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US Deprescribing Research Network

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

National Institute on Aging (R21/33-AG057289)

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Housekeeping

- All participants will be muted
- Enter **all questions** in the Zoom **Q&A/chat box** and send to Everyone
- Moderator will review questions and ask them at the end
- Want to continue the discussion? Associated podcast released about 2 weeks after Grand Rounds
- Visit impactcollaboratory.org
- Follow us on Twitter & LinkedIN:


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https://www.linkedin.com/company/65346172

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- Pilot Awards
- Junior Investigator Intensive and Webinars
- Data and Resources
- Upcoming events
  - June Webinar
  - Possible Supplement on BZRA drugs and complementary and integrative health

Disclosures

- Cynthia Boyd co-authors a chapter on multimorbidity for UptoDate and reviewed a chapter on Falls for Dyna-Med.
- Elizabeth Bayliss has no disclosures.

Publications

Perspectives on Deprescribing Communication in Primary Care *Journal of General Internal Medicine* **36**, 1122 (2021)

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JAMA Intern Med. Published online March 28, 2022. doi:10.1001/jamainternmed.2022.0502

JAMA Network™

OPTIMIZE Cluster Randomized Pragmatic Trial

Learning Objectives

Upon completion of this presentation, you should be able to:

- Understand the approach used to conduct a pragmatic trial of deprescribing education in primary care
- Describe cognitively impaired populations that may benefit from deprescribing education in primary care
- Discuss potential adaptations of a deprescribing education intervention in a large health system

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Deprescribing:
Reducing or stopping medications for which potential harms outweigh potential benefits

Optimize Trial Development (R21 phase): Develop educational materials and intervention

Aim 1: Engage patient, family caregiver (care partner), clinician, and health system stakeholders to enhance and refine a primary care based deprescribing intervention among people with Alzheimer's Disease and Related Dementia(ADRD) and Multiple Chronic Conditions(MCCs) in Kaiser Permanente Colorado.

Aim 2: Pilot test the intervention to establish feasibility and acceptability among patients, family caregivers (care partners), clinicians, and health system stakeholders.

Intervention design: Stakeholder engagement

Establish trust

"I have complete trust in the doctor... He explains things well. 'If I'm going to stop this I'll replace it with this. Or... This medication... has these side effects. Would you prefer to stop it?'" (Patient)

Frame deprescribing as positive, routine

"I'm looking at the whole person and not just one organ system... These medications take years or decades... to have an effect. And I think that we should focus on what can help you right now." (Physician)

Align deprescribing with goals of dementia care, including symptom management

"You're going down this track. What good is [this medication]?... It's not going to prolong life." (Caregiver)

"I fought for the Ativan because… I know what we go through… I hear what they are saying but I will take that chance." (Caregiver)

Provide educational materials and suggested language

"[The brochure] is a good conversation starter [for older adults who may be accustomed to a time when] you did not question the doctor." (Caregiver)

"It's not an easy conversation to say, 'I think your life expectancy is about 3 years and this statin is not going to benefit you.'" (Physician)

Engage the entire health care team

"We rely on [clinical pharmacists]—….we need their help sorting through it [or] giving us guidance on... the best plan to wean [a medication]." (Physician)

"There's not much substitute for frequent visits, close contact... And making sure they realize you care." (Physician)

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Green, A.R., et al. *J GEN INTERN MED* **35,** 3556–3563 (2020).

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Aims for pragmatic trial (R33)

Aim 1: In a cluster randomized pragmatic trial, test the effectiveness of a primary care based, clinic-level deprescribing intervention on two primary outcomes: number of chronic medications and number of PIMs among seniors with ADRD-MCC.

Hypothesis: A patient-centered intervention will reduce number of chronic medications and number of potentially inappropriate medications (PIMs) among seniors with ADRD-MCC.

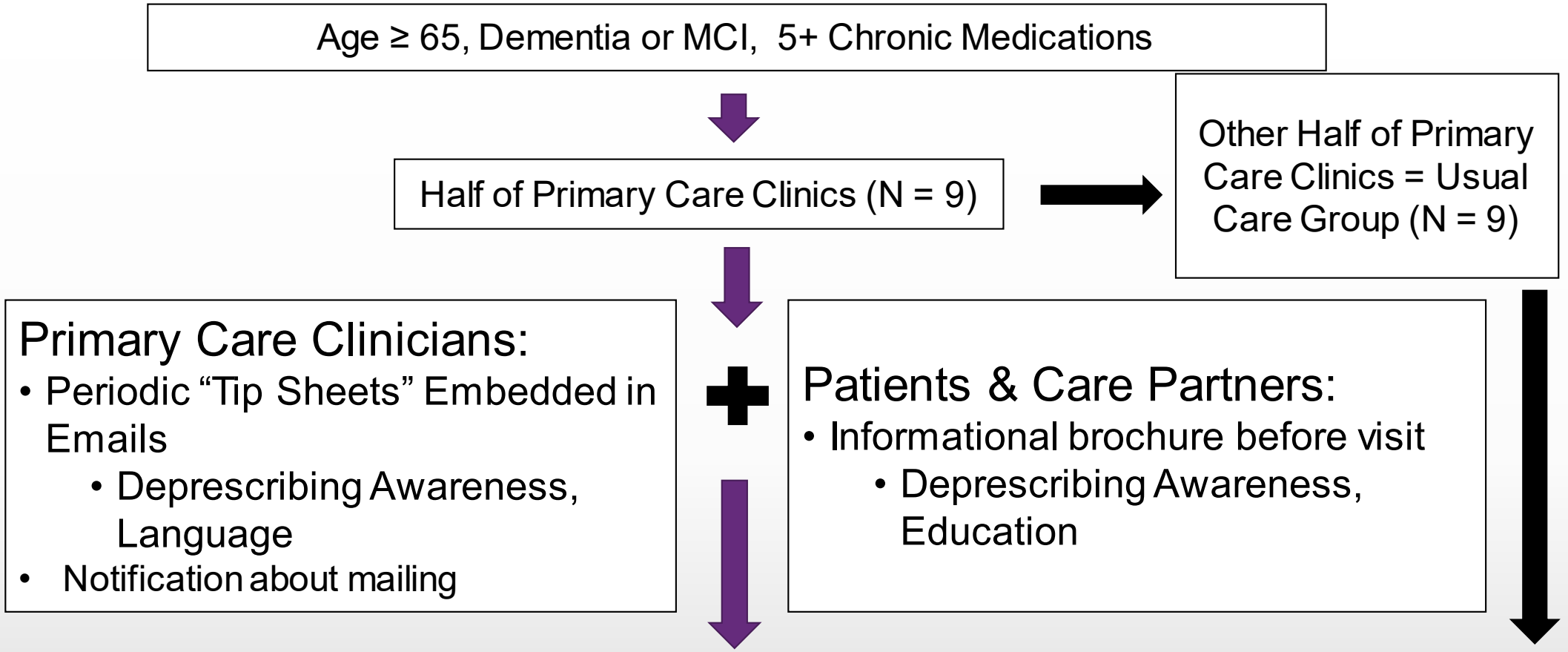
Aim 2: Evaluate the effect of the intervention on secondary outcomes of adverse drug events (falls, bleeding episodes, hypoglycemic episodes), reduction in dosage for selected PIMs (benzodiazepines, opioids, antipsychotics), hospital, emergency department and skilled nursing facility utilization, and activities of daily living.

Aim 3: Explore mechanisms of intervention effectiveness through post hoc qualitative interviews with patients, family caregivers, and clinicians and descriptive analyses quantifying outpatient office visit length.

Setting: Kaiser Permanente Colorado (KPCO)

- Integrated healthcare delivery system
  - Members choose a primary care provider (PCP)
  - Primary and specialty care
- Over 569,000 members across 30 medical offices.
  - Nineteen medical offices in the Denver/Boulder area
- Virtual data warehouse: Common data model
  - Diagnosis, utilization, EHR clinical data, demographics, health plan enrollment, pharmacy dispensing

Optimize: Cluster Randomized Trial Design



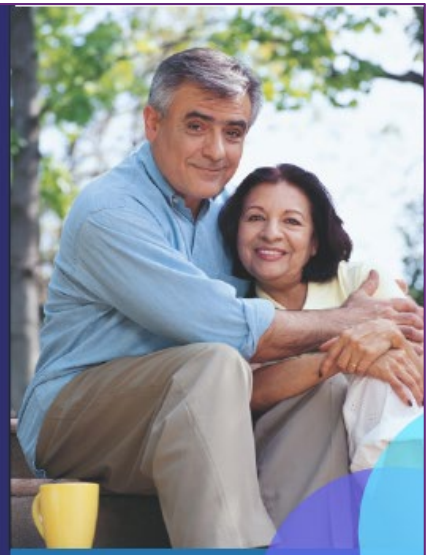
Outcomes: Number of Chronic Prescribed Medications; Proportion of Individuals with One or More Potentially Inappropriate Medications (PIMs)

Patient / Family Members Educational Brochure

QUESTIONS FOR THE DOCTOR

MANY MEDICINES SHOULD NOT BE STOPPED.

ALWAYS TALK TO THE DOCTOR BEFORE STOPPING A MEDICINE.



MANAGING MEDICATION

Could you benefit from taking fewer medicines?

KAISER PERMANENTE
INSTITUTE FOR HEALTH RESEARCH COLORADO

COULD YOU SAFELY TAKE FEWER MEDICINES?

Talking about medicines with your doctor

Consider talking to your doctor about whether one or more of your medicines could be safely stopped.

Why some people take fewer medicines

- Possible benefits and harms from medicines may change over time
- Some medicines cause sleepiness, confusion, dizziness and falls
- Many people feel better when they take fewer medicines
- There may be ways to treat your health problems without medicine

What To Do

Plan for your next visit

At your next visit start a conversation with your doctor about your medicines. If someone comes to your visits with you, share this information with them before the visit.

Review your medicines

Bring a list of your medicines to your next visit. And, if you can, bring along your pill bottles too.

Write down some notes and questions for your doctor about medicines

Write down any questions you may have about your medicines and take these notes to your next visit.

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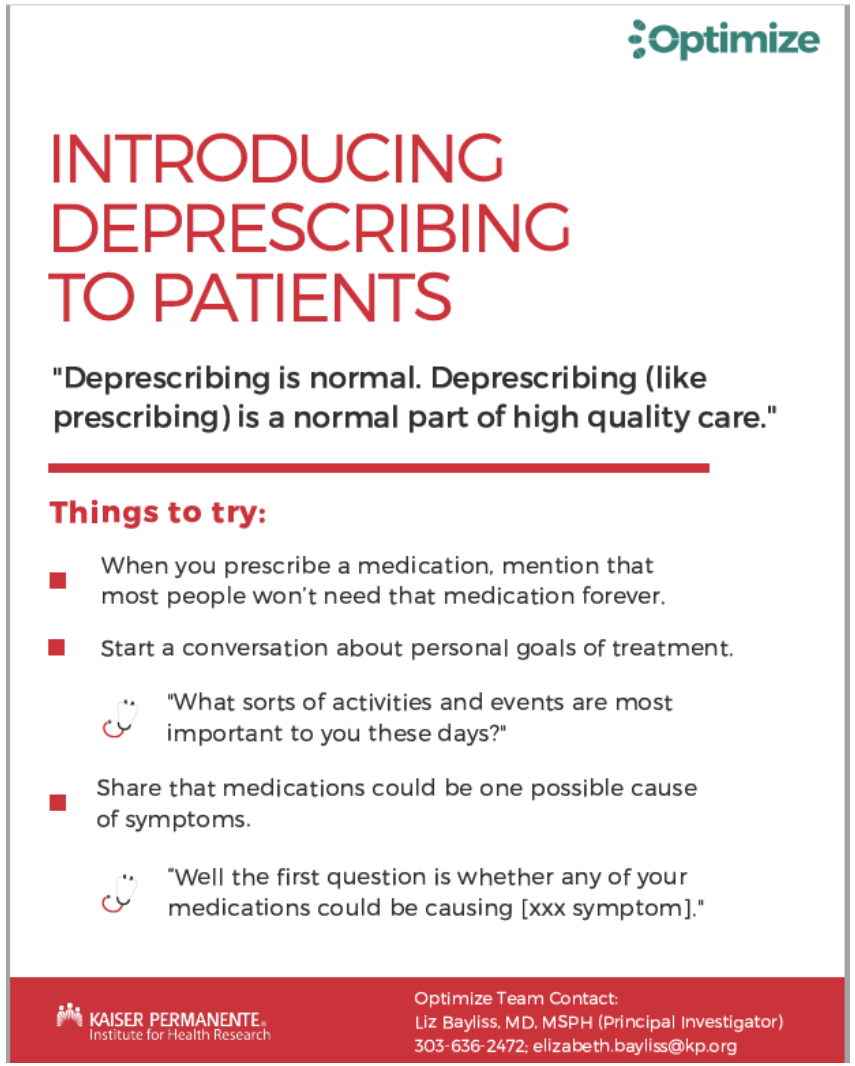
Providers: Deprescribing "Tip Sheet" for specific situations – handed out at monthly provider meetings for 1 year



Optimize

INTRODUCING DEPRESCRIBING TO PATIENTS

"Deprescribing is normal. Deprescribing (like prescribing) is a normal part of high quality care."

Things to try:

- When you prescribe a medication, mention that most people won't need that medication forever.
- Start a conversation about personal goals of treatment.
  - "What sorts of activities and events are most important to you these days?"
- Share that medications could be one possible cause of symptoms.
  - "Well the first question is whether any of your medications could be causing [xxx symptom]."

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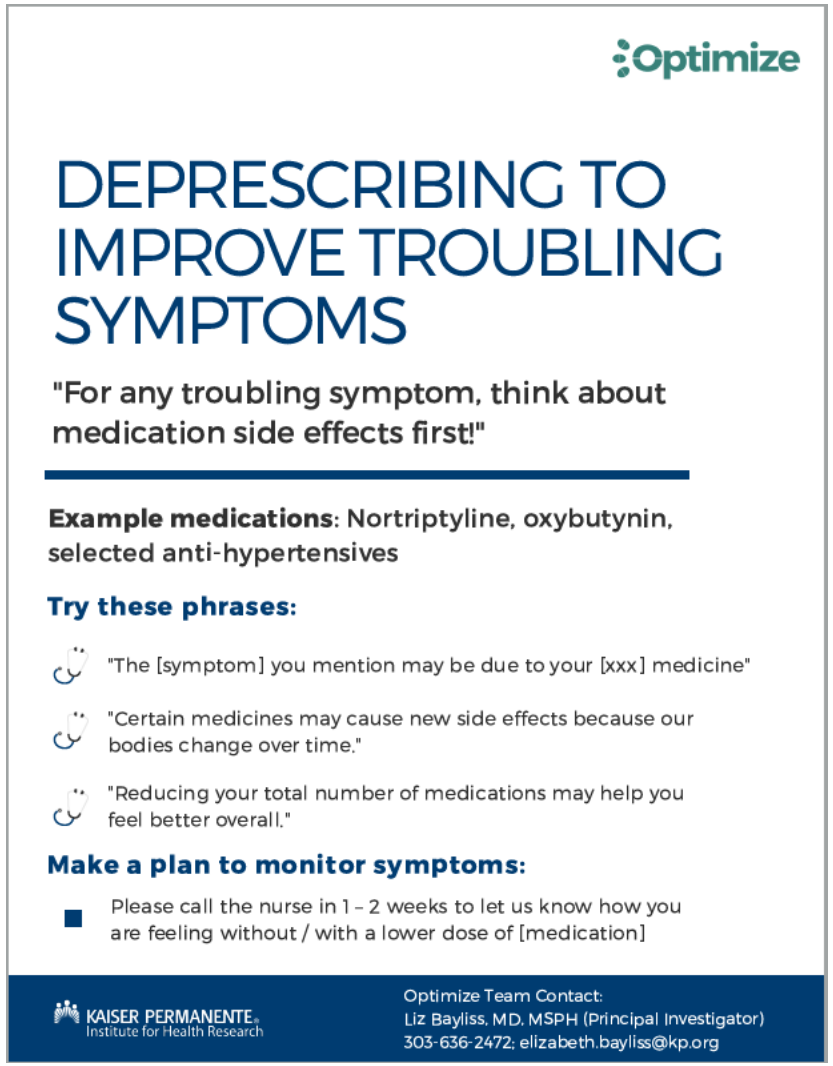

Optimize

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]

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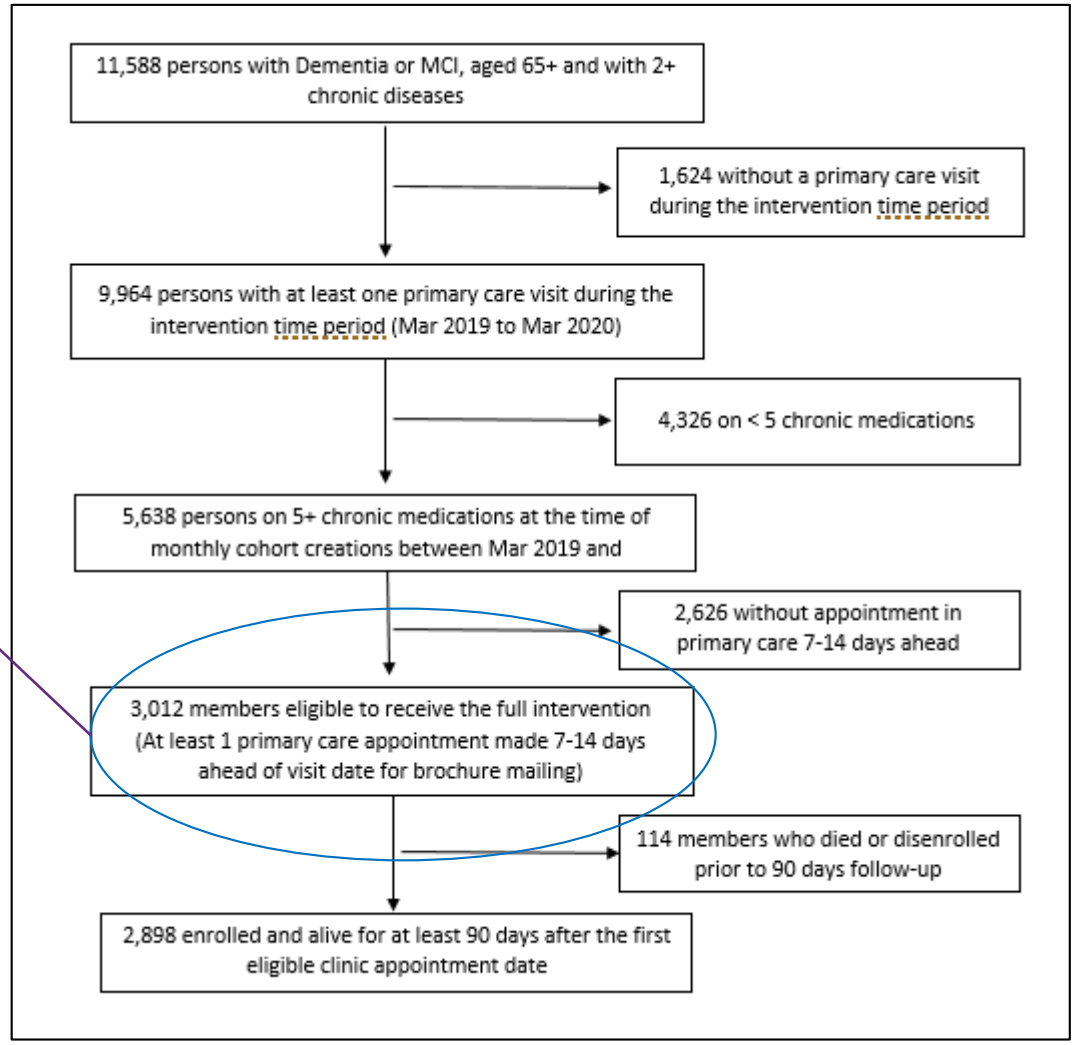
Appointment note
Optimize brochure to patient

Intervention cohort

Analyzed Results



Characteristics of study population

Characteristic	Intervention N=1,433 (47.6%)	Control N=1,579 (52.4%)	P value*
Baseline:			
Mean age in years (SD)	80.1 (7.22)	79.9 (7.48)	0.48
Female sex	56.3%	55.4%	0.62
Ethnicity / Race			<0.001
Hispanic	8.2%	16.4%	
Non-Hispanic White	77.9%	77.2%	
Non-Hispanic, non-white	12.8%	5.3%	
Missing	1.1%	1.1%	
Mean number (SD) of chronic medications at baseline	7.0 (2.13)	7.0 (2.15)	0.83
Percent with 1+ PIM at baseline	30.1%	29.6%	0.58
Mean number (SD) of chronic conditions at baseline	8.5 (3.19)	8.6 (3.20)	0.32
Mild Cognitive Impairment diagnosis only	22.3%	21.7%	0.69
Received (or eligible for) second brochure mailing	28.5%	30.7%	0.19
History of hospice at baseline	1.6%	2.1%	0.33
Follow-up:			
Died during 6-month follow up	6.2%	6.0%	0.77
Disenrolled from health plan during 6-month follow up	2.2%	1.8%	0.52
Hospice during 6-month follow up	4.2%	4.1%	0.85

*P value , 0.05 was used as a significance threshold from Chi-square tests except for age and mean number of chronic meds and conditions at baseline (T-test). SD: Standard deviation; PIM: Potentially Inappropriate Medication

Intervention vs. Control: Number of Long-term Medications

Study population	N	Group	Outcome estimates at six months (CI)[b]	Unadjusted difference (CI) p value	Adjusted difference[c] (CI) p value
Full cohort (N=3,012)	1,433	Intervention	6.42 (6.32, 6.52)	-0.10 (-0.23, 0.03) p=0.12	-0.10 (-0.23, 0.04) p=0.14
	1,579	Control	6.52 (6.43, 6.61)		
Restricted to 90+ days follow-up (N=2,898)	1,374	Intervention	6.43 (6.33, 6.53)	-0.13 (-0.27, 0.01) p=0.07	-0.12 (-0.26, 0.02) p=0.08
	1,524	Control	6.56 (6.46, 6.65)		

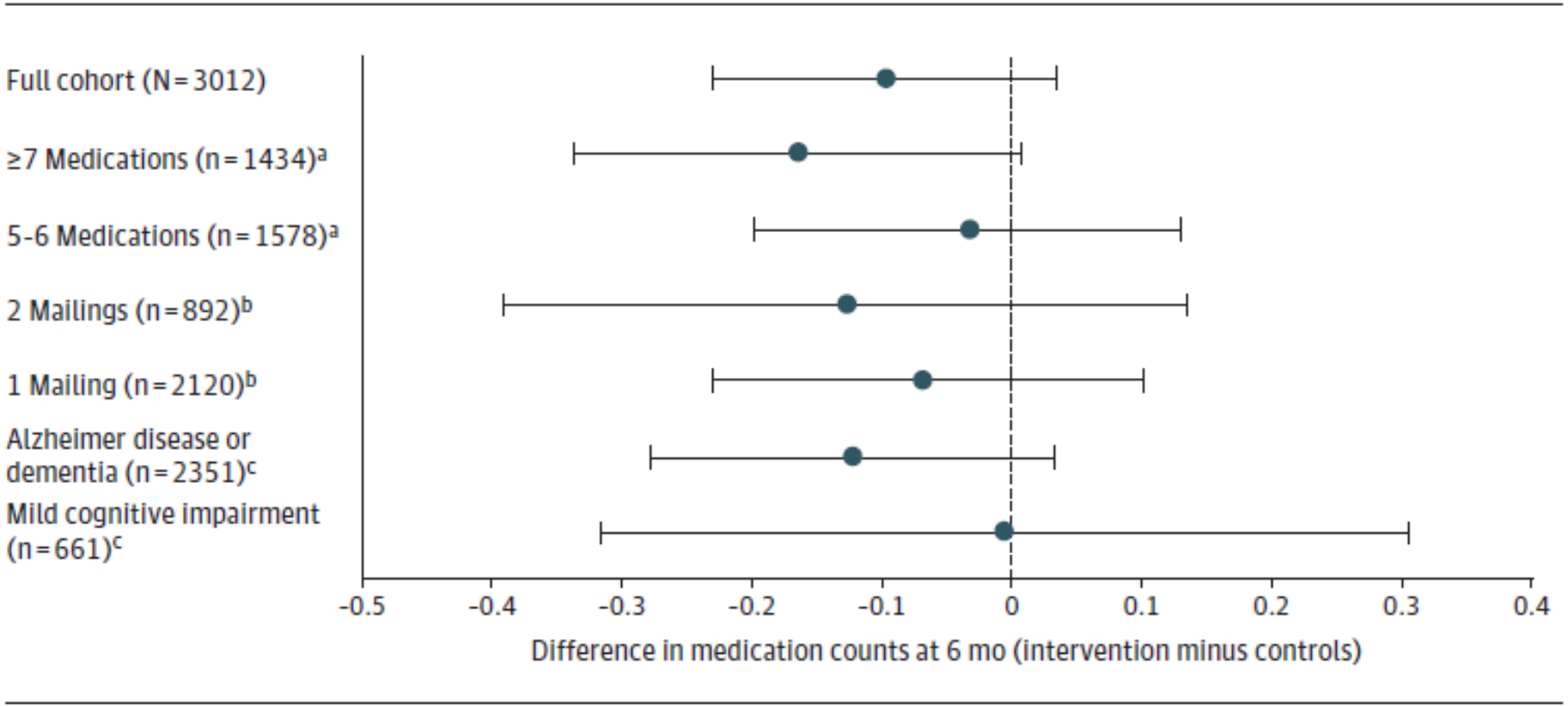
[a]Chronic medication counts at 6 months and associated intervention minus control differences were estimated using linear regression models adjusting for baseline counts of medications and a random clinic effect.
[b]CI=95% confidence intervals.
[c]Additionally adjusted for baseline age, sex and race/ethnicity.
[d]Percentage of persons on a PIM at 6 months and associated intervention minus control differences in logistic regression models adjusting for baseline number of PIMs and a random clinic effect.

Intervention vs. Control: Percentage of Persons With a PIM

Study population	N	Group assignment	Outcome estimates at six months (CI)[b]	Unadjusted difference (CI) p value	Adjusted difference[c] (CI) p value
Full cohort (N=3,012)	1,433	Intervention	17.8% (15.4, 20.5)	-3.1% (-6.2, 0.4) p=0.08	-3.2% (-6.2, 0.4) p=0.08
	1,579	Control	20.9% (18.4, 23.6)		
Restricted to persons with 90+ days follow-up (N=2,898)	1,374	Intervention	17.5% (15.0, 20.2)	-3.2% (-6.2, 0.4) p=0.08	-3.2% (-6.3, 0.4) p=0.08
	1,524	Control	20.7% (18.2, 23.4)		

[a]Chronic medication counts at 6 months and associated intervention minus control differences were estimated using linear regression models adjusting for baseline counts of medications and a random clinic effect.
[b]CI=95% confidence intervals.
[c]Additionally adjusted for baseline age, sex and race/ethnicity.
[d]Percentage of persons on a PIM at 6 months and associated intervention minus control differences in logistic regression models adjusting for baseline number of PIMs and a random clinic effect.

Subgroups: Number of Chronic Medications



Estimated differences from linear regression models accounting for baseline counts of medications, age, sex, race and ethnicity, and a random clinic effect. Subgroup models added the appropriate subgroup variable and an interaction with study group. Error bars indicate 95% CIs.

[a] Patients taking 7 or more medications vs 5 to 6 medications (P = .28 for interaction).

[b] Two mailings vs 1 mailing (P = .70 for interaction).

[c] Alzheimer disease or dementia vs mild cognitive impairment (P = .50 for interaction).

JAMA Intern Med. Published online March 28, 2022. doi:10.1001/jamainternmed.2022.0502

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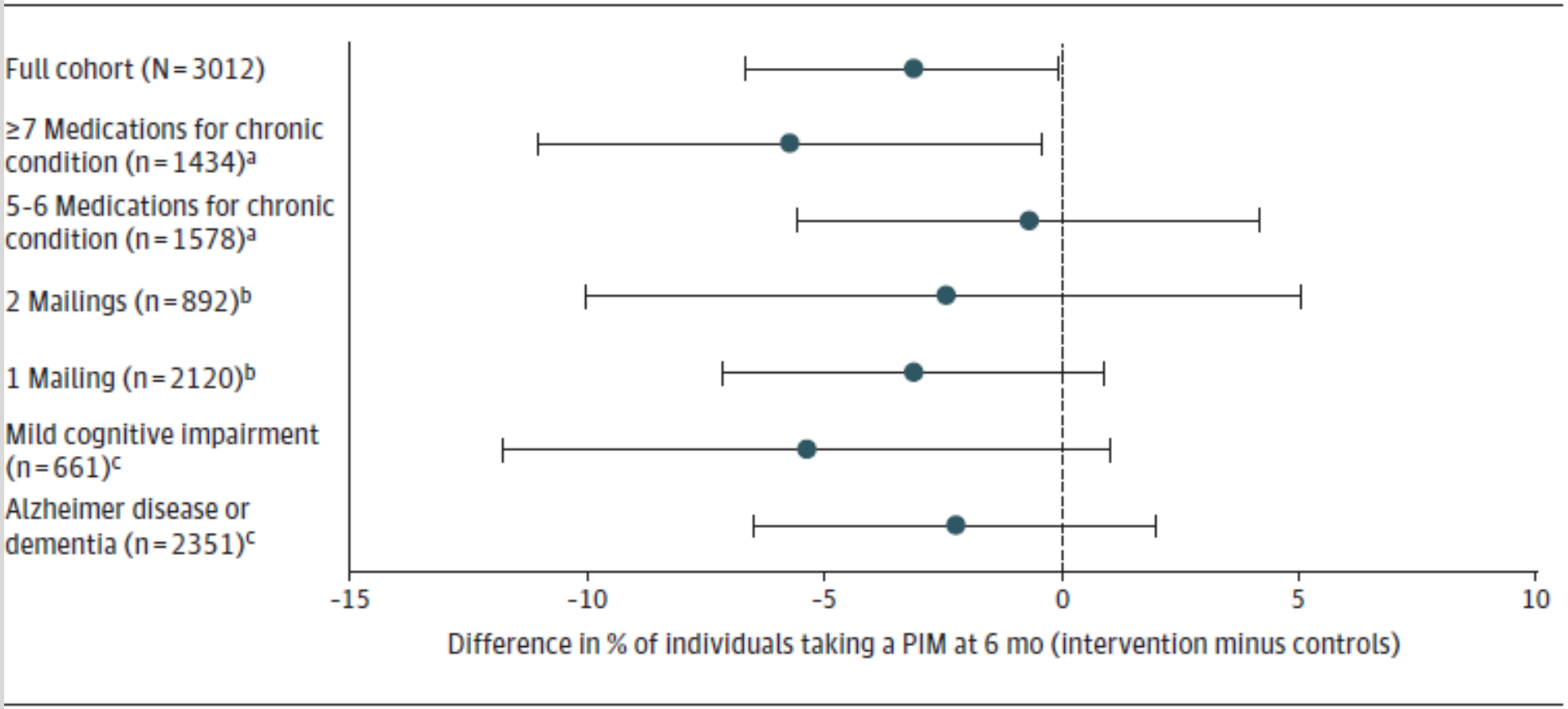
Subgroups: Proportion with ≥ 1 PIM



Estimated differences from logistic regression models accounting for baseline PIM, age, sex, race and ethnicity, and a random clinic effect. Subgroup models added the appropriate subgroup variable and an interaction with study group. Error bars indicate 95% CIs.

[a] Patients taking 7 or more medications vs 5 to 6 medications (P = .19 for interaction).

[b] Two mailings vs 1 mailing (P = .70 for interaction).

[c] Alzheimer disease or dementia vs mild cognitive impairment (P = .31 for interaction).

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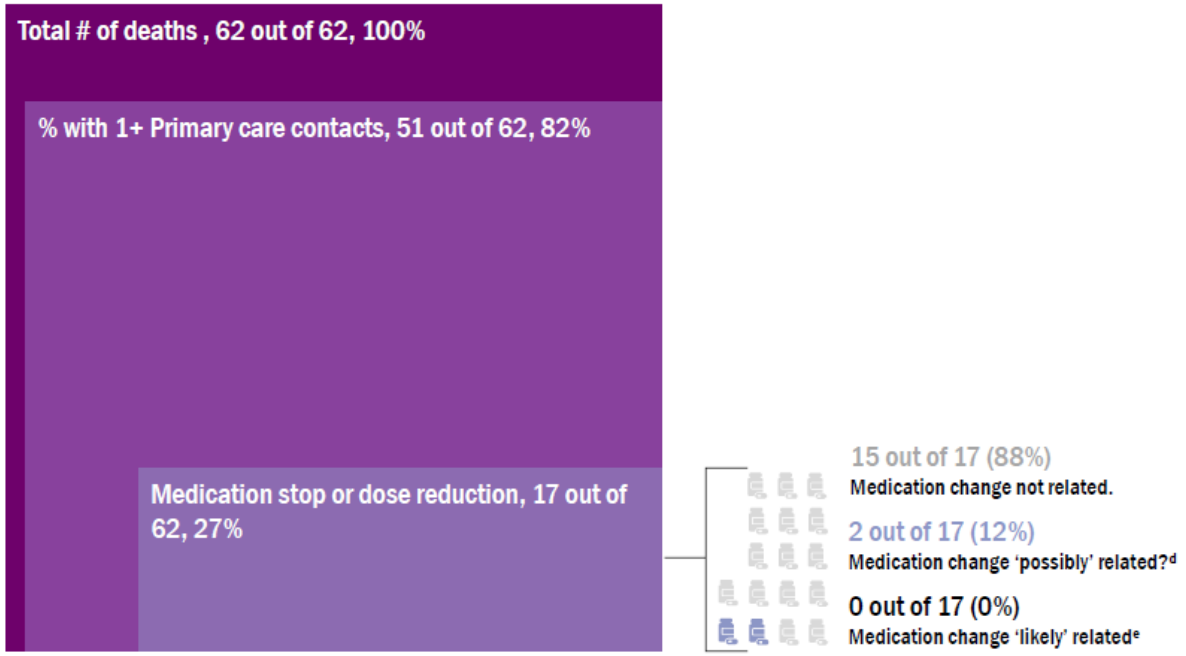
Safety monitoring: Hospitalizations 'likely' due to recent medication discontinuation intervention vs. control

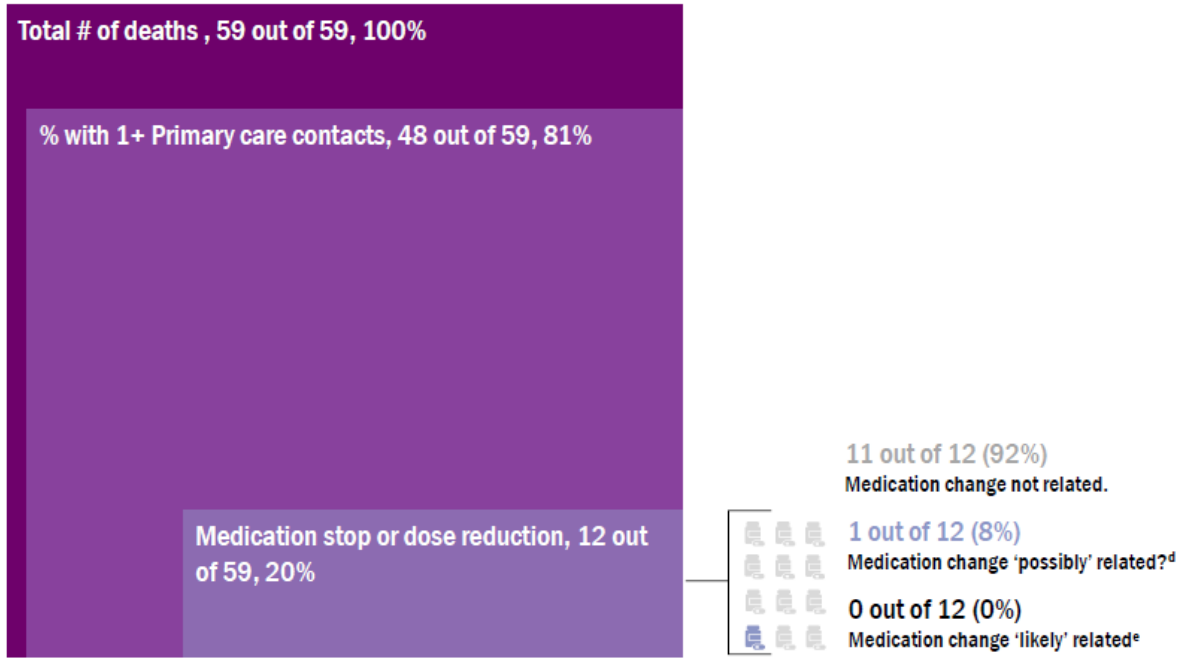
Mortality: Intervention Arm

N=1,433



Mortality: Delayed Control Arm

N=1,579



Results summary

- No reduction in number of chronic medications or proportion of individuals with PIM in primary study population
- Individuals taking 7+ medications may be better target population for similar interventions
- No evidence of serious adverse events from deprescribing education

Implications

- Feasible to conduct large scale, pragmatic cluster randomized trial in delivery system
- Taken to scale, this educational approach could….
  - Improve more distal deprescribing outcomes
  - Provide a foundation for additional medication management strategies.

Pragmatic Changes: Delayed Control Intervention

Process learnings: Patients/ family members

- Variable recollection of receiving mailings
- Caregiver role important in cognitively impaired patient population
- Appreciation for deprescribing awareness – prompted conversations with clinicians
  - Good PCP-patient relationship essential
- Limited (reported) effect on medication change
- Variable preferences on brochure mailing vs. clinic handout

Process learnings: Clinicians

- Consider handing out brochures in clinics (vs mailing)
- Translate materials into Spanish
- Expand population to include those age 75+ without cognitive impairment
- Consider focusing on 7+ medications (vs. 5+ medications)
- COVID-19 effects
  - More Virtual meetings – email Clinician Tip Sheets
  - Virtual visits could be medication review opportunities

Pragmatic changes: Delayed control design

- Expand target population
  - Age 65+, 5+ meds, with cognitive impairment
  - Age 75+, 5+ meds, without cognitive impairment
- Increase likelihood of reaching eligible patients
  - Clinic-based intervention, no need to mail brochures
  - Research team flags appointments, medical assistant hands out brochure during rooming
- Accommodate more virtual provider meetings
  - Clinician Tip Sheets sent via email (embedded)

Delayed control patient intervention process

Research team scrubs schedule daily

***MA**:*
We are working with a research team at Kaiser's Institute for Health Research. Here is a brochure on "Medication Management". Please have a look while you are waiting for the doctor.

Appointment note
Optimize brochure to patient
added to flag patient for MA
(also notifies provider)

Also available in Spanish!

Provider options during visit

Right now, you need all your medications and there is no need to discontinue any, but we may want to discuss this again in the future.

Right now, you need all your prescription medications but let's talk about OTC products.

I think you may be able to discontinue/ cut back on [medication] because [improvement in symptoms/ safety/ etc.]. Here is how you can do this…..

I think you may be able to discontinue/ cut back on [medication], but we have other important issues to address today so let's put this on the agenda for our next visit or phone call.

I think you may be able to discontinue/ cut back on [medication], and I'd like to have one of our clinical pharmacists call you to discuss all your medications

Pragmatic features of Optimize

- Embedded in healthcare delivery system
- Cluster randomization at the clinic level
- Intervention supplements but does not replace usual care (educational)
  - Delayed control intervention – education integrated with usual care
- Eligibility and Outcomes measured with clinical EHR data
- No individual level informed consent
- Prespecified sub-analyses inform future intervention deliver

Organizational engagement: Pragmatic trials

- Upper-level operations understanding, endorsement, buy-in are essential
  - Alignment with organizational goals very helpful
- Understand and work with individual clinic processes
- Follow up with clinics – maintain contact
- Clinicians are supportive of relevant projects that do not increase their work

Optimize –
How we compare to other deprescribing trials?

Differences

- Targeted drugs in general
- Pragmatic outcome measurement
- Dispensing data: unique in the U.S.
- Primary care vs. Pharmacy vs. Payor

Similarities

- Patient and family education
- Linking with a care delivery place
- Measuring number of medications

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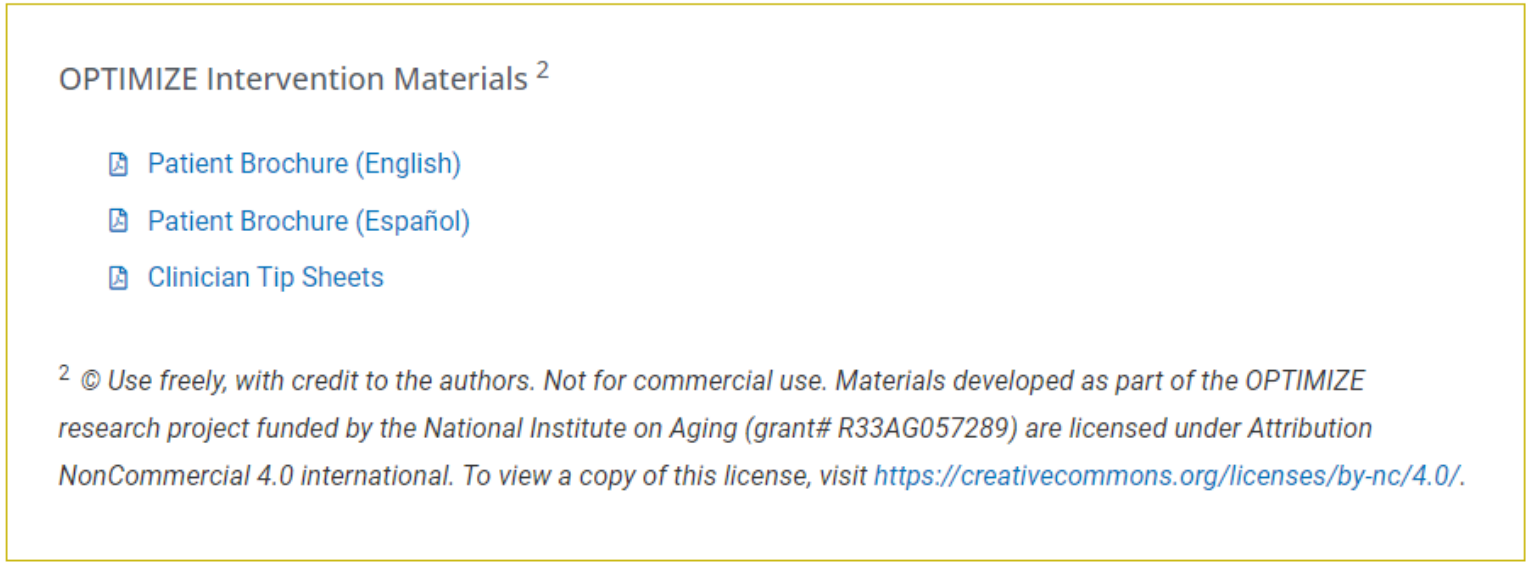
OPTIMIZE Intervention Resources

OPTIMIZE Intervention Materials

- Available for use at DeprescribingResearch.org
- https://deprescribingresearch.org/network-activities/data-and-resources/irb-dsmp-repository/optimal-medication-management-in-alzheimers-disease-and-dementia-optimize/


OPTIMIZE Intervention Materials [2]

- Patient Brochure (English)
- Patient Brochure (Español)
- Clinician Tip Sheets

[2] *© Use freely, with credit to the authors. Not for commercial use. Materials developed as part of the OPTIMIZE research project funded by the National Institute on Aging (grant# R33AG057289) are licensed under Attribution NonCommercial 4.0 international. To view a copy of this license, visit https://creativecommons.org/licenses/by-nc/4.0/.*

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Bayliss EA. Shetterly SM. Drace ML. Norton JD. Maiyani M. Gleason KS. Sawyer JK. Weffald LA. Green AR. Reeve E. Maciejewski ML. Sheehan OC. Wolff JL. Kraus C. & Boyd CM. Deprescribing Education vs Usual Care for Patients With Cognitive Impairment and Primary Care Clinicians: The OPTIMIZE pragmatic cluster randomized trial JAMA Intern Med. Published online March 28. 2022. doi.10.1001/Jamaintemmed.2022.0502

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Optimize IRB approach

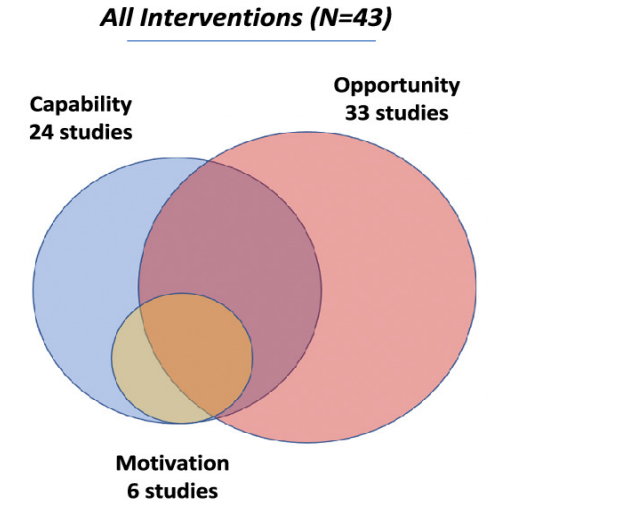
Aim	Activity	Target population	Requested consent process
Aim 1: In a cluster randomized pragmatic trial, test the effectiveness of a primary care based, clinic-level deprescribing intervention on two primary outcomes: number of chronic medications and number of potentially inappropriate medications (PIMs) among seniors with ADRD-MCC.	Send educational materials to patients (brochure and brief questionnaire). Educational presentation at department meeting. Tip sheets to clinicians at monthly department meetings.	Patients and care partners. Estimated 60-350 members per clinic. 9 clinics randomized to intervention and 9 to delayed control. Primary care clinicians who care for adults.	Waiver of informed consent. Mailing contains informational letter about the study. Letter specifies that discussing medications with PCP is optional. Waiver of informed consent. Information on the study presented to clinicians at initial department meeting as part of 15-minute deprescribing presentation. PI contact information on all clinician materials.
Aim 2: Evaluate the effect of the intervention on secondary outcomes of adverse drug events (falls, bleeding episodes, hypoglycemic episodes), reductions in dosage for selected PIMs (benzodiazepines, opioids, antipsychotics), hospital, emergency department and skilled nursing facility utilization, and activities of daily living.	Analysis of secondary outcomes.	N/ A	N/A

Deprescribing and deimplementation: Time for transformative change

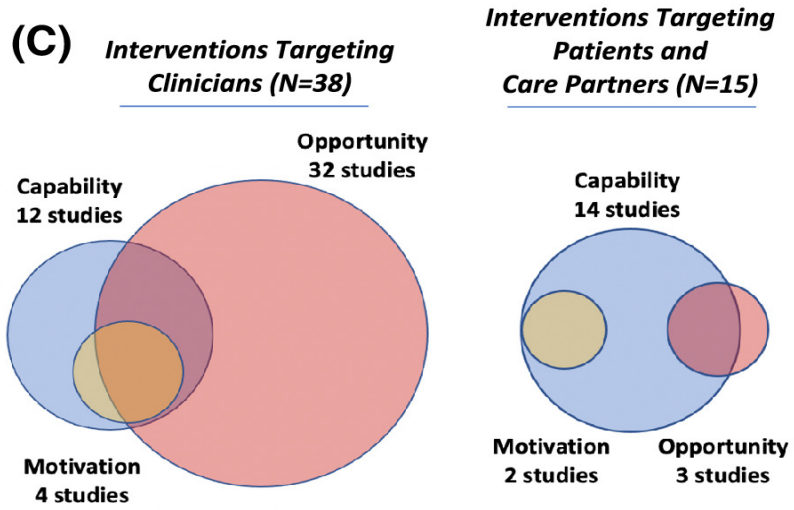
(A)

Intervention type	# of studies (N=43)	Behavior change modalities used (Capability, Opportunity, Motivation)
Interventions targeting clinicians (38 studies)		
Expert team reviews case, makes recommendations to primary clinician(s)	22	
Education provided to clinicians	7	
Decision support (e.g., point-of-care alerts), audit and feedback, other	5	
More than 1 intervention type	4	
Interventions targeting patients and/or care partners (15 studies)		
Expert team reviews case, recommendations given to patient and/or care partner	7	
Education provided to patients and/or care partner	4	
More than 1 intervention type	4	

(B)



(C)



Journal of the American Geriatrics Society, First published: 09 September 2021, DOI: (10.1111/jgs.17441)

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Thank you!

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Questions?

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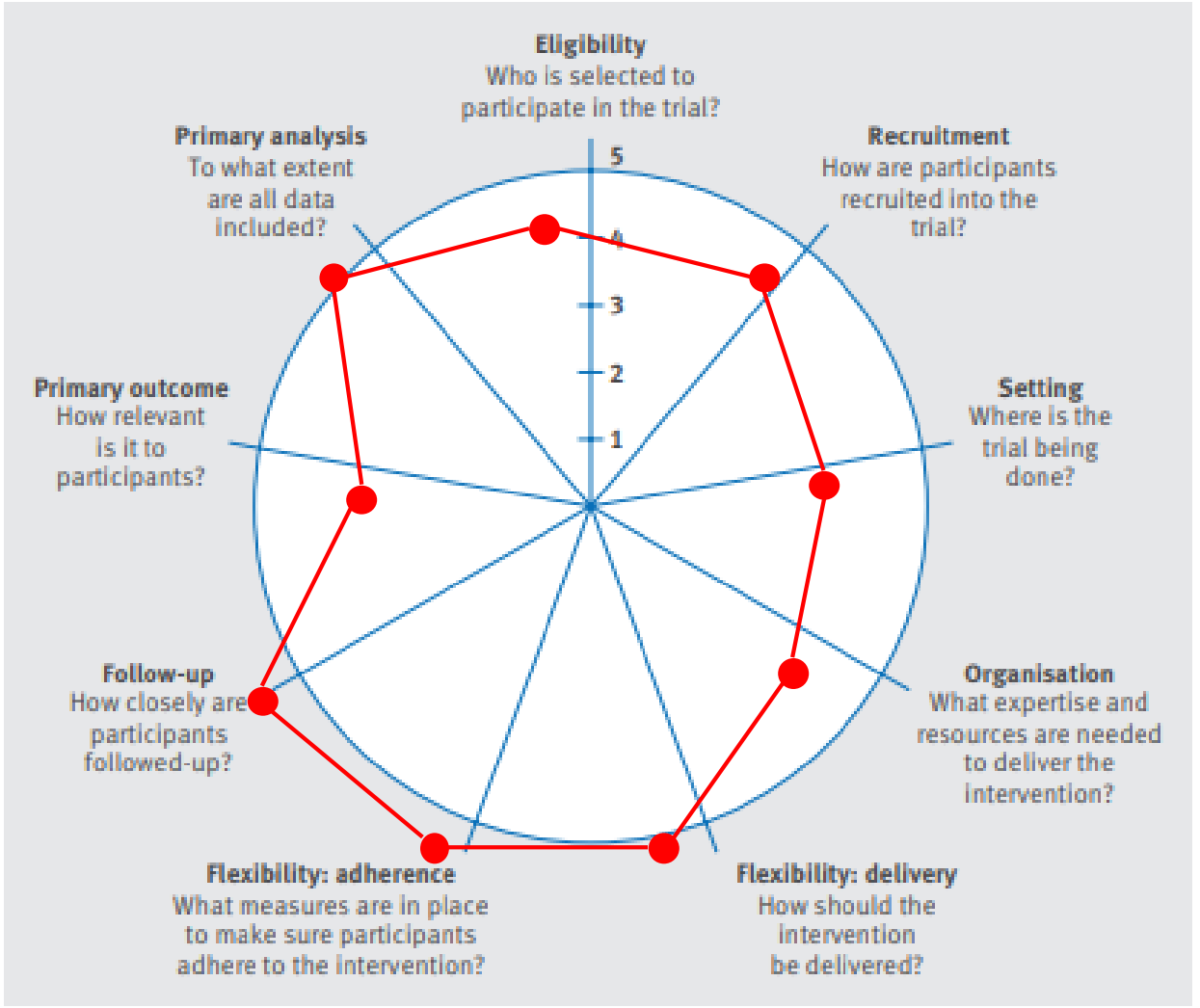
Designing a Pragmatic Trial



The PRagmatic-Explanatory Continuum Indicator Summary 2 (PRECIS-2) wheel.

Loudon K et al.
BMJ 2015;350:h2147