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Development and evaluation of an algorithm in Medication Management for best practice. Effectiveness of the intervention and translation into standard care for nursing home residents, AMBER study protocol

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ABSTRACT

INTRODUCTION:

Residents of nursing homes are susceptible for medication risks. Medication Reviews can increase medication safety and quality of drug therapy. Limited resources and barriers between health-care practitioners are potential obstructions in performing Medication Reviews in nursing homes. Focusing on frequent and relevant problems can support pharmacists in the provision of pharmaceutical care services.

METHODS AND ANALYSIS:

The study is subdivided into three phases. At phase I, structured interviews with health-care practitioners and patients are performed. At phase II, a systematic review of current literature on problems and interventions at the medication process in nursing homes is conducted. The findings of both phases are combined to develop an algorithm for Medication Reviews. For further refinement, a Delphi survey is done. In conclusion, a tool is created. In phase III the tool is tested on Medication Reviews in nursing homes. Effectiveness, acceptance, feasibility and reproducibility are assessed.

In Phase I, a mixed methods approach is chosen. Qualitative content analysis and rating of aspects concerning the frequency and relevance of problems in the medication process is performed. In phase II, literature findings are presented narratively. Primary outcome of phase III is the reduction of drug-related problems, detected by using the tool. Secondary outcomes are the proportion of drug-related problems, the acceptance of pharmaceutical recommendations, the expenditure of time and inter-rater reliability. Sensitivity of the detection of drug-related problems is measured and feasibility is tested by qualitative questionnaires.

ETHICS AND DISSEMINATION:

The study intervention is approved by the local Ethics Committee. The findings of the study will be presented at national and international scientific conferences and will be published in peer-reviewed journals. A result of the study will be a tool, which can be used by pharmacists to perform a Medication Review in standard care.

Trial registration number:
DRKS00010995 (German-Clinical-Trial-Register)

Strengths and limitations of this study

- The process to develop an algorithm for Medication Management in nursing homes is based on a wide basis with a variety of consecutive methods
- The resulting tool is tested on several aspects, as on effectiveness, feasibility and acceptance by multidisciplinary health-care providers
- The proximity to clinical practice is believed to help in translating the tool into standard care
- The algorithm needs to balance limited time and resources in community care to detect as many relevant drug-related problems as possible
- Limited duration and size of this uncontrolled study require further research and testing

INTRODUCTION

Medication Review and Medication Management are current instruments of pharmaceutical care, which have proven to be effective to reduce drug-related problems, increase the quality of the drug regimen and improve medical outcomes in various settings and indications [1–8]. Pharmaceutical care interventions are especially meaningful in high-risk populations [9]. Residents of nursing home facilities are a highly vulnerable patient group whose medication deserves special attention. Besides geriatric age, dependence on care, multimorbidity and polymedication are frequently related to this patient population [10, 11]. Inappropriate medication is related to poor quality of life, high morbidity, preventable adverse-drug events, increased risk for falls, repeated hospitalizations and manifold physician contacts [12–15]. Several approaches to optimize the quality of the drug regimen have been tested. Medication Reviews, multidisciplinary case conferences, education and coaching are examples of pharmaceutical interventions that have been studied successfully in nursing homes [16–20]. Drug- related problems could be reduced, the quality of medication could be enhanced. Effects of pharmaceutical care on further clinical outcomes, like on mortality or on quality of life is uncertain [16, 19]. This might be due to the limited size and length of most pharmaceutical studies. However, a structured and collaborative Medication Management seems to be particularly

supportive in this setting, but is rarely implemented into standard care in Germany [4, 21]. Barriers of implementation might be limited time, resources and compensation. Little experience in performing Medication Reviews and Medication Managements and entry barriers of nursing homes facilities might be a further aspect of withholding these services to the residents. Self-confidence, structure and guidance have been identified as aspects to alleviate the implementation of Medication Reviews in community pharmacies [22]. Setting higher standards of drug quality in nursing homes might be even more challenging, as further action to encounter the patients, the nurses and the physicians is required. Tailored screening tools and standardized communication forms are helpful to guide and support pharmacists in performing Medication Reviews and have been developed for various scenarios [23–25]. For pharmacists with limited experience, the TIMER©-tool has shown to be effective in performing Medication Reviews to a certain extent, but has not been updated or refined any more [26]. A contemporary tool, tailored to the demands of pharmacists willing to conduct Medication Management in a nursing home could be helpful to overcome existing barriers of implementation. It needs to take the before mentioned aspects of multidisciplinary collaboration, structured guidance and limited time and resources into account.

Aims and objectives

The aim of the AMBER study is to develop and test an algorithm, which leads to a tool that supports pharmacists in performing a structured Medication Management in an appropriate timeframe. The tool should focus on frequent and relevant problems in the medication process of residents of nursing homes and needs to consider the special circumstances of this setting. Besides effectiveness in detecting and solving drug-related problems it needs to be highly feasible for community pharmacists. To assure a high patient benefit, multidisciplinary approaches need to be facilitated by the tool. It should be developed with the utmost available evidence and serve the patient.

METHODS AND ANALYSIS

The study is registered at the German Clinical Trials Register (registration number DRKS00010995). It is funded by Apothekerstiftung Westfalen-Lippe (noncommercial foundation). The funding source has no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results. SE is the guarantor. All authors drafted the protocol.

Overview of the study

The study is performed in three phases. Phase I consists of interviews with health-care practitioners and patients. At phase II systematic review is performed and results are combined with the outcomes

of phase I to form an algorithm. Following a Delphi approach, the single aspects of the algorithm are presented to an expert panel to refine the algorithm. In phase III the algorithm is tested in patients.

Phase I: structured interviews

Purpose

Structured interviews with patients, nurses, physicians and pharmacists are performed. The involvement of different health-care practitioners is chosen to consider the different perspectives. Furthermore, this approach should assure practical relevance, feasibility and support the pragmatic attitude of the study. Patient interviews are done to consider patient goals. Results of phase I are incorporated in an algorithm.

Methods

Phase I of the study is based on a mixed methods approach, which includes qualitative and quantitative aspects. Five to ten experts of physicians, pharmacists, nurses and patients are interviewed about their experience, requirements and expectations regarding problems, risks and goals at the medication process in nursing homes. Written interviews with health-care practitioners and patients are conducted.

Physicians, pharmacists and nurses at phase I are required to have experience in nursing home care for more than one year before interview. Patients at the panel are residents of a nursing home facility and must be able to understand and answer the questions without assistance. Open-ended questions to mention uncertainties and problems in the medication process are asked. A qualitative content analysis according to Mayring [27] is performed with the software MAXQDA 12. Frequencies of coded categories are analyzed. Furthermore, 51 specific aspects on therapy and drug-related problems (DRPs) are assessed, covering general challenges, patient goals, communication barriers, medical goals and pharmaceutical aspects. Each aspect is rated separately for frequency and relevance on a scale from 1-5 (with 1 as being infrequent or irrelevant to 5 being frequent and relevant). Patients are asked to rate 24 selected aspects for relevance. Parameters rated by more than 50 % of the participants with an average score of 3 or higher are chosen as meaningful. Subsequently, top scores per group are considered for the algorithm.

Phase IIa: literature review

A literature review is performed, following the Medical Research Council guidance [28]. The protocol is prepared according to PRISMA P (2015) [29, 30] and the review is registered in PROSPERO (registration number CRD42017065002).

The objective of phase IIa is to systematically review the literature for relevant aspects of Medication Reviews in nursing homes. Interventions are analyzed and general challenges, patient goals, communication barriers, medical goals and pharmaceutical aspects are considered. The intended review aims to answer the question, which problems arise most frequently and which aspects are most relevant. It includes three consecutive steps. At step 1, a review of existing reviews is done. At step 2, interventional studies, which have been published after the last review, are searched and analyzed. At step 3 studies on frequent problems in a nursing home setting are regarded, which have not been covered by step 1 and 2.

Step 1: review of reviews

Purpose

To develop an intervention, it is recommended to use the best available evidence [28]. Reviews on interventions to optimize the medication therapy in nursing homes should provide an indication of effective interventions or parts of them. This step aims to answer the question, which interventions have already been developed, how effective they are and which aspects of the medication therapy can be improved by a medication review.

Methods

Systematic reviews, reviews and meta-analyses are included. Participants must be nursing home residents (65 years and older). Studies with geriatric population living outside nursing home facilities are excluded, except studies, which investigated both groups and provided data separately.

Any intervention, which could be part of a Medication Review is considered. Medication Review is defined as "a structured evaluation of a patient's medicines with the aim of optimizing medicines use and improving health outcomes. This entails detecting drug related problems and recommending interventions" [31].

Included studies can be either controlled or uncontrolled trials with standard care as a potential comparator. Endpoints of interest are hospitalization, mortality and falls, amongst others. In case the outcomes are DRPs or potential inadequate medication (PIM), they must be reported in detail.

Studies have to be finished and results have to be published. Articles in English and German are included.

The following electronic bibliographic databases are searched:

- **MEDLINE/ PCM (via PubMed)**
- **PsycINFO (via EBSCOhost)**
- **CDSR (via Cochrane Library)**

- **CINAHL (via EBSCOhost)**
- **International Pharmaceutical Abstracts (via EBSCOhost)**
- **NHSEED /DARE (via CRD)**

Additionally, the reference lists of included studies and reviews are hand-searched.

Articles published between January 01, 2000 and March 31, 2017 are conducted. This restriction should ensure currentness of data and consider the progress of health care. An example of a search strategy is presented in appendix 2. Citavi 5© software is used for data management and removing duplications. Additional duplications are removed by hand. One review author (SE) conducts the search in databases and extract the titles and abstracts for analyses. Two reviewers (SE; OR) independently screen publications for inclusion. Discussion and consensus resolve potential disagreements.

A data extraction form is developed for each step, which is used to collect data from eligible studies. Data extraction is carried out by one reviewer (SE) with verification by another (OR). Disagreements are resolved by discussion and consensus. At least the following data are extracted: type of intervention, used tools, conditions and outcomes. Outcomes are depending on the endpoints of the regarded studies, e.g. influence on mortality, hospitalization rate, falls, quality of life and time spending for care. Studies are checked with the AMSTAR Checklist [32].

Step 2: review of recent study

Purpose

At step 2, interventional studies on interventions to optimize medication are included, which are published after the reviews from step 1 and hence could not have been regarded by these earlier reviews.

Methods

Methods are similar to step 1. The interventional studies are examined following the template for intervention description and replication (TIDieR) Checklist [33]. Studies with poor quality are not removed, but the methods and the description of the intervention is reported as far as possible.

Step 3: review of common problems

Purpose

In addition to the results of the reviews and interventional studies, frequent problems can be described by non-interventional studies as well. The focus in this step is on reported problems and issues in the medication process in nursing homes.

Methods

Specific studies are regarded that are not covered by step 1 and 2, for example observational studies, qualitative studies and guidelines. The further procedure is similar to step 1 and 2.

Data synthesis

Narrative synthesis is provided. Descriptions of effective interventions and frequent problems are summarized. Because of potential inhomogeneity of the outcomes a meta-analysis is expected to be inappropriate.

Phase IIb

Combining the results to create an algorithm

Results of phase I are compared with the results of phase IIa. The determined aspects are checked for eligibility and feasibility in the algorithm. Every aspect is discussed by the authors and considered for inclusion. A ranking is performed and the top aspects are evaluated in a Delphi survey with 10 or more experts, using the software SurveyMonkey® with a 5-point Likert-scale. Remarks of the expert panel are incorporated in the algorithm.

Phase III

The study protocol follows the SPIRIT 2013 statement [34, 35], the study design is developed in line with the Manual for the design of non-drug trials in primary care by Joos et al. [36]. Conducting the TIDieR checklist to describe the intervention is done later on at reporting the outcomes [33].

Purpose

In phase 3 the developed algorithm is tested for effectiveness by performing a Medication Review in nursing home patients. Acceptance of the pharmaceutical recommendations is measured using a feedback form. In addition, the feasibility of the algorithm is investigated. Several pharmacists are using and rating the feasibility after conducting Medication Reviews on case scenarios.

Methods

A single-armed, prospective study design without randomization is chosen. Reduction of detected DRPs is the indicator for effectiveness of the intervention.

Study setting

The study is conducted in nursing homes in North Rhine-Westphalia, Germany.

Eligibility criteria

The following inclusion criteria are applied:

- patient age ≥ 65 years,
- residency in a nursing home facility
- multimorbidity, at least 2 chronic diseases (25)
- polymedication, at least 5 chronic systemic available medications
- signed informed consent (if necessary through a legally authorized representative)

Exclusion criteria:

- participation in other clinical studies at present time

Withdrawal of consent is possible at any time and leads to discontinuation of the intervention. Data of dropouts are not included in analyses of the primary outcome. The patient remains all rights on personal data and its deletion.

Intervention

After recruitment, a Medication Review is performed by the project manager using the developed algorithm (t_0). Patient data is collected from nursing homes and physicians. Information about the actual condition of the patient can be supplemented by the patients themselves or by the facilities` nurses. Results of the Medication Review are communicated to nurses and physicians using SOAP notes and are discussed, if required. SOAP notes cover detected problems in medication therapy and recommendations to solve them. Acceptance is measured using a feedback form. At a follow-up at three months post intervention (t_1) the medication of the patient is evaluated for changes in the number of DRPs.

Additionally, to this main analysis, an advanced Medication Review (according to the PCNE definition) is performed for ten patients as a benchmark. Results of the advanced Medication Reviews are compared to the results of the Medication Review performed by using the algorithm. Differences are presented descriptively.

Feasibility and reproducibility of the algorithm are tested by 5 or more pharmacists, using 10 similar patient cases. Experiences are presented descriptively. The study flow is shown in fig.1.

Standard care is provided during the trial, interventions are supplementary. The study will monitor for potential harms of the intervention by recording adverse-drug reactions following implemented suggestions.

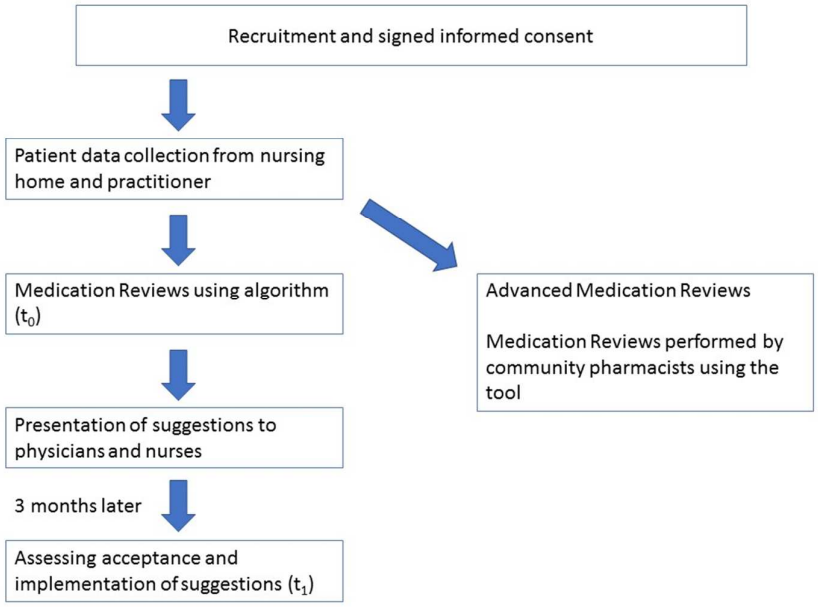

Fig.1: Participant timeline

Outcomes

Primary outcome is the change in the number of DRPs, classified according to PCNE version 8.01 and detected by using the algorithm [37]. Potential DRPs are limited to the aspects, covered by the algorithm.

Secondary outcomes

- DRPs classified according to PCNE version 8.01 (number and type)
- Acceptance measurement of physicians and nurses by using an acceptance form, classified according to PCNE version 8.01
- Number of DRPs classified according to PCNE version 8.01, detected by an advanced Medication Review
- Reproducibility of analysis and feasibility of the algorithm (time spending, inter-rater reliability)

Sample size

On the assumption of a mean reduction of one DRP per patient with a standard deviation of two, a calculation is performed by the institute for biometric and clinical research of the Westfälische Wilhelms-University Münster (IBFK). The null hypothesis, whether the number of DRPs does not

differ, is tested with a two-sided Wilcoxon signed-rank test with a significance level of 0.05. The estimate sample size to improve a power of 80 % is 75 patients. Considering dropouts, a sample size of 100 patients is intended.

Recruitment

At a first step, three nursing homes in North Rhine-Westphalia are asked to participate in the study. All patients of the participating nursing homes are screened for inclusion and exclusion criteria and subsequently asked to join the study.

In case of an insufficient number of participating patients, further nursing homes are approached.

Data collection

During the study, the following data is collected and documented using Microsoft® Excel® software (version 1707):

- Name and study number
- Age and sex of participant
- Medication, including active pharmaceutical ingredients, dosage and pharmaceutical form
- Morbidities, laboratory parameters and vital signs

This data is collected from nursing homes' and physicians' documentation.

Furthermore, the results of the Medication Reviews are documented using password-protected Excel® sheets. All reasons for withdrawal or dropout will be recorded in the study.

Data management

Patient related data is used for performing a Medication Review using the algorithm and for communication with nurses and practitioners. For all statistical analyses and other Medication Reviews anonymized data is used.

Statistical methods

Baseline and demographic characteristics are analyzed descriptively. The reduction of DRPs, is tested with a two-sided Wilcoxon signed-rank test with a significance level of 0.05.

ETHICS AND DISSEMINATION

The study intervention is approved by the local Ethics Committee (Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Westfälischen Wilhelms-Universität, approval number 2017-350-f-S) and is conducted to the principles of the Declaration of Helsinki. If amendments of the protocol are necessary, the date of each amendment, a description of the change and the rational is

given. Changes are not incorporated into the protocol. The project manager obtains informed consent from potential trial participants or legally authorized representatives. Written information is given to all study patients. Confidentiality is guaranteed by anonymizing patient data where applicable. Only the project manager has the complete data for communication with nurses and physicians. Analysis of the final data by IBFK and the project manager is performed.

The goal of the study is the development of an algorithm as underlying basis for a tool. The tool is intended to be applied into standard care and might be utilized by community pharmacies engaged in nursing home care. The findings of the study will be presented at national and international scientific conferences and will be published in peer-reviewed journals. There are no publication restrictions.

Methods against bias and for quality assurance

To ensure data quality and to avoid missing data or processes which are not adherent with the study protocol, study sites are visited for clinical monitoring. Furthermore, several routines are established to prevent or detect incorrect as well as inconsistent data entry and incomplete data. Additionally, regular training sessions are done.

DISCUSSION

The aim of this study is the development of an algorithm, which leads to a tool, aiming to support community pharmacists in performing a Medication Management in nursing homes. The tool is tested for effectiveness, feasibility and practicability.

Development

The tool needs to detect as many relevant DRPs as possible, yet take limited time and resources into account. Hence, both aspects need to be balanced. The tool can only try to constitute a good compromise. Evidence for each step of the algorithm needs to be found. To cover and rate important aspects, a mixed methods approach is chosen, which incorporates interviews with multidisciplinary practitioners and patients, a systematic review, a Delphi survey, testing and refinements of the underlying algorithm. This approach on developing the algorithm is quite comprehensive, compared to other tools as it needs to cover implicit and explicit parameters [38], in contrast to more confined medication-safety tools, which may depend on a mere Delphi survey[38] [39]. The complex method in developing the AMBER tool is believed to provide a higher probability of included items, compared to a limited approach. Taking practitioners` experience into account for example helps to rate current trends in misprescribing, as these may vary from time to time [40]. As shown by da Costa et al., tools to evaluate medication regimens differ in the number of detected DRPs, whereas it is unclear, if a higher number leads to a greater patient benefit or vice versa to an overreporting [23]. In this study,

the tool is developed solely for nursing home residents' medication and needs to cover the specific requirements of this setting.

Testing

The developed tool is aimed to be tested for effectivity in nursing homes in Germany in 100 patients. The number of relevant tool detected DRPs is compared to the results of a comprehensive Medication Management. Feasibility is evaluated by providing community pharmacists with the tool and patient cases. Results of the pharmacists' test cases are compared to the study team's results. A survey on feasibility and practicability is done, the time to perform a Medication Review using the tool is taken.

Multidisciplinary approach

Medication Management implicates further and multidisciplinary activities after a Medication Review is performed. At a nursing home, cooperation with nurses and physicians is vital to reach an effect on the patients` medication, even though attitudes on patient-oriented approaches might vary [41–43]. To take these considerations into account, the tool needs to lead pharmacists towards multidisciplinary cooperation. Nurses and physicians acceptance is measured using a standardized feedback form, based on the PCNE classification of DRPs [37].

Strengths and limitations

This study faces several limitations. Confined resources did not allow a larger and controlled study. Even though a complex method is used in developing the tool, it can be just a compromise to detect and solve a sufficient number of relevant DRPs. A comprehensive approach surely could perform better but has limited feasibility upon translation into the aspired community setting. The short duration of the study intervention and the restricted study collective might not disclose all aspects, as it is powered only for the primary endpoint. Other aspects might show up to be relevant as well during the intervention phase.

A potential strength of the study might be the variety of methods, the high number of underlying data and the large base of studies included in the development of the algorithm. The proximity to clinical practice is hoped to be a virtue for translation into standard care.

Author Contributions

Conception and design: SE, OR

Administrative support: SE

Provision of study materials or patients: SE, OR

Collection and assembly of data: SE

Data analysis and interpretation: SE, OR

Manuscript writing: SE, OR

Final approval of manuscript: SE, OR

Declaration of conflicts of interests

Susanne Erzkamp has received speaker honoraria by MSD. Olaf Rose has received speaker honoraria by Bayer, Boehringer Ingelheim, Lilly, Medac, MSD, Novartis and Omnicell. The authors declare that there is no conflict of interest regarding the publication of this article.

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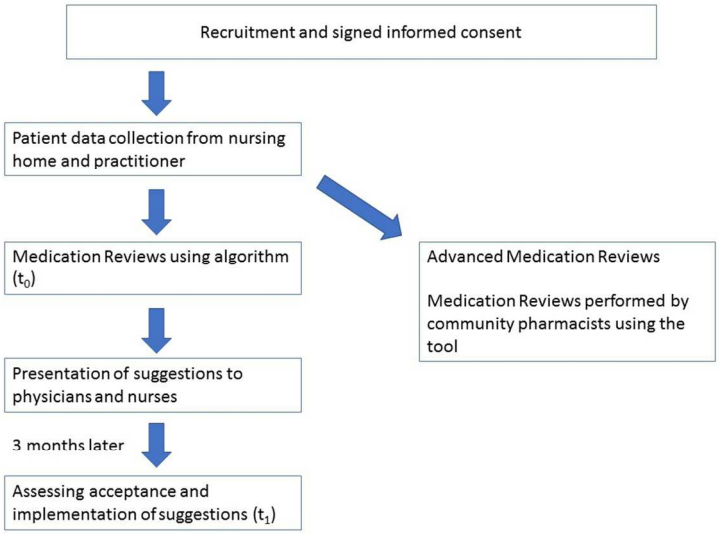

Fig.1: Participant timeline

338x190mm (96 x 96 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page (s) number
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1,4
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	4
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	2, 5, 11
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	2
Sponsor	5b	Provide name for the review funder and/or sponsor	2
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	2
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	1, 4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	4
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix 2

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	5
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	5
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	5
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	5
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	5
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	6
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Search strategy

MEDLINE/PCM via PubMed

1. Nursing Home [MeSH Terms]
2. “nursing home”
3. “nursing homes”
4. Long term care [MeSH Terms]
5. “Long-term care”
6. “Homes for the Aged”
7. “Aged care homes”
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. “intervention”
10. “interventions”
11. “Medication Review”
12. “Medication Management”
13. “Medication Therapy Management”
14. Medication Therapy Management [MeSH Terms]
15. “pharmaceutical care”
16. pharmaceutical services [MeSH Terms]
17. 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. pharmaceutical preparations [MeSH Terms]
19. “Pharmaceutical preparations”
20. “medication”
21. 18 OR 19 OR 20
22. Meta-Analysis [ptyp]
23. Review [ptyp]
24. Systematic [sb]
25. 22 OR 23 OR 24
26. "2000/01/01"[PDAT] : "3000/12/31"[PDAT]
27. English [lang]
28. German [lang]
29. 27 OR 28
30. 8 AND 17 AND 21 AND 25 AND 26 AND 29

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page(s) number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	Appendix 4
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 2
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	1
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	7, 9
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1, 2
	6b	Explanation for choice of comparators	-
Objectives	7	Specific objectives or hypotheses	6

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	7
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	10
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	8
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Methods: Assignment of interventions (for controlled trials)			
Allocation:			

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	7
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	9
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	9
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	8
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	9
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	9
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	9
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	11
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	10
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	10
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available on request (German)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

WHO Trial Registration Data Set (Version 1.2.1)

	Data category	Information
1	Primary Registry and Trial Identifying Number	German Clinical Trial Register DRKS00010995
2	Date of Registration in Primary Registry	23 August, 2017
3	Secondary Identifying Numbers	The Universal Trial Number (UTN) U1111-1186-5784
4	Source(s) of Monetary or Material Support	Apothekerstiftung Westfalen-Lippe (noncommercial foundation)
5	Primary Sponsor	Susanne Erzkamp, Elefanten-Apotheke gegr. 1575, Steinstr. 14, 48565 Steinfurt, Germany
6	Secondary Sponsor(s)	
7	Contact for Public Queries	Susanne Erzkamp, Elefanten-Apotheke gegr. 1575, Steinstr. 14, 48565 Steinfurt, Germany Telephone: 0049 2551 5435 Fax: 0049 2551 6236 Email: amber-study@gmx.de
8	Contact for Scientific Queries	7
9	Public Title	Medication Management in nursing homes- AMBER study
10	Scientific Title	Development and evaluation of an algorithm in Medication Management for best practice. Effectiveness of the intervention and translation into standard care for nursing home residents, AMBER study protocol
11	Countries of Recruitment	Germany
12	Health Condition(s) or Problem(s) Studied	Multimorbidity
13	Intervention(s)	A Medication Management for residents of nursing homes will be performed by pharmacists in collaboration with physicians and nurses by means of an innovative algorithm. There is no control group.
4		Inclusion Criteria Age: < 65 years

	Key Inclusion and Exclusion Criteria	Sex: both Residency in a nursing home facility multimorbidity (at least 2 chronic diseases) polymedication (at least 5 chronic systemic available medications) signed informed consent (if necessary through a legally authorized representative) Exclusion Criteria: participation in other clinical studies at present time
15	Study Type	Interventional single-armed, prospective study design without randomization and blinding
16	Date of First Enrollment	25 August 2017 (planned)
17	Target Sample Size	100
18	Recruitment Status	Recruiting
19	Primary outcome(s)	change in the number of drug-related problems (DRPs), classified according to PCNE version 8.01 and detected by using the algorithm
20	Key Secondary Outcomes	- DRPs classified according to PCNE version 8.01 (number and type) - Acceptance measurement of physicians and nurses by using an acceptance form, classified according to PCNE version 8.01 - Number of DRPs classified according to PCNE version 8.01, detected by an advanced Medication Review - Reproducibility of analysis and feasibility of the algorithm (time spending, inter-rater reliability)

BMJ Open

Development and evaluation of an algorithm-based tool for Medication Management in nursing homes: the AMBER study protocol

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019398.R1
Article Type:	Protocol
Date Submitted by the Author:	29-Jan-2018
Complete List of Authors:	Erzkamp, Susanne; Elefanten-Apotheke, gegr. 1575 Rose, Olaf; Elefanten-Apotheke, gegr. 1575; University of Florida College of Pharmacy, Dept. of Pharmacotherapy & Translational Research
Primary Subject Heading:	Patient-centred medicine
Secondary Subject Heading:	Evidence based practice, Medical management, Public health, General practice / Family practice, Geriatric medicine
Keywords:	GERIATRIC MEDICINE, CLINICAL PHARMACOLOGY, PUBLIC HEALTH

Development and evaluation of an algorithm-based tool for Medication Management in nursing homes: the AMBER study protocol

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ABSTRACT

INTRODUCTION:

Residents of nursing homes are susceptible to risks from medication. Medication Reviews (MR) can increase clinical outcomes and the quality of medication therapy. Limited resources and barriers between health-care practitioners are potential obstructions to performing MR in nursing homes. Focusing on frequent and relevant problems can support pharmacists in the provision of pharmaceutical care services. This study aims to develop and evaluate an algorithm-based tool that facilitates the provision of Medication Management in clinical practice.

METHODS AND ANALYSIS:

This study is subdivided into three phases. In phase I, semi-structured interviews with health-care practitioners and patients will be performed, and a mixed methods approach will be chosen. Qualitative content analysis and the rating of the aspects concerning the frequency and relevance of problems in the medication process in nursing homes will be performed. In phase II, a systematic review of the current literature on problems and interventions will be conducted. The findings will be narratively presented. The results of both phases will be combined to develop an algorithm for MRs. For further refinement of the aspects detected, a Delphi survey will be conducted. In conclusion, a tool for clinical practice will be created. In phase III, the tool will be tested on MRs in nursing homes. In addition, effectiveness, acceptance, feasibility and reproducibility will be assessed. The primary outcome of phase III will be the reduction of drug-related problems, which will be detected using the tool. The secondary outcomes will be the proportion of drug-related problems, the acceptance of pharmaceutical recommendations, and the expenditure of time using the tool and inter-rater reliability.

ETHICS AND DISSEMINATION:

This study intervention is approved by the local Ethics Committee. The findings of the study will be presented at national and international scientific conferences and will be published in peer-reviewed journals.

Strengths and limitations of this study

- The process to develop an algorithm for Medication Management in nursing homes uses a variety of consecutive methods
- The resulting tool is tested on several aspects, such as effectiveness, feasibility and acceptance, by multidisciplinary health-care providers
- The inclusion of clinical practitioners at the development of the tool is believed to support translation into standard care
- The algorithm needs to balance limited time and resources in community care to detect as many relevant drug-related problems as possible
- The limited duration and size of this uncontrolled study requires further research and testing

INTRODUCTION

Pharmaceutical Care is defined as the "pharmacist's contribution to the care of individuals in order to optimise medicines use and improve health outcomes" [1]. Medication Review and Medication Management are current instruments of Pharmaceutical Care that have proven to be effective in reducing drug-related problems, increasing the quality of the medication regimen and improving medical outcomes in various settings and indications [2–9]. Medication Review is defined by the Pharmaceutical Care Network Europe (PCNE) as "a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug related problems and recommending interventions" [10], Medication Management involves "patient-centered care to optimize safe, effective and appropriate drug therapy. Care is provided through collaboration with patients and their health care teams" [11]. Pharmaceutical care interventions are especially meaningful in high-risk populations [12]. Residents of nursing home facilities are a highly vulnerable patient group whose medication deserves special attention. In addition to geriatric age and dependence on care, multimorbidity and polymedication are frequently related to this patient population [13, 14]. Inappropriate medication is related to a poor quality of life, high morbidity, preventable adverse-drug events, increased risk for falls, repeated hospitalizations and manifold physician contacts [15–18]. Several approaches to optimize the quality of the medication regimen have been tested. Medication Reviews, multidisciplinary case

conferences, education and coaching are examples of pharmaceutical interventions that have been studied successfully in nursing homes [19–23], and drug-related problems could be reduced and the quality of medication could be enhanced. The effects of pharmaceutical care on further clinical outcomes, such as mortality or quality of life, is uncertain [19, 22]. This might be due to the limited size and length of most pharmaceutical studies. However, structured and collaborative Medication Management seems to be particularly supportive in this setting but is rarely implemented into standard care in Germany [5, 24]. Barriers of implementation might include time, resources and compensation. Limited experience in performing Medication Reviews and Medication Management and assessing entry barriers in nursing home facilities might be an additional reason for withholding these services to the residents. Structure and guidance have been identified as tools to support pharmacists in the administration of Medication Reviews [25]. Setting higher standards of medication quality in nursing homes might be even more challenging as further action to encounter the patients, nurses and physicians is required. Tailored screening tools and standardized communication forms are helpful to guide and support pharmacists in performing Medication Reviews and have been developed for various scenarios [26–28]. For pharmacists with limited experience, the TIMER©-tool has shown to be effective in performing Medication Reviews to a certain extent but has not been updated or refined any more [29]. A contemporary tool that is tailored to the demands of pharmacists willing to conduct Medication Management in a nursing home could be helpful in overcoming existing barriers of implementation. However, it needs to take the previously mentioned aspects of multidisciplinary collaboration, structured guidance and limited time and resources into account.

Aims and objectives

The aim of the AMBER study is to develop and test an algorithm-based tool that supports pharmacists in performing structured collaborative Medication Management in an appropriate timeframe. The tool should take frequent and relevant problems in the medication process of residents of nursing homes into account and needs to consider the special circumstances of this setting. In addition to demonstrating effectiveness in detecting and solving drug-related problems, which are defined as “events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes,” the tool needs to be highly feasible for community pharmacists [30]. To assure a high patient benefit, multidisciplinary approaches need to be facilitated by the tool. In addition, it should be developed with the utmost available evidence and serve the patient.

METHODS AND ANALYSIS

This study is registered at the German Clinical Trials Register (registration number DRKS00010995). It is funded by Apothekerstiftung Westfalen-Lippe (noncommercial foundation). The funding source has no role in the design of this study and will not have any role in its execution, the analysis or interpretation of the data, or the decision to submit results. Susanne Erzkamp is the guarantor for this paper and the study. All of the authors drafted the protocol.

Overview of the study

This study will be performed in three phases (figure 1). Phase I consists of interviews with health-care practitioners and patients. In phase II, a systematic review will be performed, and the results will be combined with the outcomes of phase I to form an algorithm. Following a Delphi approach, the determined aspects of the algorithm will be presented to an expert panel to refine the algorithm. In phase III, the algorithm will be tested in patients.

Phase I: practitioner and patient interviews

Purpose

Semi-structured interviews with physicians, pharmacists, nurses and patients will be performed to identify frequent and relevant aspects of the medication process in nursing homes. The involvement of different health-care practitioners was chosen to consider the different perspectives. Furthermore, this approach should assure practical relevance and feasibility and support the pragmatic attitude of the study. Patient interviews will be conducted to consider the goals of patients. The results of phase I will be to consider creation of the algorithm.

Methods

Phase I of the study is based on a mixed methods approach that includes qualitative and quantitative aspects. Physicians, pharmacists, nurses and patients will be interviewed about their experience, requirements and expectations regarding problems, risks and goals at the medication process in nursing homes. We will strive for five to ten experts in each group. Semi-structured interviews with health-care practitioners and patients will be conducted

Physicians, pharmacists and nurses at phase I are required to have more than one years' experience in nursing home care before the interview and are required to work in a facility in North Rhine-Westphalia. Participation is voluntary. Patients at the panel will be residents of a nursing home facility and will be suggested by the particular head of nursing service. In addition, they must be able to understand and answer the questions without assistance. Open-ended questions covering uncertainties and problems in the medication process will be asked. A qualitative content analysis

described previously by Mayring [31] will be performed with the software MAXQDA 12. The frequencies of coded categories are analyzed. Furthermore, 51 specific aspects of therapy and drug-related problems (DRPs) covering general challenges, patient goals, communication barriers, medical goals and pharmaceutical aspects will be assessed. The 51 aspects were elaborated together with practitioners of each profession in a first approach. Additional aspects can be added by physicians, pharmacists, nurses and patients. Each aspect will be rated separately for frequency and relevance on a scale from 1-5 (with 1 being infrequent or irrelevant to 5 being frequent and relevant). Patients will be asked to rate a limited questionnaire of 24 aspects for relevance. The restrictions are created to reduce patient burden and based on the appraisal of two nurses. The frequency of the aspects is deleted in the patient version of the questionnaire, as they do not have an overview regarding the prevalence in other patients. Parameters rated by more than 50 % of the participants with an average score of 3 or higher for frequency and relevance will be chosen as meaningful. Subsequently, the top scores per group will be considered for the algorithm.

The planned time frame for phase I is six months (07.2016-12.2016).

Phase IIa: literature review

A literature review will be performed by following the Medical Research Council guidance [32]. The protocol was prepared according to PRISMA-P 2015 [33, 34], and the review is registered in PROSPERO (registration number CRD42017065002). The PRISMA-P 2015 checklist is presented in appendix 1.

The objective of phase IIa is to systematically review the literature for relevant aspects of Medication Reviews in nursing homes. The interventions will be analyzed, and general challenges, patient goals, communication barriers, medical goals and pharmaceutical aspects will be considered. The intended review aims to answer the question of which problems arise most frequently and which aspects are most relevant. It includes three consecutive steps. In step 1, a review of the existing reviews will be done. In step 2, interventional studies that have been published after the last review will be searched and analyzed. In step 3, studies on frequent problems in a nursing home setting will be examined, especially those that have not been covered by steps 1 and 2.

Step 1: review of reviews

Purpose

To develop an intervention, the use of the best available evidence is recommended [32]. Reviews on interventions to optimize medication therapy in nursing homes should provide an indication of effective interventions or parts of them. This step aims to answer the questions of which

interventions have already been developed, how effective they are and which aspects of the medication therapy can be improved by a medication review.

Methods

Systematic reviews, reviews and meta-analyses will be included. Participants must be nursing home residents (65 years and older). Studies with a geriatric population living outside nursing home facilities will be excluded, except studies that investigated both groups and separately provide data.

Any intervention that could be part of a Medication Review will be considered.

Included studies can either be controlled or uncontrolled trials with standard care as a potential comparator. The endpoints of interest are hospitalization, mortality and falls, among others. In cases where the outcomes will be DRPs or potential inadequate medication (PIM), they must be reported in detail.

The studies will need to be finished, and the results will need to be published. Articles in English and German will be included.

The following electronic bibliographic databases will be searched:

- **MEDLINE/PCM (via PubMed)**
- **PsycINFO (via EBSCOhost)**
- **CDSR (via Cochrane Library)**
- **CINAHL (via EBSCOhost)**
- **International Pharmaceutical Abstracts (via EBSCOhost)**
- **NHSEED/DARE (via CRD)**

Additionally, the reference lists of the included studies and reviews will be hand-searched.

Articles published between January 01, 2000 and March 31, 2017 will be conducted. This restriction should ensure the current nature of the data and consider the progress of health care. An example of a search strategy is presented in appendix 2. Citavi 5© software will be used for data management and to remove duplications. Additional duplications will be removed by hand. One review author (SE) will conduct the search in the databases and will extract the titles and abstracts for analyses. Two reviewers (SE and OR) will independently screen the publications for inclusion. Discussion and consensus will resolve potential disagreements.

A data extraction form that will be used to collect data from eligible studies will be developed for each step. Data extraction will be conducted by one reviewer (SE) with verification by another (OR). Disagreements will be resolved by discussion and consensus. At least the following data will be extracted: the type of intervention, the tools used, conditions and outcomes. Outcomes will be dependent on the endpoints of the regarded studies, e.g., the influence on mortality, hospitalization

rates, falls, quality of life and time spent for care. Studies will be checked with the AMSTAR Checklist [35]. Studies with poor quality will not be removed but the methods will be reported as far as possible.

Step 2: review of recent studies

Purpose

At step 2, interventional studies for optimizing medication therapy that will be published after the reviews from step 1 will be included; hence; these studies could not have been considered by these earlier reviews.

Methods

The methods are similar to step 1. The interventional studies will be examined following the template for intervention description and replication (TIDieR) Checklist [36]. Studies with poor quality will not be removed, but the methods and the description of the intervention will be reported as far as possible.

Step 3: review of common problems

Purpose

In addition to the results of the reviews and interventional studies, frequent problems can also be described by non-interventional studies. The focus in this step is on reported problems and issues in the medication process in nursing homes that are independently detected from an intervention. We aim to supplement problems that might not be the subject of the interventional studies.

Methods

Specific studies that are not covered by step 1 and 2 will be examined, for example, observational studies, qualitative studies and guidelines (the additional procedure is similar to step 1 and 2).

Data synthesis

A narrative synthesis will be provided. This is an approach “that relies primarily on the use of words and text to summarise and explain the findings of the synthesis” [37]. Descriptions of effective interventions and frequent problems will be summarized. Because of the potential inhomogeneity of the outcomes, a meta-analysis is expected to be inappropriate.

Phase IIb: creating the algorithm and a Delphi survey

The results of phase I will be compared with the results of phase IIa. The determined aspects will be checked for eligibility and feasibility in the algorithm. Every aspect will be approved by the authors and considered for inclusion. A summarization will be conducted, and the aspects will be evaluated in a Delphi survey with 10 or more experts using the software SurveyMonkey® with a 5-point Likert-scale. The remarks of the expert panel will be incorporated into the algorithm. The experts are pharmacists and experienced researchers in the field of Medication Review, especially in the nursing home setting. They will be asked for agreement or disagreement regarding the proposed aspects. Consensus will be defined as an agreement of 70% or higher and a median higher than 3.

The planned time frame for phase II is 6 months (01.2017-06.2017).

Phase III: clinical testing

The study protocol follows the SPIRIT 2013 statement [38, 39], and the study design is developed in line with the manual for the design of non-drug trials in primary care by Joos et al. [40]. The SPIRIT 2013 checklist and the WHO Trial Registration Data Set are presented in appendix 3 and 4. Conducting the TIDieR checklist to describe the intervention will be conducted later when reporting the outcomes [36].

Purpose

In phase 3, the developed algorithm will be tested for effectiveness by performing a Medication Review in nursing home patients. Acceptance of the pharmaceutical recommendations will be measured using a feedback form. In addition, the feasibility of the algorithm will be investigated. Several pharmacists will use and rate the feasibility after conducting Medication Reviews on written case scenarios.

Methods

A single-armed prospective study design will be utilized. Reductions in the detected DRPs will be the indicator for effectiveness of the intervention.

The planned time frame for phase III is 12 months (07.2017-06.2018).

Study setting

This study will be conducted in nursing homes in North Rhine-Westphalia, Germany.

Eligibility criteria

The following inclusion criteria will be applied:

- patients aged ≥ 65 years
- residency in a nursing home facility
- multimorbidity: at least 2 chronic diseases (25)
- polymedication: at least 5 chronic systemic medications
- signed informed consent (if necessary through a legally authorized representative)

Exclusion criteria:

- participation in other clinical studies at the current time

A withdrawal of consent will be possible at any time and will lead to the discontinuation of the intervention. Data on dropouts will not be included in the analyses of the primary outcome. The patients will retain all rights regarding their personal data and its deletion.

Intervention

After recruitment, a one-time Medication Review will be performed by the project manager using the developed algorithm (t_0). The patient data will be collected from nursing homes and physicians. Information about the actual condition of the patient can be supplemented by the patients themselves or by the nurses at the facilities. The results of the Medication Review will be communicated to nurses and physicians using SOAP (subjective data, objective data, assessment, and plan) notes and will be discussed if required [41]. SOAP notes will cover detected problems in medication therapy and recommendations to solve them. Acceptance will be measured using a feedback form filled out by physicians and nurses and depending on the recommendations. At a three-month post-intervention follow-up (t_1), the medication of the patient will be evaluated for changes and the status of the detected DRPs will be reviewed. The number of solved and unsolved DRPs will be collected.

In addition to this main analysis, an advanced Medication Review will be performed for ten patients as a benchmark. This type of review is based on medication history, patient information and clinical information according to the PCNE definition [42]. In contrast to the PCNE definition, patient information can also be derived from nurses in this particular setting. The results of the advanced Medication Reviews will be compared to the results of the Medication Review performed using the algorithm. The number and type of detected DRPs will be compared and analyzed by the project manager. The differences will be descriptively presented.

Feasibility and reproducibility of the algorithm will be tested by 5 or more pharmacists using 10 similar patient cases. The case description and patient information will be handed out to the

pharmacists anonymously in a written form and the experiences will be descriptively presented. The timeline of phase III is shown in figure 2.

Standard care will be provided during the trial and interventions will be supplementary. This study will monitor for the potential harm of the intervention by recording adverse-drug reactions following the implemented suggestions.

Outcomes

The primary outcome will be the change in the number of DRPs classified according to 'The PCNE Classification V 8.01' and detected using the algorithm [30]. Potential DRPs will be limited to the aspects covered by the algorithm.

Secondary outcomes

- DRPs classified according to PCNE version 8.01 (number and type)
- Acceptance measurement of physicians and nurses using an acceptance form and classified according to PCNE version 8.01
- Number of DRPs classified according to PCNE version 8.01 and detected by an advanced Medication Review
- Reproducibility of the analysis and feasibility of the algorithm (time spent and inter-rater reliability)

Sample size

Regarding the assumption of a mean reduction of one DRP per patient with a standard deviation of two, a calculation will be performed by the institute for biometric and clinical research of the Westfälische Wilhelms-University Münster (Institut für Biometrie und Klinische Forschung, IBKF). The null hypothesis, whether the number of DRPs does not differ, will be tested with a two-sided Wilcoxon signed-rank test with a significance level of 0.05. The estimated sample size to improve a power of 80 % will be 75 patients. Considering dropouts, a sample size of 100 patients is intended.

Recruitment

As a first step, three nursing homes in North Rhine-Westphalia will be asked to participate in the study. All of the patients of the participating nursing homes will be screened for inclusion and exclusion criteria and subsequently asked to join the study.

In case of an insufficient number of participating patients, additional nursing homes will be approached.

Data collection

During the study, the following data will be collected and documented using Microsoft® Excel® software:

- Name and study number
- Age and sex of participant
- Medication, including active pharmaceutical ingredients, dosage and pharmaceutical form
- Morbidities, laboratory parameters and vital signs

This data will be collected from nursing homes' and physicians' documentation.

Furthermore, the results of the Medication Reviews will be documented using password-protected Excel® sheets. All of the reasons for withdrawal or dropout will be recorded in the study.

Data management

Patient-related data will be used for performing a Medication Review using the algorithm and for communication with nurses and practitioners. For all of the statistical analyses and other Medication Reviews, anonymized data will be used.

Statistical methods

Baseline and demographic characteristics will be descriptively analyzed. The reductions in DRPs will be tested with a two-sided Wilcoxon signed-rank test with a significance level of 0.05.

ETHICS AND DISSEMINATION

The study intervention is approved by the local Ethics Committee (Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Westfälischen Wilhelms-Universität, approval number 2017-350-f-S) and will be conducted based on the principles of the Declaration of Helsinki. If amendments of the protocol are necessary, the date of each amendment, a description of the change and the rational will be given. Changes will not be incorporated into the protocol. The project manager will obtain informed consent from potential trial participants or legally authorized representatives. Written information will be given to all of the study patients. Confidentiality will be guaranteed by anonymizing patient data where applicable. Only the project manager will have complete data for communication with nurses and physicians. An analysis of the final data by IBKF and the project manager will be performed.

The goal of the study is the development of an algorithm as an underlying basis for use as a tool. The tool is intended to be applied into standard care and might be utilized by community pharmacies engaged in nursing home care. The findings of this study will be presented at national and international scientific conferences and will be published in peer-reviewed journals. There are no publication restrictions.

Patients, nursing homes and physicians who participate in this study will be offered a final report on the study results.

Methods against bias and for quality assurance

To ensure the data quality and to avoid missing data or processes that are not adherent with the study protocol, the study sites will be visited for clinical monitoring (to determine whether the diagnoses, clinical data and medication were current). Furthermore, several routines will be established to prevent or detect incorrect and inconsistent data entry and incomplete data. Additionally, regular training sessions will be conducted.

DISCUSSION

The aim of this study is the development of an algorithm leading to the development of a tool to support community pharmacists in performing Medication Management in nursing homes. The tool is then tested for effectiveness, feasibility and practicability.

Development

The tool needs to detect as many relevant DRPs as possible but only take limited time and resources into account. Hence, both aspects need to be balanced. Each step of the algorithm needs to be based on evidence. Therefore, a mixed methods approach that incorporates interviews with multidisciplinary practitioners and patients, a systematic review, a Delphi survey, and testing and refinement of the underlying algorithm is chosen. This approach in developing the algorithm is quite comprehensive compared to other tools as it needs to cover both explicit criteria, which "can be applied with little or no clinical judgement," and implicit criteria, which also take a patient's preferences into account [43]. This is in contrast to more confined medication-safety tools, which may depend on a mere Delphi survey [43, 44]. The complex method in developing the AMBER tool is believed to provide a higher probability of included items than a limited approach. For example, taking practitioners' experience into account helps to rate current trends in mis-prescribing, as these may vary from time to time [45]. As shown by da Costa et al., tools to evaluate medication regimens differ in the number of detected DRPs, whereas it is unclear if a higher number leads to a greater patient benefit or vice versa for overreporting [26]. In this study, the tool is developed solely for the medication of nursing home residents and needs to cover the specific requirements of this setting.

Testing

The developed tool is aimed to test for effectiveness in nursing homes in Germany in 100 patients. The number of relevant tool-detected DRPs is compared to the results of an advanced Medication Review. Feasibility is evaluated by providing community pharmacists with tool and patient cases. The results of the pharmacists' test cases are compared to the study team's results. A survey on the

feasibility and practicability will be conducted, and the time to perform a Medication Review using the tool will be developed.

Multidisciplinary approach

Medication Management implicates further and multidisciplinary activities after a Medication Review is performed. At a nursing home, cooperation with nurses and physicians is vital to determine an effect on patients' medication, even though attitudes on patient-oriented approaches might vary [46–48]. In regard to these considerations, the tool needs to lead pharmacists toward multidisciplinary cooperation. Nurse and physician acceptance is measured using a standardized feedback form and based on the PCNE classification of DRPs [30].

Strengths and limitations

A potential strength of the study might be the variety of methods, the high numbers of underlying data and the large base of studies included in the development of the algorithm. Inclusion of clinical practitioners at the development of the tool is believed to support translation into standard care.

This study faces several limitations. Confined resources do not allow a larger and controlled study. Even though a complex method is used in developing the tool, it can be only a compromise to detect and solve a sufficient number of relevant DRPs. A comprehensive approach surely could perform better but has limited feasibility upon translation into the aspired community setting. The short duration of the study intervention and the restricted study collection might not disclose all aspects as it is powered only for the primary endpoint. Other aspects might show up as relevant during the intervention phase.

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Author contributions

Conception and design: SE, OR

Administrative support: SE

Provision of study materials or patients: SE, OR

Collection and assembly of data: SE

Data analysis and interpretation: SE, OR

Manuscript writing: SE, OR

Final approval of manuscript: SE, OR

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Declaration of conflicts of interests

Susanne Erzkamp received a speaker honorarium by MSD. Olaf Rose received speaker honoraria from Bayer, Boehringer Ingelheim, Lilly, Medac, MSD, Novartis and Omnicell. The authors declare that there are no conflicts of interest regarding the publication of this article.

Ethics approval:

Ethics Committee of the Medical Association of Westphalia-Lippe and of the University of Münster, approval number 2017-350-f-S

Figure 1: Study flow

Figure 2: Participant timeline

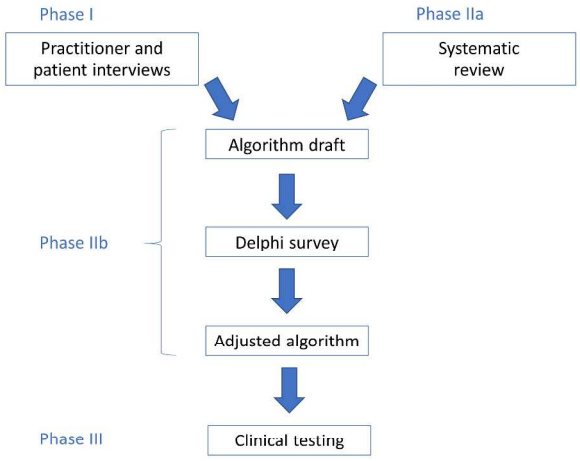

Figure 1: Study flow

338x190mm (300 x 300 DPI)

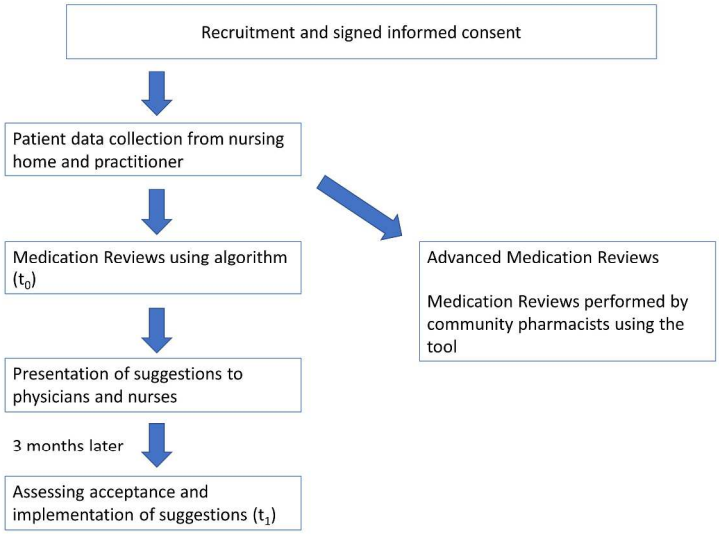

Figure 2: Participant timeline

338x190mm (300 x 300 DPI)

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page (s) number
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1,5
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	5
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	2, 4, 6, 13
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	3,4
Sponsor	5b	Provide name for the review funder and/or sponsor	3,4
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	3,4
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	2-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix 2

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	6
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	N/A
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	N/A
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	N/A

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Search strategy

MEDLINE/PCM via PubMed

1. Nursing Home [MeSH Terms]
2. “nursing home”
3. “nursing homes”
4. Long term care [MeSH Terms]
5. “Long-term care”
6. “Homes for the Aged”
7. “Aged care homes”
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. “intervention”
10. “interventions”
11. “Medication Review”
12. “Medication Management”
13. “Medication Therapy Management”
14. Medication Therapy Management [MeSH Terms]
15. “pharmaceutical care”
16. pharmaceutical services [MeSH Terms]
17. 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. pharmaceutical preparations [MeSH Terms]
19. “Pharmaceutical preparations”
20. “medication”
21. 18 OR 19 OR 20
22. Meta-Analysis [ptyp]
23. Review [ptyp]
24. Systematic [sb]
25. 22 OR 23 OR 24
26. "2000/01/01"[PDAT] : "3000/12/31"[PDAT]
27. English [lang]
28. German [lang]
29. 27 OR 28
30. 8 AND 17 AND 21 AND 25 AND 26 AND 29

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Page(s) number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
	2b	All items from the World Health Organization Trial Registration Data Set	appendix 4
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	3,4
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 4, 13
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	3, 4
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	7, 9
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	2, 3
	6b	Explanation for choice of comparators	-
Objectives	7	Specific objectives or hypotheses	11

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	8, 9
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8, 9
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	8
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	fig. 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	10
Methods: Assignment of interventions (for controlled trials)			
Allocation:			

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10, 11
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9, 11
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	11

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	9
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	11
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	11
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	11
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A

Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
	31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available on request (German)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

WHO Trial Registration Data Set (Version 1.2.1)

	Data category	Information
1	Primary Registry and Trial Identifying Number	German Clinical Trial Register DRKS00010995
2	Date of Registration in Primary Registry	23 August, 2017
3	Secondary Identifying Numbers	The Universal Trial Number (UTN) U1111-1186-5784
4	Source(s) of Monetary or Material Support	Apothekerstiftung Westfalen-Lippe (noncommercial foundation)
5	Primary Sponsor	Susanne Erzkamp, Elefanten-Apotheke gegr. 1575, Steinstr. 14, 48565 Steinfurt, Germany
6	Secondary Sponsor(s)	
7	Contact for Public Queries	Susanne Erzkamp, Elefanten-Apotheke gegr. 1575, Steinstr. 14, 48565 Steinfurt, Germany Telephone: 0049 2551 5435 Fax: 0049 2551 6236 Email: amber-study@gmx.de
8	Contact for Scientific Queries	7
9	Public Title	Medication Management in nursing homes- AMBER study
10	Scientific Title	Development and evaluation of an algorithm in Medication Management for best practice. Effectiveness of the intervention and translation into standard care for nursing home residents
11	Countries of Recruitment	Germany
12	Health Condition(s) or Problem(s) Studied	Multimorbidity
13	Intervention(s)	A Medication Management for residents of nursing homes will be performed by pharmacists in collaboration with physicians and nurses by means of an innovative algorithm. There is no control group.
4		Inclusion Criteria Age: < 65 years

	Key Inclusion and Exclusion Criteria	Sex: both Residency in a nursing home facility multimorbidity (at least 2 chronic diseases) polymedication (at least 5 chronic systemic available medications) signed informed consent (if necessary through a legally authorized representative) Exclusion Criteria: participation in other clinical studies at present time
15	Study Type	Interventional single-armed, prospective study design without randomization and blinding
16	Date of First Enrollment	25 August 2017 (planned)
17	Target Sample Size	100
18	Recruitment Status	Recruiting
19	Primary outcome(s)	change in the number of drug-related problems (DRPs), classified according to PCNE version 8.01 and detected by using the algorithm
20	Key Secondary Outcomes	- DRPs classified according to PCNE version 8.01 (number and type) - Acceptance measurement of physicians and nurses by using an acceptance form, classified according to PCNE version 8.01 - Number of DRPs classified according to PCNE version 8.01, detected by an advanced Medication Review - Reproducibility of analysis and feasibility of the algorithm (time spending, inter-rater reliability)