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Effects of a clinical decision support system and patient portal for preventing medication-related falls in older fallers: Protocol of a cluster randomized controlled trial with embedded process and economic evaluations (AD*F*ICE_IT)

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Abstract

Background

Falls are the leading cause of injury-related mortality and hospitalization among adults aged ≥ 65 years. An important modifiable fall-risk factor is use of fall-risk increasing drugs (FRIDs). However, deprescribing is not always attempted or performed successfully. The AD*F*ICE_IT trial evaluates the combined use of a clinical decision support system (CDSS) and a patient portal for optimizing the deprescribing of FRIDs in older fallers. The intervention aims to optimize and enhance shared decision making (SDM) and consequently prevent injurious falls and reduce healthcare-related costs.

Methods

A multicenter, cluster-randomized controlled trial with process evaluation will be conducted among hospitals in the Netherlands. We aim to include 856 individuals aged ≥ 65 years that visit the falls clinic due to a fall. The intervention comprises the combined use of a CDSS and a patient portal. The CDSS provides guideline-based advice with regard to deprescribing and an individual fall-risk estimation, as calculated by an embedded prediction model. The patient portal provides educational information and a summary of the patient's

Data Availability Statement: Data from the trial will be made available for other researchers after the study is completed for replication purposes and for original research questions. To obtain data, researchers will need to submit an analysis proposal, which will be evaluated by the ADFICE_IT Steering Group. More information regarding the data will be made available on our study website: http://www.onderzoeknaarvallen.nl (website information is also available in English).

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Abbreviations: AD*F*ICE_IT, Alerting on adverse Drug reactions: Falls prevention Improvement through developing a Computerized clinical support system: Effectiveness of Individualized medicaTion withdrawal; CDSS, Clinical decision support system; CI, confidence interval; DCS, Decisional Conflict Scale; EQ-5D-5L, EuroQol-5D-5L; FRID, Fall-Risk Increasing Drug; IMCQ, institute for Medical Technology Assessment Productivity Cost Questionnaire Medical Consumption Questionnaire; IPCQ, institute for Medical Technology Assessment Productivity Cost Questionnaire Productivity Cost Questionnaire; MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; MRC, Medical Research Council; NPIRQ, Netherlands Patient Information Recall Questionnaire; PrepDM, Preparation for Decision-making scale; QALY, quality-adjusted life years QPL: Question Prompt List; RCT, Randomized Controlled Trial; SDM, Shared Decision Making; TAM, Technology Acceptance Model; TOPICS-SF, The Older Persons and Informal Caregivers Survey–Short Form; UI, User Interface; WSS, Website Satisfaction Scale.

consultation. Hospitals in the control arm will provide care-as-usual. Fall-calendars will be used for measuring the time to first injurious fall (primary outcome) and secondary fall outcomes during one year. Other measurements will be conducted at baseline, 3, 6, and 12 months and include quality of life, cost-effectiveness, feasibility, and shared decision-making measures. Data will be analyzed according to the intention-to-treat principle. Difference in time to injurious fall between the intervention and control group will be analyzed using multilevel Cox regression.

Discussion

The findings of this study will add valuable insights about how digital health informatics tools that target physicians and older adults can optimize deprescribing and support SDM. We expect the CDSS and patient portal to aid in deprescribing of FRIDs, resulting in a reduction in falls and related injuries.

Trial registration

ClinicalTrials.gov NCT05449470 (7-7-2022).

Background

Falling among adults aged 65 years and older represents a serious public health problem. Approximately 30% of adults aged 65 or older falls each year. Moreover, falls are the leading cause of injury-related mortality and hospitalization, with one out of five falls resulting in severe injury [1]. In the Western European region, 8.4 million adults aged 70 and older sought medical attention due to a fall-related injury, and 54 504 older adults died due to falls in 2017 alone [2]. The incidence rate of fall-related injuries increases substantially with age [2].

Besides physical injuries such as head wounds and fractures [3, 4], falls can also lead to the development of fear of falling [5, 6], reduced perceived quality of life [7], reduced physical activity [8], physical decline [9], social isolation [10], increased healthcare utilization, and institutionalization [9, 11, 12]. Furthermore, falls pose a substantial economic burden as fall-related costs are estimated to amount to 0.85 to 1.5 percent of the total healthcare expenditures in Western countries [13].

Falls have a complex etiology and are associated with several risk factors, such as history of falls [14], impaired mobility [14], frailty [15], chronic health conditions [16], fear of falling [17], depression [18], cognitive impairment [19], increasing age [18], and female gender [18]. In addition, a large body of research has linked the use of certain medications to falls [20–22]. Medications recognized as fall-risk increasing drugs (FRIDs) include antipsychotics, antidepressants, diuretics, and opioids [23]. Studies have reported that 65 to 93 percent of older adults admitted with fall-related injuries use at least one FRID [24]. Antidepressants were the most commonly used FRID at the time of the fall-related injury, with a prevalence between 15 and 40 percent [24].

Despite the growing evidence on medication as an important modifiable risk factor, deprescribing in older adults is often not attempted or performed unsuccessfully. Physicians generally find deprescribing challenging since it requires complex decision-making in the context of polypharmacy and multi-morbidity [25]. To be precise, physicians find it difficult to identify which patients are at risk of a medication-related fall and it is not always clear which

medications should be considered for withdrawal and whether safer alternatives are available. Moreover, patients' beliefs regarding their medication use may further hinder effective FRIDs deprescribing. Research indicates patients are generally not concerned about possible adverse effects from their regular medication and not aware of medication management as an effective fall-prevention strategy [26, 27]. More effective communication may help raise awareness and consequently prompt patients to adopt to and comply with deprescribing as a treatment option. Moreover, communication is a two-way process and research suggests that interventions targeting both physicians and patients may be more effective than interventions that only target either one [28]. Given these multifaceted complications, a multicomponent intervention is expected to improve FRIDs deprescribing in older adults and thereby help prevent medication-related falls.

There is growing attention for the role of SDM in deprescribing [29–31]. SDM can be defined as an approach where clinicians and patients share the best available evidence when making decisions. In doing so, patients are supported to consider options and to achieve informed preferences [32]. In complex patient cases with multiple treatment options, as is often the case in deprescribing in older adults, SDM has been found to lead to more informed decision-making, better participation in decision-making, more self-efficacy, increased knowledge, and reduced decisional conflict of patients in disadvantaged groups, such as older patients [33–35]. Therefore, it is expected that enhanced SDM would support the FRIDs deprescribing process as well as improve patient compliance and adherence to the new treatment plan. This, in turn, may lead to a decrease in medication-related falls among older adults.

Clinical decision support systems (CDSS) may help physicians in the deprescribing process of FRIDs and may stimulate SDM. A CDSS is a computerized system that aims to support clinical-decision making by generating assessments or recommendations based on the characteristics of an individual patient. CDSSs generate patient-specific output based on an existing knowledge base or based on predictive modelling methods. CDSSs are increasingly used for improving adherence to clinical guidelines as well as for preventing prescription errors and checking for drug interactions [36]. Use of CDSSs in the prevention of falls has been studied in in- and outpatient settings [37–40]. However, these studies were all limited in scope as they focused on a select number of FRIDs, did not use utilize predictive modelling methods for generating patient-specific output, or did not address risk communication or shared decision-making (SDM) [37–40].

A tool that could stimulate patients to participate in SDM is a patient portal, which allows patients to access their clinical data through a secure website [41]. A recent systematic literature review on the impact of patient portals on health outcomes found that patient portals can enhance preventive behaviors and adherence to therapy [42]. Furthermore, a qualitative study revealed that patients thought that a portal would facilitate them in seeking medical advice in between visits (e.g., on medication side effects) and that this would stimulate patient-driven communication [43].

Given this backdrop, the AD*F*ICE_IT project (Alerting on adverse Drug reactions: Falls prevention Improvement through developing a Computerized clinical support system: Effectiveness of Individualized medicaTion withdrawal) was initiated to develop and evaluate a multicomponent intervention for optimizing FRIDs deprescribing and consequently improve patient outcomes. The intervention comprises the combined use of a CDSS and a patient portal. The CDSS includes a personalized fall risk prediction, which is used to estimate and visualizes a patient's fall risk. Furthermore, the CDSS gives insight in which of the patient's medications can contribute to this fall-risk, provides suggestions with safer medication alternatives, provides guideline-based medication advice, and provides an overview of the possible treatment actions. The patient portal provides general fall-related educational information

(e.g. information about falls prevention, FRIDs, and FRIDs deprescribing) and information to help patients prepare for their visit to the falls clinic. After the falls clinic visit, the patient portal will show a summary of the patient's treatment plan as discussed during the consultation. These features of the CDSS and patient portal may help to optimize and enhance (shared) decision making during the consultation. Consequently, it is expected that this will lead to less injurious falls among older adults and reduce healthcare-related costs.

The primary aim of the AD*F*ICE_IT cluster randomized controlled trial is to assess the effectiveness of the multicomponent intervention, comprised of a CDSS and patient portal, compared with usual care. Effectiveness will be assessed in terms of time to first injurious fall (primary outcome). In addition, as secondary aims we will study the cost-effectiveness and feasibility of the intervention.

Methods

The SPIRIT criteria were used as guideline for the reporting of this protocol paper [44] (S1 File). The *CONSORT 2010 Statement*: *extension to cluster randomised controlled trials* will be used to further guide the reporting of the results of the trial [45].

The design and the development of the AD*F*ICE_IT intervention was guided by the Medical Research Council (MRC) Framework for Complex Interventions [46]. In the preparation phase of the MRC framework, we developed a prediction model for estimating a patient's risk of falling [47]. The prediction model is currently being externally validated. In the development phase, we identified evidence and theory regarding CDSS and patient portal end users' preferences and needs, and extended these with empirical research (i.e. survey [48]), interviews) to inform our decisions regarding the design of the intervention. Furthermore, we incorporated guideline- and expert consensus-based medication advices (e.g. deprescribing advice or use of safer alternative medication) in the CDSS [23]. In the feasibility/piloting phase of the MRC framework, we tested the usability of the user interface of our intervention through usability studies. The present paper describes the protocol for the final phase of the project in which we will evaluate the effectiveness of the intervention.

Study design and settings

To evaluate the effectiveness of our multicomponent (CDSS and patient portal) intervention in preventing injurious falls among older adults, a multicenter cluster-randomized controlled trial will be conducted among new falls clinic patients of ten Dutch hospitals. These patients have been referred for a multifactorial falls assessment to the geriatrics departments by their general practitioner, the emergency department, or other specialists because of a history of falling or an increased risk of falling.

Ethical considerations

The ADFICE_IT study protocol was reviewed and approved by the Medical Ethics review board of the Amsterdam University Medical Centres (METC AMC 2021_061). All study participants will asked to sign an informed consent prior to data collection. The trial is registered with ClinicalTrials.gov (DATE; 7-7-2022, identifier: NCT05449470).

Eligibility criteria

The study population consists of older adults visiting a falls clinic. Falls clinics typically perform detailed multidisciplinary fall risk assessments and make recommendations or implement a range of targeted falls and falls injury-prevention strategies based on the assessment

findings [49]. Falls clinics at Dutch hospitals that use Epic software (Epic Systems Corporation; Verona, Wisconsin, United States) as their electronic patient record system were eligible to be included as a study center. Patients meeting the following criteria are eligible for inclusion:

- Aged 65 years and older;
- History of at least one fall in the past year;
- A Mini-Mental State Examination (MMSE) score of 21 points or higher or equivalently a Montreal Cognitive Assessment (MOCA) Dutch score of 16 points or higher [50];
- Use of at least one FRID (as defined by the Dutch Federation of Medical Specialists [51]);
- Sufficient command of the Dutch language in speech and writing; and
- Willingness to sign informed consent.

Potential subjects will be excluded if they:

- Already participate in another (intervention) study;
- Have a life expectancy of less than one year; or
- Suffer from severe mobility impairment (i.e. bedridden, e.g. inability to walk short distances with assistance of a walking aid).

Participant recruitment has started in July 2022 and is ongoing.

Randomization and blinding

Since the intervention needs to be integrated into the physician's workflow, randomization will be performed at hospital level prior to the start of inclusion. We evaluated use of the CDSS in usability studies among physicians of one of the locations of the Amsterdam UMC, i.e. location AMC. To avoid possible contamination of the intervention, the Amsterdam UMC: location AMC will be exempted from randomization and included in the intervention group by default. To assure the control and intervention hospitals remain similar with respect to their patient population, the other location of Amsterdam UMC, i.e. location VUmc, will be included in the control group by default. Randomization of the remaining hospitals will be done based on a 1:1 allocation ratio and stratified based on whether the hospital is academic or non-academic. The randomization procedure will be done by an independent statistician using computer-generated random numbers. Blinding of the intervention allocation is not possible since both physicians and patients will have to interact with the CDSS and patient portal. Researchers will be blinded to group allocation during the statistical analyses.

Intervention

The multicomponent intervention comprises the combined use of a CDSS and a patient portal. Furthermore, patients in the intervention arm will receive a Question Prompt List (QPL) prior to their consultation. Physicians in the intervention arm will be trained to work with the CDSS. The control hospitals will only receive a general overview of the study, including the procedures. Patients in the control arm will receive care-as-usual.

CDSS. Relevant FRIDs were identified based on the Dutch fall guideline [51] and STOPP-Fall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk) tool [23]. These two sources form the foundation for the CDSS' clinical knowledge base. For each class of identified FRIDs, relevant recommendations about deprescribing from more than 30

different Dutch clinical guidelines have been extracted and formalized using the Logical Elements Rule Method [52]. Thus, the CDSS provides point-of-care guideline and expert consensus based medication withdrawal advice [23] as well as a personalized fall-risk estimation based on a prediction model [47].

The CDSS will be integrated in the electronic patient record system and workflow of physicians. On the CDSS start page, the physician can check the data that was pulled from the electronic patient record system, and see the patient's estimated risk of falling. On the next screen, the physician can see the advice of the CDSS for each of the patient's prescribed current medications. Based on the given advice, the physician can decide to propose a change in treatment for a specific medication. The physician can discuss those proposed treatment changes with the patient using the consultation screen. The final screen will allow the physician to copy-paste all treatment decisions to the patient's electronic health record, print a patient-friendly summary of the individual treatment plan, and send it to the patient portal.

Patient portal. Patients in the intervention arm will receive access to the patient portal prior to their visit to the falls clinic. At that time, the patient portal provides general fall-related educational information (e.g. information about falls prevention, FRIDs, and FRIDs deprescribing) and information to help patients prepare for the falls clinic visit. After their consultation with the physician during their fall clinic visit, the patients will also receive access to the additional patient portal pages with the personalized fall-risk estimate and the treatment plan as discussed with the physician.

Question Prompt List (QPL). Patients in the intervention arm will receive a printed QPL prior to their visit to the falls clinic. A QPL is a structured list of questions designed to encourage information gathering, which patients can use as example questions to ask during the consultation [53]. A QPL stimulates agenda setting and helps patients to remember important questions. In other contexts (e.g. oncology), QPLs have been found to improve communication and stimulate participation in older patients [53]. Our QPL will consist of preparatory questions and concerns that need to be completed by the patient preceding the consultation (e.g. 'Which of the medications that I am currently taking are truly crucial for my health?'). Patients will be asked to bring it with them to consultation.

Training. Physicians will be trained in small groups (i.e., the geriatric staff of a specific intervention hospital) on how to use the system during a one-hour training session. The training addresses four components: 1) general overview of the study and its aim, 2) (issues in) FRIDs deprescribing, 3) employing SDM and the QPL during a consultation, and 4) practical instructions on how to use the CDSS. AD*F*ICE_IT project team members (i.e., an experienced geriatrician and two communication scholars) will provide the training. Afterwards, an online version of the training will be available to the physicians.

Comparator

Patients treated at the control hospitals will receive care-as-usual, e.g. a multifactorial fall assessment at a falls clinic. Usually such an assessment takes up around 3–4 hours, distributed over 1 or 2 days, and is concluded by a consultation between the patient and the physician.

Procedures

Patients who schedule an appointment at any of the participating falls clinics (i.e., intervention and control hospitals) will receive a letter containing information on the objectives and procedures of the study and an invitation to participate. For patients in the intervention arm, the invitation letter will also include a printed QPL and a link to the patient portal.

At the falls clinic, eligibility will be determined according to the in- and exclusion criteria by the hospitals' staff members. The researcher will then provide oral and written information about the study to eligible patients. Patients who are interested in participating in the study will be asked to sign an informed consent form. Next, the falls clinic assessments will be carried out as usual. In the intervention group, the physician will use the CDSS prior to the consultation to understand a patient's fall risk and medical background as well as during the consultation with the patient. Consultations in the control group are carried out according to care as usual. After the consultation, the research assistants will ask the included patients and their caregivers (if applicable) to fill out a set of questionnaires (see "Data Collection"). After the visit to the falls clinic, patients in the intervention group will be able to review information about their consultation with the physician (i.e., their treatment plan) and their estimated fall risk in the patient portal.

Data collection

We will collect a wide range of quantitative and qualitative data to assess the effectiveness and cost-effectiveness and to evaluate the implementation of the intervention (see Fig 1 for complete overview of measurements). Questionnaires will be administered at baseline and 3, 6, and 12 months after baseline (Fig 1).

Estimating the effectiveness of the intervention on trial outcomes

The primary outcome is time to first injurious fall. An injurious fall is defined as a fall resulting in wounds, bruises, sprains, cuts, medically recorded fractures, head or internal injury, requiring medical/health professional examination, accident and emergency treatment, or inpatient treatment [54]. This definition is consistent with moderate and serious injuries, as proposed by Schwenk (2012). Secondary outcomes include number of injurious falls, total number of falls, time to first fall resulting in any injuries (i.e., fall that results in minor, moderate, or severe injuries), total number of falls resulting in any injuries, time to first fall and (health-related) quality of life. Falls are defined as an unexpected event in which the participants come to rest on the ground, floor, or lower level [55]. At baseline, patients in both groups receive a falls calendar to keep track of falls, fall-related injuries, and fall-related healthcare use on a weekly basis for 12 months. The falls calendars will be returned every month by mail. Incomplete, missing or unclear data will be further inquired by telephone. Health-related) quality of life is assessed using the EuroQol-5D-5L (EQ-5D-5L) index value, EQ-5D visual analogue scale and the Older Persons and Informal Caregivers Survey Short Form (TOPICS-SF) summary score [56, 57]. EQ-5D-5L is a standardized instrument for measuring health-related quality of life [58]. The health states based on the five EQ-5D-5L domains will be converted to utility scores using the Dutch EQ-5D-5L tariff [56]. The TOPICS-SF is a 22-item questionnaire for measuring health-related quality of life, which was developed to evaluate patient-reported outcomes in the context of multidimensional geriatric care [57].

Estimating the cost-effectiveness of the intervention

Societal costs related to the intervention and care as usual will be assessed using the institute for Medical Technology Assessment Medical Consumption Questionnaire (iMCQ) [59] and the institute for Medical Technology Assessment Productivity Cost Questionnaire (iPCQ; Fig 1) [60]. The iMCQ is a non-disease specific questionnaire for measuring health care use [59]. The iPCQ is a questionnaire for measuring productivity losses of paid work due to absenteeism, presenteeism and productivity losses related to unpaid work [60]. Costs will be calculated

	STUDY PERIOD				
	Before and during enrolment	Post-enrolment			Close-out
TIMEPOINT	$-t_1$	T_0 (baseline)	t_1 (3 months)	t_2 (6 months)	t_3 (12 months)
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Cluster allocation	X				
INTERVENTIONS:					
Training sessions for physicians in intervention hospitals	X				
Use of CDSS and patient portal		X			
ASSESSMENTS:					
Questionnaires					
EuroQol-5D-5L (EQ-5D-5L)		X	X	X	X
Institute for Medical Technology Assessment Medical Consumption Questionnaire (iMCQ)		X	X	X	X
Institute for Medical Technology Assessment Productivity Cost Questionnaire (IPCQ)		X	X	X	X
The Older Persons and Informal Caregivers Survey Short Form (TOPICS-SF)		X			X
iSHARE patient		X			
iSHARE physician		◆—	—	—	—◆
Preparation for Decision-making scale (PrepDM)		X			
Netherlands Patient Information Recall Questionnaire (NPIRQ)			X		
Decisional Conflict Scale (DCS)		X			
Technology Acceptance Model (TAM)		X			
Website Satisfaction Scale questionnaire (WSS)			X		
Physicians' Satisfaction with the CDSS		◆—	—	—	—◆
Other assessments					
Attendance training physicians	X				
Patient portal logs		◆—	—	—	—◆
CDSS logs		◆—	—	—	—◆
Videotaped consultations		◆—	—	—	—◆
Falls calendar		◆—	—	—	—◆
Pharmacy records		X			X

CDSS, clinical decision support system.

Fig 1. Schedule of study procedures and assessments.

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by multiplying the volumes of healthcare use with the corresponding unit prices. Lost productivity costs will be calculated using the friction cost approach.

Process evaluation

The process evaluation will consist of two parts: a) assessing the feasibility of the intervention and b) evaluating how the intervention facilitates SDM.

Process evaluation: Feasibility

To assess the feasibility of the intervention, we will collect the following: 1) data logged by the CDSS and patient portal, 2) participation data of the CDSS training, 3) physician satisfaction regarding the CDSS, 4) the Technology Acceptance Model (TAM; [61]) questionnaire; 5) the Website Satisfaction Scale questionnaire (WSS [62]), 6) videotaped consultations, 7) pharmacy records, and 8) falls calendar entries.

Usage data of the CDSS and patient portal will be measured throughout the study period. The extent to which the intervention was implemented as intended (fidelity/dose delivered) and the extent to which the participants actively engage with the intervention (dose received/exposure) will be assessed through data logged by the CDSS and patient portal, and the videotaped consultations. Dose received/exposure will also be assessed through participation data of the CDSS training. Reach/participation rate will be assessed through data logged by the CDSS to analyze the extent to which physicians propose changes in FRID prescriptions. Patients will be asked to self-report changes in medication use on the fall calendar on a weekly basis. These falls calendar entries and pharmacy records will be used to analyze the extent to which patients adhere to the physicians' advice and changes in the treatment plan. Satisfaction with the intervention (dose received/exposure) will be measured through physician evaluations of the CDSS and the WSS questionnaire (patients). The TAM questionnaire assesses the perceived usefulness, perceived ease of use, and intended usage of the CDSS, and the WSS measures the comprehensibility, satisfaction and Emotional Support of the patient portal [62]. Finally, barriers and facilitators (context) will be assessed through the videotaped consultations, and physician evaluations of the CDSS by means of a survey.

Process evaluation: Shared decision making

SDM will be measured through self-reported questionnaires in the full sample (i.e. perceived SDM; the iSHAREpatient and iSHAREphysician [63]. In addition, we aim to measure observed SDM in a subsample (n = 50) through videos of consultations (i.e. the Observer OPTION^{MCC} Multiple Chronic Conditions coding scheme [64]). SDM will be assessed in relation to two affective-cognitive outcomes: preparation for decision-making through the Preparation for Decision-making scale (PrepDM; [65]) and decisional conflict through the Decisional Conflict Scale (DCS; low literacy version; [66]). The 'Question Format DCS– 10 item 3 response categories' version of the DCS is recommended to be used for low literacy groups [67]. In addition, recall of information will be assessed in the subsample through the Netherlands Patient Information Recall Questionnaire (NPIRQ; [68]). The iSHARE questionnaire will be used to measure perceived SDM from both the patient and physician perspective. The NPIRQ consists of multiple-choice questions, completion items, and open-ended questions related to information about treatment and recommendations on how to handle side effects [68]. Patient responses on the questionnaire will be checked against the actual communication in video recordings of the consultations. In addition, the PrepDM will be used to assess how patients evaluate the usefulness of the patient portal and QPL for preparing themselves for communicating with their physician during the consultation. Finally, we will code

observed shared (triadic) decision-making between the physician, the patient, and if relevant, the informal caregiver, in the videotaped consultations by using the Observer OPTION^{MCC} Multiple Chronic Conditions coding scheme [64].

SDM will be assessed using questionnaires in the full sample and video observations in a subsample. The subsample of 50 consultations in both intervention and control group will be video recorded to assess the level of SDM. After working with the CDSS for a couple of months, intervention-group physicians will be asked to fill out an online questionnaire about their satisfaction with the CDSS, to indicate whether they thought the advice provided by the CDSS was (sufficiently) accurate, if they perceived any barriers in using the CDSS system, and if they thought the patient perceived barriers in using the patient portal. Pharmacy records will be used to make an inventory of the prescribed medicines for individual patients at baseline and 12 months after baseline to assess adherence.

Data management

Data will be handled confidentially and only a limited number of members of the study team will have access to the complete datasets. The collected and pseudonymized questionnaire data for each local center will be transferred to the Amsterdam UMC, where it will be entered, stored and processed in Castor. In addition, the digital CDSS and patient portal data will be stored locally at each hospital. Every 3–6 months, study data will be extracted to.csv text files and stored in a secured folder. Furthermore, administrative data will be stored in a secured SQL database. Finally, data from both control and intervention patients will be extracted from Epic every 3–6 months to.csv text files (e.g. medication data, problem lists, relevant lab values, and the prediction model variables). Data from individual patients will be pseudonymized, and the different datasets can only be linked through a participant identification number, which is stored in a separate data system. These data management systems all comply in accordance with the European Union General Data Protection Regulation.

Statistical analysis

Data of the RCT will be analyzed according to the intention-to-treat principle. P-values of < 0.05 will be considered statistically significant.

Estimating the effectiveness of the intervention on trial outcomes

For every participant, we will assess fall incidents during a fixed follow-up period of 12 months, which will start after a set 1 month, during which the dose of FRIDs will be stopped or decreased. Difference in time to injurious fall between the intervention and control group in the follow-up period will be analyzed by means of a multilevel Cox regression model based on hospital level [69]. Model fit will be assessed using standard approaches (e.g., the proportional hazards assumption with Schoenfeld residuals). We will adjust all models for age, sex and type of hospital, i.e. academic versus non-academic. In a sensitivity analysis, we will additionally adjust for significant baseline differences. Difference in total number of (injurious) falls in the follow-up period between the control and intervention groups will be analyzed by means of multilevel Poisson regression models based on hospital level. In the case of overdispersion, we will apply either quasi-Poisson regression or negative binomial regression depending on the observed distribution of the data. Difference between the intervention and control group with respect to time to any fall and time to fall that results in any injuries will be analyzed by means of survival analyses, similarly to the primary outcome.

Differences in EQ-5D-5L index score, EQ-5D visual analogue scale, and TOPICS-SF summary score between the intervention and control group after 12 months will be analyzed by

means of linear mixed models. These models will be adjusted for the baseline value of the outcome [70].

Estimating the cost-effectiveness of the intervention

Differences in costs and effects between intervention and usual care will be estimated using seemingly unrelated regression to retain the correlation between costs and effects. Incremental cost-effectiveness ratios will be calculated by dividing the difference in costs between CDSS and usual care due to differences in incidence in injurious falls as well as gained quality-adjusted life years (QALYs). Bootstrapping techniques will be used to estimate the uncertainty surrounding the incremental cost-effectiveness ratios. Uncertainty will be shown in cost-effectiveness planes and cost-effectiveness acceptability curves.

Process evaluation: Feasibility

In the first part of the process evaluation we will evaluate the feasibility of the intervention, and describe 1) user data, 2) participation in and evaluation of the training, 3) physician and patient satisfaction and acceptance of the CDSS and patient portal. These descriptive statistics will be presented as percentages or means with standard deviations.

Process evaluation: Shared decision making

Differences in mean change between arms will be analyzed with the use of multi-level modelling and will be expressed as mean differences with 95% CIs. We will analyze differences in perceived SDM and observed SDM for both patients and physicians in the intervention and control groups. Finally, we will assess the differences between the intervention and control groups on recall (NPIRQ), adherence (pharmacy records), and quality of life (EQ-5D-5L).

Per protocol analysis

Logged data by the CDSS and patient portal will be used to select participants for a per protocol analysis for the primary outcome. In this analysis, we will only include patients from the experimental group that meet the following two criteria 1) physicians used the CDSS in the consult with the patients and 2) physician used the 'print' button in the CDSS or the patient visited the patient portal at least once after the consultation.

Sample size

Sample sizes of $n = 385$ in the intervention and $n = 385$ in the control group (10 clusters with 77 patients in each cluster) are needed to detect a difference in proportion of injurious falls of 0.10 with 80% power. We inferred the proportion of patients who will experience an injurious fall to be 0.22 in the control and 0.12 in the intervention group. In these calculations, we assumed the two-sided significance level of 5% and an intraclass correlation coefficient of 0.01 to account for clustering [71]. Presupposing a drop-out rate of 10%, 856 patients will need to be included.

Monitoring

A data monitoring committee will not be established since the overall risk associated with the trial is considered negligible.

Harms

All adverse events and serious adverse events reported by the subject or observed by the researchers or his staff will be recorded in an electronic database. Serious adverse events will also be reported to the medical ethics committee of the Amsterdam UMC.

Discussion

The multicenter RCT described in this paper will assess: a) the effectiveness of the multicomponent intervention (i.e., use of CDSS and patient portal) compared with usual care. Effectiveness will be assessed in terms of time to first injurious fall (primary outcome). As secondary aims, cost-effectiveness and the feasibility of the intervention will be assessed.

The deprescribing of FRIDs requires complex decision making. We expect that the implementation of our CDSS and patient portal, supported by a prediction model and guideline-based advice, will aid in optimizing deprescribing decisions for both the physician and patient, consequently reducing fall risk. In line with the expectation that the intervention will aid in the prevention of injurious falls, it is hypothesized that the intervention will be more cost-effective compared to care-as-usual regarding fall-related health care costs. The direct healthcare and follow-up care resulting from injurious falls among older adults potentially involve 0.85 to 1.5 percent of the total healthcare expenditures in Western countries [13].

The process evaluation will evaluate a) the implementation of the intervention and b) how this intervention leads to enhanced SDM and patient outcomes. A systematic review has suggested that SDM can lead to better affective-cognitive outcomes, e.g. improved satisfaction and less decisional conflict [72]. Thus, we hypothesize that physicians and geriatric patients as well as their caregivers will evaluate the intervention workflow more positively compared to the care-as-usual workflow and will engage in more SDM regarding the patient's treatment plan. Recent studies have illustrated that compliance to FRID-deprescribing is often poor. In a study by Boyé et al. [73], researchers found that compliance to their intervention of FRIDs-withdrawal was limited among patients. The researchers found that 35 percent of all deprescribing attempts were unsuccessful, either due to non-compliance, recurrence of the initial indication for prescribing, or additional medication being described for newly diagnosed conditions. Moreover, the STRIDE trial, a multicenter randomized controlled trial by Bhasin et al. [74] evaluated a multifactorial intervention that included the use of motivational interviewing to encourage patients to choose recommendations they were willing to address. Among the patients for which medication use was identified as a risk factor, only 29 percent of patients agreed to address this risk. We expect that a higher degree of SDM will lead to more recall and knowledge among patients, leading to more treatment and medication adherence among patients. This in turn, could also lead to less medication-related injurious falls among patients.

An important strength of our study is that we developed the intervention following the MRC guidelines. The aim of the framework is to ensure that feasible interventions are empirically and theoretically founded and that considerations are given both to the effectiveness of the intervention and how it works. The intervention's end-users are included in each phase of the project. This way, we will be able to optimally personalize the intervention's design to the heterogeneous needs of the end-users.

Another asset of our study is that it includes both an effect evaluation and a process evaluation. This will help us to not only assess whether the intervention was effective, but the process evaluation will also make it possible to assess whether the intervention was implemented correctly, and which implementation factors were facilitating or impeding. Gaining more insight into the context will deepen our understanding of why the intervention was (not) successful.

The findings of this study will add valuable insights about how digital health informatics tools, based on prediction models, can support SDM between physicians and older adults. This new knowledge will be especially insightful in the case of FRIDs withdrawal among older adults. Furthermore, this study will also contribute to the literature on risk communication, since it investigates how physicians will use a visualized fall-risk estimate in their consultations with the patient.

Outlook

If the AD*F*ICE_IT intervention will prove to be effective, it could be implemented in routine healthcare practices. The hospitals in the intervention group can continue using the CDSS and patient portal as they have done during the RCT, as the intervention will already be implemented in their electronic patient record systems. The hospitals in the control group could also implement the CDSS and patient portal software at the end of the study. Furthermore, the software will be available as open source to facilitate national and international implementation. We expect that once implemented at the falls clinic of the geriatric departments, the AD*F*ICE_IT intervention will contribute to individualized and cost-effective prevention of (medication-related) injurious falls among older adults.

Supporting information

S1 Checklist. *PLOS ONE* clinical studies checklist.
(DOCX)

S1 File. Filled-out SPIRIT checklist.
(DOC)

S2 File. Items from the world health organization trial registration data set.
(DOCX)

Acknowledgments

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References

1. Bergen G, Stevens MR, Burns ER. Falls and Fall Injuries Among Adults Aged ≥65 Years—United States, 2014. MMWR Morb Mortal Wkly Rep [Internet]. 2016; 65:993–8. Available from: http://dx.doi.org/10.15585/mmwr.mm6537a2
2. Haagsma JA, Olij BF, Majdan M, van Beeck EF, Vos T, Castle CD, et al. Falls in older aged adults in 22 European countries: incidence, mortality and burden of disease from 1990 to 2017. Inj Prev [Internet]. 2020; 26:i67–74. Available from: https://injuryprevention.bmj.com/lookup/doi/10.1136/injuryprev-2019-043347 PMID: 32111726
3. Alexander BH, Rivara FP, Wolf ME. The cost and frequency of hospitalization for fall-related injuries in older adults. Am J Public Health [Internet]. 1992; 82:1020–3. Available from: https://pubmed.ncbi.nlm.nih.gov/1609903 https://doi.org/10.2105/ajph.82.7.1020 PMID: 1609903
4. Centers for Disease Control and Prevention. Home and Recreational Safety Important Facts about Falls [Internet]. 2017 [cited 2020 Apr 15]. p. 10–2. Available from: https://www.cdc.gov/homeandrecreationalsafety/falls/adultfalls.html
5. Jung D. Fear of Falling in Older Adults: Comprehensive Review. Asian Nurs Res (Korean Soc Nurs Sci) [Internet]. 2008; 2:214–22. Available from: https://www.sciencedirect.com/science/article/pii/S1976131709600037 https://doi.org/10.1016/S1976-1317(09)60003-7 PMID: 25029959
6. Peeters G, Bennett M, Donoghue OA, Kennelly S, Kenny RA. Understanding the aetiology of fear of falling from the perspective of a fear-avoidance model–A narrative review. Clin Psychol Rev [Internet]. 2020; 79:101862. Available from: https://doi.org/10.1016/j.cpr.2020.101862 PMID: 32442854
7. Hartholt KA, Van Beeck EF, Polinder S, Van Der Velde N, Van Lieshout EMM, Panneman MJM, et al. Societal consequences of falls in the older population: Injuries, healthcare costs, and long-term reduced quality of life. J Trauma—Inj Infect Crit Care. 2011; 71:748–53. https://doi.org/10.1097/TA.0b013e3181f6f5e5 PMID: 21045738
8. Jefferis BJ, Iliffe S, Kendrick D, Kerse N, Trost S, Lennon LT, et al. How are falls and fear of falling associated with objectively measured physical activity in a cohort of community-dwelling older men? BMC Geriatr [Internet]. 2014; 14:114. Available from: https://doi.org/10.1186/1471-2318-14-114 PMID: 25348492
9. Tinetti ME, Williams CS. The Effect of Falls and Fall Injuries on Functioning in Community-Dwelling Older Persons. Journals Gerontol Ser A Biol Sci Med Sci [Internet]. 1998; 53A:M112–9. Available from: https://academic.oup.com/biomedgerontology/article-lookup/doi/ https://doi.org/10.1093/gerona/53a.2.m112 PMID: 9520917
10. Petersen N, König H-H, Hajek A. The link between falls, social isolation and loneliness: A systematic review. Arch Gerontol Geriatr [Internet]. 2020; 88:104020. Available from: https://www.sciencedirect.com/science/article/pii/S0167494320300145 https://doi.org/10.1016/j.archger.2020.104020 PMID: 32018091
11. Stel VS, Smit JH, Pluijm SMF, Lips P. Consequences of falling in older men and women and risk factors for health service use and functional decline. Age Ageing [Internet]. 2004; 33:58–65. Available from: https://academic.oup.com/ageing/article-lookup/doi/10.1093/ageing/afh028 PMID: 14695865
12. Tinetti ME, Williams CS. Falls, Injuries Due to Falls, and the Risk of Admission to a Nursing Home. N Engl J Med [Internet]. 1997; 337:1279–84. Available from: http://www.nejm.org/doi/abs/10.1056/NEJM199710303371806 PMID: 9345078
13. Heinrich S, Rapp K, Rissmann U, Becker C, König H-H. Cost of falls in old age: a systematic review. Osteoporos Int [Internet]. 2010; 21:891–902. Available from: http://link.springer.com/10.1007/s00198-009-1100-1 PMID: 19924496
14. Deandrea S, Lucenteforte E, Bravi F, Foschi R, La Vecchia C, Negri E. Risk Factors for Falls in Community-dwelling Older People. Epidemiology [Internet]. 2010; 21:658–68. Available from: https://journals.lww.com/00001648-201009000-00020

15. Cheng M-H, Chang S-F. Frailty as a Risk Factor for Falls Among Community Dwelling People: Evidence From a Meta-Analysis. J Nurs Scholarsh [Internet]. 2017; 49:529–36. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jnu.12322 PMID: 28755453

16. Paliwal Y, Slattum PW, Ratliff SM. Chronic Health Conditions as a Risk Factor for Falls among the Community-Dwelling US Older Adults: A Zero-Inflated Regression Modeling Approach. Biomed Res Int [Internet]. 2017; 2017:1–9. Available from: https://www.hindawi.com/journals/bmri/2017/5146378/ https://doi.org/10.1155/2017/5146378 PMID: 28459060

17. Hadjistavropoulos T, Delbaere K, Fitzgerald TD. Reconceptualizing the Role of Fear of Falling and Balance Confidence in Fall Risk. J Aging Health [Internet]. 2011; 23:3–23. Available from: http://journals.sagepub.com/doi/10.1177/0898264310378039 PMID: 20852012

18. Ambrose AF, Paul G, Hausdorff JM. Risk factors for falls among older adults: A review of the literature. Maturitas [Internet]. 2013; 75:51–61. Available from: https://doi.org/10.1016/j.maturitas.2013.02.009 PMID: 23523272

19. Muir SW, Gopaul K, Montero Odasso MM. The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis. Age Ageing [Internet]. 2012; 41:299–308. Available from: https://academic.oup.com/ageing/article-lookup/doi/10.1093/ageing/afs012 PMID: 22374645

20. de Vries M, Seppala LJ, Daams JG, van de Glind EMM, Masud T, van der Velde N, et al. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-Analysis: I. Cardiovascular Drugs. J Am Med Dir Assoc [Internet]. 2018; 19:371.e1–371.e9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1525861017306989 https://doi.org/10.1016/j.jamda.2017.12.013 PMID: 29396189

21. Seppala LJ, Wermelink AMAT, de Vries M, Ploegmakers KJ, van de Glind EMM, Daams JG, et al. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-Analysis: II. Psychotropics. J Am Med Dir Assoc [Internet]. 2018; 19:371.e11–371.e17. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1525861017307843 https://doi.org/10.1016/j.jamda.2017.12.098 PMID: 29402652

22. Seppala LJ, van de Glind EMM, Daams JG, Ploegmakers KJ, de Vries M, Wermelink AMAT, et al. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-analysis: III. Others. J Am Med Dir Assoc. 2018; 19:372.e1–372.e8. https://doi.org/10.1016/j.jamda.2017.12.099 PMID: 29402646

23. Seppala LJ, Petrovic M, Ryg J, Bahat G, Topinkova E, Szczerbińska K, et al. STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Age Ageing [Internet]. 2021; 50:1189–99. Available from: https://academic.oup.com/ageing/article/50/4/1189/6043386 https://doi.org/10.1093/ageing/afaa249 PMID: 33349863

24. Hart LA, Phelan EA, Yi JY, Marcum ZA, Gray SL. Use of Fall Risk–Increasing Drugs Around a Fall-Related Injury in Older Adults: A Systematic Review. J Am Geriatr Soc [Internet]. 2020; 68:1334–43. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jgs.16369 PMID: 32064594

25. Tinetti ME, Gordon C, Sogolow E, Lapin P, Bradley EH. Fall-Risk Evaluation and Management: Challenges in Adopting Geriatric Care Practices. Gerontologist [Internet]. 2006; 46:717–25. Available from: https://academic.oup.com/gerontologist/article-lookup/doi/10.1093/geront/46.6.717 PMID: 17169927

26. Bagge M, Tordoff J, Norris P, Heydon S. Older people's attitudes towards their regular medicines. J Prim Health Care [Internet]. 2013; 5:234. Available from: http://www.publish.csiro.au/?paper=HC13234 PMID: 23998174

27. Laing SS, Silver IF, York S, Phelan EA. Fall Prevention Knowledge, Attitude, and Practices of Community Stakeholders and Older Adults. J Aging Res [Internet]. 2011; 2011:1–9. Available from: http://www.hindawi.com/journals/jar/2011/395357/ https://doi.org/10.4061/2011/395357 PMID: 21915377

28. Légaré F, Ratté S, Stacey D, Kryworuchko J, Gravel K, Graham ID, et al. Interventions for improving the adoption of shared decision making by healthcare professionals. In: Légaré F, editor. Cochrane Database Syst Rev [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2010. Available from: https://doi.org//10.1002/14651858.CD006732.pub2

29. Jansen J, Naganathan V, Carter SM, McLachlan AJ, Nickel B, Irwig L, et al. Too much medicine in older people? Deprescribing through shared decision making. BMJ [Internet]. 2016; 353:i2893. Available from: https://www.bmj.com/lookup/doi/ https://doi.org/10.1136/bmj.i2893 PMID: 27260319

30. Weir K, Nickel B, Naganathan V, Bonner C, McCaffery K, Carter SM, et al. Decision-Making Preferences and Deprescribing: Perspectives of Older Adults and Companions About Their Medicines. Journals Gerontol Ser B [Internet]. 2018; 73:e98–107. Available from: https://academic.oup.com/psychsocgerontology/article/73/7/e98/4668532

31. Thompson W, Reeve E, Moriarty F, Maclure M, Turner J, Steinman MA, et al. Deprescribing: Future directions for research. Res Soc Adm Pharm [Internet]. 2019; 15:801–5. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1551741118307757 https://doi.org/10.1016/j.sapharm.2018.08.013 PMID: 30241876

32. Elwyn G, Laitner S, Coulter A, Walker E, Watson P, Thomson R. Implementing shared decision making in the NHS. BMJ [Internet]. 2010; 341:c5146–c5146. Available from: http://www.bmj.com/content/341/bmj.c5146.abstract https://doi.org/10.1136/bmj.c5146 PMID: 20947577

33. Simmons M, Hetrick S, Jorm A. Shared Decision-Making: Benefits, Barriers and Current Opportunities for Application. Australas Psychiatry [Internet]. 2010; 18:394–7. Available from: http://journals.sagepub.com/doi/ https://doi.org/10.3109/10398562.2010.499944 PMID: 20863175

34. O'Connor AM, Rostom A, Fiset V, Tetroe J, Entwistle V, Llewellyn-Thomas H, et al. Decision aids for patients facing health treatment or screening decisions: systematic review. BMJ [Internet]. 1999; 319:731–4. Available from: https://pubmed.ncbi.nlm.nih.gov/10487995

35. Durand M-A, Carpenter L, Dolan H, Bravo P, Mann M, Bunn F, et al. Do Interventions Designed to Support Shared Decision-Making Reduce Health Inequalities? A Systematic Review and Meta-Analysis. Malaga G, editor. PLoS One [Internet]. 2014; 9:e94670. Available from: https://doi.org/10.1371/journal.pone.0094670 PMID: 24736389

36. Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digit Med [Internet]. 2020; 3:17. Available from: https://doi.org/10.1038/s41746-020-0221-y PMID: 32047862

37. Tamblyn R, Eguale T, Buckeridge DL, Huang A, Hanley J, Reidel K, et al. The effectiveness of a new generation of computerized drug alerts in reducing the risk of injury from drug side effects: a cluster randomized trial. J Am Med Informatics Assoc [Internet]. 2012; 19:635–43. Available from: https://academic.oup.com/jamia/article-lookup/doi/10.1136/amiajnl-2011-000609 PMID: 22246963

38. Kouladjian O'Donnell L, Gnjidic D, Sawan M, Reeve E, Kelly PJ, Chen TF, et al. Impact of the Goal-directed Medication Review Electronic Decision Support System on Drug Burden Index: A cluster-randomised clinical trial in primary care. Br J Clin Pharmacol [Internet]. 2021; 87:1499–511. Available from: https://onlinelibrary.wiley.com/doi/10.1111/bcp.14557 PMID: 32960464

39. Rieckert A, Reeves D, Altiner A, Drewelow E, Esmail A, Flamm M, et al. Use of an electronic decision support tool to reduce polypharmacy in elderly people with chronic diseases: cluster randomised controlled trial. BMJ [Internet]. 2020; 369:m1822. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.m1822 PMID: 32554566

40. Damoiseaux-Volman BA, van der Velde N, Ruige SG, Romijn JA, Abu-Hanna A, Medlock S. Effect of Interventions With a Clinical Decision Support System for Hospitalized Older Patients: Systematic Review Mapping Implementation and Design Factors. JMIR Med Informatics [Internet]. 2021; 9:e28023. Available from: https://medinform.jmir.org/2021/7/e28023 https://doi.org/10.2196/28023 PMID: 34269682

41. Turner AM, Osterhage K, Hartzler A, Joe J, Lin L, Kanagat N, et al. Use of Patient Portals for Personal Health Information Management: The Older Adult Perspective. AMIA. Annu Symp proceedings AMIA Symp [Internet]. 2015; 2015:1234–41. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26958263

42. Carini E, Villani L, Pezzullo AM, Gentili A, Barbara A, Ricciardi W, et al. The Impact of Digital Patient Portals on Health Outcomes, System Efficiency, and Patient Attitudes: Updated Systematic Literature Review. J Med Internet Res [Internet]. 2021; 23:e26189. Available from: https://www.jmir.org/2021/9/e26189 https://doi.org/10.2196/26189 PMID: 34494966

43. Tieu L, Sarkar U, Schillinger D, Ralston JD, Ratanawongsa N, Pasick R, et al. Barriers and Facilitators to Online Portal Use Among Patients and Caregivers in a Safety Net Health Care System: A Qualitative Study. J Med Internet Res [Internet]. 2015; 17:e275. Available from: http://www.jmir.org/2015/12/e275/ https://doi.org/10.2196/jmir.4847 PMID: 26681155

44. Chan A-W, Tetzlaff JM, Gotzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ [Internet]. 2013; 346:e7586–e7586. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.e7586 PMID: 23303884

45. Campbell MK, Piaggio G, Elbourne DR, Altman DG. Consort 2010 statement: extension to cluster randomised trials. BMJ [Internet]. 2012; 345:e5661–e5661. Available from: https://www.bmj.com/lookup/doi/10.1136/bmj.e5661 PMID: 22951546

46. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ [Internet]. 2008; 337:a1655. Available from: https://doi.org/10.1136/bmj.a1655 PMID: 18824488

47. van de Loo B, Seppala LJ, van der Velde N, Medlock S, Denkinger M, de Groot LC, et al. Development of the ADF ICE_IT Models for Predicting Falls and Recurrent Falls in Community-Dwelling Older Adults: Pooled Analyses of European Cohorts With Special Attention to Medication. Lipsitz LA, editor. Journals Gerontol Ser A [Internet]. 2022; 77:1446–54. Available from: https://academic.oup.com/biomedgerontology/advance-article/doi/10.1093/gerona/glac080/6563350

48. Ploegmakers KJ, Medlock S, Linn AJ, Lin Y, Seppälä LJ, Petrovic M, et al. Barriers and facilitators in using a Clinical Decision Support System for fall risk management for older people: a European survey.

Eur Geriatr Med [Internet]. 2022; 13:395–405. Available from: https://doi.org/10.1007/s41999-021-00599-w PMID: 35032323

49. Hill KD, Moore KJ, Dorevitch MI, Day LM. Effectiveness of Falls Clinics: An Evaluation of Outcomes and Client Adherence to Recommended Interventions. J Am Geriatr Soc [Internet]. 2008; 56:600–8. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2007.01626.x PMID: 18266663

50. Trzepacz PT, Hochstetler H, Wang S, Walker B, Saykin AJ. Relationship between the Montreal Cognitive Assessment and Mini-mental State Examination for assessment of mild cognitive impairment in older adults. BMC Geriatr [Internet]. 2015; 15:107. Available from: https://doi.org/10.1186/s12877-015-0103-3 PMID: 26346644

51. Federation of Medical Specialists. Effect of medication on fall risk in older adults [In Dutch: Effect medicijnen op valrisico ouderen] [Internet]. 2017 [cited 2022 Jul 6]. Available from: https://richtlijnendatabase.nl/richtlijn/preventie_van_valincidenten_bij_ouderen/effect_medicijnen_op_valrisico_ouderen.html

52. Medlock S, Opondo D, Eslami S, Askari M, Wierenga P, de Rooij SE, et al. LERM (Logical Elements Rule Method): A method for assessing and formalizing clinical rules for decision support. Int J Med Inform [Internet]. 2011; 80:286–95. Available from: https://doi.org/10.1016/j.ijmedinf.2011.01.014 PMID: 21333589

53. Brandes K, Linn AJ, Butow PN, van Weert JCM. The characteristics and effectiveness of Question Prompt List interventions in oncology: a systematic review of the literature. Psychooncology [Internet]. 2015; 24:245–52. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/pon.3637 PMID: 25082386

54. Schwenk M, Lauenroth A, Stock C, Moreno RR, Oster P, McHugh G, et al. Definitions and methods of measuring and reporting on injurious falls in randomised controlled fall prevention trials: a systematic review. BMC Med Res Methodol [Internet]. 2012; 12:50. Available from: http://www.biomedcentral.com/1471-2288/12/50 https://doi.org/10.1186/1471-2288-12-50 PMID: 22510239

55. Lamb SE, JÃ¸rstad-Stein EC, Hauer K, Becker C. Development of a Common Outcome Data Set for Fall Injury Prevention Trials: The Prevention of Falls Network Europe Consensus. J Am Geriatr Soc [Internet]. 2005; 53:1618–22. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2005.53455.x PMID: 16137297

56. Versteegh M M., Vermeulen K M., Evers S M. A. A., de Wit GA, Prenger R, A. Stolk E. Dutch Tariff for the Five-Level Version of EQ-5D. Value Heal [Internet]. 2016; 19:343–52. Available from: http://dx.doi.org/10.1016/j.jval.2016.01.003

57. Santoso AMM, Lutomski JE, Hofman CS, Metzelthin SF, Blom JW, van der Wees PJ, et al. Development of a Patient-Reported Outcome Measure for Geriatric Care: The Older Persons and Informal Caregivers Survey Short Form. Value Heal [Internet]. 2018; 21:1198–204. Available from: https://doi.org/10.1016/j.jval.2018.02.011 PMID: 30314621

58. Group TE. EuroQol—a new facility for the measurement of health-related quality of life. Health Policy (New York) [Internet]. 1990; 16:199–208. Available from: https://linkinghub.elsevier.com/retrieve/pii/0168851090904219 https://doi.org/10.1016/0168-8510(90)90421-9 PMID: 10109801

59. Bouwmans C, Hakkaart-van Roijen L, Koopmanschap M, Krol M, Severens H BW. Manual iMTA medical cost ques- tionnaire (iMCQ) [in Dutch: Handleiding iMTA medical cost ques- tionnaire (iMCQ)]. 2013.

60. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Hakkaart-van Roijen L. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses. Value Health [Internet]. 2015; 18:753–8. Available from: https://doi.org/10.1016/j.jval.2015.05.009 PMID: 26409601

61. Davis FD. Technology Acceptance Model: TAM. Al-Suqri, MN, Al-Aufi, AS Inf Seek Behav Technol Adopt S. 1989;205–19.

62. Bol N, van Weert JCM, de Haes HCJM, Loos EF, de Heer S, Sikkel D, et al. Using Cognitive and Affective Illustrations to Enhance Older Adults' Website Satisfaction and Recall of Online Cancer-Related Information. Health Commun [Internet]. 2014; 29:678–88. Available from: http://www.tandfonline.com/doi/abs/10.1080/10410236.2013.771560 PMID: 24160560

63. Bomhof-Roordink H, Stiggelbout AM, Gärtner FR, Portielje JEA, de Kroon CD, Peeters KCMJ, et al. Patient and physician shared decision-making behaviors in oncology: Evidence on adequate measurement properties of the iSHARE questionnaires. Patient Educ Couns [Internet]. 2022; 105:1089–100. Available from: https://doi.org/10.1016/j.pec.2021.08.034 PMID: 34556384

64. Pel-Littel RE, Buurman BM, van de Pol MH, Yilmaz NG, Tulner LR, Minkman MM, et al. Measuring triadic decision making in older patients with multiple chronic conditions: Observer OPTIONMCC. Patient Educ Couns [Internet]. 2019; 102:1969–76. Available from: https://www.sciencedirect.com/science/article/pii/S0738399119302538 https://doi.org/10.1016/j.pec.2019.06.020 PMID: 31279614

65. Bennett C, Graham ID, Kristjansson E, Kearing SA, Clay KF, O'Connor AM. Validation of a Preparation for Decision Making scale. Patient Educ Couns [Internet]. 2010; 78:130–3. Available from: https://www.sciencedirect.com/science/article/pii/S0738399109002328 https://doi.org/10.1016/j.pec.2009.05.012 PMID: 19560303

66. O'Connor AM. Validation of a Decisional Conflict Scale. Med Decis Mak [Internet]. 1995; 15:25–30. Available from: http://journals.sagepub.com/doi/10.1177/0272989X9501500105 PMID: 7898294

67. O'Connor AM. User Manual–Decisional Conflict Scale. Https://DecisionaidOhriCa/Eval_DcsHtml. 1993;1–16.

68. Jansen J, van Weert J, van der Meulen N, van Dulmen S, Heeren T, Bensing J. Recall in Older Cancer Patients: Measuring Memory for Medical Information. Gerontologist [Internet]. 2008; 48:149–57. Available from: https://doi.org/10.1093/geront/48.2.149 PMID: 18483427

69. Austin PC. A Tutorial on Multilevel Survival Analysis: Methods, Models and Applications. Int Stat Rev [Internet]. 2017; 85:185–203. Available from: https://onlinelibrary.wiley.com/doi/10.1111/insr.12214 PMID: 29307954

70. Twisk J, Bosman L, Hoekstra T, Rijnhart J, Welten M, Heymans M. Different ways to estimate treatment effects in randomised controlled trials. Contemp Clin Trials Commun [Internet]. 2018; 10:80–5. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2451865417301849 https://doi.org/10.1016/j.conctc.2018.03.008 PMID: 29696162

71. Adams G, Gulliford MC, Ukoumunne OC, Eldridge S, Chinn S, Campbell MJ. Patterns of intra-cluster correlation from primary care research to inform study design and analysis. J Clin Epidemiol [Internet]. 2004; 57:785–94. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0895435604000459 https://doi.org/10.1016/j.jclinepi.2003.12.013 PMID: 15485730

72. Shay LA, Lafata JE. Where Is the Evidence? A Systematic Review of Shared Decision Making and Patient Outcomes. Med Decis Mak [Internet]. 2015; 35:114–31. Available from: http://journals.sagepub.com/doi/10.1177/0272989X14551638 PMID: 25351843

73. Boyé N. Effectiveness of medication withdrawal in older fallers: results from the Improving Medication Prescribing to reduce Risk Of FALLs (IMPROveFALL) trial. 2016;142–6.

74. Bhasin S, Gill TM, Reuben DB, Latham NK, Ganz DA, Greene EJ, et al. A Randomized Trial of a Multifactorial Strategy to Prevent Serious Fall Injuries. N Engl J Med [Internet]. 2020; 383:129–40. Available from: http://www.nejm.org/doi/10.1056/NEJMoa2002183 PMID: 32640131