Ensuring continuity of patient care across the healthcare interface, Telephone follow-up post hospitalisation.

Mohanad Odeh PhD[1,2] Claire Scullin PhD[1], Glenda Fleming PhD[3], Michael G. Scott PhD,[3] Robert Horne PhD[4] and James C McElnay PhD[2]

[1]Clinical and Practice Research Group, School of Pharmacy, Queen's University Belfast, Belfast BT9 7BL, [2]Faculty of Pharmaceutical Sciences, Hashemite University, Jordan, [3]Medicines Optimisation Innovation Centre (MOIC), Antrim, UK, [4]School of Pharmacy, University College London, London WC1N 1AX.

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Correspondence: James C McElnay

j.mcelnay@qub.ac.uk

'The clinical responsibility for each patient post-hospitalisation lay with his/her individual general medical practitioner (GP). '

Abstract

Aim

To implement pharmacist-led, post-discharge telephone follow-up (TFU) intervention and to evaluate its impact on rehospitalisation parameters in polypharmacy patients, via comparison with a well-matched control group.

Method

Pragmatic, prospective, quasi-experimental study. Intervention patients were matched by propensity score techniques with a control group. Guided by results from a pilot study, clinical pharmacists implemented TFU intervention, added to routine Integrated Medicines Management (IMM) service.

Results

Using an intention to treat approach, reductions in 30- and 90-day readmission rates for intervention patients compared with controls were 9.9% (Odds Ratio [OR]= 0.57; 95% CI: 0.36 - 0.90; P<0.001) and 15.2% (OR= 0.53; 95%CI: 0.36-0.79; P=0.021) respectively. Marginal mean time to readmission was 70.9 days (95% CI: 66.9 - 74.9) for intervention group compared with 60.1 days (95%CI: 55.4 -64.7) for controls. Mean length of hospital stay compared with control was (8.3 days vs 6.7 days; P<0.001). Benefit: cost ratio for 30-day readmissions was 29.62, and 23.58 for 90-day interval. Per protocol analyses gave more marked improvements. In intervention patients, mean concern scale score, using Beliefs about Medicine Questionnaire (BMQ), was reduced 3.2 (95%CI: -4.22 to -2.27; P<0.001). Mean

difference in Medication Adherence Report Scale (MARS) was 1.4 (22.7 vs 24.1; P<0.001). Most patients (83.8%) reported having better control of their medicines after the intervention.

Conclusions

Pharmacist-led post-discharge structured TFU intervention can reduce 30- and 90-day readmission rates. Positive impacts were noted on time to readmission, length of hospital stay upon readmission, healthcare costs, patient beliefs about medicines, patient self-reported adherence and satisfaction.

Keywords

Post discharge follow up; clinical pharmacists; readmission rate; rehospitalisation.

What is already known about this subject

- Telephone follow-up (TFU) is a well-established and widely used approach for exchanging information with patients. It has been applied in continuity of care after hospitalisation.
- Mixed results have been reported when TFU was combined with pre-discharge and other post-discharge interventions.

What this study adds

- This study applied the Perceptions and Practicalities Approach endorsed by the NICE Medicines Guidelines to tailor medication support to meet the needs of the individual
- We utilised propensity score matching to obtain a well-matched control group, to determine the impact of a pharmacist-led post-discharge telephone intervention on readmission rate.
- This is the first study which presents the Benefit-Cost Ratio (BCR) of the impact of TFU on readmission rate.

Introduction

Telephone follow-up (TFU) post-discharge from hospital is a well-established approach for exchanging information with patients (1,2). To ensure continuity of care after hospitalisation, TFU aims to provide reassurance to patients and it enables healthcare providers to detect problems at an early stage, shortly after discharge. Furthermore, it can be a channel to provide ongoing advice, reminders, educational interventions and help with symptom management (3,4). TFU has a number of advantages, e.g. easy to organise, economical, not time-

consuming and uses technology which is available to all patients. It has been suggested that TFU should be more widely implemented (4–7).

To date many research studies and several systematic reviews (1,8–11) as well as Cochrane reviews (2,12) have examined the effectiveness of TFU. Pharmacist-led TFU has been shown to be a cost-effective method for improving medicines engagement and adherence in community settings (13,14). However, no robust evidence is available on the effectiveness of TFU, as an isolated intervention to reduce unplanned hospital readmission rates. TFU in combination with other interventions has been shown, in a number of trials, to lead to a reduction in readmission rates (15,16). Nevertheless, other studies showed mixed results when TFU was combined with pre-discharge and other post-discharge interventions (8).

The existing hospital pharmacy led, Integrated Medicines Management (IMM) inpatient service, developed within the Antrim Area Hospital in Northern Ireland, combines pre-discharge and post-discharge planning services to all patients.

The introduction of this IMM programme has resulted in a reduced length of hospital stay, a reduced number of readmissions post discharge, an increased time to subsequent readmission (17) and improvements in the appropriateness of medications on discharge (18). Despite the success of the IMM programme in preventing and delaying hospital readmissions, there is still considerable room for improvement, particularly in relation to post-discharge follow up, with an aim to reduce readmission rates (19,20). Accordingly, tailored patient support was delivered through TFU, where a Perceptions and Practicalities Approach (PAPA) was applied (21), as recommended by NICE (22), to influence the patient's motivation and ability to adhere to treatment recommendations. Such an intervention has the potential to have an additional impact, i.e. additive to the existing IMM service.

The objective of this research was to assess the impact of TFU on 30-day post-discharge readmission rates, in polypharmacy patients who received the intervention compared with a well-matched control group within a hospital, in which IMM service provision by hospital based clinical pharmacists is a routine inpatient service. Secondary outcome measures included: 90-day readmission rates, time to re-admission to hospital (if re-admitted), length of hospital stay (during the first readmission) for intervention group patients vs matched control patients. Additional objectives were to assess the impact of TFU on a number of patient centred outcomes (intervention arm only), i.e., self-reported adherence score, and adherence-related beliefs about medicines (23), and patient satisfaction. A final objective was to evaluate the economic impact of the TFU interventions.

Methods

The study was designed as a pragmatic (24,25), prospective, quasi-experimental study (26), in which intervention patients were matched with a control group at a 1:1 matching ratio (27) using a propensity score matching technique (28,29). Ethical approval for the study was obtained from the Office for Research Ethics Committees Northern Ireland (ORECNI); reference number 14/WM/0116.

The study site was the Antrim Area Hospital, a 426-bed district general hospital within the Northern Health and Social Care Trust (NHSCT) in Northern Ireland. Patient screening and recruitment commenced on 15th Feb 2016 and was completed on 30th June 2016. The follow-up period was three months post-discharge. The service, in the present study, was delivered by three clinical pharmacists who were members of the hospital clinical pharmacy team. Eligible patients for inclusion were adult patients aged 18 years or over who were receiving at least ten prescribed medicines for the management of chronic illness**.** Patients were excluded in the following cases: suffering from a terminal illness or receiving palliative care; using a prescribed adherence support aid; unable to communicate coherently (e.g. post stroke, or severe illness that prevented communication); confused (e.g. not oriented to self, time and place); scheduled to be discharged to a nursing home, a hospice or to another hospital (rather than to own home); diagnosed with mental health illness; patients who did not manage their own medicines, i.e. totally depended on a carer for managing their medicines. In addition, patients who were alcoholic, managed by the renal disease follow up team, or who were participating in other studies, were excluded.

A sample size calculation was carried out using sample size software (Statulator®, the online beta version). Pilot study results (30) for 30-day readmission rate were used in the sample size calculation which indicated that a sample of 175 pairs, would achieve a statistical power of 90% for detecting a 6% difference in readmission rate between intervention and control groups. A sample of 211 pairs (211 intervention patients and 211 matched control patients) was recruited to account for patients lost to follow up.

For the patients who were eligible to join the intervention arm of the study and who, on invitation, provided written informed consent, TFU was scheduled. The clinical pharmacists involved in delivering the additional TFU service were asked to communicate with the intervention patients three times, i.e. structured telephone calls scheduled within ten days, at one month and at the start of the third month post-discharge. Each patient's GP was informed

of his/her participation in the study and a description of the new service was forwarded to them.

A structured guide was employed by the clinical pharmacists during interactions with patients according to the principles of medicine optimisation (20,31). During each interaction, the pharmacist noted down any issues or problems patients were experiencing with their treatment/illness. This comprised both perceptions and practicalities, for example, they discussed adherence, any concerns patients had regarding their medicines, assessed patients' ability to manage their medication regime and provided practical individual advice to help patients overcome barriers to adherence. Interventions were documented on a record form within the following subgroups: medication adherence; health promotion; adverse event management; medical related challenges such as packaging, container and printed direction; medication supply / obtaining prescriptions; over the counter products; and finally, patient self-evaluated health status. Moreover, patient medications were assessed and reviewed using a pharmacist outpatient medication review and recommendation template. The pharmacists contacted, as required, other health care providers (i.e. the GP, specialist nurse or community pharmacist) to facilitate resolving any issues identified.

To obtain the list of matched control patients, the following steps were carried out: Step 1: the Charlson comorbidity index (CCI) was calculated for each recruited intervention patient (32–34). Primary and secondary diagnoses (International Classification of Disease, ICD codes) were obtained from the hospital information system (35,36). The CCI was also calculated for all remaining adult patients (potential control cohort) who were admitted to the study site hospital during the study recruitment period. Step 2: Potential matched control patients were identified for each intervention patient, i.e. having the exact values for CCI, age (in years) at discharge and gender. Step 3: refinement of matching was carried out through a statistical matching technique, i.e. Propensity Score Matching (28,37), in which a regression equation was applied to the list resulting from step 2, to obtain a propensity score for all intervention and possible control patients. The propensity score is defined as the '*conditional probability of assignment to a particular treatment given a vector of observed covariates*'. The following covariates were used in the regression equation to calculate the propensity score: number of medicines, index length of hospital stay in days, primary diagnosis, hospital ward, month of discharge. Step 4: in the same way as for intervention patients, exclusion criteria were applied to the matched control group. Duplication was checked to avoid matching two intervention patients with the same matched control patient. Step 5: based on the exact or nearest value of the propensity score, matching was finalised. IMM service provision for inpatients was routine across the hospital at the time the study was undertaken.

Participating intervention patients were asked to complete three different questionnaires during the study. The Medication Adherence Report Scale (MARS) and the patient Beliefs about Medicines Questionnaire (BMQ) were used to assess patient self-reported adherence and perceptions about medication (Necessity beliefs and Concerns) before discharge (i.e. baseline measure pre-intervention) and at three months post-discharge (i.e. post receiving the planned interventions). A bespoke patient satisfaction questionnaire was also sent (by mail three months post-discharge) to all participating patients, who received the planned interventions. Patients were asked in the accompanying cover letter to complete the questionnaires. A reminder telephone call was made to ensure good engagement with questionnaire completion. Figure 1 summarises the intervention methodology.

Data collected for participating patients (administrative data on hospitalisation from the hospital computer system plus data set obtained from questionnaires) were transferred to SPSS (version 23) for statistical analysis. Standard statistical methodology was used to assess the impact of post-discharge telephone follow-up by comparing data from the intervention and control groups using appropriate parametric or non-parametric tests. For the economic evaluation, cost benefit analysis was used (38,39).

Results

Screening and recruiting results

During the first two weeks of the study, the research team, in collaboration with the service delivery team, explored different approaches to agree on the best screening method to identify patients who were eligible to join the study. During that period 11 patients were recruited. Figure 2 illustrates that patient screening from week 3 onwards involved 859 patients. Out of the 267 eligible patients, two hundred patients (almost 75%) consented to participate in the study. The most frequent reasons for excluding patients were severe sickness (19%); use of prescribed adherence support products (18%) and patients not managing their own medicines (17%). Figure 1 provides details on interaction between clinical pharmacists and patients, divided into Intention to treat (ITT; n= 211) and Per Protocol (PP; n=131) subgroups.

Baseline patient characteristics

Table 1 shows baseline patient characteristics. There were no significant differences between intervention sub-groups when grouped according to the number of telephone calls received. The majority of patients enrolled in the study (66.4%) were older than 65 years old. This was

similar in the per protocol (PP) group, i.e. patients who received three telephone calls, with 60.3% of the recruited patients in this group being older than 65.

Table S1 illustrates the reasons that prevented clinical pharmacists from fully delivering interventions to some recruited patients. The leading reason was transfer (discharge) of patients after recruitment to a destination other than his/her home, followed by patients who did not wish to receive further telephone calls and patients who did not respond to telephone calls.

Readmission rates

As shown in Table 2 the ITT group, when compared with the control group, demonstrated a significant reduction of 10.0% (P<0.001) and 15.2% (P=0.021) in the 30-day and the 90-day readmission rates respectively. The odds of readmission within 30 days and 90 days in the ITT group were reduced by 43% (OR= 0.57; 95% CI: 0.36 - 0.90) and 47% (OR= 0.53; 95%CI: 0.36-0.79) respectively when compared with the control group.

Tables 3 and 4 illustrate that the overall 30-day and 90-day readmission rate differences between intervention and control groups, taking account of the number of telephone calls received. For patients who received the scheduled three telephone calls, a significant reduction of 20.6% (P<0.001) in 30-day readmission rate was observed compared with corresponding control group cohort. Furthermore, odds of readmission within 30 days were significantly reduced by 78% (OR = 0.22; 95%CI: 0.11-0.46). Likewise, the corresponding observed reduction in 90-day readmission rate was significant, i.e. 24.4% (P=0.012) and odds of readmission were significantly reduced by 66% (OR =0.34; 95% CI: 0.20 - 0.57).

Time to readmission

Figure 2 presents the Kaplan–Meier curve showing readmission data vs time for the 90-day follow up period. Estimated marginal means for time to readmission were 70.9 days (95% CI: 66.9 - 74.9) in the ITT group and 60.1 days (95%CI: 55.4 -64.7) in the corresponding control group. This difference was statistically significant (Log rank=11.3, P=0.001). For the subgroup of patients who received three calls (PP group), the intervention resulted in a statistically significant longer time to readmission 19.1 days (log rank=20.0, P<0.001), in which the estimated marginal mean for readmission in the latter intervention arm was 78.0 days (95%CI: 74.1-82.0) while it was 58.9 days (95% CI:52.9– 64.9) in the control group.

Censoring, (illustrated in Figure 2), indicated no need to carry out a death-readmission competing analysis, as all cases of death (censored subjects in the present study) were reported after readmission except in two patients as follows: one case within the control group,

patient died on day 54 post-discharge and one patient in the ITT group, who received only one telephone call and died on day 77 post-discharge.

Length of hospital stay on first readmission

Compared with the control group, a significant shorter length of hospital stay on first readmission was observed for both the ITT group (8.3 days vs 6.7 days; P<0.001) and the PP group (7.8 days vs 5.3 days; P<0.001).

Economic impact

Cost benefit analysis indicated that for every pound spent on the service there will be an expected saving of £51.19 at the 30-day interval and £38.08 at the 90-day interval using the PP approach (see Tables S2 and S3). Likewise, there will be an expected saving of £29.62 at the 30-day interval and £23.58 at 90-day interval using the ITT approach for every pound spent on service delivery. Savings resulted from reduced readmission rates and subsequent expenses.

Questionnaire response

Within this section, the PP data only were utilised. The number of responders was 83 patients out of 131 patients who received the planned intervention (i.e. 63.4%), however, in the case of the BMQ two forms were blank and regarding the satisfaction questionnaire three forms were not fully completed.

Beliefs about Medicines Questionnaire (BMQ) questionnaire

The pharmacist intervention had a significant impact on patients' perceptions of their medicines. Patients receiving the intervention reported significantly higher Necessity-Concerns Differential (NCD) scores at follow up group (an increase of 3.8 points; 95%CI: 2.60 to 4.93; P<0.001). This measure provides a numerical indication of how the patient judges their personal need for the medication relative to their concerns about them. NCD scores have been shown to relate to adherence across a range of long-term conditions, countries and healthcare systems (23).

Most patients were convinced of the necessity of their medication as indicated by high scale scores at baseline. The improvement in NCD scores in the intervention group were therefore largely due to a significant reduction in medication concerns. The highest impact was noted within the concern scale in responses to the following two statements (*I sometimes worry about the long-term effects of my medicines*) and (*Having to take medicines worries me*) with

a significant improvement of 43.2% (P<0.001) and 42.7% (P<0.001) respectively. Table 5 compares mean data for the necessity scale, the concern scale and the necessity-concern differential. Significant post intervention improvement was demonstrated in the concern scores (mean reduction of 3.2 points; 95%CI: -4.22 to -2.27; P<0.001). Furthermore, the mean score for the necessity scale post intervention was numerically higher (by 0.6 points) than the baseline score, however, as the overall scores were high (i.e. >20) was not statistically significant (P=0.12).

Medication Adherence Report Scales (MARS) questionnaire

The intervention led to a significantly improved self-reported adherence as measured by the MARS. The mean adherence scale difference between pre-intervention and post-intervention was 1.4 (22.7 vs 24.1; P<0.001). Nearly one third of the 83 patients who completed the pre- and post- intervention MARS questionnaires (i.e. 24 patients, 28.9%) reported the same score at baseline and post intervention. Eight patients (9.6%) responded with a lower score after the intervention. The majority of patients (51 patients, 61.4%) responded with higher scores after the intervention.

Patient satisfaction questionnaire

Table S4 summarises patient response to the satisfaction questionnaire, that was designed to measure the satisfaction toward each aspect of the structured intervention. The highest satisfaction levels of 92.5% and 83.8% were demonstrated in response to statements one and nine respectively, which related to easement of medicine related problems and allowing better control of medicines respectively.

Discussion

To best of our knowledge this is the first pragmatic, quasi-experimental study that utilised propensity score matching to obtain a well-matched control group to determine the impact of a theory-based pharmacist-led post-discharge intervention on readmission rate. According to the Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework (40,41) pragmatic studies focus on explicit practical plans for continuation of the investigated programme after the completion of the study. Furthermore, the quasi pragmatic study outcomes were meaningful to both patients and service providers rather than simply being related to the theoretical test of the investigator's hypothesis (i.e. alignment with the

Effectiveness criterion). The study was carried out by the hospital pharmacists based on their current qualifications and experience without tailored training (i.e. alignment with the Adoption criterion) and finally the study was implemented with detailed reporting of the procedure, time allocations and costs (i.e. alignment with Implementation criterion).

To mitigate against performance bias*, i.e. 'systematic differences between groups in the care that is provided'* (42,43), detailed reasons that prevented the pharmacist from delivering the intervention as planned (i.e. three telephone calls) were recorded (Table S1). Moreover, ANOVA analysis confirmed that there were no differences in baseline characteristics between all sub-groups. This was driven by the fact that all pairs had an exact match of the basic variables (Charlson comorbidity index, age and gender) and the final matched pairs were selected based on propensity score. Propensity score matching, is considered an excellent procedure to reduce selection bias and strengthen causal argument in quasi-experimental studies (44). It can simulate the random assignment of subjects seen in a randomised trial (29).

The present study demonstrated a significant 30-day readmission rate reduction of 10.0% ($P<0.01$) for the ITT group and 20.6% ($P<0.01$) for the PP group. The results are generally in line with other studies that examined the impact of pharmacist TFU (as part of a suite of interventions) on readmission rate. For example, in a retrospective quasi-experimental study, intervention patients who received a multicomponent intervention including pre-discharge intervention (patient-centred, transition-focused care and medication review) and post-discharge TFU, demonstrated a 10% reduction ($P=0.04$) in heart failure 30-day readmission and a 7% reduction ($P=0.43$) in all cause readmission compared with standard care patients (45). In another quasi-experimental study, in which the control group involved simply those patients who did not receive the interventions (pre-discharge education, physical therapy, dietary advice and discharge planning plus post-discharge TFU and home visits in some cases) readmission rate for intervention patients was less than the control group patients during a six month follow up, i.e. at the 180-day interval, readmission rate for intervention patients was reduced by 32.8% ($P=0.01$)(46).

Other studies have reported significant impact of a range of pharmacist interventions on time to readmission and length of hospital stay during the first readmission (1,17,19,47,48). However, the present study evaluated the impact of TFU as a single intervention when

provided to patients who had received routine, inpatient, IMM services. The present data therefore provides unique evidence of the value and impact of a TFU service.

To the best of our knowledge, this is the first study which presents a cost benefit analysis, including the Benefit-Cost Ratio (BCR) of the impact of TFU on readmission rate. The BCR in the present study was as follows: 51.19 at the 30-day interval and 38.08 at the 90-day interval for the PP approach, and 29.62 for the 30-day interval and 23.58 for the 90-day interval using the ITT approach. In this respect, the present study exhibited average savings (benefits from readmission rate reduction) of £973.37 per patient at the 90-day interval using the ITT approach. A previous study that investigated a hospital-based discharge, transition programme, led by pharmacists stated that these latter interventions resulted in an annual saving of $1,034 per patient (49). i.e. saving of a similar magnitude to the present study.

The present study had a number of limitations. Firstly, the study was a single centre trial, meaning that the results may not be generalisable. Secondly, the present study considered all cause readmission. Thirdly, in the present study we were not able to verify the GP responses to recommendations made by the clinical pharmacists. Finally, the quasi-experimental design of the study was inferior to the randomised control trial design, which is considered the gold standard for clinical trials. However, a high-quality matching procedure was applied in the present study to help mitigate against this limitation and indeed such an approach can simulate the random assignment of subjects seen in a randomised trial (29).

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Conclusions

The present study clearly illustrates the benefits of a pharmacist-led intervention tailoring support to address perceptions and practicalities of regarding optimal medicines usage delivered by telephone follow-up (TFU) after discharge from hospital. The intervention was provided to adult patients receiving 10 or more prescribed medicines by clinical pharmacists. A holistic benefit was achieved across a range of clinical, economic and humanistic outcomes. These benefits were achieved despite patients receiving structured clinical pharmacy services while in hospital, in the form of a well-established integrated medicines management (IMM) service. The results suggest that this type of service should be routinely adopted in an attempt to reduce early rehospitalisation of polypharmacy patients.

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Figure legends list

References

1. Mistiaen P, Francke AL, Poot E. Interventions aimed at reducing problems in adult patients discharged from hospital to home: a systematic meta-review. BMC Health Serv Res [Internet]. 2007 Dec 4;7(1):47. Available from: http://www.biomedcentral.com/1472-6963/7/47
2. Mistiaen P, Poot E. Telephone follow-up, initiated by a hospital-based health professional, for postdischarge problems in patients discharged from hospital to home. Cochrane database Syst Rev [Internet]. 2006;(4):CD004510. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17054207
3. Jencks SF, Williams M V, Coleman EA. Rehospitalizations among Patients in the Medicare Fee-for-Service Program. N Engl J Med [Internet]. 2009 Apr 2;360(14):1418–28. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMsa0803563
4. Sanchez GM, Douglass MA, Mancuso MA. Revisiting Project Re-Engineered Discharge (RED): The Impact of a Pharmacist Telephone Intervention on Hospital Readmission Rates. Pharmacotherapy [Internet]. 2015 Sep;35(9):805–12. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26406772
5. Dudas V, Bookwalter T, Kerr KM, Pantilat SZ. The impact of follow-up telephone calls to patients after hospitalization. Am J Med [Internet]. 2001 Dec 21;111(9B):26S–30S. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11790365
6. Beaucage K, Lachance-Demers H, Ngo T, Vachon C, Lamarre D, Guévin J, et al. Telephone follow-up of patients receiving antibiotic prescriptions from community pharmacies. Am J Health Syst Pharm [Internet]. 2006 Mar 15;63(6):557–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16522892
7. Hodgins MJ, Ouellet LL, Pond S, Knorr S, Geldart G. Effect of telephone follow-up on surgical orthopedic recovery. Appl Nurs Res [Internet]. 2008 Nov;21(4):218–26. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18995164
8. Jayakody A, Bryant J, Carey M, Hobden B, Dodd N, Sanson-Fisher R. Effectiveness of interventions utilising telephone follow up in reducing hospital readmission within 30 days for individuals with chronic disease: a systematic review. BMC Health Serv Res [Internet]. 2016 Dec 18;16(1):403. Available from: http://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-016-1650-9
9. Crocker JB, Crocker JT, Greenwald JL. Telephone Follow-up as a Primary Care Intervention for Postdischarge Outcomes Improvement: A Systematic Review. Am J Med [Internet]. 2012 Sep;125(9):915–21. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0002934312004743
10. Bahr SJ, Solverson S, Schlidt A, Hack D, Smith JL, Ryan P. Integrated Literature

Review of Postdischarge Telephone Calls. West J Nurs Res [Internet]. 2014 Jan;36(1):84–104. Available from: http://journals.sagepub.com/doi/10.1177/0193945913491016

11. Leppin AL, Gionfriddo MR, Kessler M, Brito JP, Mair FS, Gallacher K, et al. Preventing 30-day hospital readmissions: a systematic review and meta-analysis of randomized trials. JAMA Intern Med [Internet]. 2014 Jul;174(7):1095–107. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24820131
12. Wise J. Cochrane review says telephone follow-up of heart failure patients is effective. BMJ [Internet]. 2012 Sep 14;345(sep14 2):e6187–e6187. Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.e6187
13. Clifford S, Barber N, Elliott R, Hartley E, Horne R. Patient-centred advice is effective in improving adherence to medicines. Pharm World Sci [Internet]. 2006 Jun;28(3):165–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17004019
14. Elliott RA, Barber N, Clifford S, Horne R, Hartley E. The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines. Pharm World Sci [Internet]. 2008 Jan;30(1):17–23. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17557211
15. Luke H, Young R, Hinami K, Leung A, Williams M. Interventions to Reduce 30-Day Rehospitalization : A Systematic Review. Ann Intern Med. 2011;155:520–8.
16. Takeda A, Taylor SJC, Taylor RS, Khan F, Krum H, Underwood M. Clinical service organisation for heart failure. Cochrane database Syst Rev [Internet]. 2012 Sep 12;(9):CD002752. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22972058
17. Scullin C, Scott MG, Hogg A, McElnay JC. An innovative approach to integrated medicines management. J Eval Clin Pract [Internet]. 2007 Oct [cited 2014 Apr 1];13:781–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17824872
18. Burnett KM, Scott MG, Fleming GF, Clark CM, McElnay JC. Effects of an integrated medicines management program on medication appropriateness in hospitalized patients. Am J Health Syst Pharm [Internet]. 2009 May 1;66(9):854–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19386949
19. Scullin C, Hogg A, Luo R, Scott MG, McElnay JC. Integrated medicines management - can routine implementation improve quality? J Eval Clin Pract [Internet]. 2012 Aug [cited 2014 Apr 17];18(4):807–15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21504517
20. Scott MG, Scullin C, Hogg A, Fleming GF, McElnay JC. Integrated medicines management to medicines optimisation in Northern Ireland (2000–2014): a review. Eur J Hosp Pharm Sci Pract [Internet]. 2015 Jul;22(4):222–8. Available from: http://ejhp.bmj.com/lookup/doi/10.1136/ejhpharm-2014-000512

21. Horne R. Compliance, adherence, and concordance: implications for asthma treatment. Chest [Internet]. 2006 Jul;130(1 Suppl):65S–72S. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16840369
22. Nunes V, Neilson J, O'Flynn N, Calvert N, Kuntze S, Smithson H et al. Medicines Adherence: Involving Patients in Decisions About Prescribed Medicines and Supporting Adherence [Internet]. Clinical Guidelines and Evidence Review for Medicines Adherence: involving patients in decisions about prescribed medicines and supporting adherence. London: National Collaborating Centre for Primary Care and Royal College of General Practitioners. 2009. Available from: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0015337/
23. Horne R, Chapman SCE, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the Necessity-Concerns Framework. PLoS One [Internet]. 2013;8(12):e80633. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24312488
24. Sackett DL. Explanatory and pragmatic clinical trials: a primer and application to a recent asthma trial. Pol Arch Med Wewn [Internet]. 2011;121(7–8):259–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21878863
25. Patsopoulos NA. A pragmatic view on pragmatic trials. Dialogues Clin Neurosci. 2011;13(2):217–224.
26. Eccles M, Grimshaw J, Campbell M, Ramsay C. Research designs for studies evaluating the effectiveness of change and improvement strategies. Qual Saf Health Care [Internet]. 2003 Feb;12(1):47–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12571345
27. Harris AD, McGregor JC, Perencevich EN, Furuno JP, Zhu J, Peterson DE, et al. The Use and Interpretation of Quasi-Experimental Studies in Medical Informatics. J Am Med Informatics Assoc [Internet]. 2006 Jan 1;13(1):16–23. Available from: https://academic.oup.com/jamia/article-lookup/doi/10.1197/jamia.M1749
28. Williamson EJ, Forbes A. Introduction to propensity scores. Respirology [Internet]. 2014 Jul;19(5):625–35. Available from: http://doi.wiley.com/10.1111/resp.12312
29. Baek S, Park SH, Won E, Park YR, Kim HJ. Propensity Score Matching: A Conceptual Review for Radiology Researchers. Korean J Radiol [Internet]. 2015;16(2):286. Available from: https://synapse.koreamed.org/DOIx.php?id=10.3348/kjr.2015.16.2.286
30. Odeh M. The clinical and economic impact of the provision of innovative pharmacy and medicine management services to post discharge patients. PhD thesis, Queen's University Belfast; 2017.

31. Royal Pharmaceutical Society. Medicines Optimisation: Medicines Optimisation: The evidence in practice. 2015.
32. Hall WH, Ramachandran R, Narayan S, Jani AB, Vijayakumar S. An electronic application for rapidly calculating Charlson comorbidity score. BMC Cancer [Internet]. 2004 Dec 20;4(1):94. Available from: http://bmccancer.biomedcentral.com/articles/10.1186/1471-2407-4-94
33. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis [Internet]. 1987;40(5):373–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3558716
34. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol [Internet]. 1994 Nov;47(11):1245–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7722560
35. Brouch K. Where in the world is ICD-10? J AHIMA [Internet]. 2000 Sep;71(8):52–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11186625
36. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol [Internet]. 2004 Dec;57(12):1288–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15617955
37. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika [Internet]. 1983;70(1):41–55. Available from: https://academic.oup.com/biomet/article-lookup/doi/10.1093/biomet/70.1.41
38. Robinson R. Cost-benefit analysis. BMJ [Internet]. 1993 Oct 9;307(6909):924–6. Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.307.6909.924
39. Malet-Larrea A, Goyenechea E, Gastelurrutia MA, Calvo B, García-Cárdenas V, Cabases JM, et al. Cost analysis and cost-benefit analysis of a medication review with follow-up service in aged polypharmacy patients. Eur J Heal Econ [Internet]. 2016 Dec 2; Available from: http://link.springer.com/10.1007/s10198-016-0853-7
40. Gaglio B, Shoup JA, Glasgow RE. The RE-AIM framework: a systematic review of use over time. Am J Public Health [Internet]. 2013 Jun;103(6):e38-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23597377
41. Gaglio B, Phillips SM, Heurtin-Roberts S, Sanchez MA, Glasgow RE. How pragmatic is it? Lessons learned using PRECIS and RE-AIM for determining pragmatic characteristics of research. Implement Sci [Internet]. 2014 Dec 28;9(1):96. Available from: http://implementationscience.biomedcentral.com/articles/10.1186/s13012-014-0096-x
42. Pannucci CJ, Wilkins EG. Identifying and Avoiding Bias in Research. Plast Reconstr

Surg [Internet]. 2010 Aug;126(2):619–25. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00006534-201008000-00034

43. Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. 5.0.2. Higgins JP, Green S, editors. John Wiley & Sons, Ltd; 2011. 840-842 p. Available from: http://handbook.cochrane.org/chapter_8/table_8_4_a_a_common_classification_scheme_for_bias.htm
44. Wang FY, Meng W, Li Y, Li T, Qin CY. Comparison of overall survival in patients with unresectable hepatic metastases with or without transarterial chemoembolization: A Propensity Score Matching Study. Sci Rep [Internet]. 2016 Dec 13;6(1):35336. Available from: http://www.nature.com/articles/srep35336
45. Record JD, Rand C, Christmas C, Hanyok L, Federowicz M, Bilderback A, et al. Reducing heart failure readmissions by teaching patient-centered care to internal medicine residents. Arch Intern Med [Internet]. 2011 May 9;171(9):858–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21555667
46. Anderson C, Deepak B V, Amoateng-Adjepong Y, Zarich S. Benefits of comprehensive inpatient education and discharge planning combined with outpatient support in elderly patients with congestive heart failure. Congest Heart Fail [Internet]. 2005;11(6):315–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16330907
47. Naylor MD, Brooten D, Campbell R, Jacobsen BS, Mezey MD, Pauly M V, et al. Comprehensive discharge planning and home follow-up of hospitalized elders: a randomized clinical trial. JAMA [Internet]. 1999 Feb 17;281(7):613–20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10029122
48. Parry C, Min S-J, Chugh A, Chalmers S, Coleman EA. Further Application of the Care Transitions Intervention: Results of a Randomized Controlled Trial Conducted in a Fee-For-Service Setting. Home Health Care Serv Q [Internet]. 2009 Oct 27;28(2–3):84–99. Available from: http://www.tandfonline.com/doi/abs/10.1080/01621420903155924
49. Saleh SS, Freire C, Morris-Dickinson G, Shannon T. An effectiveness and cost-benefit analysis of a hospital-based discharge transition program for elderly Medicare recipients. J Am Geriatr Soc [Internet]. 2012 Jun;60(6):1051–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22690981