcome measures was valued from a practice perspective.

**GP:** Audit, auditing the actual achievement rates you’re getting but of course audit it’s all very well saying we’ll do audit but it means a, you can’t audit everything every year or all the time so you’d have to focus on something and go round in a round-robin fashion to keep checking and looking at things. And the other thing is … you, often you audit the things you think you’re doing quite well at don’t you, rather than audit the thing that, because you’re not aware of the thing that you’re not doing very well so you don’t, you don’t think to do the blooming audit.

**Practice Manager:** Somebody coming in from the outside that looks at it through a different pair of eyes really…. Because you’re working all the time, it’s always the same people doing the same thing. You need that outside influence to think, ‘Oh, you need to do it like this. Or are you looking at it this way.’ So that does help.

(Focus Group, Pharmacist intervention practice 2, Nottingham)

Participants suggested that this external input could be provided through PACT data or several present PCT initiatives.
5.3.2.3 Pharmacist intervention versus simple feedback

5.3.2.3.1 Pharmacist intervention

Focus groups further indicated that practices appreciated the value of pharmacists as a designated person driving the change and the resulting face-to-face contact was viewed as particularly important.

But I think you can’t discount the human/human interaction you get when someone cajoles you and says, you know, says to you, ‘You really should be doing this, it’s just a little job to do it’. It’s so much better than a little email going ‘ping’: Email from automatic Pharmacist in some other place, they’re somewhere else, would you please look at this. It’s just not quite the same. I don’t know if that’s, in fact does that matter, that we should be professionals, we should do it anyway but we’re all human beings and…because it isn’t just the numbers that motivate people the human interaction is also what makes people think well we ought, we really ought to do something about this.

(Focus Group, GP, Pharmacist intervention practice 2, Nottingham)

The importance of face-to-face contact between pharmacists and clinicians has been documented previously\textsuperscript{128}. In relation to the diffusion of innovation literature, face-to-face contact with the change agent has been shown to facilitate adoption fitting well with the present findings\textsuperscript{97,129}.

5.3.2.3.2 Simple feedback

Simple feedback worked well in practices that were allocated to this intervention arm and they viewed it positively. This could be due to a selection bias (i.e. that only motivated and positive practices decided to participate in the trial in the first place) but could also indicate that this intervention is comparable to pharmacist intervention in terms of effectiveness. In addition, both practices participating in the focus groups stated that they were monitoring medicines anyway so they had small numbers of patients identified. This may contribute to this positive attitude.
Practices appeared positive towards having searches done periodically if these are unobtrusive and result in a manageable workload. They suggested that these searches could be build into QOF.

**GP:** Well this is certainly acceptable isn’t it?
**Practice Manager:** Yes.
**GP:** And we would have no qualms about doing this again and I think if it came on a rolling basis it’s a good reminder as well.
**GP:** Mmm, I agree with that.
**I:** So that’s important, the
**GP:** It would need to keep coming up because
**GP:** Yeah.
**GP:** for the numbers we’re looking at it’s people slipping through the net rather than people where we’re doing stuff systematically the wrong things and it’s just nice to know isn’t it?
**Practice Manager:** I think for practices this way of reporting is so commonplace now with QOF reporting and other reporting that we do for the PCT that you could almost build it into like a quarterly review idea erm, which would then capture the people who slip through the net, potentially. You’re always going to have an odd person because you might inherit them from another practice and you’ve got that interim bit where you’re adjusting stuff,

(Focus Group, Simple feedback practice 1, Nottingham)

However, it was also acknowledged that practice involvement depends very much on motivation. In addition, this model lacks a designated person driving the change and the previously mentioned all important face to face contact. Pharmacist intervention may therefore be a more effective option for laggards and practices or individuals that lack intrinsic motivation to act.

### 5.3.2.4 A flexible approach to models may be best

The research team was looking for concrete recommendations on a way forward in terms of the roll-out of the trial. Participants found this, however, relatively difficult as they felt that a flexible approach incorporating all models was preferable in order to
adequately address practices’ varying needs, degrees of motivation, issues, existing relationships and other local differences.

“… you know, it’s, I think it’s very hard for you to come up with one model because you’re dealing with people that…work and personality wise are very, you know, you don’t have one practice that’s the same and I think probably you have to use a variety of these models.”
(Pharmacist focus group)

However, it was also acknowledged that if one would let practices choose the approach, then there may be a tendency to choose the least intrusive option. Some participants suggested that a cluster-based approach may be a good way to facilitate flexibility in terms of the approach whilst still maintaining a certain level of control.

I think you know if you do it on a cluster basis it’s your way in the back door of getting the ones who are less, a bit more reluctant to actually engage in what the others are actually doing.
(PCT focus group, Manchester)

However, when asked about the feasibility of a cluster-based approach, there were some concerns in relation to individual practice differences, the perception that clusters are driven by money rather than patient safety issues and the issue that at present clusters are not mature enough and in different stages of development.

In terms of diffusion of innovations, these differences in practices can be conceptualised as differences in the inner-organisational context, which has been shown to play an important role in facilitating or inhibiting the adoption of innovations in healthcare\(^\text{67, 130, 131}\).

5.3.2.5 Incorporation into the PCT pharmacist role

The importance of PCT involvement in a potential roll-out further became apparent through participants’ recommendations to incorporate the trial pharmacists' work into the PCT pharmacist role. Although some drawbacks were acknowledged and the
extend of involvement may need further consideration, this was the model of choice for most participants.

And in my PCT role I’m now paid for by the Cluster so I have, I have sort of five, six practices, no five practices to work with because again they’ve gone for the model that actually you spend more time with the practice, you do more work for them so maybe it is going towards you being there around a lot more but you won’t sort of take on these more quality based interventions and you feed those back into the practice and you drive them from that way and the model works perhaps better that way.
(PHARMACIST 1, PHARMACIST FOCUS GROUP)

Perceived positive aspects of this PCT pharmacist model included the fact that here the PCT has overall control over the work of pharmacists, an appropriate skill-base and support structures for pharmacists already in place and the fact that PCT pharmacists are relatively established in primary care.

The recommendation to use QOF as an incentive was put forward by participants.

GP: I’m just wondering whether you could link it to QOF because, you know, in the quality and outcomes framework there’s a specific indicator around is it one or two or three prescribing, three prescribing initiatives… And whether or not you could link one of those initiatives to, in particular to a patient safety aspect of prescribing… Might be a way to start and creep with it. (…)
I: …So can I ask you now which one would you choose after discu, or if you can think of any more please erm, let us know but er, which one would you go for? (…)
GP: If we had to mainstream it and we were really serious about making it work then I think I would go with the PCT involvement model.
PRACTICE MANAGER: Link it to QOF I think that would be a wonderful way to take it forward.
GP: Yeah.
(FOCUS GROUP, SIMPLE FEEDBACK PRACTICE 2, NOTTINGHAM)
This fits in well with the diffusion of innovations literature, which shows that external imperatives such as policies can play a facilitative role\textsuperscript{97, 102}. Here, participants suggested that the searches and advice could be incorporated into prescribing meetings between the practice and the PCT pharmacist. Practices tend to have these once or twice a year.

Participants further recommended that pharmacists’ involvement could be cluster based with one PCT pharmacist looking after a group of practices. This fits in well with the recommendations of the Darzi Review introducing the idea of local versions of QOF, where PCTs have the power to choose from a set of national indicators to respond to local needs\textsuperscript{132}.

Amongst issues mentioned with the PCT pharmacist model were cost implications for PCTs in paying for the additional pharmacist resource. In addition, practices felt that PCT pharmacists are often driven too much by cost-effectiveness and that outcome measures would be based on the PCT’s priorities.

5.3.2.6 Other models

5.3.2.6.1 Computer systems

The potential of computer systems incorporating alerts and pop-ups was also discussed. Pharmacists suggested that this should be overseen by the PCT and that it would be important that these systems are tailored to individual practices’ needs and have an educational element.
The main issue with this model was, however, the acknowledgement that GPs are already faced with too many pop-ups and tend to ignore these.

As potential solutions pharmacists suggested letting practices themselves decide which alerts go on this system or creating messages that cannot be switched off.

However, IT systems lack the clinical input, face to face contact and flexibility that pharmacists can offer. They may therefore be best used in addition to a pharmacist and cannot replace a pharmacist.

Several studies have shown that computers systems can improve prescribing safety with the help of hazard alerts and monitoring reminders\textsuperscript{133-137}. However, the lack of
knowledge of certain systems amongst GPs, a lack of training, system deficiencies and the sheer volume of pop-ups have been identified as problematic in previous studies\textsuperscript{138-140}.

5.3.2.6.2 Community pharmacists

Participants felt that community pharmacists may also play a role but they should be overseen, monitored and backed-up by the PCT. Pharmacists stated that it could be incorporated into the local enhanced services or Medication Use Reviews. However, participants mostly viewed this model as most appropriate as an additional safety net (as it is at present ringing up practice if something wrong) rather than a structured intervention by itself.

*I think there’s a model there where the pharmacist could feed back to the practice, would you, would you like to look at this prescription, do you want, are you sure you want to prescribe anti-inflammatory along with the diuretic?’ ‘Would you like to, you know, given this guideline?’ And if that was routine and the practice got lots of phone calls from Pharmacists, look the Pharmacists don’t have to push it, just if every time it happened a phone call happens.*

(PCT focus group, Manchester)

Participants also stated that there are several issues that need to be considered in this model. These included the need to incentivise community pharmacists and the necessity to establish a close relationship with the practice. Problems that practices tended to have with this model were that many community pharmacies are commercially led and that there are differences in community pharmacist attributes and levels of competence.

In line with this, there is generally a policy move to promote collaboration between community pharmacies and general practices\textsuperscript{141-143}. However, our results indicate that a great deal of relationship building between pharmacists and practice staff still needs to be done in order to realise this\textsuperscript{128, 144}. 
5.3.2.6.3 Further Models

Focus groups also explored the possibility of partial pharmacist input with pharmacists working alongside other staff that could help them to deliver the intervention (e.g. pharmacy technicians at the PCT).

Remote pharmacist input, with pharmacists making use of electronic health records was also discussed but most could not envisage it working. The most commonly raised issue was the lack of face-to-face contact and issues surrounding patient consent and confidentiality.

Training practice staff to deliver the interventions was also discussed but it was generally not regarded as suitable due to workload implications for practice staff.

Altogether, it seems that a generic model lead by the PCT is most feasible. However, this should be flexible enough to accommodate local differences and still allow for local control over decisions on the approach and on the areas to focus on.

5.4 Conclusion

The combination of interviews and focus groups has identified a range of facilitators and barriers to the implementation of the interventions under study. The current study has also provided with some concrete recommendations in relation to a potential the roll-out.

Altogether, the qualitative study indicates that the interventions (or alternative models) may work under certain circumstances. In interventions not involving pharmacists these include motivational issues, attitudes, the extent of involvement of key individuals (e.g. practice manager, GPs), macro issues (especially local arrangements with secondary care) and organisational and planning issues. Additional aspects to consider in pharmacist interventions include the effective integration of the pharmacist in the practice, ongoing face-to-face contact and pharmacist job satisfaction. The involvement and support of PCTs was viewed as important in terms of both implementation and roll-out.
It has to be kept in mind that the results of the present study are highly context dependent and may not be generalisable beyond the context in which they were produced. However, they clearly provide a deeper insight into the specific issues arising when considering pharmacist intervention in UK primary care and they also provide with a practical staring point in relation to the roll-out. Diffusion of Innovation Theory has provided with a useful theoretical background and has helped to integrate the current findings with the existing literature.

Although some issues emerging from the current study were anticipated by the research team (e.g. workload, issues surrounding patients, other priorities in trial practices, technical issues), some unanticipated issues emerged especially in pharmacist intervention arm practices. This clearly supports the value of qualitative evaluation methods in complementing RCTs of complex interventions. Several valuable insights into the processes and the context in which the interventions are implemented have been gained.
Chapter 6: QRESEARCH analysis of secular trends in outcome measures
6.1 Introduction

In the PINCER trial we considered it unethical to randomise practices to a no-intervention control group. This means that we had a trial with two intervention arms. In view of this study design, we decided to undertake an additional piece of work – during the same time period – using routinely collected data, which allowed the trial results to be compared with practices where no known intervention had taken place (i.e. interpreting these findings in relation to secular trends). This analysis also gave us the opportunity to assess the external validity of the practices enrolled in this trial.

We report here findings from an epidemiological study using the large national QRESEARCH general practice database in order to estimate the changes in rates of the same clinically important errors studied in the PINCER trial, but in practices not taking part in our trial over the study time period. We also estimated the rates of patients at risk of the prescribing and monitoring errors in QRESEARCH practices comparing these with the rates of such errors in PINCER practices at baseline and the six- and 12-month assessment points. It should be noted that as the QRESEARCH component to this study involved assessments made in a non-randomised group, we have not undertaken formal statistical comparisons.

6.2 Methods

6.2.1 Study design

We conducted a cohort study in patients registered with practices in the UK contributing to the QRESEARCH database. This database is composed of practices using the EMIS (Egton Medical Information System) computer software system. Version 25 of the QRESEARCH database (downloaded 1st July 2009) was used for this analysis.
6.2.2 Practice selection

Practices were included in the study if they had their EMIS clinical computer system installed prior to 1st October 2004 and had uploaded data after 31st March 2009. The study period was the three years between 01st January 2006 and 1st January 2009.

All selected practices were included in the analysis of all trial outcomes (see Table 1), with one exception. In the PINCER trial, we found that some general practices used standalone software systems for recording INR; it was in such practices not possible to gain an accurate impression of how well patients were being monitored based on interrogation of the clinical computer system. In the seven trial practices concerned, we found apparent levels of non-recording of INR of greater than 60%. These practices were therefore excluded from the analysis of the warfarin/INR outcome measure in the main trial.

In order to allow for accurate comparison of findings, we decided to take a similar approach with the QRESEARCH analysis. Thus, we excluded from the analysis of the warfarin/INR outcome measure those practices where greater than 60% of patients did not have a recorded INR in the previous three months, the assumption being that monitoring was taking place elsewhere for patients in these practices. We took a similar approach to the monitoring composite outcome measures as this measure included patients from the warfarin/INR outcome measure.

6.2.3 Cohort definition

We identified an open cohort of patients registered at any point during the three year study period 1st January 2006 and 1st January 2009. Temporary residents were excluded. Patients were eligible for inclusion in the cohort after the date of registration with the practice or the date of the installation of the EMIS computer system, whichever was latest. The actual censor date chosen was the earliest of the following: date of death; date of leaving the practice; date of the latest download of data; or the study end date.
6.2.4 Inclusion criteria

Patients were included in the analysis if they were aged 18-100 years and had been registered with the practice for at least 15 months. All analyses, but one were run on patients aged ≥18 years; the exception to this was in relation to renal function monitoring in those on long-term diuretic or ACE inhibitor therapy. This analysis was run on patients aged ≥75 years.

6.2.5 Baseline prevalence of medication related data

We reviewed the medical history of each patient and extracted data on prescribed medications and monitoring tests undertaken within the study period. For each patient and for each of the errors of interest, we identified whether a particular patient was at risk and whether a relevant prescribing or monitoring error had been made. These data were then summarised at practice level on the basis of how many patients were at risk and in how many cases errors occurred. We used this information to calculate the proportions of patients at risk who experienced errors, describing these data using medians and inter-quartile ranges.

The criteria used for identifying patients at risk were similar to those used in the main trial; the same morbidity codes, drug codes, laboratory test codes, event dates and search criteria were used.

6.2.6 Comparing rates over the study period

In order to assess the changes in error rates, we compared the distributions of error rates using the Wilcoxon matched pairs test. To mirror the median time point at which data were collected in the PINCER trial, the compared time points were:

- Baseline to six-months post-intervention.
- Baseline to 12-months post-intervention.
- Six-months to 12-months post-intervention.
6.3 Results

6.3.1 Practices and patients

There were 532 practices which met the inclusion criteria. After removing practices with the same Strategic Health Authority (SHA) code as practices that participated in the PINCER trial, we were left with 438 practices in our database. The median practice list size was 7,036 patients (inter-quartile range (IQR): 4664 to 9759) at 1st April 2007. Quality and Outcomes Framework (QOF) data revealed that median practice list size in the UK in 2006/07 was 5582 patients (IQR: 3235 to 8781)\textsuperscript{47}.

Overall there were 3,421,174 patients registered in these participating practices; 81.5\% of patients were aged ≥18 years and 49.5\% were males.

Table 46 compares the general practices participating in the PINCER trial with QRESEARCH practices for the two main background conditions of interest studied in patients of all ages (i.e. asthma and peptic ulcer). The mean practice list size from the QRESEARCH database was slightly higher than the mean practice list size from the PINCER trial practices. The median prevalence of asthma in patients aged ≥18 years was similar in PINCER and QRESEARCH (10.9\% vs. 11.4\%) and the median prevalence of peptic ulcer was exactly the same (1.6\%) for both data sources. Data in Table 46 also shows that the findings were very similar when comparing the practices included and excluded from the QRESEARCH database on account of the INR/warfarin recording cut-off (discussed above).
Table 46. Comparison of practice list size and prevalence of asthma and peptic ulcer in QRESEARCH and PINCER practices

<table>
<thead>
<tr>
<th></th>
<th>QRESEARCH practices</th>
<th>QRESEARCH practices with INR recording ≤60% in patients on warfarin</th>
<th>PINCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of general practices</td>
<td>438</td>
<td>233</td>
<td>72</td>
</tr>
<tr>
<td>Mean (SD) practice list size</td>
<td>7,811 (4,374)</td>
<td>7,720 (4,230)</td>
<td>6,680 (3,437)</td>
</tr>
<tr>
<td>Total number of patients aged ≥18 years</td>
<td>2,779,781</td>
<td>1,460,406</td>
<td>381,561</td>
</tr>
<tr>
<td>Median (IQR) prevalence of peptic ulcer in patients aged ≥18 years</td>
<td>1.6% (1.2% to 2.2%)</td>
<td>1.7% (1.3% to 2.2%)</td>
<td>1.6% (1.1% to 1.9%)</td>
</tr>
<tr>
<td>Median (IQR) prevalence of asthma in patients aged ≥18 years</td>
<td>11.4% (10.0% to 13.1%)</td>
<td>11.8% (10.3% to 13.6%)</td>
<td>10.9% (9.2% to 12.3%)</td>
</tr>
</tbody>
</table>

Table 47 compares the age structure of patients registered in PINCER and QRESEARCH practices and the UK population as a whole as derived from 2007 Office for National Statistics (ONS) data. All samples had similar age distributions.

Table 47. Comparison of age structures in QRESEARCH database, in the PINCER trial and for UK ONS data (2007)

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Number (%) of patients in QRESEARCH</th>
<th>Number (%) of patients in PINCER</th>
<th>Percent in ONS data (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-14</td>
<td>511220 (14.9)</td>
<td>78622 (16.9)</td>
<td>17.6</td>
</tr>
<tr>
<td>15-44</td>
<td>1502470 (43.9)</td>
<td>194173 (41.7)</td>
<td>41.5</td>
</tr>
<tr>
<td>45-64</td>
<td>859212 (25.1)</td>
<td>117260 (25.2)</td>
<td>25.0</td>
</tr>
<tr>
<td>65-74</td>
<td>275796 (8.1)</td>
<td>39834 (8.5)</td>
<td>8.3</td>
</tr>
<tr>
<td>75-84</td>
<td>190469 (5.6)</td>
<td>27046 (5.8)</td>
<td>5.6</td>
</tr>
<tr>
<td>85+</td>
<td>82007 (2.4)</td>
<td>9225 (2.0)</td>
<td>2.1</td>
</tr>
</tbody>
</table>

6.3.2 Prevalence of medication related errors

6.3.2.1 Baseline prevalence of risks
Table 48 expresses the total numbers of patients at risk of an error, as a proportion of all registered patients at baseline (i.e. 1 April 2007). We also detail the numbers of patients with a recorded medication error (numerator) as a proportion of at risk patient in both the QRESEARCH database and the PINCER dataset. This reveals broadly comparable overall findings between these datasets.

The proportions of patients on warfarin (and therefore being at risk of not having INR recorded) was similar in QRESEARCH and PINCER: 1% (n=27783) in QRESEARCH and 1% (n=3183) in PINCER. The proportion of patients with this recorded monitoring error varied widely between practices in QRESEARCH, from 0-100%, reaching 11,896 (42.8%) in the total sample. After removing practices with more than 60% non-recording of INR, the proportion of patients at risk was 1.1% (16280/1460170) and the proportion of errors was 8.4% (1368/16280).

Table 48. QRESEARCH and PINCER total numbers for at risk and patients with records of errors

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>QRESEARCH</th>
<th>PINCER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total number of patients at risk (% of total N of patients of 2779781)</td>
<td>Total number of patients with errors (% of patients at risk of the measure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Peptic ulcer w/o PPI &amp; NSAID</td>
<td>30204 (1.1)</td>
<td>1182 (3.9)</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blockers</td>
<td>324778 (11.7)</td>
<td>8130 (2.5)</td>
</tr>
<tr>
<td>3 ACE/ diuretics &amp; lab test</td>
<td>79496 (2.9)</td>
<td>8461 (10.6)</td>
</tr>
<tr>
<td>4 Arterial or venous thromboembolism &amp; combined oral contraceptives</td>
<td>27225 (1.0)</td>
<td>223 (0.8)</td>
</tr>
<tr>
<td>5a Methotrexate &amp; FBC</td>
<td>6424 (0.2)</td>
<td>1435 (22.3)</td>
</tr>
<tr>
<td>5b Methotrexate &amp; LFT</td>
<td>6424 (0.2)</td>
<td>1495 (23.3)</td>
</tr>
<tr>
<td>7 Lithium &amp; Lithium levels</td>
<td>3245 (0.1)</td>
<td>985 (30.4)</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT</td>
<td>4613 (0.2)</td>
<td>2114 (45.8)</td>
</tr>
</tbody>
</table>

Table 49 shows the median (and IQR) proportions of patients in a practice being at risk of the errors of interest and the median proportions (and IQR) of patients
experiencing these errors in both the QRESEARCH database and PINCER dataset at the baseline assessment point. The highest risk of prescribing error was in patients with asthma: median proportion of patients at risk in a practice was 11.4% (IQR 10.0-13.1%). The highest risk of monitoring error was in patients aged ≥75 years that were on ACE inhibitors or loop diuretics.

Table 49. QRESEARCH and PINCER median (IQR) proportions of patients at risk in a practice and proportion of patients with records of errors among patients at risk

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>QRESEARCH</th>
<th>PINCER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Proportion of patients at risk</td>
<td>Proportion of errors in patients at risk</td>
</tr>
<tr>
<td>1 Peptic ulcer w/o PPI &amp; NSAID</td>
<td>1.01 (0.73-1.4)</td>
<td>3.45 (1.52-5.71)</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blockers</td>
<td>11.39 (9.97-13.13)</td>
<td>2.42 (1.75-3.13)</td>
</tr>
<tr>
<td>3 ACE/ diuretics &amp; lab test</td>
<td>3 (2.01-3.65)</td>
<td>9.21 (5.16-14.29)</td>
</tr>
<tr>
<td>4 Arterial or venous thromboembolism &amp; combined oral contraceptives</td>
<td>0.96 (0.71-1.2)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>5a Methotrexate &amp; FBC</td>
<td>0.23 (0.15-0.31)</td>
<td>16.7 (3.45-46.7)</td>
</tr>
<tr>
<td>5b Methotrexate &amp; LFT</td>
<td>0.23 (0.15-0.31)</td>
<td>20 (4.55-46.7)</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR*</td>
<td>1.15 (0.88-1.39)</td>
<td>4.00 (1.17-12.5)</td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels</td>
<td>0.11 (0.06-0.16)</td>
<td>28.57 (12.5-46.61)</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT</td>
<td>0.15 (0.1-0.21)</td>
<td>50</td>
</tr>
</tbody>
</table>

*Practices with >60% patients with INR not recorded excluded (these practices were excluded in the PINCER trial because they were known not to routinely record INR on their clinical computer system).

Table 50 shows the total number of cases judged to be at clinical risk by outcome measure in QRESEARCH practices compared with the practices in the PINCER trial. The distributions of risk in PINCER and QRESEARCH appear similar, but only after removing warfarin/INR errors.
Table 50. Number (%) of identified cases in QRESEARCH and PINCER practices

<table>
<thead>
<tr>
<th>Measure</th>
<th>QRESEARCH</th>
<th>PINCER*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All errors excluding warfarin &amp; INR (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cases identified</td>
<td>24025 (100)#</td>
<td>3568 (100)#</td>
</tr>
<tr>
<td>1 Peptic ulcer w/o PPI &amp; NSAID</td>
<td>1182 (4.9)</td>
<td>180 (5.0)</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blockers</td>
<td>8130 (33.8)</td>
<td>1165 (32.7)</td>
</tr>
<tr>
<td>3 ACE/ diuretics &amp; lab test</td>
<td>8461 (35.2)</td>
<td>1032 (28.9)</td>
</tr>
<tr>
<td>4 AT/VN &amp; combined oral contraceptives</td>
<td>223 (0.9)</td>
<td>21 (0.6)</td>
</tr>
<tr>
<td>5a Methotrexate &amp; FBC</td>
<td>1435 (6.0)</td>
<td>373 (10.5)</td>
</tr>
<tr>
<td>5b Methotrexate &amp; LFT</td>
<td>1495 (6.2)</td>
<td>357 (10)</td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels</td>
<td>985 (4.1)</td>
<td>199 (5.6)</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT</td>
<td>2114 (8.8)</td>
<td>241 (6.8)</td>
</tr>
</tbody>
</table>

*Total number in PINCER does not include patients with dosage errors
#Total number of cases does not include monitoring warfarin/INR errors

6.3.3 Prevalence of the outcome measures and changes over the study period

6.3.3.1 Summary

Table 51 shows the changes in proportion of errors in patients at risk on all the outcome measures. For prescribing problems (i.e. outcome measures 1, 2 and 4), there was no overall trend over the study period: error rates remained similar for Outcome 1, but decreased for Outcomes 2 and 4. For monitoring problems (i.e. Outcomes 3, 5a, 5b, 6, 7 and 8), there was a consistent and significant decrease almost for all outcome measures over the study period, apart from the lithium outcome measure where there was a significant increase. The detailed analysis below includes the distribution of median proportions of errors in practices and changes between 1st January 2006 and 1st January 2009.
Table 51. Median and IQR for proportion (%) of errors in patients in risk at baseline (i.e. 1st April 2007) and the six-month (i.e. 1st January 2008) and 12-month (i.e. 1st July 2008) assessment points

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Median and IQR for proportion of errors in patients in risk</th>
<th>1st April 2007</th>
<th>1st January 2008</th>
<th>1st July 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Peptic ulcer w/o PPI &amp; NSAID</td>
<td></td>
<td>3.45</td>
<td>3.33</td>
<td>3.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.52-5.71)</td>
<td>(1.25-5.56)</td>
<td>(1.25-5.41)</td>
</tr>
<tr>
<td>2 Asthma &amp; beta-blockers</td>
<td></td>
<td>2.42</td>
<td>2.53*</td>
<td>2.63*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.75-3.13)</td>
<td>(1.84-3.29)</td>
<td>(1.92-3.46)</td>
</tr>
<tr>
<td>3 ACE/ diuretics &amp; U&amp;E test</td>
<td></td>
<td>9.21</td>
<td>7.54*</td>
<td>6.53*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5.16-14.29)</td>
<td>(4.17-12.55)</td>
<td>(3.77-10.62)</td>
</tr>
<tr>
<td>2a Asthma w/o CHD &amp; beta blockers</td>
<td></td>
<td>1.55</td>
<td>1.63*</td>
<td>1.67*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.11-2.17)</td>
<td>(1.14-2.2)</td>
<td>(1.23-2.34)</td>
</tr>
<tr>
<td>4 AT/VN &amp; combined oral contraceptives</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0-0)</td>
<td>(0-0)</td>
<td>(0-0)</td>
</tr>
<tr>
<td>5a Methotrexate &amp; FBC</td>
<td></td>
<td>16.67</td>
<td>13.33*</td>
<td>12.83*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(3.45-46.67)</td>
<td>(2.38-33.33)</td>
<td>(0-30)</td>
</tr>
<tr>
<td>5b Methotrexate &amp; LFT</td>
<td></td>
<td>20</td>
<td>14.29*</td>
<td>13.64*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(4.55-46.67)</td>
<td>(4.08-37.98)</td>
<td>(0-33.33)</td>
</tr>
<tr>
<td>6 Warfarin &amp; INR</td>
<td></td>
<td>4.0</td>
<td>3.85*</td>
<td>3.21*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.17-12.5)</td>
<td>(1.20-10.9)</td>
<td>(1.02-12.0)</td>
</tr>
<tr>
<td>7 Lithium &amp; Li levels</td>
<td></td>
<td>28.57</td>
<td>34.58*</td>
<td>44.44*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(12.5-46.61)</td>
<td>(18.18-50)</td>
<td>(25-60)</td>
</tr>
<tr>
<td>8 Amiodarone &amp; TFT</td>
<td></td>
<td>50</td>
<td>33.33*</td>
<td>33.33*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(30-66.67)</td>
<td>(20-50)</td>
<td>(16.67-50)</td>
</tr>
<tr>
<td>C1a At least 1 prescribing problem</td>
<td></td>
<td>2.45</td>
<td>2.56*</td>
<td>2.62*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.84-3.1)</td>
<td>(1.94-3.22)</td>
<td>(2-3.37)</td>
</tr>
<tr>
<td>C2a At least 1 monitoring problem#</td>
<td></td>
<td>12.44</td>
<td>10.48*</td>
<td>9.81*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(7.82-19.01)</td>
<td>(7.08-16.31)</td>
<td>(6.41-15.19)</td>
</tr>
<tr>
<td>C1b At least 2 prescribing problems</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0-0)</td>
<td>(0-0)</td>
<td>(0-0)</td>
</tr>
<tr>
<td>C2b At least 2 monitoring problems#</td>
<td></td>
<td>0</td>
<td>0 *</td>
<td>0 *</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0-3.64)</td>
<td>(0-2.27)</td>
<td>(0-1.18)</td>
</tr>
</tbody>
</table>

*Wilcoxon test of comparison with the baseline, p-value<0.005
# Practices with >60% patients with INR not recorded excluded

6.3.3.1.1 Outcome 1: Patients with a history of peptic ulcer prescribed an NSAID without a PPI

The median percentage of patients with a history of peptic ulcer with a prescription of proton-pump inhibitors in the previous six-months was 1.0% (IQR 0.7-1.4%) at baseline. Out of the patients at risk, there was a median of 3.4% (IQR, 1.5-5.7%) patients who had at least one prescription of a NSAID. Figure 5 shows the distribution of such errors in QRESEARCH practices.
Figure 5. Percentage of patients prescribed NSAIDs out of patients with history of peptic ulcer without PPI by number of general practices

Similar histograms are available for each of the outcome measures of interest, but have not, with the exception of the INR/warfarin outcome (Figure 14) been included in this report in the interests of space. Figure 6 shows changes in those at risk of experiencing an error in relation to NSAID prescribing and those actually experiencing such an error. Although there was a slight decrease over the study period, the comparison of key time points (i.e. 1st April 2007, 1st January 2008 and 1st July 2008) did not show significant difference (Wilcoxon test for 1st April 2007 and 1st July 2008 was 0.80, P-value 0.42). Similar graphs are available for each of the other outcome measures of interest, but these have not been included in this report in the interests of space.
Figure 6. Changes in proportion of patients prescribed NSAIDs out of patients with history of peptic ulcer without PPI

![Graph showing changes in proportion of patients prescribed NSAIDs](image)

Median proportion of patients
- in a practice at risk of the error (denominator)
- in a practice with the error (numerator)
- with the error in patients at risk of the error (outcome measure)

Figure 7 compares the percentage of NSAID errors in patients with a history of peptic ulcer in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
Figure 7. Comparison of Outcome 1 in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months

6.3.3.1.2 Outcome 2: Proportion of beta-blocker users among patients with asthma

The median proportion of patients with a history of asthma in a general practice was 11.4% (IQR, 10-13.1%) on 1st April 2007. Out of the patients at risk there were median 2.4% (IQR, 1.7-3.1%) who had at least one prescription of beta-blockers (including eye-drops). Figure 8 compares the proportions of beta-blocker errors in patients with a history of asthma in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
6.3.3.1.3 **Outcome 3: Proportion of patients without check of renal function among patients aged ≥75 years on ACEI or diuretics**

The median proportion of patients aged ≥75 years with evidence of long-term (>15 months) prescription of ACE inhibitors or loop diuretics in a general practice was 3.0% (IQR 2-3.7%) on 1st April 2007. Out of the patients at risk there were median 9.2% (IQR, 5.2-14.3%) who did not have check of renal function in the last 15 months. Figure 9 compares the proportions of ACE inhibitor or loop diuretic errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
Figure 9. Comparison of Outcome 3 in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months

6.3.3.1.4 Outcome 2a: Proportion of beta-blocker users among patients with asthma and without CHD

The median proportion of patients with a history of asthma and without coronary heart disease in a general practice was 10.9% (IQR 9.5-12.4%) on 1st April 2007. Out of the patients at risk there was median 1.5% (IQR 1.1-2.2%) of patients who had at least one prescription of beta-blocker oral preparations or eye-drops. Figure 10 compares error rates in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
6.3.3.1.5 **Outcome 4: Proportion of oral contraceptive users among female patients with venous or arterial thromboembolism**

The median proportion of female patients with venous or arterial thromboembolism in a general practice was 0.96% (IQR 0.7-1.2%) on 1st April 2007. Seventy-nine percent of practices did not have any women with thromboembolism who had been prescribed combined hormonal contraceptives. Figure 11 compares error rates in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
Figure 11. Comparison of Outcome 4 in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months

![Outcome Measure 4](image)

6.3.3.1.6 Outcome 5a: Proportion of patients without full blood count among methotrexate users

The median proportion of patients with evidence of at least three months of prescribing of methotrexate in a general practice was 0.23% (IQR 0.15-0.31%) on 1st April 2007. Out of the patients at risk there was a median of 16.7% (IQR 3.4-46.7%) who did not have a full blood count check in the last three months. Figure 12 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
Figure 12. Comparison of Outcome 5a in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months

**Outcome Measure 5a**

<table>
<thead>
<tr>
<th>Proportions of patients (%) receiving methotrexate without a recorded full blood count within the previous three months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Simple Feedback</td>
</tr>
</tbody>
</table>

6.3.3.1.7 **Outcome 5b: Proportion of patients without liver function test among methotrexate users**

The median proportion of patients with evidence of at least three months of prescribing of methotrexate in a general practice was 0.23% (IQR 0.15-0.31%) on 1st April 2007. Out of the patients at risk there were median 20.0% (IQR 4.5-46.7%) who did not have a liver function test in the last three months. Figure 13 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
**Figure 13. Comparison of Outcome 5b in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months**

![Comparison of Outcome 5b](image)

**6.3.3.1.8 Outcome 6: Proportion of patients without INR among warfarin users**

The median proportion of patients with evidence of at least three-months of prescribing of warfarin in a general practice was 1.0% (IQR 0.7-1.3%) on 1st April 2007. The median proportion of patients without INR recording in the three months prior to this date calculated on all practices was 44% (IQR 3-93%), after exclusion of the practices with more than 60% of the errors, median proportion became 4% (IQR 1-13%). Figure 14 shows a histogram with frequency of general practices for different proportions of such patients. The histogram is based on all practices.
Figure 14. Percentage of patients without check of INR out of patients on warfarin by number of general practices

Data are obtained at the baseline on 1 April 2007

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Figure 15 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
6.3.3.1.9 Outcome 7: Proportion of patients without lithium level among lithium users

The median proportion of patients with evidence of at least three months of prescribing of lithium in a general practice was 0.11% (IQR 0.06-0.16%) on 1st April 2007. Out of the patients at risk there were median 28.6% (IQR, 12.5-46.6%) who did not have a lithium level check in the last three months. Figure 16 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
Figure 16. Comparison of Outcome 7 in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months

![Outcome Measure 7](image)

6.3.3.1.10 Outcome 8: Proportion of patients without TFT among amiodarone users

The median proportion of patients with evidence of at least three months of prescribing of amiodarone in a general practice was 0.15% (IQR 0.1-0.21%) on 1st April 2007. Out of the patients at risk there were median 50.0% (IQR 30.0-66.7%) who did not have a thyroid function test in the last three months. Figure 17 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
6.3.3.1.11 Outcome C1a: Proportion of patients with at least 1 prescribing problem (i.e. Outcomes 1, 2 and 4) among patients at risk of 1 prescribing problem

The median proportion of patients with at least 1 prescribing problem, in those “at risk”, in a general practice was 13.3% (IQR 11.7-15.1%) on 1st April 2007. Out of the patients at risk there were median 2.5% (IQR 1.8-3.1%) who had at least one prescribing problem. Figure 18 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
Figure 18. Comparison of Composite Outcome 1a (i.e. Outcomes 1, 2 and 4) in the two PINCER trial arms and QRESEARCH practices at baseline, six-months and 12-months.

6.3.3.1.12 Outcome C2a: Proportion of patients with at least one monitoring problem (i.e. Outcomes 3, 5 (a or b), 6, 7 and 8) among patients at risk of one monitoring problem

The median proportion of patients with at least one monitoring problem, in those “at risk” in a general practice was 4.5% (IQR 3.6-5.3%) on 1st April 2007 (after removing practices where the proportion of warfarin users without INR recording was more than 60%). Out of the patients at risk there were median 12.4% (IQR 7.8-19.0%) who had at least one monitoring problem. Figure 19 compares the rates of these errors in the two PINCER arms with those in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months.
6.3.3.1.13 Outcome C1b: Proportion of patients with at least two prescribing problems (i.e. Outcomes 1, 2 and 4) among patients at risk of two prescribing problems

The median proportion of patients with at least two prescribing problems in a general practice was 0.3% (IQR, 0.2% to 0.4%) on 1st April 2007. There were only 7 (1.6%) practices that had 1 patient with at least 2 prescribing problems.

6.3.3.1.14 Outcome C2b: Proportion of patients with at least two monitoring problems (i.e. Outcomes 3, 5 (a or b), 6, 7 and 8) among patients at risk of two monitoring problems

The median proportion of patients with at least two monitoring problems in a general practice was 0.45% (IQR 0.32-0.58%) on 1st April 2007 (after removing practices where the proportion of warfarin users without INR check was more than 60%). Out of the patients at risk there was a median 0% (IQR 0-3.6%) that had at least two monitoring problems.
6.3.3.1.15 Summary table

Table 52 summarises the comparison of the rates of errors in the two PINCER trial arms with the findings in the QRESEARCH practices at the three assessment points i.e. baseline, six-months and 12-months for the range of outcome measures of interest (see Table 52).
Table 52. Comparison of rates of errors for all Outcomes in the two PINCER trial arms and QRESEARCH practices at the at baseline, six-months and 12-months

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Assessment Point</th>
<th>Group</th>
<th>Baseline</th>
<th>6 Months</th>
<th>12-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Patients with a history of peptic ulcer who have been prescribed a NSAID without a PPI (%)</td>
<td></td>
<td>S</td>
<td>4.7</td>
<td>4.3</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>4.8</td>
<td>2.8</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>3.5</td>
<td>3.3</td>
<td>3.2</td>
</tr>
<tr>
<td>2 Patients with asthma who have been prescribed a beta-blocker (%)</td>
<td></td>
<td>S</td>
<td>3.0</td>
<td>3.0</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>2.8</td>
<td>2.5</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>2.4</td>
<td>2.5</td>
<td>2.6</td>
</tr>
<tr>
<td>3 Patients aged ≥75 years prescribed an ACE inhibitor or a loop diuretic long-term without a check of their renal function and electrolytes in the previous 15 months (%)</td>
<td></td>
<td>S</td>
<td>10.2</td>
<td>8.2</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>12.6</td>
<td>5.3</td>
<td>5.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>9.2</td>
<td>7.5</td>
<td>6.5</td>
</tr>
<tr>
<td>2a Patients with asthma who did not have CHD who have been prescribed a beta-blocker (%)</td>
<td></td>
<td>S</td>
<td>1.9</td>
<td>1.8</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>1.9</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>1.6</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>4 Women with a past medical history of thrombosis who have been prescribed the combined oral contraceptive pill (%)</td>
<td></td>
<td>S</td>
<td>0.6</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5a Patients receiving methotrexate for at least three months who have not had a recorded full blood count within the previous three months (%)</td>
<td></td>
<td>S</td>
<td>41.8</td>
<td>31.3</td>
<td>35.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>35.4</td>
<td>24.7</td>
<td>24.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>16.7</td>
<td>13.3</td>
<td>12.8</td>
</tr>
<tr>
<td>5b Patients receiving methotrexate for at least three months who have not had a recorded liver function test within the previous three months (%)</td>
<td></td>
<td>S</td>
<td>38.1</td>
<td>29.7</td>
<td>33.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>35.8</td>
<td>24.5</td>
<td>25.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>20.0</td>
<td>14.3</td>
<td>13.6</td>
</tr>
<tr>
<td>6 Patients receiving warfarin for at least three months who have not had a recorded check of their INR within the previous 12 weeks (%)</td>
<td></td>
<td>S</td>
<td>6.6</td>
<td>4.8</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>5.8</td>
<td>3.0</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>4.0</td>
<td>3.9</td>
<td>3.2</td>
</tr>
<tr>
<td>7 Patients receiving lithium for at least three months who have not had a recorded check of their lithium levels within the previous three months (%)</td>
<td></td>
<td>S</td>
<td>45.1</td>
<td>39.8</td>
<td>41.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>50.0</td>
<td>35.3</td>
<td>31.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>28.6</td>
<td>34.6</td>
<td>44.4</td>
</tr>
<tr>
<td>8 Patients receiving amiodarone for at least six-months who have not had a thyroid function test within the previous six-months (%)</td>
<td></td>
<td>S</td>
<td>51.4</td>
<td>45.1</td>
<td>37.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>46.3</td>
<td>33.5</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q</td>
<td>50.0</td>
<td>33.3</td>
<td>33.3</td>
</tr>
<tr>
<td>C1a Patients with at least one prescribing problem (%)</td>
<td></td>
<td>S</td>
<td>3.0</td>
<td>2.9</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P</td>
<td>2.8</td>
<td>2.3</td>
<td>2.4</td>
</tr>
<tr>
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<td>Q</td>
<td>2.5</td>
<td>2.6</td>
<td>2.6</td>
</tr>
<tr>
<td>C2a Patients with at least one monitoring problem (%)</td>
<td></td>
<td>S</td>
<td>15.0</td>
<td>11.7</td>
<td>11.3</td>
</tr>
<tr>
<td></td>
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<td>P</td>
<td>16.0</td>
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<tr>
<td></td>
<td></td>
<td>Q</td>
<td>12.4</td>
<td>10.5</td>
<td>9.8</td>
</tr>
</tbody>
</table>

*S = Simple Feedback P= Pharmacist Intervention Q = QRESEARCH*
6.4 Discussion

6.4.1 Main findings

Undertaking this additional analysis using the QRESEARCH database has been important for two main reasons. First, it has demonstrated that the baseline characteristics and error rates in the 72 PINCER practices were broadly comparable to those found in practices throughout the UK. We are thus confident that the errors we chose to focus on are problems facing most general practices; the practices that enrolled into the study were not therefore peculiar in this respect. This observation suggests that the external validity of our findings is likely to be high (this also being suggested by our qualitative data). Second, we have found that there appears to be some overall improvement in monitoring error rates (with the exception of Outcome 7), but not prescribing errors, as a result of secular trends and that any reductions in monitoring errors seen in the simple feedback arm are therefore likely, to a large extent, to be explained by this phenomenon rather than by the simple feedback intervention per se. This work therefore provides additional – albeit indirect – evidence on the effectiveness of the pharmacist-led IT-based intervention when compared to the simple feedback intervention.

6.4.2 Strengths and limitations

Our work has several strengths; most notably the attempt to interpret the trial results in the context of assessing secular trends. Our analyses demonstrate that QRESEARCH and PINCER practices were comparable in many key respects thereby offering some reassurance about the likely generalisability of these findings. This analysis of the QRESEARCH database is substantially larger and has greater statistical power than most previous studies on prescribing errors in general practice. It should also be noted that this work is based on computer-recorded prescribing and monitoring data collected prospectively and any bias from misclassification is unlikely because the level of accuracy and completeness on medical records in general practices has been shown to be high.

Nevertheless, there are limitations. As one might expect with a database analysis, not all patients fulfilling the criteria for being numerators in the outcome measures will
have been subject to a medication error. For example, for the prescribing errors, it is possible that in some cases there was a justification for what appears to be hazardous prescribing, or that miscoding may have been the underlying issue. In the case of the monitoring errors, lack of recording of blood test results will have resulted in spuriously high proportions of at risk patients appearing to be subject to an error. Given that we selected only practices with electronic links to local laboratories, this is unlikely to have had a major impact for outcome measures where GPs take the main responsibility for monitoring. For medications where there are shared care arrangements with secondary care, or where GPs have stand-alone systems for recording INR results, it is likely that there were spuriously high proportions of monitoring “errors” in some practices. In these cases, patients may have had monitoring done, but the results may not have been recorded on the general practice EMIS computer system. The medications potentially most affected by these issues are methotrexate, warfarin, lithium and possibly amiodarone. It is also important to emphasise that direct comparisons between PINCER and QRESEARCH practices was not possible because the QRESEARCH practices were a (large) convenience sample that was not randomly selected.
Chapter 7: General discussion
7.1 What do the findings tell us?

The PINCER trial and related studies have shown that:

- A complex pharmacist led IT-based intervention is effective at reducing the prevalence of patients at risk from prescribing and monitoring errors.

- The pharmacist-led intervention has a 95% probability of being considered cost-effective if the decision-makers ceiling willingness to pay reaches £75 (6 months) or £85 (12 months) per error avoided.

- The trial pharmacists judged that over 70% of patients identified by the outcome measures were at clinical risk (over 80% for the primary outcome measures).

- A number of factors are likely to have contributed to the success of the trial, including involvement of key individuals in the practice, support for pharmacists in their roles and support from PCTs.

- Our large parallel GP database study helped in interpretation of trial findings in two main ways: first, we were able to demonstrate that the errors we focused on are being replicated in practices throughout England; and second, we were able to demonstrate that the improvements in monitoring outcomes achieved in the simple feedback (control) arm may have been the result of secular trends.

In the rest of this section we discuss the effectiveness of the pharmacist-led intervention.

The levels of reduction of risk for the pharmacist intervention arm compared with the simple feedback arm (as represented by odds ratios) were appreciable at six-months follow-up for the three primary outcome measures and also for the secondary outcome measures. The differences were most marked for Outcomes 1 and 3 and the composite monitoring outcome measure (Outcomes 3, 5, 6, 7 and 8): reduction in odds of each outcome of 42%, 49% and 44% respectively. These reductions were less marked for Outcome 2 and the composite prescribing outcome measure (i.e. Outcomes 1, 2 and 4): reduction in odds of each outcome of 27% and 29% respectively.
It is likely that one of the reasons for the differences seen in the monitoring outcome measures was due to it being relatively straightforward for pharmacists to arrange for patients to have relevant blood tests. For example, for Outcome 3 (monitoring patients aged 75 years and older on ACE inhibitors and loop diuretics) almost 90% of recommendations to arrange blood test were completed (see Table 34).

Nevertheless, it would also have been reasonably easy for practices in the simple feedback arm of the trial to arrange blood tests for patients at risk. Although the practices in this arm appear to have had reductions in patients at risk of monitoring errors over time, these trends were largely mirrored in the QRESEARCH practices that had no involvement in the trial. Therefore, it would seem that any changes noted in the simple feedback arm of the trial were more likely to be associated with secular trends towards better blood test monitoring rather than due to the intervention itself. This suggests that in the context of our trial, simple feedback to practices had little or no impact on improving prescribing safety. This is not surprising given the results from previous studies of feedback to clinicians and indicates that a more active intervention, such as the one used in the PINCER trial, is required.

The size of the differences found in proportions of patients at risk of receiving NSAIDs without PPI cover in patients with a history of peptic ulcer were probably due to a number of factors. Firstly, there is little justification for prescribing in these circumstances. Secondly, the solutions are relatively straightforward and include the prescription of a PPI to reduce the risk of bleeding associated with the NSAID, or trying a different type of analgesic. The fact that trial pharmacists reported that nearly 80% of their recommendations were completed in relation to this outcome measure (see Table 32) supports the idea that dealing with these patients was relatively non-contentious and straightforward. For example, 73% of recommendations to stop an NSAID were completed (see Table 32). At 12-months post-intervention, however, the pharmacist-led intervention was no longer effective. This suggests that practices would have either have:

- Restarted patients on NSAIDs (where these had been stopped as a result of the intervention)
- Not continued with the PPI cover for patients on NSAIDs (where PPIs had been started as a result of the intervention), or
• Started prescribing NSAIDs without PPI cover to patients with a history of peptic ulcer who were not being prescribed NSAIDs at the baseline data collection.

Whatever the reason, it suggests that there was dropping off in the effectiveness of the pharmacist-led intervention. Therefore, it cannot be assumed that the intervention, as it stands, would result in long-term reductions in patients at risk from this medication error.

The smaller reductions in proportions of patients with asthma being prescribed beta-blockers are probably explained by this being a more challenging problem for pharmacists to deal with. While the pharmacists judged that over 80% of these patients were at clinical risk, their recommended actions were completed in only 46% of cases (see Table 33). In particular, recommendations to stop a beta-blocker were completed in only 21% of cases (see Table 33).

Possible reasons why GPs were less inclined to address recommendations in relation to this outcome measure include:

• Scepticism over whether the patient was at risk from the beta-blocker (for example in terms of the patient having relatively mild asthma and not currently being affected adversely by the beta-blocker)

• The patient being on the beta-blocker for a clinically important indication

• Difficulty in finding an alternative to the beta-blocker

In order to investigate the possibility that the patient was on beta-blockers for an important clinical indication (i.e. the second bullet above), when we excluded patients with coronary heart disease from this outcome measure, the differences between the intervention arms were no longer statistically significant at six-months post-intervention (see Table 6). This may be because the proportions of patients being prescribed beta-blockers in this group were smaller at baseline (see Table 4). Also, we did not exclude other patients, such as those with heart failure, where the benefits of beta-blockers may outweigh the risks.

Nevertheless, despite the various factors limiting the size of change seen for this outcome measure, a statistically significant difference between the intervention groups was still noted at 12-months post-intervention. This suggests that the
pharmacist intervention general practices manage to maintain some of the changes that had been introduced such as stopping the prescribing of beta-blockers to a small proportion of patients with asthma.

Overall, while the findings of the study show that the pharmacist-led intervention was effective at reducing the prevalence of patients at risk from certain prescribing and monitoring errors compared with simple feedback, the size and duration of the effect will be influenced by a number of factors. These may include the perceived clinical importance of different outcome measures, the ease with which changes can be made, and whether or not mechanisms are in place for maintaining these changes. On the basis of our findings for Outcome 1 (i.e. prescription of NSAIDs to patients with a history of peptic ulcer and no PPI cover), our findings indicate that it cannot be assumed that a once-off pharmacist-led intervention will lead to long-term changes to the prevalence of medication errors.

Also, it needs to be acknowledged that our study deliberately focused on potential medication errors rather than adverse events and therefore we cannot be certain that the pharmacist-led intervention will lead to a reduction in patient-harm. Nevertheless, a strong argument can be made for focusing on the measurement of errors rather than adverse events when assessing the quality of clinical practice, as the former relate most closely to actions that are within the control of healthcare professionals\textsuperscript{46}. Further information on the potential of the pharmacist-led intervention to reduce patient morbidity will be available from a modelling economic analysis (based on the trial findings in conjunction with literature on links between hazardous prescribing/inadequate medication monitoring and the costs of associated patient morbidity).

### 7.2 What made the pharmacist-led intervention effective?

Shortly before applying for funding for the PINCER trial, we conducted a systematic review and meta-analysis which showed some evidence of effectiveness for pharmacist-led medication reviews and educational programs using academic detailing to improve general practice prescribing\textsuperscript{8}.

In particular, this review and other studies showed that:
- Pharmacist-led interventions can lead to resolution of medication-related problems in 55-93% of patients²⁷-³¹.
- Educational outreach is a moderately powerful tool for changing professional behaviour³².
- Multifaceted interventions aimed at different barriers to change are more effective than single interventions³³.

Nevertheless, since the start of our study, there have been a number of important publications that have questioned the effectiveness of pharmacist-led interventions in general practice. For example, the HOMER trial set out to determine whether home-based medication review by pharmacists among older people would affect hospital readmission rates¹⁴⁷. The researchers found an increase in hospital admissions and no improvement in quality of life or death rate. More recently, the RESPECT trial showed no benefit from community pharmacist involvement in moderating drug management (pharmaceutical care) in older people in general practice¹⁴⁸. Indeed, the authors, drawing upon their knowledge of the literature and a recent systematic review¹⁴⁹ argue that rigorous studies “provide no evidence to support the roll-out in primary care pharmacist led medication review in general, or pharmaceutical care in particular”¹⁴⁸.

Given the conflicting evidence for the effectiveness of pharmacist-led interventions in primary care it is important to reflect on why the PINCER trial pharmacist intervention proved effective.

Firstly, we used an educational outreach approach which is known to be a moderately powerful intervention for changing professional behaviour³². Pharmacists involved in the trial received training on the use of these techniques and the evidence base for the outcome measures used in the trial. Of relevance to Outcome 1 in the PINCER trial (see Table 1), May²¹ reported a reduction in NSAID prescribing as a result of educational outreach and suggested their programme contributed to a 70% reduction in hospital admissions due to gastro-intestinal adverse events.

Secondly, we focused on specific examples of hazardous prescribing or inadequacies in medication monitoring and this may have increased our ability to impact on and detect change compared with the use of more generalised measures.
Thirdly, the pharmacists in the study worked with the practices, had access to patient records for contextual information, and were able to provide practical support in making changes to patients’ medications and organising blood tests.

Fourthly, the intervention was multifaceted and aimed simultaneously to tackle different barriers to change; such interventions are known to be more effective than single interventions\textsuperscript{33}.

Fifthly, our embedded qualitative study (see Chapter 5: Qualitative evaluation of the PINCER trial) identified a number of factors that are likely to have contributed to the success of the intervention (these were not present in all practices) including:

- The perceived value of the intervention.
- The perceived value of pharmacists in primary care.
- The perceived appropriateness of the outcome measures.
- Having an initial meeting between the pharmacist and members of the practice.
- Having a link person within the practice for the pharmacist to work with (in most cases this was the practice manager).
- Willingness of practices to accommodate the pharmacist.
- Willingness of practices to engage in the intervention.
- The non-threatening, constructive and friendly approach of trial pharmacists.
- Involvement of a wide range of staff within general practices, including doctors, nurses and administrative staff.
- Co-operation and support from PCTs.

The competence of the pharmacists themselves was also an important factor although it is worth noting that the pharmacists came from a range of backgrounds and they were not unusual in their levels of qualification (see Table 22).

Thus, there were many factors that contributed to the effectiveness of the pharmacist-led intervention. A major factor was the ability of pharmacists to facilitate change in prescribing and medication monitoring of individual patients; evidence of pharmacists teaching others how to avoid making errors was more limited.

It should be noted, that there may have been factors that limited the comparative effectiveness of the simple feedback arm of the trial. For example, the educational
materials provided (see Appendix 2) might have appeared daunting to practitioners in the simple feedback arm (where there was no additional support from a pharmacist); conveying the messages in a simpler and clearer way might have been more effective.

7.3 How well did the outcome measures perform?

The outcome measures were based upon patterns of prescribing and medicines management that were known to be associated with patient harm and/or were contrary to expert opinion\(^7\)\(^-\)\(^13\). Our analysis of reports from the trial pharmacists indicates that over 70% of patients identified by the outcome measures were considered at clinical risk. The percentages considered to be at clinical risk by pharmacists for primary Outcomes 1, 2 and 3 were 90%, 81% and 94% respectively. Nevertheless, some patients were identified as a result of computer coding errors (8% and 10% for Outcomes 1 and 2 respectively) and for other reasons that did not put the patient at clinical risk. Relatively few were identified as a result of information being available, but not coded in the clinical records.

Overall, these finding suggest that in the majority of cases the outcome measures are effective at picking up patients at clinical risk. The main exception to this was for Outcome 6 (see Table 1) for practices using stand-alone systems for recording INR results on patients prescribed warfarin. This is because, in these practices, the majority of patients appeared to be at risk only because their INR results had not been recorded on the practice computer (as noted in Section 2.2.7.1, these practices were not included in the main trial analysis for this outcome measure).

One of the reasons why the primary outcome measures were selected was because pilot work using the QRESEARCH database indicated that the numbers of patients identified, as a proportion of those at risk, was sufficiently high to allow for a feasible number of practices to be recruited according to our sample size calculations. This allowed for demonstration of proof-of-principle that the complex pharmacist-led intervention could be effective.

Apart from the composite outcome measures, the numbers of patients identified by the secondary outcome measures were relatively small compared with the primary
outcome measures, particularly Outcomes 2 and 3. This may account for the fact that few statistically significant differences were noted between the intervention groups for most of the secondary outcome measures.

In contrast, the composite outcome measures contained large numbers and demonstrated statistically significant differences between the intervention groups at both six- and 12-months follow-up. These outcome measures were included in the trial at the suggestion of referees who reviewed the grant application. The combination of different types of medication errors makes sense in that each type is likely to have similar underlying causes and the methods for tackling these errors are also likely to be similar.

Outcomes 9 and 10 (see Table 1) required extraction of dosage instructions and it was not possible to do this for one of the GP computer systems used by practices in our study. This may limit the use of such outcome measures in future studies.

Overall, the outcome measures used in the study performed reasonably well although there were issues in relation to Outcome 4 (numbers very small); Outcome 6 (INRs not recorded on the clinical computer system in some practices), and Outcomes 9 and 10 (dosage instructions cannot be reliably extracted from all GP computer systems).

7.4 Policy implications

Since the publication of An organisation with a memory and Building a safer NHS for patients the UK Government has demonstrated a strong commitment to reducing errors in the NHS. Also, while it is acknowledged that there may still be a need to understand more about medication errors and the reasons for their occurrence, the priority now must be to find effective, acceptable and sustainable ways of preventing patients from being harmed as a result of such errors.

The PINCER trial has shown that a complex pharmacist-led IT-based intervention can significantly reduce the numbers of patients at risk from clinically important prescribing and monitoring errors. The intervention appears to be acceptable to general practices, feasible in terms of the skills of pharmacists, and of relatively low cost per error avoided. The intervention would be suitable for roll-out using suitably
trained PCT pharmacists or community pharmacists. The involvement of pharmacists in such an intervention would be consistent with the Government’s aim to build on the strengths of pharmacy\textsuperscript{150}. The intervention would fit in particularly well with the PCT pharmacist role where pharmacists already have well-developed working relationships with general practices. Indeed, it is possible that pharmacists with such established working relationships with general practices would be even more effective than the pharmacists employed in the PINCER trial. Also, with increasing numbers of pharmacists becoming independent prescribers, this could enhance the ability of pharmacists to intervene to improve patient safety without needing general practitioners to action necessary changes.

Any roll-out would need to take account of all the elements of the PINCER intervention that are likely to have contributed to its success; we have no evidence to indicate that a watered-down version would be successful. Also, consideration would need to be given to maintaining the benefits of the intervention, for example by having the pharmacist revisit the practice at six-monthly intervals. In addition, further evidence would be needed to indicate whether the intervention is likely to reduce patient harm. Also, consideration should be given to the likely benefits over and above those available from computerised clinical decision support\textsuperscript{151}.

If the intervention were to be rolled out then it would be important for this to be evaluated. A Phase IV trial\textsuperscript{20} would be an appropriate approach and could work well if PCTs were randomised to start the intervention in a phased way, so that those starting the intervention later would act as controls, i.e. use of a step-wedged design\textsuperscript{152}.

The National Patient Safety Agency (NPSA) is, we believe, an appropriate body for promoting the roll-out of the PINCER trial intervention, particularly as the organisation had a pivotal role in the initiation of the study.

### 7.5 Suggestions for further research

As outlined above, an evaluation of a national roll-out of the PINCER trial intervention would be an appropriate topic for further research.
Before then, it would be useful to undertake further work aimed at optimising the intervention and considering further development of the outcome measures. With respect to optimising the intervention, the key point to note is that we were not able to eliminate the errors of interest; whilst our results were encouraging; there is still clearly scope for further improvement. In relation to extending this work, there is also the need formally to consider extending the intervention to encompass a broader range of prescribing and medication-related monitoring errors.

We already have a lot of information about the actions taken by the trial pharmacists and the factors associated with the success of the intervention. Nevertheless, we have not had time to evaluate diaries recorded by the trial pharmacists. It would be useful to examine these using qualitative research techniques with the aim of finding out whether they contain additional information that would be helpful in the further development and roll-out of the intervention.

As outlined in Section 7.3, while most of the outcome measures performed well in the study, some might not be suitable for use in a national roll-out (particularly Outcomes 9 and 10 – see Table 1). In any future study, it would make sense to retain the primary outcome measures so that the findings could be compared with the PINCER trial. It would also be worth considering developing the composite outcome measures further. For example, it would be possible to include within these outcome measures additional prescribing and monitoring errors.

There is also a need to update our systematic review and meta-analysis to incorporate findings from this new additional primary care-based trial. There is in parallel a need for a more interpretive critique of these trial data using a realist perspective, which could usefully draw on findings from our qualitative work.

We also suggest that there is ongoing monitoring of national trends in the errors investigated using large general practice databases.

Finally, in view of the conflicting evidence on the effectiveness of pharmacist interventions in primary care it would be worth reviewing the different studies to try to determine the elements most likely to be associated with success or failure.
7.6 Recommendations

As a result of this study, we have two main recommendations:

- Further developmental work to optimise and consider extending the PINCER intervention.
- Planning for a national roll-out of the PINCER intervention – preferably led by the NPSA – with this occurring in the context of a national independent evaluation.
Compared with simple feedback, the pharmacist-led intervention resulted in reductions in proportions of patients at risk of prescribing and monitoring errors for the primary outcome measures and the composite secondary outcome measures at six-months and (with the exception of the NSAID/peptic ulcer outcome measure), 12-months post-intervention. There were no differences in death rates between the two treatment arms.

The pharmacist-led intervention has a 95% probability of being considered cost-effective if the decision-makers ceiling willingness to pay reaches £75 (6 months) or £85 (12 months) per error avoided.

Analysis of data recorded by trial pharmacists indicated that over 70% of cases identified by the outcome measures were considered at clinical risk (over 80% for each of the primary outcome measures). Pharmacists recommended actions in three quarters of cases identified by the electronic searches and these recommendations were tailored to the outcome measures and individual patients. General practitioners were reported to have accepted around two-thirds of pharmacists’ recommendations.

The qualitative analysis identified a number of factors that are likely to have contributed to the success of the pharmacist-led intervention. These factors, which include involvement of key individuals in the practice, support for pharmacists in their roles and support from PCTs, need to be considered in any roll-out of the intervention.

Baseline estimates of the frequency of errors were similar in PINCER trial practices and practices contributing to the national QRESEARCH database. Examining changes in outcome measures in QRESEARCH practices over the time that the trial took place showed statistically significant reductions in the proportion of patients at risk of monitoring errors for all of the monitoring outcome measures. Informal comparison with PINCER trial practices at six- and 12-months post-intervention suggest that any apparent improvements in monitoring outcome measures in the simple intervention arm practices may have been associated more with secular trends than intervention itself.

Overall, the main trial and associated studies have shown the PINCER trial pharmacist-led intervention to be effective and cost-effective at reducing medication errors whilst also being acceptable to general practices.
Chapter 9: Additional information
9.1 Trial organisation

Professor Avery has had overall responsibility for the day-to-day management of the trial and for the conduct of the trial in the area around Nottingham. Professor Avery led the Trial Management Group.

Dr Sarah Rodgers was the trial coordinator from the start of the trial to June 2009.

Professor Cantrill had overall responsibility for the conduct of the trial in the area around Manchester.

Professor Elliott had responsibility for the economic analysis with Matthew Franklin and Matthew Boyd assisting.

Dr Sarah Armstrong was the trial statistician with Professor Kendrick also having a major role in the planning of the statistical analysis. Both Dr Armstrong and Professor Kendrick undertook the statistical analyses for the main trial outcome measures. Additional statistical advice was provided by Professors Prescott and Sheikh from The University of Edinburgh.

Professor Sheikh had overall responsibility for the conduct of the qualitative analysis.

Professor Hippisley-Cox had overall responsibility for the analysis of outcome measures using data from QRESEARCH practices.

9.2 Trial Management Group

The Trial Management Group has met on a quarterly basis throughout the study to help ensure that all trial activities were organised according to the protocol and, as far as possible, within the timescales set out in the original application for funding.

The Trial Management Group consisted of all the authors of this report with the exception of Matthew Boyd, Julia Hippisley-Cox, Caroline Morris, Scott Murray, Koen Putman and Yana Vinogradova.
9.3 Trial Steering Committee

The Trial Steering Committee (TSC) has monitored and supervised the trial and advised on any proposed amendments to the protocol. The Trial Steering Committee was headed by Professor Philip Hannaford. Professor Martin Buxton and Professor Marjorie Weiss were the other external members of the committee. The TSC and agreed to operate within the framework suggested in the *MRC Guidelines for good clinical practice in clinical trials*[^153]

9.4 Data Monitoring and Ethics Committee

The Data Monitoring and Ethics Committee (DMEC) was headed by Professor Richard Baker. Other external members of the committee were Professor Christine Bond and Professor Peter Donnan. The trial statistician reported to the DMEC, which will was responsible for reviewing the data from the trial. The DMEC agreed to operate within the framework suggested in the *MRC Guidelines for good clinical practice in clinical trials*[^153]

9.5 Ethical aspects of the trial

The trial was conducted according to the Helsinki Declaration[^154], the Good Clinical Practice Guidelines[^155] and NHS Research Governance requirements.

Patients agreeing for the study team to access their clinical records were provided written informed consent in a form designed for such purpose. Patients were able to refuse to continue participating in the study at any time after providing their consent.

Data from patients has been kept confidential and use of the data has been limited to the purposes stipulated in the protocol.

The study was approved by Nottingham 2 Research Ethics Committee (Reference: 05/Q2404/26). All staff involved in data collection had approval from the appropriate local NHS research and development offices.
9.6 Study timeline

Trial start: 1 April 2006

Start of baseline data collection and interventions in general practices: August 2006

End of interventions in general practices: February 2008

End of 12-month follow-up data collection: April 2009

Start of data analysis: May 2009

Study end date: 31st January, 2010

Duration: 3.6 years

9.7 Authors contributions

AJA, who has made substantial contributions to the conception and design of the study, was co-responsible for the overall administration and direction of the project, the analysis and interpretation of data and has given the final approval of this report.

JAC and AS are also co-responsible for the overall design, administration and direction of the study.

SR was the Trial Co-ordinator and was responsible for the day-to-day management of the trial up until June 2009. She was involved in the design of the Quest Browser queries and the piloting of the data extraction methods. She had a major role in formatting the report.

JAC, AS, SA, RE, RH, DK, CJM, SM, RJP and KC also participated in the design of the project: SA, DK, RJP and AS had a major role in designing the statistical analysis for the trial. The analysis was undertaken by SA and DK.
ME had a major role in the day-to-day running of the trial at the sites in Staffordshire and Central and Eastern Cheshire under the direction of Professor Cantrill. Under the direction of Professor Avery, he undertook the processing and cleaning of data for the main trial outcome measures. He contributed to economic analysis by piloting and undertaking data extractions and by providing data from the main trial for the economics team. He also provided comparative data for the QRESEARCH study. He assisted in the formatting of the report.

LT helped to coordinate the trial at the sites in Staffordshire and Central and Eastern Cheshire under the direction of Professor Cantrill.

RE has led on the design of the economic analysis with assistance from Koen Putman, Matthew Boyd and Matthew Franklin.

AS, SM and KC have led on the design of the qualitative analysis and KC wrote Chapter 5: Qualitative evaluation of the PINCER trial.

JHC had overall responsibility for the QRESEARCH analysis and undertook a considerable amount of work on this; YV did most of the analysis of the QRESEARCH data and wrote the first draft for Chapter 6: QRESEARCH analysis of secular trends in outcome measures; AJA, ME and SR made significant contributions to the QRESARCH study which was overseen by the TMG with particular input from SA and DK.

RH did the analysis of reports from the trial pharmacists and wrote Chapter 4: Analysis of data recorded by PINCER trial pharmacists

Glen Swanwick and Tom Turner provided useful advice on the research ethics committee application and on materials sent to general practices and patients. They attended most Trial Management Group meetings and gave constructive comments on the final report.
9.8 Acknowledgements

We thank:

- Richard Lilford and colleagues from the Patient Safety Research Portfolio and Members of the Trial Steering Committee and Data Monitoring and Ethics Committee who provided extremely valuable advice and support throughout the course of the study.
- The primary care trusts, general practices and patients involved in the study.
- PCT research and development leads, pharmacy leads, and other key individuals who helped to facilitate the study including Rachel Illingworth, Trevor Allen, Susan Noyce, Cathy Quinn, Andrew Riley and Gail Thomas.
- Tom Goodwin for acting as line manager to the trial pharmacists.
- The trial pharmacists: Stacey Sadler, Christine Butler, Sadaf Qureshi, Lisa Dutton, Reena Vedi and Robert Mason.
- Stacey Sadler for help in developing data extraction protocols for the economic study.
- Emmanuel Atsu Dodor and Brian Serumaga for help with extraction of data for the economic study and also for data input.
- Ed Longridge for help with data extractions.
- Julia Hippisley-Cox for providing data from the QRESEARCH database (www.qresearch.org) for conducting sample size calculations.
- Clive Morris, Peter Bond, Mark Poole and colleagues from The Computer Room (www.tcrnottingham.com) for their input concerning data extraction from general practices using Quest Browser software.
- April McCambridge and Clare Randall for assistance in formatting this report.
- Sharon Mills for administrative support throughout the trial.
- Sadaf Qureshi for entering the summary data collected by the pharmacists; Caroline Mulvaney and Sherie Smith for double checking the data entry, and Stacey Sadler for collating the pharmacist demographic data for this part of the project.
- Koen Putman, Lieven Annemans and Nick Verhaeghe for their input to the modelling economic analysis.
• The National Primary Care Research and Development Centre at the University of Manchester provided practice-level data on deprivation from The National Primary Care Database.
• Dr Casey Quinn for contributing to a re-analysis of the economic data.
• The referees for the time they spent reviewing our draft report, and for comments that have helped to improve the final version.

9.9 Source of funding

Patient Safety Research Program of the UK Department of Health.
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Appendix 1: Letters to general practices, information leaflets and consent forms
Appendix 1.1: Practice introductory letter

University Letterhead

Practice
Address
Date

Dear Dr Name

The PINCER Trial

We are writing to ask if your practice would be willing to participate in a research project that has been funded by the Department of Health as part of their Patient Safety Research Programme.

Research done at the Universities of Manchester and Nottingham has shown that some patients are at risk from hazardous prescribing or infrequent therapeutic monitoring in general practice. We have developed methods for identifying these patients using searches of GP computer systems and pilot studies have shown that practices find this information useful in improving patient care.

In the PINCER trial we want to find out whether an intensive pharmacist-led intervention can reduce rates of potentially hazardous prescribing more effectively than giving simple feedback about patients at risk. The study is being conducted by the Universities of Nottingham, Manchester and Edinburgh and we hope to recruit 68 general practices. The study has been granted ethical approval by the Nottingham Research Ethics Committee and organisational approval by Broxtowe & Hucknall PCT.

Please find enclosed an information sheet which explains the background to the study, requirements for participation and what would be expected of the practice during the course of the study. We would be grateful if you would read the information sheet and return the enclosed reply slip in the pre-paid envelope provided, indicating whether or not you might be interested in participating.
If you are interested in participating, a member of the research team (Sarah Rodgers or Sharon Mills) will telephone you to arrange a meeting to discuss the study in more detail and address any questions or concerns you may have. If we don’t hear from you within two to three weeks Sarah or Sharon will give your practice a ring.

Yours sincerely

Professor Tony Avery
Chief Investigator

Dr Sarah Rodgers
Trial Co-ordinator

cc Practice Partners and Practice Manager
REPLY SLIP

Practice Details

We are willing / not willing* to meeting with a researcher to discuss the PINCER trial in more detail.

* Please delete as applicable

Name and designation of practice representative we can contact to organise a meeting:

........................................................................................................................................

Practice representative telephone number:

........................................................................................................................................

Please return this reply slip using the prepaid envelope provided to:

Dr Sarah Rodgers
PINCER Trial Co-ordinator
FREEPOST MID 17779
Division of Primary Care
13th Floor, Tower Building
University Park
Nottingham
NG7 2RD
Appendix 1.2: Practice information sheet

The PINCER Trial

(A cluster randomised trial to determine the effectiveness, costs/benefits and acceptability of a pharmacist-led, IT-based intervention compared with simple feedback in reducing rates of clinically important instances of potentially hazardous prescribing in general practice)

Your practice is being invited to take part in the above study. Please take time to read this information leaflet and discuss it with other practice members before returning the reply slip. At this stage we are only asking whether you think you may be willing to participate. If you express an interest then you will be given the opportunity to meet with a member of the research team to raise any questions or concerns that you may have as a result of reading this information.

Thank you for taking the time to read this leaflet.

Purpose of the study
The purpose of this study is to determine the effectiveness, costs/benefits and acceptability of a pharmacist-led, multi-dimensional intervention (IT-based audit, the provision of evidence-based clinical information to medical staff, direct liaison with patients) compared with IT-based audit and simple feedback alone in reducing the rates of specified clinically significant instances of potentially hazardous prescribing in general practice.

Why has my practice been chosen?
Your practice has been chosen because you are located within a PCT that has given R&D approval to the study. Your practice is also within a 50 mile radius of the University of Nottingham, one of the sites from which the study is being run.
Does my practice have to take part?
It is up to you and your colleagues to decide whether you wish to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you do take part you will be given a further copy of this information sheet, and your consent form.

What will happen if we decide to take part?
If you decide to take part, your practice will be randomly allocated to one of the two arms of the trial (simple feedback or pharmacist intervention). All practices, irrespective of which arm of the study they are randomised to, will be visited by a researcher who will use Quest Browser software (www.tcr.i12.com) to extract data on patients at risk of medication-related injury from medications such as non-steroidal anti-inflammatory drugs, beta-blockers, angiotensin converting enzyme inhibitors, diuretics, amiodarone, lithium, methotrexate and warfarin. For an average sized practice, our pilot studies suggest that around 40 patients will be identified from these computer searches. Quest Browser software works with MIQUEST and has been used successfully by PCTs and practices for extracting data from GP computer systems with the aim of monitoring and improving quality of care.

In this study, the data extracted from GP computer systems will be used in two ways. Firstly, a member of your practice will be shown how to access information about those patients thought to be at risk of medication-related injury so that you can use this information to help improve
patient care (the research team will not have access to this patient-specific data). Secondly, the data will be automatically anonymised by the Quest Browser software and sent in an encrypted form to a secure email address at the University of Nottingham. Please note: All issues related to the anonymity of patient data and security of data during this process have been rigorously tested in a pilot study.

Practices allocated to the simple feedback arm of the trial will receive computerised feedback on patients who are exposed to instances of potentially hazardous prescribing, along with brief written educational materials explaining the importance of each event. The practice will be asked to try and make changes to patients' medications within 12 weeks. Practices in the pharmacist intervention arm will have a suitably experienced and trained pharmacist working with them intensively, on a part-time basis, over a 12 week period. The pharmacist will arrange an initial meeting with members of the practice team to discuss the computer-generated feedback. They will take an educational outreach ('academic detailing') approach and employ some of the principles of root cause analysis (if appropriate). The pharmacist will then work alongside practice staff to agree on the best way forward for addressing the problems identified (including dealing directly with affected patients) and for preventing further problems in the future. The pharmacist will not make changes to any patient's medication without the agreement of both the patient and their GP. In both arms of the trial the computerised searches of the clinical system will be repeated at six-months and 12-months after the end of the intervention period and this information will be sent in an anonymised and encrypted form to the University of Nottingham. Please note: the pharmacists will hold a full employment contract with a local PCT and pharmacists will not make direct contacts with patients unless those patients have given informed consent.

In both arms of the trial we would like practices to send out pre-prepared information about the study to patients. This information will be carefully worded to try to avoid generating any concerns. We will ask you to try to avoid sending the information out to certain groups of vulnerable patients (e.g. those with cognitive impairment or terminal illness).

For the patients contacted about the study, we will request their consent for a member of the research team to access their records 12-months after the completion of the study.
of the study in your practice. The reason for requesting access to patients’ records is to find out if there are any differences in the use of healthcare resources between the two arms of the trial (Please note: the member of the research team will hold an honorary contract with the PCT and will treat all patient information confidentially). In the pharmacist intervention arm of the trial we shall also ask patients to give their consent to be contacted by the pharmacist.

In order to find out what practices think to the interventions, we plan to undertake a small number of telephone interviews and focus groups with practice clinical and administrative staff from the (expected) 68 practices involved in the trial. Staff in your practice may be approached to ask if they are willing to participate in ONE of these activities. These will be audio-taped, with consent, and transcribed.

**What are the possible disadvantages or risks of taking part?**
Occasionally, MIQUEST queries can cause general practice systems to run slowly. However, we have developed and piloted the searches extensively and envisage that there will be minimal disruption to your practice’s normal routines.

Involvement in the study will take up some time for members of your practice. We have, however, piloted the study and believe that it should not be too time-consuming for most practices. We are able to pay a nominal sum of £100 to cover your administrative costs.

**What are the possible benefits of taking part?**
During the study, patients who are at risk from potentially hazardous prescribing will be identified. All practices involved in the study will have the opportunity to check these patients and to decide whether to take corrective action. In the pharmacist intervention arm, practices will receive extra help in the form of education and support.

**Will the practices’ participation in the study remain confidential?**
All information which leaves the practice will be anonymised so that neither the practice nor the individual patients can be recognised from it.
What will happen to the results of this study?
The results of this study will help to inform Government health policy on medicines management in primary care. A report will be publicly available through the Department of Health. The results of this study will be published in relevant journals and presented at conferences. No individual or practice will be identifiable in any of the published material.

Who is organising and funding this research?
The research is being organised by the Division of Primary Care, University of Nottingham in collaboration with the School of Pharmacy and Pharmaceutical Sciences, University of Manchester and the Division of Community Health Sciences, University of Edinburgh.

The study has been funded by the Patient Safety Research Programme of the Department of Health.

Who has reviewed the study?
This study has been reviewed favourably by the Nottingham Research Ethics Committee and organisational approval has been obtained from Broxtowe and Hucknall PCT.

Contact Details
For further information about this study please contact either:

Trial Co-ordinator: Dr Sarah Rodgers, Division of Primary Care, 13th Floor, Tower Building, University Park, Nottingham NG7 2RD. Tel: 0115 846 6937; Fax: 0115 8466904; email: sarah.rodgers@nottingham.ac.uk

Chief Investigator: Professor Tony Avery, Head of Division of Primary Care, School of Community Health Sciences, University of Nottingham Medical School, Nottingham, NG7 2UH. Tel: 0115 823 0207; Fax: 0115 8230214; email: tony.avery@nottingham.ac.uk
Appendix 1.3: Practice consent form

The PINCER Trial
Chief Investigator: Professor Tony Avery

Practice Details

General Practice Consent to Participate in Study

Please complete the following:  

Have you read and understood the information sheet?  

YES / NO

Have you had an opportunity to ask questions and discuss this study? 

YES / NO

Have you received satisfactory answers to all your questions?  

YES / NO

Have you received enough information about the study?  

YES / NO

Do you understand that you are free to withdraw from the study 

- at any time?  

YES / NO

- without giving a reason for withdrawing?  

YES / NO

Who explained the details of this study to you? 

The practice agrees to take part in this study.  

YES / NO

Name of practice representative: 

Designation of practice representative: 

Signed:  

Date:  

Name of researcher:  

Signed:  

Date:  

The PINCER Trial: A cluster randomised trial to determine the effectiveness, costs/benefits and acceptability of a pharmacist-led, IT-based intervention compared with simple feedback in reducing rates of clinically important instances of potentially hazardous prescribing and medicines management in general practice
Appendix 1.4: Patient invitation letter

GP Practice Headed Paper

Dear (name of patient)

Our surgery is taking part in a research project organised by the Universities of Nottingham, Manchester and Edinburgh and we are writing to you to see if you would be willing to let a researcher look at your medical records.

We have enclosed an information sheet with this letter to tell you what the study is about and what will happen should you choose to take part. If you want to ask any questions about the study before deciding whether or not to take part, then please ring Dr Sarah Rodgers at the University of Nottingham on 0115 8466937, who will be pleased to help you.

Please take time to read the leaflet and discuss the study with other people if you wish. Once you have decided whether or not to take part, please complete the enclosed consent form and return it in the postage paid envelope provided.

Please remember that it is completely up to you whether or not you take part. If you decide you do not want to take part, this will not affect the care you receive from the practice.

Yours sincerely

Dr (name) and partners
Helping your GP to review your medicines

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this information sheet.

What is the purpose of the study?
Your GP surgery is using a computer programme to help find patients who may need their medicines reviewing. The aim of the study is to find out whether the information from the computer helps GPs to review patients’ medicines, or whether it is better when a pharmacist helps out.

To do this we are going to look at two groups of general practices. In “Group One”, a pharmacist will work with the GP to help review patients’ medicines. In “Group Two” the GP will be provided with the information from the computer, but will have no pharmacist to help them. Your GP surgery is in “Group One”.

Why have I been chosen?
The computer programme that is being used by your GP surgery suggests that you may need your medicines reviewing. Your GP will decide whether any action needs to be taken. The research team would like to find out whether any changes are made to your medicines, or whether any blood tests are done, as a result of your practice being involved in this study. We would also like to know whether it makes any difference to the way you use the health service.

In order to find out more about this a pharmacist will look at your medical records and possibly contact you to discuss your medicines, if your GP thinks this is a good idea.

The pharmacist will have spoken with your GP about whether any changes are needed to your medicines or whether you need any blood tests. In some cases it will be possible to speak with you on the telephone about these changes; in other cases the pharmacist will invite you to the GP surgery, or arrange a visit if you are unable to get to the surgery.

Any changes made to your medicines will be agreed with your doctor before they take place.

If at any time you would prefer to speak directly with your doctor or a nurse at your GP surgery, the pharmacist will arrange this for you.
What will happen to me if I take part?
If you choose to take part in this study a researcher from the University of Nottingham will look at your medical records at your GP surgery in around 15 month’s time. The researcher will have been trained to deal with your records confidentially. This means that:

- they will not talk to anyone about you
- they will not write your name down on any form that they use for collecting information
- they will not take any information out of the practice that would allow anyone to know that you have been involved in the study

Information will be collected from your medical records about the medicines that you have used, any tests that you have had done and how many times you have visited the doctor, nurse or any other person dealing with your health care. Information will be recorded from around one year ago (this is one year before the study started in your general practice) until the time that the researcher visits the practice to look at your records.

Do I have to take part?
It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time, and without giving a reason. If you decide not to take part, or to withdraw from the study at a future date, this will not affect the standard of care you receive.

What are the possible disadvantages of taking part?
There are no disadvantages to taking part in this study.

What are the possible benefits of taking part?
Allowing a researcher to look at your medical records will help the research team to find out whether the information from the computer helps GPs to review patients’ medicines, or whether it is better when a pharmacist helps out.

Involving the pharmacist may help to make sure that if any changes are needed to your medicines, these will happen.

Even if you choose not to take part in this study, your GP may decide to suggest changes to your medicines, or a blood test, and this may be of benefit to you.

Will information in my medical records remain confidential?
All information which is collected about you during the course of the research will remain confidential.

What do I have to do?
Complete and return the enclosed consent form, in the postage paid envelope provided, indicating whether you wish to take part in this study or not.
What will happen to the results of the research study?
The results of the study will be published in medical journals and will be presented at conferences. There is no possibility that any individual person or doctor’s surgery could be identified in any report or article that is published.

Who is organising and funding the research?
The research is organised by the Division of Primary Care, University of Nottingham in collaboration with the School of Pharmacy and Pharmaceutical Sciences, University of Manchester and Division of Community Health Sciences, University of Edinburgh. The research is funded by the Department of Health. The official name for the study is the “PINCER trial”.

Your doctor is not being paid for including you in this study.

Who has reviewed the study?
This study has been reviewed by the ethics committee for your local area and by the Nottingham research ethics committee which governs research studies taking place in a number of different areas. It has also been approved by your local Primary Care Trust.

Contact for Further Information
If you wish to ask any questions about this study before deciding to take part, please contact one of the following people, who would be pleased to help you:

PINCER Trial Co-ordinator: Dr Sarah Rodgers, Division of Primary Care, 13th Floor, Tower Building, University Park, Nottingham, NG7 2RD.
Tel 0115 8466937; Fax 0115 8466904
email: sarah.rogers@nottingham.ac.uk

or

Chief Investigator: Professor Tony Avery, Head of Division of Primary Care, School of Community Health Sciences, University of Nottingham Medical School, Nottingham, NG7 2UH.
Tel 0115 8230209; Fax: 0115 8230528
email: tony.avery@nottingham.ac.uk

Thank you once again for taking the time to read through this information and considering taking part in this study.
Appendix 1.6: Patient information sheet simple feedback arm

University letterhead

Helping your GP to review your medicines

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this information sheet.

What is the purpose of the study?
Your GP surgery is using a computer programme to help find patients who may need their medicines reviewing. The aim of the study is to find out whether the information from the computer helps GPs to review patients’ medicines, or whether it is better when a pharmacist helps out.

To do this we are going to look at two groups of general practices. In “Group One”, a pharmacist will work with the GP to help review patients’ medicines. In “Group Two” the GP will be provided with the information from the computer, but will have no pharmacist to help them. Your GP surgery is in “Group Two”.

Why have I been chosen?
The computer programme that is being used by your GP surgery suggests that you may need your medicines reviewing. Your GP will decide whether any action needs to be taken. The research team would like to find out whether any changes are made to your medicines, or whether any blood tests are done, as a result of your practice being involved in this study. We would also like to know whether it makes any difference to the way you use the health service.

In order to find out more about this we are asking if you would allow a member of the research team to look at your medical records.

Do I have to take part?
It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time, and without giving a reason. If you decide not to take part, or to withdraw from the study at a future date, this will not affect the standard of care you receive.

What will happen to me if I take part?
If you choose to take part in this study a researcher from the University of Nottingham will look at your medical records at your GP surgery in around 15 month’s time. The researcher will have been trained to deal with your records confidentially. This means that:
they will not talk to anyone about you
they will not write your name down on any form that they use for collecting information
they will not take any information out of the practice that would allow anyone to know that you have been involved in the study

Information will be collected from your medical records about the medicines that you have used, any tests that you have had done and how many times you have visited the doctor, nurse or any other person dealing with your health care. Information will be recorded from around one year ago (this is one year before the study started in your general practice) until the time that the researcher visits the practice to look at your records.

What are the possible disadvantages of taking part?
There are no disadvantages to taking part in this study.

What are the possible benefits of taking part?
Allowing a researcher to look at your medical records will help the research team to find out whether the information from the computer helps GPs to check patients’ medicines, or whether it is better when a pharmacist helps out.

Even if you choose not to take part in this study, your GP may decide to suggest changes to your medicines, or a blood test, and this may be of benefit to you.

Will information in my medical records remain confidential?
All information which is collected about you during the course of the research will remain confidential.

What do I have to do?
Complete and return the enclosed consent form, in the postage paid envelope provided, indicating whether you wish to take part in this study or not.

What will happen to the results of the research study?
The results of the study will be published in medical journals and will be presented at conferences. There is no possibility that any individual person or doctor’s surgery could be identified in any report or article that is published.

Who is organising and funding the research?
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The research is funded by the Department of Health. The official name for the study is the “PINCER trial”.

Your doctor is not being paid for including you in this study.
Who has reviewed the study?
This study has been reviewed by the ethics committee for your local area and by the Nottingham research ethics committee which governs research studies taking place in a number of different areas. It has also been approved by your local Primary Care Trust.

Contact for Further Information

If you wish to ask any questions about this study before deciding to take part, please contact one of the following people, who would be pleased to help you:

PINCER Trial Co-ordinator: Dr Sarah Rodgers, Division of Primary Care, 13th Floor, Tower Building, University Park, Nottingham, NG7 2RD.
Tel 0115 8466937; Fax 0115 8466904
email: sarah.rodgers@nottingham.ac.uk

or

Chief Investigator: Professor Tony Avery, Head of Division of Primary Care, School of Community Health Sciences, University of Nottingham Medical School, Nottingham, NG7 2UH.
Tel 0115 8230209; Fax: 0115 8230528
email: tony.avery@nottingham.ac.uk

Thank you once again for taking the time to read through this information and considering taking part in this study.
Appendix 1.7: Patient consent form pharmacist intervention arm

University letterhead

Helping your GP to review your medicines

Principal Investigator: Professor A J Avery

Please complete the following: Please put a circle round your answers

Have you read and understood the information sheet? YES / NO

Have you had an opportunity to ask questions and discuss this study? (if you have any questions you wish to ask, please contact one of the people listed on your information sheet) YES / NO

Have you received satisfactory answers to all your questions? YES / NO

Have you received enough information about the study? YES / NO

Do you understand that you are free to withdraw from the study: YES / NO
  at any time?
  without giving a reason for withdrawing?
  and without affecting your future medical care?

I agree to allow a responsible employee from the University of Nottingham to view my medical notes as part of the above study YES / NO

Name (please print)…………………………………………………………………………………………………………………………………………

Signed……………………………………………………………………………………………………………………………………………..Date…………..

Please return in the enclosed postage paid envelope to: Dr Sarah Rodgers, PINCER Trial Co-ordinator, FREEPOST MID 17779, Division of Primary Care, 13th Floor, Tower Building, University Park, Nottingham NG7 2RD.
Appendix 1.8: Patient consent form simple feedback arm

University of Nottingham letterhead

Helping your GP to review your medicines

Principal Investigator: Professor A J Avery

Please complete the following:

Have you read and understood the information sheet? YES / NO

Have you had an opportunity to ask questions and discuss this study? (if you have any questions you wish to ask, please contact one of the people listed on your information sheet) YES / NO

Have you received satisfactory answers to all your questions? YES / NO

Have you received enough information about the study? YES / NO

Do you understand that you are free to withdraw from the study:
  at any time? YES / NO
  without giving a reason for withdrawing? YES / NO
  and without affecting your future medical care? YES / NO

I agree to allow a responsible employee from the University of Nottingham to view my medical notes as part of the above study YES / NO

Name (please print)…………………………………………………………………….

Signed……………………………………………………………..Date…………..

Please return in the enclosed postage paid envelope to: Dr Sarah Rodgers, PINCER Trial Co-ordinator, FREEPOST MID 17779, Division of Primary Care, 13th Floor, Tower Building, University Park, Nottingham NG7 2RD.
Appendix 2: Written educational materials
Appendix 2.1: NSAIDs and gastrointestinal bleeding

What are the risks of gastrointestinal injuries with NSAIDS?
NSAIDs are responsible for 3,500 hospital admissions and 400 deaths from ulcer bleeding each year in the UK.1,2 Symptomatic ulceration is thought to occur in between 1% and 4% of patients treated with NSAIDs.3 A number of factors increase the risk of gastrointestinal bleeds including age and previous history of peptic ulcer. The latter has been shown to increase the risks of further ulceration and/or gastrointestinal bleeds between three- and thirteen-fold in patients prescribed non-selective NSAIDs.3,4

What are the relative gastrointestinal risks of non-selective NSAIDs
The Committee on Safety of Medicines (CSM) advice in the British National Formulary lists the relative safety of seven non-selective NSAIDs in relation to upper GI side-effects (see table 1).5 The CSM advises that the NSAIDs associated with low risk are generally preferred. The lowest recommended dose should be initiated and not more than one oral NSAID should be used at a time.

Table 1. Relative gastrointestinal safety of non-selective NSAIDs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Risk of serious upper gastrointestinal side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Intermediate Risk</td>
</tr>
<tr>
<td>Indometacin</td>
<td>Intermediate Risk</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Intermediate Risk</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Intermediate Risk</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>Intermediate/Higher Risk</td>
</tr>
<tr>
<td>Azapropazone</td>
<td>High Risk</td>
</tr>
</tbody>
</table>

What advice is available regarding the prescribing of NSAIDs in patients with a history of a peptic ulcer?
All NSAIDs (including selective inhibitors of COX-2) are contra-indicated in patients with active peptic ulceration and non-selective NSAIDs in patients with a history of peptic ulcers.5 Patients with a history of gastrointestinal ulceration or bleeding have between a 3 and 13-fold increase in their risk of bleeding on an NSAID.3,4 In addition, the combination of NSAIDs and low-dose aspirin may increase the risk of gastrointestinal side-effects and this combination should only be used if absolutely necessary.4

How can the risk of gastrointestinal bleeding with NSAIDs be reduced?
Reviews of randomised controlled trials have found that misoprostol, proton pump inhibitors (PPIs) and double dose H2 receptor antagonists are effective at preventing chronic NSAID related endoscopic gastric and duodenal ulcers.6,7 Only misoprostol 800 micrograms per day has been directly shown to reduce the risk of ulcer complications such as perforation haemorrhage, but its usefulness is limited by diarrhoea. Lower doses of misoprostol are less effective and are still associated with diarrhoea. A review by Jacobsen and Phillips stated that in patients with a history of
ulcer complications associated with NSAID therapy, neither cox-2 selective inhibitors nor PPIs may be effective in the secondary prophylaxis of ulcer complications. The safest approach in these high-risk patients may be to avoid NSAID therapy altogether.7

What place do COX-2 selective inhibitors have?
COX-2 selective inhibitors have been shown to have a reduced risk of gastrointestinal events compared to non-selective NSAIDs.4,5,6 However, rofecoxib and valdecoxib have recently been withdrawn from the market following concerns about their cardiovascular safety profile. This is likely to be a class effect, and hence COX-2 selective inhibitors are now contraindicated in patients with established ischaemic heart disease, cerebrovascular disease, and moderate or severe heart failure. The balance of gastrointestinal and cardiovascular risk should be considered for all patients, especially those with risk factors for cardiovascular disease and those taking low dose aspirin.5 However, COX-2 selective inhibitors still have a role to play in patients at high risk of gastrointestinal ulceration, who do not have cardiovascular disease, or risk factors for it. These patients should be prescribed the lowest effective dose of COX-2 selective inhibitor for the shortest necessary time period.

References
Appendix 2.2: Betablockers in asthma

Betablockers should be avoided in asthmatics (or those with a past history of asthma) unless there is no alternative.

Traditionally, \( \beta \)-blockers have not been used in asthmatic patients because of the risk of bronchoconstriction. However, \( \beta \)-blockers are becoming increasingly useful in patients with cardiovascular disease, and the pressure to use them in asthmatics is increasing. Following case reports of bronchoconstriction in asthmatics caused by \( \beta \)-blockers, some resulting in death, the Committee on Safety of Medicines issued the following advice:

“...\( \beta \)-blockers, even those with apparent cardioselectivity, should not be used in patients with asthma or a history of obstructive airways disease, unless no alternative treatment is available. In such cases the risk of inducing bronchospasm should be appreciated and appropriate precautions taken.”

\( \beta \)-blockers vary in their affinity for \( \beta_1 \)- and \( \beta_2 \)-adrenoceptors, and are divided into two groups, cardioselective, and non-cardioselective (table 1). The majority show little selectivity for one receptor over the other, except for bisoprolol (14-fold greater affinity for \( \beta_1 \)-adrenoceptors) and timolol, sotalol and propranolol (26-fold, 12-fold, and 8-fold greater affinity for \( \beta_2 \)-adrenoceptors, respectively).

Table 1. Cardioselective and non-cardioselective betablockers

<table>
<thead>
<tr>
<th>Cardioselective beta-blockers(^1) (relative selectivity for ( \beta_1 )-adrenoceptors)(^3)</th>
<th>Non Cardioselective beta-blockers(^4) (relative selectivity for ( \beta_2 )-adrenoceptors)(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol (2.4)</td>
<td>Labetalol (2.5)</td>
</tr>
<tr>
<td>Atenolol (4.7)</td>
<td>Pindolol</td>
</tr>
<tr>
<td>Bisoprolol (13.5)</td>
<td>Propranolol (8.3)</td>
</tr>
<tr>
<td>Celiprolol</td>
<td>Sotalol (12.0)</td>
</tr>
<tr>
<td>Metoprolol (2.3)</td>
<td>Timolol (25.7)</td>
</tr>
</tbody>
</table>

Do beta-blockers cause bronchoconstriction in asthmatics?

Small-scale safety studies, detailed in table 1, confirm that non-cardioselective beta-blockers do cause bronchoconstriction, which can be severe in some asthmatics. A Cochrane review of short-term cardioselective beta-blocker use in reversible airways disease found a statistically significant 7.5% reduction in FEV\(_1\), with single-doses of beta-blockers, which was responsive to \( \beta_2 \)-agonist therapy (4.63% increase in FEV\(_1\)). However, they did not find a statistically significant increase in respiratory symptoms, compared to placebo.\(^1\) There are also a small number of case reports of \( \beta \)-blockers causing bronchoconstriction in patients with a past-history of asthma.\(^2\)

Do beta-blocker eye drops cause bronchoconstriction in asthmatics?

A number of studies, detailed in table 2, have shown that topical timolol eye drops cause bronchoconstriction, and reduce the efficacy of bronchodilator therapy. Betaxolol eye drops do not appear to have this effect. As there are safe alternatives available, the use of timolol eye drops should be avoided in asthmatics.
Should beta-blockers be used in patients with asthma?
The use of non-cardioselective β-blockers should be avoided in asthmatics and probably those with a past history of asthma, due to the high risk of bronchoconstriction. However, short-term use of cardioselective β-blockers may be safe in patients with mild to moderate asthma. In patients with cardiovascular disease and mild to moderate asthma, it may be reasonable to start therapy with a low dose of cardioselective β-blocker, and titrate up according to response. These patients should be monitored frequently for signs of exacerbation, as there is limited evidence for long-term treatment with β-blockers in this patient group. Also, there is insufficient data to confirm the safety of cardioselective β-blockers in patients with severe asthma, and hence their use should be avoided.

Table 1. Summary of studies of the effects of non-cardioselective beta-blockers on airway function in asthmatics.

<table>
<thead>
<tr>
<th>Beta-blocker</th>
<th>Effect on airways</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carvedilol⁵</td>
<td>6/12 patients with asthma withdrew from therapy secondary to wheezing.</td>
<td>Open-label study of carvedilol in patients with CHF and COPD or asthma.</td>
</tr>
<tr>
<td>Oxprenolol⁶</td>
<td>Worsening of airways obstruction in 6/11 patients without airways disease, and 7/12 patients with bronchitic asthma.</td>
<td>Double-blind controlled trial in COAD and non-COAD patients</td>
</tr>
<tr>
<td>Pindolol⁷</td>
<td>Pindolol caused a significant total decrease in FEV₁ compared to placebo in &gt; 50% of patients.</td>
<td>Placebo controlled study in asthmatics.</td>
</tr>
<tr>
<td>Pindolol⁸</td>
<td>No significant reduction in pulmonary function at rest or on exercise with Pindolol. However, a trend towards a reduction in airway function was observed.</td>
<td>Safety trial in mild to moderate, controlled asthmatics.</td>
</tr>
<tr>
<td>Propranolol⁹</td>
<td>Worsening of pulmonary function following propranolol 40mg, lasting for over four hours compared to placebo (p&lt;0.01)</td>
<td>Randomised, double blind crossover, placebo controlled trial</td>
</tr>
<tr>
<td>Sotalol¹⁰</td>
<td>Sotalol induced a significant reduction in FEV₁.</td>
<td>Placebo controlled, double blind, single-dose, crossover study in asthmatics.</td>
</tr>
<tr>
<td>Timolol¹¹</td>
<td>Asthmatic patients suffered bronchoconstriction following topical timolol eye drops, accompanied by a 32% reduction in FEV₁. No change was seen in non-asthmatics.</td>
<td>Double blind, randomised, cross over trial in mild asthmatics and non-asthmatics.</td>
</tr>
<tr>
<td>Timolol &amp; Betaxolol¹²</td>
<td>Significant reduction in FEV₁ seen with timolol eye drops, but no change seen with betaxolol eye drops</td>
<td>Double blind, randomised, cross over trial in patients with reactive airway disease</td>
</tr>
<tr>
<td>Timolol &amp; Betaxolol¹³</td>
<td>Significant reduction in FEV₁ seen with timolol, and reduction in response to bronchodilator. No change seen with betaxolol.</td>
<td>Double blind cross over study in asthmatics</td>
</tr>
</tbody>
</table>

References
Appendix 2.3: Monitoring Angiotensin Converting Enzyme Inhibitors

Why monitor urea and electrolytes during ACE Inhibitor therapy?
ACE Inhibitors are known to cause renal dysfunction and hyperkalaemia, to varying degrees.\(^1,2\) However, they are also known to improve outcomes in a variety of cardiovascular conditions such as congestive cardiac failure, post-myocardial infarction and renal failure etc. Therefore, the benefits of treatment with ACE Inhibitors outweigh the risks in most cases. However, monitoring urea and electrolytes may reduce the risk of severe morbidity or mortality due to renal dysfunction and hyperkalaemia with ACE inhibitors.

How many patients will develop renal dysfunction or hyperkalaemia?
The proportion of patients who have suffered from renal dysfunction or hyperkalaemia during trials with ACE-Inhibitors is shown in table 1. In the first month of treatment, around 1% of patients experienced renal dysfunction or hyperkalaemia.\(^3\) This proportion increased with the duration of treatment, with over 8% of patients experiencing renal dysfunction after four years of treatment. Hence, there is an ongoing risk of developing renal dysfunction with continuing treatment, and renal function should be monitored at intervals (see below).

Do all patients experiencing renal dysfunction or hyperkalaemia need to stop treatment with ACE Inhibitors?
Table 1 shows that not all patients who experienced renal dysfunction or hyperkalaemia required cessation of their ACE inhibitor. Some patients were controlled by dose reduction, or changes in other medication (e.g. cessation of drugs which can exacerbate renal dysfunction or hyperkalaemia). The NICE guideline for the treatment of congestive heart failure advises that:\(^6\)
- An increase in creatinine to 50% above baseline (or 200µmol/L) and a rise in potassium to ≤ 5.9mmol/L is acceptable.
- If serum potassium rises to ≥ 6.0mmol/L or creatinine to >100% above baseline (or >350µmol/L) then the ACE inhibitor should be stopped, and specialist advice sought.

How often should patients taking ACE Inhibitors have their urea and electrolytes monitored?
The NICE guidelines for CCF\(^6\) state that stable patients with proven heart failure should be monitored every 6 months. In addition, urea and electrolytes should be checked prior to initiation of ACE-inhibitors, and following each significant dose increase.\(^7\) Other guidelines recommend that urea and electrolytes are checked annually, once a stable dose of ACE Inhibitor has been achieved.\(^8\)

Patients aged 75 years and older taking ACE Inhibitors should have their urea and electrolytes monitored at least every 15 months
Table 1. Proportion of patients suffering from renal dysfunction and/or hyperkalaemia in studies of ACE-inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trial, Duration of study</th>
<th>Renal dysfunction and hyperkalaemia</th>
<th>Hyperkalaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ACEI</td>
<td>Placebo</td>
</tr>
<tr>
<td>Captopril</td>
<td>ELITE, 48 weeks.(^4)</td>
<td>0.8(^\text{dis})</td>
<td>1.6(^\text{dis})</td>
</tr>
<tr>
<td>Enalapril</td>
<td>SOLVD, 40 months.(^5)</td>
<td>1.2(^\text{ob}) (0.7(^\text{dis}))</td>
<td>0.4(^\text{ob}) (0.1(^\text{dis}))</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>ATLAS, 4 weeks.(^3)</td>
<td>1.4(^\text{dis})</td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>ATLAS, 4 years.(^3)</td>
<td>7.9(^\text{ob}) (2.3(^\text{dis}))</td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>ATLAS, 4 years.(^3)</td>
<td>8.4(^\text{ob}) (2.4(^\text{dis}))</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>Systematic review, average 35 months.(^1)</td>
<td>5.2(^\text{ob})</td>
<td>3.6(^\text{ob})</td>
</tr>
<tr>
<td>Mixed</td>
<td>Systematic review, average 30 days.(^2)</td>
<td>1.3(^\text{ob})</td>
<td>0.6(^\text{ob})</td>
</tr>
</tbody>
</table>

\(^*\) p<0.05 and/or significant difference between ACE inhibitor and placebo.
\(^\text{dis}\) Treatment discontinued as a result of renal dysfunction and/or hyperkalaemia
\(^\text{ob}\) Observed cases of renal dysfunction and/or hyperkalaemia

References

Appendix 2.4: Monitoring Diuretics

Why monitor urea & electrolytes with loop and thiazide diuretics?
Loop and thiazide diuretics are known to cause a dose-related reduction in sodium and potassium, as well as causing renal dysfunction through dehydration. Traditionally, thiazide diuretics have been associated with a higher risk of causing electrolyte disturbances. However, thiazide diuretics are now used in lower doses (i.e. bendroflumethiazide 2.5mg daily) for hypertension, and the risk of electrolyte disturbance is much lower than previously. Patients taking a combination of a loop and thiazide diuretics are the most likely to suffer a clinically important electrolyte disturbance.

How frequently do diuretics cause electrolyte disturbances?
Studies show varying frequencies of electrolyte disturbance, depending on the diuretic used, other medication taken by the patient, and the patient group studied. Table 1 shows frequencies up to 9.1% with serum sodium levels <130mmol/L and ranging from 2% to 5.6% with serum potassium levels ≤ 3.0mmol/L. In a large community-based cohort study, diuretics were the second most important group of drugs associated with preventable adverse drug events. Despite the wide range of frequencies of electrolyte disturbance shown, table 1 confirms that this is an important problem, where up to 9% of patients are at risk of morbidity as a result of electrolyte disturbance.

How frequently do diuretics cause renal dysfunction?
There is very little data on the frequency of renal dysfunction in patients taking diuretics. This is because patients are often taking other medication which will increase the risk of renal dysfunction (e.g. ACE Inhibitors or NSAIDs).

Which patients have the highest risk of electrolyte disturbance?
Elderly female patients, patients with liver cirrhosis and those with severe cardiac failure complicated by secondary hyperaldosteronism are at the highest risk of electrolyte disturbance. Patients taking digoxin or QT interval prolonging drugs, and those with serious organic heart disease are the most likely to experience arrhythmias as a result of hypokalaemia.

How often should urea and electrolytes be monitored?
There are no strict guidelines for monitoring electrolytes with diuretics. However, the NICE guidelines for Congestive Heart Failure recommend that patients should have urea and electrolytes taken 6 monthly at minimum. In addition, urea and electrolytes should be checked following dose changes and when patients are unstable (patients may require daily monitoring of urea and electrolytes when they are unstable). Patients being treated for CHF appear to be at the highest risk of electrolyte disturbance as they are often elderly, have poor renal function, and are taking higher doses of diuretics.

Patients being treated for hypertension are usually prescribed low doses of thiazide diuretics, and are at a lower risk of electrolyte disturbance. However, patients still require their urea and electrolytes to be checked following initiation of treatment, dose changes and at regular intervals to ensure there has not been a progressive change in urea and electrolytes. There are no strict guidelines as to when this regular check should be done, but an annual check is often suggested.
## Table 1. Frequency of electrolyte disturbance in patients taking diuretics

<table>
<thead>
<tr>
<th>Drugs studied</th>
<th>Frequency of hyponatraemia</th>
<th>Frequency of hypokalaemia</th>
<th>Summary of study participants</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop or Thiazide diuretics, with or without potassium sparing diuretics or potassium supplements¹</td>
<td>11.2% &lt;135mmol/L 0% &lt;125mmol/L</td>
<td>13.7% &lt;3.5mmol/L 5.6% ≤3.0mmol/L</td>
<td>Retrospective review of 161 nursing-home residents taking diuretics</td>
<td>No significant difference in prevalence of hypokalaemia seen between those taking or not taking potassium sparing diuretics or potassium supplements</td>
</tr>
<tr>
<td>Loop or Thiazide diuretics, with or without potassium sparing diuretics or potassium supplements²</td>
<td>29.2% &lt;135mmol/L 9.1% &lt;130mmol/L</td>
<td>20.1% &lt;3.5mmol/L 4.0% &lt;3.0mmol/L</td>
<td>353 patients taking diuretics out 929 patients consecutively admitted to a geriatric hospital</td>
<td>Of those not taking diuretics: 22.5% had serum sodium &lt;135mmol/L and 20.1% had serum potassium &lt;3.5mmol/L</td>
</tr>
<tr>
<td>Hydrochlorothiazide 50mg daily⁴</td>
<td>56% 3.0 – 3.5mmol/L 2.3% &lt;3.0mmol/L</td>
<td>447 hypertensive patients</td>
<td>Data from literature review – original paper not seen.</td>
<td></td>
</tr>
<tr>
<td>Loop or Thiazide diuretics ⁴</td>
<td>24.9% &lt;3.5mmol/L</td>
<td>870 patients taking loop or Thiazide diuretics in Sweden</td>
<td>Data from literature review – original paper not seen.</td>
<td></td>
</tr>
<tr>
<td>Loop diuretics⁵</td>
<td>4% &lt;3.5mmol/L 2% &lt;3.0mmol/L</td>
<td>1110 patients with normokalaemia on hospital admission, started on loop diuretics, not taking potassium supplements, potassium sparing diuretics or ACEI’s, with hypokalaemia on discharge.</td>
<td>Patients aged 75 years and over had a mean drop of 0.11mmol/L in potassium levels, compared to a drop of 0.01mmol/L in patients aged &lt;75 years.</td>
<td></td>
</tr>
</tbody>
</table>

## References


**PINCER trial evidence base for monitoring diuretics**

Updated on 21st September 2005  Version 4
Appendix 2.5: Combined Oral Contraceptives and Thrombosis

Combined oral contraceptives are contraindicated in patients with a past history of venous or arterial thrombo-embolism

Combined oral contraceptives (COCs) are associated with an increased risk of thrombosis. Women with risk factors for thrombosis (see overleaf) are at an increased risk of thrombosis whilst taking a COC. The greatest risk factor for thrombosis is a previous history of thrombosis, and this represents an absolute contraindication to the use of COCs. If a woman is receiving warfarin, then the use of a COC can be considered, but when warfarin therapy ceases, the COC should stop also.1

What is the risk of venous thromboembolism with COC use?
Venous thromboembolism (VTE) is thought to occur in 5 per 100,000 healthy non-pregnant women each year. The risk of VTE in pregnancy is much greater at 60 cases per 100,000 pregnancies per year. The risk with COCs lies between these figures, with levonorgestrel and norethisterone containing COCs associated with 15 cases per 100,000 women per year and desogestrel and gestodene containing COCs possibly having a higher risk at 25 cases per 100,000 women per year.2,3 This represents a three to five fold increase in VTE risk with COC use which becomes apparent within four months of starting and returns to that of non users within three months of discontinuation.3 Although there is an increased risk of VTE with COC use, it is still less than the risk of VTE in pregnancy. The magnitude of risk with topical contraceptives is not known.

What is the risk of myocardial infarction or stroke (arterial thrombosis) with COC use?
The risk of myocardial infarction in young, healthy, non-smoking women taking COCs containing between 20mcg and 35mcg oestrogen is not raised.4 However, there appears to be a 2 to 3-fold increase in risk of ischaemic stroke for women who are smokers, and a 10-fold in crease in risk of MI.1, 5 There is a 1.5 fold increase in risk of ischaemic stroke in young, healthy women taking COCs, however, the baseline risk in this population is so low, the increase is not clinically significant. Women with risk factors such as increasing age, hypertension, migraine and/or smoking have at least an additional 3-fold increase in risk of haemorrhagic and ischaemic stroke with COCs, which is clinically significant.1, 4

What effect does oestrogen and progestogen content have on the thrombotic potential of COCs?
The increased risk in thrombosis results from the oestrogenic effects of the COCs. Hence, high doses of oestrogen (>35 micrograms/day) are associated with a higher risk. To confuse matters further, progestogens can effect the oestrogenic activity. Levonorgestrel and norethisterone (second generation progestogens) have an antioestrogenic effect, whilst desogestrel and gestodene (third generation progestogens) do not. This is thought to be why the risk of VTE is slightly higher with third generation COCs, than second generation COCs.
When should combined oral contraceptives be avoided?
Women with a past history of, or two or more risk factors for, venous thromboembolism or arterial thrombosis, should not be prescribed COCs.²

Risk factors for venous thromboembolism include:
- **Past history of venous thromboembolism**
- **Family history** of venous thromboembolism in first degree relative aged under 45 years (avoid contraceptives containing desogestrel or gestodene) or if known prothrombotic coagulation abnormality e.g. factor V Leiden or antiphospholipid antibodies (including lupus anticoagulation)
- **Obesity**: body mass index above 30kg/m² (avoid if body mass index above 39kg/m²)
- **Long-term immobilisation** e.g. in a wheelchair (avoid if confined to bed or leg in a plaster cast)
- **Varicose veins** (avoid during sclerosing treatment or where definite history of thrombosis)

Risk factors for arterial thrombosis include:
- **Past history of arterial thrombosis**
- **Family history** of arterial disease in first degree relative aged under 45 years (avoid if atherogenic lipid profile)
- **Diabetes mellitus** (avoid if diabetes complications present)
- **Hypertension**: blood pressure above systolic 140 mmHg and diastolic 90 mmHg (avoid if blood pressure above systolic 160 mmHg and diastolic 100 mmHg)
- **Smoking** (avoid if smoking 40 or more cigarettes daily)
- **Age** over 35 years (avoid if over 50 years)
- **Obesity** (avoid if body mass index above 39 kg/m²)
- **Migraine**: contra-indicated in migraine with typical focal aura; severe migraine regularly lasting over 72 hours despite treatment; migraine treated with ergot derivatives; use with caution in migraine without focal aura; migraine controlled with 5HT1 agonist

Providing that women are informed of, and accept the relative risks of venous and arterial thrombosis, a joint decision on which kind of oral contraceptive to use should be made between the prescriber and the woman. The decision should be based on an individual’s medical history and any contra-indications.

References
What are the risks associated with methotrexate?
Methotrexate has a range of potentially serious, dose related side effects, including:

- Significant elevations in liver enzymes which can progress to atrophy, necrosis and cirrhosis
- Haematological toxicities e.g. leucopenia, thrombocytopenia and anaemia
- Gastrointestinal toxicities e.g. nausea, vomiting and diarrhoea

In addition, methotrexate can also cause a pneumonitis (not thought to be dose-related).

Why should methotrexate be prescribed weekly not daily?
Early trials with methotrexate showed that longterm toxicity of the liver was less common with weekly dosing than with daily dosing (e.g. 17.5mg weekly vs 2.5mg daily). Acute toxicity is less common at low doses of methotrexate (≤ 15mg per week). Of 25 deaths and 26 episodes of serious morbidity identified by the NPSA in England over a ten-year period, methotrexate prescribed daily rather than weekly was the most common error. Great care needs to be taken to avoid this very preventable prescribing error, which can result in severe toxicity or death. This issue is of such significance that the NPSA have released a patient safety alert about prescribing of methotrexate (see www.npsa.nhs.uk).

Why should methotrexate be closely monitored?
The severity of adverse effects such as liver and haematological toxicity can be minimised if they are caught early. A review of 673 patients taking methotrexate at a Staffordshire clinic between 1986 and 1999 found that 244 (36%) stopped taking methotrexate following adverse effects (including 36 (5.3%) gastrointestinal symptoms; 37 (5.5%) abnormal LFTs; 25 (3.7%) low white cell counts), 117 (48%) patients restarted treatment. 102 (15.2%) had potentially serious and 12 (1.8%) had life threatening side effects. Only one patient died as a direct result of methotrexate therapy. Patients were closely monitored by the clinic, and the potential severity of many side effects was reduced by early identification.

When should methotrexate be monitored?
The CSM advises that patients being treated with low dose, weekly, methotrexate, have full blood count, renal and liver function tests checked before starting treatment and repeated weekly until therapy is stabilised, thereafter patients should be monitored every 2–3 months.

The British Society for Rheumatology recommends more frequent monitoring. Once therapy is stabilised full blood count and liver function tests should be undertaken fortnightly until six weeks after the last increase in dose, and providing they are stable, monthly thereafter.
References
Appendix 2.7: Monitoring the INR of patients taking warfarin

**Patients treated with warfarin should have their INR monitored at least every 12 weeks**

What proportion of patients suffer bleeding complications during oral anticoagulant therapy?
The proportion of patients suffering any bleeding complication whilst on oral anticoagulants varies between studies, ranging from 4%\(^1\) to 18%\(^2\). Major bleeding complications range from 2%\(^3\) to 11%\(^4\), depending on the study. Randomised controlled trials (RCTs) show a lower rate of bleeding than observational studies, this may be a reflection of tighter INR control in RCTs, and the inclusion of patients with a lower baseline risk of bleeding.

What proportion of time are patients’ INRs within the recommended therapeutic range?
The proportion of time when patients’ INRs are within the recommended therapeutic range ranges from 32%\(^5\) to 68%\(^4\) of patient years, depending on the study. Patients newly started on warfarin spend less time in the recommended therapeutic range than patients that have been taking warfarin for at least 3 months.\(^1\) More frequent INR monitoring results in more time spent within the therapeutic range.\(^4\)

What are the risk factors for bleeding in patients taking oral anticoagulation?
Numerous risk factors for bleeding have been identified in patients receiving oral anticoagulation. These include:
- Alcohol abuse\(^2\)
- Concomitant disease: Chronic renal insufficiency\(^2,6\), Serious heart disease\(^6\), Cerebrovascular disease\(^6\)
- Previous gastrointestinal bleeding\(^2\)
- INR raised on last test\(^7\) or INR >3.5\(^8\)
- Patients in their first year of oral anticoagulation\(^1\)
- Indication for anticoagulation\(^6\)
- Concomitant medications\(^9\)
- Aged >85 years\(^8\)
- Infrequent monitoring

This list is not exhaustive, and other risk factors do exist. For instance, the prescription of drugs which have the potential to increase the efficacy of warfarin, will increase the risk of a raised INR, and therefore the risk of bleeding.

How can the risk of bleeding in patients taking oral anticoagulation be reduced?
Studies have shown that the risk of bleeding is associated with an INR outside the therapeutic range, and the higher the INR\(^7,8,10\), the greater the risk of bleeding. In addition, specific indications for anticoagulation and concomitant diseases will increase the risk of bleeding in individual patients. Although these conditions are not contraindications to anticoagulation, they should be treated as reasons for caution with anticoagulation. Less frequent testing of the INR is associated with less time spent in the therapeutic range.\(^4\) This means that patients are more likely to have a raised INR, and an increased risk of bleeding complications. By increasing the frequency of INR monitoring in high risk patients e.g. newly started on oral anticoagulation, INR raised on last test, introduction of interacting drugs etc. the risk of major bleeding should be reduced.
How frequently should patients taking warfarin have their INR monitored?
Specific guidance is available for the frequency of INR monitoring. The BNF states that it is essential for the INR to be determined daily or on alternate days in early days of treatment, then at longer intervals (depending on the response) then up to every 12 weeks. The British Society of Haematology concur in their guidelines that once stabilised the frequency of monitoring can be extended up to an interval of 12 weeks. However, The Scottish Intercollegiate Network’s guidelines for antithrombotic therapy are more cautious, suggesting that a well stabilised patient may only need an INR check every four to eight weeks.

References
Appendix 2.8: Lithium monitoring

During lithium therapy, levels should be checked every three months

What are the risks associated with lithium therapy?
Lithium therapy has a narrow therapeutic range (0.4 to 1.0mmol/L 12 hours post dose)\(^1\) and is associated with potentially serious, dose-dependent, side effects including: cardiac arrhythmias; ataxia; seizures; thyroid dysfunction; nausea, vomiting and diarrhoea; nephrogenic diabetes insipidus and renal impairment.\(^2\) Chronic toxicity increases the risk of severe neurotoxicity.\(^3\)

A survey of 10,615 patients aged over 65 years taking lithium found that 413 (3.9%) were admitted to hospital at least once with lithium toxicity between 1992 and 2001. Of these hospitalisations, 5.4% were attributed to the recent introduction of a loop diuretic or angiotensin converting enzyme inhibitor.\(^4\) A number of drugs can interfere with the renal excretion of lithium, and careful monitoring is necessary.

How frequently should lithium levels be monitored?
Guidance on the frequency of monitoring lithium levels varies. The BNF states that serum lithium concentration should be measured every three months in patients on stabilised regimes.\(^5\) The SPCs for Priadel\(^6\) (lithium citrate) and tablets\(^6\) (lithium carbonate) and Li-Liquid\(^7\) (lithium citrate) state that after stabilisation monitoring should not normally exceed three months. The SPC for Liskonum\(^8\) (lithium carbonate) advises that levels are checked a minimum of once every two months after stabilisation, whilst that for Camcolit\(^9\) (lithium carbonate) specifies monthly monitoring.

Guidelines from Southdowns NHS Trust also recommend monitoring lithium levels in stable patients every three months\(^10\) whilst a review in the drugs and therapeutics bulletin recommends monitoring every three to six-months once therapy is stable (but more frequently in elderly patients).\(^1\)

References
Appendix 2.9: Monitoring Thyroid Function with Amiodarone

Thyroid function should be checked before starting amiodarone, and every six-months during treatment

How common are hypo- and hyperthyroidism with amiodarone?
Studies show that thyroid dysfunction is relatively common with amiodarone, occurring in up to one-third of patients. The proportion of patients suffering from hypothyroidism with amiodarone ranges from 1 to 32% in the reported studies, but is usually around 3% in randomised controlled trials.¹⁻⁴ There is a similarly wide range for the proportion of patients suffering from hyperthyroidism with amiodarone (1% to 23%), but again, in randomised controlled trials, usually around 1% of patients are affected.¹⁻⁴ More detail of these studies is shown in Table1.

What are the risk factors for the development of thyroid dysfunction?
The incidence of hypo- and hyperthyroidism is dependent on the dietary intake of iodine. In areas with low iodine intake, hyperthyroidism is more prevalent. However, in countries with a high iodine intake e.g. UK, hypothyroidism is more prevalent.⁵,⁶ Other risk factors for thyroid dysfunction are thought to be:
- Dose of amiodarone – the lower the dose, the lower the risk.⁵ However, not all studies support dose as a risk factor.²,⁷
- Pre-existing thyroid disease as a risk factor for hypothyroidism.⁶
- Female sex as a risk factor for hypothyroidism.⁵,⁷

When should thyroid function be monitored?
Since pre-existing thyroid dysfunction is a risk factor for hypothyroidism with amiodarone, it is advisable to test thyroid function before initiating treatment. Thyroid function tests should be repeated after 3 months, and if symptoms suggestive of thyroid disease occur. Thyroid dysfunction can occur at any time during treatment with amiodarone and it is advisable to continue monitoring thyroid function at intervals throughout therapy. The summary of product characteristics for amiodarone (Cordarone X) and the BNF advise 6 monthly monitoring.⁸,⁹

Thyroid dysfunction has been reported to occur within 2 months of starting amiodarone therapy, and as long as 2 months after amiodarone has stopped.⁶,⁷ It is thought that thyroid dysfunction continues to be a risk for months after amiodarone has been stopped.¹⁰

References


Table 1. Proportion of patients suffering hyper- or hypothyroidism with amiodarone.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients:</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Taking amiodarone</td>
<td>Suffering hypothyroidism</td>
</tr>
<tr>
<td>Tavackoli et al (1997)</td>
<td>2461</td>
<td>7% (9% subclinical)</td>
</tr>
<tr>
<td>Thorne et al (1999)</td>
<td>92</td>
<td>15%</td>
</tr>
<tr>
<td>Harjai et al (1997)</td>
<td>NA</td>
<td>1% to 32%</td>
</tr>
<tr>
<td>Vorperian et al</td>
<td>738 (amiodarone) 27 (placebo)</td>
<td>27 (3.7%) amiodarone 3 (0.4%) placebo</td>
</tr>
<tr>
<td>Cairns et al (1997)</td>
<td>606 (amiodarone) 596 (placebo)</td>
<td>20 (3.3%) amiodarone 1 (0.2%) placebo 4 (0.6%) amiodarone 4 (0.7%) placebo</td>
</tr>
<tr>
<td>Julian et al (1997)</td>
<td>743 (amiodarone) 743 (placebo)</td>
<td>11 (1.5%) amiodarone 0 placebo 12 (1.6%) amiodarone 4 (0.5%) placebo</td>
</tr>
</tbody>
</table>
Appendix 2.10: Amiodarone dosing

The lowest possible dose of amiodarone should be used to avoid unnecessary toxicity

Dose Related Side Effects of Amiodarone
Amiodarone has a broad range of toxicities, many of which are related to the daily dose, or cumulative dose administered. These include pulmonary fibrosis, gastrointestinal effects, neuropathies, and thyroid and hepatic dysfunction (Table 1).  

Table 1. Dose related toxicities of amiodarone

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Toxicity</th>
<th>Relation to dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Pulmonary fibrosis</td>
<td>Related to daily dose</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, anorexia, constipation</td>
<td>Related to daily dose</td>
</tr>
<tr>
<td></td>
<td>Hepatic dysfunction</td>
<td></td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>Ataxia, paraesthesias, peripheral polyneuropathy, sleep disturbance, impaired memory</td>
<td>Related to daily dose</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Hyperthyroidism or hypothyroidism</td>
<td>Related to cumulative dose</td>
</tr>
<tr>
<td>Skin</td>
<td>Blue discolouration</td>
<td>Related to cumulative dose</td>
</tr>
</tbody>
</table>

Mechanisms of Thyroid Toxicity
Amiodarone has a high iodine content (two atoms per molecule) and is structurally related to thyroid hormones. The type of thyroid toxicity caused by amiodarone largely depends on two factors:
- Dietary intake of iodine (high in developed countries, low in developing countries)
- Underlying thyroid disease

In patients with a high iodine intake, the high iodine content of amiodarone inhibits the production of triiodothyronine, causing a drop in levels of 20-25%. If a patient has a predisposition to hypothyroidism or hyperthyroidism (e.g. subclinical disease), then the amiodarone will likely cause progression to either hyper- or hypothyroidism. In patients with a low dietary iodine intake, the increased iodine consumption can stimulate production of triiodothyronine, resulting in hyperthyroidism. Hypothyroidism caused by amiodarone can be safely treated with thyroxine, and pre-existing hypothyroidism does not represent a contraindication to starting amiodarone. However, hyperthyroidism will often necessitate withdrawal of amiodarone and treatment of the hyperthyroidism; Amiodarone is contraindicated in pre-existing hyperthyroidism.
Loading Doses
Amiodarone has a long half-life and its onset of action can be delayed when used orally. Hence, a loading dose is used.\(^1\) There are two commonly used regimens:

- 200mg three times daily for seven days, 200mg twice daily for seven days, then 200mg once daily as maintenance.\(^1\)
- 400mg three times daily for seven days, then 200mg daily as maintenance.

Because amiodarone should be started in hospital, knowledge of these loading regimens may be limited in primary care, and patients may be inadvertently continued on inappropriately high doses once they are discharged to home. Continuing higher doses increases the risk of serious toxicity.\(^8\)

Maintenance Doses
The maintenance dose of amiodarone for the majority of patients is 200mg daily. However, it is good practice to use the minimum dose which controls the arrhythmia, which can be as little as 50mg daily.\(^1,9,10\) In contrast, some patients will need up to 400mg daily to control their arrhythmia, however this is rare, and the need for the increased dose should be regularly reviewed.

References
Appendix 3: Protocol for dealing with serious adverse events in the pincer trial
### Background
Below is a list of serious adverse events that might occur in study practices in patients identified by the PINCER Trial outcome measures.

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Potential adverse event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serious GI bleed in a patient with a history of peptic ulcer receiving a non-selective NSAID without PPI cover</td>
</tr>
<tr>
<td>2</td>
<td>Serious asthma attack in a patient with a history of asthma who has been prescribed a beta-blocker</td>
</tr>
<tr>
<td>3</td>
<td>Admission to hospital with a serious electrolyte disturbance or dehydration in a patient aged 75 years and older who has been prescribed an angiotensin converting enzyme inhibitor (ACEI) or a loop diuretic long-term who has not had a recorded check of their renal function and electrolytes in the previous 15 months</td>
</tr>
<tr>
<td>4</td>
<td>Venous or arterial thrombosis in a woman with a past medical history of venous or arterial thrombosis who has been prescribed a combined hormonal contraceptive (CHC)</td>
</tr>
<tr>
<td>5</td>
<td>Serious haematological or liver problem in a patient receiving methotrexate for at least three months who has not had a recorded full blood count and/or liver function test within the previous three months</td>
</tr>
<tr>
<td>6</td>
<td>Serious bleed associated with high INR, or thromboembolic event associated with low INR, in a patient receiving warfarin for at least three months who has not had a recorded check of their international normalised ratio (INR) within the previous 12 weeks</td>
</tr>
<tr>
<td>7</td>
<td>Lithium toxicity in a patient receiving lithium for at least 3 months who has not had a recorded check of their lithium levels within the previous 3 months</td>
</tr>
<tr>
<td>8</td>
<td>Thyrotoxicosis in a patient receiving amiodarone for at least 6 months who has not had a thyroid function test within the previous 6 months</td>
</tr>
<tr>
<td>9</td>
<td>Toxic effects from methotrexate overdose in a patient receiving prescriptions of methotrexate without instructions that the drug should be taken weekly</td>
</tr>
<tr>
<td>10</td>
<td>Toxic effects from amiodarone overdose in a patient receiving prescriptions of amiodarone for at least one month without instructions to take a dose of 200mg or less per day</td>
</tr>
</tbody>
</table>

Given that the outcome measures are based on identifying patients at risk from a serious adverse event, rather than adverse events themselves, the study team will not automatically be made aware of all patients suffering such events.

In some cases we will learn of adverse events, if they occur. For example, we intend to collect information on adverse events for the health economic analysis, but this will take place only for those patients giving prior consent (currently 30-40% of patients are giving consent to be involved in this part of the study). Also, for these patients, data collection will take place at least one year after the intervention has been completed in a particular practice. In general practices receiving pharmacist intervention, it is possible that the pharmacists will come across patients who have suffered a serious adverse event.

Overall, it is clear that we do not have a reliable way of identifying all serious adverse events involving patients identified by the PINCER Trial outcome measures. The main reason for this (as outlined above) is that the trial was designed to investigate changes in proportions of patients at risk rather than adverse events themselves.
Also, we decided to use anonymised data in order to increase the generalisability of the results and not to adversely affect the relationship between general practices and their patients.

Assuming that it would not be appropriate to alter the study protocol to include obtaining information on individual patients without their consent, we suggest that the protocol for dealing with serious adverse events should relate only to those adverse events that the study team is made aware (e.g. through the study pharmacists or the health economic analysis).

Protocol

It is the responsibility of general practices to deal appropriately with serious adverse events involving their patients. This includes:

- Prompt action to deal with the adverse event, which might include referral to hospital
- An explanation to the patient of what has gone wrong and why, including admission of fault if an error has occurred

For serious adverse events that come to the attention of study pharmacists, or the study team (through viewing patients’ records as part of the health economic analysis), we will ensure that information about these events is fed back to the practices with a request that they deal with the information through their usual mechanisms of handling significant events (e.g. discussion at a significant events audit meeting).

If study pharmacists, or member of the study team, have very serious concerns about the performance of a practice in relation to an adverse event, they will discuss this with the Chief Investigator to agree on the most appropriate course of action, which may include a formal report to PCT Clinical Governance Lead. Any such actions will be recorded in project files and the DMEC (Data Monitoring and Ethics Committee for the trial) will be provided with an anonymised report.

Professor Tony Avery
February 2007
Appendix 4: Mortality data letter
Dear Practice Manager

Re: The PINCER Trial

I am writing to thank your practice for taking part in the PINCER Trial and to ask for your help in reporting our findings.

Would you be able to check the list of names from our initial audit dated Baseline date to see if any of your patients deceased or left the practice on or before date 12-months post end of intervention, please?

The names will be inside the PINCER practice file on a sheet headed ‘Exceptions’. We only need to know how many PINCER patients died or left during that 15 month period – we do not need to know any of their personal details (e.g. names, identification numbers, etc.).

We would be very grateful if you could complete the enclosed ‘PINCER patient numbers’ sheet and return it in the pre-paid addressed envelope.

If you need any help locating the original audit contact Martin Eden on 0161 275 8356 or martin.eden@manchester.ac.uk.

Thanks again for all your help over the past couple of years.

Yours sincerely

Martin Eden
PINCER Trial Researcher
Martin.eden@manchester.ac.uk
0161 275 8356

Professor Tony Avery
PINCER Trial Chief Investigator

Practice Code

The PINCER Trial: A cluster randomised trial to determine the effectiveness, costs/benefits and acceptability of a pharmacist-led, IT-based intervention compared with simple feedback in reducing rates of clinically important instances of potentially hazardous prescribing and medicines management in general practice
PINCER Patient Numbers

Please enter the relevant number of patients in each of the yellow boxes below. Use ‘Not applicable’ if none of your patients died or left your practice.

| Number of patients identified on Baseline date at your practice | 99 |
| Number of those identified patients who left your practice between Baseline date and date 12-months post end of intervention | |
| Number of those identified patients who died between Baseline date and date 12-months post end of intervention | |

Please complete and return this sheet using the pre-paid addressed envelope provided to:

Martin Eden  
School of Pharmacy and Pharmaceutical Sciences  
1st Floor, Stopford Building  
University of Manchester  
Oxford Road  
Manchester  
M13 9PL
Appendix 5: Analyses adjusted only for stratum and for stratum and baseline medication-related problems and sub-group analyses
Appendix 5.1: Prevalence of prescribing and monitoring problems at 6 months follow-up by treatment arm (with subgroup analyses and interactions shown)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Simple feedback arm (%)</th>
<th>Pharmacist intervention arm (%)</th>
<th>Odds ratio (95% CI)*</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome measures</strong></td>
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<tr>
<td>History of peptic ulcer with NSAID and without PPI prescription/History of PU without PPI prescription</td>
<td>86/2014 (4.3)</td>
<td>51/1852 (2.8)</td>
<td>0.64 (0.43, 0.93) p=0.02 n=3866 (S)</td>
<td>0.017</td>
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<tr>
<td></td>
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<td></td>
<td>0.63 (0.42, 0.95) p=0.03 n=3434 (S,B)</td>
<td>1.02x10^{-6}</td>
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<td></td>
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<td>0.58 (0.38, 0.89) p=0.01 n=3434 (S,B,D,T)</td>
<td>4.68x10^{-7}</td>
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<td></td>
<td><strong>Interaction with list size (S) p=0.91</strong></td>
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<td><strong>Interaction with list size (S,B) p=1.00</strong></td>
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<td><strong>Interaction with deprivation (S) p=0.59</strong></td>
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<td><strong>Interaction with deprivation (S,B) p=0.38</strong></td>
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<td>Asthmatics prescribed a beta-blocker/Asthmatics</td>
<td>658/22224 (3.0)</td>
<td>499/20312 (2.5)</td>
<td>0.83 (0.71, 0.98) p=0.03 n=42536 (S)</td>
<td>0.014</td>
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<td></td>
<td>0.76 (0.62, 0.94) p=0.01 n=39235 (S,B)</td>
<td>2.39x10^{-7}</td>
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<td></td>
<td>0.73 (0.58, 0.91) p=0.006 n=39235 (S,B,D,T)</td>
<td>3.50x10^{-7}</td>
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<td><strong>Interaction with list size (S) p=0.82</strong></td>
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<td><strong>Interaction with list size (S,B) p=0.41</strong></td>
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<td><strong>Interaction with deprivation (S) p=0.29</strong></td>
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<td><strong>Interaction with deprivation (S,B) p=0.54</strong></td>
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<td>Aged ≥ 75 on long term ACEI or diuretics without U&amp;E in last 15 months/-aged ≥ 75 on long term ACEI or diuretics</td>
<td>436/5329 (8.2)</td>
<td>255/4851 (5.3)</td>
<td>0.69 (0.45, 1.06) p=0.099 n=10180 (S)</td>
<td>0.16</td>
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<td>0.54 (0.35, 0.82) p=0.006 n=8185 (S,B)</td>
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<td>0.51 (0.34, 0.78) p=0.003 n=8185 (S,B,D,T)</td>
<td>0.14</td>
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<td><strong>Interaction with list size (S) p=0.56</strong></td>
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<td><strong>Interaction with list size (S,B) p=0.90</strong></td>
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<td><strong>Interaction with deprivation (S) p=0.48</strong></td>
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<td><strong>Interaction with deprivation (S,B) p=0.43</strong></td>
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<tr>
<td>Outcome</td>
<td>Simple feedback arm (%)</td>
<td>Pharmacist intervention arm (%)</td>
<td>Odds ratio (95% CI)*</td>
<td>ICC</td>
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<td>-------------------------------------------------------------------------</td>
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<td><strong>Secondary outcome measures</strong></td>
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<tr>
<td>Asthmatics without a CHD code prescribed a beta-blocker/ Asthmatics</td>
<td>387/21048 (1.8)</td>
<td>299/19286 (1.6)</td>
<td>0.83 (0.69, 1.01), p=0.07, n=40334 (S)</td>
<td>0.01</td>
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<tr>
<td>without a CHD code (excludes those without a CHD code at 6 months)</td>
<td></td>
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<td>0.84 (0.66, 1.06), p=0.14, n=37159 (S,B)</td>
<td>1.02x10^{-6}</td>
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<td></td>
<td>0.81 (0.63, 1.04), p=0.10, n=37159 (S,B,D,T)</td>
<td>4.94x10^{-6}</td>
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<tr>
<td><strong>Women with a past history of venous or arterial thrombosis who have</strong></td>
<td>8/2783 (0.3)</td>
<td>3/2490 (0.1)</td>
<td>0.42 (0.08, 2.32), p=0.31, n=5273 (S)</td>
<td>0.35</td>
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<td>been prescribed the combined oral contraceptive pill/ Women with a past</td>
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<td>0.36 (0.07, 1.92), p=0.21, n=4835 (S,B)</td>
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<tr>
<td>history of venous or arterial thrombosis</td>
<td></td>
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<td>0.39 (0.07, 2.15), p=0.26, n=4835 (S,B,D,T)</td>
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<tr>
<td><strong>Patients receiving methotrexate for at least 3 months who have not</strong></td>
<td>162/518 (31.3)</td>
<td>122/494 (24.7)</td>
<td>0.75 (0.42, 1.34), p=0.33, n=1012 (S)</td>
<td>0.22</td>
</tr>
<tr>
<td>had FBC in the previous 3 months</td>
<td></td>
<td></td>
<td>0.87 (0.48, 1.59), p=0.66, n=817 (S,B)</td>
<td>0.17</td>
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<td>0.80 (0.45, 1.43), p=0.45, n=817 (S,B,D,T)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Patients receiving methotrexate for at least 3 months who have not</strong></td>
<td>154/518 (29.7)</td>
<td>121/494 (24.5)</td>
<td>0.78 (0.44, 1.40), p=0.41, n=1012 (S)</td>
<td>0.22</td>
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<tr>
<td>had LFT in the previous 3 months</td>
<td></td>
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<td>0.87 (0.47, 1.59), p=0.65, n=817 (S,B)</td>
<td>0.19</td>
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<td></td>
<td>0.79 (0.43, 1.45), p=0.44, n=817 (S,B,D,T)</td>
<td>0.17</td>
</tr>
<tr>
<td><strong>Patients receiving warfarin for at least 3 months who have not</strong></td>
<td>78/1618 (4.8)</td>
<td>52/1720 (3.0)</td>
<td>0.63 (0.36, 1.09), p=0.10, n=3338 (S)</td>
<td>0.14</td>
</tr>
<tr>
<td>had INR in the last 3 months/patients prescribed warfarin for at least</td>
<td></td>
<td></td>
<td>0.57 (0.32, 1.01), p=0.05, n=2519 (S,B)</td>
<td>7.86x10^{-7}</td>
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<td>3 months</td>
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<td>0.53 (0.29, 0.95), p=0.03, n=2519 (S,B,D,T)</td>
<td>1.11x10^{-6}</td>
</tr>
<tr>
<td>Outcome</td>
<td>Simple feedback arm (%)</td>
<td>Pharmacist intervention arm (%)</td>
<td>Odds ratio (95% CI)*</td>
<td>ICC</td>
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<td>Patients prescribed lithium for at least 3 months who have not had lithium level in the last 3 months/patients prescribed lithium for at least 3 months</td>
<td>84/211 (39.8)</td>
<td>67/190 (35.3)</td>
<td>0.80 (0.38, 1.68), p=0.56, n=401 (S)</td>
<td>0.25</td>
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<td>0.55 (0.25, 1.21), p=0.14, n=350 (S,B)</td>
<td>0.24</td>
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<td>0.53 (0.24, 1.19), p=0.12, n=350 (S,B,D,T)</td>
<td>0.24</td>
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<tr>
<td>Patients prescribed amiodarone for at least 6 months who have not had TFT in the last 6 months/patients prescribed amiodarone for at least 6 months</td>
<td>106/235 (45.1)</td>
<td>81/242 (33.5)</td>
<td>0.56 (0.35, 0.90), p=0.02, n=477 (S)</td>
<td>0.06</td>
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<td>0.66 (0.43, 1.00), p=0.05, n=404 (S,B)</td>
<td>9.75x10^-6</td>
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<td></td>
<td>0.57 (0.36, 0.92), p=0.02, n=404 (S,B,D,T)</td>
<td>4.86x10^-7</td>
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<tr>
<td>Patients prescribed methotrexate without instructions that the drug should be taken weekly/patients prescribed methotrexate</td>
<td>16/310 (5.2)</td>
<td>2/268 (0.8)</td>
<td>0.08 (0.005, 1.20), p=0.04, n=578 (S)</td>
<td>0.68</td>
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<td>0.60 (0.05, 6.66), p=0.67, n=482 (S,B)</td>
<td>5.56x10^-7</td>
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<td></td>
<td>0.72 (0.06, 9.25), p=0.80, n=482 (S,B,D,T)</td>
<td>5.20x10^-7</td>
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<tr>
<td>Patients prescribed amiodarone for at least 1 month who are prescribed a dose of more than 200mg daily/patients prescribed amiodarone for at least 1 month</td>
<td>1/228 (0.4)</td>
<td>1/228 (0.4)</td>
<td>0.96 (0.06, 15.55), p=0.97, n=456 (S)</td>
<td>2.1x10^-5</td>
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<td>Not calculable (S,B)</td>
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<td>Not calculable (S,B,D,T)</td>
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<tr>
<td>Patients with at least one prescribing problem/patients at risk of at least one prescribing problem</td>
<td>752/26329 (2.9)</td>
<td>553/24073 (2.3)</td>
<td>0.80 (0.69, 0.93), p=0.006, n=50402 (S)</td>
<td>0.01</td>
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<td>0.75 (0.63, 0.89), p=0.001, n=46378 (S,B)</td>
<td>3.44x10^-7</td>
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<td>0.71 (0.59, 0.86), p=0.0003, n=46378 (S,B,D,T)</td>
<td>9.16x10^-7</td>
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<tr>
<td>Patients with at least one monitoring problem/patients at risk of at least one monitoring problem</td>
<td>868/7409 (11.7)</td>
<td>584/6963 (8.4)</td>
<td>0.71 (0.55, 0.91), p=0.01, n=14372 (S)</td>
<td>0.07</td>
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<td>0.58 (0.46, 0.74), p&lt;0.001, n=11584 (S,B)</td>
<td>0.04</td>
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<td>0.56 (0.44, 0.70), p&lt;0.001, n=11584 (S,B,D,T)</td>
<td>0.04</td>
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</tbody>
</table>

* adjusted for randomisation stratum (S), baseline prevalence of errors (B), deprivation (D), training status (T)
** includes interaction between treatment arm and continuous covariate
### Appendix 5.2: Prevalence of prescribing and monitoring problems at 12-months follow-up by treatment arm (with subgroup analyses and interactions shown)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Simple feedback arm (%)</th>
<th>Pharmacist intervention arm (%)</th>
<th>Adjusted odds ratio* (95% CI)</th>
<th>ICC</th>
</tr>
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<tr>
<td>History of peptic ulcer with NSAID and without PPI prescription/History of PU without PPI prescription</td>
<td>78/2035 (3.8)</td>
<td>61/1852 (3.3)</td>
<td>0.87 (0.62, 1.23) p=0.43, n=3887 (S)</td>
<td>7.94x10^-7</td>
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<tr>
<td></td>
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<td></td>
<td>0.93 (0.62, 1.41) p=0.75, n=3331 (S,B)</td>
<td>6.75x10^-7</td>
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<td></td>
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<td></td>
<td>0.91 (0.59, 1.39) p=0.65, n=3331 (S,B,D,T)</td>
<td>6.54x10^-7</td>
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<td><strong>Interaction with list size (S) p=0.76</strong></td>
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<td><strong>Interaction with list size (S,B) p=0.61</strong></td>
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<td><strong>Interaction with deprivation (S) p=0.52</strong></td>
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<td></td>
<td><strong>Interaction with deprivation (S,B) p=0.36</strong></td>
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<tr>
<td>Asthmatics prescribed a beta-blocker/Asthmatics</td>
<td>692/23520 (2.9)</td>
<td>545/21359 (2.6)</td>
<td>0.87 (0.73, 1.03) p=0.11, n=44879 (S)</td>
<td>0.02</td>
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<td>0.77 (0.63, 0.95) p=0.02, n=39221 (S,B)</td>
<td>0.009</td>
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<td></td>
<td>0.78 (0.63, 0.97) p=0.02 n=39221 (S,B,D,T)</td>
<td>0.008</td>
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<td><strong>Interaction with list size (S) p=0.77</strong></td>
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<td><strong>Interaction with list size (S,B) p=0.85</strong></td>
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<td><strong>Interaction with deprivation (S) p=0.21</strong></td>
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<td><strong>Interaction with deprivation (S,B) p=0.19</strong></td>
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</tr>
<tr>
<td>Aged ≥ 75 on long term ACEI or diuretics without U&amp;E in last 15 months/Aged ≥ 75 on long term ACEI or diuretics</td>
<td>452/5813 (7.8)</td>
<td>306/5242 (5.8)</td>
<td>0.72 (0.49, 1.06) p=0.10, n=11055 (S)</td>
<td>0.13</td>
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<td>0.60 (0.39, 0.90) p=0.02, n=7848 (S,B)</td>
<td>0.14</td>
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<td></td>
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<td></td>
<td>0.63 (0.41, 0.95) p=0.03, n=7848 (S,B,D,T)</td>
<td>0.13</td>
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<td><strong>Interaction with list size (S) p=0.50</strong></td>
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<td><strong>Interaction with list size (S,B) p=0.37</strong></td>
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<td>†Interaction with deprivation (S) p=0.78</td>
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<td>†Interaction with deprivation (S,B) p=0.88</td>
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<tr>
<td>Outcome</td>
<td>Simple feedback arm (%)</td>
<td>Pharmacist intervention arm (%)</td>
<td>Adjusted odds ratio* (95% CI)</td>
<td>ICC</td>
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<td>------------------------------------------------------------------------</td>
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<tr>
<td><strong>Secondary outcome measures</strong></td>
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</tr>
<tr>
<td>Asthmatics without a CHD code prescribed a beta-blocker/ Asthmatics without a CHD code</td>
<td>414/22294 (1.9)</td>
<td>326/20283 (1.6)</td>
<td>0.84 (0.68, 1.04), p=0.11, n=42577 (S)</td>
<td>0.03</td>
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<td></td>
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<td></td>
<td>0.76 (0.60, 0.97), p=0.03, n=37108 (S,B)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.79 (0.62, 1.02), p=0.06, n=37108 (S,B,D,T)</td>
<td>0.009</td>
</tr>
<tr>
<td>Women with a past history of venous or arterial thrombosis who have been prescribed the combined oral contraceptive pill/ Women with a past history of venous or arterial thrombosis</td>
<td>15/2987 (0.5)</td>
<td>4/2640 (0.2)</td>
<td>0.53 (0.09, 3.04), p=0.48, n=5627 (S)</td>
<td>0.46</td>
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<td>0.53 (0.05, 5.40), p=0.59, n=4840 (S,B)</td>
<td>0.30</td>
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<tr>
<td></td>
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<td></td>
<td>0.57 (0.05, 6.17), p=0.64, n=4840 (S,B,D,T)</td>
<td>0.24</td>
</tr>
<tr>
<td>Patients receiving methotrexate for at least 3 months who have not had FBC in the previous 3 months</td>
<td>194/552 (35.1)</td>
<td>130/531 (24.5)</td>
<td>0.54 (0.28, 1.07), p=0.08, n=1083 (S)</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>0.49 (0.26, 0.93), p=0.03, n=787 (S,B)</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.51 (0.27, 0.99), p=0.05, n=787 (S,B,D,T)</td>
<td>0.22</td>
</tr>
<tr>
<td>Patients receiving methotrexate for at least 3 months who have not had LFT in the previous 3 months</td>
<td>186/552 (33.7)</td>
<td>134/531 (25.2)</td>
<td>0.62 (0.34, 1.13), p=0.12, n=1083 (S)</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.48 (0.27, 0.87), p=0.01, n=787 (S,B)</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.50 (0.28, 0.91), p=0.02, n=787 (S,B,D,T)</td>
<td>0.16</td>
</tr>
<tr>
<td>Patients receiving warfarin for at least 3 months who have not had INR in the last 3 months/patients prescribed warfarin for at least 3 months</td>
<td>69/1752 (3.9)</td>
<td>76/1877 (4.1)</td>
<td>1.09 (0.72, 1.67), p=0.68, n=3629 (S)</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.90 (0.47, 1.71), p=0.75, n=2487 (S,B)</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.98 (0.52, 1.85), p=0.94, n=2487 (S,B,D,T)</td>
<td>0.10</td>
</tr>
<tr>
<td>Outcome</td>
<td>Simple feedback arm (%)</td>
<td>Pharmacist intervention arm (%)</td>
<td>Adjusted odds ratio* (95% CI)</td>
<td>ICC</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>--------------------------------</td>
<td>-------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Patients prescribed lithium for at least 3 months who have not had lithium level in the last 3 months/patients prescribed lithium for at least 3 months</td>
<td>88/213 (41.3)</td>
<td>56/176 (31.8)</td>
<td>0.63 (0.36, 1.09), p=0.10, n=389 (S)</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.52 (0.30, 0.91), p=0.02, n=329 (S,B)</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.50 (0.29, 0.85), p=0.01, n=329 (S,B,D,T)</td>
<td>0.02</td>
</tr>
<tr>
<td>Patients prescribed amiodarone for at least 6 months who have not had TFT in the last 6 months/patients prescribed amiodarone for at least 6 months</td>
<td>92/247 (37.3)</td>
<td>80/233 (34.3)</td>
<td>0.81 (0.43, 1.51), p=0.50, n=480 (S)</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.82 (0.46, 1.47), p=0.50, n=376 (S,B)</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.77 (0.41, 1.43), p=0.41, n=376 (S,B,D,T)</td>
<td>0.11</td>
</tr>
<tr>
<td>Patients prescribed methotrexate without instructions that the drug should be taken weekly/patients prescribed methotrexate</td>
<td>13/309 (4.2)</td>
<td>0/271 (0.0)</td>
<td>Not calculable (S)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not calculable (S,B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not calculable (S,B,D,T)</td>
<td></td>
</tr>
<tr>
<td>Patients prescribed amiodarone for at least 1 month who are prescribed a dose of more than 200mg daily/patients prescribed amiodarone for at least 1 month</td>
<td>1/231 (0.4)</td>
<td>1/232 (0.4)</td>
<td>0.95 (0.06, 15.45), p=0.97, n=463 (S)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not calculable (S,B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Not calculable (S,B,D,T)</td>
<td></td>
</tr>
<tr>
<td>Patients with at least one prescribing problem/patients at risk of at least one prescribing problem</td>
<td>785/27808 (2.8)</td>
<td>610/25246 (2.4)</td>
<td>0.85 (0.72, 1.01), p=0.07, n=53054 (S)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.78 (0.64, 0.95), p=0.01, n=46287 (S,B)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.78 (0.64, 0.94), p=0.01, n=46287 (S,B,D,T)</td>
<td>0.01</td>
</tr>
<tr>
<td>Patients with at least one monitoring problem/patients at risk of at least one monitoring problem</td>
<td>901/8011 (11.3)</td>
<td>652/7449 (8.8)</td>
<td>0.76 (0.59, 0.98), p=0.04, n=15460 (S)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.64 (0.50, 0.81), p=0.0005, n=11193 (S,B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.64 (0.51, 0.82), p=0.0006, n=11193 (S,B,D,T)</td>
<td></td>
</tr>
</tbody>
</table>

* adjusted for randomisation stratum (S), baseline prevalence of errors (B), deprivation (D), training status (T)
** includes interaction between treatment arm and continuous covariate
† includes interaction between treatment arm and covariate dichotomis
Appendix 6: Pharmacist record forms
Pharmacist Record Forms

Name of Pharmacist:

Practice:

Code number:
Outcome Measures

Primary Outcome Measures

1. Patients aged 16 and over with a history of peptic ulcer who have been prescribed a non-selective NSAID
   • More specifically, those with a computer-coded diagnosis of peptic ulcer disease, at least six-months prior to data collection, who have a computer record for one or more prescriptions for a non-selective NSAID in the six-months prior to data collection who have NOT also had a prescription for a PPI within that six-month period

2. Patients aged 16 and over with asthma who have been prescribed a beta-blocker:
   • More specifically those with a computer-coded diagnosis of asthma, at least six-months prior to data collection, who have a computer record of one or more prescriptions for a beta-blocker (oral or eye drops) in the six-months prior to data collection

3. Patients aged 75 years and older who have been prescribed an ACE inhibitor or a loop diuretic long-term who have NOT had a computer-recorded check of their renal function and electrolytes in the previous 15 months:
   • More specifically, long-term prescribing implies a first prescription for an ACE inhibitor or a loop diuretic at least 15 months before the time of data collection and at least one prescription in the six-months beforehand

Secondary outcome measures

Contraindicated prescribing

4. Women with a past medical history of venous or arterial thrombosis who have been prescribed the combined oral contraceptive pill

Inadequate monitoring

5. Patients receiving methotrexate for at least three months who have not had a recorded full blood count and/or liver function test within the previous three months

6. Patients receiving warfarin for at least three months who have not had a recorded check of their INR (International Normalised Ratio) within the previous 12 weeks

7. Patients receiving lithium for at least 3 months who have not had a recorded check of their lithium levels

8. Patients receiving amiodarone for at least 6 months who have not had a thyroid function test within the previous 6 months

Dosing problems

9. Patients receiving prescriptions of methotrexate without instructions that the drug should be taken weekly

10. Patients receiving prescriptions of amiodarone for at least one month without instructions to take a dose of 200mg or less per day
# Pharmacist Record Form – summary sheet

<table>
<thead>
<tr>
<th>Date</th>
<th>Patient ID*</th>
<th>Age</th>
<th>Gender (M/F)</th>
<th>Initials</th>
<th>GP</th>
<th>Outcome Measure Number</th>
<th>Reason for patient being identified by Quest Browser search (please tick)</th>
<th>Action recommended by pharmacist</th>
<th>Action completed</th>
<th>Time taken (mins)</th>
<th>Pharmacist initials and date completed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Coding error</td>
<td>Info available in records but not coded</td>
<td>Patient “at risk”</td>
<td>other</td>
<td></td>
</tr>
</tbody>
</table>

*patient’s unique number within the practice

**Codes for action recommended/completed:**

1. Correct coding error
2. Add codes (e.g. blood test results)
3. Add PPI
4. Stop NSAID
5. Stop beta blocker
6. Stop combined oral contraceptive pill
7. Arrange blood tests
8. Alter dose instructions for methotrexate
9. Alter dose instructions for amiodorone
10. Other action not specified above
11. No action
Pharmacist Record Form – action plan for each patient

Practice code: ____________________________ Date: ____________

Patient ID: ____________________________ Initials pharmacist: ____________________________

Outcome measure number: ____________________________ Initials GP: ____________________________

Action recommended by pharmacist: 

please write in the box below

GP comments (optional): 

please write in the box below

Action taken (including who took action and time taken) or reason for no action: 

please write in the box below

Time taken: ____________________________
Patient Contact Form

Practice code:               Initials pharmacist:
Patient ID:                  Initials GP:
Outcome measure number:

Type of contact:  please tick  Letter  ☐  please attach anonymised copy  Date:
Telephone call  ☐  Date:
Personal contact  ☐  please indicate:  Date:
  GP  ☐
  Pharmacist  ☐
  Practice Nurse  ☐

Summary of contact:


## Pharmacist Record Form – general action plan

**Practice code:**

**Initials pharmacist:**

**Action taken:** *please write in the box below giving the date of the action, the action taken, the job title of the person who took the action and the time taken*

<table>
<thead>
<tr>
<th>Date</th>
<th>Action taken and by whom</th>
<th>Time taken</th>
</tr>
</thead>
</table>
Appendix 7: Interview schedules and focus group topic guides for qualitative study
Appendix 7.1: Interview Schedules Brief Interviews

Introduction (used for all telephone interviews):

- Thanks a lot for taking part in this part of the PINCER trial. The interview should take no longer than … minutes.
- Brief reminder of the aims
- Do you have any questions about the study or do you feel the information you received is sufficient?
- And you are still ok with the interview being audio-taped and transcribed?
- The transcripts will be anonymised, anything you say during the interview will be confidential, you can ask for the interview to be stopped at any time

Please note: Theses schedules/topic guides were used as guidance only and not in all interviews all of the topics were covered as participants were encouraged to raise issues important to them.

Pharmacists

1. In your opinion, which are the main issues in prescribing safety in general practice?
2. Is there anything that particularly appeals to you in this project? What? Why?
3. In your opinion, what are the positive and negative aspects of the PINCER trial? (Any concerns/problems? Which aspect is running particularly smoothly/effectively? Why?)
4. What do you feel about the outcome measures that have been chosen for the trial?
5. What is your experience of the training? (Did the training prepare you for the task? Is there anything that you would have done differently in the training?)
6. How do you feel the PINCER trial is working so far? (What is your experience of the PINCER trial? How was it to be introduced in the practice? How is your relationship with the practice staff? How do you feel received in the practice?)
7. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn't work, why do you think this will be? Do you think after you left things will be kept up?)
8. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)
9. What are your expectations of this project? (What do you think it will achieve/lead to?)
10. How do you see your role in bringing this about? (Do you think you can contribute to these expectations with your behaviour?)
11. If the PINCER trial was shown to be effective, what do you think will help to make it work if it is to be rolled-out on a larger scale? (Across England)
12. How do you think practices can be motivated to implement interventions like the PINCER trial?
13. If after the study has finished, you were offered a pharmacist post similar to that in the PINCER trial, would you want to do the job? Why/why not?
14. Is there anything else that you would like to say? Do you have any suggestions?
GPs – Pharmacist Intervention Arm

1. In your opinion, which are the main issues in prescribing safety in general practice?
2. What is your sense of what the PINCER trial is?
3. Is there anything that particularly appeals to you in this project? What? Why?
4. In your opinion, what are the positive and negative aspects of the PINCER trial? (Any concerns/problems? What aspect is running particularly smoothly/effectively? Why?)
5. What do you feel about the outcome measures that have been chosen for the trial?
6. What is your involvement in the PINCER trial? (Do you have regular contact with the pharmacists?)
7. How do you feel the PINCER trial is working so far? (What is your experience of working with the pharmacists? How does the PINCER trial affect your day-to-day work as a GP?) (Workload)
8. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)
9. In your opinion, does the PINCER trial affect the work-dynamics in your practice? If so, how?
10. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)
11. What are your expectations of this project? (What do you think it will achieve/lead to?)
12. How do you see your role in bringing this about? (Do you think you can contribute to these expectations with your behaviour?)
13. If the PINCER trial was shown to be effective, what do you think will help to make it work if it is to be rolled-out on a larger scale? (Across England)
14. How do you think practices can be motivated to implement interventions like the PINCER trial?
15. If after the study has finished, you were offered a pharmacist service similar to that being provided in the PINCER trial, would you or your practice want to use the service? Why/why not?
16. Is there anything else that you would like to say? Do you have any suggestions?

GPs – Simple Feedback Arm

1. In your opinion, which are the main issues in prescribing safety in general practice?
2. What is your sense of what the PINCER trial is?
3. Is there anything that particularly appeals to you in this project? What? Why?
4. In your opinion, what are the positive and negative aspects of the PINCER trial? (Any concerns/problems? What aspect is running particularly smoothly/effectively? Why?)
5. What do you feel about the outcome measures that have been chosen for the trial?
6. What is your involvement in the PINCER trial? (Have you read the educational material? Have you had a look at the potentially at-risk patients identified/reviewed their medication?)
7. How do you feel the PINCER trial is working so far? (How does the PINCER trial affect your day-to-day work as a GP?) (Workload)
8. Do you feel the PINCER trial will be effective in reducing prescribing errors in
genral practice? (If it works, why do you think this will be? If it doesn't work,
why do you think this will be?)

9. In your opinion, does the PINCER trial affect the work-dynamics in your
practice? If so, how? (Is everyone working on it together?)

10. Is there anything that you would have done differently in implementing the
PINCER trial? (Thinking about what has been happening in the practice and
your role during the intervention period)

11. What are your expectations of this project? (What do you think it will
achieve/lead to?)

12. How do you see your role in bringing this about? (Do you think you can
contribute to these expectations with your behaviour?)

13. If the PINCER trial was shown to be effective, what do you think will help to
make it work if it is to be rolled-out on a larger scale? (Across England)

14. How do you think practices can be motivated to implement interventions like
the PINCER trial?

15. If after the study has finished, you were offered a service similar to that being
provided in the PINCER trial, would you or your practice want to use it?
Why/why not?

16. Is there anything else that you would like to say? Do you have any
suggestions?

Practice Managers - Pharmacist Intervention Arm

1. In your opinion, which are the main issues in prescribing safety in general
practice?

2. What is your sense of what the PINCER trial is?

3. Is there anything that particularly appeals to you in this project? What? Why?

4. In your opinion, what are the positive and negative aspects of the PINCER
trial? (Any concerns/problems? What aspect is running particularly
smoothly/effectively? Why?)

5. What do you feel about the outcome measures that have been chosen for the
trial?

6. What is your involvement in the PINCER trial? (Do you have regular contact
with the pharmacists?)

7. How do you feel the PINCER trial is working so far? (What is your experience
of working with the pharmacists? How does the PINCER trial affect your day-
to-day work as a practice manager? How does the PINCER trial affect the
day-to-day work of others in the practice e.g. reception staff?) (Workload)

8. Do you feel the PINCER trial will be effective in reducing prescribing errors in
genral practice? (If it works, why do you think this will be? If it doesn't work,
why do you think this will be?)

9. In your opinion, does the PINCER trial affect the work-dynamics in your
practice? If so, how? (Is everyone working on it together?)

10. Is there anything that you would have done differently in implementing the
PINCER trial? (Thinking about what has been happening in the practice and
your role during the intervention period)

11. What are your expectations of this project? (What do you think it will
achieve/lead to?)

12. How do you see your role in bringing this about? (Do you think you can
contribute to these expectations with your behaviour?)

13. If the PINCER trial was shown to be effective, what do you think will help to
make it work if it is to be rolled-out on a larger scale? (Across England)

14. How do you think practices can be motivated to implement interventions like
the PINCER trial?
15. If after the study has finished, you were offered a pharmacist service similar to that being provided in the PINCER trial, would you or your practice want to use the service? Why/why not?

16. Is there anything else that you would like to say? Do you have any suggestions?

**Practice Managers – Simple Feedback Arm**

1. In your opinion, which are the main issues in prescribing safety in general practice?
2. What is your sense of what the PINCER trial is?
3. Is there anything that particularly appeals to you in this project? What? Why?
4. In your opinion, what are the positive and negative aspects of the PINCER trial? (Any concerns/problems? What aspect is running particularly smoothly/effectively? Why?)
5. What do you feel about the outcome measures that have been chosen for the trial?
6. What is your involvement in the PINCER trial? (Have you read the educational material? Have you had a look at the potentially at-risk patients identified?)
7. How do you feel the PINCER trial is working so far? (How does the PINCER trial affect your day-to-day work as a practice manager? How does the PINCER trial affect the day-to-day work of others in the practice e.g. reception staff?) (Workload)
8. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)
9. In your opinion, does the PINCER trial affect the work-dynamics in your practice? If so, how? (Is everyone working on it together?)
10. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)
11. What are your expectations of this project? (What do you think it will achieve/lead to?)
12. How do you see your role in bringing this about? (Do you think you can contribute to these expectations with your behaviour?)
13. If the PINCER trial was shown to be effective, what do you think will help to make it work if it is to be rolled-out on a larger scale? (Across England)
14. How do you think practices can be motivated to implement interventions like the PINCER trial?
15. If after the study has finished, you were offered a service similar to that being provided in the PINCER trial, would you or your practice want to use it? Why/why not?
16. Is there anything else that you would like to say? Do you have any suggestions?

**NHS Prescribing Leads (or similar)**

1. In your opinion, which are the main issues in prescribing safety in general practice?
2. How would you address prescribing safety issues in general practice?
3. Are you aware that the PINCER trial is taking place? (Are you involved in it? If yes, How?)
4. What is your sense of what the PINCER trial is?
5. Is there anything that particularly appeals to you in this project? What? Why?
6. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)
7. What do you feel about the outcome measures that have been chosen for the trial?
8. In your opinion, is there anyone or anything that could hinder the progress of the PINCER trial? (Or keep it from running smoothly?)
9. What are your expectations of this project? (What do you think it will achieve/lead to?)
10. How do you see your role in bringing this about? (Do you think you can contribute to these expectations with your behaviour?)
11. If the PINCER trial was shown to be effective, what do you think will help to make it work if it is to be rolled-out on a larger scale? (Across England)
12. How do you think practices can be motivated to implement interventions like the PINCER trial?
13. If after the study has finished, you were offered a pharmacist service similar to that being provided in the PINCER trial, would you want to use the service? Why/why not?
14. Is there anything else that you would like to say? Do you have any suggestions?

Researchers
1. How do you feel the PINCER trial is working so far? (How is it to go into practices?)
2. How do the practices appear to receive the trial? (Intervention arm differences?)
3. How is your relationship with the practice staff? (How do you feel received in the practices?)
4. Any concerns/problems? (logistical (organisational, planning), technical (computer))
5. How do problems affect the practice staff?
6. How to problems affect you/your work?
7. Are things getting better with time? How?
8. Which aspect is running particularly smoothly/effectively?
9. What are the motivations to take part for practices in your opinion?
10. Is there anything else that you would like to say? Do you have any suggestions?
Appendix 7.2: Interview Schedules In-depth Interviews

Community pharmacists

[Modify questions depending on if they know about PINCER or not, do they welcome or resent trial? How can trial be integrated into community pharmacy?]

Questions relating to the PINCER trial:
1. Were you aware that the PINCER trial is taking place? (Are you involved in it? If yes, How?)
2. Is there anything that particularly appeals to you in this project? What? Why? (Do you feel the trial adequately addresses issues surrounding prescribing safety?)
3. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)
4. How do you feel about the outcome measures of the trial? (After initial answer can focus on beta blocker and asthma in particular: risks and benefits of beta-blockers, how does that influence prescribing behaviour? Try to get specific examples)
5. In your opinion, is there anything that could hinder the progress of the PINCER trial? (Or keep it from running smoothly?) potential problems?
6. What are your expectations of this project? (In what way will outcomes of the trial (or the trial itself) affect you as a community pharmacist and/or pharmacists in general?)
7. Do you think the interventions will make a long term impact on prescribing behaviour? Why? Why not? (What will help to keep things up in practices long-term? What will hinder the long-term success of the interventions (if found to be successful)?)
8. How is the relationship between community pharmacists and PINCER trial pharmacists? (e.g. are there any territorial issues?)

Roll-out of the PINCER trial:
9. If the PINCER trial was shown to be effective, what do you think will help to roll it out in other practices? (Across England)
10. If the PINCER was to be rolled out, which other things could pharmacists do/look at in practices (beyond the outcome measures of the trial)? Do you need a pharmacist to do these things? Who else could do them?
11. If the trial was to be rolled out, do you think community pharmacists could incorporate some of the functions of the PINCER trial pharmacists in their current role? (What would have to be done to make this possible? e.g. more resources, more training)
12. If the trial was to be rolled out, who would be the employing authority for pharmacists working on the trial?

More general questions:
13. From your perspective, what influences prescribing safety in general practice? (How is the issue addressed by the PCT? How is it developing?)
14. How do you see the role of pharmacists developing within primary care? (What can help to make pharmacists a more integral part of the primary care team? Do you feel they are?)
15. How would you describe the relationship between pharmacists and GPs (both community and PCT pharmacists – is there a difference?)?
16. Is there anything else that you would like to say? Do you have any suggestions?

**GPs and Nurses – Pharmacist Intervention Arm**

Questions relating to the PINCER trial:

1. Could you tell me how your practice decided to get involved in this project? (How does the trial benefit the practice?)
2. How do you feel about the outcome measures of the trial? (after initial answer can focus on beta blocker and asthma in particular: risks and benefits of beta-blockers, how does that influence prescribing behaviour? try to get specific examples)
3. When you had a look at the patients identified – did the outcome measures of the trial still make sense to you? (Why? Why not?)
4. What is your involvement/role in the PINCER trial? (Do you have regular contact with the pharmacists? For what reasons do you tend to see the pharmacist? How is it working with a pharmacist?)
5. How do you feel the PINCER trial is working so far? (Any concerns/problems with the trial? Why? How can problems be addressed/dealt with? How does the PINCER trial affect your day-to-day work as a GP?)
6. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)
7. In your opinion, does the PINCER trial affect the work-dynamics in your practice? If so, how? (Is everyone working on it together?)
8. How important is the role of the pharmacist in the trial? (keeping in mind that there is also a simple feedback arm, do you feel your practice could have done it without the pharmacist? Do you feel that this kind of work could be done by someone else? Who? Practice nurse, GPs? How could that be made possible?)
9. Have you had a pharmacist working in your practice before? How do you think this influences the outcome of the trial?
10. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)
11. Are there things that the pharmacist is doing in your practice that are not trial related? Which are these?
12. Do you think things will be kept up after the pharmacist has left? (What will help to keep things up long-term? What will hinder the long-term success of the intervention (if found to be successful)?)
13. What are your expectations of this project? [can leave out if no time]

**Roll-out of the PINCER trial:**

14. If the PINCER trial was shown to be effective, what do you think will help to roll it out in other practices? (Across England)
15. How do you think practices can be motivated to participate in trials like the PINCER?
16. If the PINCER was to be rolled out, which other things could pharmacists do/look at in practices (beyond the outcome measures of the trial)? (How could the pharmacists’ time be used most effectively?)
17. If after the study has finished, you were offered a service similar to that being provided in the PINCER trial, would you or your practice want to use the service? Why/why not?
More general questions:

18. From your perspective, what influences prescribing safety in general practice? (How is the issue addressed by your practice? How is it developing?)

19. The literature has shown that in certain circumstances GPs can feel threatened by pharmacists’ expanding clinical role – how do you feel about this? (inter-professional boundaries) e.g. Mark A. Mesler (1991) ‘Boundary encroachment and task delegation: clinical pharmacists on the medical team.’ Sociology of Health & Illness 13 (3), 310–331

20. How do you see the role of pharmacists developing within primary care? (What can help to make pharmacists a more integral part of the primary care team? Do you feel they are?)

21. Is there anything else that you would like to say? Do you have any suggestions?

GPs and Nurses – Simple Feedback Arm

Questions relating to the PINCER trial:

1. Could you tell me how your practice decided to get involved in this project? (How does the trial benefit the practice?)

2. How do you feel about the outcome measures of the trial? (after initial answer can focus on beta blocker and asthma in particular: risks and benefits of beta-blockers, how does that influence prescribing behaviour? try to get specific examples)

3. When you had a look at the patients identified – did the outcome measures of the trial still make sense to you? (Why? Why not?)

4. What is your involvement/role in the PINCER trial? (Have you read the educational material? Have you had a look at the potentially at-risk patients identified/reviewed their medication?)

5. How do you feel the PINCER trial is working so far? (Any concerns/problems with the trial? Why? How can problems be addressed/dealt with? How does the PINCER trial affect your day-to-day work as a GP?)

6. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)

7. In your opinion, does the PINCER trial affect the work-dynamics in your practice? If so, how? (Is everyone working on it together?)

8. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)

9. Do you think things will be kept up after the project has finished? (What will help to keep things up long-term? What will hinder the long-term success of the intervention (if found to be successful)?)

10. What are your expectations of this project?

Roll-out of the PINCER trial:

11. If the PINCER trial was shown to be effective, what do you think will help to roll it out in other practices? (Across England)

12. How do you think practices can be motivated to participate in trials like the PINCER?

13. If after the study has finished, you were offered a service similar to that being provided in the PINCER trial, would you or your practice want to use the service? Why/why not? (Was simple feedback useful or has it thrown up more questions than answers? Would you want to receive pharmacist intervention?)
More general questions:

14. From your perspective, what influences prescribing safety in general practice? (How is the issue addressed by your practice? How is it developing?)

15. The literature has shown that in certain circumstances GPs can feel threatened by pharmacists’ expanding clinical role – how do you feel about this? (inter-professional boundaries) e.g. Mark A. Mesler (1991) ‘Boundary encroachment and task delegation: clinical pharmacists on the medical team.’ Sociology of Health & Illness 13 (3), 310–331

16. How do you see the role of pharmacists developing within primary care? (What can help to make pharmacists a more integral part of the primary care team? Do you feel they are?)

17. Is there anything else that you would like to say? Do you have any suggestions?

Trial Pharmacists

Questions relating to the PINCER trial:

1. How are things going now that you have worked on the trial for a while?
2. Any concerns/problems? (How can these be addressed/dealt with? Are there any issues that you feel might influence the results of the trial?)
3. Which aspect is running particularly smoothly/effectively? Why? (identify conditions)
4. What do you feel about the outcome measures now that you have worked on the trial for a while? (after initial answer can focus on beta blocker and asthma in particular: risks and benefits of beta-blockers, how does that influence prescribing behaviour? try to get specific examples)
5. How is your relationship with the practice staff? How do you feel received in the practice? Does the relationship/your role change with time?
6. How do you feel you are integrating into the practice teams? (What can help to make you a more integral part of the primary care team?)
7. How would you describe the relationship between pharmacists and GPs? (in general and in the trial)
8. What do practices think about the trial?
9. Is your workspace in the practices (accommodation) appropriate? Does the way you are accommodated in the practice affect your performance/work/outcome of trial? (What could be done to improve things?)
10. If you encounter a problem during your work on the trial, where do you go?
11. How do you see the GPs role in the trial? How is their attitude/involvement?
12. How do you see your role in the trial?
13. How do you see the practice manager’s role in the trial?
14. Anyone else you can think of, who is crucial for the implementation of the trial? (could you rank?)
15. What do you feel is the crucial “ingredient” of the trial? (What are the differences between pharmacist intervention and simple feedback?)
16. What other (unanticipated) effects do/might the interventions have on prescribing safety in practices (those that are not related to the outcome measures)? (these can be either positive or negative)
17. Do you think the intervention will make a long term impact on prescribing behaviour? Why? Why not? (Will things be kept up in practices after you left? What will help to keep things up in practices long-term? What will hinder the long-term success of the intervention?)
18. Any advice for someone who just started working as a pharmacist for the PINCER trial? (Capture aspect of time – what would have helped? Do things get easier over time? What have you learned?)
19. Are there things that you are doing in the practices that are not trial related? Which are these?
20. What difference will the results of the trial make for future developments in prescribing safety?

Possible roll-out:
21. How was your job profile reconfigured while working for the PINCER? Would there be anything that you would like to see included in the job profile if the trial is to be rolled out?
22. If the PINCER was to be rolled out, would it be appropriate to broaden the remit of the pharmacists beyond the outcome measures of the trial?
23. If the trial was to be rolled out, who would be the employing authority for pharmacists?
24. If the trial was to be rolled out, do you think community pharmacists could incorporate some of the functions of the PINCER trial pharmacists in their current role? (What would have to be done to make this possible? e.g. more resources, more training)

More general questions:
25. From your perspective, what influences prescribing safety in general practice? (How is the issue addressed by the PCT? How is it developing?)
26. How do you see the role of pharmacists developing within primary care? (In what way does the PINCER influence these developments?)
27. Is there anything else that you would like to say? Do you have any suggestions?

Practice Managers - Pharmacist Intervention Arm

Questions relating to the PINCER trial:
1. Why did your practice decide to get involved in this project? (How does the trial benefit the practice?)
2. What is your involvement/role in the PINCER trial? (Do you have regular contact with the pharmacists? How does the PINCER trial affect your day-to-day work as a practice manager?)
3. What is the GPs role in the PINCER trial? (How does it affect them? Are they heavily involved in it? Do they have regular contact with the pharmacist? How are they getting on with the pharmacist?)
4. How is the trial received by the GPs? How are the GPs reacting to seeing the list of patients identified/the pharmacist's recommendations?
5. How do you feel the PINCER trial is working so far? (Any concerns/problems with the trial? Why? How can problems be addressed/dealt with? How does the PINCER trial affect the day-to-day work of others in the practice e.g. reception staff?)
6. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)
7. In your opinion, how important is the role of the pharmacist in the trial? (keeping in mind that there is also a simple feedback arm, do you feel your practice could have done it without the pharmacist? Do you feel that this kind of work could be done by someone else? Who? Practice nurse, GPs? How could that be made possible?)
8. Have you had a pharmacist working in your practice before? How do you think this influences the outcome of the trial?
9. In your opinion, does the PINCER trial affect the work-dynamics in your practice? If so, how? (Is everyone working on it together?)
10. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)
11. How is the pharmacist accommodated in the practice?
12. Are there things that the pharmacist is doing in your practice that are not trial related? Which are these?
13. Do you think things will be kept up after the pharmacist has left? (What will help to keep things up long-term? What will hinder the long-term success of the intervention (if found to be successful)?)
14. What are your expectations of this project?

Roll-out of the PINCER trial:
15. If the PINCER trial was shown to be effective, what do you think will help to roll it out in other practices? (Across England)
16. How do you think practices can be motivated to participate in trials like the PINCER?
17. If the PINCER was to be rolled out, which other things could pharmacists do/look at in practices (beyond the outcome measures of the trial)? (How could the pharmacists’ time be used most effectively?)
18. If after the study has finished, you were offered a pharmacist service similar to that being provided in the PINCER trial, would you or your practice want to use the service? Why/why not?

More general questions:
19. What does your practice do to address issues of prescribing safety? (Are there systems in place? What are they? Which are the main areas for improvement?)
20. How do you see the role of pharmacists developing within primary care? (What can help to make pharmacists a more integral part of the primary care team? Do you feel they are?)
21. Is there anything else that you would like to say? Do you have any suggestions?

Practice Managers – Simple Feedback Arm

Questions relating to the PINCER trial:
1. Why did your practice decide to get involved in this project? (How does the trial benefit the practice?)
2. What is your involvement/role in the PINCER trial? (Have you read the educational material? Have you had a look at the potentially at-risk patients identified? How does the PINCER trial affect your day-to-day work as a practice manager?)
3. In your opinion, what is the GPs role in the PINCER trial? (How does it affect them? Are they heavily involved in it?)
4. How is the trial received by the GPs? How are the GPs reacting to seeing the list of patients identified?
5. How do you feel the PINCER trial is working so far? (Any concerns/problems with the trial? Why? How can problems be addressed/dealt with? How does the PINCER trial affect the day-to-day work of others in the practice e.g. reception staff?)
6. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (If it works, why do you think this will be? If it doesn’t work, why do you think this will be?)

7. In your opinion, does the PINCER trial affect the work-dynamics in your practice? If so, how? (Is everyone working on it together?)

8. Is there anything that you would have done differently in implementing the PINCER trial? (Thinking about what has been happening in the practice and your role during the intervention period)

9. Do you think things will be kept up after the trial has finished? (What will help to keep things up long-term? What will hinder the long-term success of the intervention (if found to be successful)?)

10. What are your expectations of this project?

Roll-out of the PINCER trial:

11. If the PINCER trial was shown to be effective, what do you think will help to roll it out in other practices? (Across England)

12. How do you think practices can be motivated to participate in trials like the PINCER?

13. If after the study has finished, you were offered a service similar to that being provided in the PINCER trial, would you or your practice want to use the service? Why/why not? (Was simple feedback useful or has it thrown up more questions than answers? Would you want to receive pharmacist intervention?)

More general questions:

14. What does your practice do to address issues of prescribing safety? (Are there systems in place? What are they? Which are the main areas for improvement?)

15. How do you see the role of pharmacists developing within primary care? (What can help to make pharmacists a more integral part of the primary care team? Do you feel they are?)

16. Is there anything else that you would like to say? Do you have any suggestions?

**NHS Prescribing Leads (or similar)**

Questions relating to the PINCER trial:

1. Were you aware that the PINCER trial is taking place? (Are you involved in it? If yes, How?)

2. Do you feel the PINCER trial will be effective in reducing prescribing errors in general practice? (Do you feel the trial adequately addresses issues surrounding prescribing safety?)

3. How do you feel about the outcome measures of the trial? (after initial answer can focus on beta blocker and asthma in particular: risks and benefits of beta-blockers, how does that influence prescribing behaviour? Try to get specific examples)

4. If applicable: how do you feel the interventions are received by (a) practices and (b) pharmacists (c) others in the PCT?

5. Are there or do you anticipate any problems with the trial (design and/or how it is received by key players)?

6. Do you think the interventions will make a long term impact on prescribing behaviour? Why? Why not? (What will help to keep things up in practices long-term? What will hinder the long-term success of the interventions (if found to be successful)?)
Roll-out of the PINCER trial:
7. If the PINCER trial was shown to be effective, what do you think will help to roll it out in other practices? (Across England) (How do you see the PCT’s role in this?)
8. How do you think practices can be motivated to participate in trials like the PINCER?
9. If the PINCER was to be rolled out, which other things could pharmacists do/look at in practices (beyond the outcome measures of the trial)? (How could the pharmacists’ time be used most effectively? Do you need a pharmacist to do these things? Who else could do them?)
10. If the trial was to be rolled out, who would be the employing authority for pharmacists working on the trial? PCT’s, practices themselves? How can you make this possible?
11. If the trial was to be rolled out, do you think community pharmacists could incorporate some of the functions of the PINCER trial pharmacists in their current role? (What would have to be done to make this possible? e.g. more resources, more training)

More general questions:
12. From your perspective, what influences prescribing safety in general practice? (How is the issue addressed by the PCT? How is it developing?)
13. How do you see the role of pharmacists developing within primary care? (What can help to make pharmacists a more integral part of the primary care team? Do you feel they are?)
14. Is there anything else that you would like to say? Do you have any suggestions?

Trial Pharmacists – Exit Interviews
1. Could you tell me about how you’ve come to decide to leave?
2. What are your reasons for leaving? (Anything to do with the nature of your work for the PINCER or external?)
3. Is there anything that could have been done early on to prevent you from leaving?
4. What has been good/enjoyable/satisfying for you in your time working as a PINCER pharmacist?
5. What has been frustrating/difficult/upsetting to you in your time working as a PINCER pharmacist? Is this job boring?
6. How could the PINCER team/trial have enabled you to make fuller use of your capability and potential?
7. Do you think that pharmacists should be doing this job or could it be done by others e.g. admin staff? Who else could do it? Why? How could this be made possible? Discuss alternative models!!! pros and cons – any other suggestions?
8. What training would you have liked or needed that you did not get? What difference would that have made?
9. How could the team/trial have enabled you to have made better use of your time?
10. What suggestion would you make to improve working conditions of PINCER pharmacists?
11. How did reality differ from your expectations of working as a PINCER pharmacist (when you applied)?
12. Would you apply again for a job like this? Why/why not? (Short term contract – does that make a difference?)
13. Can I ask where you are going (if you have decided)? (Why are you going there?)
14. Is there anything else that you would like to say?
Appendix 7.3: Topic Guides Focus Groups

PINCER Trial pharmacists

5 min - Introduction, welcome from organiser & ground rules

- The purpose of the group today is to discuss your experiences/opinions of the PINCER trial and to discuss potential alternative interventions to reduce prescribing errors in primary care
- What you say is confidential and whatever views you express will be anonymised so that no one outside of this room will know who has said what.
- You should therefore treat information and views expressed in this room as confidential
- Please feel free to say what you want and feel free to discuss comments or add your own experiences
- Please allow others to have their say (even if you disagree)
- With your consent the discussions will be recorded so that we can analyse them later, but the data will be anonymised
- It’s not so much a question and answer session as a forum for discussion
- I may need to stop a discussion if going over time in order to get all topics discussed

10 Minutes
GROUP INTRODUCTIONS
Researcher and participants (names and professions)
Record names/positions
State the two topics to keep the structure of the discussion

30 - 40 Minutes
TOPIC 1 – the wider usability of the trial
Rationale:
The trial has included two ways of reducing medication errors (pharmacist intervention and simple feedback) but there may be other more effective ways to achieve this.
We have some concerns regarding the sustainability of the PINCER models and therefore want to explore alternatives.

Question 2: In your opinion, how might the trial interventions be modified or adapted in order to maximise their effectiveness when implemented in routine general practice?

Prompts
Do you think the interventions are fine as they are or is there anything that could be changed?
What would need to be changed and why?

30 - 40 Minutes
TOPIC 2 – possible alternative interventions
Question 3: What alternative interventions/strategies might be both acceptable to you and effective in reducing prescribing errors in general practice?

Prompts
Can they think of any themselves?
Introduce our four potential models:
1. Simple feedback: practices themselves setting up and conducting searches on a monthly basis (and, crucially, act on the results), based on written educational material, within this scenario, modified simple feedback versions may be possible, e.g. simple feedback with incentives (e.g. money) to motivate practices to implement and drive change or remote access to a pharmacist (potential of electronic health records)

2. Training practice staff to provide relevant clinical input: clinical staff (e.g. nurses) within the practice may provide this clinical input, this may be possible through attending additional training courses, but would probably need additional incentives, trained clinical staff may then work in collaboration with admin staff, healthcare assistants or technicians

3. Pharmacist intervention: may take a number of different forms e.g. PINCER pharmacists going into practices as in the trial (employed by the practices themselves or the PCT or both), community pharmacists, the introduction of the electronic health record/summary care record may facilitate a remote solution for both

4. Partial pharmacist input: a designated person driving change is necessary. This may either come from inside the practice or outside the practice. This person does, however, not necessarily need to have a clinical background – there may be a potential role for admin staff, healthcare assistants or technicians. Clinical input is needed for some aspects of the intervention. There may be a potential role for pharmacists (PCT or community) in an advisory capacity – this may also be done remotely (e.g. on the phone or computer) - if this would be the case less resources would have to be spent on training

What are the strengths and limitations of each alternative approach?
Which model would you pick if you had to chose?

5 Minutes
CLOSURE
All know what I am trying to do - anything else to add?

Pharmacist Intervention Practices

5 min - Introduction, welcome from organiser & ground rules as above

5 Minutes
GROUP INTRODUCTIONS
Researcher and participants (names, professions and involvement in trial if applicable)
Record names/positions
State the 3 topics to keep the structure of the discussion:
• experiences and opinions of the PINCER trial
• the wider usability of the trial
• possible alternative interventions

15 Minutes
TOPIC 1 – experiences and opinions of the PINCER trial
How would you describe your experiences of being involved with the trial? (positive and negative)

15 Minutes
TOPIC 2 – the wider usability of the trial
Rationale: The trial has included two ways of reducing medication errors (pharmacist intervention and simple feedback) but there may be other more effective ways to achieve this. We have some concerns regarding the sustainability of the PINCER models and therefore want to explore alternatives. Do you think the interventions are fine as they are or is there anything that could be changed or adapted to maximise their effectiveness? What would need to be changed and why?

20 Minutes
TOPIC 3 – possible alternative interventions
What alternative interventions/strategies might be both acceptable to you and effective in reducing prescribing errors in general practice?
Prompts: Can they think of any themselves?
Introduce our four potential models: (emerged from interviews with those involved in trial)
What are the strengths and limitations of each alternative approach?

- Remote pharmacist input – potential of electronic health records
- Community pharmacists taking over some of the functions of PINCER pharmacists
- Partial pharmacist input with technicians, healthcare assistants or admin staff taking over some functions of PINCER pharmacists (interviewees stated that especially monitoring outcome measures would not require a pharmacist but clinical input is needed for some aspects of the intervention e.g. beta-blockers)
- Training clinical staff to provide relevant clinical input (might then work in collaboration with admin staff, technicians or healthcare assistants)

Which model would you pick if you had to chose?
We did a focus group with PINCER pharmacists and they favoured a flexible option with the approach taken tailored to individual practices (potentially lead by clusters), when pushed they stated that they would prefer the community pharmacist model, or a collaboration of community pharmacists and PCT pharmacists. How do you feel about this?

Closure as above

PCT Focus Group

As above except TOPIC 3 – possible alternative interventions
What alternative interventions/strategies might be both acceptable to you and effective in reducing prescribing errors in general practice?
Prompts: Can they think of any themselves?
Introduce our four potential models: (emerged from interviews with those involved in trial)
What are the strengths and limitations of each alternative approach?

- Remote pharmacist input – potential of electronic health records
- Community pharmacists taking over some of the functions of PINCER pharmacists
- Partial pharmacist input with technicians, healthcare assistants or admin staff taking over some functions of PINCER pharmacists (interviewees stated that especially monitoring outcome measures would not require a pharmacist but clinical input is needed for some aspects of the intervention e.g. beta-blockers)
- Training clinical staff to provide relevant clinical input (might then work in collaboration with admin staff, technicians or healthcare assistants)
Which model would you pick if you had to chose?
We did a focus group with PINCER pharmacists and they favoured a flexible option with the approach taken tailored to individual practices (potentially lead by clusters), when pushed they stated that they would prefer the community pharmacist model, or a collaboration of community pharmacists and PCT pharmacists. Practices not so keen on Community Pharmacist option but thought PCT pharmacist option was ok – felt they needed some input on specific issues/problems to focus on. How do you feel about this?

**Simple Feedback Practices and PCT Interview**

**As above except TOPIC 3 – possible alternative interventions**
What alternative interventions/strategies might be both acceptable to you and effective in reducing prescribing errors in general practice?
Prompts: Can they think of any themselves?
Introduce our potential models: (emerged from interviews with those involved in trial)
What are the strengths and limitations of each alternative approach and how could each be put into practice?
- Remote pharmacist input – potential of electronic health records
- Community pharmacists taking over some of the functions of PINCER pharmacists
- Partial pharmacist input with technicians, healthcare assistants or admin staff taking over some functions of PINCER pharmacists (interviewees stated that especially monitoring outcome measures would not require a pharmacist but clinical input is needed for some aspects of the intervention e.g. beta-blockers)
- Incorporate into existing role of PCT pharmacist
- Cluster based flexible approach
Which model would you pick if you had to chose?
Focus on practicalities of implementing these models - need to come up with concrete recommendations
 Appendix 7.4: Graphical representation of results

**Brief interviews**

Interviewees were asked what they perceived to be the main issues in prescribing safety in general practice. Other perceived issues frequently mentioned included the data quality of patient records, the lack of integration between primary and secondary care and medication side effects.

Participants were also asked about their expectations of the trial. Here, across participants, the most commonly mentioned issue was the trial's potential to improve prescribing safety. All pharmacists had the expectation that the trial would raise the profile of pharmacists in general practice.

Diagrams summarising facilitators/barriers and themes and sub-themes identified can be viewed in Figure 1 and Figure 2 below. Here, the green circles are the facilitators identified, backed up with extracts from participants’ accounts. The brown boxes are conceptual categories designed to facilitate the reader’s understanding. Arrows indicate to what extent identified themes are grounded in the data (the thicker the arrow, the more participants mentioned the theme). An attempt was made to follow a similar conceptual structure in both diagrams.
Figure 1. Visual presentation of facilitators
In-depth interviews

The analysis of in-depth interviews resulted in themes and sub-themes capturing the context in which the interventions were most and least likely to work. In addition, the analysis has identified issues to consider if the outcome interventions were rolled out and helped to gain an insight into potential alternative components of the interventions. Although the focus of this analysis was on the pharmacist intervention arm, the results can easily be applied to the simple feedback arm.

A diagram summarising the results obtained in the in-depth qualitative phase can be viewed in Figure 3. Here, red circles are conceptual categories of the trial design, implementation and potential roll-out whilst the other boxes are backed up by citations in the qualitative data. Arrows indicate to what extent identified themes are grounded in the data (the thicker the arrow, the more participants mentioned the theme).
Figure 3. Visual presentation of the results obtained in the in-depth qualitative phase

Course of the project - timing
Pharmacist job construction
Pharmacist meetings
Integration of pharmacist
Practice meetings
Accommodation of pharmacist

Outcome measures
Feedback of performance
Money
Computer systems
Practice workload

Organisation and planning

Practice context
Practice attitude
Practice characteristics
Integration of pharmacist

Implementation

Key players
Admin staff
Practice manager
GPs
Nurses
Pharmacist characteristics

Roll-out

Motivate practices through e.g. emphasis on best practice, financial incentives, making it compulsory, documenting benefits, sharing positive experiences

Outcome measures
(Drop some and include others)

Employing authority
PCT
Both?

Who else could deliver (parts of) the intervention?

Need support from PCT and improved communication with secondary care throughout
Focus groups

GPs usually dominated the focus group discussion in practices. Some administrative staff hardly spoke at all during the focus groups. This may be due to their limited involvement in the trial.

The analysis resulted in themes and sub-themes capturing models (with both strengths and weaknesses) of a potential roll-out of the PINCER trial. A diagram summarising the results obtained in focus groups can be viewed in Figure 4. Elements of this visual representation will be discussed in detail in the results section.
Figure 4. Graphical presentation of the results obtained in focus groups

**Outcome measures** (generally viewed positively, specific suggestions on other outcome measures, external input as to what to focus on important to practices)

- PCT overseeing
  - Ideally flexibility but the following concrete models were considered
    - Pharmacist Intervention
    - Practices themselves
      - Computer Systems
      - Simple Feedback
    - Remote Pharmacist input
    - Partial Pharmacist input

Macro context (the need to develop wider systems)