

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

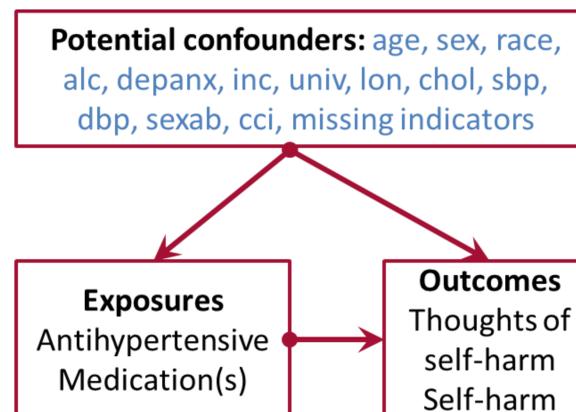
- Touchscreen questionnaire “taking regular prescription medication”, followed by verbal interview with trained nurses – collected in 2006-2010

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):

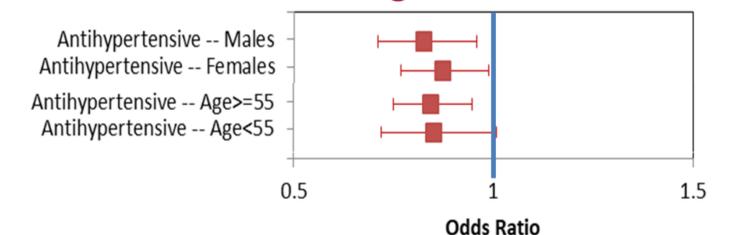
- Univariable logistic regression model with use of antihypertensive medications as primary exposure and thought of self-harm as primary outcome or self-harm as secondary outcome
- Multivariable logistic regression models with covariates
- Effect modification: by sex (Schaffer'00; Rhodes'14) and age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

RESULTS

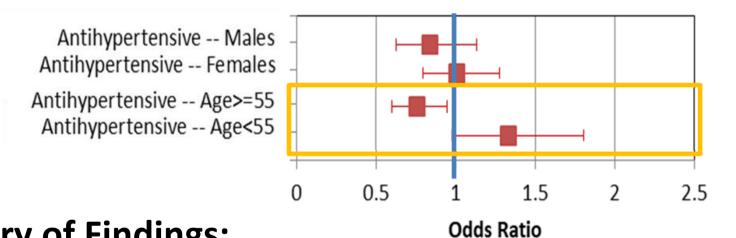
| | Univariable/Crude analysis | | Multivariable/Adjusted analysis ** | |
|---|---|----------------|---|----------------|
| Primary Outcome: Thoughts of self-harm | | | | |
| Medication | Odds ratio (95% confidence interval) | P-value | Odds ratio (95% confidence interval) | P-value |
| (A) Antihypertensive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

**Adjusted for: age, sex, race, alc, dep anx, 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