Medicines - Can less be more?

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WESTERN AUSTRALIAN CENTRE FOR HEALTH AGEING

Acknowledgements

Utilises work of Richard Lindley, Andrew McLachlan, Vasi Naganathan and Sue Kurrle.

Reports data from papers led by Kathleen Potter and Pascalle Bosboom.

Nil COI

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Overview

1. Use of medicines for dementia
2. Understand the dangers and consequences associated with polypharmacy
3. The impacts of some common medications
4. MDT communication for consistency
5. Help! Where to go if you have a patient with a specific medication problem
6. Define de-prescribing and outline current research into de-prescribing

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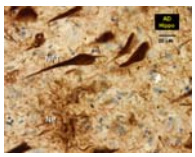
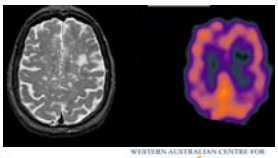
Overview of the Major Dementias

Alzheimer's Dementia (AD)
- most common dementia
- gradual decline in memory
- social skills preserved
- Three As; Amnesia (short term), agnosia (naming), apraxia (motor planning)



Vascular Dementia (VaD)
- second most common cause
- memory loss associated with focal neurology

Mixed Dementia (VaD + AD)



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Other Major Dementias

Lewy Body Dementia (DLB)
- dementia with early visual hallucinations, parkinsonism, and fluctuations
- very sensitive to neuroleptics

Frontotemporal Dementia (FTD)
- disinhibition and personality changes early, with memory loss later on (good short term memory, and score well on SMMSE)

Other Dementias
- NPH, CJD, Wernickes Psychosis, Parkinson's Dementia, Huntington's Dementia, AIDS related Dementia, etc.

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differential dx: “3 Ds”

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Meducation use for dementia

Prevent disease or delay onset
Cure disease
Slow progression of disease
Treat primary symptoms eg memory
Treat secondary symptoms eg depression, hallucinations

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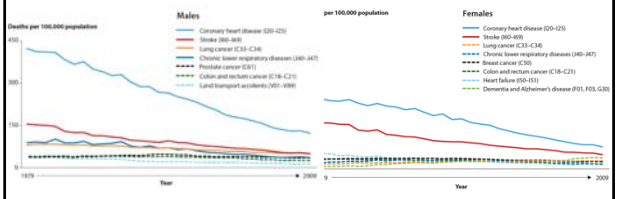
Good news! Deaths in Australia



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The effectiveness of lifestyle changes (such as smoking cessation), antiplatelet therapy, and the control of hypertension, dyslipidemia, and diabetes in the prevention of vascular events is well established.

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Medication use for PWD

Prevent disease or delay onset

~~Cure disease~~

Slow progression of disease

Treat primary symptoms eg memory

Treat secondary symptoms eg depression, hallucinations

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1. Control of vascular risk factors assumed to be beneficial

2. Vitamin E

Initial data (Sano 1996) suggested a significant delay in functional decline

thought to work through its antioxidant effect

NOT recommended (ref: Cochrane)

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Medication use for PWD

Prevent disease or delay onset
~~Cure disease~~
Slow progression of disease
Control cognitive symptoms
Treat secondary symptoms eg depression, hallucinations

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Medications to treat primary symptoms

cholinesterase inhibitors:
donepezil, rivastigmine, galantamine

Memantine

ginkgo biloba

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Cholinesterase inhibitors

modest improvement in cognition and function

response: 1/3 improve, 1/3 stabilise, 1/3 have no response

do not prevent progression of underlying disease

ADR – GI, cardiac

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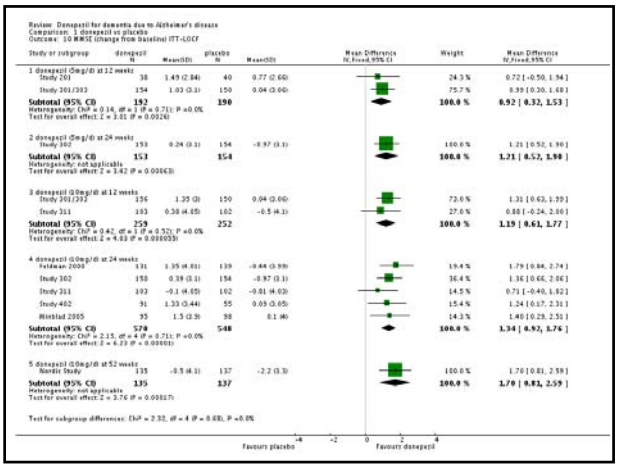

Ginkgo biloba

anti-inflammatory, anti-oxidant properties

Some trials suggest modest improvements in some measures of function and memory

reasonably safe and well tolerated, but watch for bleeding

Cochrane: insufficient evidence of predictable, clinically important effect

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Souvenaid®

- Three RCTs showed that there were no significant benefits on QoL, ADL function or cognition in RCTs
- statistically significant benefit on memory function in people with mild AD

→ not recommended

- Any small effects may be outweighed by cost

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Medications use for PWD

Prevent disease or delay onset
~~Cure disease~~
Slow progression of disease
Treat primary symptoms eg memory
Treat other symptoms eg BPSD

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Medications for BPSD

Antidepressants eg SSRI

antipsychotics:
- typical antipsychotics (eg haloperidol)
- atypical antipsychotics (eg risperidone)
- modest effect on symptoms

mood stabilisers:
- anticonvulsants (carbemazepine)

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Polypharmacy

- 5 or more drugs
- 20-40% of older people
- Iatrogenesis is one of the 'geriatric giants'
- 'Hyperpolypharmacy'

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Causes of Polypharmacy

- Comorbidities
- Age
- Prescriber (*what influences prescribers?)*

- Reluctance to cease another prescriber's prescription

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Risks of Polypharmacy

- Adverse drug reactions common cause of
  - hospital admission
  - morbidity and mortality
- Falling, delirium and the other geriatric syndromes may be drug-related
- Medication errors

polypharmacy, *per se*, *appears* to be a risk factor for adverse outcomes

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Adverse reactions- how big is the problem?

The Quality in Australian Health Care Study 1995

~ 2% of hospital admissions associated with ADEs

=140,000 hospital admissions annually!

Wilson R McL, Runciman WB, Gibberd RW et al Med J Aust 163:458-71

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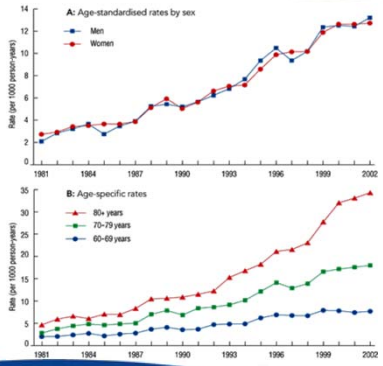

Hospital admissions coded as 2º to ADRs in WA

Burgess et al MJA 2005 biggest increase is CV medications >20% of AEs > 80 yrs

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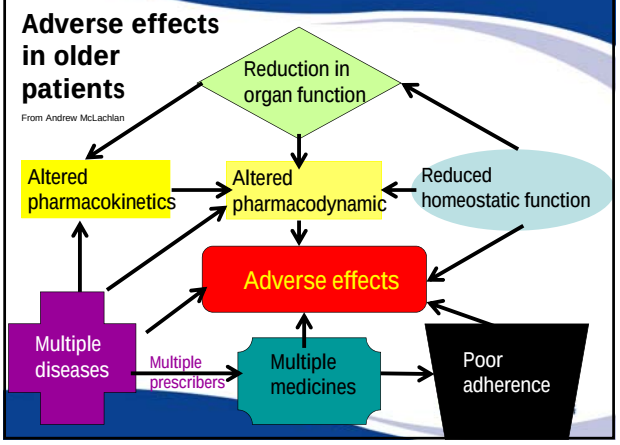
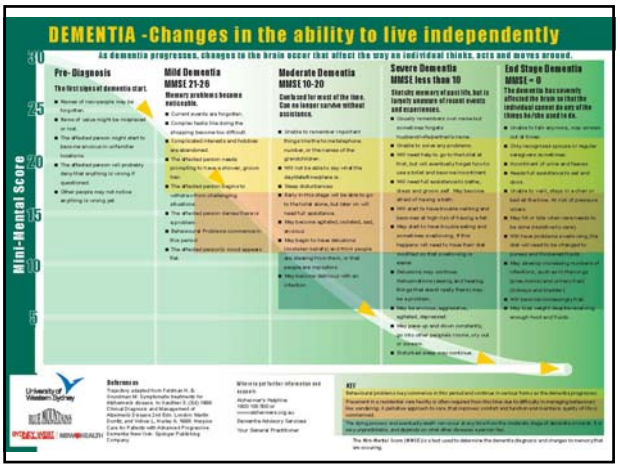
Adverse effects in older patients

From Andrew McLachlan





Our data suggest polypharmacy and DBI>0 associated with worse QoL among PWD living in RACF

Table 2. Differences in self-reported QoL-AD ratings (i.e. %MaxSc on the QoL-AD) according to exposure to PHM

Measure	No exposure		Exposure		Crude		Adjusted[1]		Adjusted[2]	
	n	mean ± SD	n	mean ± SD	mean difference (95% CI)	p	mean difference (95% CI)	p	mean difference (95% CI)	p
PIM(s) by Beers criteria	102	70.21 ± 10.32	124	68.41 ± 9.51	−1.79 (−4.40 to 0.81)	0.175	−1.68 (−4.04 to 0.68)	0.163	−1.49 (−3.86 to 0.88)	0.217
DBI >0	48	73.02 ± 10.77	178	68.20 ± 9.43	−4.82 (−7.94 to −1.70)	0.003	−4.38 (−7.51 to −1.24)	0.006	−4.07 (−7.25 to −0.89)	0.012
Polypharmacy[3]	18	74.17 ± 10.71	208	68.79 ± 9.74	−5.37 (−10.12 to 0.61)	0.027	−5.54 (−10.26 to −0.82)	0.022	−4.96 (−9.79 to −0.12)	0.045

[1] Adjusted for age, gender, MMSE total score and NPI total score using linear regression modeling. [2] Adjusted for age, gender, MMSE total score, NPI total score and number of comorbidities using linear regression modeling. [3] Number of medications consumed per day ≥5.

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Improvements in medical care a definite contributor to improved heath outcomes - Why the concern about use of medicines?

In addition to risks of ADR

- Industry has strong interest in doctors prescribing
- Most research about using drugs (rather than alternatives)
- Prescribers receive a lot of advice on starting medications but very little guidance on when to stop treatment.
- Prescribers' reluctance to cease specialist prescriptions

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	Pro	Anti
Cholinergic	Dementia treatments Cholinesterase inhibitors eg donepezil	Bladder overactivity Eg oxybutinin ADR of many drugs eg tricyclic antidepressants
Dopaminergic ("extra-pyramidal")	Parkinson's	Anti-emetics; anti-psychotics

ORIGINAL INVESTIGATION

A Prescribing Cascade Involving Cholinesterase Inhibitors and Anticholinergic Drugs

Sudeep S. Gill, MD, MSc, FRCPC; Muhammad Mamdani, PharmD, MA, MPH; Gary Naglie, MD, FRCPC; David L. Streiner, PhD; Susan E. Bronskill, PhD; Alexander Kepp, BSc; Kenneth I. Shulman, MD, SM, FRCPC; Philip E. Lee, MD, FRCPC; Paula A. Rochon, MD, MPH, FRCPC

Background: The prescribing cascade model involves the misinterpretation of an adverse reaction to 1 drug and the subsequent, potentially inappropriate prescription of a second drug. We present a new example of the prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs used to manage urinary incontinence.

Methods: A population-based retrospective cohort study was carried out in Ontario, Canada. Participants included 44 884 older adults with dementia (20 491 were dispensed a cholinesterase inhibitor and 24 393 were not), enrolled between June 1, 1999, and March 31, 2002. Subjects were observed until they received an anticholinergic drug, stopped the cholinesterase inhibitor treatment, died, or the study period ended (March 31, 2003). The main outcome measure was receipt of an anticholinergic drug to manage urinary incontinence.

Results: After adjusting for potential confounding factors, we observed that older adults with dementia who were dispensed cholinesterase inhibitors had an increased risk of subsequently receiving an anticholinergic drug (4.5% vs 3.1%; P<.001; adjusted hazard ratio, 1.55; 95% confidence interval, 1.39-1.72), relative to those not receiving cholinesterase inhibitors. This finding was consistent in a series of subgroup analyses.

Conclusions: Use of cholinesterase inhibitors is associated with an increased risk of receiving an anticholinergic drug to manage urinary incontinence. The use of an anticholinergic drug in this setting may represent a clinically important prescribing cascade. Clinicians should consider the possible contributing role of cholinesterase inhibitors in new-onset or worsening urinary incontinence and the potential risk of coprescribing cholinesterase inhibitors and anticholinergic drugs to patients with dementia.

Arch Intern Med. 2005;165:808-813

Class	Common problematic ADR
Antihypertensive	Hypotension (postural dizziness)
Psychotropics, antihistamines, anticholinergics; analgesics	Sedation, cognitive impairment, falls
Calcium, opiates, Metformin, anitbiotics	GI upset
B Blockers	Bad dreams, cool peripheries
Polypharmacy	ERRORS, interactions

Most controversial……

Families count cost of dementia drugs prescriptions

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Under treatment

- Aspirin and anticoagulation
- Analgesia
- ACE – inhibitors and B-blockers
- Ca and Vit D (v bisphosphonates)

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Weigh risks and benefits

- Efficacy
- Risk of ADR
- Pt wishes

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Is Discontinuation Safe?

- Psychotropic withdrawal reactions
- Anti anginals
- Anticonvulsant medications

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The medication management cycle

Guiding principles to achieve continuity in medication management

Reviewing Medications

- Have patient bring in all medications, including OTC's, herbs, dietary supplements
- Ask about other prescribers
- POMB
- Consider home visit if high risk
- Cautious medication withdrawal where indicated

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Medication Reconciliation

- Process of creating the most accurate list possible of all medications a patient is taking – including drug name, dosage, frequency, and route
- Comparing best possible medication history against the admission, transfer, and/or discharge orders for each hospitalised patient.
- Aims to remedy communication errors, ensuring correct medications provided to the patient at all transition points – coming into a hospital, moving within it, or being discharged home or to another hospital.

Source: OSQHC, WA Health

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Communicate with patients, carers other prescribers

Consumers often can engage sophisticated concepts

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Use aids

- Simplify regimens
- Medication cards
- Dosette Boxes
- 'Webster Pack'
- visiting nurses
- involving caregiver

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Aim for concordance

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- DBMAS
- Pharmacist - HMR/RMMR
- Increasing resources for polypharmacy

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NHS SCOTLAND

The Scottish Government

Polypharmacy Guidance

October 2012

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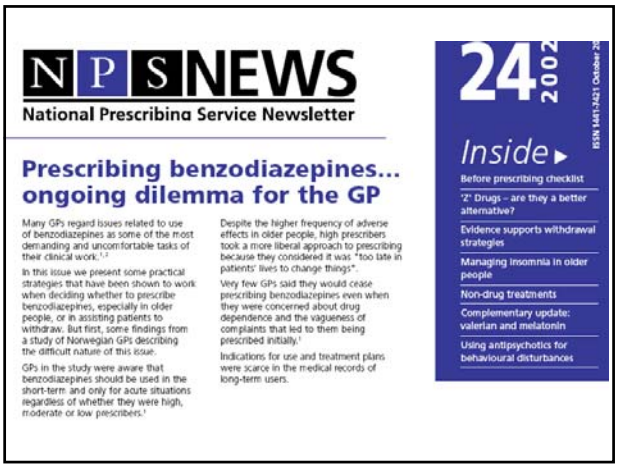


NPS NEWS
National Prescribing Service Newsletter

Prescribing benzodiazepines... ongoing dilemma for the GP

Many GPs regard issues related to use of benzodiazepines as some of the most demanding and uncomfortable tasks of their clinical work.[1,2]

In this issue we present some practical strategies that have been shown to work when deciding whether to prescribe benzodiazepines, especially in older people, or in assisting patients to withdraw. But first, some findings from a study of Norwegian GPs describing the difficult nature of this issue.

GPs in the study were aware that benzodiazepines should be used in the short-term and only for acute situations regardless of whether they were high, moderate or low prescribers.[1]

Despite the higher frequency of adverse effects in older people, high prescribers took a more liberal approach to prescribing because they considered it was "too late in patients' lives to change things".

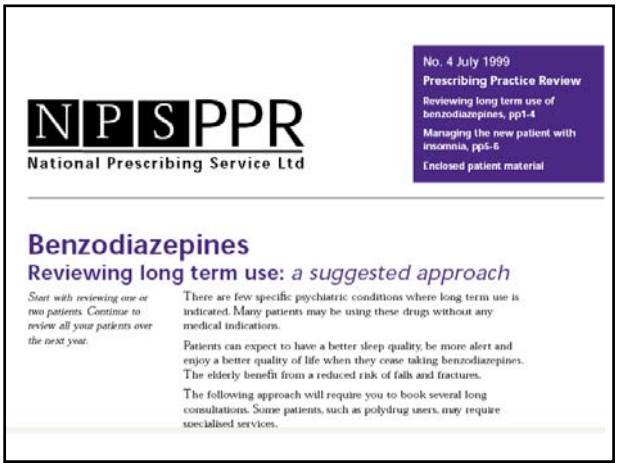
Very few GPs said they would cease prescribing benzodiazepines even when they were concerned about drug dependence and the vagueness of complaints that led to them being prescribed initially.[1]

Indications for use and treatment plans were scarce in the medical records of long-term users.

24 2002

ISSN 1441-7421 October 20

Inside ▸



NPS PPR
National Prescribing Service Ltd

No. 4 July 1999
Prescribing Practice Review

Enclosed patient material

Benzodiazepines
Reviewing long term use: *a suggested approach*

Start with reviewing one or two patients. Continue to review all your patients over the next year.

There are few specific psychiatric conditions where long term use is indicated. Many patients may be using these drugs without any medical indications.

Patients can expect to have a better sleep quality, be more alert and enjoy a better quality of life when they cease taking benzodiazepines. The elderly benefit from a reduced risk of falls and fractures.

The following approach will require you to book several long consultations. Some patients, such as polydrug users, may require specialised services.

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"De-prescribing"

"process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes"

Only 45 citations in PubMed, over half of those since last year

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Why are medications ceased?

- Adverse drug reactions
  - common in older people
  - hospital admissions and mortality
  - associated with polypharmacy
  - drug burden linked to cognitive and physical function
- Medication efficacy
  - often no evidence base in older people
  - *or* evidence suggests lack of efficacy
- On this basis, medications are often stopped in older people *but without clear evidence base for risks and benefits of this practice*

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Psychoactive medication withdrawal

- Campbell et al
  - Any psychoactive medication
  - n = 93, mean age 75, community, 44 weeks
  - Reduction in falls, 66% reduction in falls
- Curran et al
  - Benzodiazepine withdrawal
  - n = 138, mean age 77, community, 24 weeks
  - Cognitive performance benefits
  - No difference in withdrawal/insomnia symptoms

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Psychoactive medication withdrawal II

- Ballard et al
  - Antipsychotic withdrawal
  - n = 100, mean age 83, Nursing home, 3 months
  - 70% successful withdrawal
  - No difference between groups in agitation/behavioural scores
  - Subgroup analysis (small numbers)
    - ↓ behav scores (baseline) = ↓ agitation
    - ↑ behav scores (baseline) = ↑ agitation

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Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia (Review)

Declercq T, Petrovic M, Azermai M, Vander Stichele R, De Sutter AIM, van Driel ML, Christiaens T

THE COCHRANE COLLABORATION®

March 28 2013

- 9 trials (7 in Nursing homes) 606 subjects
- 8 of 9 no difference in success of withdrawal
- Do difference in psychiatric symptoms except subsets with severe symptoms or psychosis/agitation and have responded
- "We recommend that programmes that aim to withdraw older nursing home residents from long-term antipsychotics should be incorporated into routine clinical practice, especially if the NPS are not severe"

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The war against Polypharmacy: A New Cost-Effective Geriatric-Palliative Approach for Improving Drug Therapy in Disabled Elderly People

Doron Garfinkel MD[1], Sarah Zur-Gil MA[2] and Joshua Ben-Israel MD[3]

Methods: The study group comprised 119 disabled patients in six geriatric nursing departments; the control group included 71 patients of comparable age, gender and co-morbidities in the same wards.

Results: A total of 332 different drugs were discontinued in 119 patients (average of 2.8 drugs per patient) and was not associated with significant adverse effects. The overall rate of drug discontinuation failure was 18% of all patients and 10% of all drugs. The 1 year mortality rate was 45% in the control group but only 21% in the study group (P < 0.001, chi-square test).

Successful discontinuation of all target drugs in 82% of patients. Antidepressants and antipsychotics were the most difficult drugs to cease, with failure of withdrawal in 26% and 31% of patients respectively.

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Local deprescribing studies

- STOPAT
- Midwest Deprescribing Study
- Opti-Med

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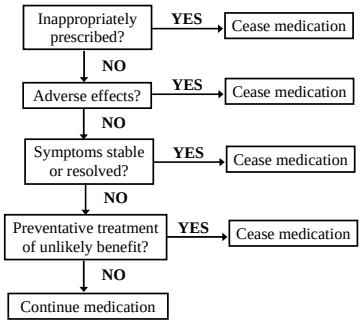
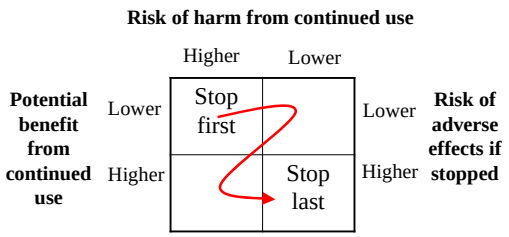
Step One: Identify Targets!



Step Two: Withdrawal Order



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Midwest outcomes

- Reduced the number of regular medicines by ~2.5 per person
- Increase in the number of PRN medicines over 12 months
- No change in the total number of prescribed medicines
- No apparent adverse effects of deprescribing on quality of life or level of independence

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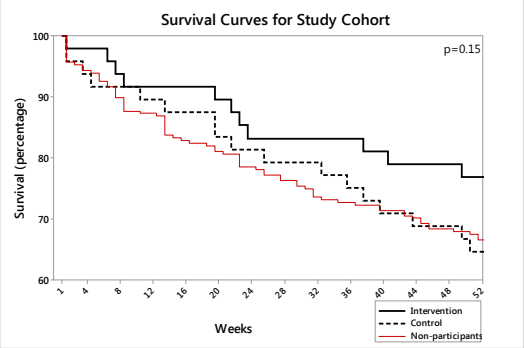
Survival at 12 months



Consider de-prescribing

Deprescribing

***David Le Couteur**, Professor of Geriatric Medicine,[1] **Emily Banks**, Professor and National Health and Medical Research Council Senior Research Fellow,[2] **Danijela Gnjidic**, Postdoctoral scientist,[1,4] and **Andrew McLachlan**, Professor of Pharmacy (Aged Care)[3]*

1. Centre for Education and Research on Ageing, University of Sydney and Concord Hospital, Sydney
2. National Centre for Epidemiology and Population Health, The Australian National University, Canberra
3. Faculty of Pharmacy, University of Sydney and Concord Hospital, Sydney
4. Departments of Pharmacology and Aged Care, Royal North Shore Hospital, Sydney

Summary

Medicines have adverse effects and the use of multiple medicines, polypharmacy, can be associated with poorer outcomes. Health professionals need to recognise when medicines

in older people. A feasibility study to reduce polypharmacy in people over 70 years of age suggested that over half of their medicines could be discontinued. Only 2% of the drugs needed to be restarted because the original indication re-emerged. Overall there was improvement in cognition and the patients' global health.[2] A review of medicine withdrawal studies in

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Fig. 1
General approach to deprescribing

Prepare	discuss deprescribing at start of therapy
Recognise	polypharmacy, adverse drug reactions (including falls in older people), lack of efficacy, and change in treatment goals, often due to the onset of terminal illness, dementia and/or frailty
Prioritise	one medicine at a time starting with the medicine suspected of causing the adverse drug reaction or consider using risk assessment tools
Wean	always wean central nervous system-active medicines (especially benzodiazepines, opioids), beta blockers, corticosteroids, levodopa typically over weeks and months
Monitor	withdrawal syndromes, discontinuation syndromes, rebound, recurrence of illness, cognition, falls and quality of life

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Special Communication | **LESS IS MORE**

Reducing Inappropriate Polypharmacy
The Process of Deprescribing

Ian A. Scott, MBBS, FRACP, MHA, MEd; Sarah N. Hilmer, MBBS, FRACP, PhD; Emily Reeve, BPharm (Hons), PhD; Kathleen Potter, PhD, FRACGP; David Le Couteur, PhD, FRACP; Deborah Rigby, BPharm, GradDipClinPharm, FASCP, FACP, FAICD; Danijela Gnjidic, PhD; Christopher B. Del Mar, MB, BChir, MD, FRACGP; Elizabeth E. Roughead, PhD; Amy Page, MClinPharm; Jesse Jansen, MPsych, PhD; Jennifer H. Martin, MB, ChB, FRACP, PhD

Inappropriate polypharmacy, especially in older people, imposes a substantial burden of adverse drug events, ill health, disability, hospitalization, and even death. The single most important predictor of inappropriate prescribing and risk of adverse drug events in older patients is the number of prescribed drugs. Deprescribing is the process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes. Evidence of efficacy for deprescribing is emerging from randomized trials and observational studies. A deprescribing protocol is proposed comprising 5 steps: (1) ascertain all drugs the patient is currently taking and the reasons for each one; (2) consider overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention; (3) assess each drug in regard to its current or future benefit potential compared with current or future harm or burden potential; (4) prioritize drugs for discontinuation that have the lowest benefit-harm ratio and lowest likelihood of adverse withdrawal reactions or disease rebound syndromes; and (5) implement a discontinuation regimen and monitor patients closely for improvement in outcomes or onset of adverse effects. Whereas patient and prescriber barriers to deprescribing exist, resources and strategies are available that facilitate deliberate yet judicious deprescribing and deserve wider application.

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Invited Commentary
Related article

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Deprescribing

- Data on the effects of deprescribing are scarce
- Small observational studies and a few RCTs have examined withdrawing a single class of medication in older people
- Antihypertensives, benzodiazepines and psychotropic agents can often be stopped without causing harm
  (Iyer S, Naganathan V, McLachlan AJ, Le Conteur DG. Drugs & Aging 2008; 25:1021)
- Serious ADWE rare, the majority of adverse reactions are caused by only a few types of medication, and adverse effects are easily treated by restarting the medication

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Conclusions

1. Medicines contribute to benefits in preventing dementia, and improving symptoms in PWD.
2. However medicine use is associated with risks. Polypharmacy is common, and probably increases risk.
3. Common medication classes can impact on patients' functional status
4. Consistent messages from the MDT can support concordance
5. There are several useful resources to assist caring for patients with polypharmacy or challenging medication related issues.
6. There is an emerging evidence base for cautious deprescribing

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