DEPRESCRIBING IN NURSING HOME RESIDENTS: AN IMPLICIT ALGORITHM

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ABSTRACT

Background: Inappropriate medication use and its associated harm is a relevant problem among nursing home residents. An important solution for this problem may be deprescribing: the process of safe withdrawal of inappropriate medication, with the goal of managing polypharmacy as well as improving outcomes. Several explicit tools are available to identify potentially inappropriate medication, but these tools consist of closed questions and closed answers that are often not easily applicable for nursing home patients with their multimorbidity and complex care needs. Tools based on implicit criteria do fit into the individual patient centred care, but are sparse and the underlying evidence is lacking. **Objective**: The aim was to create an implicit patient centred, evidence-based deprescribing algorithm for nursing home residents. **Methods**: A systematic literature search of proposed deprescribing strategies was used to develop the deprescribing algorithm. All recommendations and their evidence were reviewed and eventually combined and supplemented in the implicit algorithm. **Results**: We identified 29 deprescribing strategies and organized these into five deprescribing steps: review all current medication; identify medications to be targeted for cessation, plan a deprescribing regimen; create partnership with patients and monitoring and documentation of the outcomes. The goal of this implicit algorithm is to guide safe and rational deprescribing for nursing home residents. **Conclusions**: The implicit algorithm presented in this article provides a good basis for implicit deprescribing, but needs further validation in the clinical setting.

KEYWORDS: Deprescribing, nursing home residents, polypharmacy.

1. INTRODUCTION

The prevalence of chronic diseases increases with age. Therefore, frail older people in nursing homes should benefit from medication that treats diseases or cures or reduces symptoms. The Benefit-Risk-Balance (BRB) compares the positive therapeutic effects and negative safety or tolerability risks of medication, taking into account interactions and side effects. The BRB decreases because of age, frailty, a decrease in life expectancy and due to dementia and comorbidity.[1] At higher age medication is often less effective, whereas there are more side effects and drug interactions, increasing the risk of complaints and complications.[2] In frail older people this may lead to a higher risk of falling, hospitalization and even death.[3] This is especially the case in the VOCODFLEX-population described by Garfinkel: "the **V**ery **O**ld, with **CO**morbidity, **D**ementia, **F**railty and limited **L**ife-**Ex**pectancy".[4]

The problem with research for evidence in this population is that the quality of 'evidence-based medicine' decreases with age of the target population.

This makes high quality reviews or meta-analyses of the VOCODFLEX-population practically impossible.[4] Despite this lack of evidence, there is a lot of research about polypharmacy and preventing polypharmacy in frail old people.

An important and emerging approach in this context concerns deprescribing: the process of withdrawal of inappropriate medication, with the goal of managing polypharmacy and improving outcomes.[5] Garfinkel's prospective cohort study within a VOCODFLEX population proved that the number of hospital admissions and 1-year mortality had decreased significantly after using a deprescribing algorithm. It was also shown that sustainable deprescribing medication failed in only 17% of the study population.[6] Other studies showed similar results, with significantly improved health outcomes.[7-12]

The decreased BRB of many medicines and the associated risks are known to physicians, just as the dangers of polypharmacy. Nevertheless, it has been found difficult for physicians to sustainably stop

potentially inappropriate medication, partly because guidelines often describe when to start medication, not when to stop. Therefore, there is a demand for a general deprescribing guideline.[13]

Several tools are available, based on explicit criteria, such as the Beers criteria and the STOPP-criteria.[14] These screening tools detect the use of potentially inappropriate medicines in the elderly and are user-friendly, but represent a rigid system with closed questions and answers that do not fit well within the personalized care that is being pursued in nursing homes.[1,4]

Tools based on implicit criteria, such as pill burden, Fatigue or increased fall risk, may fit better within the aimed personalized care for nursing home patients, but are sparse and the underlying evidence is lacking. For this reason, we conducted an extensive literature study that resulted in an evidence based implicit algorithm, to support safe and sustainable deprescribing for nursing home patients. We will also discuss the pros, cons and feasibility of this algorithm. Research into the use of this algorithm in practice is currently taking place.

2. METHOD

The development of the algorithm was based on a systematic literature search conducted in February 2019. We searched the following databases: Cochrane Central Register of Controlled Trials, MEDLINE, Embase and clinicaltrials.gov. As deprescribing is a relatively new concept in the literature, we used a broad range of key words in the search string, including deprescribe, unprescribe, cease, cessation, withdraw, discontinue and stop. We hand searched the reference lists of all relevant studies. We screened 816 articles (784 identified through search strategy, 32 through hand-searching the reference lists of potentially eligible articles). Of these articles, 41 were considered potentially eligible. Articles were included if they proposed (steps of) the deprescribing process. The term 'deprescribing' was not essential, but the included articles had to discuss how potentially inappropriate medication could be stopped safely. We included 29 articles, which are shown in table 1. This table forms the base of this article and algorithm we created.

Table 1: List of included articles. 1. Medication review; 2. Identify potentially inappropriate medication; 3. Deprescribing regimen; 4. Create partnership with patient; 5. Monitoring and documentation. EBU = Evidence based underpinning, based on references provided within the articles: High, moderate, low.

Reference	Study description		Strategy	EBU
Ailabouni (2017)[15]	Feasibility study	1-3	Pharmacist using peer-reviewed deprescribing guidelines, to recommend to general practitioners (GPs), sedative and anticholinergic medicines that can be deprescribed.	Mod
Alexander (2006)[16]	Review	3	Prioritizing before stopping medicines.	Low
Bain (2015)[17]	Review	1	Revising the prescribing stage of the medication-use process to include discontinuing medications.	Mod
Blenke (2018)[18]	Prospective cohort study	1-5	Structured medication reviews performed by pharmacists and nursing facility physicians in newly admitted psychogeriatric nursing facility patients.	Mod
Cullinan (2016)[19]	Review	4	Involve patient in deprescribing process. Be aware of potential barriers patient, family or doctor can experience.	Low
Garfinkel (2007)[20]	Feasibility study	1-3, 5	Introduced a geriatric-palliative approach and methodology to safely cease medication.	Mod
Gordon (2012)[21]	Review	1-3	Informed rational prescribing.	Low
Hardy (2011)[22]	Review	1-4	An algorithm to guide safe, rational deprescribing for patients who are believed to be in their last year of life.	Mod
Harrison (2018)[23]	Review	1-5	Person-centred and individualised deprescribing protocol, followed by careful monitoring of the individual.	Low
Hilmer (2012)[24]	Review	1-3, 5	8 steps, including patient assessment, therapeutic goals, medical history, correlate, assess medicines, optimise medicines with net benefit, cease medicines without net benefit, monitor.	Mod
Kua (2017)[25]	Review	1-5	5-step (reviewing, checking, discussion, communication and documentation) team-care deprescribing practice coupled with the use of a deprescribing guide	Mod
Le Couteur (2011)[26]	Review	1-5	Proposes a general approach to deprescribing, including the following steps: Prepare, recognise, prioritise, wean and monitor.	Low
Lindsay (2015)[27]	Prospective cohort study	2	Onc-Pal deprescribing guideline: to identify potentially inappropriate medication.	High
McIntyre (2017)[28]	Quality improvement study	1-2	Developed a deprescribing tool for target medications with poor evidence for efficacy and safety.	High

McKean (2016)[29]	Prospective pilot study	1-3	Education programme and a paper-based or computerised proforma listing clinical and medication data linked with a five-step decision support tool for selecting drugs eligible for discontinuation.	Mod
Meeks (2011)[30]	Review	2	Reviews the rationale for why various types of medications are deemed inappropriate.	Low
O'Connor (2012)[31]	Review	2	Describes the inappropriate prescribing detection tools most frequently cited in the literature and examines their role in preventing inappropriate prescribing	Mod
Ostini (2012)[32]	Systematic review	3, 4	Identifies effective strategies for stopping pre-existing prescribing in situations where continued prescribing may no longer be clinically warranted.	Mod
Potter (2016)[33]	RCT	2, 3	Individualised medicine review followed by the planned cessation of non-beneficial medicines.	Mod
Puskowski (2017)[34]	Pilot study	1-4	Pharmacist-Driven Deprescribing Initiative in a Nursing Facility.	Mod
Reeve (2016)[35]	Review	1-5	Proposes an evidence-based, patient-centred deprescribing process.	High
Rodriguez-Perez (2017)[36]	Review	1-3, 5	Tool to identify drugs and clinical situations that offers an opportunity of deprescribing in patients with multimorbidity.	Mod
Scott (2015)[37]	Review	1-3, 5	A deprescribing protocol is proposed comprising 5 steps.	Mod
Thillainadesan (2018)[38]	Systematic review	2,3,5	Describes deprescribing interventions in older hospitalised patients.	High
Todd (2018)[39]	Review	4	Proposes a conceptual framework highlighting the importance of patient context when stopping medication.	Mod
Triantafylidis (2018)[40]	Review	2, 3	Describes a deprescribing intervention in older adults with chronic kidney disease.	Mod
Whitman (2018)[41]	Pilot study	1-3	Pharmacist-led medication assessment and deprescribing intervention for older adults with cancer and polypharmacy	Mod
Woodward (2003)[42]	Review	1-5	5 steps: reviewing all current medications, identifying medications to be ceased, planning a deprescribing regimen in partnership with the patient and frequently reviewing and supporting the patient.	Low
Wouters (2017)[43]	Cluster RCT	1-5	Multidisciplinary Multistep Medication Review (3MR) consisting of an assessment of the patient perspective, medical history, critical appraisal of medications, a meeting between the treating elder care physician and the pharmacist, and implementation of changes.	High

3. DEVELOPMENT OF THE DEPRESCRIBING ALGORITHM

Woodward proposed one of the first deprescribing strategies, following five principles of deprescribing:[16]
1. Review all current medication;
2. Identify medications to be targeted for cessation;
3. Plan a deprescribing regimen;
4. Create partnership with patients and carers;
5. Monitoring and documentation.

Several experts modified this model, but the principles remained the same.[17-19] Other deprescribing models were reviewed as well, for example those developed by Reeve, Scott, Garfinkel and Hilmer.[6,17-19] For this study, we compared all deprescribing strategies suggested in the included articles to the five deprescribing principles as listed above. We combined and supplemented the groups and explored the evidence behind each of the recommendations.

3.1. Medication review. The first deprescribing principle involves a medication review. Nineteen of the included articles report this as an essential element of the deprescribing process. Only eleven of these articles cite relevant research, based on references provided within

the articles [15, 17, 18, 20-26, 28, 29, 34-37, 41-43 respectively 15,18, 24, 25, 29, 24, 35-37, 41, 43]. All relevant facts are documented and taken into account in our deprescribing algorithm.

3.2. Identify potentially inappropriate medications. Identifying medication to be targeted for cessation is the second deprescribing principle. Twenty-four of the included articles report this as an element of the deprescribing process and eighteen of these cite relevant research, based on references provided within the articles [15, 18, 20-31, 33-38, 40-43 respectively 15,18, 20, 22, 24, 25, 27, 29, 31, 33-38, 40, 41, 43]. While comparing the different articles, we recognised several returning implicit questions. First, several articles state that life expectancy often changes treatment goals. Therefore, our first question is '*what is the indication for the prescribed medication: primary prevention, secondary prevention or symptom control*'? This makes it easier to answer the second question '*Is the indication for the prescribed medication still correct?*'.

Almost all explicit criteria lists (e.g. Beers Criteria) concern identifying potentially inappropriate medication that might provide more potential harm than benefit.

Therefore, we formulated our third question: '*Does the medication provide more potential harm than benefit*'.

3.3. Withdrawing medication. The third deprescribing principle is to plan a deprescribing regimen. Twenty-two of the included articles report this as an element of the deprescribing process [15, 16, 18, 20-26, 29, 32-38, 40-43] and twelve of these cite relevant research [15, 18, 24, 25, 33-36, 38, 41, 43]. All relevant facts are documented and taken into account in our deprescribing algorithm.

3.4. Consultation with patient, family and caregivers. Partnership with patient and carers is the fourth deprescribing principle. Twelve of the included articles report this as an element of the deprescribing process and seven of these cite relevant research [18, 19, 22, 23, 25, 26, 32, 34, 35, 39, 42, 43 respectively 18, 22, 25, 34, 35, 39, 43]. It is stated several times that shared decision making is an important cornerstone for patient-oriented care and increases the chances of successful deprescribing.[51] Therefore, we emphasize the importance of this step. All relevant facts are documented and taken into account in our deprescribing algorithm.

3.5. Monitoring and documentation. The last deprescribing principle is monitoring and documentation. Twelve of the included articles report this as an element of the deprescribing process and nine of these cite

relevant research [18, 20, 23-26, 35-38, 42, 43 respectively 18, 20, 24, 25, 35, 36, 37, 38, 43]. Several of the included articles describe the importance of this step for sustainable deprescribing. All relevant facts are documented and taken into account in our deprescribing algorithm.

4. RESULTS

The resulting patient centred, evidence-based deprescribing algorithm, is specifically made for nursing home patients (Figure 1). It is intended for all nursing home patients and not only for patients with polypharmacy. Each step in the algorithm is based on a search of relevant literature and contains tips and tricks that have been suggested in other deprescribing tools, in a logical sequence. These concrete steps will help identifying potentially inappropriate medication and guide how to deprescribe.

We have chosen for an implicit algorithm with open questions to structurally guide physicians through the deprescribing process. An explicit algorithm consists of closed questions and closed answers that are often not easily applicable for nursing home patients with their multimorbidity. An implicit algorithm fits the individualised patient-centred care, because it supports physicians to combine evidence based medicine, clinical expertise and the patient's context.[31,44]
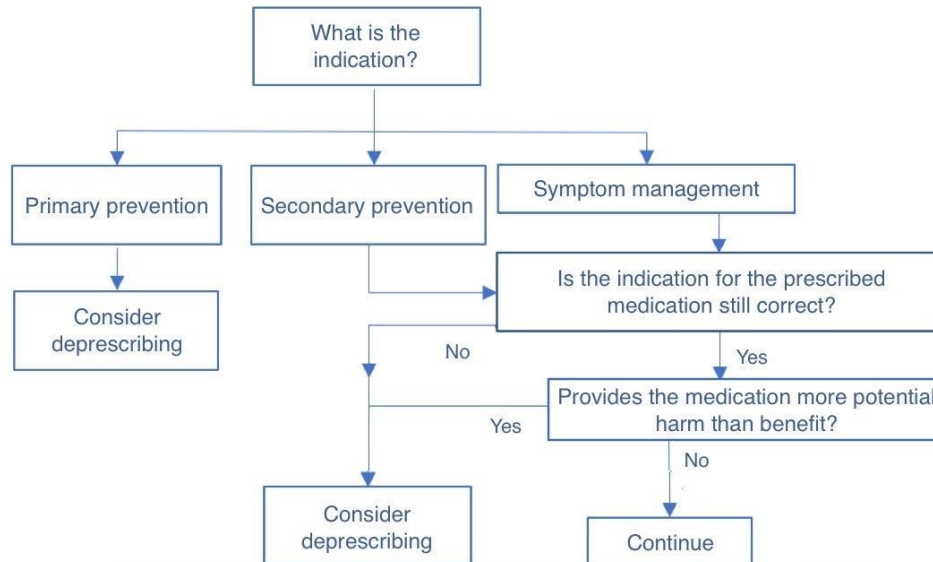

Figure 1: Algorithm for identifying potentially incorrect medication

Figure 1: Shows the algorithm. This algorithm supports identifying potentially inappropriate medication and ceasing this. Under here, we will go through the different steps.

4.1. Medication review
A regular and structured medication review is the starting point of the deprescribing process. This can take place every time new medication is started or on a regular base with a pharmacist for example. A

medication review is also perfect to follow up the deprescribing process.[42]

For deprescribing it is essential to obtain a complete medical and medication history.[35,42] The medication history should include dose, frequency, indication and

start date. Allergies, intolerabilities and observed side effects should be included in the medical history.[35]

It is important to predict the patient's life expectancy, which can be challenging in multimorbid nursing home patients. The PROFUND-index is a prognostic index that provides an accurate method of stratifying 1-year death risk in this specific population, using nine independent mortality predictors.[45] For the nursing home population, this index is more accurate and specific than the 'surprise question' or the Lawton-Brody index.[46] It is user friendly too, which makes it a practical support while using the deprescribing algorithm.[47]

4.2. Identify potentially inappropriate medications
Step 2 is to identify potentially inappropriate medications. This is the central step in the deprescribing process. It includes checking the indication for each individual medicine and to consider the medication's pros and cons.

What is the indication for the prescribed medication?
Primary and secondary prevention and symptom management are differentiated. Physicians should always consider to stop medication for primary prevention in the nursing home population: these medicines are often accompanied by a higher *number needed to treat* (NNT) than *numbers needed to harm* (NNH).[48] The NNT and NNH are measures to indicate how many patients benefit **or** are harmed using the medication. For example: a patient using a statin for five years for primary prevention, has a chance of 1:104 to prevent a myocardial infarction, a chance of 1:50 to develop diabetes and a chance of 1:10 to develop muscle damage.[49]

The time to benefit is 3 to 5 years, whilst for nursing home patients the average life expectancy is less than 2 years.[50] The typical nursing home patients will not benefit from taking this medication, but might suffer from the increased pill burden, side effects and interactions of the medication provided.
For secondary prevention and symptom management the NNT and NNH are more balanced, so there is less reason to cease them immediately.[49]

Is the indication for the prescribed medication still correct?
If there is an indication, medication can be easily (re)started. Absence of indication could be a reason to cease medication.[8] Helpful questions are:[51]
- Are the symptoms still there or newly present?
- Does the medication have the intended effect?
- Did the patient's risk change?
- Is there a (non-)pharmacological alternative?
- Is it part of a prescribing cascade, in which medication is started to prevent complaints from other medicines?
- Are there potential side effects present or might the medication cause any possible damage in the future?

Does the medication provide more potential harm than benefit?
Then consider the risks and benefits of the medication for this specific patient. This depends on different patient-related and medication-related factors.[31,46] For example polypharmacy, side effects, pill burden, pharmacological interactions, possible side effects in the future, life expectancy, patient's medication necessity and benefit, cognitive and functional limitations, comorbidity, wishes of patients and their family and their care goals.[51,52]

All factors listed above and many more affect the costs benefit consideration, which shows how complicated this step is. The outcome is not as unambiguous as with the STOPP-criteria. In absence of strong clinical evidence regarding the risks and benefits of medication for older people, it is almost impossible to identify undoubtedly inappropriate medication.[31,53] A more likely outcome is that medication *might be* incorrect. It is uncertain and that makes this step in the deprescribing process difficult. While guidelines frequently explain how and when a medication should be initiated, there is often no information concerning when and how the medications should be reduced or stopped.[54] The individual recommendations of a guideline may be rational, but the sum of all recommendations for the individual multimorbid patient is often inappropriate.[54] Moreover, these clinical guidelines are often taken too literally by the absence of qualitatively good research, and not seldom there is great pressure not to deviate from these guidelines, even in individual cases.[54,55]

During the first implementation experiences with this deprescribing algorithm in practice, we noticed that several physicians would not stop undoubtedly inappropriate medication, because stopping was against the guidelines. How to stop medication without the backup of a guideline? It is the tough job of a physician to combine the (lack of) evidence about nursing home patients with the patient's context and then, together with patient and family, make the decision what is desirable.[35,54] This might be a different decision than recommended in the guideline.

This step in the deprescribing process helps ceasing inappropriate medication, but also stimulates dose reduction and switching to other/better (non-) pharmacological interventions.

There are various barriers to successful deprescribing: lack of knowledge about the effectiveness, potential side effects and interactions of medicines.[35] If one does not know which medication can be safely stopped for nursing home patients, no medicine will be stopped. It is difficult to detect side effects, partly because older people often do not associate their symptoms with medication use, but for example, with their age.[56]

Older people often will not recognise side effects, nor the nursing staff if they are not aware of possible side effects. Nevertheless, it is important to explore whether the patient experiences side effects, otherwise these side effects will certainly be missed.

4.3. Withdrawing medication

In step 2 the physician identified certain potentially inappropriate medication or medication that is not useful (anymore). This does not mean that the medication can be stopped immediately. The decision to "deprescribe or not to describe" will depend on the patient's consent, and optionally the patient's family consent and the opinion of other involved caregivers as well. To engage in such a conversation, it is good to be convinced that stopping is possible (being convinced does not mean being 100% confident).

It is important to have a plan which medication can be discontinued and how. The most effective regime to stop medication has not yet been established.[17] The most common regimes are sequentially stopping, simultaneous stopping and gradually reduce medicine. We will discuss these options below.

If several drugs are potentially incorrect, it is good to rank these by priority. Studies in adults show that it is best to stop sequentially.[17,57] In this way it is easier to trace which medicine is responsible for any withdrawal symptoms.

As mentioned above, sequential cessation was found to be better for adults. However, Garfinkel states that it is better for frail elderly people with reduced life expectancy to stop multiple drugs at the same time. By ceasing medication faster, they can benefit longer.[4] The physician should decide how to cease the medication in consultation with the individual patient, representative and/or family. The reduction of medication is sensible if withdrawal symptoms are known. Then recurrence symptoms be registered earlier and one can prescribe the lowest effective dose and thus increase patient comfort. If this dose is lower than the starting dose, a profit has already been made.[17,51]

It is always good to draw up a personalized patient-related management plan. This should describe the symptoms that caregivers should pay attention to, the action plan in the event of recurrence symptoms or withdrawal symptoms. It should also describe agreements with the patient and its family and in which cases a doctor should be contacted.[51]

4.4. Consultation with patient, family and caregivers

Shared decision making is an important cornerstone for patient-oriented care and increases the chances of successful deprescribing.[51]

Up to 80% of patients would be hypothetically interested in stopping medication.[57-59] What the patient thinks of deprescribing depends partly on external influences such as family, friends, media and medical family history.[57,58,59] The most important influence, however, is the physician's attitude.[58] Therefore, it is good to be aware of possible barriers that both doctor and patient can experience. Deprescribing becomes difficult if one of the involved individuals is convinced that the treatment is effective or if one is afraid of withdrawal syndromes or recurrence symptoms.[57] For the patient and family, negative experiences of others may change their opinion on deprescribing.[60] The doctor might experience the following barriers: lack of time, not wanting extra consultations, the complex prescribing environment with multiple providers and multimorbid patients or the lack of guidelines.[61]

Possible approaches to increase patients' (and their families') willingness to deprescribing:[59,60]

- Introduce deprescribing without the patient experiencing stress or anxiety. Initially, the doctor-patient relationship is more important than deprescribing.
- Emphasize that deprescribing has a therapeutic goal. Medication is not stopped because the patient is not worth the treatment.
- Discuss the lack of benefits or necessity of medication for the patient and identify the possible risks that the medication has.
- Discuss various deprescribing options and ask what is preferred by patient, representative, family and/or caregivers. Discuss the steps that need to be taken to reduce the risks of deprescribing and confirm that deprescribing is a 'trial': it is not certain that it will succeed, but it's worth trying.

4. 5. Monitoring and documentation

It is important to monitor the patient during and after the deprescribing process.[62] This is an important step in sustainable deprescribing and can easily be implemented during a medication review.

The decrease in polypharmacy and incorrect medication that is achieved in the first period, can come to a standstill within a few months after deprescribing and the number of medicines can increase again.[62] Given their daily contact, nurses and/or carers have an important role in monitoring the patient.

Follow up, support and good documentation are the key to success in long-term deprescribing, but there is little evidence about how this follow-up should take place.[53] The purpose of this last step of the deprescribing process is to report. This way we can prevent medication errors and re-introduction of medication.[63] Describe the reason for deprescribing, the process and the outcome. If deprescribing was not successful, describe why it did not work.

5. DISCUSSION

In this article, we propose a patient centred-deprescribing algorithm, which provides a systematic approach to review current medication, identify potentially inappropriate medication, plan a deprescribing regimen, create partnership with patient and family and monitor the sustainability of the deprescribing process.

Deprescribing has the potential to improve clinical outcomes, but there is no evidence yet. Using this algorithm will help identifying potentially inappropriate medication and will be a guidance to deprescribe in a structured way. However, we acknowledge that there might be practical difficulties in using this algorithm, such as obtaining a comprehensive and complete medical history.

Deprescribing can be difficult and time-consuming in older individuals with polypharmacy and multiple comorbidities. No algorithm is capable to cover the complexity of this task, but still be simple and specific. It might be helpful to use the already mentioned NNT, NNH and time to benefit or time to harm.[48] The website www.theNNT.com can help with these considerations.[49] Another tool to support deprescribing, is the website Medstopper.com.[64] On this website, you fill in the medicines with corresponding indication. This site provides an overview of which medication can best be discontinued first, in which way this can be done, possible withdrawal or recurrence symptoms and the Beer's criteria and STOPP criteria.

Still, there is a lack of an evidence base to support the recommendation made and on which to conduct deprescribing. In this population, it is almost impossible to create a study with enough power to proof deprescribing is completely safe and increasing clinical outcomes. With trial and error our knowledge will progress and improve this algorithm. The main goal remains the patient's quality of life and safety.

Deprescribing with this algorithm in practice is feasible, but may require a change in attitude for physicians, patients and its family. Physicians will need to invest time in deprescribing, patients and their family have more decisions to make. Both physicians and patients might experience barriers. We are aware that this implicit tool might be time consuming and depends on the knowledge and experience of the physician.

We acknowledge the utility of the algorithm in routine clinical practise needs to be evaluated, so we are currently working on an intervention study with this algorithm. In the meantime, current prescribers might find this algorithm of use, and we welcome feedback as to their perceptions of its utility.

6. CONCLUSION

Inappropriate medication use and its associated harm is a relevant problem among nursing home patients. Deprescribing by using a patient centred algorithm might be (part of) the solution. Although there are many literature studies on deprescribing, there is still a lack of thorough intervention research. The algorithm presented here provides a good basis for this, because it is not product-specific. Yet it needs further validation. The authors are currently working on an intervention study regarding the deprescribing of statins and proton pump inhibitors in Dutch nursing homes, for which this algorithm is used.

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