Interventions for improving medication reconciliation across transitions of care (Protocol)

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effect of medication reconciliation on medication discrepancies, patient related outcomes and healthcare utilisation in patients receiving this intervention during transitions of care compared to patients not receiving medication reconciliation.

BACKGROUND

Errors in the prescribing and administration of medication are frequent, costly and harmful (Bates 2007). More than 40% of medication errors take place as a result of inadequate reconciliation of medications at transitions of care (Hughes 2008). Transitional care provides for the continuity of care as patients move between different stages and settings of care (Coleman 2004). The prevalence of medication discrepancies arising at transitions of care have been reported in many different settings (hospital, community and long-term care facilities) and stages of care (admission, transfer and discharge); in particular transitioning from an inpatient to an outpatient setting is associated with an increase in medication errors relative to other stages of care (Boockvar 2006; Coleman 2004; Moore 2003; Tam 2005). Prevalence of adverse events post-hospitalisation as high as 19% have been reported with the major-

ity of these related to adverse drug events, which may be the result of medication error. (Forster 2003). Medication discrepancies as patients transition to home from hospital have also been linked with increased re-hospitalisation rates (Coleman 2005).

"Medication reconciliation is a conscientious, patient centred, inter-professional process that supports optimal medicines management" (Greenwald 2010). It is an attempt to prevent medication errors at patient transition points. It is intended to be the process of creating the most accurate list of medications at all transition points, with the goal of providing the correct medications to the patient (Karapinar-Carkit 2011). Different patient groups and locations have been subject to study. A variety of intervention types have been investigated for the reconciliation of medicines including information technology (Kramer 2007; Schnipper 2009), pharmacist-led (Gillespie 2009), and more complex multi-faceted

interventions (Koehler 2009). The benefits of medication reconciliation interventions are often assessed by comparing medication regimens across transitions and reporting discrepancy reduction as the primary outcome. A previous systematic review reported that although unintended medication discrepancies are common, clinically significant discrepancies may affect only a few patients (Kwan 2013). Challenges arise in identifying those discrepancies that are considered clinically significant and which may give rise to patient harm.... The recognised difficulty in undertaking appropriate comparisons and selection of relevant outcome measures is seen by the fact that while reported interventions have a positive effect on reducing the prevalence of medication discrepancies, the evidence for the presumed subsequent reduction in patient harm or healthcare utilisation is equivocal (Mueller 2012).

Therefore despite reconciliation being recognised as a key aspect of patient safety there remains a lack of consensus and evidence as to the most effective methods of implementing reconciliation and calls have been made to strengthen the evidence base prior to widespread adoption (Greenwald 2010).

Description of the condition

Transitional care describes the care provided to patients to ensure the coordination and continuity of healthcare as they transfer between different settings and/or different stages of care within the same settings (Coleman 2003b). Examples of care settings include locations such as hospitals, subacute and long term nursing facilities, patients' homes, primary care offices, and assisted living facilities (Coleman 2003b). Stages of care within these care settings may include admission, transfer and discharge. Transitions of care are associated with medication errors and patient harm. Greater coordination and attention to care transitions have been brought about by regulatory changes and financial penalties for "hospital-acquired conditions" (Jenq 2012). Furthermore, improved continuity of prescribed medication via medication reconciliation for patients at transitions of care is recommended by national standard setting bodies and internationally led initiatives e.g. World Health Organization (WHO)'s High 5's project (IHI 2011; NICE 2007; WHO 2006). However, the most effective method of conducting reconciliation remains unclear.

Description of the intervention

Medication reconciliation consists of the following three steps (IHI 2011).

1. **Verification:** A current medication list is developed using one or more sources of information (e.g. general practitioner medical records, patient's own supply, pharmacy records).

2. **Clarification:** Medication and dosages are checked for appropriateness. Here appropriateness means ensuring that there

are no unintentional changes, rather than a medication review leading to optimal medication appropriateness).

3. **Reconciliation:** Newly prescribed medications are compared to old and any changes made are documented.

How the intervention might work

Failure to reconcile medications can result in medication error and subsequent adverse drug events (IHI 2011). Interventions to improve medication reconciliation may work by improving the communication between all those involved in the medication use process (dispensing, administration, monitoring across settings and stages of care), including the patient. Additionally these interventions may well help in reducing transcribing errors, improved monitoring of prescriptions, information technology systems and reorganisation of care delivery.

Why it is important to do this review

Medication reconciliation is incorporated into the National Patient Safety Goals of the Joint Commission under the umbrella of improving the safety of using medications (The Joint Commission 2013). The National Institute for Health and Care Excellence (NICE) in collaboration with the National Patient Safety Agency in the UK encouraged the standardisation of reconciliation processes within healthcare organisations (NICE 2007). The Canadian Patient Safety Institute and the Institute for Safe Medication Practices (Canada) have advocated for medication reconciliation and the WHO launched the High 5's project in 2006, with an emphasis on patient safety with the standard operating procedure - 'assuring medication accuracy at transitions in care' focused on reducing medication discrepancies (WHO 2006). Despite the high level of interest in implementing medication reconciliation the most effective process of conducting reconciliation remains unclear. A consensus statement from key stakeholders has called for further efforts to identify the best practices surrounding medicine reconciliation and their wider dissemination (Greenwald 2010). The seminal Institute of Medicine report titled "To Err is Human: Building a Safer Health System" highlighted medication error as being widely prevalent, costly and contributing to preventable causes of patient injury (IOM 1999).The findings of this proposed review are relevant at both a national and international level. Regulatory bodies, healthcare institutions, patient safety advocates, healthcare practitioners and the wider public would be receptive audiences for the findings from a systematic review of the most effective method of medicines reconciliation.

O B J E C T I V E S

To assess the effect of medication reconciliation on medication discrepancies, patient related outcomes and healthcare utilisation in patients receiving this intervention during transitions of care compared to patients not receiving medication reconciliation.

METHODS

Criteria for considering studies for this review

Types of studies

We will include the following types of studies:
- randomised controlled trials (RCTs);
- non-RCTs;
- controlled before after studies;
- interrupted time series studies;
- repeated measures studies.

Studies will be eligible for inclusion, irrespective of language or publication status.

Non-RCTs, controlled before after studies, interrupted time series studies and repeated measures studies will be eligible for inclusion, subject to the criteria stated in the *Cochrane Handbook for Systematic Reviews of Interventions* and inclusion criteria developed by the Cochrane Effective Practice and Organisation of Care (EPOC) Group (Higgins 2011). It was felt necessary to include these types of studies due to the potentially small number and difficulty of designing randomised controlled trials in the area of medication safety.

We will exclude case series, cohort studies, studies using historical controls or cross-sectional studies.

We will report results from randomised studies separately.

Types of participants

We will include all studies involving patients experiencing a transition of care. Transitions of care refer to changes in the level, location, or providers of care as patients move within the health care system (Coleman 2003a; Kim 2013). This may include but is not limited to hospital admission/discharge, acute and sub acute facilities/units/wards, primary and speciality care, long term care institutions and patients' homes. Transition may be in either direction e.g. admission and/or discharge to an intensive care unit from a general ward.

There will be no restriction on age, gender, ethnicity, location or patient population.

Types of interventions

We will select studies where the intervention is broadly compliant with the process of medication reconciliation as outlined by the Institute for Healthcare Improvement (IHI 2011): *"the process of creating the most accurate list possible of all medications a patient is taking - including drug name, dosage, frequency, and route - and comparing that list against the physician's admission, transfer, and/ or discharge orders, with the goal of providing correct medications to the patient at all transition points..."*. Medication reconciliation involves three steps (IHI 2011):

1. create an accurate and complete list of current medications (verify);
2. check appropriateness of medication regimes (clarify);
3. document the reason for medication changes (reconcile).

The intervention must be applied as patients transition from different levels and/or locations of care.

Medication reconciliation interventions may be aligned to a number of broad interventional categories including professional interventions, financial, organisational and regulatory (EPOC 2013b). These can include pharmacist delivered reconciliation (Kwan 2007; Makowsky 2009; Nazareth 2001; Walker 2009), complex multi-faceted interventions (Scullin 2007), and information technology solutions (Jack 2009; Schnipper 2009). It may be possible within the review to perform subgroup analysis to compare different approaches within these categories of interventions.

We will exclude trials investigating interventions to improve the quality of prescribing during transitions of care, with no medication reconciliation focus.

The comparator group will be those patients receiving no intervention or "usual care" as provided by the relevant healthcare provider.

Types of outcome measures

The outcomes chosen reflect the Cochrane EPOC Group guidance as those being important to the population of interest as well as decision makers in healthcare (EPOC 2013a). We will exclude studies reporting secondary outcomes only. We will include process measures, patient related outcomes and healthcare utilisation.

Primary outcomes

Discrepancies in prescription per:
- patient;
- medication (e.g. drug/dose/name/mode of administration/ frequency).

Medication discrepancies have previously been defined as unexplained differences in documented medication regimes across different sites of care (Mueller 2012).

Secondary outcomes

Patient related and process outcomes:

- medication discrepancy with the potential for adverse drug events, which have been previously described as "incidents with potential for injury related to a drug" (Bates 1995);
  - adverse drug events;
  - mortality.

Health care utilisation:
  - primary care visits;
  - emergency department visits;
  - unplanned re-hospitalisation;
  - length of stay.

Additional outcomes:

- adverse effects of interventions (e.g. unanticipated increased workload, health worker attrition);

- resource use (dependent on studies of effectiveness selected for inclusion in the review, a narrative summary of the characteristics of economic analysis undertaken may be possible e.g. comparisons of study design, methodology and outcome, measures of incremental resource use, cost and cost effectiveness etc. These results may be useful in future full economic evaluations).

The order of the chosen outcomes (with a process measure being identified as the primary outcome) is a reflection of the current efforts in the study of medication reconciliation. The majority of completed and planned interventional studies in this area have chosen medication discrepancy as their primary outcome. Indeed many trials reporting clinical measures such as re-hospitalisations are underpowered to adequately report such findings. In addition, reporting potential for adverse drug events acknowledges previously-raised concerns that some discrepancies may have little or no impact on patient safety (Kwan 2013).

Search methods for identification of studies

The Cochrane EPOC Group will search the Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of Effects (DARE) for related systematic reviews and the following databases for primary studies.

Electronic searches

- Cochrane EPOC Group Specialised Register
- Cochrane Central Register of Controlled Trials (CENTRAL), *The Cochrane Library*
- MEDLINE and MEDLINE In-Process and other non-indexed citations, OvidSP (Appendix 1)
- EMBASE, OvidSP
- PsychINFO, OVIDSP

- CINAHL (Cumulative Index to Nursing and Allied Health Literature), EbscoHost
- Dissertations and Theses Database, ProQuest
- Science Citation Index, ISI Web of Knowledge
- Web of Science, Conference Proceedings Citation Index-Science, ISI Web of Knowledge
- Pharmline, National Electronic Library for Medicines
- International Pharmaceutical Abstracts (IPA), ProQuest

We will translate the MEDLINE search strategy for other databases using appropriate syntax and vocabulary for those databases. The strategy includes medical subject headings and synonyms for medication reconciliation and transitions of care. We will limit results using the "Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); Ovid format" , to identify RCTs, as well as the Cochrane EPOC Group methodology filter to identify non-RCTs.

Searching other resources

We will conduct a grey literature search to identify studies not indexed in the databases listed above. Sources will include the sites listed below. Additional sources, if any, will be documented in the review.

- Open Grey (http://www.opengrey.eu/).
- Grey Literature Report (New York Academy of Medicine) (http://greylit.org/).
- Agency for Healthcare Research and Quality (AHRQ) (http://www.ahrq.gov/).
- National Research Register (NRR) Archive (http://www.nihr.ac.uk/Pages/NRRArchive.aspx).
- Joanna Briggs Institute (http://joannabriggs.org/).
- National Institute for Health and Care Excellence (NICE) (http://www.nice.org.uk/).
- NHS Evidence Search (https://www.evidence.nhs.uk/).

We will search the following Registries:
- International Clinical Trials Registry Platform (ICTRP) search portal, WHO (http://apps.who.int/trialsearch/);
- ClinicalTrials.gov, US National Institutes of Health (NIH) (http://clinicaltrials.gov/).

We will also:
- screen individual journals and conference proceedings;
- review reference lists of all included studies, relevant systematic reviews/primary studies/other publications;
- contact authors of relevant studies or reviews to clarify reported published information/seek unpublished results/data;
- contact researchers with expertise relevant to the review topic/Cochrane EPOC Group interventions.

Data collection and analysis

Selection of studies

A combination of two authors (PR,TG, RMcD, FB) will independently screen titles and abstracts to decide which studies satisfy the inclusion criteria as well as identification of multiple reports from single studies. Any papers not meeting the inclusion criteria will be excluded at this stage. If there is uncertainty, consensus will be reached by discussion with another co-author. If agreement cannot be reached, we will involve an Cochrane EPOC Group editor to resolve it. Following this, two authors (PR, TG) will independently assess the full text articles to ensure the studies still fulfil the inclusion criteria.

Data extraction and management

A combination of two authors (PR,TG, RMcD, FB) will independently undertake data abstraction using a modified version of the Cochrane EPOC Group data collection checklist to include: study design, study population, intervention, usual care, outcome measures used and length of follow-up data (EPOC 2013c). Any disagreement will be resolved by discussion between the co-authors. Where necessary, we will contact authors for missing information or clarification. Information from data extraction forms will guide the extraction of numerical data for meta-analysis in the Cochrane Collaboration's statistical software, Review Manager 2013.

Assessment of risk of bias in included studies

The criteria against which the risk of bias in a study is judged will depend upon its study design. The domains by which studies with a control group (RCTs, non-RCTs and controlled before and after studies) will be assessed include (EPOC 2011; Higgins 2011):

1. sequence generation;
2. allocation concealment;
3. baseline characteristics;
4. baseline outcome measurement;
5. blinding;
6. incomplete outcome data;
7. protection against contamination;
8. selective outcome reporting;
9. other biases.

We will tabulate the description of the domains for each included study, along with a judgement on the risk of bias (low, high or unclear), using one key domain of a study-level entry (allocation concealment) and one key domain of an outcome-level entry (incomplete outcome data) based on the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will undertake a summary assessment of the risk of bias for the primary outcome across the studies (Higgins 2011). For each study, we will provide a summary assessment of risk of bias as shown below:

1. low risk when there is a low risk of bias across all key domains;
2. unclear risk of bias when there is an unclear risk of bias in one or more of the key domains;
3. high risk of bias when there is a high risk of bias in one or more of the key domains.

We will use the following criteria for interrupted time series studies and repeated measures studies (EPOC 2011):

1. the intervention was independent of other changes;
2. the shape of the intervention effect was pre-specified;
3. the intervention was unlikely to affect data collection;
4. incomplete outcome data were adequately addressed;
5. the study was free from selective outcome reporting.

A combination two authors (PR,TG, RMcD, FB, CH, TF) will independently perform the quality assessment. We will resolve disagreements by discussion and, if needed, arbitration by a third author.

Measures of treatment effect

Randomised and non-randomised studies will be reported separately. We will report outcomes for each study in natural units. We will calculate, where possible, absolute change from baseline with 95% confidence intervals. We will report estimates for dichotomous outcomes (e.g. adverse drug events) as risk ratios. We will report estimates for continuous outcomes as mean differences if they are measured on the same scale, if continuous outcomes are measured on multiple scales, we will report the standardised mean difference. We will report pre-intervention and post-intervention means or proportions where baseline results are available for both intervention and control groups from RCTs, quasi-RCTs and controlled before and after studies.

For RCTs, we will combine findings from independent studies using standard meta-analysis techniques provided enough study data is obtained and taking account of heterogeneity between studies. The size of the study will determine the study's weight and an overall treatment effect will be estimated.

For interrupted time series design studies, we will extract the difference in slope and the difference in pre to post-intervention levels. We will analyse the post- versus pre-intervention difference (adjusted for trends) at specific time points (three months, six months and six-monthly thereafter). If the differences are not available in the primary reports, we will attempt re-analysis using data from graphs or tables

We will exclude studies ignoring secular changes and performing simple pre-post analyses unless re-analysis is possible. Re-analysis, to estimate the effect of an intervention, will include a segmented time-series regression analysis, taking into account secular time trends and any autocorrelation between any individuals observations. This allows the change in level and change in trend, after the intervention, to be estimated. Meta-analysis will be performed for the changes in level and changes in trend using the generic inverse

variance method in Review Manager 2013.

We will tabulate all relevant information of studies included in the review. This will include all pre- and post-intervention results (sample sizes, means, proportions, 95% confidence intervals, etc.) for each group for each outcome of interest. Additionally, we will examine the pre- and post-intervention difference for each group for each outcome of interest as well as the differences across groups. We will conduct a meta-analysis combining the results of the individual studies.

Unit of analysis issues

Cluster-randomised trials selected for inclusion will be assessed in order to ensure that appropriate analysis was carried out to address cluster effects and to avoid overestimating the significance of differences. In cluster randomised studies where the analysis was carried out ignoring the effect of clustering, efforts will be made to obtain the data needed to correct for this. Should the data not be forthcoming we will use the intra cluster correlation coefficient (ICC) or design effect from external sources (other trials included in the review) to inflate the standard error so as to account for clustering as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). As stated above, we will assess all non-RCTs, controlled before and after studies, interrupted time series studies and repeated measures studies selected for inclusion to ensure that the appropriate analysis was carried out and, as for the cluster randomised trials efforts, will be made to obtain the data if necessary.

Dealing with missing data

We will contact lead study investigators or corresponding authors for any missing trial data or data missing from published reports or for additional clarification. If there are any missing data from a study, we will explicitly state this. Sensitivity analyses will be undertaken as per the *Cochrane Handbook for Systematic Reviews of Interventions* to assess how sensitive results are to reasonable changes in the assumptions that are made (Higgins 2011). We will comment on the potential impact of missing data on the review findings in the Discussion section.

Assessment of heterogeneity

We intend to assess contextual heterogeneity on the basis of information collected on the context in which the intervention was implemented. We will assess for variability in the participants, interventions and outcomes studied to identify clinical heterogeneity, and for variability in study design to describe methodological diversity. Statistical heterogeneity will be identified and measured as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The following will be used as a guide for interpretation:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

Assessment of reporting biases

We will examine assymetry in funnel plots of the primary outcome to assess the potential for study effects such as publication bias, if a sufficient number of trials are available. We will conduct formal statistical tests for funnel plot asymmetry, namely the Begg's and Egger's methods (Higgins 2011), again if a sufficient number of trials are available. Furthermore, we will assess reporting bias by scrutinising the study results using the 'Risk of bias' tables (e.g. selective outcome reporting). Where there is a possibility of publication bias and small-study effects, we will undertake a sensitivity analysis as described below (Sensitivity analysis). In addition to searching trial registries for relevant trials not identified in our main database searches, we will also search for protocols of studies selected for inclusion, to compare planned with actual methods, interventions and outcomes. Furthermore a thorough search of the grey literature and contact with known experts in the field will also reduce the influence of publication bias on our review.

Data synthesis

We will perform statistical analysis using Review Manager 2013. We will conduct the meta-analysis of included randomised controlled trials and observational trials separately. Pooled estimates (risk ratios (RRs) with 95% confidence intervals (CIs)) of the evaluated outcome measures will be calculated by the generic inverse variance method.

Results will not be depicted as 'not statistically significant' or 'non significant', but we will report the CIs together with the exact P value. In the absence of statistical and clinical heterogeneity we will apply a fixed-effects model to pooled data. The I^2 statistic will be examined to describe the proportion of the variability in the results that reflects real differences in effect size. However, variation in studies with respect to populations, interventions, outcomes and settings is likely. Thus, the true effect is likely to be related, but not the same for all studies. We will therefore choose the random-effects model or choose not to perform a meta-analysis.

If it is not possible to synthesise the data from the included studies, we will provide a narrative synthesis of the results, grouping together studies that used similar interventions and provide a comparison of different approaches. The data will eventually be synthesised using a 'Summary of Findings' table that will provide key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on all primary outcomes for a given comparison. We will conduct quality assessment of the results using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which specifies four levels of quality (high, moderate,

low and very low) where the highest quality rating is for a body of evidence based on randomised trials. Quality will be assessed separately for each outcome.

Subgroup analysis and investigation of heterogeneity

We will pursue subgroup analyses with sufficient data. Exploratory search results suggest the following subgroup analysis may be possible.

- Patients with polypharmacy (≥4 long-term medications), older (>65), and/or chronic illnesses as these groups are known to suffer more errors in prescribing (Gleason 2010; Grimes 2011).

- Comparison of different approaches to medication reconciliation (e.g. information technology, pharmacist delivered, integrated medicines management) may be undertaken, particularly where the methods are supported by the literature and are of interest in developing and implementing reconciliation interventions.
- Patients admitted to or discharged from acute hospital care (hospital admission and discharge are well studied transitions of care for applying medication reconciliation interventions).

The number of subgroups will be kept to a minimum and priority will be given to subgroups that are of specific interest to the potential implementation of any future intervention.

Sensitivity analysis

We will conduct a sensitivity analysis to calculate the effect of risk of bias (including missing data) within studies on effect size, by calculating the effect of excluding or including studies with a higher risk of bias.

A C K N O W L E D G E M E N T S

R E F E R E N C E S

Additional references

Bates 1995
Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, et al.Incidence of adverse drug events and potential adverse drug events. Implications for prevention. ADE Prevention Study Group. *JAMA* 1995;**274**(1):29–34.

Bates 2007
Bates DW. Preventing medication errors: a summary. *American Journal of Health-System Pharmacy* 2007;**64**(14 Suppl 9):S3–9.

Boockvar 2006
Boockvar KS, Carlson LaCorte H, Giambanco V, Fridman B, Siu A. Medication reconciliation for reducing drug-discrepancy adverse events. *American Journal of Geriatric Pharmacotherapy* 2006;**4**(3):236–43.

Coleman 2003a
Coleman EA. Falling through the cracks: challenges and opportunities for improving transitional care for persons with continuous complex care needs. *Journal of the American Geriatrics Society* 2003;**51**(4):549–55.

Coleman 2003b
Coleman EA, Boult C. Improving the quality of transitional care for persons with complex care needs. *Journal of the American Geriatrics Society* 2003;**51**(4):556–7.

Coleman 2004
Coleman EA, Berenson RA. Lost in transition: challenges and opportunities for improving the quality of transitional care. *Annals of Internal Medicine* 2004;**141**(7):533–6.

Coleman 2005
Coleman EA, Smith JD, Raha D, Min SJ. Posthospital medication discrepancies: prevalence and contributing factors. *Archives of Internal Medicine* 2005;**165**(16):1842–7.

EPOC 2013a
Cochrane Effective Practice and Organisation of Care (EPOC) Group. What outcomes should be reported in Cochrane Effective Practice and Organisation of Care (EPOC) reviews?. http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/06%20What%20outcomes%20should%20be%20reported%20in%20EPOC%20revi (accessed 17–10–2013).

EPOC 2013b
Cochrane Effective Practice and Organisation of Care (EPOC) Group. EPOC Resources for review authors. Oslo: Norwegian Knowledge Centre for the Health Services; 2013. http://epocoslo.cochrane.org/epoc-specific-resources-review-authors (accessed 17–10–2013).

EPOC 2013c
Cochrane Effective Practice and Organisation of Care (EPOC) Group. Effective Practice and Organisation of Care (EPOC). EPOC Resources for review authors. Data collection checklist. Oslo: Norwegian Knowledge Centre for the Health Services; 2013.. http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/datacollectionchecklist.pdf (accessed 17–10–2013).

Forster 2003
Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting

patients after discharge from the hospital. *Annals of Internal Medicine* 2003;**138**(3):161–7.

Gillespie 2009
Gillespie U, Alassaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H, et al.A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. *Archives of Internal Medicine* 2009;**169**(9):894–900.

Gleason 2010
Gleason KM, McDaniel MR, Feinglass J, Baker DW, Lindquist L, Liss D, et al.Results of the Medications at Transitions and Clinical Handoffs (MATCH) study: an analysis of medication reconciliation errors and risk factors at hospital admission. *Journal of General Internal Medicine* 2010;**25**(5):441–7.

Greenwald 2010
Greenwald JL, Halasyamani L, Greene J, LaCivita C, Stucky E, Benjamin B, et al.Making inpatient medication reconciliation patient centered, clinically relevant and implementable: a consensus statement on key principles and necessary first steps. *Journal of Hospital Medicine* 2010;**5**(8):477–85.

Grimes 2011
Grimes TC, Duggan CA, Delaney TP, Graham IM, Conlon KC, Deasy E, et al.Medication details documented on hospital discharge: cross-sectional observational study of factors associated with medication non-reconciliation. *British Journal of Clinical Pharmacology* 2011;**71**(3):449–57.

Higgins 2011
Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hughes 2008
Hughes RG (ed.). Patient safety and quality: An evidence-based handbook for nurses. (Prepared with support from the Robert Wood Johnson Foundation). AHRQ Publication No. 08-0043. Rockville, MD: Agency for Healthcare Research and Quality; March 2008. http://www.ahrq.gov/professionals/clinicians-providers/resources/nursing/resources/nurseshdbk/nurseshdbk.pdf (accessed 17–10–2013).

IHI 2011
Institute for Healthcare Improvement. How-to Guide: Prevent Adverse Drug Events by Implementing Medication Reconciliation. http://www.ihi.org/_layouts/ihi/login/login.aspx?ReturnURL=%2fknowl-edge%2fPages%2fTools%2fHowtoGuidePreventAdverseDrugEvents.aspx (accessed 17–10–2013).

IOM 1999
Institute of Medicine. In: Kohn L Corrigan J Donaldson M editor(s). *To Err Is Human: Building a Safer Health System.*. Washington, DC: National Academies Press, 1999.

Jack 2009
Jack BW, Chetty VK, Anthony D, Greenwald JL, Sanchez GM, Johnson AE, et al.A reengineered hospital discharge program to decrease rehospitalization: a randomized trial. *Annals of Internal Medicine* 2009;**150**(3):178–87.

Jenq 2012
Jenq G, Tinetti ME. The journey across the health care (dis)continuum for vulnerable patients: policies, pitfalls, and possibilities. *JAMA* 2012;**307**(20):2157–8.

Karapinar-Carkit 2011
Karapinar F, Terry DRP. Medication reconciliation : a necessity for continuity of care (EAHP 16th Congress Report). *European Journal of Hospital Pharmacy: Practice* 2011;**17**:32–3.

Kim 2013
Kim CS, Flanders SA. Transitions of care. *Annals of Internal Medicine* 2013;**158**(5 Pt 1):ITC3–1.

Koehler 2009
Koehler BE, Richter KM, Youngblood L, Cohen BA, Prengler ID, Cheng D, et al.Reduction of 30-day postdischarge hospital readmission or emergency department (ED) visit rates in high-risk elderly medical patients through delivery of a targeted care bundle. *Journal of Hospital Medicine* 2009;**4**(4):211–8.

Kramer 2007
Kramer JS, Hopkins PJ, Rosendale JC, Garrelts JC, Hale LS, Nester TM, et al.Implementation of an electronic system for medication reconciliation. *American Journal of Health-System Pharmacy* 2007;**64**(4):404–22.

Kwan 2007
Kwan Y, Fernandes OA, Nagge JJ, Wong GG, Huh JH, Hurn DA, et al.Pharmacist medication assessments in a surgical preadmission clinic. *Archives of Internal Medicine* 2007;**167**(10):1034–40.

Kwan 2013
Kwan JL, Lo L, Sampson M, Shojania KG. Medication reconciliation during transitions of care as a patient safety strategy: a systematic review. *Annals of Internal Medicine* 2013;**158**(5 Pt 2):397–403.

Makowsky 2009
Makowsky MJ, Koshman SL, Midodzi WK, Tsuyuki RT. Capturing outcomes of clinical activities performed by a rounding pharmacist practicing in a team environment: the COLLABORATE study [NCT00351676]. *Medical care* 2009;**47**(6):642–50.

Moore 2003
Moore C, Wisnivesky J, Williams S, McGinn T. Medical errors related to discontinuity of care from an inpatient to an outpatient setting. *Journal of General Internal Medicine* 2003;**18**(8):646–51.

Mueller 2012
Mueller SK, Sponsler KC, Kripalani S, Schnipper JL. Hospital-based medication reconciliation practices: a systematic review. *Archives of Internal Medicine* 2012;**172**(14):1057–69.

Nazareth 2001

Nazareth I, Burton A, Shulman S, Smith P, Haines A, Timberal H. A pharmacy discharge plan for hospitalized elderly patients - a randomized controlled trial. *Age and Ageing* 2001;**30**(1):33–40.

NICE 2007

National Institute for Health and Care Excellence. Technical patient safety solutions for medicines reconciliation on admission of adults to hospital: Guidance. Available from http://guidance.nice.org.uk/PSG001.

Review Manager 2013

The Nordic Cochrane Centre, The Cochrane Colllaboration. Review Manager (RevMan). 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Colllaboration, 2013.

Schnipper 2009

Schnipper JL, Hamann C, Ndumele CD, Liang CL, Carty MG, Karson AS, et al.Effect of an electronic medication reconciliation application and process redesign on potential adverse drug events: a cluster-randomized trial. *Archives of Internal Medicine* 2009;**169**(8):771–80.

Scullin 2007

Scullin C, Scott MG, Hogg A, McElnay JC. An innovative approach to integrated medicines management. *Journal of Evaluation in Clinical Practice* 2007;**13**(5):781–8.

Tam 2005

Tam VC, Knowles SR, Cornish PL, Fine N, Marchesano R, Etchells EE. Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. *Canadian Medical Association Journal* 2005;**173**(5):510–5.

The Joint Commission 2013

The Joint Commission. National Patient Safety Goals. http://www.jointcommission.org/standards_information/npsgs.aspx (accessed 17–10–2013).

Walker 2009

Walker PC, Bernstein SJ, Jones JN, Piersma J, Kim HW, Regal RE. Impact of a pharmacist-facilitated hospital discharge program: a quasi-experimental study. *Archives of Internal Medicine* 2009;**169**(21):2003–10.

WHO 2006

World Health Organization. Action on Patient Safety - High 5s. http://www.who.int/patientsafety/implementation/solutions/high5s/en/index.html (accessed 17–10–2013).

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. MEDLINE search strategy

1   Medication Reconciliation/ (145)

2   ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formularies or prescription? or prescrib$) adj3 (reconcil$ or review or reviewing)).ti,ab. (7628)

3   ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formularies or prescription? or prescrib$) adj3 (assess$ or audit?)).ti,ab. (12053)

4   (stopp or beer's criteria).ti,ab. (248)

5   (medication? adj2 discrepanc$).ti,ab. (131)

6   ((medication? or prescribing) adj2 error?).ti,ab. (3382)

7   stewardship.ti,ab. (1172)

8   or/1-7 [Medication Reconciliation] (23888)

9   Medication Systems, Hospital/ [ML] (3045)

10   Pharmacy service, hospital/ [ML] (9482)

11   ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) and (inpatient? or hospital$ or WARD? or UNIT or UNITS)).ti. (2877)

12   ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) adj2 (inpatient? or hospital$ or WARD? or UNIT or UNITS)).ab. (2451)

13   ((medication? or prescribing or prescription? or dispensing) adj2 system?).ti,ab. and (hospital$ or WARD or WARDS or (CARE adj2 UNIT?) or INPATIENT?).ti,hw. (500)

14   or/9-13 [Med systems/Pharm service hospitals] (13912)

15   Pharmacists/ or Pharmacists' Aides/ [ML] (10039)

16   Pharmaceutical Services/ or Drug Information Services/ or Clinical Pharmacy Information Systems/ (8273)

17   Drug Monitoring/ or Medication Therapy Management/ or Drug Therapy/ or Drug Therapy, Computer-Assisted/ (46901)

18   Prescriptions/ or Drug Prescriptions/ or Pharmaceutical Preparations/ or Drug Therapy/ or Drug Dosage Calculations/ or Electronic Prescribing/ or Medication Systems/ (97267)

19   medication errors/ or polypharmacy/ or inappropriate prescribing/ (11544)

20   Drug utilization review/ (2759)

21   (pharmacy or pharmacies or pharmacist? or prescription? or prescribing).ti. (39315)

22   (pharmacist-led or pharma$ initiated or ((driven or lead or led) adj2 pharmacist?)).ab. (227)

23   (PRESCRIBING adj2 PATTERN?).ab. (1406)

24   ("physician-pharmacist?" or "doctor-pharmacist?").ti,ab. (138)

25   ((IMPROV$ or OPTIMI?ING or OPTIMI?E? or OPTIMAL$) and (DOSING or DOSAGE or PHARMAC$ or PRESCRIB$ or PRESCRIPT$)).ti. or ((IMPROV$ or OPTIMI?ING or OPTIMI?E? or OPTIMAL$) adj2 (PHARMACEUTICAL CARE or PHARMACY or PRESCRIB$ or PRESCRIPT$)).ab. (4492)

26   ((pharmaceutical adj (care or consult$)) or (pharmacist? adj2 (care or consult$ or intervention? or managed))).ab. (2182)

27   ((drug therapy or drug regime? or medication? or medicineS or pharmacy or pharmacist? or pharmaceutical or PRESCRIB$ or prescription?) adj2 (audit$ or monitor$ or RECONCIL$ or review?)).ti,ab. (4569)

28   ((medication? or prescrib$ or pharmac$) adj2 (manage? or management or service? or system?)).ti,ab. (12779)

29   (("drug therapy" or dosage? or dose? or medication? or PRESCRIPTION? or PRESCRIB$ or PHARMACIST? or PHARMA-CEUTICAL CARE) adj2 (managing or management or monitor$)).ti,ab. (6310)

30   ("drug utili?ation" adj2 (review? or reconcil$ or audit?)).ab. or ("drug utili?ation" and (review? or reconcil$ or audit?)).ti. (284)

31   (inappropriate$ adj2 (medicine? or medication? or prescrib$ or drug?)).ti,ab. [Term added Aug 2011] (1506)

32   Drug utilization/ (15915)

33   or/15-32 [Drug use/misuse. Pharmacy services] (176303)

34   ((care or patient?) adj3 transition$).ti,ab. (4365)

35   (hospital adj3 releas$).ti,ab. (455)

36   "hospital to home".ti,ab. (1686)

37   Patient admission/ or Patient discharge/ or Patient readmission/ or Patient transfer/ [ML] (42670)

38   (patient? or hospital$ or medical centre or medical centres or medical center?).ti,hw. and (discharg$ or admission? or admitting or readmission? or readmit$ or transfer? or transferred or transferring).ti. (23404)

39   ((patient? or care facility or medical facility or hospital? or medical centre or medical centres or medical center? or emergency or ward or wards or unit or units or (intensive adj2 care) or ICU or acute care or (hospital? adj2 department?)) adj2 (discharg$ or admission? or admitting or readmission? or transfer? or transferring or transferred)).ab. (79034)

40   (exp Academic Medical Centers/ or exp Hospital Units/ or exp Hospitals/ or exp Ambulatory Care Facilities/) and (transfer or transferred or discharge or admission? or readmission? or re-admission?).ti. (5865)

41   ((earlie$ or early) adj2 discharg$).ab. (2897)

42   ((icu or (intensive adj2 care) or acute care or unit or units or ward or wards or department) adj3 transition$).ti,ab. (361)

43   (transfer$ adj3 emergency).ti,ab. (473)

44   (hospital adj8 (transfer? or transferred)).ti,ab. (4063)

45   discharge.ti. (13765)

46   (discharge adj3 (medication? or prescription? or communication? or (information adj2 exchang$))).ab. (1020)

47   or/34-46 [Discharge/transition care] (133107)

48   8 and 47 [Medication Reconciliation & Transition of Care] (904)

49   (and/14,47) not 48 [Hospital Med Systems & Transition of Care] (464)

50   (and/33,47) not (or/48-49) [Drug Use/Misue Pharm services & Transition of Care] (2403)

51   (randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti. (811019)

52   exp animals/ not humans.sh. (3744372)

53   51 not 52 [Cochrane RCT Filter 6.4.d Sens/Precision Maximizing] (749158)

54   intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individuali?e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care)).ab. (134843)

55   (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab. [added 2.4] (7924)

56   (hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw. (663628)

57   demonstration project?.ti,ab. (1789)

58   (pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab. (55792)

59   (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab. (519)

60   trial.ti. or ((study adj3 aim?) or "our study").ab. (529459)

61   (before adj10 (after or during)).ti,ab. (324911)

62   ("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab,hw. (90765)

63   ("time series" adj2 interrupt$).ti,ab,hw. (776)

64   (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab. (7385)

65   pilot.ti. (34027)

66   Pilot projects/ (73602)

67   (clinical trial or controlled clinical trial or multicenter study).pt. (587846)

68   (multicentre or multicenter or multi-centre or multi-center).ti. (25106)

69   random$.ti,ab. or controlled.ti. (662937)

70   (control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt. (361452)

71   "comment on".cm. or review.ti,pt. or randomized controlled trial.pt. (2661748)

72   (rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti. (1270457)

73   exp animals/ not humans.sh. (3744372)

74   (or/54-70) not (or/71-73) [EPOC Methods Filter 2.4 Medline] (1905394)

75   ((or/48-50) and 53) not placebo$.ti,ab,hw. [RCT Results] (377)

76   ((or/48-50) and 74) not (placebo$.ti,ab,hw. or 75) [EPOC Filter Results] (2135)

77   Medication reconciliation/ (145)

78   ((medication? or prescription?) and reconcil$).ti. (210)

79   ((medication? or prescription?) adj3 reconcil$).ab. (307)

80   (or/77-79) not ((or/75-76) or placebo?.ti,ab,hw.) [Unfiltered results; screen all] (307)

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No conflicts of interest are reported.

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