



The OPTIMIZE Trial: A Clinician's Reflection on the Challenges of Deprescribing

International Deprescribing Journal Club

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Presenter Disclosure

Faculty :

- Louise Papillon-Ferland, B. Pharm., M. Sc.

Relationship with commercial interests

- None, either related or unrelated to this presentation

Other

- Clinical professor affiliated to the Michel Saucier Chair in Pharmacy, Health and Aging

Objectives

1. Present key learnings from the OPTIMIZE trial.
2. Discuss enablers and barriers of deprescribing, as applied to real-life clinical cases.



Clinical case – Mrs M.*



84 y.o. referred to geriatric clinic
Living alone (retired orderly/pt attendant), support from friend

Pharmacy consultation requested re:

- Medication review – Polypharmacy with possible compliance issues

Diagnosis :

- Mild neurocognitive disorder – MMSE 26/30
- Hypertension
- Anxiety-depression
- Hip fracture 1 year ago (hip prosthesis)
- Chronic pain (osteoarthritis)
- eGFR \cong 55 mL/min

Family physician + 5 specialists involved in care

Mrs M. – Medication list from her pharmacy

- Telmisartan 40 mg po Daily
- Amlodipine 5 mg po Daily
- Bupropion SR 150 mg po Daily
- Clonazepam 0.5 mg qAM + 1mg qHS
- Lorazepam 1 mg po qHS
- Betahistine 8 mg po TID prn
- Bimatoprost 0.01% both eyes qHS
- Oxycodone 5 mg po QID
- Esomeprazole 40 mg po BID
- Dicyclomine 20 mg po TID prn
- Dimenhydrinate 50 mg po q6h prn
- Lactulose 15-30 mL po HS prn
- PEG 3350 17 g po Daily prn
- Fosfomycine as directed for UTI



Mrs M. : Potentially inappropriate medications to consider for deprescribing ?

- Telmisartan 40 mg po Daily
- Amlodipine 5 mg po Daily
- Bupropion SR 150 mg po Daily
- Clonazepam 0.5 mg qAM + 1mg qHS
- Lorazepam 1 mg po qHS
- Betahistine 8 mg po TID prn
- Bimatoprost 0.01% both eyes qHS
- Oxycodone 5 mg po QID
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- Fosfomycine as directed for UTI



Study

JAMA Internal Medicine | [Original Investigation](#)

Deprescribing Education vs Usual Care for Patients With Cognitive Impairment and Primary Care Clinicians The OPTIMIZE Pragmatic Cluster Randomized Trial

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National Institute on Aging



Background - Rationale

- Patients with NCD or MCI:
 - Multiple chronic conditions
 - Multiple medications



Deprescribing
?

Increased risk of
adverse outcomes

Preliminary work

Qualitative study by research team prior:

Elements identified to facilitate deprescribing in primary care in patient with cognitive impairment :

- ✓ Establish Trust
- ✓ Frame Deprescribing as Positive, Routine
- ✓ Align Deprescribing with Goals of Dementia Care (Symptom Management)
- ✓ Provide Direct-to-Patient Educational Materials and suggested language
- ✓ Engage Entire Health Care Team in Deprescribing



Objective

- To examine the effectiveness of increasing **patient and clinician awareness** about the potential to **deprescribe unnecessary or risky** medications among patients with **dementia or mild cognitive impairment**



Design

- Pragmatic, patient-centered, 12-month cluster randomized clinical trial (April 2019- March 2020)
- Hypothesis :
 - Deprescribing intervention → Reduction of # of long-term medications prescribed and % taking 1 or more PIMs at 6 months

Design - Setting

- 18 primary care clinics (Colorado, USA)
 - 9 Intervention + 9 control clinics
 - Clinics randomized using uniform distribution block of 2 by clinic size (170-1125 patients/clinic)
- Control clinics : receiving the intervention in a delayed manner (24 months after the start of the « intervention clinics »)

Eligibility criteria - Patients

Inclusion criteria

- ≥ 65 years old
- With primary care clinician in the clinic targeted for trial
- Major NCD or MCI
- ≥ 1 additional chronic medical conditions
- ≥ 5 chronic medications
(Informed consent waived)

Exclusion criteria

- Patients living in long-term care facilities or enrolled in hospice care

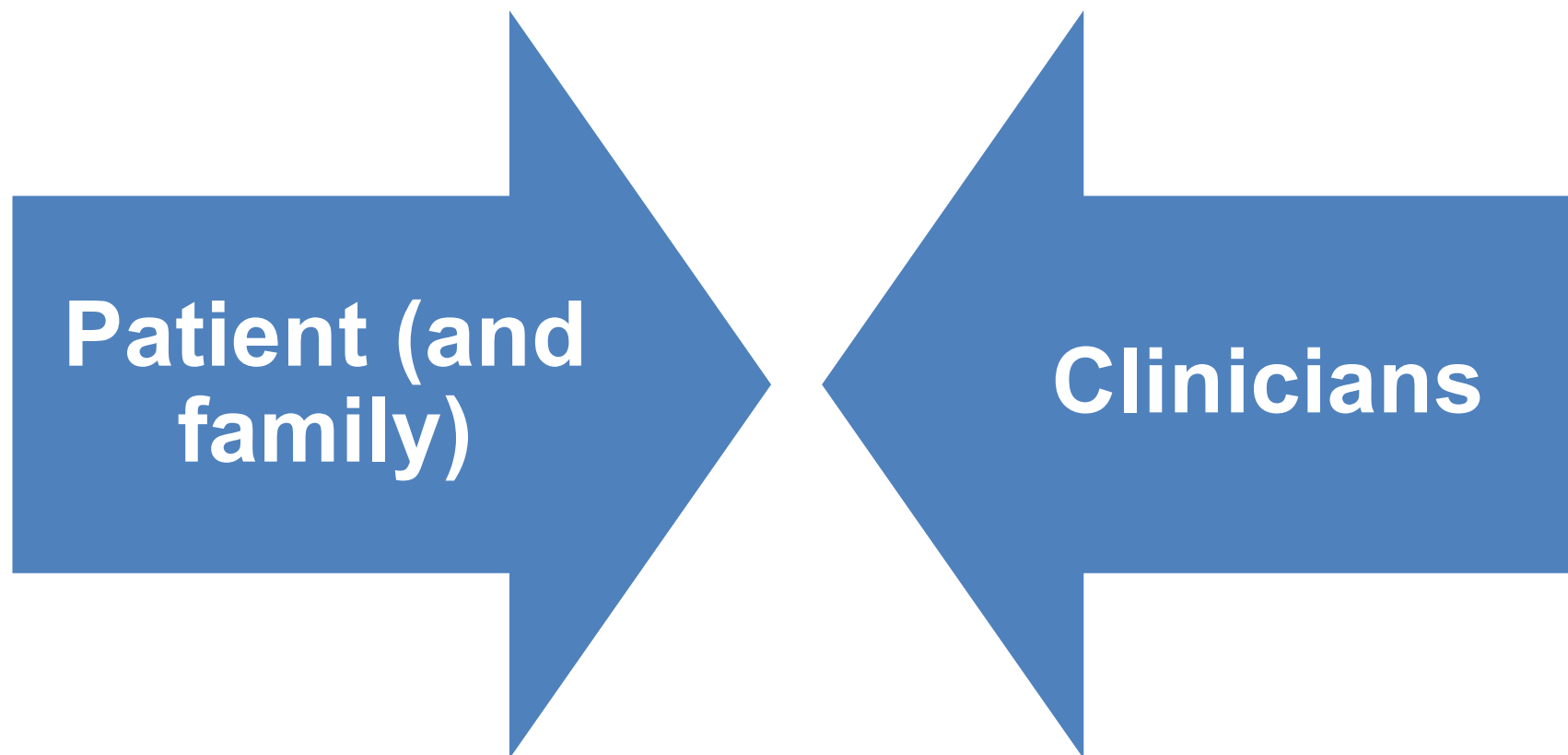


**Appointment
scheduled at least
7 days in advance
in PCC**

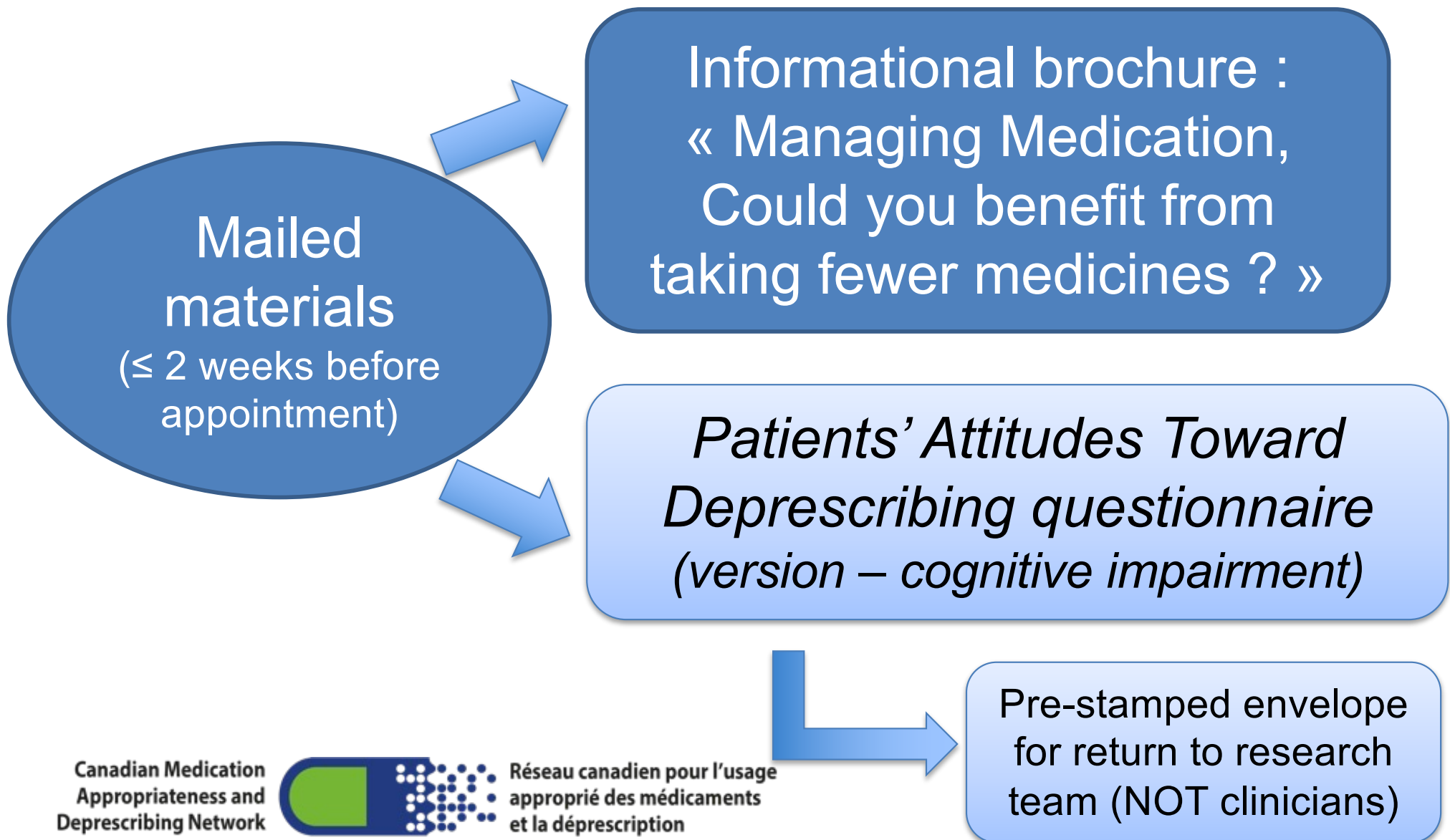
Inclusion criteria - Clinicians

- Clinicians caring for adult patients in clinic area targeted for trial
- Primary target = PHYSICIANS
 - Other clinical staff (ex: advanced practice nurses) included if they attend PCC provider meetings.

Intervention : Two components



Intervention – Patient (and family) component




Intervention – Clinician component

Educational presentation (15-20 min) + PPMD

Monthly « Tip sheets » x 11 and 1 poster

Electronic notification (patient mailing)

Table 1 Tip Sheet topics for OPTIMIZE clinician intervention




1	Clinician guidance for deprescribing – an overview
2	Introduce deprescribing to patients
3	Deprescribing to improve troubling symptoms 
4	Prescribing is a discussion opportunity
5	Recognize prescribing cascades
6	Reduce burden through deprescribing
7	Consider treatment deintensification
8	Discontinue risky medications to avoid adverse outcomes
9	Deprescribing as patients approach the end of life
10	Discuss deprescribing with family and friends
11	Don't forget about over the counter products
12	Summary document: deprescribing poster listing Tip Sheet topics

DEPRESCRIBING TO IMPROVE TROUBLING SYMPTOMS

"For any troubling symptom, think about medication side effects first!"

Example medications: Nortriptyline, oxybutynin, selected anti-hypertensives

Try these phrases:

-  "The [symptom] you mention may be due to your [xxx] medicine"
-  "Certain medicines may cause new side effects because our bodies change over time."
-  "Reducing your total number of medications may help you feel better overall."

Make a plan to monitor symptoms:

- Please call the nurse in 1 – 2 weeks to let us know how you are feeling without / with a lower dose of [medication]

Outcomes : at 6 and 12 months

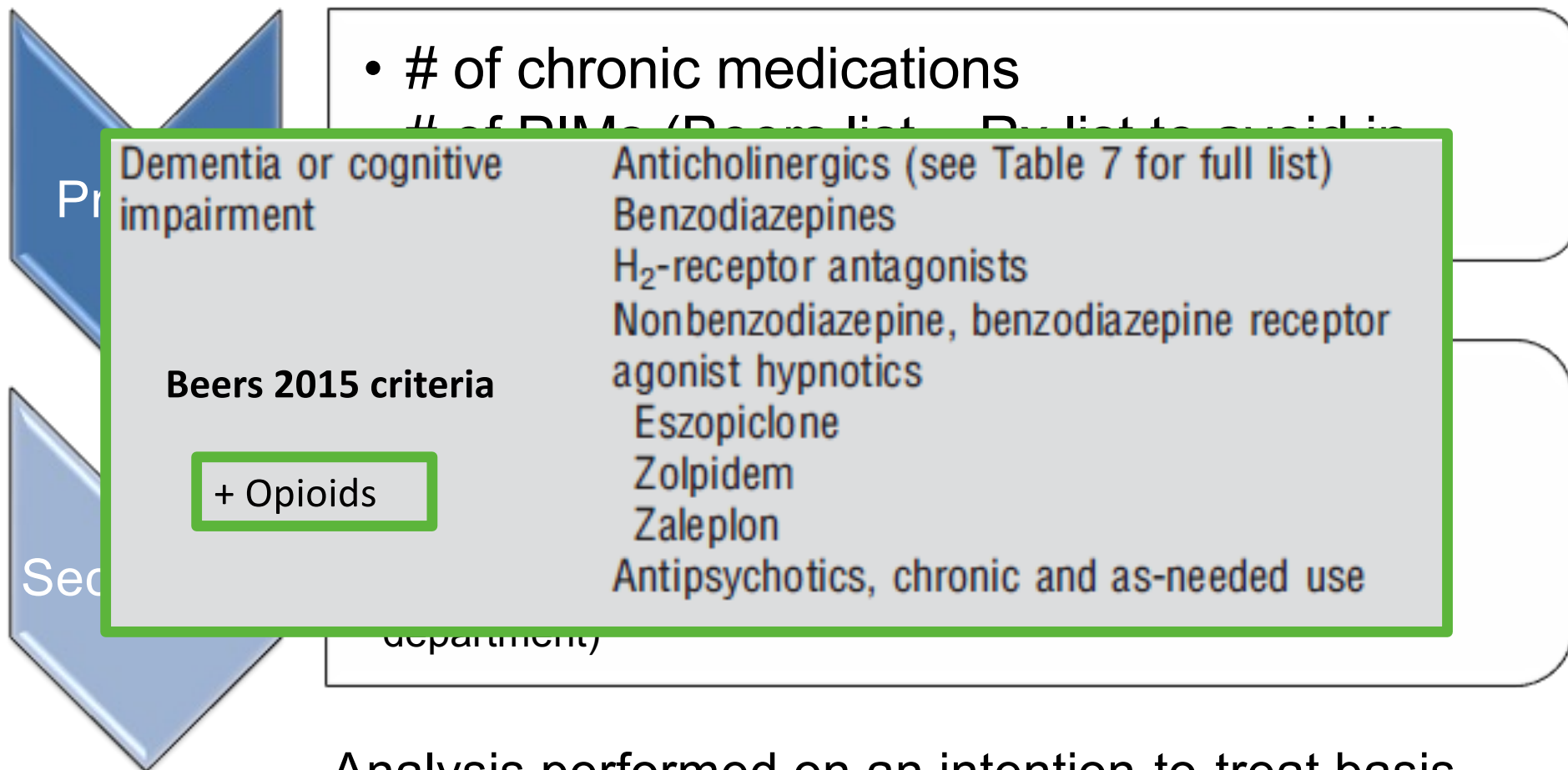


- # of chronic medications
- # of PIMs (Beers list – Rx list to avoid in cognitive impairment + opioids)



Analysis performed on an intention-to-treat basis

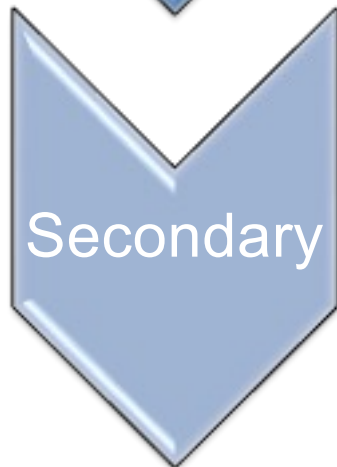
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Outcomes : at 6 and 12 months



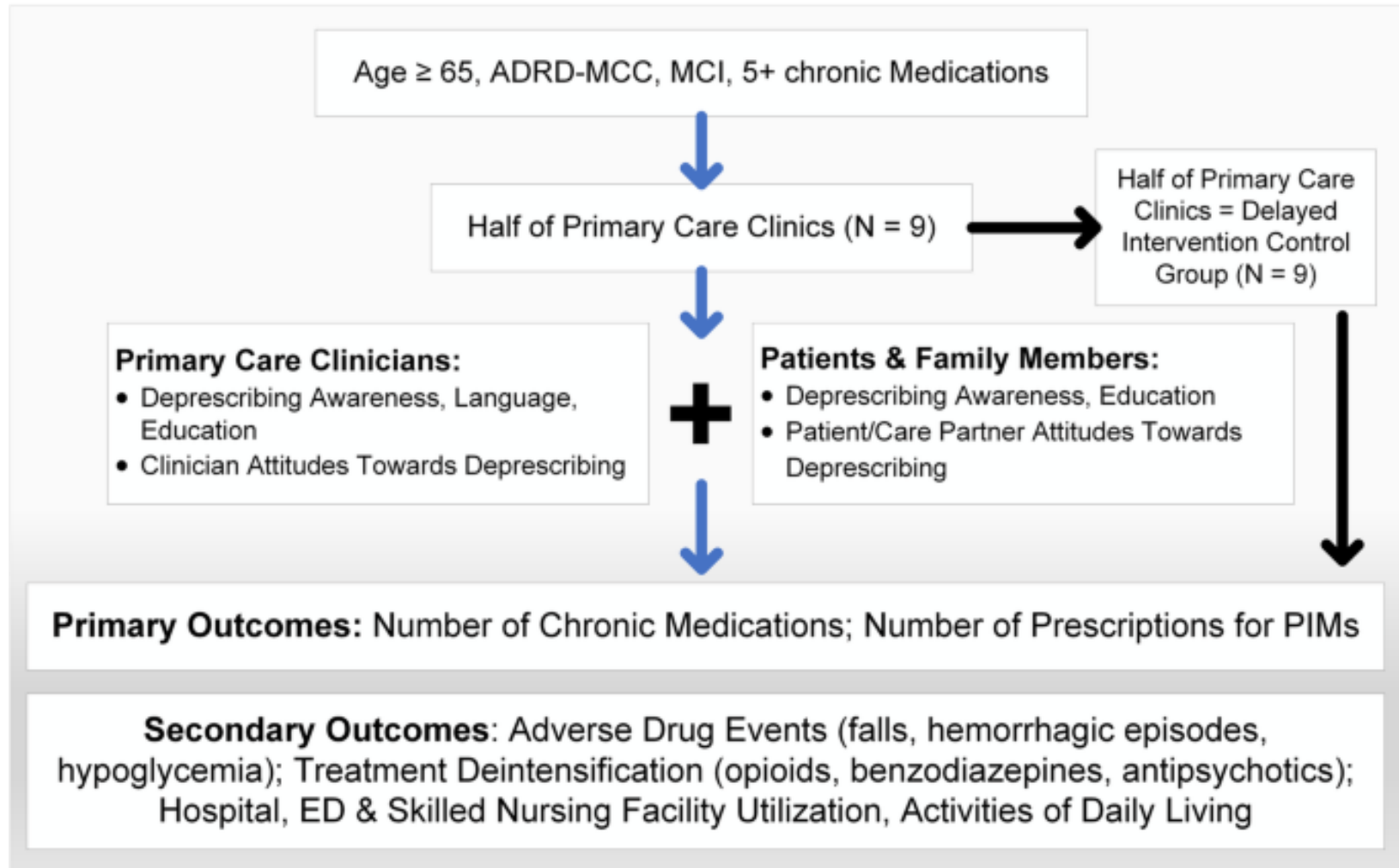
- # of chronic medications
- # of PIMs (Beers list – Rx list to avoid in cognitive impairment + opioids)



- # PIM starts
- Dose reductions for selected PIMs *
- Rates of ADEs (falls, hemorrhagic events, hypoglycemia)
- Ability to perform ADLs
- Admissions (Skilled nursing facility, hospital, emergency department)

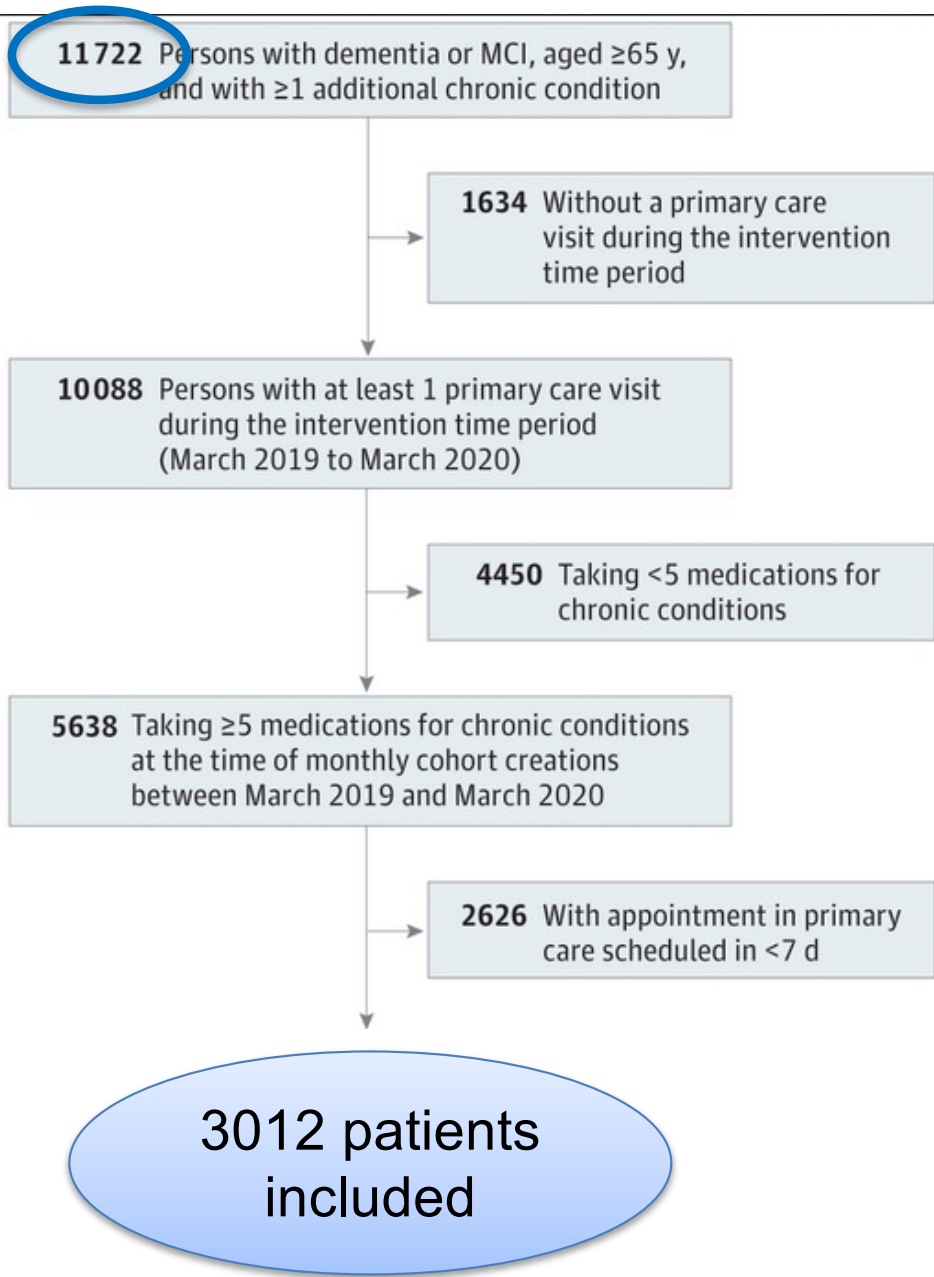
Analysis performed on an intention-to-treat basis

Optimize Cluster Randomized Trial Design

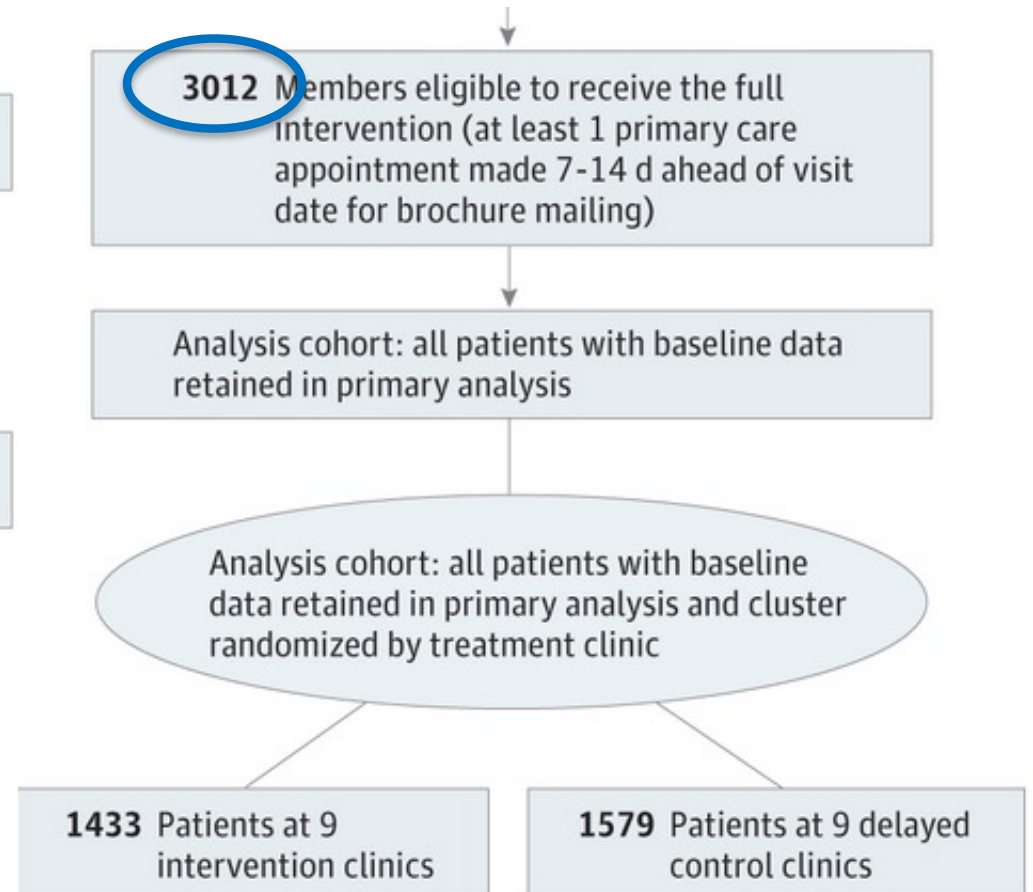


ADRD: Alzheimer's Disease and Related Dementias; MCC: Multiple Chronic Conditions; MCI: Mild Cognitive Impairment; PIM: Potentially Inappropriate Medications; ED: Emergency Department

Bayliss EA. *Trials*. 2020;21(1):542.



Flow diagram



Population- comparable groups

Baseline characteristic	Intervention (n = 1433)	Control (n = 1579)
Age, mean (SD)	80.1 (7.2)	79.9 (7.5)
Female sex (%)	56	55
Non-Hispanic, White (%)	78	77
Long-term medications, mean (SD)	7.0 (2.1)	7.0 (2.2)
≥ 1 PIM (%)	30.5	29.6
Chronic conditions, mean (SD)	8.5 (3.2)	8.6 (3.2)
MCI only (%)	22.3	21.7
2 nd brochure mailing (%)	28.5	30.7

PIMs targeted for outcomes

Classes	Most common examples (<i>Number of persons with 1+ in full cohort</i>)
Anticholinergics	
Antidepressants	
Antihistamines	
Antimuscarinics (Overactive bladder)	
Antispasmodics	
Antipsychotics	
Benzodiazepines	
Nonbenzodiazepine hypnotics	
H2-receptor antagonists	
Opioids	

Which class of PIMs do you think was most frequently used ?



PIMs targeted for outcomes

Classes	Most common examples (<i>Number of persons with 1+ in full cohort</i>)
Anticholinergics	
Antidepressants	Nortriptyline (53), paroxetine (20)
Antihistamines	Hydroxyzine (32)
Antimuscarinics (Overactive bladder)	Trospium (589), oxybutynin (49)
Antispasmodics	Dicyclomine (65), atropine (46)
Antipsychotics	Quetiapine (670), olanzapine (206), risperidone (161)
Benzodiazepines	
Nonbenzodiazepine hypnotics	
Zolpidem	(30)
H2-receptor antagonists	
Opioids	
Oxycodone SA (1245), hydrocodone (890), morphine (368)	



PIMs targeted for outcomes

Classes	Most common examples (<i>Number of persons with 1+ in full cohort</i>)
Anticholinergics	
Antidepressants	Nortriptyline (53), paroxetine (20)
Antihistamines	Hydroxyzine (32)
Antimuscarinics (Overactive bladder)	Trospium (589) , oxybutynin (49)
Antispasmodics	Dicyclomine (65), atropine (46)
Antipsychotics	Quetiapine (670), olanzapine (206), risperidone (161)
Benzodiazepines	Lorazepam (208), clonazepam (203)
Nonbenzodiazepine hypnotics	Zolpidem (30)
H2-receptor antagonists	Ranitidine (362), famotidine (309)
Opioids	Oxycodone SA (1245), hydrocodone (890), morphine (368)

Results – Primary outcome (at 6 months)

of Chronic Medications

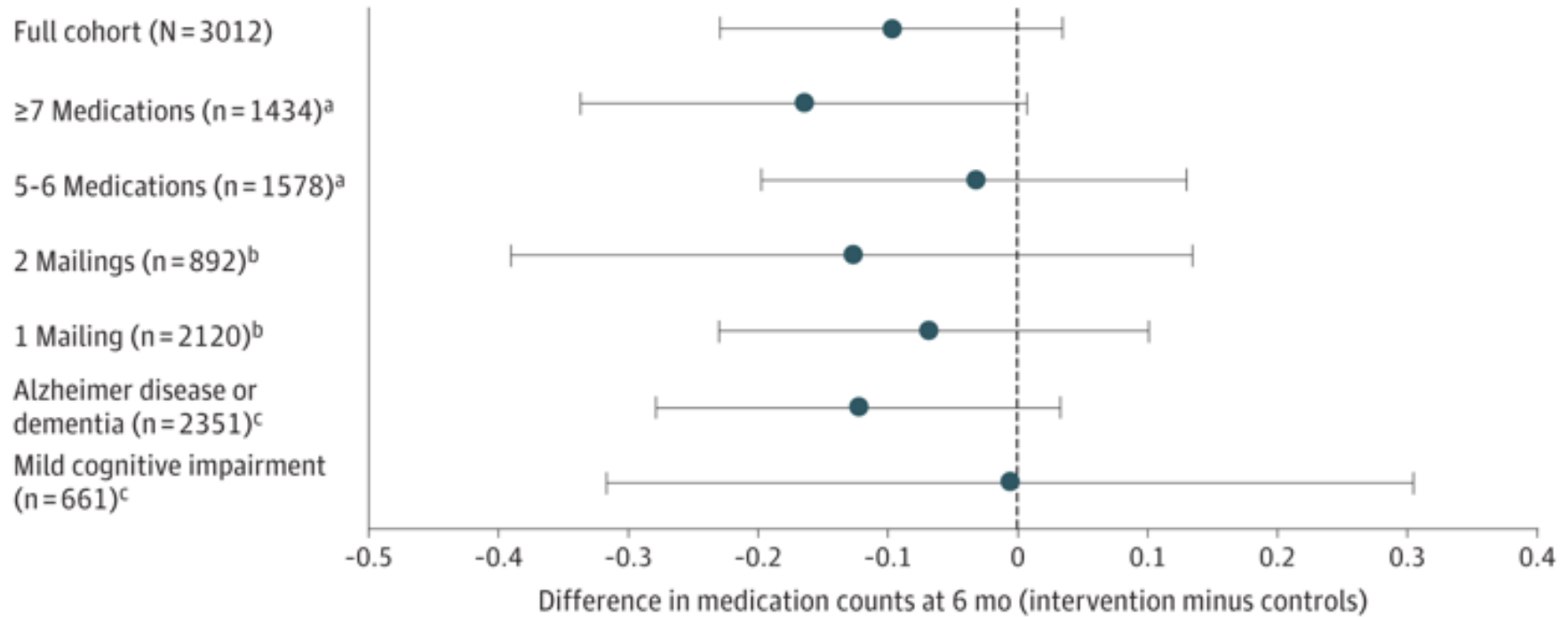
	Baseline	At 6 months	Adjusted difference at 6 months (95% CI)
Control	7.0	6.5	-0.1 (-0.2 to 0.04) P = 0.14
Intervention	7.0	6.4	

% of Persons Prescribed ≥ 1 PIMs

	Baseline	At 6 months	Adjusted difference at 6 months (95% CI)
Control	29.6 %	20.9 %	-3.2 (-6.2 to 0.4) P = 0.08
Intervention	30.5 %	17.8 %	

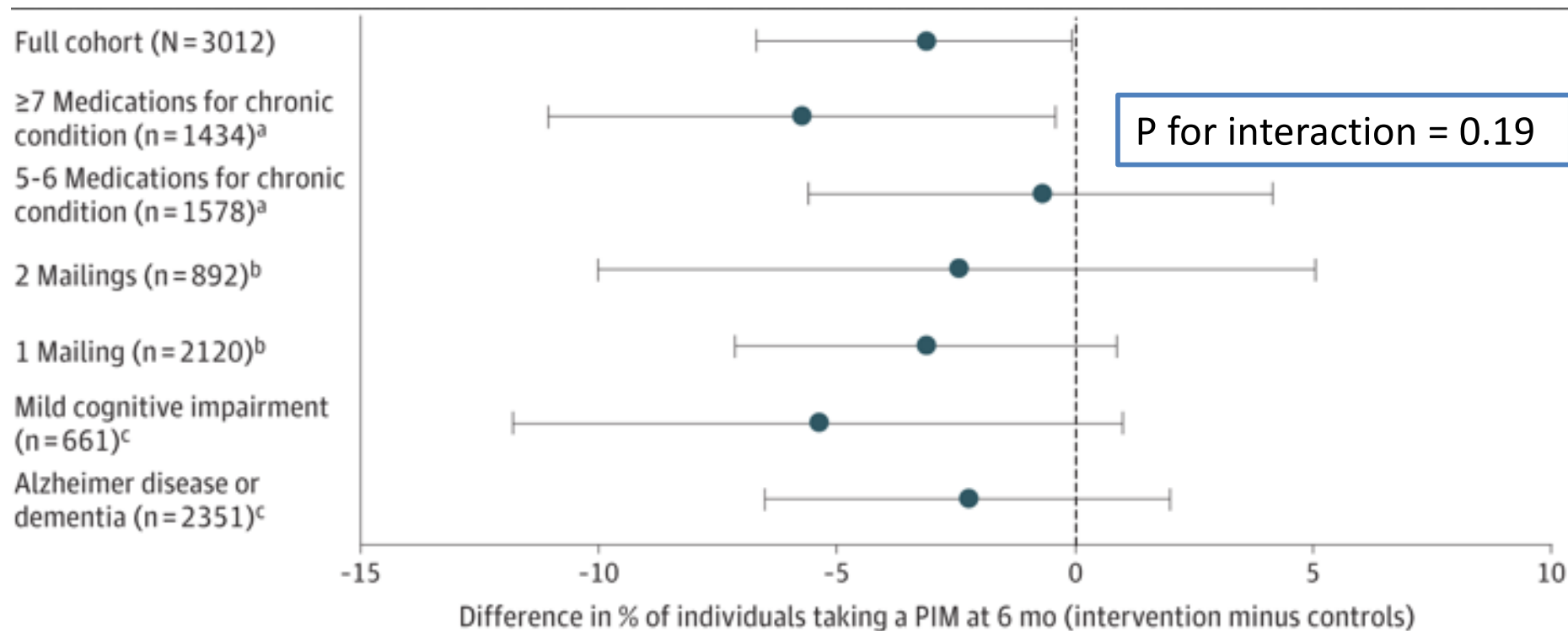
Results - Subgroup analysis

chronic medications:



Results - Subgroup analysis

% of Persons Prescribed ≥ 1 PIMs:



Authors conclusion

- Large-scale educational deprescribing intervention for older adults with cognitive impairment taking 5 or more long-term medications and their primary care clinicians demonstrated small effect sizes and did not significantly reduce the number of long-term medications and PIMs.
- Such interventions should target older adults taking relatively more medications.

Back to clinical case



Mrs M. : Eligible for study ?

- ✓ Cognitive impairment
- ✓ ≥ 65 years old
- ✓ ≥ 5 chronic medications
- ✓ ≥ 1 additional chronic medical conditions

Mrs M. – REAL Medication list reviewed with her

- ~~Telmisartan 40 mg po Daily (not taking since amlodipine started recently)~~
- Amlodipine 5 mg po Daily
- Bupropion SR 150 mg po Daily (Stopped x 1 week)
- Clonazepam 0.5 mg qAM + 1mg qHS
- ~~Lorazepam 1 mg po qHS~~
- Betahistine 8 mg po TID prn (occasionally)
- Bimatoprost 0.01% both eyes qHS
- Oxycodone 5 mg po QID ~~7.5 mg BID~~
- Acetaminophen LA 650 mg TID
- Esomeprazole 40 mg po BID
- Dicyclomine 20 mg po TID prn (occasionally)
- Dimenhydrinate 50 mg po q6h prn (occasionally)
- Lactulose 15-30 mL po HS prn
- PEG 3350 17 g po Daily prn
- Fosfomycine as directed for UTI
- OTC: Vitamine D



Clinical case – Mrs M.

Geriatric screening (chart review/interview)

Autonomy/Mobility :

- Walks with cane; Balance disorder (Berg 39/56) with fall last year;
- Partially dependent for iADLs; managing ADLs with some difficulties

Nutrition :

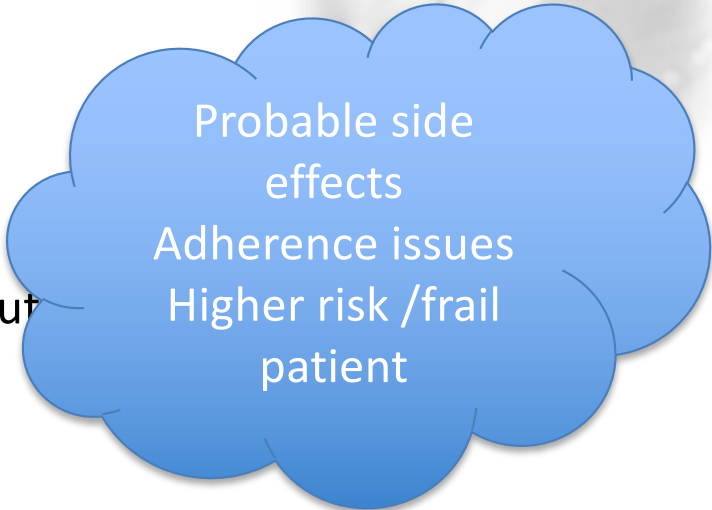
- Weight loss since hip fracture; reduced appetite; frequent nausea/heartburn
- 49 kg – BMI 21

Cognition/Mood : Anxious ++, mild memory impairment

Sleep : Good sleep; napping during daytime

Elimination : Chronic constipation; urinary urgency without

Pain : Limiting mobility – Hip, knees, back



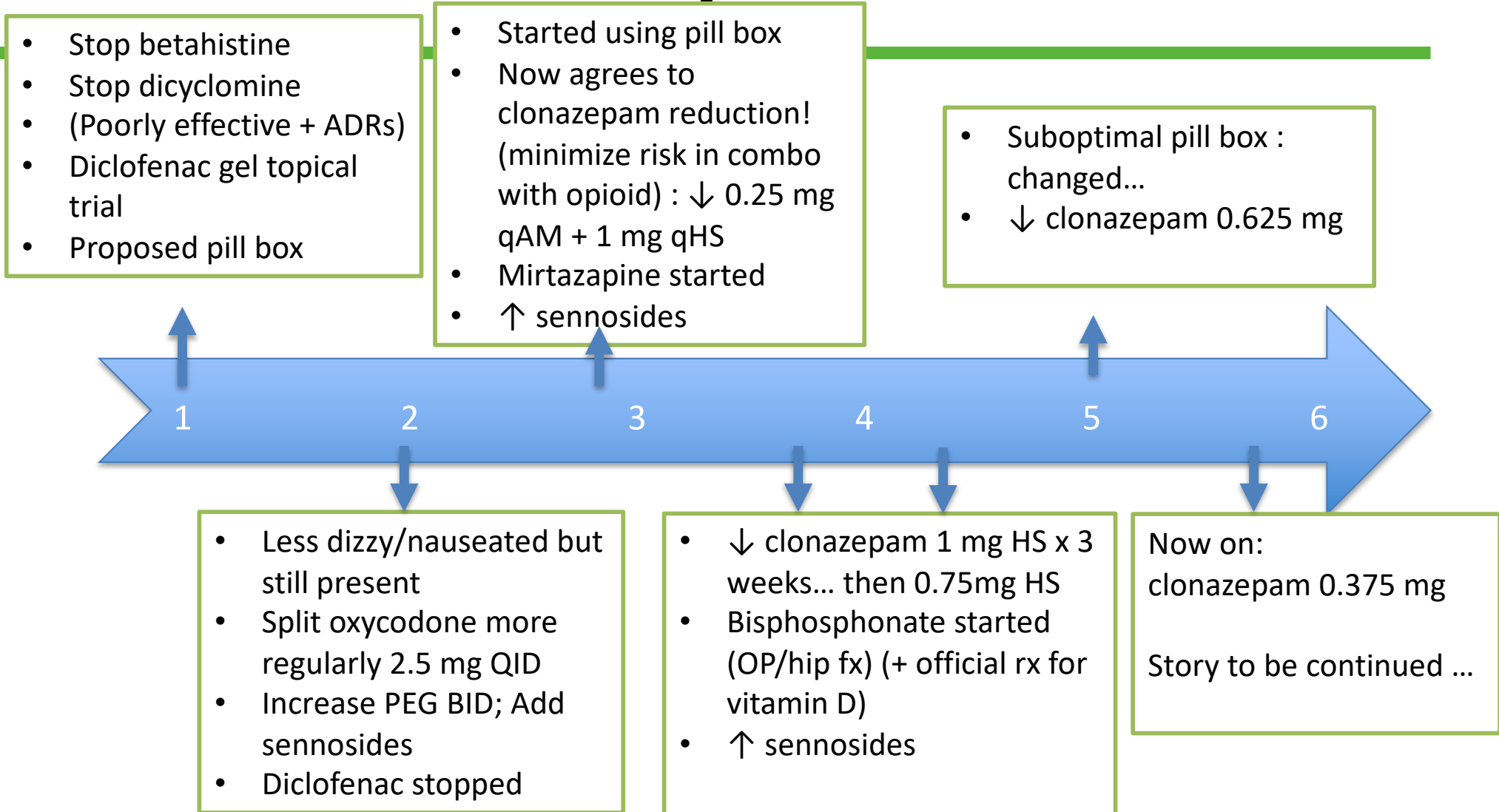
Probable side effects
Adherence issues
Higher risk /frail patient

Mrs M. – Patient attitudes toward deprescribing (selected items)

- Taking a large number of medicines ?
 - « *I'm taking only what's necessary* »
- Feeling comfortable with the number of medications taken ?
 - « *Unsure...* »
- Believing that all my medications are necessary
 - « *Uncertain...* »
- Believing one or more of my medicines may be currently giving side effects
 - « *Possibly nausea...* »
- Would be in agreement to reduce medications with appropriate follow-up of healthcare team : **YES**



Mrs M. follow-up over 6 months...



Mrs M. – Medication list (prescribed)

Baseline

- Amlodipine 5 mg po Daily
- Clonazepam 0.5 mg qAM + 1mg qHS
- Betahistine 8 mg po TID prn
- Bimatoprost 0.01% both eyes qHS
- Oxycodone 7.5 mg BID
- Acetaminophen LA 650 mg po TID
- Esomeprazole 40 mg po BID
- Dicyclomine 20 mg po TID prn
- Dimenhydrinate 50 mg po q6h prn

« Study – Primary outcome » :

➤ # medications: 12 → 13

➤ ≥ 1 PIMs : YES → YES

At 6 months

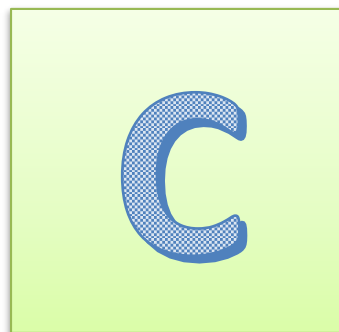
- Amlodipine 5 mg po Daily
- Clonazepam 0.325 mg qHS
-
- Bimatoprost 0.01% both eyes qHS
- Oxycodone 5 mg qAM + 2.5 mg TID
- Acetaminophen LA 650 mg po TID
- Esomeprazole 40 mg po BID
-
-
- Lactulose 15-30 mL po HS prn
- PEG 3350 17 g po BID
- Fosfomycine as directed for UTI
- Mirtazapine 15 mg qHS
- Sennosides 8.6 mg qAM + 17.2mg qHS
- Zoledronic acid IV
- Vitamine D

Reflection on Mrs M...

Challenges addressed... over many follow-ups !

- Initially resistant to change benzo:
 - Trust built over time
 - Deprescribing framed in context of actual ADRs (including geriatric syndromes)
- Education provided but limited uptake – repeated info over follow-up
- Links with other physicians done as needed

Discussion



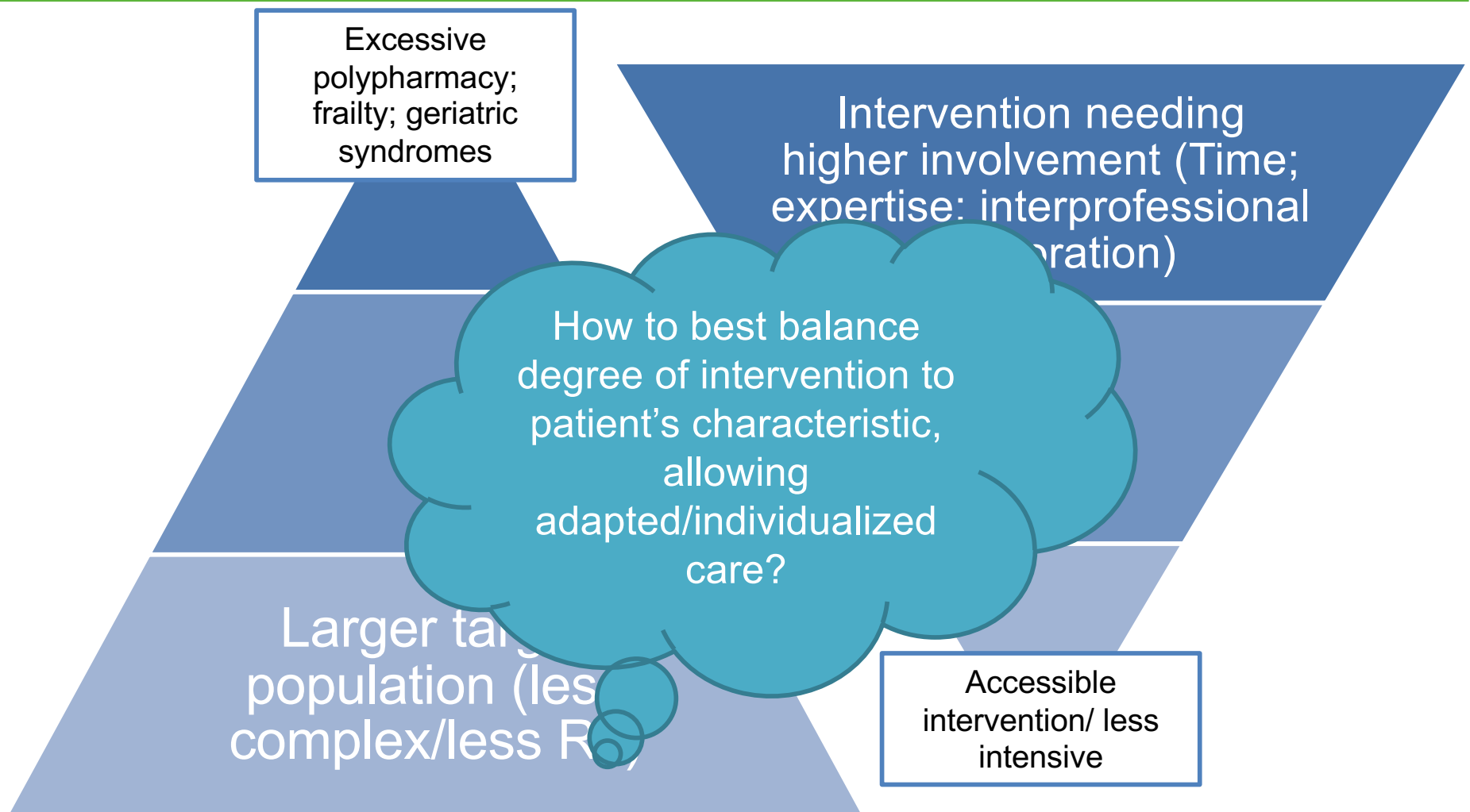
For discussion...

A green square with a blue letter 'P' inside, representing the 'Population' component of a study.

- Population :
 - + Broad inclusion criteria for pragmatic « real life » study; large sample size
 - Select more complex patient (polypharmacy?)
 - Select higher risk patient ?
- Intervention
 - + Targeted patient + clinicians (Education/empowerment)
 - ? Time sufficient / Specific follow-up required
 - ? Targeted patient education needed (ex: class specific with specific risk and non pharmacologic approaches)
 - ? More support needed for clinician (ex: coaching)
 - ? PATD helpful for clinician
 - ? Degree of pharmacist involvement

A green square with a blue letter 'I' inside, representing the 'Intervention' component of a study.

For discussion...

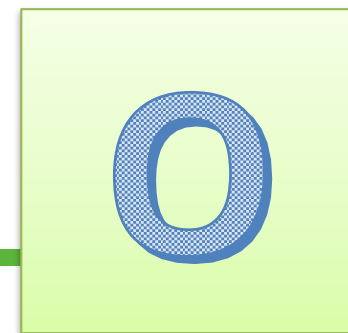


For discussion...



- Control group :
 - Reduction of PIM also seen in control group
 - Deprescribing as hot topic... Increasing as part of usual care ?
 - How to differentiate specific intervention...
 - « Trospium » case...

For discussion...



Primary outcomes : NS but are they the real target?

- Total number of Rx: Not reflecting quality of prescribing (may be unchanged... or increased!)
 - % with at least 1 PIM : Difficult to change if multiple PIMs
- NB: 12 months results not reported in article

Secondary outcomes:

- Not reported in article (Dose reduction; new PIM; ADEs; ADLs performance; admissions/visits)

Targeting PIMs for cognitive impairment vs global review (in context of multiple chronic conditions):

- Other medications might be the priority depending of clinical status
- Missing information on « real prevalence »... (? Antipsychotics for BPSD/sleep vs psychiatric diagnosis)
- Anti-H2 : Removed from Beers 2019 criteria (vs PPI)
- Opioids : Stopping often difficult in practice for chronic pain. Limited efficacy of coanalgesics (and many are also PIMs !)

What is the ideal «Rx outcome » ?

- Ex: Total # of PIMs; PIMs with other tool (ex: STOPPFall); Drug Burden Index

Intervention designed to activate patient/clinicians ... Did a conversation about Rx occurred ?



And what is your perspective ?



References

- Bayliss EA, Shetterly SM, Drace ML, et al. Deprescribing Education vs Usual Care for Patients With Cognitive Impairment and Primary Care Clinicians: The OPTIMIZE Pragmatic Cluster Randomized Trial. *JAMA Intern Med.* 2022;182(5):534-542.
- Bayliss EA, Shetterly SM, Drace ML, et al. The OPTIMIZE patient- and family-centered, primary care-based deprescribing intervention for older adults with dementia or mild cognitive impairment and multiple chronic conditions: study protocol for a pragmatic cluster randomized controlled trial. *Trials.* 2020;21(1):542.
- Green AR, Boyd CM, Gleason KS, et al. Designing a Primary Care-Based Deprescribing Intervention for Patients with Dementia and Multiple Chronic Conditions: a Qualitative Study. *J Gen Intern Med.* 2020;35(12):3556-3563.