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The Effects of a Web Application and Medical Monitoring on the Quality of Medication, Adverse Drug Events and Adherence in the Elderly Living at Home: a Protocol of the Study

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ABSTRACT

Background: In more than half of elderly chronically-ill family clinic attendees, drug prescribing deviates from the internationally acknowledged STOPP/START recommendations. Our study will determine whether it is possible to improve the quality of drug prescriptions in chronically-ill elderly people living at home by regularly monitoring the prescribed drugs according to STOPP/START criteria. **Methods:** The project started in 2014 and will run until 2017. Forty general practitioners (GPs) are participating in a pragmatic randomized controlled trial. From the patient register, GPs randomly selected 20 patients older than 65 years who regularly receive at least one drug and invited them to participate in the study. We will use the START/STOPP criteria to determine the (in)adequacy of drug prescribing in the elderly by a web application (WA). Expected **Results:** The use of the WA will be the basis of the implementation of the final version of the application into the regular family medicine practice, thereby reducing the problems of inappropriate prescribing, correct medication, polypharmacy and adherence; we will identify the stability of the factors of drug prescribing in the elderly. By comparing the test and control groups, it will be possible to distinguish which are related to the WA and which act independently.
Keywords: patient, family medicine, elderly, chronic illness, multi morbidity, depression, drug prescription, polypharmacy, adherence, ADE – adverse drug events.

1. INTRODUCTION

Up to 99% of women and 97% of men over 65 years of age have more than one chronic disease or condition (1); the number of prescriptions per 100 inhabitants increases with age. Of the almost 17 million prescriptions written in Slovenia in 2011, more than 9 million were prescribed to people older than 60 years (with just over 20% of the total population receiving 54% of all the prescriptions issued), and the value of these drugs reached EUR 262.5 million (2). It was found that 20% of people over 70 years of age were being treated with five or more drugs at once. Polypharmacy is associated with adverse drug events (ADE) (drug-drug interactions, adverse drug effects, frequency and length of hospitalizations, re-admissions, and higher mortality), it is by itself a risk factor for ADE and geriatric syndromes which affect the functional status of elderly people (1, 3).

Appropriate prescribing comprises both the scientific and technical rational basis and the general well-being of patients (4). Inappropriate prescribing means the use of a drug for which the risk of ADE outweighs the clinical benefits, and which could result in harmful effects, either through interactions between drugs or through the non-use of a drug with proven efficiency for patients with sufficiently long life expectancy and a good quality of life (5). A major risk factor for the occurrence of inappropriate prescribing is a large number of drugs administered to a patient (6, 7). The explicit criteria for assessing the appropriateness of medication are screening tools based on a review of the literature or a consensus of experts, and they determine, in advance, inappropriate combinations of drugs or contraindications; nevertheless, most individuals fail to take into account the problems arising from the non-use of potentially beneficial drugs (8-10).

The STOPP criteria (STOPP = Screening Tool of Older Persons' potentially inappropriate Prescriptions) (11) were developed in Europe. According to the STOPP criteria, the presence of potentially inappropriate drugs is significantly related to ADE, which can cause or contribute to urgent hospitalization of the elderly and could be avoided (12, 13). More than half of the patients hospitalized due to acute illness do not receive drugs, which would be beneficial according to evidence-based medicine. To address this issue, the START tool was developed to alert physicians to potentially useful drugs (14). Possibly inappropriate prescriptions according to the STOPP and START criteria were identified in 21-36% and 22% respectively of elderly people living at home (15, 16) and between 60% and 80% of patients living at home had at least one prescription from the STOPP list and more than 42% had at least one non-prescribed drug from the START list (17, 18). As with other groups of prescriptions criteria, their limitation was that they had not been produced for multimorbid patients, i.e. most elderly patients (19).

Literature reviews indicate that the STOPP/START criteria are appropriate and indicate an 85% higher risk of ADE; yet there is not enough evidence that the use of these criteria contribute to optimal prescribing; there has been no research to investigate the impact of the use of the STOPP/START criteria on quality of life, and there is no solid evidence related to the impact of the STOPP/START criteria in financial considerations (20).

Prescribing drugs to the elderly is poorly supported by evidence, since they are rarely included in clinical trials, and, in research intended specifically for the elderly, the researchers usually study non-typically healthy subjects instead of the more numerous fragile elderly with several illnesses (21). In many cases, comorbidity is a usual exclusion criterion, and multimorbidity is also poorly researched (22).

2. PROBLEM AND OBJECTIVES

In this study, we were interested in finding out whether it is possible to improve the quality of drug prescriptions in chronically-ill elderly people living at home by regularly monitoring their prescribed drugs according to the internationally accepted STOPP/START criteria. Physicians are aware of the problem of inappropriate prescribing in old age, but they lack the tools to improve their prescribing technique. A systematic overview of the appropriateness of prescribed drugs with a software-web application (WA), developed to identify inappropriate drug prescribing in the elderly according to the START/STOPP criteria, could reduce both the incidence of inappropriate prescribing of drugs and the number of drugs prescribed to an individual.

2.1. Objectives of the study

A randomized controlled longitudinal study was begun in 2014 to find out whether it is possible to improve the quality of drug prescriptions in chronically-ill elderly people living at home, by regularly monitoring the prescribed drugs according to the STOPP/START criteria.

The objectives were set as follows:

1) To design and implement a computerised program (WA) to determine the (in)adequacy of drug prescribing in the elderly according to the START/STOPP criteria.

2) By using the WA in elderly patients in GP practices the quality of drug prescriptions will be determined according to the STOPP/START criteria. We expect the factors that predict the quality of prescribing drugs to elderly people living at home to be related to the patient, the number and type of chronic illnesses, the physician, and the environment in which the treatment is carried out.

3) The WA will be used to determine whether it is possible to improve the quality of prescribing. We expect a change in the quality of prescribing for an individual GP, and in the number of potentially inappropriate prescriptions the patient receives during the first and the second data collections.

4) The WA will be used to reduce the incidence of inappropriate prescribing. It is expected that the number of inappropriate drug prescriptions in the intervention group will be lower after year 1 than in the group with standard care. The same results are expected during the second data collection.

5) The WA will be used to reduce the number of drugs prescribed to an individual. It is expected that the average number of drugs per person in the test group will be equal to or smaller than that of the control group after year 1, and adherence to medication will be better. The same results are expected during the second data collection.

6) To establish a multivariate model explaining the factors influencing the quality of drug prescriptions for the elderly living at home. Multivariate modelling will be performed after all three data collection periods to identify the stability of the factors associated with drug prescriptions.

7) To identify the factors which predict poor adherence to treatment. We expect them to be related to the number of different prescribed drugs, the amount of the daily doses of the drugs, the multimorbidity index, and the number of hospitalizations in the previous year.

Prior to the beginning of the research, a pilot programme was carried out in two outpatient clinics, primarily with the aim of making the use of the WA as simple and intuitive as possible.

The use of the WA may also alter the need of individual elderly patients for medical services, resulting in reduced polypharmacy, improved adherence and a reduced number of visits to the GP.

3. METHODS/DESIGN

Forty general practitioners (GPs) are participating in a pragmatic randomized controlled trial. From the patient register, GPs randomly selected 20 patients older than 65 years who regularly receive at least one drug and invited them to participate in the study. We will use the START/STOPP criteria to determine the (in)adequacy of drug prescribing in the elderly by a web application (WA).

3.1. Participating General Practitioners

Since 2014, 40 GPs from different environments have been participating in the trial. The GP practices were selected from urban, suburban and rural areas to ensure an appropriate socioeconomic and ethnic diversity; however, the GP practices and GPs were selected pragmatically, not systematically. The physicians participated on a voluntary basis, according to their interest in chronic diseases and multimorbidity in the elderly, the problem of prescribing medication for the elderly living at home, and general computer

literacy (because it is important that they do not consider the use of WA as an additional burden and stress factor).

At the beginning of the study, the GPs filled in a questionnaire with basic demographic data on the clinic, and then at the end of each year, with data on the use and functioning of the WA.

3.2. Participating patients

A review of the scientific literature revealed that potentially inappropriate prescribing occurs on average in one fifth to one quarter of the elderly receiving medication for chronic illnesses. To change all the potentially inappropriate regulations, i.e. to add a potentially missing drug or remove a potentially inappropriate one, it was decided that a relatively small sample was sufficient for the research, namely about 500 patients; based on the available data following a review of the scientific research, we expected that at least 20% of the prescriptions in population would be inappropriate.

From each GP's patient register, 20 people older than 65 years who regularly take at least one drug were randomly selected in 2014 and invited to participate in the study. Patients with dementia who were unable to answer the questionnaire, and those with a terminal illness, e.g. advanced cancer or the terminal phase of chronic obstructive pulmonary disease, were excluded, while bed-ridden patients were visited by their physicians at home. We were aiming for a final sample of 800 patients, i.e. for each GP to select 20 patients.

3.3. Procedures and Instruments

Intervention focused on appropriate drug prescribing in the form of a WA which was designed as a tool for reducing the occurrence of adverse drug events (ADE), taking into account (i) multimorbidity, (ii) the number of drugs taken by the patient (polypharmacy), (iii) the current prescriptions in multimorbid elderly patients, (iv) data on the amount and duration of the use of the drugs, and (v) the use, potential inappropriateness or non-use of drugs that have been shown to reduce morbidity and mortality in certain conditions or diseases. The WA allows for constant medication monitoring which can prevent or mitigate between one quarter and one half of all ADEs.

We decided to include the STOPP criteria in the WA because the presence of potentially inappropriate drugs is significantly related to undesired drug-related events which can cause or contribute to avoidable urgent hospitalizations of the elderly. The WA includes data on polypharmacy, the frequency and length of hospitalizations, re-admissions, and higher mortality, and which has itself been shown to be a risk factor for drug-related and geriatric syndromes, which affect the functional status of elderly people. The last set of data considered by the WA is data on adherence, defining the extent to which the patient's behavior coincides with medical advice; data on appropriate and regular taking of drugs was also recorded.

The GPs have access to the WA based on a user name and password. The basic data on the patient and all drugs prescribed to them were entered in the program, which allows the entry of generic or brand names. The strength and dosage of the prescribed drug were also added. At the same time, GPs filled in all the patient's diagnoses; they were also sometimes asked to answer additional questions, based on the data they entered. The WA randomly placed the patient into the trial or control group without displaying the selection to the physician. For the trial group, in the final step, the program displayed potentially inappropriate prescriptions or the lack of prescriptions that could be recommended, together with justification from the START/STOPP criteria.

Other collected data and instruments: at the first and both control checks, i.e. in the 2nd and 3rd year of the study (in 2015, 2016 and 2017), the following data will be collected and assessed: demographic data; multimorbidity (CIRS-G index) (23, 24); depression (Zung Self-Rating Depression Scale) (25); quality of life index (EQ-5D) (26); quality of prescribing – the presence of inappropriate prescribing according to the START/STOPP criteria (at least one criterion from both lists was violated) or the presence of polypharmacy (more than 5 concomitant medications); the number of active ingredients regularly taken by the patient; adherence according to the Morisky 4-item questionnaire (27, 28); non-planned hospitalizations and non-planned/urgent visits to a clinical specialist; number of visits to the emergency room or the emergency physician's home visits in the previous year; number of visits to the GP in the year concerned; number of inappropriate prescriptions according to the START/STOPP criteria; and number of interactions between the prescribed medications marked "major". All these data were first entered into the WA by the physician, together with the diagnoses and drugs (strength and dosage), in 2015.

At the end of the second (2016) and third (2017) years of the study, data will be collected again at a control examination and the number of visits to the family clinic will be added, as well as non-planned hospitalizations and non-planned/urgent visits to a clinical specialist or emergency medical assistance. Comparability of patients in both groups will be checked against gender, the multimorbidity index, health-related quality of life at the time of joining the research, and the number of drugs being taken on joining the research. The factors associated with drug prescribing for the elderly will be identified; by comparing the test and control groups it will be possible to distinguish which are related to the WA and which act independently. The number of inappropriate drug prescriptions in the test group will be compared to the number of inappropriate drug prescriptions in the control group with standard care. The average number of drugs per person will be compared to the average number of drugs per person in the control group.

Adherence to medication will be compared in both groups.

3.4. Data Analysis

Reliability will be estimated using the Cronbach alpha, and descriptive statistics will be used to analyze the main characteristics of the patients; differences between the control and trial groups will be assessed using difference tests for two or more independent samples, i.e. the t-test, the Mann-Whitney U test and the Kruskal-Wallis test. Data normality will be analyzed by the Kolmogorov-Smirnov test. Multivariate modelling will be used to evaluate the associations between the dependent (quality of prescribing, number of drugs prescribed, adherence to medication, number of visits to the GP, quality of life index) and the independent

variables, e.g. demographic data, multimorbidity index (CIRS-G), and self-rated depression. Data analysis will be performed using IBM SPSS Statistics for Windows (version 22.0). The confidence level will be set at $p<0.05$.

4. DISCUSSION

4.1. Expected results

Factors associated with drug prescribing for the elderly will be identified; by comparing the test and control groups it will be possible to distinguish which are related to the WA (in the test group) and which act independently (in the control group). The number of inappropriate drug prescriptions at follow-up (years 2 and 3) should be lower in the test group than in the control group with standard care. The average number of drugs per person in the test group should be equal or smaller, and adherence to medication should be better.

We hope that the use of the WA will effect a change in the quality of prescribing for an individual GP, the number of potentially inappropriate prescriptions the patient receives, and that it will also reduce patients` need for health services (less polypharmacy, improved adherence rate leading to less reliance on health services, and fewer visits to a family clinic). This could also mean significant financial savings. Furthermore, we expect an impact on the quality of life of the elderly living at home and less frequent and severe depressive episodes.

4.2. Relevance to the development of family medicine

Prescribing for the elderly is poorly researched. The planned introduction of more appropriate drug prescribing in the form of a WA in family medicine practice in Slovenia could bring about important changes in the quality of prescribing to GPs in Slovenia (more than 900 physicians) and the number of potentially inappropriate prescriptions received by the elderly, which accounted for a good quarter of population in 2014 (29). The change in prescribing quality should also have significant financial consequences (savings).

The intervention focused on appropriate drug prescribing in the form of a WA, designed, tested and, if necessary, modified in the proposed research, will be used as the basis for the introduction of the final version of the WA in the daily work and practice of a family medicine practitioner, resulting in reduced problems of inappropriate prescribing and correct medication, polypharmacy and adherence. This will be the first such intervention in the region.

The stability of the factors of prescribing drugs to the elderly will be identified. After the completion of the research, we would like to monitor patients for a further year, as this is the only way to gather additional information on other possible outcomes and compare them.

Given that approaches to optimizing prescribing to the elderly should be prepared in consideration for these patients, who usually suffer from several concomitant illnesses, and that the related polypharmacy and treatment goals differ from younger adults, GPs are unable to use the clinical guidelines prepared for a specific chronic disease. Approaches involving the use of geriatric medical services, support of the pharmacist in providing care for a patient, and computer systems supporting decisions can therefore improve the appropriateness of prescribing for the elderly in different environments.

One of the reasons for the poor effects of computer systems on the termination of inappropriate treatment was the physicians' concern that patients would reject the change, or that physicians felt uncomfortable terminating a drug prescribed by another physician. Therefore, when devising the final intervention focused on appropriate drug prescribing in the form of a web application (WA), these reasons will be taken into account, while its introduction will also consider the differences between the patients, prescribing physicians and the environment.

Long-term introduction of the WA, bringing about a change in the quality of prescribing for an individual GP and the number of potentially inappropriate prescriptions the patient receives, could have a significant impact on the quality of life of the elderly, reducing co-morbid depressions in this age group. All of the above will be beneficial for the health system.

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