

Updates in Deprescribing Research Not a Trivial Pursuit!

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Disclosures

- There are no conflicts of interest.
- The views expressed are those of the presenters and do not necessarily represent the views of the Department of Veterans Affairs



Objectives



Highlight novel deprescribing literature (Jan 2019-Sept 2020)



Discuss key findings and implications



Identify gaps in knowledge and needs for future research



Stay awake. Have some fun!



1 Setting the Stage: Deintensification in long-term care

Deintensification of Diabetes Medications among Veterans at the End-of-Life in VA Nursing Homes

Joshua D. Niznik, I Maria K. Mor, PhD¹ Sydney P. Springe MPH^{1,10}, Loren J. § Thorpe, PhD, MPH

CLINICAL INVESTIGATION

Discontinuation of Statins in Veterans Admitted to Nursing Homes near the End of Life

Carolyn T. The Xinhua Zhao, I Sydney Springe Michelle Vu, Pl	Original Study Antihypertensive Deprescribing in Older Adult Veterans at End of Life Admitted to Veteran Affairs Nursing Homes
Jacob Hunnicu Joseph T. Hanl	Michelle Vu PharmD, MPH ^{a,b} , Florentina E. Sileanu MS ^a , Sherrie L. Aspinall PharmD, MSc ^{a,b,c} , Joshua D. Niznik PharmD, PhD ^{a,d,e} , Sydney P. Springer PharmD, MS ^{a,f} , Maria K. Mor PhD ^a , Xinhua Zhao PhD ^a , Mary Ersek PhD, RN ^{g,h} , Joseph T. Hanlon PharmD, MS ^{a,c,i} , Walid F. Gellad MD, MPH ^{a,i} , Loren J. Schleiden MS ^{a,j} , Joshua M. Thorpe PhD, MPH ^{a,e} , Carolyn T. Thorpe PhD, MPH ^{a,e,*}



Deintensification in long-term care

Objective: Determine the incidence and predictors of deintensification in long-term care residents

Methods: Multivariable competing risk survival analysis

- Older adults with limited life expectancy (LLE) or advanced dementia (AD)
- Admitted to US Veterans Affairs Community Living Centers, FY2009-2015

Diabetes (n=3,056)	Lipids (n=13,110)	Hypertension (n=10,574)
Hgb a1c <7.5% rx'd <u>></u> 1 hypoglycemic med	>65 yo, with CAD, CVA/TIA, DM rx'd statin for secondary prevention	SBP <120 rx'd <u>></u> 1 HTN med
Deintensification (<u>></u> 7days)	Deintensification (<u>></u> 14days)	Deintensification (7days) w/o increase/addition of HTN med
90-day follow-up	90-day follow-up	30-day follow-up



1 Deintensification in long-term care

	Diabetes (n=3,056)	Lipids (n=13,110)	Hypertension (n=10,574)
Cumulative deintensification	46%	31% (EoL documented 52%; No EoL documented 25%)	41%
Factors associated with <u>increased</u> deintensification	Sulfonylurea regimen (alone or in combo)	>15 meds	Very low SBP with multiple meds (vs. low SBP with one med)
	Documented LLE, AD	Documented LLE, AD, Age >85 (vs. 65-74) ADL dependence, poor appetite, dehydration, change in mental status, cancer, very severe aggressive behavior, swallowing difficulty,	ADL dependence, weight loss, poor appetite, dehydration, pain
		South (vs. NW)	NOK sibling (vs. spouse)
Factors associated with <u>decreased</u> deintensification	Basal insulin only Higher a1c (7-7.5 vs 6)		
	PVD	Obesity, CHF	CV risk-related conditions, DM, CHF, overweight/obesity, shortness of breath
	Admission from home/ALF (vs. hosp)	Admission from home/ALF/NH (vs. hosp)	Admission from home/ALF/NH (vs hosp) lower facility complexity



2 Clinicians: Differences in Specialties

Physician Perspectives on Deprescribing Cardiovascular Medications for Older Adults

Parag Goyal, MD, MSc, *¹ ^[D] Timothy S. Anderson, MD, MAS, MA, ^{†1} ^[D] ^[] Gwen M. Bernacki, MD, MHSA, ^{‡§} ^[] Zachary A. Marcum, PharmD, PhD, [¶] ^[] ^[] Ariela R. Orkaby, MD, MPH, ^{||} ** ^[] Dae Kim, MD, MPH, ScD, ^{††} ^[] ^[] Andrew Zullo, PharmD, PhD, ^{‡‡§§} ^[] ^[] Ashok Krishnaswami, MD, MAS, ^{¶¶|||} ^[] Arlene Weissman, PhD, *** Michael A. Steinman, MD, ^{†††‡‡‡2} ^[] and Michael W. Rich, MD^{§§§2}



2 Differences in Specialties

Objective: Characterize and compare geriatricians, general internists, and cardiologists on behaviors and attitudes via:

- 1. Frequency of reported behaviors in clinical practice
- 2. Reasons for and barriers to deprescribing

Methods: Cross sectional survey

- Deprescribing practices in the prior month
- Reasons for deprescribing
- Deprescribing selections, if any, in 9 clinical scenarios for hypothetical 79 yo woman with multiple comorbidities taking 4 cardiovascular medications
- Barriers to deprescribing



2 Differences in Specialties: Behaviors

Geriatricians General Internists Cardiologists



≪ USDeN

2 Differences in Specialties: Facilitators





Differences in Specialties: Scenarios





2

*Statistically significant differences

2 Differences in Specialties: Barriers

Geriatricians

Concern about interfering with other physicians Patient reluctance toward deprescribing Lack of patient understanding of depresribing Insufficient time to describe deprescribing to patients Medicolegal concerns Insufficient evidence of deprescribing benefits Concern about upsetting patient and/or family Insufficient time to engage in complex decision making Limited formal training on deprescribing Deprescibing is not reimbursable 0 10 20 30 40 50 60 70 80 % of Respondents

General Internists

Cardiologists



3 Compelling Clinical Arguments

JAMA | Original Investigation

Effect of Antihypertensive Medication Reduction vs Usual Care on Short-term Blood Pressure Control in Patients With Hypertension Aged 80 Years and Older The OPTIMISE Randomized Clinical Trial

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3 Clinical Arguments: OPTIMISE

Objective: Evaluate antihypertensive medication reduction and subsequent changes in systolic blood pressure and adverse events during 12-week follow-up

Methods: randomized, unblinded, non-inferiority study

- Participants: age <a>80 years, SBP <150mmHg, receiving <a>2 HTN meds
- Deprescribe single HTN medication (n = 282) versus usual care (n = 287)
- Primary outcome: SBP < 150 at 12 weeks (non-inferiority margin, RR 0.90)
- Secondary outcomes: proportion of participants maintaining medication reduction; differences in blood pressure, frailty, quality of life, adverse effects, and serious adverse events



3 Clinical Arguments: OPTIMISE

Table 2. Primary Outcome Difference in the Proportion of Patients With Clinically Acceptable Systolic Blood Pressure Lower Than 150 mm Hg at 12 Weeks

	Group, No. (%)		RD, % (97.5% 1-sided CI)		RR (97.5% 1-sided CI) ^a		_
	Medication reduction	Usual care	Unadjusted	Adjusted ^b	Unadjusted	Adjusted ^b	P value ^c
Primary analysis, No.	265	269					
SBP <150 mm Hg	229 (86.4)	236 (87.7)	-1.3 (-7.0 to ∞)	-1.5 (-7.4 to ∞)	0.98 (0.92 to ∞)	0.98 (0.92 to ∞)	.01
Per-protocol analysis, No. ^d	185	269					
SBP <150 mm Hg	161 (87.0)	236 (87.7)	-0.7 (-6.9 to ∞)	-1.6 (-8.1 to ∞)	0.99 (0.92 to ∞)	0.98 (0.92 to ∞)	.007

n = 80 excluded from analyses --66 (33.7%) restarted med --14 excluded for other reasons



3 Clinical Arguments: OPTIMISE

Table 3. Secondary Outcomes and Post Hoc Outcomes at 12 Weeks

	Medication reduction group		Usual care group			
	No. analyzed	Mean (95% CI)	No. analyzed	Mean (95% CI)	Adjusted mean difference (95% CI)	P value ^a
SBP ^{b,c}	265	133.7 (131.7 to 135.6)	269	130.8 (128.9 to 132.7)	3.4 (1.0 to 5.8)	.005
DBP ^{b,d}	265	70.9 (69.6 to 72.1)	269	69.7 (68.5 to 70.8)	2.2 (0.9 to 3.6)	.001
Post hoc outcomes						
SBP (per-protocol analysis, mm Hg) ^{c,h}	185	134.4 (132.1 to 136.7)	269	130.8 (128.9 to 132.7)	4.9 (2.4 to 7.5)	<.001
DBP (per-protocol analysis, mm Hg) ^{d,h}	185	71.6 (70.2 to 73.1)	269	69.7 (68.5 to 70.8)	3.4 (1.8 to 4.9)	<.001
Change in antihypertensive prescriptions	276 ^g	-0.68 (-0.74 to -0.61)	283 ^g	-0.05 (-0.08 to -0.01)	-0.63 (-0.70 to -0.56)	<.001



4 Compelling Arguments: Money talk\$

Research Article

Economic Evaluation of Sedative Deprescribing in Older Adults by Community Pharmacists

Justin P. Turner, PhD,^{1,2,} Chiranjeev Sanyal, PhD,^{3,*} Philippe Martin, PhD,^{1,2,} and Cara Tannenbaum, MD, MSc^{1,4}



4 Money talk\$: Economic Evaluations

Objective: Evaluate cost-effectiveness of a community pharmacist-led benzodiazepines and z-drugs deprescribing intervention (D-PRESCRIBE)

Methods: Cost-utility

analysis

- Costs and QALYs over 1-year time-horizon
- Payor perspective
- 1-month cycle for moving between states in Markov model
- Examined willingnessto-pay thresholds and scenario analyses





4 Money talk\$: Economic Evaluations

Table 2.	Reference	Case-	 Cost-Effectiveness 	s of D-PRESCRIBE	Intervention	Compared With	Usual Care
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Strategy	Mean Costs, \$	Mean QALYs	Incremental Costs, \$	Incremental QALYs	ICER, \$/ QALY gained
Usual care	2717.06 (1668.03; 4131.51)	0.6463 (0.6132;	-	-	-
D-PRESCRIBE	1325.01 (825.41; 2025.09)	0.6734) 0.7232 (0.6839; 0.7704)	-1392.05 (-2287.93; -775.39)	0.0769 (0.0434; 0.1191)	Dominant

- Increasing incremental net benefit with greater willingness-to-pay
- Remained dominant with:
 - 1) extra primary care visit
 - 2) increased pharmacist fee for expert opinion
 - 3) varying deprescribing rates



4 Compelling Arguments: Money Talk\$

Financial advantage or barrier when deprescribing for seniors: A case based analysis

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4 Money talk\$: Financial Consequences

Objective:

- 1. Determine the financial loss to the community pharmacy for deprescribing meds for a publicly funded older adult
- 2. Determine financial impact on patient and payor

Methods: Created case scenario to represent a typical older adult and 8 scenarios, each with different changes to medication regimen, to calculate baseline and average change to:

- 1. Pharmacy margin
- 2. Government share
- 3. Patient share



4 Money talk\$: Financial Consequences

Scenario	Pharmacy margin	Government Savings	Patient Savings
Stop ASA			
Abrupt DC simvastatin			
Slow lorazepam taper			
Rapid omeprazole taper			
Switch lorazepam to melatonin			+
Dose reduction of lorazepam			
Switch liraglutide to pre-filled detemir	♣♣♣♣		
Switch irbesartan/HCTZ to irbesartan		+	+



5 Patients: Predictability and Participation

Patients' Attitudes Towards Deprescribing Alpha-Blockers and Their Willingness to Participate in a Discontinuation Trial

Malou Edelman¹ · Petra Jellema¹ · Eelko Hak² · Petra Denig³ · Marco H. Blanker¹



5 Patients: Predictability and Participation

Objective: To describe attitudes of men with lower urinary tract symptoms (LUTS) towards deprescribing alpha-blockers, and to assess willingness to participate in a planned discontinuation research trial

Methods: Cross-sectional survey of men age <a>30 with LUTS receiving alphablocker from one of 20 pharmacies in the Netherlands

- General revised Patient Attitudes Toward Deprescribing (rPATD)
- Alpha-blocker specific rPATD
- Clinical measures of LUTS (IPSS, OAB-q)
- One item "willingness to participate" (y/n) in a discontinuation research trial



5 Patients: Predictability and Participation





6 Filling the Void: Researchers' Needs

Health professionals' and researchers' opinions on conducting clinical deprescribing trials

Alexander J. Clough^{1,2} | Sarah N. Hilmer² | Lisa Kouladjian-O'Donnell² | Sharon L. Naismith^{3,4} | Danijela Gnjidic^{1,4}



6 Researchers' Needs

Objective: Explore health professionals' and researchers' perspectives, attitudes, interests, barriers and enablers of <u>conducting</u> clinical deprescribing trials

Methods: Cross-sectional survey of international deprescribing, pharmacological, and pharmacy organizations, with targeted recruitment of published researchers



6 Researchers' Needs: Conducting Trials

- n = 96 respondents; 41% with experience conducting trials
- Primary rationale: "optimise clinical and/or patient centered outcomes" (79%)

Enablers

- "The beliefs of other health professionals regarding benefits of deprescribing" (24%)
- "Willingness of patients to participate" (21%)

Barriers

- "Time and effort required" (18%)
- "Establishing and/or maintaining relationships with other health professionals" (17%)



6 Filling the Void: Implementation Science

Interventions to deprescribe potentially inappropriate medications in the elderly: *Lost in translation*?

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6 Filling the Void: Implementation Science

Objective: Determine the extent to which implementation factors were identified in deprescribing trials

Methods: Narrative review of controlled trials or prospective cohort studies intended to reduce medications in the elderly that used hospitalizations and/or emergency department visits as outcome measures (2000-2019)

• Mentions of implementation factors were mapped to a construct according to the Consolidated Framework for Implementation Research (CFIR)



6 Filling the Void: Implementation Science

- 548 abstracts → 14 eligible articles → 10 articles discussed implementation factors
- 1-4 factors per article
 - Inner Setting (n=8)
 - Individual characteristics (n=3)
 - Intervention characteristics (n=1)
- Within Inner Setting, most common domain construct was networks and communication





Take-Home Messages

We aren't deprescribing enough in eligible patients 2 There are differences between medical specialties 3 Clinical evidence is needed to put us on the same page It makes economic sense 5 Patients are interested and are willing to enroll in research trials Researchers need support for trials and to 6 be cognizant of implementation factors



Thank you

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