Antihypertensive Deprescribing in Nursing Home Residents: A Target Trial Emulation

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Cardiovascular benefits of antihypertensives may not outweigh potential harms in older adults

→ Patient and provider interest in deprescribing

Antihypertensive deprescribing is common in the NH

NH residents with low BP who fell → 11% experienced drug deintensification within 1 week

Song, W, Intrator, O, Lee, S, et al. Antihypertensive Drug Deintensification and Recurrent Falls in Long-Term Care. Health Serv Res 2018.

NH residents with limited life expectancy or advanced dementia → 35% deprescribed over 30 days

Vu, M, Sileanu, FE, Aspinall, SL, et al. Antihypertensive Deprescribing in Older Adult Veterans at End of Life Admitted to Veteran Affairs Nursing Homes. J Am Med Dir Assoc 2020.

NH long-term stay residents → 11-42% deprescribed within 1 month after a potential deprescribing event (incident low blood pressure, fall, electrolyte imbalance, acute renal event)

Odden MC, Lee SJ, Steinman MA, Deprescribing Blood Pressure Treatment in Long-Term Care Residents. J Am Med Dir Assoc 2022.

Recent deprescribing trials have shown no harm

Cochrane review of studies found suggestive evidence of a greater risk of MI (odds ratio [OR]: 1.86, 95% CI: 0.19, 1.98) and stroke (OR: 1.44, 95% CI: 0.25, 8.35)

Reeve E, Jordan V, Thompson W, Sawan M, Todd A, Gammie TM, et al. Withdrawal of antihypertensive drugs in older people. Cochrane Database Syst Rev. 2020

DANTE trial in 385 adults aged 75+ years with mild cognitive deficits

→ No change in cognitive, psychological, general daily function or adverse events

Moonen JE, Foster-Dingley JC, de Ruijter W, van der Grond J, Bertens AS, van Buchem MA, et al. Effect of Discontinuation of Antihypertensive Treatment in Elderly People on Cognitive Functioning--the DANTE Study Leiden: A Randomized Clinical Trial. JAMA Intern Med. 2015

OPTiMISE trial in 569 older adults in primary care

→ No change in systolic BP control or adverse events

Sheppard JP, Burt J, Lown M, Temple E, Lowe R, Fraser R, et al. 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. JAMA. 2020

Target Trial Emulation (TTE) can help build evidence base

What TTE is:

- A systematic way of analyzing observational data using the design principles of RCT
- A method to address many sources of bias common in observational data
- A powerful way to estimate treatment benefits and harms
  - A recent investigation found a Pearson correlation of 0.93 (0.79, 0.97) among 16 RCT/TTE studies with similar design

What TTE is not:

- A magic bullet
- Easy
- Always feasible

Emulation of Randomized Clinical Trials With Nonrandomized Database Analyses Results of 32 Clinical Trials. Wang S, Schneeweiss S, and the RCT-DUPLICATE Initiative. JAMA. 2023;329(16):1376-1385.

Outline

1. My background and motivation
2. Study design of VA long-term care cohort
3. Intro to target trial emulation
4. Results from our cohort

1. Background

Journal of Gerontology: MEDICAL SCIENCES
2003, Vol. 58A, No. 7, 653–658

Review Article

Embracing Complexity: A Consideration of Hypertension in the Very Old

James S. Goodwin

Department of Internal Medicine, School of Medicine, and Sealy Center on Aging, The University of Texas Medical Branch, Galveston.

The consequences of hypertension and its treatment differ in very old men and women compared to younger populations. In populations aged 85 years and older, higher levels of systolic and diastolic blood pressures are

"The consequences of hypertension and its treatment differ in very old men and women compared to younger populations."

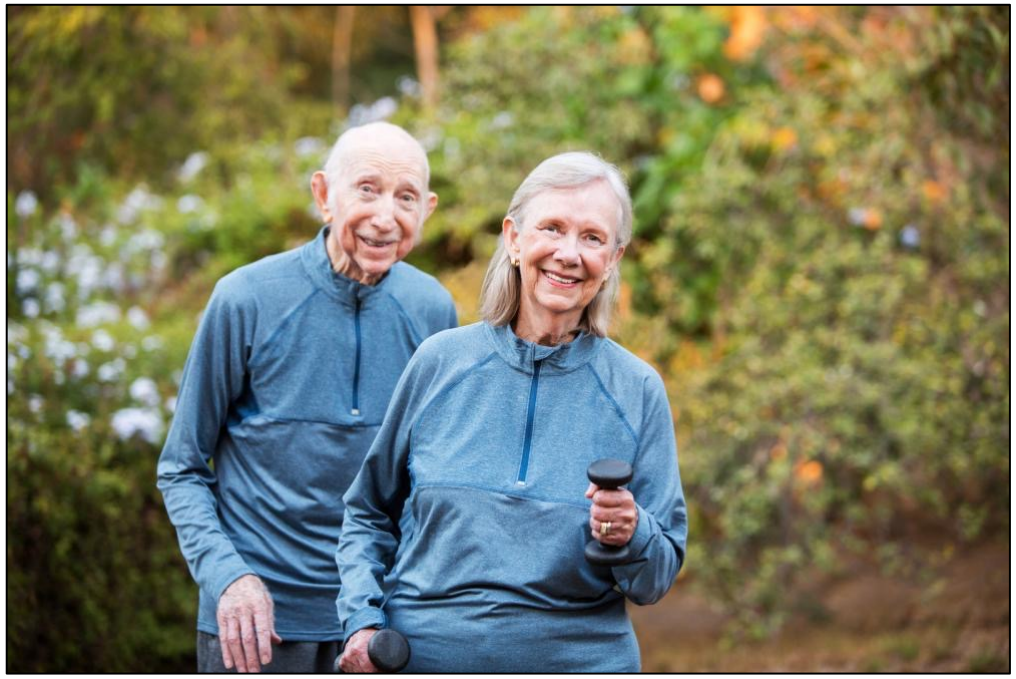
"There are many ways to define potential categories of very old individuals, such as age, walking speed, level of cognition, ejection fraction, level of affect, and self-rated health"

1. Background

UCSF
University of California
San Francisco

"They've revised the standards again. Your blood pressure should be 110/70 ÷ 417^2 + XY^5 ÷ 49X + 160/16 X .999% – 5^3."

1. Functional Status as a Marker of Heterogeneity in Aging



1. The Risk of High BP on Mortality Depends on Functional Status

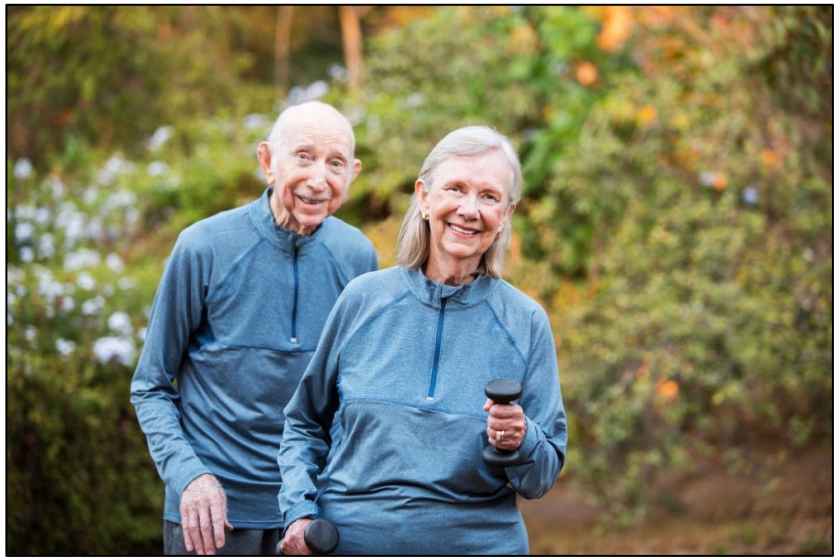
Among older adults in NHANES…

	Faster Walkers (n = 1,307)
Systolic BP ≥ 140 mmHg	
Hazard ratio for mortality* (95% CI)	1.35 (1.03, 1.77)

*Adjusted for survey year, age, gender, black race, education, smoking status, cholesterol, coronary heart disease, heart failure, and stroke

Odden MC, Peralta CA, et al. Rethinking the association of high blood pressure with mortality in elderly adults: the impact of frailty. Arch Intern Med. 2012 Aug 13;172(15):1162-8

1. A New Paradigm for Hypertension in the Elderly – Beyond Age (R01-AG046206)



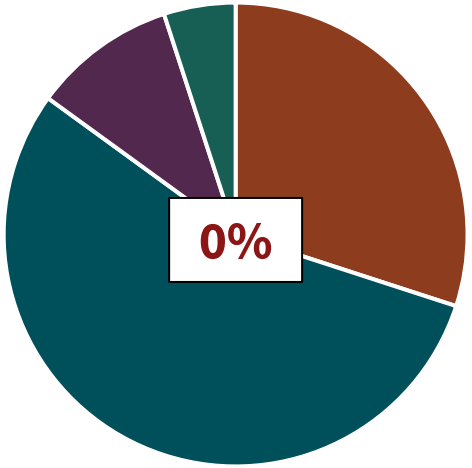
Low blood pressure -> benefit

Low blood pressure -> harms

Treatment Beneficial

Treatment Value ?

2. None of the large RCTs of antihypertensive medications have included nursing home residents



2. Management of Hypertension among Persons with and without Dementia in Long-Term Care - RF1AG062568

n = 45,183

2. VA CLC as a Setting for Deprescribing Research

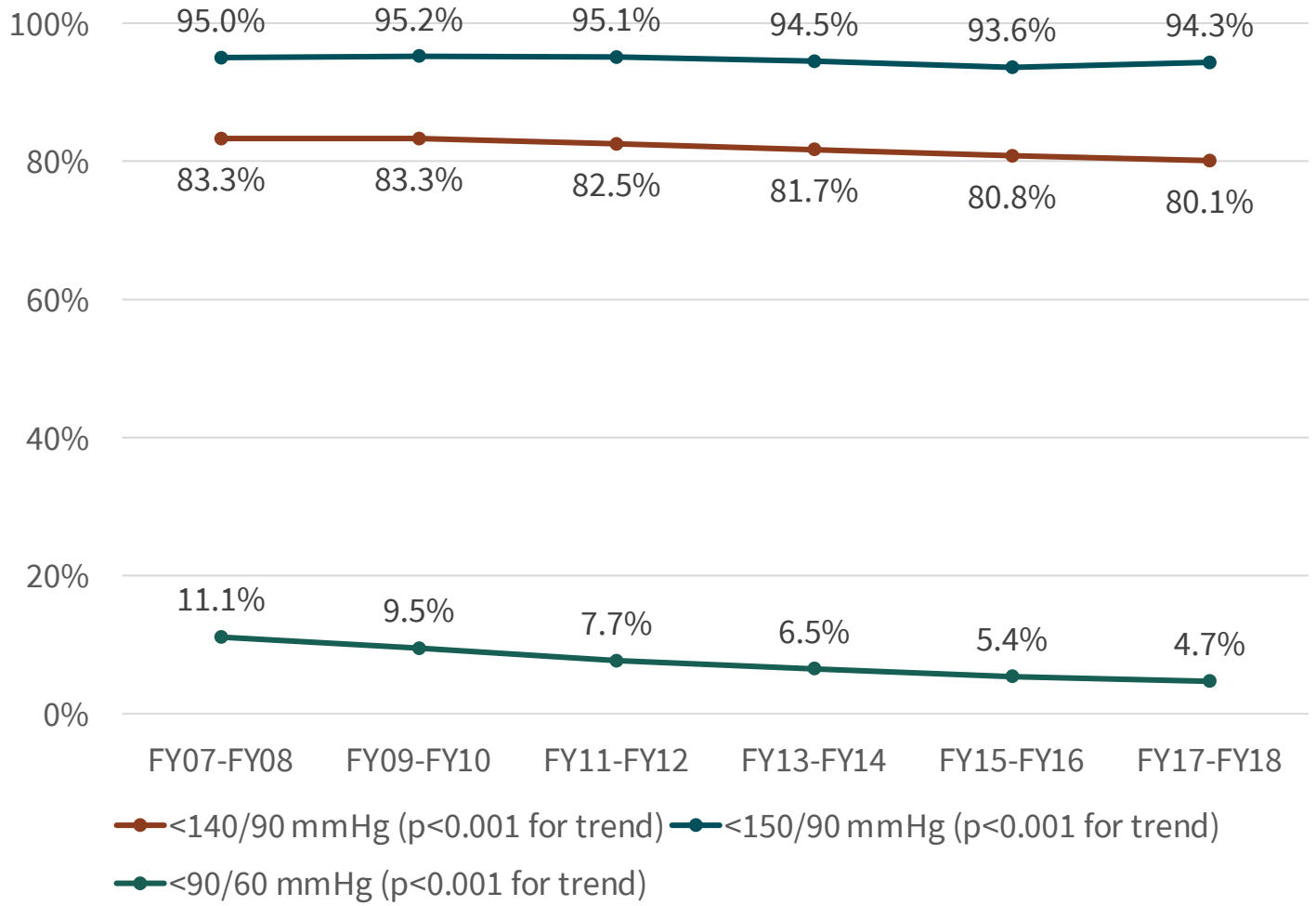
Benefits

- VA is a single payer system
- Knit together nursing home and hospital time
- BCMA data
- Vitals
- CMS-linked data

Limitations

- Mostly men
- Comorbidity may not represent non-VA population

2. Trends in Blood Pressure Diagnosis, Treatment, and Control among VA Nursing Home Residents, 2007-2018



Odden MC, Li Y, et al. Trends in Blood Pressure Diagnosis, Treatment, and Control among VA Nursing Home Residents, 2007-2018. J Am Geriatr Soc. 2022

2. Factors associated with BP treatment and Control

Antihypertensive Treatment	
Age	↓
Black race	
Hispanic ethnicity	↓
Diabetes	
Renal Disease	
Stroke	
Heart Failure	
Myocardial Infarction	
Cancer	↓
Dementia	↓

BP Control <140/90 mmHg	
Age	↓
Black race	↓
Hispanic ethnicity	↓
Diabetes	↓
Renal Disease	↓
Stroke	↓
Heart Failure	↑
Myocardial Infarction	↑
Cancer	↓
Dementia	–

2. Exploring the Dynamics of Week-to-Week Blood Pressure in Nursing Home Residents Before Death

Blood Pressure Dynamics at the End of Life

Setting & Participants

- Prospective Observational Cohort
- 17,953 Nursing Home Residents
- Last 6 months of life

- **Blood pressure** assessed 2-3 times per week

Results

- **Systolic blood pressure**
  decreases an average of 1.2 mmHg each month and 4.4 mmHg in the last month of life.

- **Diastolic blood pressure**
  remains stable.

- **Week-to-week variability**
  for both diastolic and systolic increases 30% in the last month of life.

- What influences variability?

Hospitalizations

Medication Changes

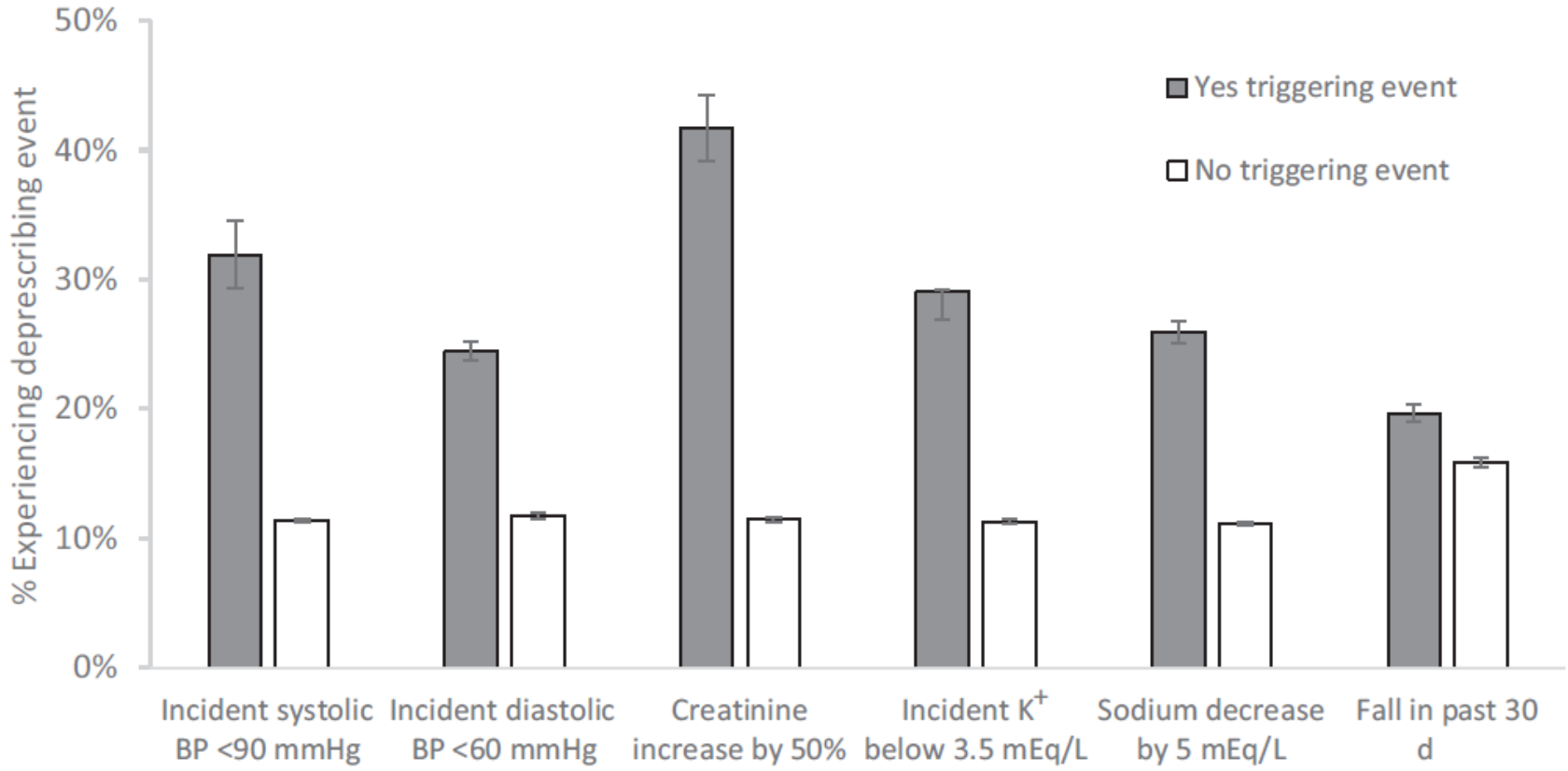
Hospice Care

Graham LA, Lee SJ, Steinman MA, Peralta CA, Rubinsky A, Jing B, Fung K, Odden MC. Am J Hypertens. 2021

2. Deprescribing Blood Pressure Treatment in Long Term Care

Deprescribing rate: 3.5/100 person-weeks

70.4% experienced a deprescribing even at some point during nursing home stay



Odden MC, Lee SJ, Steinman MA, Rubinsky A, Graham LA, Jing B, Fung K, Marcum ZA, Odden MC. JAMDA. 2021

Emulated trial of deprescribing antihypertensive medications

Protocol Component	Description
Eligibility Criteria	Adults 65+ years residing in long-term care on 1+ antihypertensive medication
Treatment Strategies	A reduction in the # of antihypertensives or a ≥ 30% reduction in dose, maintained for 2 weeks, verses no change/increase
Assignment Procedures	Pseudorandomized
Follow-up Period	2 years
Outcome Ascertainment	Hospitalization for myocardial infarction or stroke
Analysis Plan	Intention-to-treat; per-protocol multivariable adjustment, IPTW, TMLE to account for confounding

3. Eligibility criteria

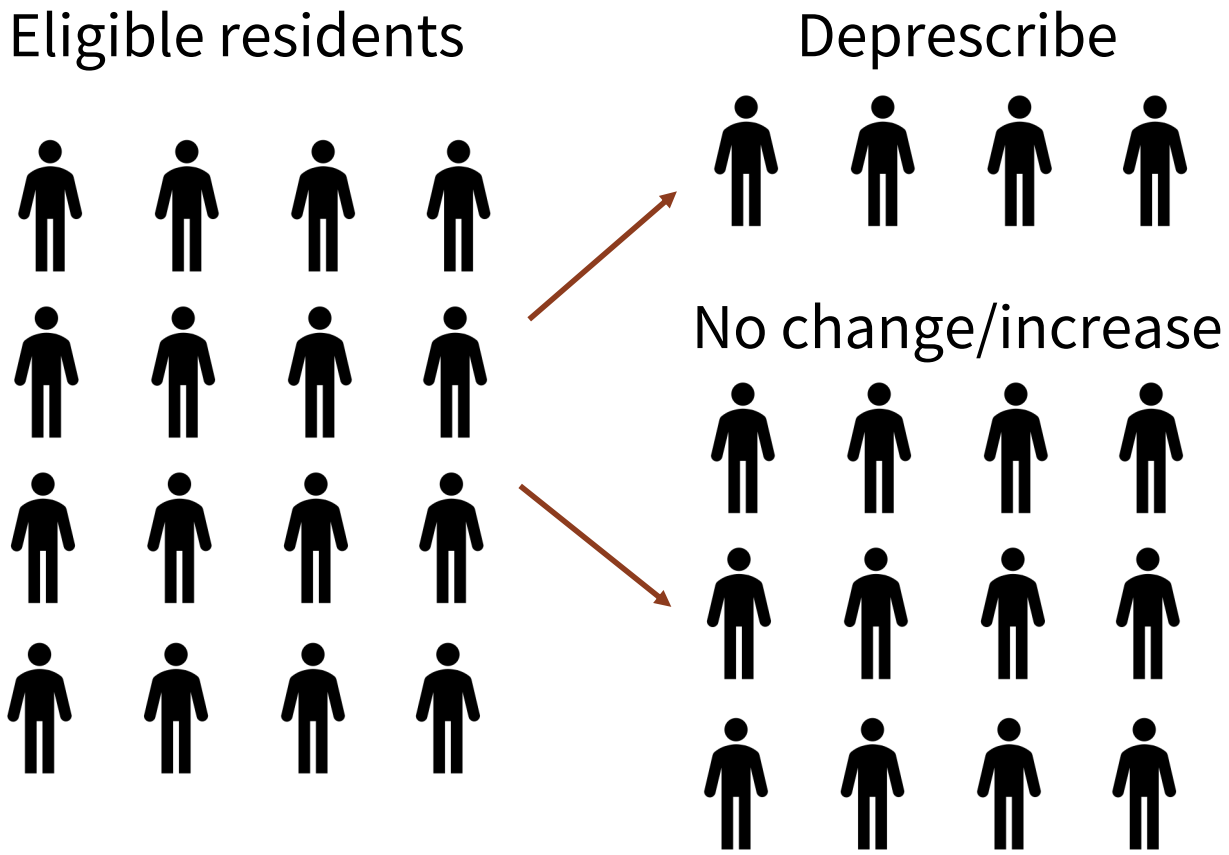
1) were <65 years at admission;
2) had a CLC stay <90 days to exclude those undergoing post-acute rehabilitation
3) had an acute hospital stay lasting >30 days during their CLC stay (n=14; those with hospital stays ≤ 30 days were included)
4) were not on antihypertensive medications at admission
5) had a history of heart failure or metastatic cancer at admission
6) had systolic blood pressure >160 mmHg at the time of deprescribing

Immortal time bias: When your cohort or treatment definition requires participants to survive X amount of time

→ If everyone was deprescribed in first month and then died, deprescribing would look more beneficial then it is

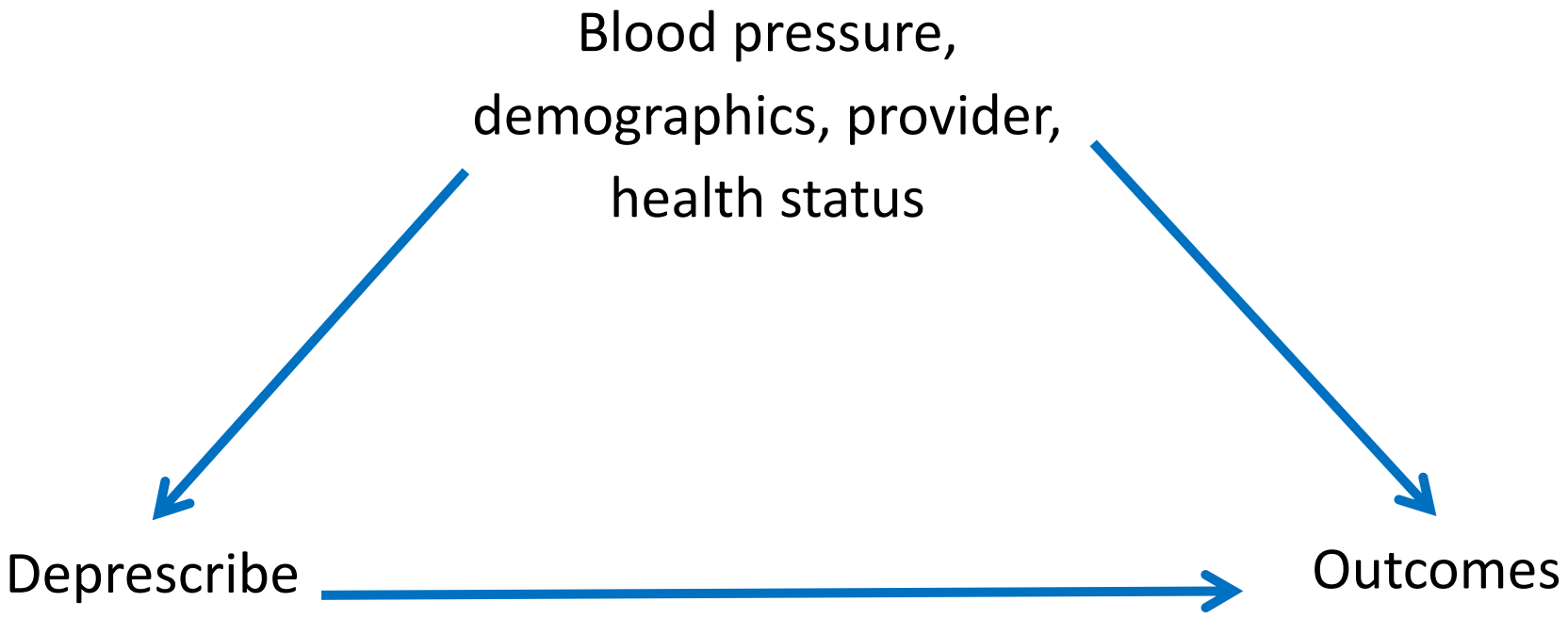
Solution – start entry into "trial" after 90 days

3. Treatment Strategies



- Each week, residents are divided into those who deprescribe and those who do not
- By allowing “rolling” entry, this increases sample size of deprescribing group

3. Assignment Procedures



Problem: Deprescribing is not random

Solution: "Causal" methods including targeted maximum likelihood estimation

3. Analysis Plan

ITT

- Best represents the clinical decision
- Only account for confounding prior to “assignment”

Per protocol

- Can account for changes in tx after initial “assignment”
- Per protocol estimates from TTE tend to better approximate ITT in trials

Summary

- TTE remains the best available approach when trials are unavailable
  - Trials remain strongly affected by selection (Anderson TS et al. J Am Heart Assoc. 2021 Apr 6;10(7):e019707; JAMA Intern Med. 2020 May 1;180(5):795-797.)
- Deprescribing is associated with no CVD harm and may provide small benefit on function
- New antihypertensive medications are associated with an elevated risk of fall-related injuries
- Unmeasured and residual confounding remains a potential source of bias

Next Steps:

Pending R01 to study deprescribing of:

- Aspirin
- Statins
- Anticoagulants
- Other antiplatelet agents

Thank you & Questions?

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