A systematic review of the effectiveness and cost-effectiveness of interventions aimed at preventing medication error (medicines reconciliation) at hospital admission

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Glossary

Term	Definition
Medicines reconciliation	It is defined as "being the process of identifying the most accurate list of a patient's current medicines – including the name, dosage, frequency and route – and comparing them to the current list in use, recognizing and discrepancies, and documenting any changes, thus resulting in a complete list of medications, accurately communicated". (IHI 2005)[1]
Gold standard	A term used in this review to refer to the most complete and accurate medication history that can be obtained.
Adverse Drug Event	An unwanted or harmful effect that occurs as a result of a medication error.
Medicines error	Medication errors include prescriptions that have never been considered appropriate for the diagnosed condition and preventable events that cause a deviation in the medication received by an inpatient from an appropriate prescription intended by the prescriber, excluding patient non-compliance.
Medication discrepancy	This refers to differences found between either the medication history and prescription chart or between the medication histories and charts of different intervention groups.
Errors of omission	An error which occurs as a result of an action not taken, for example, when a drug received prior to admission inadvertently omitted from a patients' in hospital prescription order.
Errors of commission	An error that occurs as a result of an action taken. Examples include when a drug is administered at the wrong time, in the wrong dosage, or using the wrong route.

Abbreviations

A&E..... Accident and emergency
ADE ..... Adverse drug event
pADE..... Preventable adverse drug event
CI ..... Confidence interval
CP ..... Clinical pharmacist
NA..... Not applicable
NR..... Not reported
OTCs ..... Over the counter drugs
PODs..... Patient own drugs
QALY ..... Quality adjusted life years
RCT ..... Randomised controlled trial
SHO ..... Senior house officer
UKCPA ..... United Kingdom Clinical Pharmacy Association

Executive Summary

Background: Medication errors are one of the leading causes of injury to hospital patients leading to increased morbidity, mortality and economic burden to health services. Over half of all hospital medication errors occur at the interfaces of care and most commonly at admission. The causes of the problem are multiple including, patient, practitioner and existing medicines management systems. Interventions that ensure effective medicines reconciliation are the focus of this review.

Objectives: To review the clinical and cost effectiveness of interventions aimed at the prevention of medication error at the point of admission to hospital. If data permitted we intended to perform a subgroup analysis of patients admitted as emergencies and outside of office hours. We wanted to explore the hypothesis that this type of intervention may be particularly effective for this subgroup of patients.

Methods: Searches were carried our for studies published in English in or after 1950 until June 2007 that addressed any intervention designed to improve medicines reconciliation and prevent medication error at the point of admission into hospital. The search also looked for papers on the cost effectiveness and comparative costs of the different medicines reconciliation procedures. Eleven databases were searched, sources of 'grey' literature, the internet were all searched for relevant studies. In order to capture work in progress or unreported the views of the wider pharmacy community were sought via e-discussion forums on the UKCPA website.

Studies were selected if they included an intervention that was designed to improve medicines reconciliation or accurate medication history at the point to admission to hospital. The review only included studies of adults. It included any type of comparative study and studies which had an indication of medication accuracy or prevention of error or discrepancy or prevention of adverse drug event.

The results of the data extraction and quality assessment were presented in structured tables and as a narrative summary. The possible effects of study quality on the effectiveness data and review findings were discussed.

Results of clinical effectiveness review: In total 3111 references were screened for relevance and full copies of 106 studies were retrieved and assessed for eligibility. Twelve studies were included in the review; 1 randomised controlled trial, six before and after studies, and five uncontrolled comparative studies. An additional five studies of poor methodological quality were excluded on the basis of their design and lack of relevance to a UK setting.

The clinical effectiveness review evaluated three types of intervention, increased involvement of a clinical pharmacist (8 studies), a package of medicines reconciliation interventions (3 studies) and transfer of information by fax from a GP to the admitting ward (1 study).

The pharmacist led interventions involved a greater involvement of the pharmacist at the point of admission, collecting a medication history from patients and verifying the doctors' medication history. Medication errors and discrepancies were reported. Pharmacists appeared to be more effective than doctors in making fewer errors and

gathering a more complete medication history from the patient. Discrepancies identified could be checked and errors corrected. The design of the included studies and the lack of information reported means these conclusions are drawn with caution. Only one study was randomised, none of the studies reported blinding at outcome assessment, differences in the information made available to participating physicians and pharmacists would bias the results in favour of the intervention rather than the control.

Three US based studies looked at a package of interventions at admission including the improved documentation of medication history, a health care professional designated as responsible for accurate collection of medication history and checking these against the doctors prescription. These also showed a positive effect in reducing medication error. One UK based study looked at the effectiveness of faxing information about a patients medication history from the GP to the admitting ward. This again showed a positive effect. While study design means all of these studies findings must be interpreted with caution there is a consistent picture that interventions to reduce medication error at admission have a positive and significant effect. Where a 'gold standard' measure was in place it was clear that errors, despite the interventions, still occurred.

Discussion

The effects of increased pharmacist involvement at admission, a package of interventions including personnel and documentation changes and systems to better transfer information from the GP to hospital all appeared to be beneficial in reducing medication error. The impact of this on adverse drug event was not described in any of the studies. The results of these studies are likely to have been biased by aspects of their design and so conclusions are drawn with caution.

The literature search did also suggest that there is a range of new and developing technologies that all appear to have benefits in reducing medication error. Many are evolving from practice based initiatives and are not designed or reported in such a way that their findings can be drawn into a clinical effectiveness review of the literature.

Results and discussion for cost effectiveness analysis

The economic evaluation estimated the incremental costs and quality adjusted life years (QALYs) of five interventions aimed at improving the medicines reconciliation process: Pharmacist-led reconciliation, Standardised forms, pharmacy technicians, hospital policy, Nurses taking histories with standardised form, Computerised assessment and feedback by pharmacist, and Current medication faxed from the GP practice. QALY gains were derived from reduction in the number of preventable adverse drug events (pADEs). Incorporating the effects of medication errors that do not result in harm into a unitary outcome measure is beyond the scope of this evaluation, and so rates of medication errors are presented separately.

A medication errors model was adapted that estimated the impact of three types of medication errors on patient outcome. The incidence of errors of omission, errors of commission, and errors in the recording of known allergies were described, with subsequent probabilities of detection, and of causing harm if undetected were described. The baseline model was calibrated to estimates of the number of pADEs

caused by the different error types. Costs were estimated for the intervention and for the treatment of occurring pADEs, QALY losses were estimated for different categories of pADEs.

The results showed that the pharmacist-led reconciliation intervention is predicted to prevent the most medication errors, reducing costs associated with errors by £3,002 compared to the baseline scenario and gaining 2.2 QALYs. The next most effective intervention is the 'GP fax' system, which reduces error-related costs by £778 and gains 2 QALYs. There is significant overlap between all of the confidence intervals for all of the output variables. The incremental cost per QALY gained results show that all five interventions are estimated to be extremely cost-effective when compared to the baseline scenario. Three of the interventions are shown to dominate the baseline scenario (i.e. cost less and gain more), whilst the upper CI for all five interventions is below £5,000.

The medication errors model provides reasonably strong evidence that some form of intervention to improve medicines reconciliation is a cost-effective use of NHS resources. The results indicate that pharmacist-led medicines reconciliation is likely to be the most cost-effective intervention, though it is difficult to assess whether the model has captured all of the relevant uncertainty around the model's input parameters. There are also likely to be other interventions, particularly IT-based interventions, for which evidence of effectiveness was not available.

Conclusions: The current evidence, though poor, suggests the initiatives described in the studies included in this review, particularly pharmacist led initiatives, are positive. Any effort to formulate a recommendation for a medicines reconciliation strategy must take into account the large gap in the current evidence. The current evidence as it stands does not sufficiently reflect the many promising and emerging technologies that may be effective in medicines reconciliation. There is a need for those with research design expertise to work alongside innovators of emerging technologies to ensure that the benefits of new interventions are measured and evidence found for their effectiveness and wider applicability.

1. Background

1.1 The extent of the Problem

Medication error is a leading cause of avoidable harm suffered by patients. The cost burdens of these are considerable with significantly increased morbidity, prolonged length of stay in hospital and increased mortality.[2] Medication error occurs most commonly at the interfaces of care[3] in particularly at admission. Variances between the medications patients were taking prior to admission and their prescriptions on admission ranged from 30-70% in two recent literature reviews.[4,5]

Given the scale of the problem, its considerable costs and its potential for prevention, there is clear need to identify effective interventions that can reduce medication error at admission. Indeed, the need for improvements in medicines management arrangements at admission were highlighted by the Audit Commissions report, 'A Spoonful of Sugar'[6] and the NPSA report, 'Moving patients medicines safely' guide.[7] Government health policy in both this country and America has made reducing the number of serious errors in the use of prescribed medicines a target

The purpose of this review is to address the evidence around interventions aimed at reducing errors in the medicines reconciliation process, and to estimate the incremental costs and quality adjusted life years (QALYs) of such interventions.

1.2 The cause of the Problem

There are many factors that are described within the literature that may disrupt the flow of information about the prescribed medications being taken by a patient prior to admission and what is recorded in the medication history and transferred to a medication chart and subsequently administered to a patient in hospital. The accurate recording of a medication history should also include information about the patients allergy status and their use of over the counter drugs (OTCs).

The potential causes are multi-factorial. They include those relating to the patient, such as an inability to recall medicines, confusion and impaired communication function. Carers' knowledge of the medications may also be limited. Wrong medicines may be brought to hospital or wrong information given to the admitting staff. The causes or medication error may relate to the systems of care which fail to transfer information from a GP to a hospital in a timely way. Letters from GPs may be incomplete or absent. Errors may be caused by an absence of checking and verification of medication charts where mistakes may be made by staff admitting patients. The information may not be collected in a standardized way so that key information may be inadvertently omitted. In addition to documenting inadequate information, errors may also occur when transcribing accurate information. These causes may be exacerbated by time constraints on the admitting staff, particularly at night when pressures are greatest. Hand-written prescriptions may contribute to errors if they are illegible, incomplete, or use inappropriate shorthand.

1.3 Medicines Reconciliation

The process of collecting and communicating accurate information about a patient's medication at a point of transfer is summarised by the term medicines reconciliation (Canadian Council on Health Services Accreditation 2005).[8] It is defined as "being

the process of identifying the most accurate list of a patient's current medicines – including the name, dosage, frequency and route – and comparing them to the current list in use, recognizing and discrepancies, and documenting any changes, thus resulting in a complete list of medications, accurately communicated".[1] Any intervention seeking to achieve this purpose will be considered in the review.

2. Methods

This report is based on a systematic review of the literature on interventions that address the problem of medication error occurring at admission to hospital from a community setting. A comprehensive range of databases was searched for studies published in English of interventions that sought to improve the transfer of accurate information about medication use by patients in the community in order to prevent inaccuracies in medication prescriptions at the point of hospital admission.

2.1 Search Strategy.

Eleven databases were searched in April 2007 and an updated search carried out in July 2007.See Appendix 1. These databases covered a wide range of types of data (including economic, grey literature, conference abstracts and ongoing studies.) Key terms used to conduct the search were identified in consultation with clinical experts and included: medication reconciliation, medical history, medication record, patient admission and any related cost-effectiveness. This was broadened further to include electron medication system, clinical pharmacists, pharmacist, admission order, adverse drug error, drug related error, and drug related problem, safety and one-stop dispensing. See Appendix 1.

The search also included horizon scanning the internet. Additional efforts were made to identify relevant studies and current examples of good practice in the UK by contacting clinical experts and contacting the wider pharmacy community via an e-discussion list on the UKCPA website.

2.2 Inclusion and exclusion criteria

One reviewer screened all title and abstracts. Full paper manuscripts of any records that were potentially relevant were obtained, were possible, and the relevance of each study assessed according to the criteria listed below.

2.3 Study design

It was anticipated that there may be a small number of randomised controlled trials in this field, reflecting in part the challenges of undertaking a randomised controlled trials that explore medication error. We therefore broadened our inclusion criteria to incorporate studies that were non-randomised, well-designed controlled studies. Studies were graded in accordance with guidelines from the Centre for Reviews and Dissemination (CRD) and quality assessment findings. Since non-randomised studies are subject to a number of potential methodological biases that make findings hard to interpret we planned a narrative analysis of the findings.

2.4 Interventions

Medicines reconciliation is defined as "being the process of identifying the most accurate list of a patient's current medicines – including the name, dosage, frequency and route – and comparing them to the current list in use, recognizing and discrepancies, and documenting any changes, thus resulting in a complete list of medications, accurately communicated".[1] Interventions that sought to achieve medicines reconciliation were included in the review. The types of interventions identified included personnel led programs, IT initiatives, data management initiatives, educational programs and patient focused interventions such as patients own drugs (PODs) and one-stop dispensing.

2.5 Population

The population included adults being admitted to hospital. Adults being admitted to any type of ward were considered. In order to anticipate potential heterogeneity we undertook a subgroup analysis of emergency, unplanned and out of hours admissions. We excluded children from the review because of the differences in service provision to children and the additional risk factors children present for medication error and associated harm.

2.6 Outcomes

Data on the following categories of outcome measures were included:

- Accuracy of the documented medication history
- Discrepancies in medication prescription
- Medication errors per patient or per medication
- Adverse or harms caused by medication error

2.7 Data extraction strategy

Data relating to both the study design and quality were extracted by one reviewer (FC). Additional checking and clarification was provided as needed by a second reviewer (CM). The key aspects of the studies were summarized, including the type of intervention, which country and which type of hospital was it carried out in, inclusion and exclusion criteria, number of participants, baseline comparability, proportion of patients admitted our of hours. Details were extracted about the intervention including the personnel involved, length of time of intervention and duration of study. Note was made if the intervention sought to establish allergy status. Outcomes as described above were recorded. Where non-randomised trials ere included in the review, potential confounding factors were documented. These included changes in the control group as a result of information about medicines already being recorded, differences in experience between control interventions, differences in between intervention and control in terms of understanding about participation in the study

2.8 Quality assessment strategy

One reviewer independently assessed the quality of the studies, using one of two separate checklists depending on study design. Randomised controlled trials were assessed on 4 key quality parameter; randomisation, allocation concealment, blinding and intention to treat analysis (Schulz). A 14-question checklist was used to assess the quality of non-randomised comparative studies (see Appendix 2). The checklist for non-randomised studies was adapted from several sources, including the NHS Centre for Reviews and Dissemination's guidance for those carrying out or commissioning reviews[9] Verhagen and colleagues[10] and Downs and Black.[11] The checklist was developed through the Review Body for Interventional Procedures (ReBIP). Additional adjustments were made by the reviewer so the tool more closely fit the current review.

3. Results of the Systematic Review

When the searching was complete and duplicates had been removed there were 3111 references. Following sifting 106 papers were retrieved for further consideration. Of these 90 were excluded as they did not meet the inclusion criteria. The remaining 16 studies were examined for inclusion in this review. These included one randomised controlled trial[12] 6 before and after studies [13,14,15,16,17,18] and 9 studies which used a comparator as a control but were not randomised and did not control for potential confounders.[19,20,21,2223,24,25,26,5] Eight studies were carried out in the UK[13,14,19,20,21,22,23,15] and nine in America.[12,24,25,26,5,16,17,27,18] Twelve studies explored the effect of a pharmacist led intervention, three studies explored the effects of a medicines reconciliation process incorporating both personnel, information management and policy changes and one study looked at systems to transfer details of patients medicines from the community to hospital. Table 1 summarises the type of intervention for these studies along with an unpublished study that examined an IT based/Information transfer initiative.[15]

Table 1: Intervention by Study Type

Types of intervention				**Country**	
	Randomised trial	**Before and after studies**	**Uncontrolled studies**	**UK**	**USA**
Total	1	7	9	8	9
Pharmacist	1[12]	2[14,13]	9[19,20,21,22,23,24,25,26,5]	7[13,14,19,20,21,22,23]	5[12,24,25,26,5]
Medicines reconciliation 'package'		4[15,16,17,27,18]			4[15,16,17,27,18]
IT/information transfer		1[15]		1[15]	

3.1 Additional Excluded Studies

Given the lack of randomised controlled trials we incorporated non-randomised studies in the review. In order to determine relevance and value to this review an additional ranking scale was developed (table 2).

Table 2: Ranking Scale

Rank	**Location**	**Method of comparison**	**Outcomes measures**
1	UK	Randomised with independent assessment of gold standard	Adverse drug events
2	Developed western world	Randomised with non-independent assessment of gold standard	Potential adverse drug events
3	Other developed nations	Non-randomised with independent assessment of gold standard	Medication errors
4	Other nations	Non-randomised with non-independent assessment of gold standard	Other, e.g. completed forms, allergy documentation, etc.

We excluded all of those studies which fell into rank four. This included four studies undertaken in the US were excluded. A number of features of their study design will have introduced bias and compromised their internal validity. As they are US based they were felt to offer less value to this review as the systems of care between the UK and USA differ substantially.

3.2 Pharmacist led interventions

This section presents a narrative description of findings from the included studies. See Appendix 3 and Table 3 for study characteristics.

Eight studies explored pharmacist led interventions with a total of 3078 patients. Seven of the studies were based in the UK and explored the effectiveness of pharmacists working in acute admissions settings. One study was based in the US on a surgical preadmission clinic. The studies looked at a medication error or discrepancies in medication charts as outcome measures.

Kwan et al 2005[12] undertook a randomised controlled trial that compared a pharmacist medication assessment with a nurse-conducted medication history and prescription written by a surgeon. The study took place in the USA and was based on a surgical pre-admission clinic. It did not include out of hours patients. This study found that the incidence of medication discrepancy between hospital and home medication was much lower when the history and medication order form were taken and written by the pharmacist than by the nurse and doctor. There was a reduction in medicine discrepancies between home and hospital prescribed medications of 55.3% with the number of discrepancies per 100 patients falling from 43.6% to 19.5% following the intervention. Both arms of the intervention were compared against a 'gold standard', i.e. a medication history considered to be as accurate and complete as possible. The data was retrieved form a conference abstract so much detail of the study design were not reported.

Brady 2004[13] and Dutton 2003[14] reported the results of before and after studies. Both studies explored the effects of a pharmacist offering more intense involvement on the medical admissions ward. This included increased visiting to the wards, participation in post-admission ward rounds and taking medication histories. Dutton 2003 also incorporated a greater use of patients own drugs (PODs – prescribed drugs brought into hospital from home) in order to assist in an accurate medication history. Both interventions were compared with the same setting prior to the more intense pharmacy intervention starting. In both studies the intervention of the pharmacist allowed a greater number of medication errors to be identified and corrected than in the control arm of the study. In Dutton 2003, 43% more errors were identified than during the control period compared with 17.9% in Brady's 2004 study. The greater use of PODs may also have meant more errors were identified in the Dutton 2003 study. Anecdotal evidence from UK based examples of innovative practice has seen a positive effect with increased use of PODs at admission.[28] There was, however, no 'gold standard' measure to establish the true rate of medication error and any adverse events that may have arisen as a result. These studies do not reveal the errors the pharmacist may have made so do not give a full picture of the effectiveness of the intervention. It is also unclear whether the physicians involved in the study were aware that their drug prescriptions would be scrutinised, while the pharmacists were aware of their

participation in the study. This may have introduced performance bias and influenced the findings.

Five prospective studies[20,22,19,21,23] based in the UK compared a pharmacist obtained medication history with that obtained by the admitting physician. In two studies the pharmacist was based in the accident and emergency department,[21,19] in two[22,20] the pharmacists were based in admissions units and in one clinical pharmacists were covering all medical admissions in seven hospitals over a 5 day period.[23]

In three studies[23,21,19] medication error was determined by comparing the pharmacist's medication history with the physician's. Any unintended discrepancy was counted as an error when compared against the pharmacists record. There was no 'gold standard' medication history against which both could be compared and errors in the pharmacists record also identified. In these studies, where calculable, the number of errors per patient was 202 per 100 patients[23] and 136.4 per 100 patients.[19] Differences in error rates may reflect differences in the range of discrepancies being measured. The errors measured in Akwagyria's 1996 study apply only to drugs omitted but those in Slee's 2006 paper include any unnecessary drug therapy, wrong drug, wrong dose, incomplete prescription, adverse drug reaction and drug omissions. In all three studies the pharmacist appeared to make considerably fewer errors.

In two studies a third source or 'gold standard' medication history was used to verify the errors found in both the pharmacist and the physician's medication history.[22,20] In Collins 2004 paper, in contrast to all the other studies, pharmacists appeared to omit more medicines (137 omissions per 100 patients) than physicians (128 omissions per 100 patients) McFadzean 2003, findings were consistent with the other studies in finding a higher error rate in physicians (65 errors per 100 patients) than pharmacists (5 errors per 100 patients). In both of these studies the physicians were unaware that they were participating in a study while the pharmacists were aware. In addition where the same group of patients were used for both arms of the study[19,23,22] patients ability to recall their medication history may be influenced by their initial interview with the physician and hence improve recall for the pharmacist. Both these factors could introduce bias and influence the results.

None of the studies clearly described the time taken to gather the medication history. The difference in time available and time taken to gather a medication history may make a significant difference to its subsequent accuracy and completeness. Once again this difference may introduce bias into the results.

3.3 Medicines reconciliation packages

Three, before and after studies[18,17,16] undertaken in the US explored the effects of a medicines reconciliation package. See Appendix 3 and Table 3 for study characteristics. All three involved the development of a standardised medication form providing a template for information to be gathered. In one study this was computerized.[17] In two studies the pharmacist was to collect the medication history and in one this process was undertaken by a nurse.[16] Any discrepancies with the physicians order form were identified and reconciled. In all three studies this led to a reduction in the number of errors in medicines prescribed at admission (see table). Insufficient data was reported in this conference abstract to ascertain information regarding the external validity of the study findings such as the total number of

Deleted: DeCarolis 2005 reported the greatest reduction of errors with a 74% reduction in patients with unintended discrepancies following the intervention.

patients, inclusion criteria and baseline comparability. In Rozich 2004 the number of errors fell 62% from 213 to 80 errors per 100 admissions and in Michels 2003 they fell 47.6% from 145 to 76 errors per 100 patients.

3.4 IT based/Information transfer initiatives

One UK based before and after study[15] implemented a system of care which supported the transfer of current medication and other relevant information for an accurate medication history. See Appendix 3 and Table 3 for study characteristics. They developed a template that could be faxed by the GP practice to the admitting ward. This new pattern of care reduced the number of incorrect medication sheets by 69% with errors falling from 55 per 100 patients to 17. This data was drawn from unpublished literature and little information was available regarding the study design.

Table 3: Summary of Included Studies - Pharmacist led interventions

Study	Study Design	Participants/ Settings n	Interventions I1:	Control I2	Outcomes	Reviewers comments
Randomised controlled trials						
Kwan 2004	RCT	USA, surgical pre-admission clinic	Pharmacist medication assessment and a post-operative medication order form.	Nurse-conducted medication histories and surgeon-generated orders	Incidence of medication discrepancy related to home medications: I1: 30/154 (19.5%) I2: 68/154 (43.6%) 55.3% reduction in medicine discrepancies when compared to home medications	Conference abstract. The 'gold standard' medication history against which the other medication histories compared not described.
Before and after studies						
Brady 2004	Before and after study Control data was collected retrospectively .	UK, medical admissions ward, teaching hospital. n = 305 (I1) NR (I2)	The MAP attended post-admission ward rounds on a daily basis (excluding weekends), confirmed patient's medication histories and ensured patients regular medications were prescribed appropriately on admission. Three one-month periods were chosen to serve as study periods.	Typical UK ward pharmacy service, visited each weekday by a pharmacist Interventions recorded prior to the appointment of the MAP (medical admissions pharmacist) were retrieved from the in-house pharmacy intervention database. Three one week periods were selected for analysis as the control.	Interventions (ie any communication between a pharmacist and a clinician, whether verbal or written , made with the intention of influencing prescribing) concerning possible omissions or other discrepancies in the medication history. I1:232/413 (56.2%) CI: 210.6-251.9 I2:31/81 (38.3%) CI: 26.7-43.8 NB: the denominator for the above is the total number of interventions. There is no reported total number of medications or total number of patients for the control period. There was a significant increase in the number of inaccuracies identified between the patient's confirmed medication history and drug regimen prescribed on admission during the intervention period.	Studies with no 'gold standard' measure for overall medication prescription error assume that the baseline rate of errors in the same in both time periods.
Dutton 2003	Before and	UK	More intense	Clinical	Number of errors identified concerning	Factors to consider when

Study	Study Design	Participants/ Settings n	Interventions I1:	Control I2	Outcomes	Reviewers comments
	after study	Patients admitted to medical admissions ward.	clinical pharmacy involvement (visited twice each weekday) and was available by bleep to take as detailed a medication history as possible. Greater use of PODs (patients own drugs).	pharmacist visited ward each weekday morning. Did not include routine drug history taking and limited use of PODs	regular medication: I1: 393/506 I2: 182/526 Number of patients on regular medication who had ≥ 1 error: I1: 228/506 I2: 106/526 The largest number of errors involved the omission of medication (177 vs 80). Of the errors found in I1 74.8 % could not have been identified from checking the drug chart alone. More than 50% (202/506) errors were considered likely to cause destabilization of a chronic medical condition, or serious adverse events..	comparing error data from the two phases. New intake of junior doctors meant that during the intervention period the doctors will have been more experienced than during baseline collection of data.
Comparative/observational/uncontrolled? – UK based						
Slee 2006	prospective	UK, medical admissions in seven acute NHS trusts in England and Wales. n=791	Clinical pharmacist review of medication at the point of admission using a standardised reporting form	Existing prescription made by admitting physician.	Discrepancies between intervention and control identified and amended. 464 discrepancies found 391 amendments to physician order made (72 unresolved) 38% required an intervention Potential severity: Fatal 10 2.2% Serious 82 17.7% Moderate/ Minor 369 79.5% Missed	NB total number of admissions and total included different – to do with out o f hours admissions. Need to flag up

Study	Study Design	Participants/ Settings n	Interventions I1:	Control I2	Outcomes	Reviewers comments
					Opportunity 3 0.6% Errors per 100 patients: 202	
Collins 2004	prospective	UK n=177	Pharmacist obtained medication history.	Physician history	**Omission of medicines from medication histories.** Medicines obtained by pharmacist interview but not on physicians chat: 227/553 Medicines on physicians chart but not obtained from pharmacist interview: 243/553 **Differences in doses from the medication histories:** Medicines with a different dose documented on the chart by the doctor from that obtained from pharmacist interview: 45/352 **Errors per 100 patients:** I1: 128	NB problem with the denominator. Each group differed so there was no 'gold standard' against which they could compare their results
Cavin 2005	Retrospective comparative study	UK, A&E admissions n=400	Pharmacist based in A&E	Junior doctor medication history	Accurate medication history I1: 100% I2: 12.5% **Errors per 100 patients** No error rates reported	Doctors unaware they would participate in study but pharmacist was aware. Pharmacist had access to doctors history and medication chart. Pharmacist medication history considered 'gold standard' but not verified by additional source.
McFadzean 2003	Prospective, comparative	UK, medical admissions	Clinical pharmacists taking	Junior doctor medication	**Prescribing errors:** I1: 3/60 patients	'gold standard' in place to verify medication histories.

Study	Study Design	Participants/ Settings n	Interventions I1:	Control I2	Outcomes	Reviewers comments
	study	ward n=120	drug history	history	I2: 39/60 patients **Histories with drug allergies recorded:** **I1:** 56 (93%) **I2:** 13 (23%) **Average time to write medication history and drug chart:** **I1:** 32 mins **I2:** not reported **Errors per 100 patients** I1:5 I2: 65	Doctors unaware of participation in study.
Akwagyriam 1996	Propective study	UK, inpatients admissions through A&E n=33	Pharmacist	A&E SHO	**Omissions** **Number of currently prescribed drugs identified** **I1:** 125 **I2:** 77 Rate of omission: 62% **Over the counter drugs prescribed:** **I1:** 33 **I2:** 4 **Previous adverse drug reactions:** **I1:**17 **I2:** 6 **Length of interview:** 11.8 (5.8) mins (unclear – this appears to just refer to pharmacists) In six cases the extra information gathered by the pharmacist may have contributed to the need for admission.	We don't know how many omissions the pharmacist made or whether the doctor had deliberately decided not to record the drug. We also don't know if the process of remembering drugs taken favoured second interview by pharmacist. Pharmacist may have had doctors notes when they conducted their own interview, therefore not fair comparison. In addition the questionnaire that the pharmacists used may have provided prompts for elucidating a full drug history.

Study	Study Design	Participants/ Settings n	Interventions I1:	Control I2	Outcomes	Reviewers comments
					Omission errors per 100 patients I2: 136	

3.5 Methodological Quality of Included Randomised Controlled Trials

Only one randomised controlled trial was included in this review.[12] It did not describe the method used to randomise and it is not clear whether the trial concealed allocation or used blinding at outcome assessment. It did not describe any participants withdrawing from the trial and any loss to follow-up.

3.6 Methodological Quality of Non-randomised Studies

The quality criteria checklist sought to ascertain the external and internal validity of the included studies by exploring how representative the findings can be to a broader patient group and the extent to which their findings are subject to bias.

Five studies[19,21,22,20,23] limited their inclusion criteria to patients who were admitted during office hours and not at weekends. In five it was not reported clearly in the text.[13,14,17,16,15] In six studies the inclusion and exclusion criteria was not clearly described.[22,23,18,17,16,15]

Patients were selected consecutively in six studies as each admission was included in the study.[13,14,19,21,22,20] In five studies the method for selecting patients was not evident from the text.[23,18,17,16,15]

Only three studies reported sufficient information to assume the studies were comparable at baseline and did not introduce factors that distorted the comparability of the groups.[22,18,17] Methodological features that may have biased the results included the comparison of retrospective data with prospective data,[13] the control arm of one study may have included out of hours admissions,[21] professionals participating in the intervention arm of the study aware of their participation whilst the professionals in the control arm were not,[21] the impact of one professional having access to the records of another professional in the intervention arm but not in the control arm.[23]

In three studies the problems of comparability were in part addressed by using the same patients for both arms of the study,[22,20,23] however this may also have introduced factors that could have biased the results. Patient's ability to recall their medications may have been altered by having to firstly go through their medication history with one professional before being questioned later by a second professional.

Seven studies used an external 'gold standard' against which to compare both arms of the intervention[13,19,22,20,18,17,15] providing a more meaningful assessment of the effectiveness of both interventions in the studies. Four studies used the pharmacist's assessment as both a comparator and the standard to which the other intervention was compared.[14,21,23,16]

None of the studies described methods to blind at outcome assessment. Six studies did not have any patients withdraw from the study or lost to follow-up.[14,19,21,22,20,18] Two did report this information[13,23] and in three it was not reported.[17,16,15]

4. Cost Effectiveness

4.1 Background

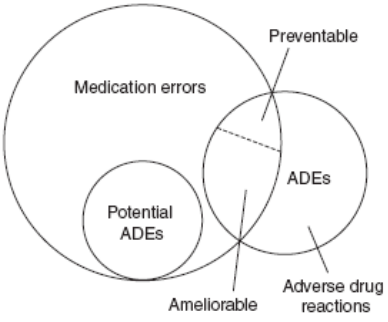
The systematic review of the medicines reconciliation literature identified a range of studies that investigated the effectiveness of alternative methods for improving the medicines reconciliation process. Most of the interventions involved the additional use of pharmacists to assist in the taking of patients' medication histories on admission to hospital. No economic evaluations of such interventions were identified.

The objective of the presented economic evaluation is to estimate the incremental cost per QALY gained of alternative interventions aimed at improving the medicines reconciliation process on admission to hospital. The interventions included in the analysis are informed by the literature review presented in the previous sections. The analysis is presented from the perspective of the UK National Health Service (NHS) and includes only costs incurred by the health service. Relevant costs and outcomes are discounted at an annual rate of 3.5%.

The economic evaluation of interventions aimed at preventing, or reducing the impact of medication errors is usefully informed by the distinctions represented in Figure 1, which was developed by Morimoto and colleagues.[29] Four categories of medication errors are defined: no harm caused and no potential for harm, no harm caused but potential for harm existed, harm caused that could and the severity or duration or harm could have been substantially reduced if different actions had been taken, and harm caused that could have been prevented. The recognition of ameliorable ADEs is a relatively new concept and one that is not reflected in most empirical studies, so the current analysis does not distinguish between preventable and ameliorable ADEs.

Non-preventable ADEs are defined as adverse drug reactions, where no error occurs, for example, an allergic reaction in a patient not previously known to be allergic to the medication.

Figure 1 Structural relationship between medication errors and adverse drug events[29]



The standard quality adjusted life year (QALY) paradigm for the economic evaluation of health care technologies incorporates only the effects that impact on a patient's well being (survival and/or quality of life effects). Applying this paradigm to the evaluation of medicines reconciliation interventions, an analysis would measure the

benefits of an intervention in terms of the QALYs gained as result of reducing events that cause harm to the patient. Incorporating the effects of medication errors that do not result in harm into a unitary outcome measure is beyond the scope of this evaluation, and so rates of medication errors are presented separately.

4.2 Methods

The economic analysis used an adapted version of a previously developed medication errors model. This model was developed to inform research priorities into reducing the impact of medication errors across secondary care by identifying interventions with the greatest potential for the cost-effective reduction of the impact of medication errors on costs and health outcomes from the perspective of the NHS. The initial model structure covered three phases of hospital care at which medication errors could occur: prescribing, dispensing, and administration. At each stage four error types were described. Subsequent to the occurrence of an error, the error could be detected prior to reaching the patient. If the error reached the patient, it was assigned a probability of causing harm, categorised into minor, moderate, and severe.

Prior estimates of the model's parameters (error incidence, detection, and probability of harm parameters) were estimated from a wide ranging literature review. However, significant gaps in the model remained and so the model was calibrated to calculated values for preventable ADE rates by type and stage of origination in the medication pathway. Resource requirements for potential interventions, the additional treatment of ADEs, and monetary valuations of the health effects of ADEs on patients were also included in the analysis.

The original model described the incidence of pADEs that occurred as a result of errors originating at different stages of the medication pathway within hospital. Four alternative prescribing errors were described by the original medication errors model: wrong drug, wrong dose, wrong route, and wrong frequency. The adapted model is specific to errors occurring as a result of errors in the medicines reconciliation process, and describes the incidence and pathway of the most common errors in that process. The choice of error types included was based on an analysis of the most common error types occurring at the reconciliation stage, combined with an assessment of the error types most likely to result in a pADE.

The literature on pADEs was reviewed to identify the most common error types implicated in the occurrence of pADEs. Winterstein et al collected 2571 ADR reports from 1994 through 2000 from a US teaching hospital's ADR database.[30] 317 reports of pADEs occurring in 275 inpatients were analysed, including an analysis of the error types that caused the ADEs (some ADEs had multiple error type categories). The most common error type was an inappropriate dose, route, or frequency of administration (216, 49%), followed by known drug interactions (18.6%) and inadequate monitoring (17%). Known allergies were documented in 3.7% of cases, and inappropriate drugs in 2.8% of cases. Interestingly, errors of omission were not defined within any of the 8 categories, implying that such errors were not responsible for any of the 317 preventable ADEs.

Other studies of preventable ADEs by error type have similarly not found any ADEs that were caused by an error of omission.[31,32] Another study of medication errors identified 202 errors of omission, but did not define any of these as significant errors

(i.e. as having potential for adverse consequences and a reasonable potential to be carried out as ordered).[33]

Bobb et al identified 16 errors of omission within 342 errors that were either rated as likely to have required monitoring (214) or likely to have produced patient harm (128). It is not clear whether this definition of significant errors incorporates any judgement as to the likelihood of the errors being detected.[34]

As noted by Winterstein et al, non-identified known allergies do appear to have significant potential for causing harm. Lesar et al identified 61 allergy errors, all of which were defined as significant errors.

A literature review that included an assessment of types of errors related to pADEs found that the majority of reported pADEs were attributed to errors of commission. Only four studies reported errors of omission in addition to errors of commission. However, the description of omission errors that were associated with pADEs did not mention drugs omitted from patients' medication history, but included underdoses or missed doses, and failure to recognize, prevent, or treat a disease or symptom).[35] Table 4 presents the median and ranges of the percentages of pADEs by error type.

Table 4 Median (ranges) of the percentages of pADEs by error type

Error type	Median (range)
Overdose or underdose	22.4 (7.9-29.6)
Inappropriate drug	17 (9.0-20.9)
Inappropriate drug administration	16.5
Inadequate patient monitoring	12 (1.8-46.7)
Wrong frequency	8.8 (4.6-12.9)
Known allergy	6.9 (5.7-8.1)
Lack of preventive therapy	6.7
Missed dose	6.1 (5.0-7.2)
Drug-drug interaction	2.8 (2.7-2.8)
Other	12.2

The literature indicates that few pADEs occur as a result of omitted drugs (i.e. drugs patients were receiving before admission that are not prescribed in hospital). However, as these are one of the most frequently cited error types occurring at the medicines reconciliation stage, drug omission is included as a category of error. The other defined error types include errors of commission and known allergy errors. Known allergy errors are assumed to originate from errors in recording patients' allergies on admission. Technically, ascertaining allergies is not medicines reconciliation, but it is a closely linked task and some of the intervention studies refer to improvements in allergy ascertainment.

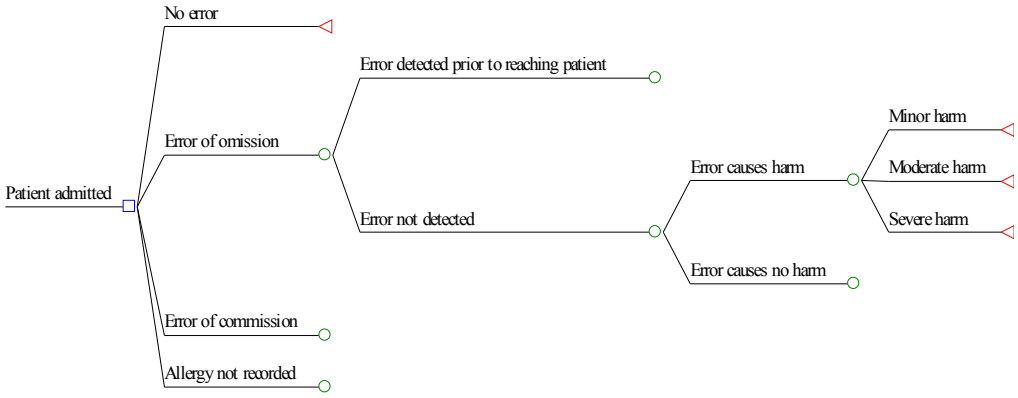
The decision to aggregate the wide range of drug errors of commission into a single category was due to the following reasons:

- few of the intervention studies presented separate error rates for different error of commission types
- of the studies presenting separate error rates, wrong dose or strength was by far the most common error of commission.[14,23]
- there is very little evidence to inform alternative estimates of detection, and probability of harm, for different types of errors of commission

The general process of populating the adapted model is the same as for the original model, requiring the estimation of following input parameters as represented in Figure 2, which presents the defined model structure describing the incidence and progression of errors that occur during the medicines reconciliation process:

- incidence rates of alternative medication error types occurring during medicines reconciliation
- detection rates for the defined prescription medication errors
- probabilities of harm, and severity of harm for errors that remain undetected and reach the patient.

Figure 2 Medication errors model structure



The latter two parameter categories combine to predict the rate at which errors convert into pADEs. The distinction is made in order to estimate, albeit with very large uncertainty, the number of errors that reach the patient.

In addition, to calibrate the model it is necessary to estimate the rates of pADEs occurring as a result of the defined error types at the medicines reconciliation stage of the secondary care pathway. The following sections describe the data, analyses, and assumptions used to populate each of the above parameter categories.

4.3 Incidence of alternative medication error types

In estimating the frequency of medication errors occurring at the point of admission, it is important to distinguish between errors in the obtained drug histories and prescription errors. An example is the case where a drug history does not note the

dose of a drug prescribed prior to admission – this may not lead to a prescription error as the appropriate dose may be investigated before the prescription order is made.

The estimation of the baseline rate of prescription errors occurring due to deficiencies in medicines reconciliation (including notification of drug allergies) was informed by the control arm of the only UK intervention studies that included an independent assessment of errors. McFadzean et al[20] undertook a prospective audit of drug histories undertaken by junior doctors and by clinical pharmacists, and employed a research nurse and pharmacist to assess the accuracy of drug charts in both arms of the study. It is assumed that the error rates observed in the junior doctors arm, who were unaware of the study, are representative of the baseline error rates with no specific intervention in place.

The study identified 110 prescribing errors (1.83 per patient) in 39 patients (65%), of which 78 errors (71%) were errors of omission. The study also noted that drug allergies were recorded for only 13 (23%) patients. In the intervention arm drug allergies were recorded in 93% of patients, indicating that some reference to drug allergies should be made in all cases. It is assumed, therefore, that drug allergies are not recorded in 77% of patients in the baseline scenario.

The medication errors model requires estimates of the rates of errors per prescription order, as prescription orders are the denominator for the rate of pADEs against which the model is calibrated. A recent audit undertaken at the Royal Hallamshire Hospital in Sheffield reported the mean number of regularly prescribed items to be 8.44 in a general hospital population.[36] To account for additional 'when required' and single doses, this figure is rounded up to 9, which is taken as the average number of prescription orders received per inpatient stay. No information on the number of prescription orders received at the start of an inpatient stay (i.e. after the medicines reconciliation process) was identified. It is assumed that two thirds of prescription orders (6) are received following admission, with a range of 4 to 8. Thus, the mean rate of errors per prescription order is estimated to be 1.83 / 6 = 0.3 (0.23 to 0.46). Table 5 presents the error rate ranges estimated for the three error type categories.

Table 5 Error rate frequencies per prescription order following admission

Error type	Error rate per patient	Error rates per prescription order		
		Mean	95% CI	
Errors of omission	1.30	0.4	0.3	0.59
Errors of commission	0.53	0.16	0.12	0.24
Errors due to known allergies	0.23	0.07	0.05	0.11

4.4 Detection rates for medication errors at subsequent stages of the medication pathway

Five studies were identified that presented a wide range of detection rates, which is likely to be due to differences in the definition of undetected errors and methods of data collection. In the US, Kaushal et al[37] and Bates et al[31] presented detection rates for potential ADEs (errors that had the potential to cause harm if undetected) of 68% and 57%, respectively. In a UK study, Wilson et al reported that around 68% of all errors were detected,[38] though only 2% of undetected errors resulted in additional actions undertaken as a consequence of the error (i.e. pADEs). The proportion of

detected errors that had the potential for harm was not presented. The studies reported by Kaushal et al, and by Wilson et al, were undertaken in paediatric wards. Dale et al[39] presented a lower detection rate of 18% for all prescription errors on a control (baseline) ward. Scarsi et al[40] presented similarly low detection rates in their control group, where 12.5% of all prescription errors were detected.

Though the study by Wilson et al was conducted in the UK, it is the least methodologically rigorous study. The other studies involved the prospective identification of errors, whilst Wilson et al relied on error reports and was therefore likely to significantly underestimate error incidence.

As the medication errors model describes the pathway of all errors (not just those with the potential to cause harm), it is likely that the relevant detection rates are lower than the reported detection rates for potential ADEs[31,37] which are a subset of all medication errors. The estimated detection rates are based, therefore, on the aggregate rates reported by Wilson,[38] Dale[39] and Scarsi,[40] with adjustments for the higher detection rate for prescription errors reported by Scarsi et al as well as the calibrated detection rates from the previous medication errors model. The differentiation between the error types is informed by the relative likelihood of pADEs being caused by the different error types (as described in the following sections). The estimated ranges are presented in Table 6.

Table 6 Detection rate input parameter values

Parameter	Range
Error of omission	40-70%
Error of commission	20-50%
Allergy not documented	40-70%

4.5 Probabilities of harm, and severity of harm for errors that reach the patient

The severity of the impact of undetected errors on patients' health is a key parameter determining the potential cost-effectiveness of medication error interventions. Studies have used different thresholds for the potential severity of medication errors when collecting error data or reporting the number of errors that reached patients undetected. Some studies report all errors, whilst others report only those errors that have the potential to cause harm,[31] or have the potential to cause harm and have a non-negligible probability of remaining undetected.[41] In the current analysis, errors that reach the patient may be in one of three categories: errors that do not have the potential to cause harm (non-potential ADEs); errors that have the potential to cause harm, but do not cause harm (potential ADEs); and errors that cause harm (preventable ADEs).

In a UK study, Wilson et al[38] provide some evidence around the proportion of undetected errors without the potential for harm, which showed that 9 of 143 (6.3%) undetected errors were classified as requiring increased monitoring or worse. As noted above, this study relied on error reports and so is subject to the assumption that probabilities of harm are similar in reported and unreported errors.

Kaushal et al[37] and Bates et al[31] present data describing the numbers of non-intercepted potential ADEs and the number of pADEs, from which the proportion of undetected errors with the potential for harm that actually cause harm can be estimated. In aggregate, Kaushal et al reported that 9.6% of non-intercepted ADEs with the potential to cause harm actually caused harm in a paediatric unit, the corresponding figure reported by Bates et al for all units was 38.5%.

As the model is not limited to potential ADEs, the estimated ranges for the probabilities of harm are set lower than those reported by Bates et al (for all inpatient potential ADEs), as described in Table 7.

Table 7 Original and revised values for 'probability of harm' input parameters

Parameter	Range
Error of omission	0.1-1%
Error of commission	1-5%
Allergy not documented	0.1-1%

The relevant results of five studies reporting the severity of preventable ADEs are presented in Table 8. The error frequency model requires estimates of severity only for pADEs that reach the patient, so the most relevant sources are the two studies reported by Bates and colleagues.[31,42] The weighted average proportions from these two studies are 20% fatal/life threatening; 41% serious; 39% significant.

Table 8 Reported medication error and ADE severity

Author	Setting	Event definition	Fatal/life threatening		Serious		Significant	
			No.	%	No.	%	No.	%
Bates[42]	General inpatient	Preventable ADEs	14	20%	30	43%	26	37%
Bates[31]	General inpatient	Preventable ADEs	1	20%	1	20%	3	60%
Kaushal[37]	Paediatrics	Preventable ADEs	0	0%	4	80%	1	20%
Gurwitz[43]	Nursing home	Preventable ADEs	26	9%	145	53%	105	38%
Weingart[44]	General medical	Preventable ADEs	0	0%	3	100%	0	0%
Bates[31]	General inpatient	Intercepted potential ADEs	0	0%	2	12%	15	88%
Kaushal[37]	Paediatrics	Intercepted potential ADEs	16	24%	28	41%	24	35%
Bates[42]	General inpatient	Non-intercepted potential ADEs	13	12%	43	39%	55	50%
Bates[31]	General inpatient	Non-intercepted potential ADEs	4	19%	5	24%	12	57%
Kaushal[37]	Paediatrics	Non-intercepted potential ADEs	2	4%	24	51%	21	45%
Gurwitz[43]	Nursing home	Potential ADEs	16	9%	149	79%	23	12%
Gandhi[45]	Outpatient	Preventable or ameliorable ADEs	11	6%				

4.6 Rates of pADEs occurring as a result of the defined error types

The pADE literature reviewed above to estimate the proportion of pADEs that occurred as a result of alternative error types was also analysed to inform the rate at which these pADEs occur. These rates were informed by estimates of the proportion of pADEs occurring at different stages of the medication pathway and the aggregate pADE rate.

Four studies reported the proportion of ADEs that originate at different stages of the medication process. The four main stages defined by these studies include ordering, transcription, dispensing, and administration, of which the most relevant stages from a UK NHS perspective are the ordering, dispensing, and administration stages. Table 9 presents the adjusted proportions of errors originating from these three stages.

These data show that fewest ADEs originate at the dispensing stage, but that there is variation between studies over the proportion of ADEs that originate at the ordering and administration stages. The proportion of events originating as ordering errors ranges from 0.41 for preventable and potential (intercepted & non-intercepted) ADEs in ICU to 0.91 for potential ADEs in paediatrics.

Table 9 Stage of origination of medication errors and ADEs

Study	Setting	Definition	No.	Prescription	Dispensing	Administration
Bates[46]	General	ADEs	27	0.60	0.04	0.36
Kaushal[37]	Paediatrics	Errors	616	0.84	0.01	0.14
	Paediatrics	Potential ADEs	120	0.91	0.04	0.05
Cullen[47]	Non-ICU	Preventable & potential ADEs*	106	0.46	0.14	0.40
	ICU		158	0.41	0.11	0.48

* intercepted & non-intercepted ADEs

Six studies were identified that reported aggregate rates across error types and medication stages for variously defined ADEs, including preventable ADEs, non-intercepted potential ADEs, intercepted potential ADEs, and all potential ADEs. All of the studies were undertaken in the US, one study was specific to paediatrics. Only two studies report ADE rates with prescription orders as the denominator,[31,37] with the majority reporting errors per 1,000 patient days. The rates per 1,000 patient days presented by the other four studies are converted to rates per 1,000 patient days using the average of the ratio of days to orders presented by three papers,[31,37,48] with ranges presented that are based on the range of the ratios. The adjusted data are presented in Table 10.

The adjusted rate for Bond appears to be an outlier,[49] and whilst the adjusted rates are generally higher than the reported rates per 1,000 orders it appears that the preventable ADE rate is unlikely to be above 3 per 1,000 orders. The highest combined intercepted and non-intercepted potential ADE rate is 6.1 per 1,000 orders.

Table 10 Aggregate ADE estimates

Author	Data period	Inpatient setting	NISME definition	No. Errors	Error rates
Bates[46]	Pub 1993	General	Preventable ADEs	12	1.3 (0.7-1.8)*
	Pub 1993	exc.Obstetrics	Preventable ADEs	12	1.7 (0.9-2.2)*
Bates[42]	1993	General	Preventable ADEs	70	1 (0.5-1.4)*
Bates[31]	1993	General	Preventable ADEs	5	0.5
Bond[49]	1992	General	Preventable ADEs		13 (6.8-17.6)†
Cullen[47]	1993	Medical ICU	Preventable ADEs	15	2 (1.1-2.7)*
	1993	Surgical ICU	Preventable ADEs	14	1.5 (0.8-2)*
	1993	Medical	Preventable ADEs	41	0.8 (0.4-1.1)*
Kaushal[37]	1999	Paediatrics	Preventable ADEs	5	0.05
Cullen[47]	1993	Medical ICU	Potential ADEs	46	6.1 (3.2-8.3)*
	1993	Surgical ICU	Potential ADEs	31	3.2 (1.7-4.4)*
	1993	Medical	Potential ADEs	117	2.4 (1.3-3.3)*
Bates[42]	1993	General	Non-intercepted potential ADEs	111	1.7 (0.9-2.3)*
Bates[31]	1993	General	Non-intercepted potential ADEs	8	0.8
Kaushal[37]	1999	Paediatrics	Non-intercepted potential ADEs	47	0.44
	1999	Paediatrics	Intercepted potential ADEs	68	0.63

All studies were undertaken in the US
* converted from rates per 1,000 patients days
† converted from rates per occupied bed year

The range of aggregate preventable ADE rates is estimated to be between 1 and 4 per 1,000 orders. Lower and upper bounds of the proportion of preventable ADEs originating at the prescription stage are defined as 0.5 and 0.85, respectively. Thus, the range for rate of preventable ADEs originating at the prescription stage is between 0.5 and 3.4 per 1,000 orders.

To use these estimates of the pADE rate in the context of errors in the medicines reconciliation process, it is assumed that:

- Individual patients experience no more than 1 pADE
- The rate of pADEs per 1,000 orders at admission is the same as the estimated rate of pADEs for all prescription orders
- The distribution of error types responsible for pADEs occurring as a result of errors at admission is the same as the estimated distribution of error types for all prescription order-related pADEs

The data on the median proportion of pADEs by error type (presented in Table 4[35]) was used to estimate the distribution of pADE error types using the following assumptions:

- the 'inappropriate drug administration' and 'missed dose' errors are removed as these are most likely to describe errors occurring at the administration stage
- one quarter of the 'other' error type category was assumed to represent 'errors of omission', as these errors were not explicitly represented. The other three quarters of the 'other' errors were assumed to be errors of commission
- the remaining median percentages were weighted proportionately so that they summed to 100
- the specified ranges from the review paper were combined with assumed ranges for three of the error types. Values were randomly sampled from assumed uniform distributions for each error type, which were proportionally adjusted to sum to 100. The 95% confidence intervals from 5,000 sets of sampled values were estimated to represent the uncertainty in the distribution of error types according the three specified categories.

The results of the above analysis are presented in Table 11, which show that errors of commission are the dominant error types causing pADEs.

Table 11 Distribution of error type-related pADEs

Error type	Median	Range	
Overdose or underdose	25.2	8.9	33.3
Inappropriate drug	19.1	10.1	23.5
Inadequate patient monitoring	13.5	2.0	52.6
Wrong frequency	9.9	5.2	14.5
Known allergy	7.8	6.4	9.1
Lack of preventive therapy*	7.5	6.0	9.0
Drug-drug interaction	3.2	3.0	3.2
Other (error of commission)*	10.3	5.3	15.3
Other (error of omission)*	3.4	1	5.8
Sum	100	95% CI	
Total errors of omission	3.4	1.0	6.1
Total errors of commission	88.8	84.2	93.0
Total errors due to known allergies	7.8	5.2	10.7

* assumed ranges

4.7 Calibration methods

The process of calibration for the medication errors model involved sampling a large number of sets of input parameter values (10,000), collecting the associated output parameter values, and comparing each set of outputs to the observed range of output values for the 3 pADE rates. The number of sampled input parameter sets was chosen on the basis of providing a reasonable sample, without overloading the software used to analyse the model [Microsoft Excel 2003].

The comparison between the predicted and observed outputs is based on the differences between the predicted output parameters and the estimated 95% confidence intervals (CIs) for the rate of pADEs occurring as a result of each error type. The difference for each output parameter value is estimated as:

- if a predicted output parameter is within the estimated CI for that parameter the difference is zero
- if the predicted value is below the estimated CI, the difference is estimated as the 'lower bound value minus the predicted value'
- if the predicted value is above the estimated CI, the difference is estimated as the 'the predicted value minus the upper bound value'

The first stage of the calibration process involves identifying eligible input parameter sets. Eligibility is defined as sets that predict aggregate pADE rates that fall within the estimated 95% CIs for all pADEs originating from errors occurring as a result of deficiencies in the medicines reconciliation process. Within the eligible set, the following steps involve:

- summing the distances for each of the 3 output parameters to estimate the aggregate absolute difference
- defining the reciprocal of the aggregate difference (1 divided by the difference) as the weight for each input parameter set that reflects how closely each set predicts the observed output parameter values (for iterations with a sum of differences of zero, the weight is assumed equal to the weight for the lowest non-zero sum of differences)
- probabilities that each input parameter set is the optimal set (i.e. the set that most accurately predicts the estimated output parameters) are defined as the estimated weight for each parameter set divided by the sum of the weights across all eligible sets.

4.8 Calibration results

Given the input parameter ranges specified in the above sections, the calibration process identified 2,328 eligible input parameter sets from the 10,000 sets that were analysed. The weighted mean and 95% CIs for the input parameters within the eligible sets are presented in Table 12.

Table 12 Mean and 95% confidence intervals for included input parameters

Input parameters	Mean	Lower 95% CI	Upper 95% CI
Error probabilities per prescription order			
No error	0.382	0.204	0.479
Errors of omission	0.364	0.302	0.551
Errors of commission	0.173	0.123	0.234
Errors due to known allergies	0.081	0.051	0.109
Prescription error detection probabilities			
Errors of omission	0.617	0.433	0.699
Errors of commission	0.379	0.224	0.490
Errors due to known allergies	0.558	0.415	0.693
Probabilities of harm for undetected errors			
Errors of omission	0.001	0.001	0.002
Errors of commission	0.020	0.011	0.036
Errors due to known allergies	0.005	0.001	0.010

4.9 Intervention effectiveness

Intervention effectiveness was described as the relative risk (RR) of medication errors occurring with an intervention in place compared to the baseline scenario, which then feeds through the model to estimate the corresponding reduction in pADEs.

In line with the structure of the literature review in the previous chapters, separate estimates of effectiveness were derived within three broad categories of intervention aimed at preventing errors during the medicines reconciliation process: pharmacist involvement in the medicines reconciliation process; medicines reconciliation package involving the development of a standardised medication form; and IT based/Information transfer initiatives. However, three separate interventions within the medicines reconciliation package category were evaluated (described below).

As discussed in the review section, the variation in methods, settings, and definitions precluded any meaningful combination of the results of studies evaluating similar interventions. As such, the effectiveness parameters for the economic evaluation are defined as subjectively defined ranges describing the relative risk (RR) of medication errors with the interventions in place compared to the baseline scenario of no specific intervention.

The defined RRs were applied to all error types as it was not considered feasible to estimate alternative levels of effectiveness for different types of errors. It is also necessarily assumed that the relationship between medication errors and pADEs is constant, i.e. a reduction in the incidence of medication errors leads to a proportional reduction in the incidence of pADEs.

Five UK-based studies evaluated the effectiveness of pharmacist involvement in the medicines reconciliation process, though only two studies used a third source to verify the errors found in both the pharmacist and the physician's medical history.[22] In contrast to all the other studies, Collins et al found that pharmacists found fewer additional medicines than was on the drug chart (128 per 100 medications) than the drug chart found in addition to those found by the pharmacist (137 per 100 medications). It is stated that the majority of the cases in which physicians identified

additional medicines were cases in which the pharmacist had been unable to obtain histories. Though a third source was used (contacting GPs, nursing homes, etc.), the medicines identified from the third source were not compared in any useful way to the physician or pharmacist histories. This study did show that histories undertaken by physicians were quite different to the prescriptions made on drug charts. It is also likely that there will be differences between pharmacist histories and the medications that end up on drug charts. This indicates that emphasis should be placed on studies that compare drug charts of separate cohorts of patients based on baseline drug histories and, in this case, pharmacist-based interventions.

McFadzean et al did include separate patient cohorts and found a higher error rate in physicians (5 vs 65 errors per 100 patients), whilst drug allergies were recorded in 23% and 93% of physician and pharmacist-based charts.[20] These results lead to RRs of 0.08 and 0.09 for prescription errors and allergy recording, respectively. As in the Collins study, the physicians were unaware that they were participating in a study while the pharmacists were aware.

The only RCT compared a pre-operative structured pharmacist medication assessment with standard care in Canada[12] The pharmacist assessment reduced the number of patients with at least one medication discrepancy from 43.6% to 19.5%, a RR of 0.45.

The RR reported by McFadzean et al is increased to account for the potential biases arising from the study design. A mean RR of 0.25 is specified for additional pharmacist involvement, with a 95% CI of 0.10 to 0.40 to represent uncertainty.

Three US-based studies evaluating medicines reconciliation packages were reviewed. The interventions included:

- a combination of standardised forms, pharmacy technicians, and hospital policy initiative to improve the quality of orders. [18] Defects per drug order reduced from 0.25 to 0.12, a RR of 0.48.
- the use of nurses to take medication histories aided by a standardised form.[16] errors per admission decreased from 213 to 80, a RR of 0.375.
- a systematic medicines reconciliation process (involving the computerised assessment and feedback to physicians of patients' medication profiles by a pharmacist).[17] A RR of 0.43 for patients with order discrepancies

The included evidence on IT based systems was restricted to one UK based before and after study that evaluated the transfer of current medication and other relevant information by fax from the GP practice to the admitting ward.[15] The fax system reduced the number of incorrect medication sheets by 69% with errors falling from 55 per 100 patients to 17, a RR of 0.31. Assuming this is representative of reductions in medication errors, a subjectively defined 95% CI of 0.11 to 0.51 is specified to represent uncertainty.

The set of interventions evaluated and their corresponding RRs (and 95% CIs) for reductions in error rates are presented in Table 13. The summary data for the RRs are represented as log normal distributions in the model, as these distributions are bounded at zero and have a long tail representing the small likelihood of limited, and even negative effectiveness.

Table 13 Intervention effectiveness relative risks for the prevention of medication errors occurring as a result of medicines reconciliation

Intervention	Mean	95% CI	
Pharmacist-led reconciliation	0.25	0.1	0.4
Standardised forms, pharmacy technicians, hospital policy	0.48	0.33	0.63
Nurses taking histories with standardised form	0.375	0.225	0.525
Computerised assessment and feedback by pharmacist	0.43	0.28	0.58
Current medication faxed from the GP practice	0.31	0.16	0.46

4.10 Cost and quality adjusted life year (QALY) effects

This section describes the cost and QALY parameters used in the medication errors model. Cost parameters are restricted to the costs of implementing the interventions for which effectiveness estimates were estimated (as reported in the previous section), and costs associated with the treatment of pADEs or additional monitoring to prevent pADEs as a result of medication errors. QALY effects are estimated as the QALYs lost as a result of the harmful effects of pADEs. Separate cost and QALY effects are estimated for the different severities of pADES, defined as:

Significant: resulted in temporary harm to the patient and required intervention

Serious: resulted in temporary harm to the patient and required initial or prolonged hospitalisation

Severe, life threatening, or fatal: resulted in permanent patient harm, required intervention to sustain life, or contributed to a patient's death.

Interventions may have some additional cost savings related to reductions in ancillary test usage (mostly laboratory) and reductions in length of stay via guideline embedding and variance analysis. However, these potential savings are not included due to a lack of evidence.

The following sections describe the data, analyses and assumptions used to estimate the necessary cost and QALY parameters.

4.11 Intervention implementation costs

The following sections describe the methods and estimated implementation costs for a range of medication error interventions. The cost are estimated as additional costs relative to the baseline scenario.

The main cost of a system of pharmacist-led medicines reconciliation is assumed to be the additional time requirements for the pharmacists. Dutton et al report that the mean time spent on a ward per day was 68.8 minutes (95% CI 60.8-76.8) in the routine practice phase, which involved checking drug charts but not taking medication histories. This increased to 150.4 minutes (95% CI 139-161.8) in the intervention phase in which pharmacists visited the ward twice daily and did take medication histories. The average ward is assumed to contain 30 beds, whilst the average length of stay is reported as 8.1 days (Department of Health, Hospital Episode Statistics,

2001-2). Thus, 3.7 new patients would be expected to be admitted to a 30 bed ward each day. The mean additional time per patient receiving pharmacist-led medicines reconciliation is (150.4 – 68.8) / 6 = 22 minutes. Assuming a 95% CI of 2.2 to 5.2 for daily admissions, the 95% CI for time per patient is 12 to 46 minutes.

An hourly cost of a pharmacist of £28 is based on the mid-point of Agenda for Change (AfC) salaries band 6 of the April 2005 pay scale.[50] The mean cost per patient receiving pharmacist-led medicines reconciliation is £10.28 (95% CI £5.58 to £21.39).

The second intervention evaluated involved the use of standardised forms, pharmacy technicians, and the implementation of new hospital policy aimed at improving the quality of medicines reconciliation.[18] Michels & Meisel state that the most experienced technicians were chosen for this role, though no details of the time spent in the role were provided. The time costs were assumed to be similar to that reported by Dutton et al for pharmacists. The hourly staff cost was based on the midpoint of the AfC salaries band 5, which is 19% less than the band 6 cost of a pharmacist. Thus, the cost per patient is estimated to be £8.33 (£4.52 to £17.33).

The costs of the other elements of this intervention are less tangible. It is assumed that the development and maintenance of the standardised form requires the equivalent of one week's work of a pharmacist (£1,050) each year. Based on a 14 ward, 420-bed hospital, the expected number of new admissions per year is 18,926 [(420*365) / 8.1] the assigned development and maintenance cost of the form is £0.06 per admission.

The implementation of a new hospital policy is assumed to incur costs of dissemination, equivalent to 15 minutes of every prescriber's time per year. The policy impacts on all prescription orders, not just those following admission. In line with previous assumptions, it is assumed that two thirds of prescription orders are completed on admission and so two thirds of the policy-related costs are assigned to the interventions effects on improved medicines reconciliation.

The number of beds in the NHS was 145,218 in 2004,[51] and the number of hospital doctors employed in 2005 was 78,000.[52] The mean numbers of doctors per hospital bed is 0.54, so in a 420 bed hospital 226 doctors would be expected to be employed. The total cost of disseminating a new hospital policy is estimated to be £3,045, based on the salary costs of a specialist registrar (£54 per hour on duty). The cost per admission is £0.11 [(18,926 x 0.66) / 3045].

The third intervention involves nurses taking histories with a standardised form. In the US, Nester et al found that pharmacists and nurses took mean lengths of 13.4 and 24.3 minutes to obtain medication histories, respectively.[53] Applying the 81% increase in time to the previously estimated times for UK pharmacist-led medicines reconciliation, the mean time for a nurse-led medicines reconciliation is 40 minutes (95% CI 16.3 to 103.9, assuming a 25% decrease and increase in the additional time required, respectively). Using the AfC salaries mid-point for Band 5, the hourly cost of a nurse on a day ward is £22,[50] so the cost per patient is £14.65 (£5.96 to £38.09). The same cost per admission of £0.06 to develop and maintain the standardised form is assumed.

The fourth intervention involved computerised assessment and feedback by a pharmacist to inform doctor-led medicines reconciliation. This intervention is very difficult to cost, but it is assumed that additional staff includes 11 minutes per admitted patient of pharmacists' time (half the amount required to take a medication history), and an additional 5 minutes of prescribing physicians' time. The total additional cost per admission is estimated to be £9.63 (95% CI £7.2 to £12.04, based on a 25% decrease and increase, respectively). The cost of setting up the computerised system is based on estimated costs of setting up a Computerised Physician Order Entry (CPOE) system, which was estimated to cost between £0.35 and £4.9 million to develop, and £0.12 to £1 million to maintain each year.[54] The lower bounds for the CPOE system are taken as the upper bounds for setting up a more specific, simpler computerised system. Lower bounds are specified as one quarter of the upper bounds. Assuming a 10-year useful life for the system, annuitised at 3.5%, the annual development cost is estimated to be between £6,914 and £27,656. Adding maintenance costs, the annual cost increases to between £36,914 and £147,656. The cost of the system per admission is between £1.95 and £7.80.

The final intervention assessed involved current medication lists being faxed from the patients' GP practice using a standardised form. Again, little information to guide the costing of this intervention was available. It is assumed that the development of the standardised form had similar costs to those estimated above. It is assumed that a member of the practice's clerical staff could complete the form and submit it, requiring a mean time of 10 minutes. The AfC salaries mid-point for Band 2 is assumed clerical staff, which 48% less than the band 6 cost of a pharmacist. The cost per faxed form is estimated to be £2.45 (95% CI £1.22 to £3.67, assuming a range of 5 to 15 minutes). In addition, the use of the form by the prescribing physician is assumed to add 7.5 minutes to the prescribing time at a mean cost of £4.50 (95% CI £1.22 to £3.67, assuming a range of 5 to 10 minutes).

Based on the data, analyses, and assumptions described in the preceding paragraphs, Table 14 presents the total costs of each intervention per admission, based on the use of the interventions in a single 400 bed hospital. The summary data for the costs are represented as log normal distributions in the model, as these distributions are bounded at zero and have a long tail representing the small likelihood of large costs. In the medication errors model, the intervention costs are divided by the expected number of prescriptions per admission (range 4 to 8), as the intervention costs represent the cost per admission and the model describes events per prescription order.

Table 14 Intervention implementation costs per inpatient admission (£s)

Intervention	Mean	95% CI	
Pharmacist-led reconciliation	10.28	5.58	21.39
Standardised forms, pharmacy technicians, hospital policy	8.5	4.69	17.5
Nurses taking histories with standardised form	14.71	6.02	38.15
Computerised assessment and feedback by pharmacist	14.505	9.15	19.84
Current medication faxed from the GP practice	9.26	5.78	12.73

4.12 Costs of pADEs

As with the identified costs of implementing medication error interventions, all of the identified data describing additional treatment costs for patients experiencing an adverse drug event are US-based. The identified sources are reviewed below.

Bates et al[55] undertook a case control costing study that defined two sets of cases as patients with an ADE, and patients with a preventable ADE. Controls were selected as patient on the same unit as the case with the most similar pre-event length of stay (LoS). Charges for LoS on ICU, intermediate and routine care units, as well as pharmacy, laboratory and surgery charges were converted to costs using ratios of costs to charges.

Comparing all patients who had ADEs with controls, length of stay was 2.2 days longer for patients (P=.04), total charges were $6341 higher for patients (P=.04), and total costs were $3244 higher for patients (P=.04). Differences were even greater for patients with preventable ADEs compared with controls: length of stay was 4.6 days longer for patients (P=.03), total charges were $11 524 higher for patients (P=.06), and total costs were $5857 higher for patients (P=.07). This is equivalent to an additional cost of $1,273 per additional inpatient day. The costs associated with preventable ADEs were almost twice as high as the costs for the full set of ADEs.

Pinilla et al undertook a case control study of the costs of medication errors in a Spanish hospital.[56] Based on 63 errors defined as category C or worse on the National Co-ordinating Council on Medication Error Reporting and Prevention (NCC MERP) scale (where category C describes an error that reached the patient but did not cause harm), an increased length of stay (LoS) of 7 days was identified in patients experiencing a medication error. When the analysis was restricted to the 37 patients in whom an error required additional monitoring (n=31), may have contributed to temporary injury (n=5), or may have contributed to permanent harm (n=2), the additional LoS was over 10 days. The reported mean cost difference for the cohort of 63 medication errors was €1,641, which is equivalent to an additional cost of €234 per additional inpatient day.

Classen et al[57] report a case control study to estimate the excess length of stay, extra costs, and mortality attributable to ADEs in hospitalised patients where controls were matched to cases on primary discharge diagnosis related group (DRG), age, sex, acuity, and year of admission; varying numbers of controls were matched to each case. Matching was successful for 71% of the cases, leading to 1580 cases and 20 197 controls. The unmatched case patients had higher mortality, acuity score, more

severe ADEs, and more drug exposures, but the causal drugs and types of ADEs did not differ from the cases. Cost outcomes were determined from a transaction-based microcosting system.

In the analysis of the matched cases, a linear regression model for total cost of hospitalisation that controlled for severity of illness, several DRGs, sex, and age, estimated that the mean additional cost of an ADE was $2262.

Nordgren et al[58] also used a matched case-control design to evaluate excess length of stay and costs associated with all types of errors, including falls and surgical mishaps. The mean LoS for 300 cases was 10.8 days, and the mean LoS for the 300 matched controls was 6.8 days (mean difference was 4.0 days ($p < 0.001$), 59% longer stays than the controls). The mean total variable cost for the 300 cases was $8,687, and the mean total variable cost for the 300 matched controls was $6,276. The mean difference was $2,411 ($p = .016$), which is consistent with the cost estimates reported by Bates et al.[55]

Schneider et al[59] estimated the costs of different types of medication errors, including errors requiring extra laboratory tests or treatment without an increased LoS ($95 to $227); errors prolonging length of stay ($2,596); and errors resulting in near-death experience ($2,640).

Douglas & Larrabee[60] present a range of cost estimates as part of a presentation on the use of bar coding, for which information on the source of the estimates were not identified. The Joint Commission on Accreditation of Healthcare Organisations (JCAHO) reported cost estimates of $2,000 for an ADE (excluding malpractice), whilst the Leapfrog Group (comprising more than 170 companies and organizations that buy health care in the US) reported that 1 medication error costs $10 and that 1 ADE costs $2,000. The CA HealthCare Foundation is reported to have defined the cost of a preventable ADE as $5,000.

The range of identified mean cost estimates for all ADEs is quite narrow, varying from $2,000 to around $3,300. However, the medication errors analysis is concerned with pADEs, for which only Bates et al[55] and Pinilla et al[56] present separate cost estimates. These studies show the estimated mean cost of preventable ADEs to be significantly higher than the cost of the full set of ADEs. Separate costs were estimated for preventable ADEs that are assumed to result in no additional inpatient stay (significant ADEs) and those that are assumed to require an additional period of inpatient care (serious/severe/life threatening ADEs), which are presented in Table 15.

The range of cost estimates for a significant preventable ADE that did not result in an increased LoS is taken directly from Schneider et al.[59] The cost of a serious pADE estimated using the reported additional LoS by Bates et al[55] (4.6 days) and the lower estimate of additional LoS reported by Pinilla et al (7 days). The cost of severe, life threatening, or fatal pADEs takes the 7 day estimate as the lower bound, and the upper estimate by Pinilla et al of 10 days as the upper bound. The mean NHS reference cost of £176 (95% CI £155 to £212, informed by the quartiles of the returned cost estimates) for a day spent on a non-ICU ward was applied to the LoS estimates.

A range of costs for the correction of identified medication errors is also specified, based on the estimated cost presented by the Leapfrog group, though the range does include a zero cost estimate.

Table 15 Cost parameters for preventable ADEs

Cost parameter	Range
Detected medication errors	£0 - £6
Significant (non-increased LoS) pADEs	£65 - £150
Serious pADEs	£713 - £1,484
Severe, life threatening, or fatal pADEs	£1,085 - £2,120

4.13 QALY effects

The losses of QALYs due to each category of severity of pADEs were estimated using two distinct methods. Data were available from the NHS Litigation Authority (NHSLA) describing the litigation payments to patients who have experienced adverse health consequences as a result of health service error. Using the NICE implied range of a value of a QALY of between £20,000 and £30,000 per QALY gained, the ordered litigation payments were analysed to provide a very crude estimate of QALYs lost per pADE.

The dataset contains 655 cases in which a medication error was alleged to have resulted in injury to a patient. To inform the valuation of the health effects of medication errors, only those cases that were closed (i.e. had been settled) were included. After excluding all closed cases in which the claim value was £0 (assumed to indicate that the case was not proven), the number of cases reduced to 251.

A short description of the error and the resulting injury is given for each case, which were qualitatively reviewed to identify ranges for the litigation costs for each of the three severity categories. The payouts ranged from £17 to over £0.5 million, though there seems to be little consistency, for example, the prescription of a wrong dose of phenobarbitone resulted in a payment of £140, whilst a negligent injection of phenytoin that resulted in scarring to a patient's hand was awarded £194,000. These inconsistencies may be due to the limited description provided for some of the cases.

The lowest payment made for a fatality was £387 in 1996, in which a diagnosis of bacterial endocarditis was made, high dose antibiotics did not improve the condition, the patient was transferred for mitral valve replacement and subsequently died. The highest payment for a fatality was £317,009 in 1998, which was due to medication errors from dealing with gall stones/bile duct problems.

Given the inconsistencies in the database and difficulties in linking injuries to the defined categories of injury, the payments were arranged in order and ranges for each of the three ADE severity categories are specified in Table 16, based on the reported percentiles.

Table 16 Percentile-based ranges for the value of alternative severities of preventable ADEs

ADE severity	Percentile range	Value range	QALY loss range
Significant	0.01 – 0.2	£145 - £1,951	0.005 – 0.1
Serious	0.3 – 0.6	£2,812 - £13,242	0.09 – 0.66
Severe/life threatening/fatal	0.7 – 0.99	£21,000 - £373,088	0.7 – 18.65

The QALY effects of ADEs may also be described directly. No relevant data estimating the utility effect of the broadly defined severity categories were identified. Very approximate estimates of the QALY impact may be made by assuming a utility decrement for each category and an accompanying duration of effect. The utility decrement describes the reduction in the quality of life of a patient as a result of an ADE, a utility decrement of 0.1 indicates a 10% reduction in utility relative to perfect health. If patients' health is assumed to be less than perfect in the absence of an ADE, the utility decrement of 0.1 describes a greater relative decline, for example, if pre-ADE utility is 0.5 a utility decrement of 0.1 represents a 20% decline in utility.

Table 17 describes the assumptions behind the direct estimation of QALY effects for each category of pADE. The ranges specified for significant, and serious ADEs are based on discussions within the research team. The range for severe, life threatening, or fatal ADEs are also defined by the research team, though they are also informed by study of preventable deaths occurring due to medical errors (including errors occurring across the broader spectrum of medical care, e.g. including timely diagnosis) that also assessed the likelihood of death in the absence of the error, and the patients' underlying short-term prognosis.[61] Hayward and Hofer found that when reviewers rated a death as at least possibly preventable, the estimated probability that these patients would have left hospital alive was 20% (95% CI, 12%-27%). For deaths identified as definitely or probably preventable, the mean estimate of the likelihood that these patients would have left the hospital alive given optimal care was 43% (95% CI, 35%-51%). These cases inform our estimates of the lower bound QALY loss for severe ADEs.

Table 17 Assumed QALY-based monetary valuations of the preventable ADE severity categories

Significant: resulted in temporary harm to the patient and required intervention		
Utility decrement	0.1	0.2
Effect duration	3 days	14 days
Serious: resulted in temporary harm to the patient and required initial or prolonged hospitalisation		
Utility decrement	0.2	0.4
Effect duration	14 days	56 days
Severe, life threatening, or fatal: resulted in permanent patient harm, required intervention to sustain life, or contributed to a patient's death.		
Utility decrement	1	0.3
Effect duration	1 year	20 years

The two sets of QALY loss estimates are presented in Table 18. The estimated QALY losses for significant pADEs are small and similar between the two methods and the full range of uncertainty is incorporated. The other categories show more variation. As the model requires estimates of the mean QALY loss across all pADEs within each category, the extreme values are discarded from the four presented estimates for each category, and the middle values used in the model.

Table 18 QALY loss values from two different methods

ADE severity	Litigation	Health effects assumptions	Model input range
Significant	0.005 – 0.1	0.001 – 0.008	0.001 – 0.008
Serious	0.09 – 0.66	0.008 – 0.061	0.061 – 0.09
Severe/life threatening/fatal	0.7 – 12.8*	1 – 4.41*	1 – 4.41

* discounted at 3.5% per annum (the litigation effects are estimated assuming lost life is equivalent to 25 years with a utility weight of 0.75)

4.14 Model analysis

The model was analysed by sampling input parameter sets based on the probability that they represent the optimal set. The sampled sets of input parameters informed the baseline epidemiological model, i.e. the number of pADEs occurring with no specific intervention in place. To evaluate cost-effectiveness, additional parameter values were sampled from the defined probability distributions that represented the implementation costs and the effectiveness of the five interventions, the severity categories of the incident pADEs, and the costs and QALYs effects of the occurring medication errors and pADEs.

The main analysis involved 10,000 iterations of the model to provide 10,000 matched estimates of intervention costs, costs associated with medication errors and pADEs,

and QALY losses due to pADEs for the baseline scenario and the five interventions. These outputs were analysed to estimate the mean incremental cost per QALY gained of each intervention compared to the baseline scenario, as well as a cost-effectiveness acceptability frontier. Frontiers describe the probability that the intervention with the highest mean net benefits (estimated using the mean total cost and QALY outputs) at alternative QALY values is the most cost-effective intervention (estimated as the proportion of iterations in the probabilistic sensitivity analysis in which that intervention has the highest net benefits). Net benefits are estimated as the number of QALYs gained multiplied by the assumed value of a QALY (varied from £0 to £50,000) minus the costs incurred by patients receiving each intervention.

4.15 Results of the economic evaluation

The main outputs from the model are described in Table 19, which show the costs and numbers of non-intercepted medication errors and pADEs occurring with every 1,000 prescription orders, and the corresponding loss of QALYs. The results show that the nurse-based reconciliation intervention has the highest intervention costs, due to the observation that nurses take considerably longer than pharmacists to take a medication history. The computerised assessment approach has the second largest cost, due to assumptions made about the cost of setting up such a system.

In terms of effectiveness, the pharmacist-led reconciliation intervention is predicted to prevent the most medication errors. This reduction is shown to reduce costs associated with errors by £3,002 compared to the baseline scenario. The next most effective intervention is the system involving faxed details from a patient's General Practice, which reduces error-related costs by £778. The health gains show that the prevention of one pADE corresponds to a gain of approximately one QALY, and that the largest QALY gain is 2.2 QALYs per 1,000 orders from the pharmacist-led reconciliation intervention. It should be noted that there is significant overlap between all of the confidence intervals for all of the output variables.

The incremental cost per QALY gained (ICQ) results presented in Table 20 show that all five interventions are estimated to be extremely cost-effective when compared to the baseline scenario. Three of the interventions are shown to dominate the baseline scenario (i.e. cost less and gain more), whilst the upper CI for all five interventions is below £5,000.

Table 19 Model outputs: mean values (95% confidence intervals) per 1,000 prescription orders

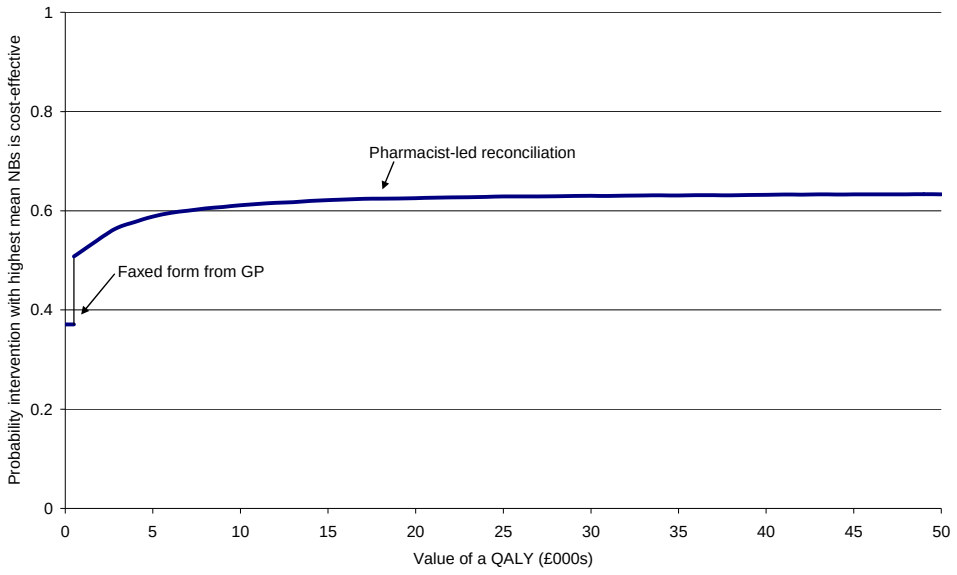
Intervention	Intervention costs	Error costs	Total costs	Non-intercepted medication errors	Preventable ADEs:	Total QALYs lost
Baseline	£0 (£0-£0)	£4092 (£2072-£6758)	£4092 (£2072-£6758)	323 (215-456)	2.8 (1.5-4.5)	3.0 (0.9-7.0)
Pharmacist-led reconciliation	£1897 (£811-£3785)	£1090 (£390-£2362)	£2987 (£1565-£5229)	86 (36-170)	0.7 (0.3-1.6)	0.8 (0.2-2.2)
Standardised forms, pharmacy technicians, hospital policy	£1552 (£689-£3059)	£1990 (£922-£3538)	£3543 (£2029-£5632)	157 (93-243)	1.4 (0.7-2.4)	1.5 (0.4-3.6)
Nurses taking histories with standardised form	£2866 (£897-£6868)	£1567 (£697-£2938)	£4433 (£2106-£8525)	124 (68-205)	1.1 (0.5-2.0)	1.1 (0.3-2.9)
Computerised assessment and feedback by pharmacist	£2542 (£1469-£4230)	£1783 (£822-£3222)	£4325 (£2752-£6445)	141 (81-225)	1.2 (0.6-2.2)	1.3 (0.3-3.1)
Current medication faxed from the GP practice	£1632 (£923-£2737)	£1314 (£542-£2596)	£2945 (£1816-£4588)	104 (52-184)	0.9 (0.4-1.8)	1.0 (0.2-2.5)

Table 20 Incremental cost per QALY gained of the five interventions compared to the baseline scenario

Intervention	Mean	95% CI	
Pharmacist-led reconciliation	Dominates	Dominates	£1,177
Standardised forms, pharmacy technicians, hospital policy	Dominates	Dominates	£1,695
Nurses taking histories with standardised form	£184	Dominates	£4,402
Computerised assessment and feedback by pharmacist	£138	Dominates	£3,124
Current medication faxed from the GP practice	Dominates	Dominates	£623

Figure 3 presents the cost-effectiveness acceptability frontier. This shows the probability that the intervention with the highest mean net benefits at consecutive values of a QALY (i.e. values that society is assumed to be willing to pay to gain additional QALYs) is the most cost-effective intervention. The curve shows that the 'GP fax' intervention has the highest mean net benefits when the QALY value is zero, but that as soon as any value is attached to a QALY gain the pharmacist-led reconciliation intervention becomes the preferred intervention. The probability that this intervention is cost-effective rises to over 60% by a QALY value of £10,000, at which point it plateaus.

Figure 3 Cost-effectiveness acceptability frontier for interventions aimed at improving medicines reconciliation



5. Discussion

5.1 Clinical Effectiveness

This report has assessed the evidence on the effectiveness of interventions aimed at preventing medication errors occurring at the point of admission to hospital, through improvements in reconciling medicines received prior to admission and medicines received in-hospital. The evidence was then applied in a decision analytic framework to estimate the incremental cost per QALY gained of a range of the identified interventions. The results of the effectiveness review are discussed first, followed by a discussion of the cost-effectiveness analysis.

Increased pharmacist involvement
A small number of studies met our inclusion criteria, and only one randomised controlled trial was identified. The inclusion of eleven studies using less strong methodologies, and differences in the interventions evaluated and outcomes measured prevented the statistical combination of the data that would have provided an overall indication of effectiveness. This means that conclusions around questions of effectiveness must be drawn with caution.

Most evidence was identified on the effectiveness of some form of pharmacist-led medicines reconciliation process. The subjective interpretation of the combined evidence is that the increased involvement of a clinical pharmacist at the point of admission does improve the accuracy and completeness of a patient's medication history and subsequent medication prescription. Seven out of the eight studies looking at the effects of increased clinical pharmacy input were based in the UK where the comparator was usual care. Usual care in the UK involves the medication history and complication of medication sheet being undertaken by a junior doctor – although variations may exist – however it makes it more likely that the findings can apply to secondary care settings in the UK.

Interventions by clinical pharmacists also address and correct some of the recognized weaknesses in prescribing arrangements that contribute to an environment where medication error can more readily occur. Prescribing decisions at admission are most usually decided by a house officer and senior house officer who may have little experience of medicines.

There does however need to be caution in our endorsement of the results of these studies. Four of the studies did not use a 'gold standard' against which to compare the results of the physician and the pharmacist's interventions, the assumption being that the pharmacist will be correct. Where a 'gold standard' was used the pharmacist was also found to have made errors. This would suggest that additional interventions need to be considered to reduce the risks of errors occurring. In all of the non-randomised studies, the potential biases that exist and the lack of blinding are factors that may overestimate the effectiveness of the interventions. The presence of only one randomised study and no studies which report adequate methods of randomisation will also increase the risk of bias in favour of the intervention.[62]

None of these studies looked at patients admitted out of hours. Patients admitted outside of office hours may be at additional risk of medication error with less access to primary care services that may be able to give advice on pre-admission medication. They may also be being admitted during times when fewer staff are on duty and doctors may be prone to increased error rates.[6] The absence of data on out of hours admissions means that the findings of these studies are limited and cannot be applied to all admissions.

While these studies suggest that the increased involvement of a clinical pharmacist means that more corrections are made and fewer inaccuracies are present in medication charts they do not address the problem of improving the transfer of information about pre-admission prescribed medication, over the counter medications and drug allergy status.

The studies looking at the effectiveness of medicines reconciliation packages also reported positive effects in terms of reducing the number of errors on medication prescription charts. These studies were all carried out in the US so their application to the UK setting is limited because of different systems of care delivery and funding. These studies also suggest that additional interventions can have a positive effect. All three packages included the identification of a health professional with a specific responsibility for accurate medication history but this was also combined with efforts to improve the documenting of information and policy changes ruling out poor practice such as blanket prescribing. The causes of medication error at admission are multi-factorial and strategies that integrate different initiatives are more likely to be beneficial.

As for the studies described above the methodological quality of these studies was poor and may have introduced biases that will have influenced the findings.

Transfer of Information

The remaining study was a UK based study that demonstrated that a system of faxing information about a patient's medication history from the GP to the admitting hospital ward had benefits in reducing the number of incorrect medication sheets at admission. Although it appears to have benefits, errors continued to occur. The study introduced an intervention that directly addressed the most common cause of medication error which is a lack of access to accurate information about either the medicine or the patient.[31]

This study was not randomised and the data were drawn from an unpublished abstract so little information about the study methodology was available. Once again the quality of the study methodology means that there should be caution in interpreting these findings.

Gaps in the evidence and innovative practice

Despite an extensive and rigorous search for research evidence there were only 12 studies that met our inclusion criteria and these described only a small number of interventions, primarily pharmacist focused.

However, it was apparent that there are a wide range of interventions, UK based, for which no research evidence that met our inclusion criteria were available. These

interventions include a wide range of initiatives including better use of IT systems to improve the availability of accurate, up to date and secure key clinical information about a patient. This includes the development of the electronic prescription service which can provide health care professionals with up to date and accurate information about the range of medications a patient might be taking at any point in time.

Other initiatives which are more patient focused are also being developed. These types of interventions work cooperatively with patients so that they become a part of the process in ensuring accurate information about their home medication usage is transferred to the admitting clinician. These include one-stop dispensing which refers to the practice of combining drugs taken in a community setting with those taken as an inpatient, where the use of patients' own drugs (PODs) in hospital is encouraged. Patients are encouraged to self-administer their own drugs and these are kept in a locked bedside cabinet.[63]

The reason that research on so much innovative practice is not being reported and added to the evidence base is worth addressing. It may be that these innovations appear so intuitively positive in improving health and without possible harmful effects that slowing their progress or incurring additional costs by researching them is not seen as necessary. It may also be too early in their development for research evidence to be available.

It may be that innovations that derive from the 'real world' clinical setting which is less subject to the controls needed for a randomised controlled trial makes designing this type of intervention study much more difficult. Designing studies that focus on preventing an adverse drug event are complex and outcomes difficult to measure. These too may act as disincentives to practitioners concerned to improve care in their settings.

5.2 Discussion – Economic analysis

The effectiveness review was the starting point for the economic analysis. Five separate interventions for which some effectiveness evidence was identified were evaluated with respect their incremental costs and QALYs compared to a baseline scenario. The relative risks of medication errors for each intervention were applied to a baseline model that described the incidence and progression of medication errors occurring as a result of deficiencies in the medicines reconciliation process.

The presented results show that a pharmacist-led medicines reconciliation intervention is likely to provide the largest net benefits to the NHS. This result is observed despite the conservative assumption that the additional employment of pharmacists to assist in the medicines reconciliation process will not free up physicians time to be spent on other activities that would provide health benefits.

In the absence of capacity to provide the required increase in pharmacists, it may be more feasible to implement the second most cost-effective intervention that involved a system of faxed medication sheets from patients' General Practices. This intervention was assumed to be handled by clerical staff who could extract relevant information from patient's notes.

However, the presented analysis is subject to a range of potentially important limitations. Firstly, the medication errors model extrapolates from the point of incidence of a

medication error to the final impact of an error on a patient. There were few reliable data to populate the full model, though data describing some of the outputs from the model were available. The approach taken, therefore, was to estimate ranges for all input parameters (based on empirical observations where possible), to specify ranges for the observed output parameters, and then to sample a large number of sets of input parameter values and assign weights to each set that reflect the accuracy with which they predicted the observed range of output parameter values.

The main issues concern the relevance of the empirical data used to inform both the input and output parameters, and the choice of ranges for parameters for which no data were observed. A hierarchy was defined by which priority was given to UK-based studies when defining parameter ranges, though few UK studies reporting relevant outcomes, particularly the incidence of pADEs, were identified. In these cases US studies were used. The relevance of US estimates to the UK is unknown, though specific differences in the systems of health care delivery can be described, and hence inform the interpretation of the US from a UK perspective. Key differences include the requirement that transcribed prescriptions for medicine must be clinically checked by a hospital pharmacist in the US before supplies can be made, and that there is little or no assessable ward stock, whilst the available ward stock model is used in the UK. In the US, medicine supplies are made in the form of individual unit doses supplied in individual drawers for named patients for 24 hours, as opposed to the UK where patient packs and bottles are supplied for 14 – 28 days use, or where the preparation of doses of injectable medicines by ward staff in clinical areas.

It was difficult to adjust these data to a UK context as the overall direction of the many differences between the UK, in terms of increasing or decreasing the aggregate rate of preventable ADEs, is unclear.

No direct comparisons of error rates in the UK and the US were identified, though Taxis et al[64] report an observational study that directly compared administration errors in two German hospitals and a UK hospital. Significant differences were observed between all three settings, with the UK ward pharmacy setting having the highest number of medication errors. One explanation for the differences between the UK and German sites was that one researcher observed at all three sites, whilst the other researcher who observed only at the UK site had a higher error detection rate (9.5% vs 6.5%).

In specifying ranges for the input parameters, one approach would have been to specify a range of 0 to 1 for all of the input parameters as the calibration process assigns weights to all input parameter sets that reflects the likelihood that each set matches the defined output parameters. However, this approach ignores the possibility that some inconceivable combinations of input parameter values may result in reasonable predictions of the outputs, for example, the combination of unfeasibly high probabilities of error detection and that undetected errors cause harm may result in an accurate estimate of preventable errors (a case of two or more wrongs making a right). It was necessary, therefore, to specify ranges for each input parameter that were broadly feasible.

The input parameters describing the level of severity of preventable ADEs are of particular concern as these have a significant impact on the estimated net benefits of the interventions and were based solely on a couple of related US studies.[31,42] Until the validity of incident reporting is assured (i.e. that incident reporting identifies a complete and unbiased set of ADEs), the accurate estimation of the severity of preventable ADEs will be reliant on empirical studies that use more reliable identification techniques, such as observation or case note review. Few such studies have been undertaken, particularly in the UK. Incident reporting may be validated by comparative studies of alternative ADE detection methods that show no difference between incident reporting and other detection methods.

Other key drivers of the analysis are the cost and QALY values attached to pADEs, which were not covered by the calibration process. The parameter estimates for these variables are based on limited empirical data, for example, QALY effects are based on explicit, but subjective assumptions and a summary analysis of the NHS Litigation Authority database of medication error cases. Additional research on both of these parameter categories would increase the certainty of the presented analysis, though this research would ideally be undertaken in the context of evaluations of interventions aimed at reducing the impact of medication errors.

The valuation of the health effects of ADEs in the context of primary research is difficult as the ideal would involve administering quality of life surveys to all patients on intervention or control wards, which will require large resources and be subject to significant missing data. An alternative is to develop vignettes describing a range of effects of preventable ADEs, and to obtain QALY estimates using standard techniques, or monetary valuations using available methods, such as the relativities approach.[65]

The majority of the reviewed studies specified the number of medication errors occurring as the primary outcome measure. Decision models evaluating a health care technology for a specific disease usually extrapolate intermediate endpoints to the full lifetime of patients, for example, a cancer trial may describe the relative frequency of cancer recurrence in different treatment groups, which is then extrapolated beyond the trial period based on the predicted effects of recurrence. Such extrapolations are based on the assumption that a recurrence (or recurrences of particular types, if multiple recurrence sites are modelled) in the control and treatment groups have the same prognostic impact, i.e. the subsequent pathways are the same irrespective of the initial treatment group.

The assumption of proportionality between the prevention of medication errors and the occurrence of pADEs is difficult to justify. This is because there is such a wide range of potential medication errors with different potential health impacts, as well as different likelihoods of detection. The assumption of equal effects of medication errors occurring in the presence and absence of an intervention would require that an intervention prevents an entirely random sample of medication errors. This is unlikely because interventions generally prevent alternative types of errors differentially. Bates et al[66] provide an extreme example, in which the RR for all medication errors for a CPOE system compared to baseline (in the first implementation period) was 0.37 (145.2 versus 53.6 errors per

1,000 patient days), whilst the RR for pADEs was 1.97 (2.9 versus 5.7 per 1,000 patient days).

Prospective studies that investigate the relationship between medication errors and ADEs from a UK perspective, may improve the accuracy of the results. However, it should be considered that there are almost infinite types of medication errors, each of which will have different probabilities of detection prior to administration, of causing harm, and of causing different levels of severity of harm. This makes the model-based extrapolation of medication error frequencies to pADEs very difficult as ideally a separate error state would be created for every medication error, to which individual estimates of the likelihood of detection, harm, and severity of harm would be attached. It may be the case, therefore, that interventions aimed at reducing the impact of medication errors cannot be definitively evaluated through the synthesis of data from disparate sources within the framework of a decision modelling approach, as is commonly undertaken for the evaluation of other health care technologies.

The precise specification of alternative interventions is likely to alter their effectiveness, including factors such as rates of clinician acceptance and ease of use. A recent, primarily qualitative study of an implemented CPOE system identified a range of medication error risk associated with a widely used CPOE(95). The conclusion from this study was that as CPOE systems are implemented, clinicians and hospitals must try to minimise errors that these systems cause in addition to errors that they prevent. Such studies will assist the design of new generation CPOE systems that will hopefully increase their effectiveness. Similar issues may be hypothesised for other potential interventions, for example, the ground rules specified for the interaction between pharmacists and clinicians whilst jointly attending ward rounds.

Given the scope for improvement in all of the specified interventions, combined with the problems with available data describing their current effectiveness, the modelled analysis of the effectiveness of the five defined interventions was based on the specification of wide RR ranges for each intervention. The specified RRs for each of the five interventions were based on the assumption that the interventions were well designed, or appropriately implemented.

Another limitation of the analysis concerns the estimation of the costs of the interventions. As described in the report, intervention costs were based primarily on the assumptions of the authors and are subject to large uncertainty.

5.3 Conclusions – clinical effectiveness

The scale of the problem and the inadequacy of the current system to minimize risk of medication error means that a medicines reconciliation intervention is likely to bring benefit. No data describing any harmful side effects as a result of any of the interventions was described. The current evidence, though poor, suggests the initiatives described in the studies included in this review, particularly pharmacist led initiatives, are positive. There needs to be, however, more work to get a truer measure of their effectiveness. This includes conducting better designed studies that include adequate methods to control for

bias such as randomisation, allocation concealment, blinding at outcome assessment and intention to treat analysis. Specific challenges to study designs in the area of medicines reconciliation include controlling for baseline variability between groups when comparing the effectiveness of interventions by different health care personnel and the need to have a 'gold standard' medication history against which the intervention and control can be compared.

Any effort to formulate a recommendation for a medicines reconciliation strategy must take into account the large gap in the current evidence. The current evidence as it stands does not sufficiently reflect the many promising and emerging technologies that may be effective in medicines reconciliation.

The reasons for this include their infancy in terms of development, the lack of cohesive working between innovators in a clinical setting and health service researchers with research design expertise. It also reflects the way this type of work evolves and a natural assumption of its clinical effectiveness.

Multiple factors contribute to create an environment where medication error at admission occurs. It would seem fitting that a variety of intervention that address these different causes is likely to be the most effective way of minimizing risk.

5.4 Conclusions - economic analysis

The medication errors model provides reasonably strong evidence that some form of intervention to improve medicines reconciliation is a cost-effective use of NHS resources. The results indicate that pharmacist-led medicines reconciliation is likely to be the most cost-effective intervention, though it is difficult to assess whether the model has captured all of the relevant uncertainty around the model's input parameters. There are also likely to be other interventions, particularly IT-based interventions, for which evidence of effectiveness was not available.

The broad-brush analysis presented in this report may inform research allocation decisions by identifying those interventions with the largest potential for reducing the impact of medication errors and providing net benefits to the health service. The variation in the reported effectiveness of the few identified studies of medication error interventions illustrates the need for extreme attention to detail in the development of interventions, but also in their evaluation and may justify the evaluation of more than one specification of included interventions.

Key drivers of cost-effectiveness should be specifically addressed in the design of primary evaluations of medication error interventions, in particular, data should be collected on the severity of ADEs occurring in the different intervention groups and additional research should be undertaken on the value attached to the prevention of such effects.

If further research confirms the cost-effectiveness of pharmacist-led medicines reconciliation, the capacity of the NHS to employ more pharmacists will be a key factor

in the implementation of this intervention. Solutions to the supply issue should be considered at the same time as the evaluation of the intervention as some solutions may affect the design of evaluation studies. Critical incidence studies may be undertaken to define the attributes of pharmacists that contribute most to the reduction of medication errors, which may identify interventions such as new training programmes for other health professionals and new processes of health care delivery.

5.5 Implications for research – effectiveness and economic analysis

There is a need to address the current evidence gap by implementing research that assesses the effects of new and emerging technologies.

There is also a need to design studies of methodological rigor to look at medicines reconciliation interventions so that the results are useful in measuring effectiveness. This includes further work on the initiatives that have been described in this review.

There is a need for better links between health service research units and areas of innovative practice in order to ensure a growing body of high quality research that can keep pace with innovations and usefully inform the evidence base.

A second systematic review exploring medicines reconciliation initiatives that span the patient journey from hospital admission to discharge. This review focused on admission meaning that interventions that were trying to address the problem of medication error at all patient transfer points were not included. A broader review may yield additional useful evidence that can inform our current understanding of interventions that will reduce the risk of medicines error at admission.

6. Appendices

Appendix 1 – Search Strategy

Search strategies
A comprehensive literature search was performed in April 2007. Searches were designed to retrieve:

- Papers describing the use of medicines reconciliation procedures
- Papers on the cost effectiveness and comparative costs of the different medicines reconciliation procedures.

In July 2007 further focused searches were performed to retrieve papers on the following terms related to medicines:

- Electronic medication system
- Computerized medication system
- Computerized physician-order entry
- Admission order

The following electronic bibliographic databases were searched:

1. Cumulative index to nursing and allied health literature (CINAHL)
2. Cochrane Database of Systematic Reviews (CDSR)
3. Cochrane Central Register of Controlled Trials (CENTRAL)
4. Embase
5. Medline
6. Medline In-Process & Other Non-Indexed Citations
7. NHS Database of Abstracts of Reviews of Effects (DARE)
8. NHS Economic Evaluations Database (EED)
9. NHS Health Technology Assessment (HTA) Database
10. Science Citation Index (SCI)
11. Social Sciences Citation Index (SSCI)

Attempts were also made to identify 'grey' literature by searching current research registers (e.g. National Research Register, Current Controlled Trials Register) and relevant websites (e.g. Institute for Healthcare Improvement http://www.ihi.org/ihi). The reference lists of included studies and relevant review articles were also checked.

No date or language restrictions were applied to these searches.

The search strategies used in Medline (Ovid) are provided below:

Medicines reconciliation searches

Database: Ovid MEDLINE(R) <1950 to April Week 1 2007>
Search Strategy:
---

1. medication$ reconciliation.tw.
2. medicine$ reconciliation.tw.
3. Medical History Taking/
4. Medication Systems/
5. medication$ histor$.tw.
6. medicine$ histor$.tw.
7. discharge document$.tw.
8. medication$ management.tw.
9. medicine$ management.tw.
10. manag$ medicine$.tw.
11. manag$ medication$.tw.
12. medication$ record$.tw.
13. medicine$ record$.tw.
14. or/1-13
15. patient admission/ or patient discharge/ or patient transfer/
16. discharg$.tw.
17. admission$.tw.
18. admit$.tw.
19. or/15-18
20. 14 and 19

The medicines reconciliation terms (1-13) were combined the with patient admission, discharge and transfer terms (15-18).

Cost effectiveness searches
To retrieve papers on cost-effectiveness and comparative costs of the different medicines reconciliation procedures searches were conducted in Medline, CINAHL, Embase, NHS Economic Evaluations Database (EED). The search terms given above were utilised. Search filters designed to retrieve economic evaluations, were applied to the Medline CINAHL and Embase searches. An example of the Medline (Ovid) search filter is provided below:

1. Economics/
2. exp "Costs and Cost Analysis"/
3. economic value of life/
4. exp economics hospital/
5. exp economics medical/
6. economics nursing/
7. exp models economic/
8. Economics, Pharmaceutical/
9. exp "Fees and Charges"/

10. exp budgets/
11. ec.fs.
12. (cost or costs or costed or costly or costing$).tw.
13. (economic$ or pharmacoeconomic$ or price$ or pricing$).tw.
14. quality adjusted life years/
15. (qaly or qaly$).af.
16. or/1-15

Additional focused searches

Database: Ovid MEDLINE(R) <1950 to June Week 3 2007>
Search Strategy:
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1. electronic medication system$.tw.
2. Pharmacists/
3. clinical pharmacist$.tw.
4. cpoe.tw.
5. computerized physician-order entry.tw.
6. computerised physician order entry.tw.
7. computerized medication system$.tw.
8. computerised medication system$.tw.
9. admission order.tw.
10. pharmacy pharmacist$.tw.
11. or/1-10
12. Patient Admission/
13. admission$.tw.
14. admit$.tw.
15. or/12-14
16. 11 and 15

Terms related to medicines reconciliation (1-10) were combined with patient admission terms (12-14).

To retrieve cost effectiveness papers the above strategy was combined with search filters designed to retrieve economic evaluations as discussed above.

Appendix 2: Quality Assessment of Included Studies

Study characteristics

	Brady '04	Dutton '03	Akwagyiram '96	Cavin '05	Collins ,03	McFadzean '03	Slee '06	Michels '03	De Carolis '05	Rozich '04	Featherstone '06
Type of intervention	P	P	P	P	P	P	P	MR	MR	MR	IT
Study Design	B/A	B/A	C	C	C	C	C	B/A	B/A	B/A	C
Were participants a representative sample selected from a relevant patient population?[2]	N	U	U	N	N	N	N	N	NR	NR	Y
Were the inclusion/exclusion criteria clearly described?	Y	Y	Y	Y	N	Y	N	N	N	N	N
Was selection of patients consecutive	Y	Y	Y	Y	Y	Y	U	U	U	U	NR
Was the method used to assign participants to the treatment groups random?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NR
Was the allocation of treatment concealed?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NR
Within subject comparison?	N	N	N	N	Y	Y	Y	N	N	N	N
Were the groups comparable on demographic characteristics and clinical features? Was the setting the same for both groups and both interventions? Did the differences raise the risk of bias and was this documented?	N[1]	N[6] N discusses doctors varying levels of experience in different phases	NR	N[5,6]	Y	N[6]	N[7]	Y	Y	NR	NR
Were the analyses adjusted for confounding factors?	N-mentioned seasonal variation		NR	N	NA	N	N	NA	NA	NA	NR
Was data collection undertaken propsectively?	Y&N [1]	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Was the intervention (and comparison) clearly defined?	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N
Were objective (valid and reliable) outcome measure/s used? (presence of a 'gold standard')	Y	N	Y[3]	N	Y	Y	N	Y	Y	N	NR
Was the assessment of main outcomes blind?	N	N	N	N	N	N	N	N	NR	N	NR
Was information provided on non-respondents, dropouts?	Y	NoR	NoR	NoR	NoR	NoR	Y	NoR	NR	NR	NR
Were participants lost to follow-up likely to introduce bias? (e.g. high drop-out rate; differential drop-out, no description of those lost)	N	NoR	NoR	NoR	NoR	NoR	U	NoR	NR	NoR	NR

(1) before data was collected retrospectively and compared with prospective data
B/A - before and after studies
P - pharmacist led interventions
NA - not applicable
(2) in after study
NoR-none reported
NR-not reported
I - inadequate
2 - N if study limited only to office hours admissions
3- yes, GPs records but few responded
4 yes, only for one arm of study
5-the control may have included out of hours admissions

6-doctors unaware of participation in intervention
C- comparative

7- pharmacists had the physician's assesment
U - unclear
MR medicines reconciliaiton package

Appendix 3 – Characteristics of Included Studies

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
Kwan 2004[12] **Study design**: RCT **Location:** USA, surgical pre-admission clinic **Length of intervention:** 6 weeks and 3 days **Randomisation:** NR **Concealment:** NR **Blinding:** NR **Withdrawal/dropout:** 0	To measure the impact of a combined intervention of structured pharmacist medication assessments in a surgical pre-admission clinic and a post-operative order form on reducing medication discrepancies.	**Number of patients:** 310 **Inclusion criteria:** Pre-admission appointment for a surgical procedures **Exclusion criteria:** Cancelled surgeries and scheduled for discharge the same day as their surgery **Baseline Comparability:** NR **Age (mean):** NR **Gender:** NR **Number of patients admitted out of hours:**0	**I1:** Structured pharmacist medication assessment and a post-operative medication order form. **I2:** Nurse-conducted medication histories and surgeon-generated orders.	Incidence of patients with at least one post-operative medication discrepancy related to home medications. Discrepancies were systematically characterized and their clinical impact was independently assessed. I1: 30/154 (19.5%) I2: 68/156 (43.6%) Potential for discrepancy to result in probably patient discomfort and/or clinical deterioration I1: 8/30(17.0%) I2:46/68 (36.8%)	**Definition of drug error:** unclear how the 'gold standard' medication history was obtained against which the intervention medication histories were compared. Conference abstract
Dutton2003[14] **Study design**: before and after design **Location:** UK, acute admissions ward	To determine the impact of a clinical, ward-based pharmacist on the prescribing practices of an acute admission ward.	**Number of patients:** 1247 **Inclusion criteria:** Patients admitted to the medical admissions ward. **Exclusion criteria:** NR **Baseline Comparability:** yes **Age (mean):** NR **Gender:** NR **Number of patients admitted out of hours:**	**I1: Intervention** More intense clinical pharmacy involvement (visited twice each weekday) and was available by bleep to take medication history. Greater use of PODs. CP also attended the daily 'post-take' ward round Three month run-in followed up by repeating the data collection over a 11 week period **I2: Baseline** The CP visited	**Number of errors identified concerning regular medication:** **I1:** 393/506 **I2:** 182/526 **Number of patients on regular medication who had ≥ 1 error:** **I1:** 228/506 **I2:** 106/526 The largest number of errors involved the omission of medication (177 vs 80). Of the errors found in I1 74.8 % could not have been	**Definition of drug error:** A prescribing error was defined as a mistake in detailing a patient's pre-admission medication on the prescription chart. Intentional changes made to pre-admission medication and errors involving medication initiated in hospital were excluded. The clinical severity of each error was graded. Factors to consider when comparing error data from the two phases. New intake of junior doctors meant that during the intervention period the doctors will have been more experienced than during baseline collection of data.

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
		NR	admissions ward every weekday morning over an 11 week period. Did not include routine drug history taking and limited use of PODS.	identified from checking the drug chart alone. More than 50% (202/506) errors were considered likely to cause destabilization of a chronic medical condition, or serious adverse events.	
Brady 2004[13] **Study design**: before and after - however baseline data was recorded retrospectively and compared with prospective data **Location:** UK, 22 bed medical admissions ward	The aim of the study was to evaluate the impact of a full-time medical admissions pharmacist in a London teaching hospital.	**Number of patients:** 290 in intervention group. Number in control group not reported. **Inclusion criteria:** Patients admitted to the medical admissions ward. **Exclusion criteria:** NR **Baseline Comparability:** NR **Age (mean):** NR **Gender:** NR **Number of patients admitted out of hours:** NR	**I1:** The MAP attended post-admission ward rounds on a daily basis (excluding weekends), confirmed patient's medication histories and ensured patients regular medications were prescribed appropriately on admission. Three one-month periods were chosen to serve as study periods. **I2:** Typical UK ward pharmacy service, visited each weekday by a pharmacist Interventions recorded prior to the appointment of the MAP were retrieved from the in-house pharmacy intervention database. Three one week periods were selected for analysis as the control.	Interventions (ie any communication between a pharmacist and a clinician, whether verbal or written , made with the intention of influencing prescribing) concerning possible omissions or other discrepancies in the medication history. I1:232/413 (56.2%) CI: 210.6-251.9 I2:31/81 (38.3%) CI: 26.7-43.8 NB: the denominator for the above is the total number of interventions. There is no reported total number of medications or total number of patients for the control period. There was a significant increase in the number of inaccuracies identified between the patient's confirmed medication	**Definition of drug error:** The study looked at pharmacy interventions. A pharmacy intervention was defined as any communication between a pharmacist and a clinician made with the intention of influencing prescribing. Studies with no 'gold standard' measure for overall medication prescription error assume that the baseline rate of errors in the same in both time periods.

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
				history and drug regimen prescribed on admission during the intervention period.	
Akwagyriam 1996[19] **Study design**: prospective study of 33 elderly patients survey **Location:** UK, inpatients admissions through A&E **Randomisation:** NR **Allocation Concealment:** NA **Blinding:** no **Withdrawal/dropout:** none	To determine the incidence of drug related problems that fail to be noted on casualty cards in patients subsequently admitted, and to compare medication histories as recorded by accident and emergency (A&E) senior house officers (SHOs) and a pharmacist	**Number of patients:** 33 **Inclusion criteria:** All patients attending the A&E department who were then admitted as medical inpatients **Exclusion criteria:** Unconscious or confused or unable to give a coherent history. Those admitted and discharged overnight. **Baseline Comparability:** **Age (mean):** 80 (5.81) **Gender:** NR **Number of patients admitted out of hours:** NR	**I1:** Pharmacist interview assisted by a structured questionnaire. **I2:** A&E SHO	**Omissions -Number of currently prescribed drugs identified** **I1:** 125 **I2:** 77 Rate of omission: 62% **Over the counter drugs prescribed:** **I1:** 33 **I2:** 4 **Previous adverse drug reactions:** **I1:**17 **I2:** 6 **Length of interview:** 11.8 (5.8) mins (unclear – this appears to just refer to pharmacists). In six cases the extra information gathered by the pharmacist may have contributed to the need for admission.	**Definition of drug error:** SHO may have identified the problems without making a record on the patients cards Pharmacist may have had doctors notes when they conducted their own interview, therefore not fair comparison. In addition the questionnaire that the pharmacists used may have provided prompts for elucidating a full drug history. Poor response from the GPs meant their records could not be used as a standard against which the others could be assessed, and the accuracy of GP records may also be questioned.
McFadzean 2003[20] **Study design**: prospective, comparative study **Location:** Scotland, medical admissions ward **Randomisation:** NA **Allocation**	To compare the accuracy with which junior doctors and pharmacists take a drug history and write a drug chart.	**Number of patients:** 120 patients **Inclusion criteria:** all patients admitted as emergencies to the medical admissions unit between 8:30 am and 5 pm, Monday to Friday **Exclusion criteria:** patients not taking regular medication just	**I1:** Drug histories taken by four clinical pharmacists who knew they were in the study **I2:** Drug histories taken by one of 12 junior doctors who did not know they were in the study **Duration of**	**Prescribing errors** **I1**: 3 in 3 patients/60 (5%) **I2**: 110 in 39 patients/60 (110%) **I2:** 78 drug omission (71% of total errors) 23 errors of drug dose (21% total errors) **Histories with drug allergies recorded:**	**Definition of drug error:** Prescribing errors were defined as drugs omitted or prescribed in error, drug dosage or frequency errors or known drug allergies not recorded. Did not include recording if patients were taking herbal or over the counter medicines. These errors are over and above those already documented. Junior doctors were unaware that they

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
concealment: NA **Blinding:** NR **Withdrawal/dropout:** none		before admission and patients admitted following an overdose. **Baseline Comparability:** yes Average number of drugs taken per patient: **I1:** 6.4 **I2:** 6.9 **Age (mean):** **I1:** 67.4 **I2:** 68.3 **Gender:** **I1:** 31 (52%) **I2:** 25 (42%) **Number of patients admitted out of hours:** 0	**intervention:** 1month In both arms the drug history was then reassessed by a research nurse who interviewed the patient or carer as appropriate, contacted the GP or community pharmacist, reviewed the patients own drugs, matched the drug chart and admission chart to document any errors	**I1:** 56 (93%) **I2:** 13 (23%) **Average time to write medication history and drug chart:** **I1:** 32 mins **I2:** not reported	were participating in the study but the clinical pharmacist did.
Collins 2004[22] **Study design**: Prospective/comparative **Location:** UK **Randomisation:** NA **Allocation concealment:** NA **Blinding:** no **Withdrawal/dropout:** none	To assess the accuracy of physician-acquired medication histories for patients admitted to medical, surgical and trauma admissions units and to identify problems encountered when taking a medication history.	**Number of patients:** 117 **Inclusion criteria:** Included all patients who were admitted onto the acute medical, surgical and orthopaedic admissions between 9 am-530 pm. All aged over 16 years. **Exclusion criteria:** NR **Baseline Comparability:** same group of patients in both intervention arms	**I1:** The pharmacist obtained a medication history by interviewing the patient as per routine clinical practice. Allergy status confirmed during this interview. **I2:** medication history compared with the physician's history as documented in the medical notes and what was prescribed on the inpatient prescription chart.	Discrepancies between the different sources of medication information identified and grouped into a series of categories. **Omission of medicines from medication histories.** Medicines obtained by pharmacist interview but not on physicians chat: 227/553 Medicines on physicians chart but not obtained from pharmacist interview: 243/553 **Differences in doses from the medication histories:**	**Definition of drug error:** Third data source was used for corroboration – either a phone call to the GP's surgery, a patient's repeat prescription form or a current nursing home medication list. There were significant numbers of discrepancies between the histories obtained from different sources.

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
		Age (mean): NR **Gender:** NR **Number of patients admitted out of hours:**0	**Duration of intervention:** 5 days	Medicines with a different dose documented on the chart by the doctor from that obtained from pharmacist interview: 45/352	
Cavin 2005[21] **Study design**: retrospective comparative study **Location:** UK, A&E department **Randomisation:** yes for baseline data, method NR **Allocation concealment:** NA **Blinding:** NR **Withdrawal/dropout:** none	To determine the DRP rate and to compare the extent to which these and complete medication histories are recorded by clinical pharmacists and doctors. To describe the activities of a clinical pharmacist in an A&E department.	**Number of patients:** 400 (for doctors 200 randomly selected from A&E department cards and for pharmacists 200 during a trial phase – 175 taken as a result of noticing that the medication history taken by the doctor was incomplete and 25 taken by pharmacists before patients were seen by a doctor. **Inclusion criteria:** Patients who attended the A&E department during the clinical pharmacist working hours and who were subsequently admitted. **Exclusion criteria:** Patients who were not taking any medicines before admission **Baseline Comparability:** NR	**I1:** A&E department pharmacist medication history **I2:** Medication history taken by a junior doctor when a patient first attended A&E	**Accurate medication history:** **I1:** 100% **I2:** 12.5% Of the medication histories taken by doctors, 61.5% included the drug name, but the dose and the frequency of administration were missed on 75% of occasions	**Definition of drug error:** DRP = number of DRPs per 100 patients attending the A&E department and then admitted to hospital in an inner city teaching hospital Complete medication history required: confirming if taking medicines regularly, their name, dose, frequency of administration and any OTCs. They did not include allergies. Problems: cannot compare interventions. The pharmacy histories were taken in 175 patients after a problem was noticed. Therefore a 2 stage intervention. The timing of the interventions was also different and changes in the experience of the doctors or support may have influenced their history taking. Doctors unaware they were going to participate in study but pharmacist was.

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
		Age (mean): NR **Gender:** NR **Number of patients admitted out of hours:** 0			
Slee 2006[23] **Study design**: prospective comparative study **Location:** UK, acute medical patients in seven acute NHS trusts in England and Wales **Randomisation:** No **Concealment of allocation:** No **Blinding:** No **Withdrawal/dropout**: 72 discrepancies unresolved	To identify whether a proactive clinical pharmacy review of a patient's treatment at the point of admission could potentially avoid adverse events	**Number of patients:** 791 **Inclusion criteria:** All acute medical patients including care of the elderly (Monday to Friday) **Exclusion criteria:** NR **Baseline Comparability:** same group of patients **Age (mean):** NR **Gender:** NR **Number of patients admitted out of hours:** 0	**I1:** Measured over a five day period. Clinical pharmacy review of a patient's treatment at the point of admission using a standardized reporting form. Assessment included details from patient or carer, medications brought to hospital, details from the admitting physician, clarification from community. The outcome of this assessment was then compared with the existing prescription. Any anomalies identified were then discussed with the prescriber. **Duration of intervention:** NR **I2:**	**Total number of patients requiring an intervention:** 38% 464 interventions recorded with an average of 1.5 interventions per patient (in the 38%). 391 (84%) accepted by physicians 72 (16%) unresolved **Potential severity:** Fatal 10 2.2% Serious 82 17.7% Moderate/ Minor 369 79.5% Missed Opportunity 3 0.6%	**Definition of drug error:** Interventions classified as need for additional drug, unnecessary drug therapy, wrong drug, dose too low, adverse drug reaction, dose too high, compliance, miscellaneous eg incomplete prescriptions. NB total number of admissions and total included different – to do with out o f hours admissions.

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
			Existing prescription made by admitting physician. **Duration of intervention:** NR		
Geibig 1991[27] **Study design**: Before and after **Location:** USA, 600 bed teaching hospital no withdrawals or loss to follow-up	To examine the completeness of drug allergy documentation following the implementation of a policy for documenting drug allergies that involved nurses, pharmacists and physicians, with pharmacists having the key role in ensuring the policy's effectiveness.	**Number of patients:** 84 **Inclusion criteria:** Patients from all inpatient areas **Exclusion criteria:** None described **Baseline Comparability:** Not descrbied **Age (mean):** Not described **Gender:** Not described **Number of patients admitted out of hours:** not described	Interventions focused on recording of drug allergies **I1:** Modification of existing framework of care. Multidisciplinary responsibilities for obtaining allergy information. Creation of a 'control point' in allergy documentation with one professional responsible for ensuring that documentation be complete. The dispensing of drugs by pharmacists was identified as this control point. Nurses and doctors independently solicit allergy information and the nurse is responsible for resolving any discrepancies with the physician. **Baseline** **I2:** Nurses and doctors separately gathered information on drug allergies and recorded it	**Outcomes measured2 months after intervention** **Documentation of drug allergy by physician on first drug order:** **I1:** 86% (n-43) **I2:** Baseline 0 (n=41) **Documentation of allergy information by nurse on admission assessment form** **I1:** 65% (n=43) **I2:** 71% (n=41) **Documentation of allergy information by pharmacist in drug profiles** **I1:** 93% (n=43) **I2:** 2% (n=41)	**Definition of drug error:**

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
			on admission assessment form and in the patients' medication record. Pharmacy received the allergy information from the nurses. The approach was uncoordinated and one employee often assumed that another was responsible.		
Michels2003[18] **Study design**: before and after study **Location:** US, 390 bedded community hospital	To describe a program in which pharmacy technicians were used to reduce potential ADE's during the processing of outpatient medication orders to active inpatient orders	**Number of patients:** 767 **Inclusion criteria:** Surgical patients **Exclusion criteria:** NR **Baseline Comparability:** NR **Age (mean):** no data **Gender:** no data **Number of patients admitted out of hours:** none	**I1:** Pharmacy technicians in the admission department to collect medication history, use of a special home-medication order form and a hospital policy prohibiting the use of blanket orders. Pharmacists history included nonprescription medications and allergy status. History taken prior to admission over the phone **Duration:** 16 weeks **I2: Baseline** Nurse recorded home medication onto a data base which was not used or easily accessible to physicians and pharmacists. Mediation orders would be written by physicians on the	**Number of defects per order form** **I1:** 0.76 (0.07)/585 **I2:** 1.45 (0.39)/182 **Defects per individual drug order:** **I1:** 0.12/3620 **I2:** 0.25 /1056	**Definition of drug error:** Defects on admission medication history used as a marker of potential ADEs. The omission of key information (eg drug dosage, route, or frequency) the presence of incorrect information (eg incorrect dosage for the drug), the ordering of an inappropriate drug for the condition, an illegible order, a serious drug interaction and the continuation of a previously discontinued drug. A pharmacist reviewed all completed forms, identifying any defects that remained unresolved at the time of order activation by the surgeon.

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
			basis of a combination of printed lists from patients, the nurse's records, community pharmacists and family members.		
Rozich JD 2004[16] **Study design**: before and after study **Location:** America, 'health system'	**Number of patients:** Not described **Inclusion criteria:** not described **Exclusion criteria:** not described **Baseline Comparability:** not described **Age (mean):** not described **Gender:** not described **Number of patients admitted out of hours:** not described	Change the system of care to reduce unneeded variances and also decrease inefficiencies.	**I1:** At admission a nurse conducts the medication process, which includes gathering information from the patient and family and patient's pharmacy. A medication reconciliation form is used as a template for the process. Any discrepancies with the physician's records will be evident on the form and the nurse contacts the physician. **Duration of intervention:** **Duration of follow-up:** seven months **I2:** usual care – not a uniform approach **Duration of measurement of baseline data:** 6weeks	'The introduction of admission reconciliation resulted in a decrease from about 213 to nearly 80 errors per 100 admissions'.	**Definition of drug error:** Medication error included incorrect dose given, incorrect route of administration and incorrect time of administration. Also measured ADEs defined by the WHO as 'a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or the modification of physiological function'

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
			(3months between baseline and intervention)		
DeCarolis 2005[17] **Study design**: Before and after design **Location:** USA	**Number of patients:** Not described **Inclusion criteria:** NR **Exclusion criteria:** NR **Baseline Comparability:** NR **Age (mean):** NR **Gender:** NR **Number of patients admitted out of hours:** NR	To compare the current process of ordering medications upon admission to hospital vs a systematic medication reconciliation process.	**I1:** A medication reconciliation system using pharmacist analysis of computerized profiles and documentation before initial inpatient orders written. A tool in obtaining the initial medication history **I2:** Usual care	Baseline data revealed the computerized profile to be inaccurate in 71% of patients, medication histories by providers not routinely performed and unintended order discrepancies in 58% of patients. The medication reconciliation system reduced the number of patients with unintended discrepancies by 43%. The number of unintended discrepancies per patient decreased by 53%.	'gold standard' was patients reported medication history. However patients may not be able to remember the names of all the medicines that they are taking, and those who can remember the names may not be able to remember all of the doses they are taking. Patients who are intentionally non-compliant with their medication may be reluctant to disclose this. (NB will these cautions to using patient history as a gold standard apply in a US setting ?) Conference abstract – little information given.
Featherstone 2006[15] **Study design**: non randomized comparative study **Location:** UK	To reduce the number of patients admitted without appropriate and timely medicines management information with the aim of increasing patient safety and reducing risk, whilst at the same time improving patient flow.	**Number of patients:** Five GP practices were recruited and found admission areas **Inclusion criteria:** patients admitted from the selected GP practices and admission areas **Exclusion criteria:** NR **Baseline Comparability:** NR	**I1:** Template containing key information – namely current medication, past medication, allergies and clinical aspects that could be faxed by the GP practice to the admitting ward. **I2:** usual care	**Percentage of treatment sheets written correctly within 24 hours of admissions:** I1: 83% I2: 45%	**Definition of drug error:** NR

Study details	Purpose	Participant characteristics	Intervention characteristics	Results/Outcomes	Comments
		Age (mean): NR **Gender:** NR **Number of patients admitted out of hours:** NR			

7. References

1. The Institute for Healthcare Improvement (IHI). 2007.

2. Pirmohamed, M., James, S., Meakin, S., Green, C., Scott, A. K., Walley, T. J., Farrar, K., Park, B. K., and Breckenridge, A. M. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *Bmj* 3-7-2004; **329** 15-19.

3. Rozich JD and Resar RK Medication Safety: One Organization's Approach to the Challenge. *Journal of Clinical Outcomes Management* 2001; **8 (10)** 27-34.

4. Cornish, P. L., Knowles, S. R., Marchesano, R., Tam, V., Shadowitz, S., Juurlink, D. N., and Etchells, E. E. Unintended Medication Discrepancies at the Time of Hospital Admission. *Archives of Internal Medicine* 2005; **165** 424-429.

5. Gleason, K. M., Groszek, J. M., Sullivan, C., Rooney, D., Barnard, C., and Noskin, G. A. Reconciliation of discrepancies in medication histories and admission orders of newly hospitalized patients. *American Journal of Health-System Pharmacy* 2004; **61** 1689-1695.

6. Audit Commission A Spoonful of Sugar. Medicines Management in NHS Hospitals. 2001.

7. The Royal Pharmaceutical Society of Great Britain Moving patients medicines safely. Guidance on Discharge and Transfer Planning. 2006.

8. Canadian Council on Health Services Accreditation CCHSA Patient/Client Safety Goals & Required Organizational Practices. Frequently Asked Questions - Updated June 6, 2005 Ottawa. 2005.

9. University of York, NHS Centre for Reviews and Dissemination Undertaking systematic reviews of research effectiveness. CRD's guidance for those carrying out or commissioning reviews. 2001; **CRD Report No 4**

10. Verhagen, AP, de Vet, HC, de Bie, RA, Kessels, AG, Boers, M, Bouter, LM, and et al The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 1998; **51** 1235-1241.

11. Downs, SH and Black, N The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998; **52** 377-384.

12. Kwan, Y., Fernandes, O., Nagge, J., Wong, G., Huh, J., Hurn, D., and Bajcar, J. Implementation and a randomized controlled evaluation of pharmacist medication assessments in a surgical pre-admission clinic. *Pharmacotherapy* 2005; **25** 1462-1462.

13. Brady, D. and Franklin, B. D. An evaluation of the contribution of the medical admissions pharmacist at a London teaching hospital. *International Journal of Pharmacy Practice* 2004; **12** 1-6.

14. Dutton, K., Hedger, N., Wills, S., Brown, D., and Davies, P. Prevent medication errors on admission. *British Journal of Clinical Governance* 2003; **8** 128-137.

15. Featherstone, P, Giles, P, Browne, M, Baugh, A., Hare, J, Jinks, T, Kennerley, P, Mann, V, Patel, N, Payne, E, and Wilson, T Improving In-Patient Medicines Treatment Sheet Accuracy Within Hospitals. 2006.

16. Rozich JD, Resar, R. K., and et al Standardization as a mechanism to improve safety in health care: impact of sliding scale insulin protocol and reconciliation of medications initiatives. *Joint Commission Journal on Quality & Safety* 2004; **30** 5-14.

17. DeCarolis, D. D., Leraas, M. C., and Rowley, C. Medication reconciliation upon admit using an electronic medical record. *Pharmacotherapy* 2005; **25** 1505-1505.

18. Michels, R. D. and Meisel, S. B. Program using pharmacy technicians to obtain medication histories. *American Journal of Health-System Pharmacy* 2003; **60** 1982-1986.

19. Akwagyriam, I., Goodyer, L. I., Harding, L., Khakoo, S., and Millington, H. Drug history taking and the identification of drug related problems in an accident and emergency department. *Journal of Accident & Emergency Medicine* 1996; **13** 166-168.

20. Mcfazdean E, Isles C, Moffat J, Norrie J, and Steward DI Is there a role for a prescribing pharmacist in preventing prescribing errors in the medical admissions ward? *Pharm J* 2003; **270** 896-899.

21. Cavin, A. and Sen, B. Improving medication history recording and the identification of drug-related problems in an A&E department. *Hospital Pharmacist* 2005; **12** 109-112.

22. Collins, D. J., Nickless, G. D., and Green, C. F. Medication histories: Does anyone know what medicines a patient should be taking? *International Journal of Pharmacy Practice* 2004; **12** 173-178.

23. Slee, A., Farrar, K., Hughes, D., and Constable, S. Optimising medical treatment - How pharmacist-acquired medication histories have a positive impact on patient care. *Pharmaceutical Journal* 2006; **277** 737-739.

24. Carter, M. K., Allin, D. M., Scott, L. A., and Grauer, D. Pharmacist-acquired medication histories in a university hospital emergency department. *American Journal of Health-System Pharmacy, AJHP* 15-12-2006; **63** 2500-2503.

25. Walchle, R. D., McKercher, P. L., Cooper, J. W., Walchle, R. D., McKercher, P. L., and Cooper, J. W. Physician-, nurse-, and pharmacist-conducted patient drug histories. *Contemporary Pharmacy Practice* 1980; **3** 75-78.

26. Truitt, C. A., Longe, R. L., Taylor, A. T., Truitt, C. A., Longe, R. L., and Taylor, A. T. An evaluation of a medication history method. *Drug Intelligence & Clinical Pharmacy* 1982; **16** 592-596.

27. Geibig, C. B., Mansur, J. M., Medema, P. G., and Nold, E. G. Pharmacy-controlled documentation of drug allergies. *American Journal of Hospital Pharmacy* 1991; **48** 260-264.

28. Nottingham City Hospital, Improvement in Action. 2005; **Vol 1**

29. Morimoto, T, Gandhi, T. K., Seger, AC, Hsieh, TC, and Bates, D. W. Adverse Drug Events and Medication Errors, Detection and Classification Methods. *Qual.Saf.Health Care* 2004; **13** 306-314.

30. Winterstein, A. G., Hatton, R. C., Gonzalez-Rothi, R, Johns, T. E., and Segal, R Identifying Clinically Significant Preventable Adverse Drug Events Through a Hospital's Database of Adverse Drug Reaction Reports. *Am J Health-Syst Pharm* 2002; **59** 1742-1749.

31. Bates, D. W., Boyle, D. L., Vliet, M. V. V, Schneider, J, and Leape Relationship between medication errors and adverse drug events. *Journal of internal medicine* 1995; **10** 199-205.

32. Kaushal, R., Bates, D. W., Landrigan, C., McKenna, K. J., Clapp, M. D., Federico, F., and Goldmann, D. A. Medication errors and adverse drug events in pediatric inpatients. *Jama* 2001; **285** 2114-2120.

33. Lesar, T. S., Briceland, L. L., Delcoure, K., Parmalee, J. C., Masta-Gornic, V., and Pohl, H. Medication prescribing errors in a teaching hospital. *Journal of the American Medical Directors Association* 1990; **263** 2329-2334.

34. Bobb, A., Gleason, K., Husch, M., Feinglass, J., Yarnold, P. R., and Noskin, G. A. The Epidemiology of Prescribing Errors: The Potential Impact of Computerized Prescriber Order Entry. *Archives of Internal Medicine* 2004; **164** 785-792.

35. Kanjanarat, P, Winterstein, A. G., Johns, T. E., Hatton, R. C., Gonzalez-Rothi, R, and Segal, R Nature of Preventable Adverse Drug Events in Hospitals: A Literature Review. 2003; **60** 1750-1759.

36. Nicky Thomas Personal communication: Nicky Thomas, Sheffield Teaching Hospitals NHS Foundation Trust. 2007.

37. Kaushal, R., Bates, D. W., Landrigan, C., McKenna, D. J., Clapp, M. D., and Federico, F. Medication errors and adverse drug events in pediatric inpatients. 2001; **285** 2114-2120.

38. Wilson, D. G., McArtney, R. G., Newcombe, R. G., McCartney, R. J., Gracie, J., and Kirk, C. R. Medication errors in paediatric practice: insights from a continuous quality improvement approach. *European journal of pediatrics* 1998; **157** 769-774.

39. Dale, A., Copeland, R, and Barton, R. Prescribing errors on medical wards and the impact of clinical pharmacists. 2007; **11** 19-24.

40. Scarsi, K. K., Fotis, M. A., and Noskin, G. A. Pharmacist participation in medical rounds reduces medication errors. *American Journal of Health-System Pharmacy, AJHP* 1-11-2002; **59** 2089-2092.

41. Lesar, T. S. Errors in the use of medication dosage equations. *Archives of pediatrics & adolescent medicine* 1998; **152** 340-344.

42. Bates, D. W., Cullen, D. J., Laird, N., Petersen, L. A., Small, S. D., Servi, D., Laffel, G., Sweitzer, B. J., Shea, B. F., Hallisey, R., Vandervliet, M., Nemeskal, R., and Leape, L. L. Incidence of Adverse Drug Events and Potential Adverse Drug Events - Implications for Prevention. *Jama-Journal of the American Medical Association* 1995; **274** 29-34.

43. Gurwitz, J. H., Field, T. S., Avorn, J., McCormick, D., Jain, S., Eckler, M., Benser, M., Edmondson, A. C., and Bates, D. W. Incidence and preventability of adverse drug events in nursing homes. *American Journal of Medicine* 2000; **109** 87-94.

44. Weingart, SN, Callanan, LD, Ship, AN, and Aronson, MD A physician-based voluntary reporting system for adverse events and medical errors. *Journal of General Internal Medicine* 2001; **16** 809-814.

45. Gandhi, T. K., Weingart, S. N., Borus, J., Seger, A. C., Peterson, J., Burdick, E., Seger, D. L., Shu, K., Federico, F., Leape, L. L., and Bates, D. W. Adverse drug events in ambulatory care. *New England Journal of Medicine* 2003; **348** 1556-1564.

46. Bates, D. W., Leape, L. L., and Petrycki, S. Incidence and Preventability of Adverse Drug Events in Hospitalized Adults. *Journal of General Internal Medicine* 1993; **8** 289-294.

47. Cullen, D. J., Sweitzer, B. J., Bates, D. W., Burdick, E., Edmondson, A., and Leape, L. L. Preventable adverse drug events in hospitalized patients: A comparative study of intensive care and general care units. *Critical care medicine* 1997; **25** 1289-1297.

48. Lesar, T. S., Lomaestro, B. M., and Pohl, H. Medication-prescribing errors in a teaching hospital - A 9-year experience. *Archives of Internal Medicine* 1997; **157** 1569-1576.

49. Bond, C. A., Raehl, C. L., and Pitterle, M. E. 1992 National Clinical Pharmacy Services Study. *Pharmacotherapy* 1994; **14** 282-304.

50. Netten, A and Curtis, L Unit Costs of Health and Social Care 2003, Personal Social Services Research Unit. *PSSRU* 2007.

51. The NHS Confederation. *NHS* 2007.

52. Society Guardian. *Guardian* 2007.

53. Nester, T. M. and Hale, L. S. Effectiveness of a pharmacist-acquired medication history in promoting patient safety. *American Journal of Health-System Pharmacy* 2002; **59** 2221-2225.

54. Karnon, J, McIntosh, A, Bath, P, and et al A prospective hazard and improvement analysis of medication errors in a UK secondary care setting. *Report for the NHS Patient Safety Programme* 2006.

55. Bates, D. W. The cost of adverse drug events in hospitalized patients. *Journal of the American Medical Association* 1997; **277** 307-311.

56. Pinilla, J, Murillo, C, Carrasco, G, and Humet, C Case-control analysis of the financial cost of medication errors in hospitalized patients. *Eur J Health Economics* 2006; **7** 66-71.

57. Classen, D. C. Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. *Journal of the American Medical Association* 1997; **277** 301-306.

58. Nordgren, LD, Johnson, T, Kirschbaum, M, and Peterson, ML JHQ 144 - Medical Errors: Excess Hospital Costs and Lengths of Stay. *NAHQ* 2004.

59. Schneider, P. J., Gift, M. G., Lee, Y. P., Rothermich, E. A., and Sill, B. E. Cost of medication-related problems at a university hospital. *American Journal of Health-System Pharmacy* 1995; **52(21)** 2415-2418.

60. Douglas, J and Larrabee, S Bringing barcoding to the bedside. Challenges and benefits of implementing a barcode point of care medication administration system. *Health* 2007.

61. Hayward, R. A. and Hofer, T. P. Estimating hospital deaths due to medical errors - Preventability is in the eye of the reviewer. *Jama-Journal of the American Medical Association* 2001; **286** 415-420.

62. Schulz, K. F., Chalmers, I., Hayes, R. J., and Altman, D. G. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Jama* 1-2-1995; **273** 408-412.

63. Rankine, G. P. Redesign of medicine suppl systems in a rehabilitation hospital. *Nursing Standard* 2005; **20** 48-53.

64. Taxis, K., Dean, B., and Barber, N. Hospital drug distribution systems in the UK and Germany--a study of medication errors. *Pharmacy World & Science* 1999; **21** 25-31.

65. Karnon, J, Tsuchiya, A, and Dolan, P Developing a relativities approach to valuing the prevention of non-fatal work-related accidents and ill health. *Health Economics* 2007.

66. Bates, D. W., Teich, J. M., Lee, J., Seger, D., Kuperman, G. J., Ma'Luf, N., Boyle, D., and Leape, L. The impact of computerized physician order entry on medication error prevention. *Journal of the American Medical Informatics Association* 1999; **6** 313-321.