

Selecting the right patient for medication reviews

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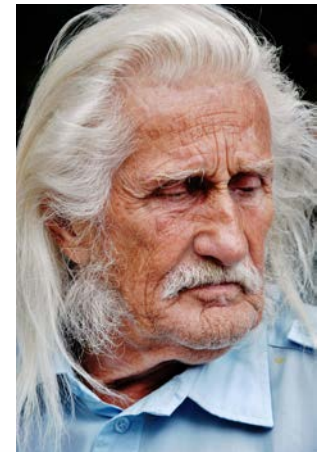


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Who is in need of medication review: can you make an educated guess?



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Health insurers criteria

- Polymedication check in Switzerland
 - **≥4 prescribed drugs** taken over **≥3 months**, if patient agrees
- Medication Therapy Management in USA
 - **Multiple chronic conditions** and **multiple chronic drugs** prescribed and **medication costs** that exceed a certain level
- Medicines Use Review in UK
 - Regular users of pharmacy with **high risk medicines** or recently discharged with **medication changes** or **respiratory disease or cardiovascular disease** and **≥4 chronic drugs**
- Advanced Medication Reviews in the Netherlands
 - **≥65 year old** and **≥5 chronic drugs** prescribed (and 1 risk factor: low eGFR, low cognition, low adherence, high fall risk, unplanned hospitalisation, nursing home)



What can you expect

- Medication reviews and drug related problems
- Overview of possible criteria for selecting patients
- Tools developed for selecting patients in need
- Prediction models for identifying patients in need

What is a medication review?

- Medication review is a **structured evaluation of a patient's medicines** with the aim of **optimising medicines use** and **improving health outcomes**
 - including patient-reported outcomes
- This entails detecting of **drug related problems (DRP)** and **recommending / conducting interventions**
 - DRP: event or circumstance involving drug therapy that **actually or potentially** interferes with desired outcomes

Different Medication Reviews

1. Simple MR: based on medication history pharmacy

- drug interactions, unusual dosages/choices, duplicates, some adherence issues

2A. Intermediate MR: based on medication history and patient information

- drug interactions, unusual dosages, issues, drug-food interactions, effectiveness issues, side effects, problems with OTC, adherence issues, concerns, medication burden

3. Advanced MR: based on medication history, patient information and clinical information

- all above plus: indication without a drug, drugs without indication, dosage/duration issues, suboptimal/inappropriate choices, contra-indications => **patient's needs and wants**

Adapted from **PCNE statement on medication review 2013**

Why do we need to select patients?



- Large numbers of (elderly) patients with polypharmacy
- Not all need, want or benefit from medication review
- Different reviews
- Limited resources



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Simple MR: select on medication history?

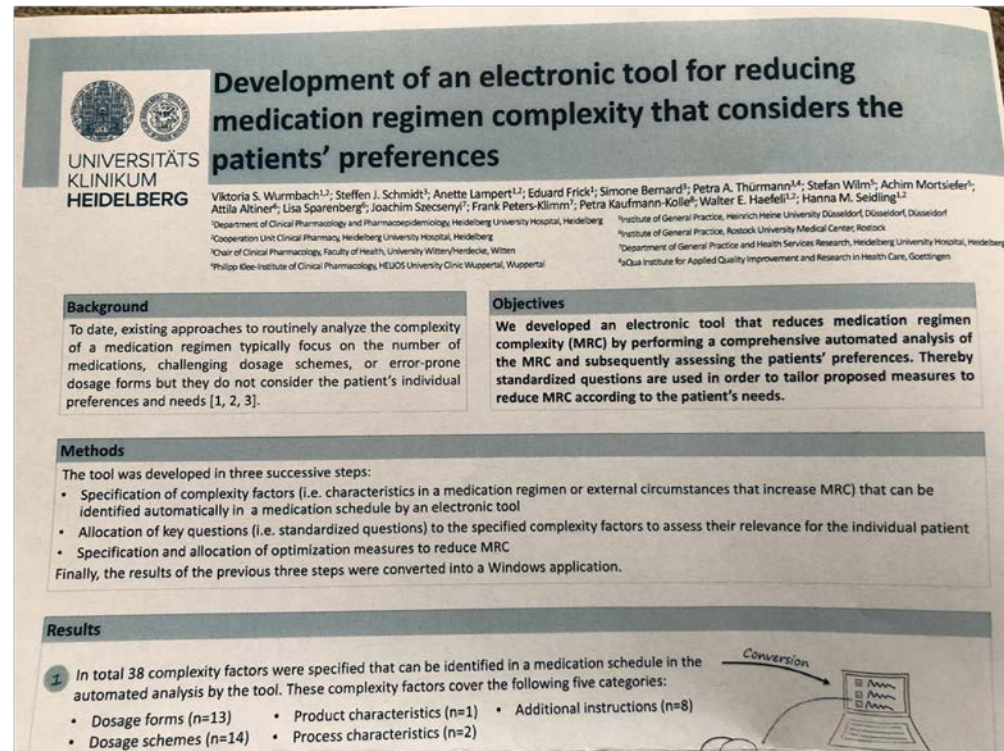
- **Polypharmacy, number of drugs**
- **High risk medication (ADR, hospitalisation, TDM)**
- **PIM/PIP lists:** Beers, EU-7; potentially inappropriate medications for elderly
- **Drug Burden Index (DBI):** cumulative exposure to anticholinergic/ sedative drugs
- **Medication regimen complexity**
- **STOPP/START criteria:** limited without clinical information

Selection on DBI

- Medication review in ≥ 65 years, ≥ 5 chronic drugs including 1 psycholeptic/analeptic and DBI of ≥ 1
- Advanced reviews did **not** reduce DBI
- Prevalent use may be difficult to change
- High risk medication may be really needed
- Really inappropriate medication use may be low
- Many patients with low DBI may also need review
- Pilot to use **potential rise in DBI (start of new 'DBI' drug)** as trigger to intervene / prevent

Selection 'bias' -> specific intervention

- Medication regimen complexity algorithm
- Key questions for patients
- Optimization actions allocated to each complexity factor



Criteria for selecting patients for medication reviews

- Medication characteristics

High risk?

High need or
want?

- P
 - age, literacy, adherence, beliefs, concerns, medication taking issues, (lack of) support, communication issues

- C
 - Actual risk vs potential risk
 - Medication error vs suboptimal treatment
 - Treatment complexity vs patient-perceived burden

DRPs detected by medication reviews

DRP categories	n	%
Overtreatment	2915	25.5
Undertreatment	1814	15.9
Drug not effective	975	8.5
Contra-indication	971	8.5
Side effect	923	8.1
Difficulty using dosage form	756	6.6
Interaction	664	5.8
Non adherence	645	5.6
Dose too low	622	5.4
Dose too high	568	5.0
Inappropriate dosage form	96	0.8
Miscellaneous problem ^a	470	4.1
Total DRPs	11,419	100

^a Besides drug-related problems, the category 'miscellaneous problem' also contained non-drug-related problems, for example, lifestyle advice given such as smoking cessation



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Chau SH e.a. Int J Clin Pharm 2016

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Proposed interventions by pharmacists

	Number	Percentage (%)	Implemented (%)	Other intervention (%)	No intervention (%)
Stop drug	2238	19.6	46.6	21.4	32.0
Provide monitoring	2099	18.4	52.8	23.1	24.1
Adjust dose	1684	14.7	43.3	25.1	31.6
Add drug	1601	14.0	36.3	27.4	36.3
Switch drug	1307	11.5	38.5	26.0	35.5
Provide education	1225	10.7	67.9	12.3	19.8
Synchronise medication	304	2.7	82.6	12.5	4.9
Switch dose form	176	1.5	60.2	24.4	15.4
Other	766	6.7	15.5	21.5	63.0
Total	11,419	100.0	46.2 ^a	22.4 ^a	31.3 ^a

^a These percentages were calculated based on the known outcomes (11,400) as a proportion of the total interventions (11,419). 0.2 % of the interventions (n = 19) was not attributed to a specific category



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Tools for selecting patients: proposed by pharmacists/experts



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Identifying patients in need or at risk

1. ≥ 5 drugs
 2. ≥ 12 doses per day
 3. regimen changed ≥ 4 times in past year
 4. ≥ 3 concurrent disease states
 5. drugs requiring therapeutic drug monitoring
 6. history of non-adherence
- Associated with drug-related adverse outcomes
 - Adds to healthcare provider 'subjective' selection
 - Patient survey: patients can reliably answer questions
 - Applied to electronic pharmacy / medical records



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Koecheler JA e.a. Am J Hosp Pharm 1989
Langford BJ e.a. Pharmacotherapy 2006
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Isaksen SF e.a. Ann Pharmacother 1999
Makowsky MJ e.a. JMCP 2017



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Extended Medication Risk Questionnaires

1. ≥ 5 drugs
2. ≥ 12 doses per day
3. regimen changed ≥ 4 times in past year
4. ≥ 3 medical conditions
5. history of non-adherence
6. drugs requiring therapeutic drug monitoring
- 7. ≥ 1 target condition (9 were defined)**
- 8. > 1 prescribing physician**
- 9. > 1 pharmacy / location for collecting drugs**
- 10. not collecting drugs themselves**
- 11. not knowing reason for taking particular drug
/ unanswered questions / worried about drugs**



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Barenholtz Levy H e.a. Ann Pharmacother 2003
Makowsky MJ e.a. JMCP 2017



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Medication Risk Assessment Questionnaire (MRAQ): detecting high risk patients *

Criteria	Percentage of Charts Meeting Criteria				Specificity	
	Electronic Medical Record		Self-Administered			
5-item MRAQ	EMR-based risk fairly predicted ER visit/hospitalisation, with high sensitivities but low specificities					
≥ 3 medical conditions						23.9
≥ 1 target condition						33.3
≥ 5 medications						51.0
≥ 11 pills per day						77.2
≥ 5 medication changes	10-item self-administered MRAQ fairly detected low medication adherence, with low sensitivity but high specificity					
Overall MRAQ ≥ 3 criteria met						70.2
Overall MRAQ ≥ 3 criteria met						49.0
Additional SA-MRAQ						
≥ 1 physician prescribing	140	-	66 (47.1)	-	-	
≥ 1 location	140	-	29 (20.7)	-	-	
≥ difficult to take medications	140	-	5 (3.6)	-	-	
Unanswered questions ≥ occasionally	140	-	29 (20.7)	-	-	
Worried about medications ≥ occasionally	141	-	61 (43.3)	-	-	
Overall 10-item SA-MRAQ ≥ 6 criteria met	102	-	18 (17.6)	31.5	97.9	
Sensitivity analysis						
Overall classic ≥ 3 criteria met		46/105 (43.8)	19/105 (18.1)	84.2	65.1	

EMR = emergency medical record; MRAQ = medical record medication risk assessment questionnaire; SA = self-administered.

* 5-item self-administered as gold standard

Risk factors for DRPs: literature review

BMJ Open Determination of risk factors for drug-related problems: a multidisciplinary triangulation process

Carole P Kaufmann,^{1,2} Dominik Stämpfli,¹ Kurt E Hersberger,¹ Markus L Lampert^{1,2}

To cite: Kaufmann CP, Stämpfli D, Hersberger KE, *et al.* Determination of risk factors for drug-related problems: a multidisciplinary triangulation process. *BMJ Open* 2015;5:e006376. doi:10.1136/bmjopen-2014-006376

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2014-006376>).

Received 13 August 2014
Revised 28 January 2015
Accepted 29 January 2015

ABSTRACT

Introduction and objectives: Drug-related problems (DRPs) constitute a frequent safety issue among hospitalised patients leading to patient harm and increased healthcare costs. Because many DRPs are preventable, the specific risk factors that facilitate their occurrence are of considerable interest. The objective of our study was to assess risk factors for the occurrence of DRPs with the intention to identify patients at risk for DRPs to guide and target preventive measures where they are needed most in patients.

Design: Triangulation process using a mixed methods approach.

Methods: We conducted an expert panel, using the nominal group technique (NGT) and a qualitative analysis, to gather risk factors for DRPs. The expert panel consisted of two consultant hospital physicians (internal medicine and geriatrics), one emergency physician, one independent general practitioner, one

Strengths and limitations of this study

- This research project followed a comprehensive triangulation method to gather risk factors for drug-related problems (DRPs), integrating expert opinion and literature data, which represents—to the best of our knowledge, a new approach in this topic.
- Participating experts represented a wide variety of settings of patient care and steps in the medication process. This allowed a broad view on the topic of DRPs.
- Inviting actively practising healthcare professionals as experts ensures the practical relevance of gathered risk factors.
- The restricted number of participants in the nominal group technique may have limited the diversity of risk factors.

healthcare costs. The term DRP embraces



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Risk factors for drug related problems

- Literature review & expert panel
 - excluding risk factors mentioned in only 1 publication, with low-ranking in expert panel, related to care system
 - eliminating synonyms/duplicates
- 42 risk factors
 - **Patient characteristics:** cognition, medication-related understanding/education, non-adherence, impaired manual skills, impaired vision, age, living alone, need for caregiver, language issues
 - **Medical issues:** morbidity (cardiac, respiratory, diabetes, dementia, renal impairment, hepatic impairment), motion issues/fall risk, recent hospitalisation, experience of ADR
 - **Medication:** polypharmacy, 21 specific drugs/ drug groups/ drug combi's, difficult to handle medication

27 risk factors with high ratings

Table 2 Final ranking list of the 27 risk factors contributing to the occurrence of DRPs rated by the expert panel as 'important' (Likert scale: 4) or 'rather important' (Likert scale: 3)

Risk factor	Delphi		NGT Ranking list	Qualitative analysis	Literature
	Median	IQR			
Dementia, cognitive situation, low IQ, confused patient	4	4.00–4.00	Yes		10, 17, 18, 19, 20
Polypharmacy (number of drugs >5)	4	4.00–4.00	Yes	Yes	10, 17, 18, 21, 22, 5
Antiepileptics	4	4.00–4.00		Yes	23, 24, 20, 25
Anticoagulants	4	4.00–4.00		Yes	10, 21, 23, 26, 5
Combinations of NSAID and oral anticoagulants	4	4.00–4.00		Yes	20
Insulin	4	4.00–4.00	Yes		10, 23, 24
Missing information, half-knowledge of the patient, the patient does not understand the goal of the therapy	4	4.00–3.25	Yes		11
Medication with a narrow therapeutic window	4	4.00–3.25	Yes	Yes	5
Non-adherence	4	4.00–3.00	Yes		10
Polymorbidity	3.5	4.00–3.00	Yes	Yes	10, 22
Digoxin	3	4.00–3.00			24, 20, 27
Renal impairment (eGFR <30 mL/min)	3	4.00–3.00	Yes		10, 22, 20
NSAIDs	3	4.00–3.00		Yes	5, 10, 21, 23, 24, 25
Experience of ADR	3	3.75–3.00	Yes	Yes	22
Medication that is difficult to handle	3	3.75–3.00	Yes		
Language issues (ie, non-native speakers)	3	3.00–3.00	Yes	Yes	
Diuretics	3	3.00–3.00		Yes	5, 10, 19, 23, 24, 26, 25
Tricyclic antidepressants	3	3.00–3.00			21, 20
Hepatic impairment	3	3.00–3.00	Yes		22, 20
Self-medication with non-prescribed medicines	3	3.00–3.00	Yes	Yes	
Impaired manual skills (causing handling difficulties)	3	3.00–3.00	Yes		
Visual impairment	3	3.00–3.00	Yes	Yes	17
Anticholinergic drugs	3	3.00–3.00			28
Benzodiazepines	3	3.00–3.00			21, 20, 28, 25, 29
Opiates/opioids	3	3.00–3.00			10, 23, 26, 20, 25
Corticosteroids	3	3.00–2.00			10, 23, 24
Oral antidiabetics	3	3.00–2.00			10, 23, 24

Kaufmann CP e.a. BMJ Open 2015

Drug Associated Risk Tool (DART)

Questionnaire for patients

General information
What is your preferred language of communication? _____
What is your current age? _____

My state of health
Yes No
<input type="checkbox"/> <input type="checkbox"/> I have a restricted kidney function/kidney dysfunction/kidney disease
<input type="checkbox"/> <input type="checkbox"/> I have a liver disease/liver dysfunction
<input type="checkbox"/> <input type="checkbox"/> I have a heart weakness/heart performance weakness
<input type="checkbox"/> <input type="checkbox"/> I have a chronic respiratory disease
<input type="checkbox"/> <input type="checkbox"/> I have diabetes
<input type="checkbox"/> <input type="checkbox"/> I have trouble remembering things or tend to be forgetful

If you do not take any medication, the questionnaire is finished for you.

My medicine
Yes No
<input type="checkbox"/> <input type="checkbox"/> I regularly take medicine, which I bought myself without (including vitamin supplements)
<input type="checkbox"/> <input type="checkbox"/> I take more than 5 drugs every day, which are prescribe
I use the following drugs at home (before my hospital stay):
Yes No
<input type="checkbox"/> <input type="checkbox"/> Sleeping pills
<input type="checkbox"/> <input type="checkbox"/> Cortison
<input type="checkbox"/> <input type="checkbox"/> Medicine against epilepsy
<input type="checkbox"/> <input type="checkbox"/> Marcoumar, Xarelto, Sintrom or Pradaxa
<input type="checkbox"/> <input type="checkbox"/> Surmontil (Trimipramin), Saroten (Tryptizol, Limbitrol)
<input type="checkbox"/> <input type="checkbox"/> Medicine against rheumatism / inflammation
<input type="checkbox"/> <input type="checkbox"/> Medicine for drainage (Diuretics)
<input type="checkbox"/> <input type="checkbox"/> Digoxin
<input type="checkbox"/> <input type="checkbox"/> Detrusitol
<input type="checkbox"/> <input type="checkbox"/> Insulin / Medicine against diabetes

Yes No
<input type="checkbox"/> <input type="checkbox"/> Do you sometimes forget to take your medicine?

Yes	Partially	No
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I feel well informed about my medicine.		
Strongly disagree	Disagree	Agree
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Strongly agree		
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Application of medicine
I am having trouble with the application of my medicine
Yes No
<input type="checkbox"/> <input type="checkbox"/> when splitting
<input type="checkbox"/> <input type="checkbox"/> when identifying
<input type="checkbox"/> <input type="checkbox"/> when swallowing

- Self-assessment tool may save time and resources of caregivers
- Can reveal more issues
- Allows better patient involvement

Thank you very much for taking the time to fill out this questionnaire.



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Kaufmann CP e.a. BMJ Open 2018

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DART validation

Statements or questions of DART	Number of answers (n)	Missing data	True positive	False positive	True negative	False negative	Prevalence of the Rf (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
I have a restricted kidney function/kidney dysfunction/ kidney disease											
I have a liver disease/liver dysfunction											
I have a heart weakness/heart performance weakness											
I am suffering from a chronic respiratory disease											
I am suffering from diabetes											
I have troubles remembering things or tend to forget things											
I take more than five drugs every day, prescribed by my physician											
Sleeping pills	147	17	15	10	121	1	11	93	92	60	99
Cortisone or other steroids	149	15	11	2	129	7	12	61	98	85	95
Antiepileptic drugs	149	15	0	0	149	0	00	NA	100	NA	NA
Oral anticoagulants	149	15	21	5	123	0	14	100	96	81	100
Tricyclic antidepressants	149	15	2	2	145	0	01	100	99	50	100
Drugs for rheumatism/inflammation											
Drugs for drainage (diuretics)											
Digoxin											
Anticholinergic drugs											
Insulin/drugs used in diabetes											
Do you sometimes forget to take your medicine?											
BMQ											
I use some of these application forms: spray for inhalation, skin patch, syringe for self-injection											
Mean value											
Range											

*Rephrased statements for DART V.2.0, revalidated with BMQ, Beliefs about Medicines Questionnaire; DART, Drug Attitudes Rating Test

- poor regarding kidney/liver problems
- poor regarding the use of some specific drugs

- item reduction: >5 medicines, missing doses, concerns about dependency, diabetes, heart failure
- tested in hospitalised patients without cognitive impairments

Risk factors for need for intervention in hospital setting: literature review

Drugs - Real World Outcomes (2016) 3:241–263
DOI 10.1007/s40801-016-0083-4



SYSTEMATIC REVIEW

Risk Factors Associated with the Requirement for Pharmaceutical Intervention in the Hospital Setting: A Systematic Review of the Literature

Emma Suggett¹ · John Marriott²



Criddle D e.a. PCNE poster 2019

	MRAQ	DART	Hospital
Polypharmacy / number of drugs	x	x	x
Elderly patients	n.a.	-	x
Female gender	n.a.	n.a.	x
Poor renal function	n.a.	x	x
Poor liver function	n.a.	x	x
Polymorbidities	xx	x	x
History allergy / ADR	n.a.	x	x
Compliance / reconciliation	x	x	x
High risk drugs	x	x	x
Trigger drugs	n.a.	x	n.a.
Concerns / questions	xx	x	n.a.
Medication complexity	x	n.a.	n.a.
Many regimen changes	x	n.a.	n.a.
>1 prescriber/pharmacy	xx	n.a.	n.a.
Length hospital stay/recent hosp	n.a.	-	x



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Makowsky MJ e.a.
JMCP 2017

Kaufmann CP e.a.
BMJ Open 2015

Suggett E e.a.
Drugs- RWO 2016

Selection criteria based on prediction models



- Predicting medication-related preventable hospital admissions
- Predicting relevant medication-related improvements after medication review
- Predicting need for medication review



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Which outcome is relevant?

- Problems that require a pharmacist intervention
 - DRPs, ADEs, ADRs, medication errors
 - Patient concerns, worries, difficulties, adherence
 - Medication burden, treatment complexity, need for deprescribing
- Not all are reflected in preventable medication related hospitalisations

Predicting medication improvement

- **Outcome:** relevant improvement in medication appropriateness (MAI) after medication review
- **Included:** ≥ 65 year old and ≥ 5 drugs and ≥ 3 chronic diseases from ≥ 2 organ systems including 1 cardiovascular
- **Potential predictors:**
 - age, gender, number of GP visits
 - eGFR, number of diagnoses, illness score, number of healthcare providers
 - number of drugs, number of differences between prescribed and used drugs
- **Final predictors:** number of drugs, number of differences between prescribed and used drugs

Tool to select for simple or advanced MR

Screening algorithm for patients ≥ 65 years with ≥ 5 chronic medications

- Simple MR for patients with low complexity
- Advanced MR for patients with high complexity

Development of the algorithm

- Two expert panels of general practitioners and community pharmacists assessed complexity/need
- 80 cases of elderly patients
 - Medication & medical history, diagnostic assessments, background information (e.g. mobility, cognition, recent falls, hospital admissions)
- Modified Delphi method
 - Cases judged on their complexity on a 9 point Likert scale

Simple case						Complex case		
1	2	3	4	5	6	7	8	9
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- Backward stepwise regression analyses to develop the algorithm predicting the expert ratings

Results

**'number of drugs'×1 +
'number of prescribers'×3 +
'recent fall incident'×7 +
'does not collect own medication'×4**

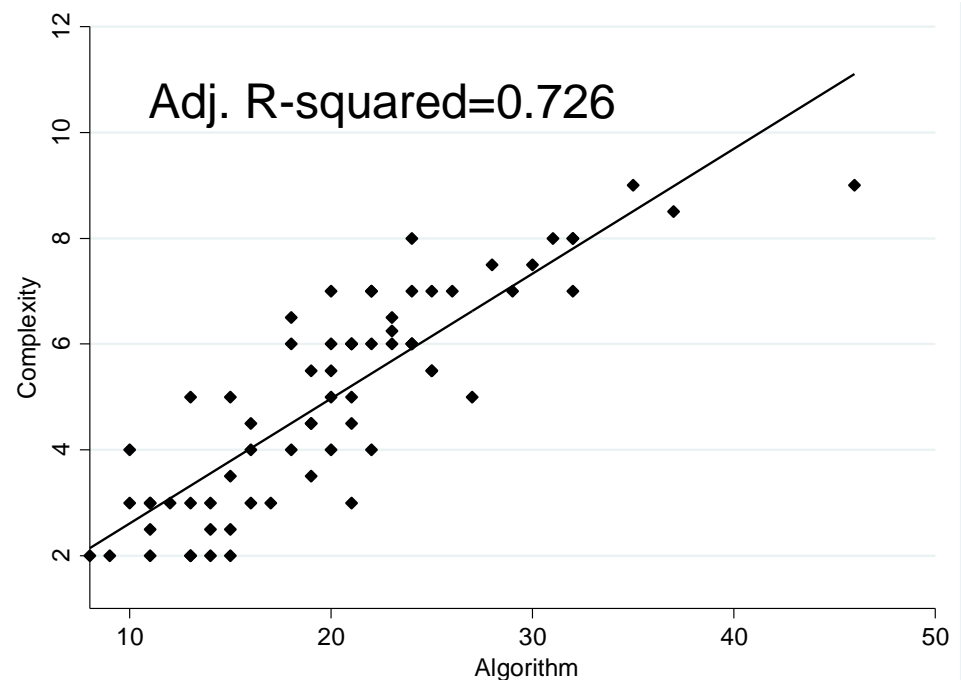


Figure 1: Regression model of the complexity rating of the expert panel vs the algorithm

Small pilot to study feasibility

- Implemented in 4 pharmacies, using a short patient questionnaire to collect data

Question 1.

Do you collect your own medication at the pharmacy?

Yes ☐
No ☐

Question 2.

Do you use medication which is prescribed by a different physician than your general practitioner? For instance, a pulmonologist or a cardiologist from the hospital or a psychiatrist.

Yes ☐
No ☐

In case of a yes: How many different physicians besides your general practitioner prescribe your medication?

Question 3.

In the last 12 months, have you had a fall so severe that you needed help from other people? For instance, you needed to go to the general practitioner or the emergency room because of this fall. Or you needed extra help in or around the house because of this fall.

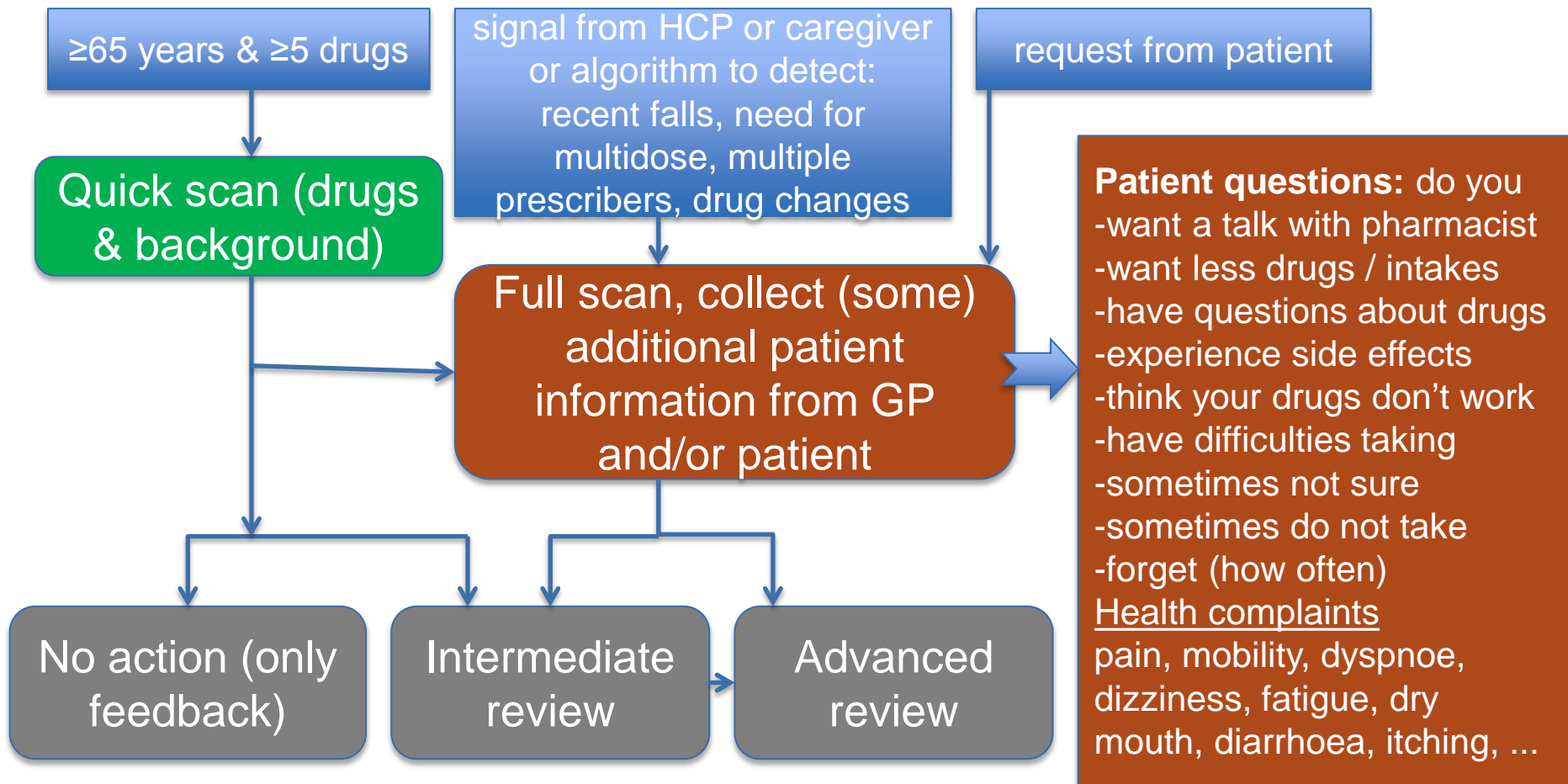
Yes ☐
No ☐

- Mixed opinions about feasibility and validity
 - Sending questionnaires to all eligible patients was feasible
 - Doubts about getting reliable information on fall incidents
 - Information on Q1/2 may be derived from pharmacy records
 - Agreement with selections was moderate

Where does this bring us?

- There is not yet an optimal algorithm to select patients for different levels of medication review
- Possible screening criteria
 - number of chronic medicines (not using a cut-off level)
 - signals: falls, dizziness, pain, specific drugs/combi's, ..
 - adherence issues: missing doses, concerns, discrepancies
- Separate programs for specific subgroups
 - patients not visiting the pharmacy
 - poor communication skills, poor health literacy
- Combine electronic algorithms with some key patient questions in a hybrid or dynamic model

Dynamic model for patient selection



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Verdoorn S e.a. DREAMer study

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