Systematic review - Research protocol

TITLE

A systematic review of nurse interventions to improve medication adherence among discharged older adults

Authors

H. Verloo RN PhD (HV)a, A. Chiolero MD PhD (AC)b, B. Kiszio Health BiS (BK)a, T. Kampel, Bsc MSN (TK)a; V. Santschi PharmD PhD (VS)a,c

Affiliation

a. La Source School of Nursing Sciences, University of Applied Sciences Western Switzerland Lausanne, Switzerland

b. Institute of Social and Preventive Medicine, Lausanne University Hospital, Lausanne, Switzerland

c. Service of Nephrology and Hypertension; Lausanne University Hospital, Lausanne, Switzerland
### Planning of the components of the systematic review

Table 1. Time frame

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Selection of the research topic</td>
<td>VS &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Development of research question</td>
<td>VS &amp; AC &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Development of first components of the protocol</td>
<td>VS &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Development and writing the background</td>
<td>VS &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Development and writing the objectives</td>
<td>VS &amp; AC &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developing the inclusion/exclusion criteria</td>
<td>VS &amp; AC &amp; BK &amp; HV &amp; TK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developing search strategy</td>
<td>VS &amp; AC &amp; BK &amp; TK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conducting literature search</td>
<td>BK &amp; TK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selection of the studies</td>
<td>BK &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developing extraction form</td>
<td>VS &amp; TK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appraise the studies</td>
<td>BK &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opinion third reviewer</td>
<td>VS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extract data</td>
<td>BK &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analyze data – meta analysis</td>
<td>AC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Writing results</td>
<td>VS &amp; AC &amp; BK &amp; HV &amp; TK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Writing discussion</td>
<td>VS &amp; AC &amp; BK &amp; HV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Writing paper (discussion journal ?)</td>
<td>Together</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Green: 1st version; orange: work in progress; red: still to be done
**Background**

Adherence to medications, defined as the extent to which a patient take medications as prescribed by their healthcare professionals, is an important aspect in terms of treatment efficacy, healthcare costs and patient safety (1-4). According to a WHO report, inadequate adherence medication averages 50% among patients with chronic disease (5) and represents a significant problem that leads to increased morbidity and mortality from various illness, as well as increased healthcare costs (6, 7).

Typically, older adults suffer from multiple chronic disease and are treated with numerous medications, therefore they are at a high risk of medication adherence problems, including poor adherence to non-adherence to medications, discontinuation, overuse/abuse or forgetfulness with alteration of schedules and doses (8, 9). Estimates of non-adherence vary from 21 to 55% among older adults (10-12), with 3-10% of hospital admissions attributable to non-adherence (7). Consequences of non-adherence are important because of the resulting of poor clinical outcomes (i.e., exacerbation of chronic medical conditions), of more frequent hospitalizations, and greater healthcare costs (13, 14).

Studies demonstrated that insufficient adherence to medication is complex and common among discharged older adults (12, 14-16). Firstly, older adults experienced changes in their medications regimes during a hospitalization (17) and in the first month following hospital discharge, as demonstrated by Mansur et al (13). Such changes tend to decrease adherence to medications. Secondly, older adults may continue to take medications that were discontinued during the hospitalization, fail to start new medications initiated during the hospitalization, or take the incorrect dosage (14, 18, 19). Moreover, medication changes are poorly communicated to the patient at the time of discharge (20).

Hence, older adults are at particularly high risk of non-adherence, i.e. in the first days to weeks following hospital discharge (12, 14). Therefore, it is important for healthcare professionals, especially the community health care nurses, to proceed with an early and frequent follow-up to keep discharged older adults adherent to therapy (21). Nurses are well positioned to provide and coordinate adherence care collaborating inter-professionally by their presence in the majority of healthcare settings, by their closeness to patients (22) by interfacing with patient and physician.

Previous studies have shown that interventions, for example therapeutic education of patients, medication management tools or electronic monitoring reminder supported by a
monitoring device), may help increasing medication adherence and continuity of care among older adults (23-29). However, studies have not evaluated the effectiveness of interventions to improve medication adherence after hospital discharge. More specifically, there is little evidence related to the impact of nurse interventions (alone or in collaboration with other health professionals) on medication adherence among discharged older adults (14, 17).

The purpose of this systematic review is therefore to determine if nurse interventions are effective in improving medication adherence among recently hospital discharged home dwelling older adults of 65 years or more compared with usual care.

**Methods and materials**

This review will be conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations (30) and using methods outlined in the Cochrane Handbook for Systematic Reviews of Interventions (31).

**Inclusion criteria**

**Types of studies**

This review will include randomized controlled trials (RCT), cluster randomized controlled trials, and controlled studies. All papers, without language restrictions, will be searched.

**Types of participants**

This review will consider studies that include recently discharged (< two weeks after discharge) older adults (aged 65 years and over), living at home and taking at least one prescribed medication for any kind of medical condition.

**Types of intervention(s)**

We will examine all types of nurse interventions aimed at improving medication adherence among older adults recently discharged and living at home, compared with usual care defined by the study. We will include all types of interventions delivered by a nurse alone or in collaboration with other healthcare professionals, at hospital discharge or at home shortly after discharge (< two weeks).

Based on the Cochrane Effective Practice and Organization of Care (EPOC) taxonomy interventions (32, 33), we will consider interventions targeted at healthcare
professionals-level and at patient-level. We will exclude interventions targeted at healthcare organization, regularization and financial level.

a) Interventions targeted at healthcare professionals:
   - Educational meetings aimed at healthcare professionals
   - Local consensus processes
   - Distribution of educational materials
   - Educational outreach visits with audit and feedback (i.e., medication review from medical records; monitoring of medication therapy (assessment, adjustment or change of medication); verbal or oral recommendation to pharmacist or physician; meeting with team to discuss care; reference to physician)
   - Influencing local opinion leaders
   - Individual and group interviewing and discussions (focus groups)

b) Interventions targeted at patients:
   - Patient educational interventions (single or multi-professional conducted by nurse, pharmacist or physician, such as counselling about medications and medication compliance; patient teaching sessions)
   - Mass media communication targeting the participants including newspapers, posters, leaflets, brooklets, radio and television, alone or in conjunction with other interventions
   - Patient-reminder systems (single or multi-professional conducted by nurse, pharmacist or physician, such as telephone contact, discharge planning; medication adherence aids such as electronic monitors, or pill dispenser; meeting with healthcare professional’s team in patient’s home)

**Types of outcome measures**

The primary outcome measures for this review will be:

- Adherence with medications including change and follow-up in medication adherence (measured by different methods (1, 22), for example such as electronic monitors, prescription refills, pill counts and patient self-report (1)) focused on dichotomous (yes/no), ordinal or continuous adherence rate/score.

**Search methods for identification of studies**

In collaboration with a medical librarian (BK), we will conduct a systematic literature search of the following electronic databases from the start date until 31 July 2015 in Medline via Pubmed (1946 to 2015), Embase (1947 to 2015), CINAHL (1937 to 2015), the Cochrane...)

The PubMed search syntax (Appendix A) served as the basis for all search strategies, using Medical Subject Headings (MeSH) and text terms with Boolean operators. The syntax consisted of four search themes intersected by the Boolean term “AND”.

MeSH terms included:

1) Older adults related term (“Aged”, “Older adults”, “Elderly”, “Aged patients”, “65 years and older”, “65 years and over”, “Home dwelling older adults”)
2) Medication adherence-related terms (“Medication adherence”, “Medication compliance”, “Medication abuse”, “Medication education” and “Treatment adherence” and “Medication adherence intervention”)

In addition to the electronic database searches, we will conduct a hand search of bibliographies of all relevant articles and a search of unpublished studies with Google Scholar, Proquest, Mednar, Worldcat. We will consider publications in any language.

Data collection and analysis

Study selection

Two authors (HV and BK) will electronically screen titles and abstracts identified in searches independently to assess which studies meet the inclusion criteria. Disagreements will be resolved by discussion or if needed, a consensus will be reached by discussion with authors (VS and AC).

Two authors (HV and BK) will obtain and will independently assess full-text articles to ensure they meet the inclusion criteria. Disagreements will be discussed and resolved with the other authors (VS and AC). A flowchart of the process of trial selection will be made in accordance with the PRISMA statement (30).

Data extraction
Data extraction will be conducted independently by two authors (HV and BK) using a specially designed and standardized data extraction form (Appendix B). Discrepancies will be resolved through discussion and consultation with the other authors (VS and AC).

From each included study, information will be extracted: (1) study author, year of publication, and country where the study will be conducted; (2) study characteristics (including study setting and design, duration of follow-up, and sample size); (3) characteristics of participants (including gender, age, medication, medical conditions); (4) characteristics of interventions (including description and frequency of nursing interventions, healthcare professionals involved); (5) characteristics of usual care group; (6) types of outcome measures (including medication adherence rate or score, self-assessment of medication adherence).

Assessment of risk of bias in included studies

Two authors (HV and BK) will independently assess the risk of bias for all included studies using the Cochrane Risk of Bias Tool (34), a validated tool for randomized trials based on six domains: adequate sequence randomization; concealment of allocation; blinding of participants and outcome assessors; adequately addressed incomplete outcome data; selective outcome reporting; other risk of bias. Each of these 6 domains in the tool will be rated as (1) low risk of bias; (2) unclear risk of bias; (3) high risk of bias. Any disagreement in quality assessment will be resolved by discussion.

Statistical analyses

Statistical analyses will be conducted following the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (31) and the PRISMA statement (35). Data will be analyzed using STATA version 13.0 (StataCorp, College Station, Texas).

For dichotomous outcomes, average intervention effects will be calculated as relative risks with 95% confidence intervals (CIs) using a random effects model (36). For continuous data, a random effects model will be used to calculate weighted mean differences with 95% CIs. If required, we will calculate standard deviations from standard errors or 95% CIs presented in the articles. Heterogeneity will be quantified using the I² and the chi² test of heterogeneity. Funnel plots will be drawn and Egger tests will be computed to explore the possibility of publication bias (37).

Reasons for heterogeneity in effect estimates should be sought in meta-analyses (38, 39). To explore possible determinants of heterogeneity, we will conduct subgroup analyses according to selected study characteristics (e.g., age of the participants; country where the
study was conducted; type of diseases; type of intervention). Furthermore, sensitivity analyses will be conducted by (1) excluding relatively small studies (with fewer than ?? participants per randomization group); (2) restricting analysis to studies of good quality.
Records identified through database searching (n = )

Additional records identified through other sources (n = )

Records after duplicates removed (n = )

Records screened (n = )

Records excluded (n = )

Full-text articles assessed for eligibility (n = )

Full-text articles excluded, with reasons (n = )

Studies included in qualitative synthesis (n = )

Studies included in quantitative synthesis (meta-analysis) (n = )

**Figure 1. Flow diagram based on the PRISMA guidelines (35)**

**Funding**
No fundings are implicated in this systematic review.
References
