Leveraging Real-World Healthcare Data to Examine Deprescribing of Medications of Questionable Benefit in Older Nursing Home Residents Nearing the End of Life

#### Carolyn T. Thorpe, PhD, MPH

Associate Professor, Division of Pharmaceutical Outcomes & Policy, University of North Carolina

Research Scientist, Center for Health Equity Research & Promotion, VA Pittsburgh Health System

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## Outline

#### Background

- Chronic disease medications of questionable benefit in the context of limited life expectancy/advanced dementia (LLE/AD)
- Value of real-world healthcare data and observational study designs in deprescribing research

Share results from large VA R01-equivalent study
Statins, hypoglycemic agents, antihypertensives

## Collaborators

#### Co-investigators

- VA Pittsburgh Healthcare System:
  - Joshua Niznik, Michelle Vu, Sydney Springer, Jacob Hunnicutt, Maria K. Mor, Florentina Sileanu, Xinhua Zhao, Wendy He, Song Zhang, Sherrie L. Aspinall, Walid F. Gellad, Loren J. Schleiden, Joshua M. Thorpe, Joseph Hanlon
- Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA:
  - Mary J. Ersek

#### National VA Operations Partners

- Geriatrics & Extended Care
- Pharmacy Benefits Management (PBM), Center for Medication Safety (VA MedSAFE)

## Disclosures

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- J. Hunnicutt (previous VA fellow) is now employed by GlaxoSmithKline.
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- The views expressed are those of the authors, and no official endorsement by the Department of Veterans Affairs or the United States government is intended or should be inferred.

## Medication Burden in Older Adults near End of Life

 ~50% of seriously ill older adults take 10+ medications in the last year of life<sup>1,2</sup>

• 38%-54% are on regimens including at least one medication of questionable benefit<sup>3,4</sup>

I. Morin et al. Am J Med 2017; 130(8):927-936.

2. McNeil et al. J Pain Symptom Manage 2016; 51(2):178-183.

Morin et al. J Am Med Dir Assoc 2017; 18(6):551-557.
 Tjia et al. JAMA Intern Med 2014;174(11): 1763-71.

# Improving Appropriateness of Medications in Late Life via Deprescribing

#### **Deprescribing:**

Discontinuing or reducing the dose of drugs when risks outweigh expected benefits in context of patient's goals of care, life expectancy, values, and preferences

Scott IA, et al. JAMA Int Med 2015; 175(5):827-834.

Holmes's Framework for Prescribing in Late Life



Adapted from Holmes et al. Arch Intern Med 2006;166:605-609

#### Improving Appropriateness of Medications in Late Life via Deprescribing

• Reducing "inappropriate" medications in older adults

- Drugs/dosages that should be avoided in all adults, or in combination with certain diseases or other drugs (e.g., Beers criteria)
- Not the focus today

 Also: de-intensifying meds to treat/prevent complications of chronic conditions with increased risks/reduced benefits in context of limited life expectancy/advanced dementia (LLE/AD)

- Statins for secondary prevention of CV events
- Antihypertensives for blood pressure control
- Hypoglycemic agents for diabetes control

#### The Case for Deprescribing Statins

- High potential for drug interactions, adverse effects<sup>1</sup>
- RCT of discontinuation in adults with <1-year life expectancy: increased quality of life, no increase in mortality<sup>2</sup>
- Inconsistency between geriatric vs. other guidelines
- One of the most commonly used medications of questionable benefit near the end of life<sup>3,4</sup>
  - 34% of residents with life-limiting illnesses in US Medicare/Medicare nursing homes<sup>5</sup>

<sup>1</sup> Thai et al. Drugs Aging 2015;32(10):849-856.
 <sup>2</sup> Kutner et al. JAMA Int Med 2015; 175(5): 691-700.
 <sup>3</sup> Matlow et al. JAGS 2017; 65(7):1535-1542.

#### The Case for Deprescribing Hypoglycemic Agents

- Guidelines recommend "less intense" HbAIc control in adults aged ≥65 with <5 years life expectancy, comorbidities, complications
  - AGS Choosing Wisely and Department of Veterans Affairs: 8-9%
- Trials in older adults (not LLE) suggest increased harms, reduced benefits of pursuing tight HbA1c control with medications
  - 个 hypoglycemic events/hospitalizations
  - $\leftrightarrow$  or  $\uparrow$  cardiovascular events/mortality
- In patients with LLE/AD, risks & burden likely even greater

#### The Case(?) for Deprescribing Antihypertensives

- Evidence on the optimal intensity of blood pressure (BP) control for older adults with LLE/AD is lacking
  - CV risk reduction benefits vs. risks of postural hypotension, falls/fractures, mortality
- Guidelines are inconsistent
  - <u>2017 AHA/ACC</u>: Treat to <130/80 mmHg for ambulatory older adults; individualize targets for adults with LLE
  - <u>ACP/AAFP</u>: Treat to SBP <150 mmHg (vs. 140); individualize targets
  - <u>CRIME project (2015)</u>: Avoid treating to <140 mmHg; avoid >3 antihypertensives

# Knowledge Gap & Opportunity

- Information on real-world deprescribing patterns in older adults with LLE/AD is limited
- Nursing home admission is an opportunity for medications of questionable benefit to be reviewed, identified, & deprescribed
- Data resources available for VA NH residents provide a unique opportunity

# Observational Studies as a Complement to Drug Withdrawal Trials

#### Advantages

- Avoid barriers to recruiting and enrolling participants
- Larger, more generalizable samples
- Allow us to track and evaluate real-world deprescribing patterns

#### Challenges with observational studies

- Ascertaining clinical characteristics
  - Identifying "potentially overtreated" patients
  - More limited range of outcomes
  - Measurement of confounders
- Accurately identifying "de-prescribing"
- Non-randomized exposure (deprescribing vs. continuing)

## **Overall Study Objectives**

- Examine incidence, predictors, and outcomes of deprescribing of statins, antihypertensives, and hypoglycemic agents in Veterans with LLE/AD who are potentially overtreated at admission to a VA nursing home
- National, retrospective cohort study of Veterans admitted to a Community Living Center (CLCs)
- Today: Completed work on incidence and predictors

### Deprescribing of Statins (secondary prevention) in CLC Residents

- Thorpe CT et al. Discontinuation of statins in Veterans admitted to nursing homes near the end of life. Under review.
- **Thorpe CT,** et al. Statin discontinuation in Veterans Affairs (VA) Community Living Center residents with limited life expectancy. Oral presentation at the 2019 Department of Veterans Affairs HSR&D/QUERI National Conference, Baltimore, MD, October 29-31, 2019.
- **Thorpe CT,** et al. Statin discontinuation in Veterans Affairs (VA) nursing home residents with limited life expectancy. Poster presented at the 2019 Annual Scientific Meeting of the American Geriatrics Society, Portland OR, May 2-4, 2019.

## Data Sources

- Residential History File<sup>1,2</sup>
- VA Minimum Dataset (MDS) v2.0 and v3.0 assessments
- VA bar-coded medication administration (BCMA) data
- VA Corporate Data Warehouse
- Medicare claims
- VHA Support Service Center

Intrator O, Hiris J, Berg K, et al. *Health Serv Res.* 2011;46(1 Pt 1):120-137.
 Intrator O, Makinei R, Cai S, et al. VA HSR&D Research Meeting; July 2015; Philadelphia, PA

# Sample – Statin Deprescribing

- CLC admission with completed MDS FY 2009-2015 (n=200,333)
- Meet at least I of 3 criteria for LLE/AD (n=81,273,41%)
  - MDS item for "end-stage disease, <6 months to live"
  - Score  $\geq$ 36 on MDS Mortality Risk Index-Revised (MMRI-R)<sup>a,b</sup>
  - Brief Interview for Mental Status<sup>c</sup>  $\leq$ 7 or Cognitive Performance Scale<sup>d</sup>  $\geq$ 4
- Age ≥65 years (n=61,137,75%)
- Minimum LOS ≥7 days (n=58,782,96%)
- Coronary artery disease, stroke/transient ischemic attack, or diabetes (n=43,968,75%)
- Received statin medication during first week of CLC stay (n=16,473,38%)
- Remained in CLC for  $\geq$ 14 days after medication index date (n=13,110,80%)

## **Defining Statin Discontinuation**

- ≥14 consecutive days after the statin index date with no statin doses given (≥30 days in sensitivity analysis)
- First day of gap (d) is the discontinuation date



## **Conceptual Model: Predictors of Deprescribing**



dehydration, acute change in mental status, shortness of breath, cancer, pain, infection, activities of daily living, aggressive behavior, swallowing difficulties, parenteral/tube feeding, mechanically altered diet, recent falls

## Analytic Approach

- Time-to-event analysis, with death as a competing risk
- 90-day cumulative incidence of statin discontinuation
- Fine & Gray subdistribution hazard models
  - Standard errors adjusted for clustering by facility
- Stratified by whether or not the Veteran's limited prognosis (LP) was explicitly documented at admission
  - MDS item for end-stage disease, MDS item for hospice use in past 14 days, or admission to VA hospice treating specialty

# Sample Characteristics (selected)

Characteristic	Percent
Age 65-74 75-84 85+	32% 40% 28%
Race White, non-Hispanic	79%
CV risk factors >I qualifying condition (CAD, stroke/TIA, diabetes) Hypertension Hyperlipidemia Myocardial infarction in past year Stroke/TIA in past year	61% 94% 79% 7% 26%
Limited prognosis explicitly documented at admission	18%
Advanced dementia	29%

#### Cumulative Incidence of Statin Discontinuation

Stratified by Explicit Documentation of Limited Prognosis, 14-Day Gap



	I4-Day Gap	30-Day Gap
Full Sample	31% (30%-32%)	26% (25%-28%)
Explicit LP	52%	48%
Documentation	(50%-55%)	(45%-51%)
No Explicit LP	25%	21%
Documentation	(24%-26%)	(20%-23%)

#### Factors Associated with Statin Discontinuation, p<.05 Residents with <u>No</u> Explicit Documentation of LP (n=10,736)



#### Factors Associated with Statin Discontinuation, p<.05 Residents with Explicit Documentation of LP (n=2,374)



#### Statin Deprescribing – Summary

- (at least through 2015) most VA CLC residents with LLE/AD taking a statin at admission did not have it discontinued, but...
- Discontinuation much more likely if their limited prognosis is documented at admission, but...
- Even among those with LP documented, almost half remained on statins
  - CV risk factors discourage deprescribing?

### Diabetes: Deprescribing of Hypoglycemics in Potentially Overtreated CLC Residents

- Niznik JD, Hunnicutt J,...Thorpe CT. Deintensification of diabetes medications among Veterans at the end-of-life in VA nursing homes. *Journal of the American Geriatrics Society* Feb 17 2020 [epub ahead of print].
- Hunnicutt J...Thorpe C. Deprescribing hypoglycemic medications among older Veterans with overtreated diabetes and limited life expectancy in Veterans Affairs (VA) nursing homes. Oral presentation at the 2019 Annual Scientific Meeting of the American Geriatrics Society, Portland OR, May 2-4, 2019.

# Sample – Hypoglycemic Deprescribing

- CLC admission with completed MDS FY 2009-2015
- Meet at least 1 of 3 criteria for LLE/AD
- Age ≥65 years
- Minimum LOS ≥7 days
- Diabetes diagnosis (n=25,341,43%)
- Had HbAIc measured during first 90 days of CLC stay (n=6,960, 28%)
- HbAIc <7.5% and taking ≥1 hypoglycemic medication (n=3,421,49%)
- Remained in CLC for  $\geq$ 7 days after medication index date (n=3,056, 89%)

# Defining Hypoglycemic Deprescribing

- $\geq$ 7 consecutive days after the index date with
  - Decreased daily dose or discontinuation of a non-insulin agent, and/or
  - Discontinuation of a type of insulin (type = short-acting or basal)
     WITHOUT
  - Increasing daily dose or adding a non-insulin agent or adding a new type of insulin
- ≥14 days in sensitivity analysis



## Analytic Approach

• Similar set of covariates, but also diabetes-related factors

- Baseline HbAIc, medication regimen, diabetes complications, past hypoglycemic events
- Time-to-event analysis, with death as a competing risk
- 90-day cumulative incidence of hypoglycemic de-intensification
- Fine & Gray subdistribution hazard models
- Converted subdistribution hazard ratios to risk ratios for easier interpretation
  - 95% CIs estimated using 1,000 bootstrap resamples

#### Sample Characteristics (selected) n=3,056 Veterans Potentially Overtreated for Diabetes at Nursing Home Admission

Characteristic	Percent
Age 65-74 75-84 85+	38% 41% 21%
Race White, non-Hispanic	76%
Number of comorbidities 0-1 2-3 4-5 >5	9% 22% 30% 39%
Limited prognosis or hospice documented at admission	14%
Advanced dementia	29%

Medication Regimens at Baseline				
Number of diabetes medications used				
1	53.1			
2	41.9			
≥3	5.0			
Most common treatment regimens				
Short-acting insulin and basal insulin	28.6			
Short-acting insulin only	16.0			
Basal insulin only	13.7			
Sulfonylureas only	13.8			
Non-insulin / non-sulfonylurea agent only	9.8			
Short-acting insulin and sulfonylureas	5.0			
Sulfonylureas and non-insulin / non-sulfonylurea agent	3.5			
Short-acting insulin and non-insulin / non-sulfonylurea	2.6			
agent				
Other regimens	7.1			
≥1 high-risk hypoglycemic agents	75.3			
Short-acting insulin	56.7			
Sulfonylurea	26.4			

## 90-day Cumulative Incidence of De-intensification of Diabetes Medications



Sensitivity analysis using 14-day gap: 36.1%

#### Factors Associated with De-intensification, p<.05

#### **Risk Ratios and 95% Confidence Intervals**



Comparator group for HbA1c was HbA1c <6.0%; Comparator group for medication regimens was non-insulin/non-sulfonylurea agent only.

#### Diabetes Deprescribing – Summary

- One-third to just under one-half of residents with LLE/AD had diabetes medications de-intensified in response to below-guideline HbA1c levels (depending on gap length)
  - Once again, no strong time trends
- HbA1c and nature of medications used were strongest predictors of de-intensification
- Documentation of limited prognosis only showed modest association

#### Hypertension: Deprescribing of Antihypertensives in Potentially Overtreated CLC Residents

- Vu M...Thorpe CT. Antihypertensive deprescribing in older adult Veterans at end-of-life admitted to Veterans Affairs nursing homes. Under review.
- Vu M...Thorpe CT. Antihypertensive Deprescribing among Veterans with Limited Life Expectancy after Admission to Veteran Affairs (VA) Nursing Homes. Accepted for oral presentation at the 2020 Annual Scientific Meeting of the American Geriatrics Society, Long Beach, CA May 6-8.

# Sample – Antihypertensive Deprescribing

- CLC admission with completed MDS FY 2009-2015
- Meet at least 1 of 3 criteria for LLE/AD
- Age ≥65 years
- Minimum LOS ≥7 days
- Hypertension diagnosis (n=50,334,86%)
- Had BP measured and taking ≥1 antihypertensive during first week of stay (n=32,923,77%)
- Remained in CLC for  $\geq$ 7 days after medication index date (n=30,940, 94%)\*
- Potentially overtreated for hypertension (n=10,574, 34%)
  - Receipt of  $\geq 1$  antihypertensive and mean systolic BP  $< 120 \text{ mmHg}^{a}$

# Defining Antihypertensive Deprescribing

- $\geq$ 7 consecutive days after the index date with
  - Decreasing the daily dose or discontinuing an antihypertensive without increasing/adding another agent
- $\geq$  14 days in sensitivity analysis
- Shorter follow-up (30 days maximum)

Song W et al. Health Serv Res. 2018;53(6):4066-4086.



### Selected Characteristics: N=10,574

Sociodemographic: age at admission	
65-74	33%
75-84	37%
≥85	30%
CV risk factors	
Coronary artery disease	68%
Diabetes	47%
Congestive heart failure	51%
Atrial fibrillation	22%
Recent myocardial infarction (past year)	6%
Recent stroke/transient ischemic attack (past year)	17%
Poor prognosis factors	
History of fall/fracture in past 180 days	52%
Advanced dementia	25%
Limited prognosis documented at admission	36%

#### Antihypertensive Regimens at Baseline

		Intensity of Overtreatment			
	Overall	Low BP 1 class	Very Low BP 1 class	Low BP >1 class	Very Low BP >1 class
Treatment Administered n (row %)	N=10,574	3,579 (34)	600 (6)	5 <i>,</i> 489 (52)	906 (9)
Number of antihypertensive classes on admission	(col %)	(col %)	(col %)	(col %)	(col %)
1	40	100	100	-	-
2	32	-	-	54	52
3	20	-	-	33	36
>3	8	-	-	13	13
Most common antihypertensive classes (column %)	(col %)	(col %)	(col %)	(col %)	(col %)
Beta blockers	67	50.	49	78	81
Loop diuretics	38	13	20	54	59
Alpha-1 blockers (non-uroselective)	37	14	12	52	56
Calcium channel blockers	20	12	8	27	14
ACE/ARB	16	8	7	21	18
Thiazide diuretics	8	2	2	12	12

Very Low BP = SBP <100 mmHg Low BP = SBP 100 to <120 mmHg

## Antihypertensive Regimens at Baseline

		Intensity of Overtreatment			
	Overall	Low BP 1 class	Very Low BP 1 class	Low BP >1 class	Very Low BP >1 class
Treatment Administered n (row %)	N=10,574	3,579 (34)	600 (6)	5 <i>,</i> 489 (52)	906 (9)
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#### 30-day Cumulative Incidence of Deprescribing



Sensitivity analysis using 14-day gap: 35%

#### Factors Associated with Deprescribing, p<0.05



#### Factors Associated with Deprescribing, p<0.05



### Hypertension Deprescribing – Summary

- 35-41% of residents with LLE/AD had antihypertensive medications de-intensified after low SBP readings (depending on gap length)
  - More likely in more recent years
- Similar to diabetes:
  - Intensity of overtreatment was strongest predictor of deintensification
  - Documentation of limited prognosis did not play much role
- Cardiovascular risk factors ightarrow less deprescribing
- Markers of poor prognosis  $\rightarrow$  more deprescribing
- History of falls/fracture  $\rightarrow$  no association

#### Limitations – All 3 Studies

• Optimal gap for defining deprescribing is unknown

- Cumulative incidence estimates somewhat sensitive to gap length, esp. in diabetes
- Generalizability to non-Veterans, other settings, unknown
- Data ended in 2015 and may not reflect current practice
- Observational design cannot necessarily interpret associations as causal
- Diabetes:
  - Many had no recent HbAIc and were excluded
  - Decreases in insulin dose intensity not captured

#### **Conclusions and Implications**

- Deprescribing of chronic disease medications of questionable benefit appears to occur in one-third to one-half of VA nursing home residents with LLE/AD
- Predictors of deprescribing varied to some degree across disease states
  - Documentation of LP most salient for statins
  - Intensity of overtreatment most salient for diabetes and hypertension
- Further efforts are needed to encourage appropriate deprescribing and further develop evidence base regarding outcomes

## Ongoing work

 Identify and learn from facilities with different likelihood of deprescribing

 Interviews with providers and family caregivers at "highdeprescribing" and "low-deprescribing" facilities

• Examine effect of de-prescribing on outcomes

 Hospitalization/ED visits, mortality, falls/fractures, cardiovascular events

#### Other Deprescribing Work by Our Team

- Aspirin deprescribing patterns in VA CLC residents with LLE/AD
  - Springer SP...**Thorpe CT.** Incidence and predictors of aspirin discontinuation in older Veteran nursing home residents at end-of-life. *Journal of the American Geriatrics Society* 2020 Feb 13 [epub ahead of print].
- Patterns and outcomes of deprescribing acetylcholinesterase inhibitors in Medicare-enrolled nursing home residents with advanced dementia
  - Niznik JD...**Thorpe CT.** Impact of deprescribing AChEls on aggressive behaviors and antipsychotic prescribing. *Alzheimer's & Dementia:The Journal of the Alzheimer's Association* 2020 Feb 13 [epub ahead of print].
  - \*Niznik JD...**Thorpe CT.** Risk for health events after deprescribing AChEls in nursing home residents with severe dementia. *Journal of the American Geriatrics Society* 2020 Nov 26 [epub ahead of print].
  - \*Niznik J... Thorpe CT. Factors associated with deprescribing AChEls in older NH residents with severe dementia. *Journal of the American Geriatrics Society* 2019 67(9): 1871-1879.



# Questions?

carolyn\_thorpe@unc.edu