

# The association between antihypertensive medications and suicidality in the UK Biobank sample

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## INTRODUCTION

- Suicide claims >800K lives worldwide each year, and in US (CDC, 2019): >47K suicides, 1.4M attempts, 12M with suicidal thoughts
- Renin-Angiotensin System in mood disorders (Chrissobolis'20)
- Angiotensin Converting Enzyme gene associated with suicide (Fudalej'09;10Sparks'09;11Hishimoto'06)
- Certain antihypertensive medications reported to increase risk of suicide (Lindberg'98;Callreus'07;Sorensen'01;Mamdani'19), but also negative findings (Gasse'00; Lin'20; Dent'20)

**Gap:** Overall, few studies on the topic of antihypertensive medications on self-harm or thoughts of self-harm

## AIM & HYPOTHESIS

### Primary Aim:

To evaluate the association of exposure to antihypertensive medications with thoughts of self-harm among individuals with hypertension

### Hypothesis:

Individuals with hypertension on antihypertensive medications are at increased risk of thoughts of self-harm compared to those not on these medications, controlling for covariates

## METHODS

### Study Design:

Cohort study: UK Biobank (N=503,328) 40-69 years of age being followed for at least 30 years

### Inclusion Criteria:

- Reporting hypertension at baseline visit
- With available baseline data on medication use
- With available data on thought of self-harm / self-harm

## METHODS

**Exclusion Criteria:** Missing values for exposures or outcomes

**Primary Exposure: Antihypertensive medications (binary):** angiotensin converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, beta-adrenergic receptor blockers, and diuretics

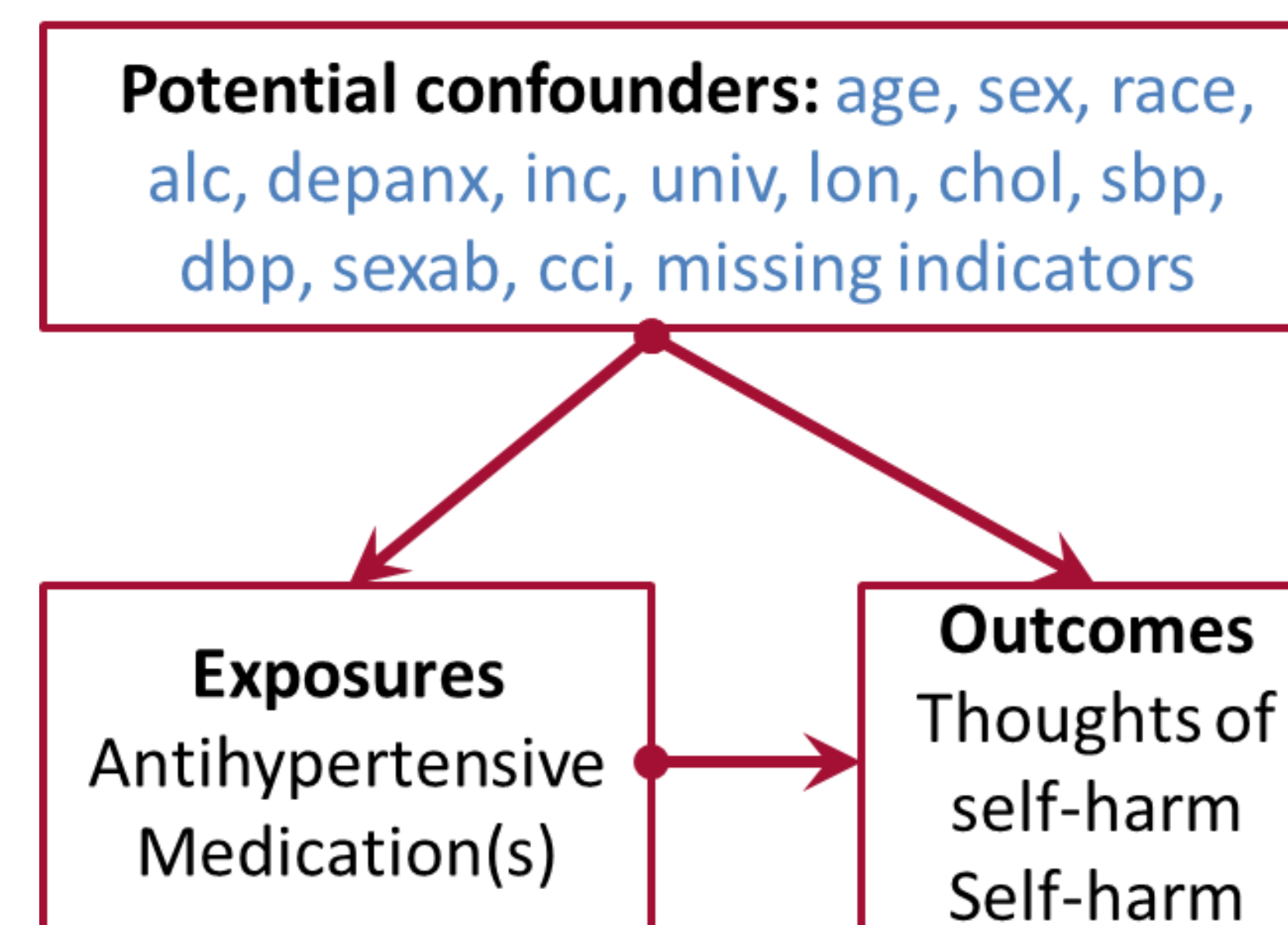
- Touchscreen questionnaire “taking regular prescription medication”, followed by verbal interview with trained nurses – collected in 2006-2010

**Primary Outcome: Thoughts of self-harm (binary)**

**Secondary Outcome: Self-harm (binary)**

- collected as part of the online mental health “Thoughts and Feelings” questionnaire administered to (N=339,092) study participants who agreed to email contact in 2016-2017 (Davis'20); N=157,366 completed

**Covariates:** (see Directed Acyclic Graph)



cci: MI, Congest ht fail, periph vasc dis, dem, cvd, cpd, pept ulcer d, livd, diabetes, hemi/paraplegia, rend, malig, aids (Carlson'87)

### Statistical Analysis (R):

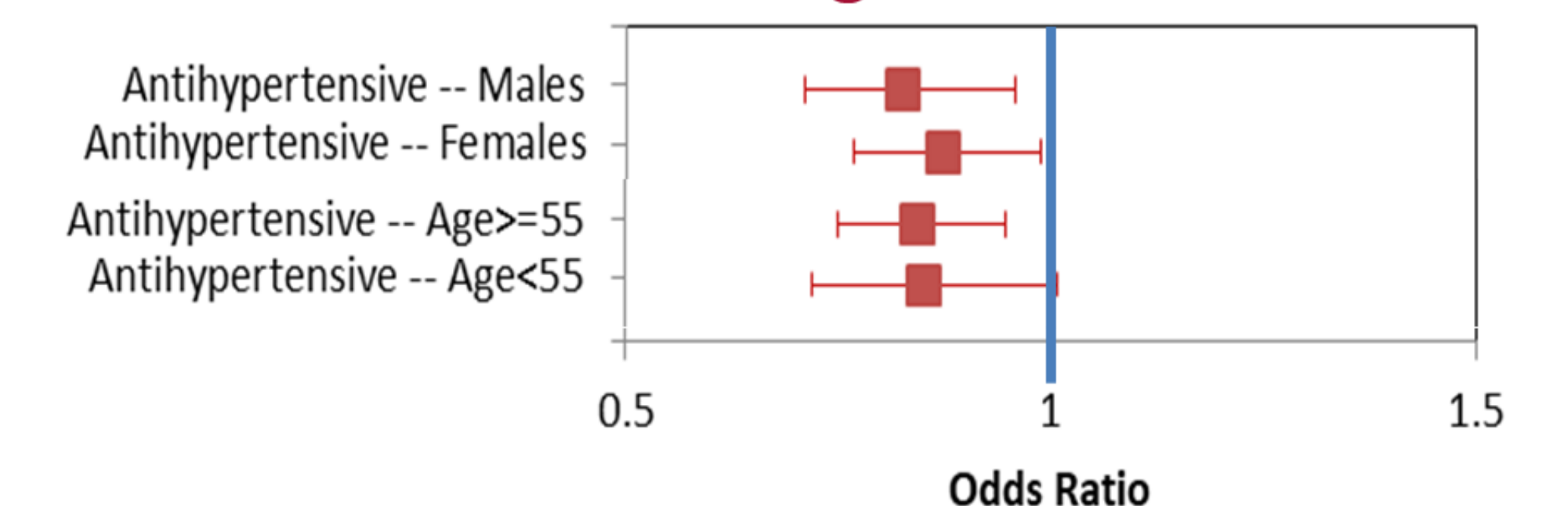
- Univariable logistic regression model with use of antihypertensive medications as primary exposure and thought of self-harm as primary outcome or self-harm as secondary outcome
- Multivariable logistic regression models with covariates
- Effect modification: by sex (Schaffer'00; Rhodes'14) and age (Dennis'07) (recoded as binary (<55 vs ≥55 years))

## RESULTS

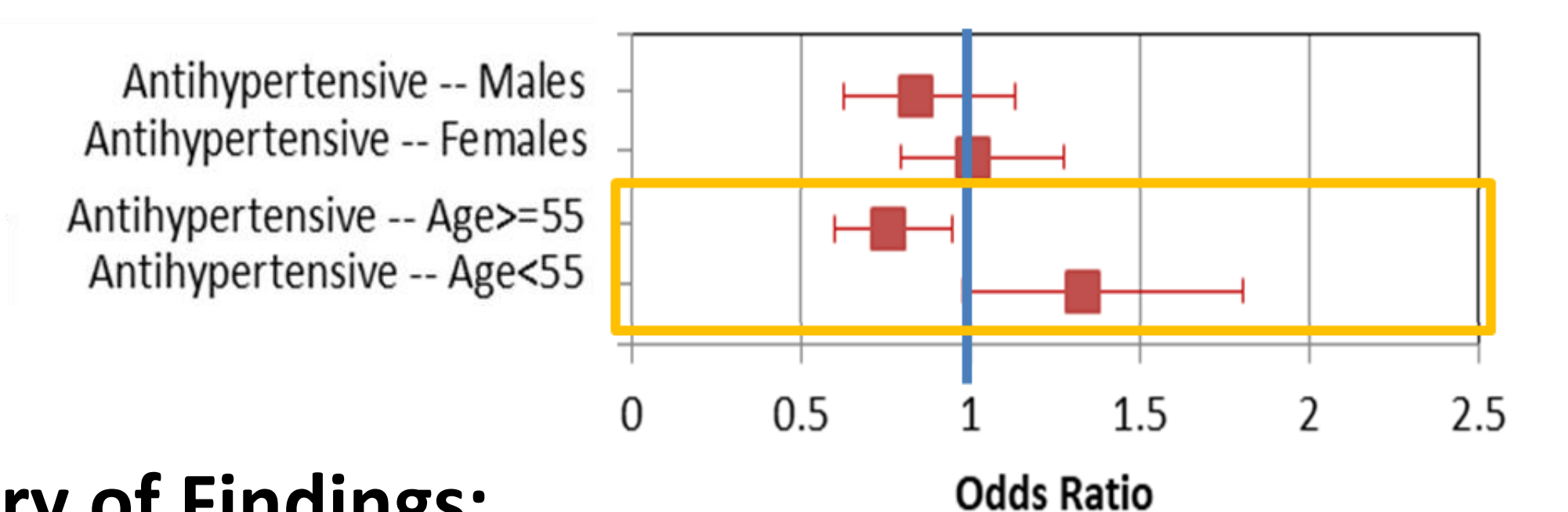
|   | Univariable/Crude analysis                  |                | Multivariable/Adjusted analysis **          |                |
|---|---|----------------|---|----------------|
| <b>Primary Outcome: Thoughts of self-harm</b> |   |                |   |                |
| <b>Medication</b>                             | <b>Odds ratio (95% confidence interval)</b> | <b>P-value</b> | <b>Odds ratio (95% confidence interval)</b> | <b>P-value</b> |
| (A) Antihypertensive                          | 0.73 (0.67-0.80)                            | <0.001         | 0.85 (0.77-0.93)                            | <0.001         |
| <b>Secondary Outcome: Self-harm</b>           |   |                |   |                |
| (A) Antihypertensive                          | 0.78 (0.66-0.93)                            | 0.004          | 0.93 (0.78-1.12)                            | 0.469          |

\*\*Adjusted for: age, sex, race, alc, depanx, inc, educ, lon, chol, sbp, dbp, sexab, CCI, and missing indicators  
(A) N=29,372

### Thoughts of self-harm\*\*



### Self-harm\*\*



### Summary of Findings:

- Antihypertensive med. associated with a 15% decrease in risk of thoughts of self-harm compared to non-use among those with hypertension, controlling for covariates
- Potential effect modification by age
- ≥55: 24% lower risk vs. <55: 33% higher risk of self-harm

## DISCUSSION

**Limitations:** Generalizability, Data collection (Fry'17; Wu Y'19), Sample sizes, mix of new and prevalent users

**Implications:** For older adults with hypertension, antihypertensive medications in general appear to be safe in terms of risk of thoughts of self-harm and self-harm  
In line with biological studies

**Future work:** Replications, other potential confounders