OPtimising thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly: a cluster randomised controlled trial

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Overall ObjectiveThe objective of this RCT is to evaluate whether the Systematic Tool to Reduce Inappropriate Prescribing (STRIP) including STRIP assistant (STRIPA) implemented by an appropriately qualified team will lead to an improvement in…

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47041

Source
ToetsingOnline

Brief title
OPERAM

Condition

- Other condition

Synonym
medication use, Multipel medications

Health condition

polyfarmacie, multimorbiditeit

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Europese Unie;Zwitserse Overheid

Intervention

Keyword: Hospital admissions, Medication review, Multimorbid elderly, Polypharmacy

Outcome measures

Primary outcome

Primary Outcome

The primary outcome is defined as the first confirmed DRA after discharge from the index hospitalisation or departure from the ambulatory clinic, within a period of 12 months (365 days) after enrolment into the study.

The following criteria must be fulfilled in order for an event to qualify as a DRA:

• The hospitalisation must be preceded by an ADR, and the ADR must be at least a contributory factor for admission of the patient. This includes harm due to a non-preventable ADR or a preventable medication error related to over-, mis-, or underuse or over-, mis-, or underprescribing of prescription and non-prescription medications.

• It must be an inpatient hospitalisation for longer than 24 hours

• It must not be a visits to the emergency room (even if overnight) without inpatient hospitalisation

• It must not be a hospitalisation or a prolongation of a current

hospitalisation for a diagnostic or elective (surgical) procedure for a pre-existing condition

• Further criteria that must be fulfilled as specified in the adjudication guidelines

Secondary outcome

Secondary Outcomes

The following secondary endpoints will be analysed

Up to 365 days after baseline:

• Inpatient re-hospitalisations for any cause, including planned hospitalisations, but excluding hospitalisations for a diagnostic procedure

• Survival (including causes of death). Death caused by cancer will be used as a negative control outcome - see section 11.4.3 for details)

• Number of falls and fractures reported by participants (see corresponding SOP for the definition of falls in the context of this study)

• Formal care received (number and length of stay of planned and unplanned hospitalisations, visits to the emergency room without inpatient hospitalisation, scheduled and unscheduled primary care physician and medical specialist [differentiated by profession] visits, hospital outpatient clinic visits, inpatient stays and length of stay at a rehabilitation facility, physiotherapist and other therapist visits; patient living in nursing home admissions and length of stay (in patients who were living in the community at baseline); home nursing visits)

• Informal care received (unpaid care by e.g. family members, relatives, friends)

• Quality-adjusted life years (QALYs) accrued during one year

• Direct medical costs during one year

• Cost-effectiveness of the trial intervention by combining clinical data, quality of life data, and healthcare utilisation data collected within the trial and unit costs for participating countries that will stem from external sources.

At discharge from the index hospitalisation or departure from the ambulatory clinic, and on days 60, 184, and 365 after inclusion:

• Quality of life as assessed by the 5-level version of the European Quality of Life-5 Dimensions questionnaire (EQ-5D), including pain/discomfort

• Degree of polypharmacy, defined as the number of regular long-term medications

• Activities of daily living as assessed by the Activities of Daily Ling questionnaire (ADL)

On days 60 and 365 after inclusion:

• Drug compliance as assessed by the Medication Adherence Questionnaire (MMAS-8) developed by Morisky with the addition of one question based on Gehi et al. (*In the past month, how often did you take your medications as the doctor prescribed?*)

On day 60 after inclusion:

• Clinically significant drug-drug interaction (DDI) as assessed by currently used medication and diagnoses at baseline/discharge. Assessment will be done at the end of the trial, when all data is collected.

Unnecessary drugs as assessed by currently used medication and diagnoses at baseline/discharge. Assessment will be done at the end of the trial, when all data is collected.

• Drug underuse as assessed by currently used medication and diagnoses at baseline/discharge. Assessment will be done at the end of the trial, when all data is collected.

• Potentially inappropriate medications as assessed by currently used medication and diagnoses at baseline/discharge. Assessment will be done at the end of the trial, when all data is collected.

During the index hospitalisation or stay at the ambulatory clinic

• Direct costs of the trial intervention by combining staff time per profession required to perform study intervention or standard of care activities relating to reconciliation of medication, and unit costs for participating countries that will stem from external sources

• Acceptance of STRIPA recommendations (intervention arm only)

Safety Outcomes

Up to 365 days after inclusion:

• SAEs, including unplanned inpatient hospitalisations and death

• Device deficiencies

Study description

Background summary

Global life expectancy at birth has increased by a further 6 years from 1990 until 2012, and average life expectancy in the EU is projected to further increase to 89.1 years for females and 84.6 years for males by 2060. The population aged >=65 years is growing rapidly in the EU region. Multimorbidity is the coexistence of several chronic diseases . Multimorbidity is associated with increased mortality, decreased QoL, increased healthcare utilisation, hospital admissions, and higher rates of drug prescriptions. Two-thirds of the overall healthcare expenditures are spent for multimorbid patients, because these patients are usually older, have more activity limitations, and present with more complex clinical pictures.Despite the large number of multimorbid patients, they were excluded in more than 60% of the RCTs published in high impact journals during the last 15 years. Only 2% of RCTs explicitly included multimorbid patients.

Polypharmacy may have detrimental effects in the elderly
Polypharmacy can be defined as the concurrent use of multiple drugs. A clear and consistent definition is lacking, but >=5 chronic medications is a commonly used approach to defining polypharmacy. Appropriate polypharmacy can improve QoL and prevent consequences of diseases, whereas inappropriate polypharmacy is often harmful.16 Inappropriate polypharmacy can have detrimental effects especially in elderly patients for several reasons. Age-related changes in pharmacokinetics and pharmacodynamics increase the risk of adverse drug events (ADEs) in elderly. With polypharmacy, there is also an increased risk of drug-drug and drug-disease interactions. In addition to its relation with adverse drug reactions (ADRs) and ADEs, polypharmacy is associated with poor drug compliance and other negative health outcomes, such as drug-related hospital admissions (DRAs), cognitive decline, falls, and an increased risk of hip fractures. Awareness of the related problems of polypharmacy and inappropriate drug treatment in resource-rich countries is increasing.

Drug-related hospital admissions are common and costly
Drug-related morbidity and mortality is an increasing problem in European healthcare systems. In the US, the overall costs of drug related morbidity and mortality have been estimated to more than 170 billion dollars every year, of which nearly 70 % are due to DRAs.

Study objective

Overall Objective
The objective of this RCT is to evaluate whether the Systematic Tool to Reduce Inappropriate Prescribing (STRIP) including STRIP assistant (STRIPA)

implemented by an appropriately qualified team will lead to an improvement in clinical and economic outcomes among patients aged 70 years and more with multimorbidity and polypharmacy.

Primary Objective
The primary objective is to assess the effect of pharmacotherapy optimisation, using STRIP, on DRAs.

Secondary Objectives
Secondary objectives is to assess the impact of pharmacotherapy optimisation by STRIP on parameters listed below (objectives 1-12) as well as to asssess the patient*s acceptance of the STRIPA recommendations (objective 13):

1. Number of inpatient re-hospitalisations for any cause
2. Mortality
3. Number of falls and fractures
4. Health economics parameters, including direct costs of the intervention and overall cost-effectiveness
5. Quality of life, including pain/discomfort
6. Degree of polypharmacy
7. Activities of daily living
8. Drug compliance
9. Clinically significant drug-drug interaction (DDI)
10. Unnecessary drug use
11. Drug underuse
12. Use of potentially inappropriate medications
13. Acceptance of the STRIPA recommendations

Study design

General study design and justification of design

OPERAM is a European multi-centre, cluster randomised, controlled trial of people aged 70 years or older, with multimorbidity and polypharmacy, being on an ambulatory visit or on a hospital stay in one of the four participating centres in Ireland, Belgium, Switzerland, and the Netherlands. The primary objective is to assess the effect of pharmacotherapy optimisation on DRAs over one year of follow-up. Clusters will be randomised 1;1 to either the intervention arm receiving STRIP or to the control arm undergoing usual clinical care. The cluster is defined by one or two prescribing physicians, i.e. physicians that are responsible for the pharmacotherapy of the participant at the time of inclusion in the trial (cluster-defining physician). The patients assigned to a cluster which was allocated to the intervention arm will undergo a systematic pharmacotherapy optimisation by a research physician and a pharmacist using the STRIP, including the STRIPA software. Patients assigned to a cluster allocated to the control arm will receive usual care. Patients will be followed for 1 year with follow-up phone calls to either the patient or his

or her carer(s) at 2, 6, and 12 months after inclusion. For the purpose of this trial, all hospitalisations during follow-up of the participants will be adjudicated at each site, based on common guidelines, to assess their relationship to drugs. To assess the occurrence of selection bias, data on a negative control outcome will be analysed. Assessment of the time needed for the intervention will be collected in a subsample of patients.

Intervention

The intervention will take place during the initial hospital stay (corresponding to the index hospitalisation) or an equivalent situation for outpatients (i.e. a visit at an ambulatory clinic). STRIP is a structured method to perform pharmacotherapy optimisation. The STRIP-intervention consists of 9 steps:
1. Structured history taking of medication (SHIM): Conducted by any trained member of the trial team
2. Recording medication and diagnoses in STRIPA: Conducted by any trained member of the trial team
3. Structured drug review based on the STRIPA with the integrated STOPP/START criteria: Conducted by the research pharmacist and the research physician
4. Communication and discussion of the structured drug review with prescribing physician with possible adaptation of the recommendation: Between the research pharmacist and/or the research physician and the prescribing physician
5. Shared decision-making with the patient with possible adaptation of the recommendation: To be conducted by the prescribing physician, the research physician, or the research pharmacist
6. Optional revision based on new accumulating data during hospitalisation (e.g. new diagnoses, ADRs): Adapted by the research pharmacist and the research physician
7. Generation of medication report for patient*s GP: Conducted by the research pharmacist and the research physician
8. Delivery of the report to the GP (optional additional direct communication): Conducted by any trained member of the trial team
9. Follow-up: Conducted by any trained member of the trial team

Changes in therapy will be implemented according to discussions between the research physician, the research pharmacist, and the prescribing hospital physician. The prescribing hospital physician must determine the ultimate potential net risk and benefit associated with any such management change in the context of the individual patient*s circumstances and it is thus the clinician who exclusively determines the most appropriate course of action for the patient and who remains responsible for it. Changes will only be performed after shared decision-making with the patient. The GP will be provided with the STRIP suggestions including reasons for suggested changes..

Control Intervention (standard / routine / comparator treatment / medical device)

Participants in the control group will receive medication review by the prescribing physicians in accordance with usual care.

Study burden and risks

Changing medication may also lead to disadvantages or risk for patients. Changes in medication will only be recommended after a careful review of all drugs and weighing of all potential benefits and risks according to guidelines about polypharmacy in elderly. Changes will be implemented only if agreed with the patient and the treating physician at the hospital. He or she remains responsible for these changes. Therefore, the risk is equal to that of patients in the usual care group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• People 70 years of age or older
• Multimorbidity: 3 or more coexistent chronic conditions (either defined by 3 distinct ICD-10 codes or based on clinical decision) with an estimated duration of 6 months or more or based on a clinical decision
• Polypharmacy i.e. five or more different regular drugs (defined as authorised medications with registration numbers) for more than 30 days
• If inpatient: Estimated minimal length of stay within the cluster is sufficient to apply the intervention
• If outpatient: Prescribing physician has GP-function and has a planned appointment to conduct intervention

Exclusion criteria

• Inability to provide informed consent or to obtain informed consent from a proxy for patients with cognitive impairment
• Direct admission to palliative care (planned within < 24 hours after index hospital admission or visit at the ambulatory clinic)
• Has passed or is planned to pass a systematic structured drug review other than the study intervention during the index hospitalisation or stay at the ambulatory clinic or within the last two months

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-01-2017
Enrollment:	500

Type:	Actual

Medical products/devices used

Generic name:	Webbased decision support system: Systematic Tool to Reduce Inappropriate Prescribing (STRIP) Assist
Registration:	No

Ethics review

Approved WMO Date:	06-12-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	27-07-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-03-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-03-2019
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28225
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL58279.041.16
Other	Universal Trial Number: U1111-1181-9400. Registratie in Nederlands Trial Register onder nummer: NTR6012
OMON	NL-OMON28225

Study results

Date completed: 16-09-2019

Results posted: 02-08-2021

Actual enrolment: 452

First publication
01-01-1900