



## **University of Groningen**

### Deprescribing for frail older people - Learning from the case of Mrs. Hansen

Granas, Anne Gerd; Stendal Bakken, Marit; Ruths, Sabine; Taxis, Katja

Published in: Research in Social and Administrative Pharmacy

DOI:

10.1016/j.sapharm.2017.07.003

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version Publisher's PDF, also known as Version of record

Publication date:

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Granas, A. G., Stendal Bakken, M., Ruths, S., & Taxis, K. (2018). Deprescribing for frail older people -Learning from the case of Mrs. Hansen. Research in Social and Administrative Pharmacy, 14(6), 612-616. https://doi.org/10.1016/j.sapharm.2017.07.003

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverneamendment.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 12-10-2022

FISEVIER

Contents lists available at ScienceDirect

# Research in Social and Administrative Pharmacy

journal homepage: www.rsap.org



# Deprescribing for frail older people — Learning from the case of Mrs. Hansen



Anne Gerd Granas <sup>a</sup>, Marit Stendal Bakken <sup>b</sup>, Sabine Ruths <sup>c, d</sup>, Katja Taxis <sup>e, \*</sup>

- <sup>a</sup> School of Pharmacy, The Faculty of Mathematics and Natural Sciences, University of Oslo, Norway
- b Kavli Research Centre for Geriatrics and Dementia, Haraldsplass Deaconess Hospital, PB 6165, N-5892, Bergen, Norway
- <sup>c</sup> Research Unit for General Practice, Uni Research Health, Bergen, Norway
- <sup>d</sup> Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway
- <sup>e</sup> University of Groningen, Groningen Research Institute of Pharmacy, Unit of PharmacoTherapy, -Epidemiology and —Economics, Ant Deusinglaan 1, 9713 AV. Groningen. The Netherlands

#### ARTICLE INFO

#### ABSTRACT

Article history: Received 10 July 2017 Accepted 10 July 2017 Drug treatment is often an essential part in treatment and prevention of diseases in older people, but there is much concern about inappropriate medication use. This paper aims to describe the complexity of medication safety issues and clinical judgments when optimizing prescribing in older individuals. It uses the case of Mrs. Hansen, an aged nursing home resident, to illustrate the facilitators and barriers of this process. With decreasing life expectancy, medication use should shift from cure to care, focusing on symptomatic treatment to increase the patient's well-being. In Mrs. Hansen's case, the number of (potentially) dangerous medications were reduced, and non-pharmacological alternatives were considered. There were some medicines added, as underprescribing can also be a problem in older people. Deprescribing long-standing treatment can be interpreted by the patient and family as "giving up hope". More clinical evidence and practical communication tools are needed to guide deprescribing decisions, taking medical and patient-centered priorities into account. Studies evaluating such interventions should select outcome measures that are particularly relevant for frail old individuals.

© 2017 Elsevier Inc. All rights reserved.

#### 1. Introduction

Over the last decades, there has been a major increase in drug use, particularly in older people. Although drug treatment is essential in both treatment and prevention of diseases among older people, this is of concern. Firstly, most evidence regarding medication efficacy and safety is derived from small samples of younger and healthier populations. Secondly, older people are extra vulnerable to adverse effects of drug use due to age- and disease-related changes, multimorbidity, and complex drug regimens. Research on prescribing quality in older people is rapidly expanding. A range of assessment tools have been developed to identify and measure inappropriate prescribing. Although helpful in increasing awareness, such tools can never replace good clinical judgement. Multiple intervention studies have demonstrated improvements in prescribing quality based on reductions in

inappropriate prescribing; however, the question remains if the interventions also result in improved clinical outcomes. Thus, there is no gold standard on how to ensure high quality of prescribing for older people. The aim of this paper is to describe the complexity of medication safety issues and clinical judgments when optimizing the prescribed medication of a frail old lady.

#### 2. Medical history and diagnoses

Mrs. Hansen, a 90-year old widow, was admitted to the local nursing home four weeks ago. During the last months living at home she had severe functional decline, became disorientated and could no longer cope with daily activities. Her comprehensive care needs and increasingly demanding behavior for attention could no longer be met by her 65 year old daughter and the home care services. They flagged the need for admission to a nursing home. According to her general practitioner, Mrs. Hansen has had hypertension and intermittent atrial fibrillation for decades, a stroke 15 years ago, and an abdominal hernia 10 years ago. She complained repeatedly about back pains. Previously conducted X-ray and bone

E-mail address: k.taxis@rug.nl (K. Taxis).

<sup>\*</sup> Corresponding author.

density measurement revealed osteoporosis with multiple vertebral compression fractures. She also had hearing problems but refused to use hearing aids.

Her daughter reported that Mrs. Hansen used to like gardening but lost the interest in flowers and being outdoors. Her daily activities in the last two years were restricted to cooking simple meals and shopping with her daughter. She has never been particularly socially active.

Prior to admission, the nursing home primary nurse obtained a list of prescribed medicines from the general practitioner and asked the daughter to bring along all the medicines used at home, including any "as required" medications. After reconciliation, the nurse recorded Mrs. Hansen's actual medication regimen to consist of 13 regular medicines and 1 as required medicine, as shown in Table 1. For three medicines (oxycodone, paracetamol and acetylcysteine), it was difficult to establish the exact frequency of use at home.

On the third day after admission, the nursing home physician conducted an admission consultation, focusing on the patient's complaints and expectations, known conditions and possible dementia. Mrs. Hansen suffered from constant back pains and frequently asked for more painkillers. Also, she complained about constipation and itching legs. Clinical examination revealed arrhythmia, ankle edema, dry skin and scratches on both legs. She was clearly agitated and unable to complete the Mini Mental State Examination. After consulting a geriatric psychiatrist and the daughter, the nursing home physician decided to prescribe risperidone to alleviate agitation and restlessness.

The following week, a multidisciplinary medication review was performed. The primary nurse performed relevant measurements in advance, such as weight, blood pressure, heart rate, and ECG, as well as blood tests such as hemoglobin, renal function, electrolytes, HbA1C, glucose, thyroidal function, and cholesterol levels. The clinical pharmacist received the list of the patients' current medication in advance and applied different tools (STOPP & START, Beers list, Interaction database 10) to check for potentially inappropriate medication use, under-prescribing and drug interactions. The physician, the primary nurse and the pharmacist then performed a medication review, discussing pros and cons of the current drug regimen, taking into consideration the overall clinical picture and patient perspectives. 11

#### 3. Polypharmacy late in life

Table 1 illustrates that Mrs. Hansen was exposed to excessive polypharmacy, i.e. > ten drugs, including six drugs affecting the central nervous system (analgesics and psychotropic drugs). In other words, Mrs. Hanson is a typical polypharmacy patient commonly seen in nursing homes.<sup>12</sup> Frail, older individuals like Mrs. Hansen have an increased risk to experience side effects from medicines, emphasizing the need to be cautious about prescribing. Holmes suggested a model with four components to guide the reconsideration of medication use late in life<sup>13</sup>: Remaining life expectancy of the patient, the time until benefit for each medication, pinpointing treatment targets for each medication, and shared decision-making among physicians, patients, and families all should inform the goals of care. Ideally, there is consistency among all four components. With decreasing life expectancy, medication use should shift from cure to care. Late in life, the focus should be on symptomatic treatment to increase the patient's well-being. Consequently, the number of medicines prescribed should decrease, and non-pharmacological alternatives should be considered whenever possible. So, what would be a sensible way forward regarding the medical treatment of Mrs. Hansen? Firstly, one should address potentially dangerous medications, then those considered unnecessary or troublesome. Lastly, one must consider any missing treatment options, as underprescribing can be a problem even in older people.<sup>14</sup>

#### 4. The medication review

For Mrs. Hansen, the top priority was pain relief. Her complaints continued despite an excessive use of analgesics. Her constant pain may partly explain her demanding behavior and craving for the staff's attention. The first drug the team decided to stop was ibuprofen due to the high risk of older individuals to develop gastrointestinal bleeding and a decrease in renal function due to taking NSAIDs. Because of an interaction with the ACE inhibitor, this was also increasing the risk for renal and heart failure. The team decided to stop amitriptyline as the patient presumably did not get any pain relief and because of the very strong anticholinergic side effects in older people. Likewise, pregabalin was stopped by stepwise reduction of the dose over the course of two weeks to prevent the patient from experiencing withdrawal symptoms. The team decided to tackle the pain by prescribing an immediate-release formulation of oxycodone six times daily and paracetamol four times daily for dose titration. If this regimen was sufficient, the patient would be changed to receive a modified released formulation of oxycodone twice daily and paracetamol four times daily (not more than 2 g to reduce the risk of liver toxicity on chronic use) as well as receive immediate-release oxycodone for breakthrough pain.

The team also decided to initiate a number of other options to address the patient's pain, including physiotherapy and encouragement to take part in social activities. They also considered deprescribing her sleeping tablets zopiclone, being used long-term in the highest available strength. Sleeping tablets lose effectiveness in long-term use; additionally, they increase the risk for delirium, falls and fractures. The team decided to initiate a step-wise dose reduction leading to cessation and was looking for nonpharmacological alternatives for her. In addition, a number of other medications were stopped. Acetylcysteine was stopped due to lack of evidence for treatment effects. Estriol was stopped because there was no clear clinical indication for use. Iron was stopped as the patient's hemoglobin was normal and because it may worsen the patient's constipation. The itching on her legs improved when a moisturizing lotion for dry skin was applied, so it was decided to discontinue the dermatological preparation. She had not been prescribed secondary prevention for stroke, but considering that her stroke occurred 15 years ago, her high age and heavy drug load, a full cardiovascular risk management was not initiated. 15 Finally, vitamin D and calcium was started after the multidisciplinary medicating review because of her clinically manifest osteoporosis and low vitamin D-levels in an attempt to decrease her fracture risk. Table 2 shows her updated list of pharmacotherapy.

#### 5. Deprescribing

So, what was done to optimize Mrs. Hansen's treatment? Overall, eight medicines were stopped due to high risk of side effects and the lack of effectiveness. Two medicines were added, Vitamin D/calcium and risperidone. The latter was then stopped within three months. What happened in Mrs. Hansen's case can be called deprescribing. This was recently defined as "the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes". A small number of studies have examined the impact of deprescribing, suggesting benefits and an absence of harm. Examples include withdrawal of neuroleptics in older

 Table 1

 Details of the prescribed medicine for nursing home patient Mrs. Hansen at admission, and comments from the multidisciplinary medication review.

Medication use details	ATC code	Indication	Drug initiation	Comments from the medication review	Consequence of the review	
1. Ibuprofen tablets 200 mg Two tablets	M01A E01	Pain	Before admission	Adverse drug profile	Cessation	
2. Amitriptyline tablets 10 mg Once daily	N06A A09	Pain	Before admission	Lack of effect, adverse drug profile	Cessation	
3. Pregabalin tablets 25 mg Once daily	N03A X16	Pain	Before admission	Lack of effect, adverse drug profile	Dose reduction, cessation	
A. Oxycodone 5 mg sustained release tablets Frequency of administration before admission unclear	N02A A05	Pain	Before admission	Optimize pain treatment by dose titration using immediate release formulation and then convert to modified release formulation to be administered twice daily with an immediate release formulation for breakthrough pain.	Dose titration with immediate release formulation then conversion to modified release formulation	
5. Paracetamol 500 mg Frequency of administration before admission unclear	N02B E01	Pain	Before admission	Ensure stable pain management. Water-soluble, with shorter half-life in old people. Chronic use should be no more than 2 g/day.	Now given 4 times/day	
6. Zopiclone tablets 7.5 mg Once daily	N05C F01	Insomnia	Before admission	Lack of effect, adverse drug profile	Dose reduction, cessation	
7. Movicol powder Makrogol, NaCl, NaHCO3, KCl Two sachets per day	A06A D65	Constipation	Before admission	Valid indication. Need for two laxatives?	Continuation, increase dose?	
8. Sennosid A + B 20 mg syrop 2–3/ week	A06A B06	Constipation	Before admission		Dose reduction, cessation?	
9. Iron sulphate sustained release tablets 100 mg	B03A A07	Anemia	Before admission	Normal hemoglobin levels measured	Cessation	
Once daily 10. Enalapril tablets 5 mg	C09A A02	Hypertension	Before admission	Valid indication	Continuation	
Once daily 11. Hydrocortisone/ Miconazol cream Twice daily	D01A C20	Fungal infection feet	Before admission	Symptoms (itch?) Duration? Effect? Long-term use in elderly not recommended.	Cessation	
12. Estriol tablets 1 mg Once daily	G03C A04	Unknown	Before admission	Duration, symptoms (urinary tract infections, senile colpitis?)	Cessation and re-evaluation. If indicated, local application is	
13. Nitroglycerine spray 0.4 mg/dose As required	C01D A02	Angina pectoris	Before admission	Symptoms? Still indicated?	preferred Continuation	
14. Acetylcystein 200 mg Frequency of administration before admission unclear	R05C B01	Cough	Before admission	No documented effect	Cessation	
15. Risperidon tablets 0.5 mg One tablet at night	N05A X08	Agitation, restlessness	Added 3 days after admission	Limited effectiveness, not indicated for long-term use	Cessation after 3 months	
16. Calcium 1000 mg/ Vitamin D 800 International Units Once daily	A12AX	Reduce fracture risk	Added after medication review	Osteoporosis	Initiation after medication review	

nursing home residents,<sup>17</sup> antidepressants in older patients with dementia,<sup>18</sup> and antihypertensives in older persons.<sup>19</sup> In Mrs. Hansen's case, the STOPP criteria<sup>8</sup> and the Beer's criteria<sup>9</sup> were used to guide decisions on which medication to discontinue. Studies have shown that these tools are useful in detecting drugrelated problems.<sup>6</sup> Other tools may be also very useful, such as the Drug Burden Index<sup>20,21</sup> measuring the cumulative and anticholinergic drug load of patients. Their practical applicability however should be further developed from a research point-of-

view, to become a fully integrated part of prescribing support systems. <sup>22,23</sup> There are initiatives to develop deprescribing guidelines (e.g. <sup>24</sup>). Tools have also been proposed to support the decision-making around deprescribing. <sup>25</sup> But more research is needed to broaden the clinical evidence around some of the choices, e.g. when to discontinue antihypertensive medication. <sup>26</sup> Little is known to what extent deprescribing is implemented in clinical practice. A Norwegian study showed that 72.5% of deceased nursing home patients still had standing prescriptions of curative/

**Table 2**Details of the prescribed medicine for nursing home patient Mrs. Hansen following the medication review.

Medication use details	ATC code	Indication	Drug initiation	Follow-up
1. Movicol powder Makrogol, NaCl, NaHCO3, KCl	A06A D65	Constipation	Before admission	Both medicines were kept. Likely to be constipated from the oxycodone. Evaluate the need for two laxatives in the following
Two sachets per day				weeks.
2. Sennosid A + B	A06A B06	Constipation		
20 mg syrop 2-3/week				
3. Enalapril tablets 5 mg	C09A A02	Hypertension		Blood pressure should be measured regularly.
Once daily				
4. Oxycodone 5 mg immediate release formulation, 6 times daily	N02A A05	Pain		Monitor effect; if pain is under control, then convert to modified release formulation to be administered twice daily; use oxycodone
				5 mg immediate release formulation for breakthrough pain.
5. Paracetamol 500 mg	N02B E01	Pain		Chronic use should be no more than 2 g/day.
Four times daily				
6. Nitroglycerine spray 0.4 mg/dose	C01D A02	Angina pectoris		Continuation, but the patient does not seem to have symptoms.
As required				Evaluate the need in the following weeks.
7. Risperidon tablets 0.5 mg	N05A X08	Agitation,	Added 3 days after	Monitor effects on behavior, cessation after 3 months.
One tablet at night		restlessness	admission	
8. Calcium 1000 mg/Vitamin D 800 International Units	A12AX	Reduce fracture risk	After medication review	Continuation for prevention of osteoporosis.
Once daily				

preventive drugs on the day of death, and 47.3% of them also received palliative drugs.<sup>27</sup> This evidence argues the case for a more proactive approach to deprescribing in frail older people.

How should optimization of the pharmacotherapy in older people be organized? Mrs. Hansen received a medication review by a multidisciplinary team including a physician, a nurse and a clinical pharmacist. This is a mix of health professionals, each with different and complementary competences. The specific role of the pharmacist in this cooperation has been highlighted.<sup>28</sup> Direct collaboration between different professionals is very important.<sup>29</sup> Furthermore, a patient-centered approach is vital to allow for shared decision-making on pharmacotherapy. Deprescribing longstanding treatment can be interpreted by the patient and family as "giving up hope". Good communication with the patient, family and carer is therefore crucial, but in many cases a challenge to realize, especially in patients with dementia. Important ethical implications of deprescribing such as how to deal with autonomy of patients are very important to overcome barriers in implementing deprescribing in practice.<sup>30</sup> Schuling et al.<sup>31</sup> suggested using a communication tool based on work by Fried et al.<sup>32</sup> to guide such conversations. Patients are asked to rank four components: staying alive as long as possible, being free of symptoms, being free of pain and remaining independent. More work has to be done to develop such tools for the nursing home setting. Planning and thorough follow-up of effects are other essential elements of the deprescribing process.<sup>33</sup>

What is the evidence that medication reviews are effective in older individuals? On one hand, a range of studies report positive effects of medication reviews on reducing the number of (inappropriate) medications and lowering the drug costs in different settings including nursing homes. <sup>34,35</sup> On the other hand, a systematic review and meta-analysis by Wallersted et al. <sup>36</sup> found no effects of medication reviews on mortality and hospitalization rates in nursing home residents. Similarly, a Cochrane Review by Alldred et al. <sup>37</sup> showed that interventions in nursing home residents, including medication reviews, did not have an effect on adverse drug events, hospital admissions or mortality.

Is it realistic to expect that medication reviews in patients like Mrs. Hansen will have any effects on mortality or hospital admission? In general, nursing home residents have a high mortality, and mortality is influenced by many co-variables. In line with policy for many other nursing home residents, the multidisciplinary team decided in collaboration with her daughter that Mrs. Hansen was

not to be admitted to hospital for intensive life-prolonging treatment, should her health deteriorate. The deprecribing of eight medicines may or may not have an impact on her life expectancy. Considering her case, relevant research outcomes would be improved quality of life, activities of daily living, satisfaction with treatment, and absence of adverse drug events. She may experience fewer side effects, but in a complex case like hers, causality would be difficult to establish. Mrs Hansen's own concern has mainly been the unsatisfactory pain treatment. Careful follow-up is needed to ensure that the new regimen is effective. Mrs. Hansen (and her daughter) was overall more satisfied with the pain treatment. The nursing staff found that Mrs. Hansen appeared to be calmer after the changes to her medication, possibly related to her experiencing less pain. More work is needed to develop a set of relevant outcome measures to evaluate health care interventions such as medication reviews.38

#### 6. Conclusions

In recent years, some advances have been made to optimize polypharmacy late in life. Mrs. Hansen's case serves as an example of the complexity and difficulty of the decision making process during medication reviews. Further clinical evidence around deprescribing, alongside practical communication tools to support shared decision making, are needed for wider implementation. Studies evaluating such interventions should select outcome measures that are particularly relevant for frail old individuals.

#### **Authors' contributions**

AGG and KT wrote the initial draft of the paper based on a nursing home patient from AGG. Personal and clinical details are changed to protect privacy. SR and MB contributed with clinical aspects to add depth and applicability to prescribers.

#### Conflict of interest disclosures

We have no conflict of interest to report.

#### References

1. Taxis K, O'Sullivan D, Cullinan S, Byrne S. Drug utilization in older people. In: Elseviers M, Wettermark B, Almarsdóttir AB, et al., eds. *Drug Utilization* 

- Research: Methods and Applications. London: Wiley-Blackwell; 2016.
- Duijnhoven RG, Straus SM, Raine JM, de Boer A, Hoes AW, De Bruin ML. Number of patients studied prior to approval of new medicines: a database analysis. PLoS Med. 2013;10:e1001407.
- Beers E, Egberts TC, Leufkens HG, Jansen PA. Information for adequate prescribing to older patients: an evaluation of the product information of 53 recently approved medicines. *Drugs Aging*, 2013;30:255–262.
- Davies EA, O'Mahony MS. Adverse drug reactions in special populations the elderly. Br I Clin Pharmacol. 2015;80:796–807.
- Kaufmann CP, Tremp R, Hersberger KE, Lampert ML. Inappropriate prescribing: a systematic overview of published assessment tools. Eur J Clin Pharmacol. 2014:70:1–11.
- Cooper JA, Cadogan CA, Patterson SM, et al. Interventions to improve the appropriate use of polypharmacy in older people: a cochrane systematic review. BMJ Open. 2015;5(12), e009235—2015-009235.
- Wouters H, Quik EH, Boersma F, et al. Discontinuing inappropriate medication in nursing home residents (DIM-NHR study): protocol of a cluster randomised controlled trial. *BMJ Open*. 2014;4(10). e006082–2014-006082.
- O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/ START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing, 2015;44(2):213–218.
- By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2015;63:2227–2246.
- Royal dutch association of pharmacists (KNMP) kennisbank, versie 2.1.9 (dutch drug information database). https://kennisbank.knmp.nl/. Accessed 7/6, 2015.
- Halvorsen KH, Ruths S, Granas AG, Viktil KK. Multidisciplinary intervention to identify and resolve drug-related problems in Norwegian nursing homes. Scand J Prim Health Care. 2010;28:82–88.
- **12.** Taxis K, Kochen S, Wouters H, et al. Cross-national comparison of medication use in Australian and Dutch nursing homes. *Age Ageing*. 2017;46:320–323.
- Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. Arch Intern Med. 2006;166:605–609.
- Cherubini A, Corsonello A, Lattanzio F. Underprescription of beneficial medicines in older people: causes, consequences and prevention. *Drugs Aging*. 2012;29:463–475.
- Bushnell CD, Colon-Emeric CS. Secondary stroke prevention strategies for the oldest patients: possibilities and challenges. *Drugs Aging*. 2009;26:209–230.
- Reeve E, Gnjidic D, Long J, Hilmer S. A systematic review of the emerging definition of 'deprescribing' with network analysis: implications for future research and clinical practice. Br J Clin Pharmacol. 2015;80:1254–1268.
- Ballard C, Lana MM, Theodoulou M, et al. A randomised, blinded, placebocontrolled trial in dementia patients continuing or stopping neuroleptics (the DART-AD trial). PLoS Med. 2008;5(4):e76.
- Bergh S, Selbaek G, Engedal K. Discontinuation of antidepressants in people with dementia and neuropsychiatric symptoms (DESEP study): double blind, randomised, parallel group, placebo controlled trial. BMJ. 2012;344:e1566.
- Iyer S, Naganathan V, McLachlan AJ, Le Couteur DG. Medication withdrawal trials in people aged 65 years and older: a systematic review. *Drugs Aging*. 2008:25:1021–1031.
- **20.** Wouters H, van der Meer H, Taxis K. Quantification of anticholinergic and sedative drug load with the drug burden index: a review of outcomes and methodological quality of studies. *Eur J Clin Pharmacol.* 2017;73:257–266.

- **21.** Kouladjian L, Gnjidic D, Chen TF, Hilmer SN. Development, validation and evaluation of an electronic pharmacological tool: the Drug Burden Index Calculator. *Res Soc Adm Pharm.* 2016;12:865–875.
- 22. van der Meer HG, Wouters H, van Hulten R, Pras N, Taxis K. Decreasing the load? is a multidisciplinary multistep medication review in older people an effective intervention to reduce a patient's drug burden index? protocol of a randomised controlled trial. BMI Open. 2015;5(12), e009213–2015-009213.
- Pont LG, Nielen JT, McLachlan AJ, et al. Measuring anticholinergic drug exposure in older community-dwelling australian men: a comparison of four different measures. Br J Clin Pharmacol. 2015;80:1169–1175.
- 24. Lindsay J, Dooley M, Martin J, et al. The development and evaluation of an oncological palliative care deprescribing guideline: the 'OncPal deprescribing guideline'. *Support Care Cancer*. 2015;23(1):71–78.
- 25. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med.* 2015;175:827–834.
- 26. Benetos A, Rossignol P, Cherubini A, et al. Polypharmacy in the aging patient: management of hypertension in octogenarians. *JAMA*. 2015;314(2):170–180.
- 27. Jansen K, Schaufel MA, Ruths S. Drug treatment at the end of life: an epidemiologic study in pursing homes. *Scand J Prim Health Care* 2014;32:187–192
- miologic study in nursing homes. *Scand J Prim Health Care*. 2014;32:187–192.

  28. Spinewine A, Fialova D, Byrne S. The role of the pharmacist in optimizing pharmacotherapy in older people. *Drugs Aging*. 2012;29:495–510.
- 29. Kwint HF, Bermingham L, Faber A, Gussekloo J, Bouvy ML. The relationship between the extent of collaboration of general practitioners and pharmacists and the implementation of recommendations arising from medication review: a systematic review. *Druss Aging*. 2013:30:91–102.
- a systematic review. *Drugs Aging*. 2013;30:91–102.

  30. Reeve E, Denig P, Hilmer SN, Ter Meulen R. The ethics of deprescribing in older adults. *J Bioeth Inq*. 2016;13:581–590.
- **31.** Schuling J, Gebben H, Veehof LJ, Haaijer-Ruskamp FM. Deprescribing medication in very elderly patients with multimorbidity: the view of Dutch GPs. A qualitative study. *BMC Fam Pract*. 2012;13, 56–2296-13-56.
- 32. Fried TR, Tinetti M, Agostini J, Iannone L, Towle V. Health outcome prioritization to elicit preferences of older persons with multiple health conditions. *Patient Educ Couns*. 2011;83:278–282.
   33. Jansen J, Naganathan V, Carter SM, et al. Too much medicine in older people?
- Jansen J, Naganathan V, Carter SM, et al. Too much medicine in older people? deprescribing through shared decision making. BMJ. 2016;353:i2893.
- 34. Geurts MM, Talsma J, Brouwers JR, de Gier JJ. Medication review and reconciliation with cooperation between pharmacist and general practitioner and the benefit for the patient: a systematic review. Br J Clin Pharmacol. 2012;74: 16–33.
- 35. Patterson SM, Hughes CM, Cardwell C, Lapane KL, Murray AM, Crealey GE. A cluster randomized controlled trial of an adapted U.S. model of pharmaceutical care for nursing home residents in northern Ireland (fleetwood northern Ireland study): a cost-effectiveness analysis. J Am Geriatr Soc. 2011;59:586–593.
- 36. Wallerstedt SM, Kindblom JM, Nylen K, Samuelsson O, Strandell A. Medication reviews for nursing home residents to reduce mortality and hospitalization: systematic review and meta-analysis. Br J Clin Pharmacol. 2014;78:488–497.
- Alldred DP, Raynor DK, Hughes C, Barber N, Chen TF, Spoor P. Interventions to optimise prescribing for older people in care homes. *Cochrane Database Syst Rev.* 2013;2:CD009095.
- **38.** Beuscart JB, Pont LG, Thevelin S, et al. A systematic review of the outcomes reported in trials of medication review in older patients: the need for a core outcome set. *Br J Clin Pharmacol*. 2017;83:942–952.