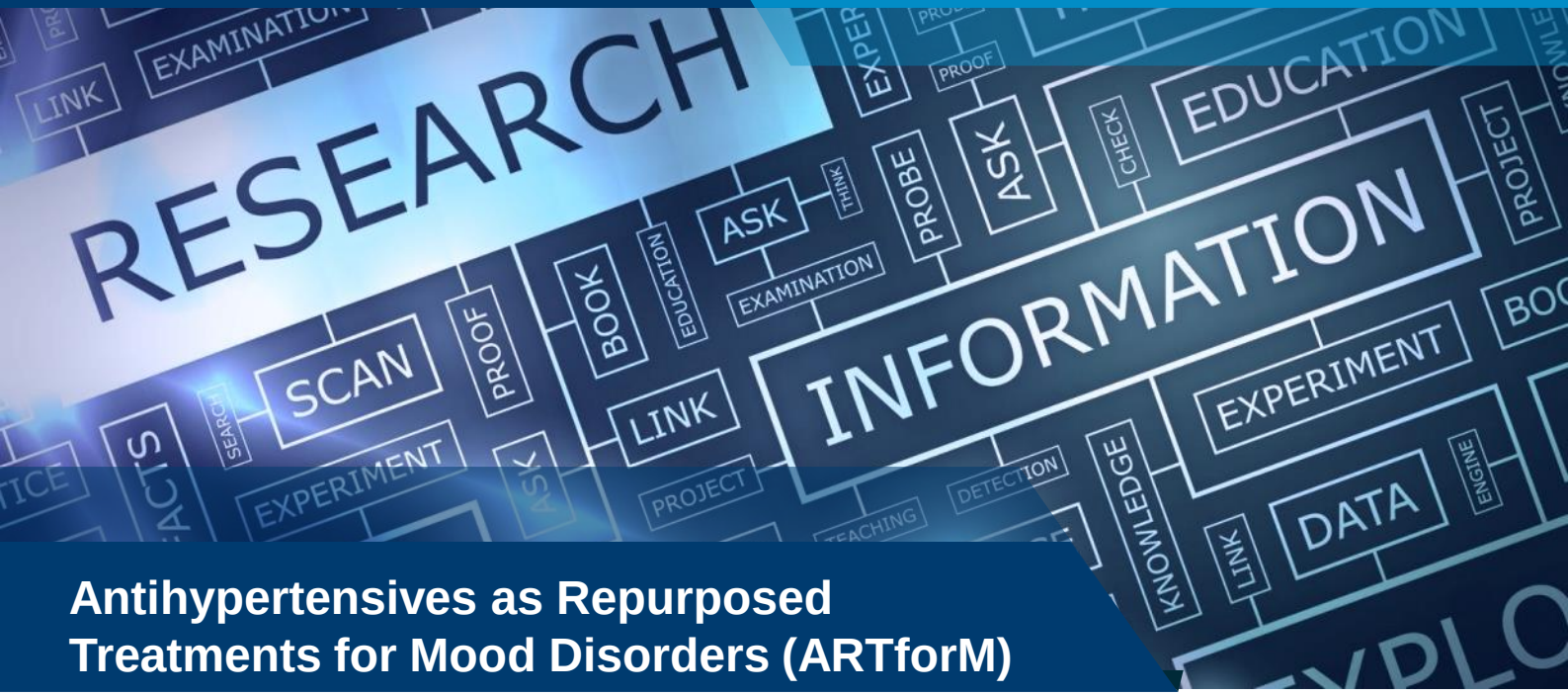
CHIEF SCIENTIST OFFICE

CODE: TCS/16/06

RESEARCH PROJECT BRIEFING




# Antihypertensives as Repurposed Treatments for Mood Disorders (ARTforM)

## AIMS

Using national-level healthcare data linkage in Scotland, we assessed how treatment with different types of antihypertensives was associated with risk of developing new-onset major depressive disorder and bipolar disorder. We also assessed how these antihypertensive classes affected the recurrence of mood disorder episodes in people with a known history of major depressive disorder or bipolar disorder.

## KEY FINDINGS

For people with no previous history of mood disorder:

- Treatment with most classes of antihypertensives was associated an **increased risk of new-onset depression but a reduced risk of new-onset bipolar disorder.**
- Angiotensin antagonists were associated with the lowest risk of developing bipolar disorder.

For people with a previous history of mood disorder:

- All classes of antihypertensive treatment were associated with **increased risk of depressive episodes**; there was no clear pattern with bipolar disorder.

## WHAT DID THE STUDY INVOLVE?

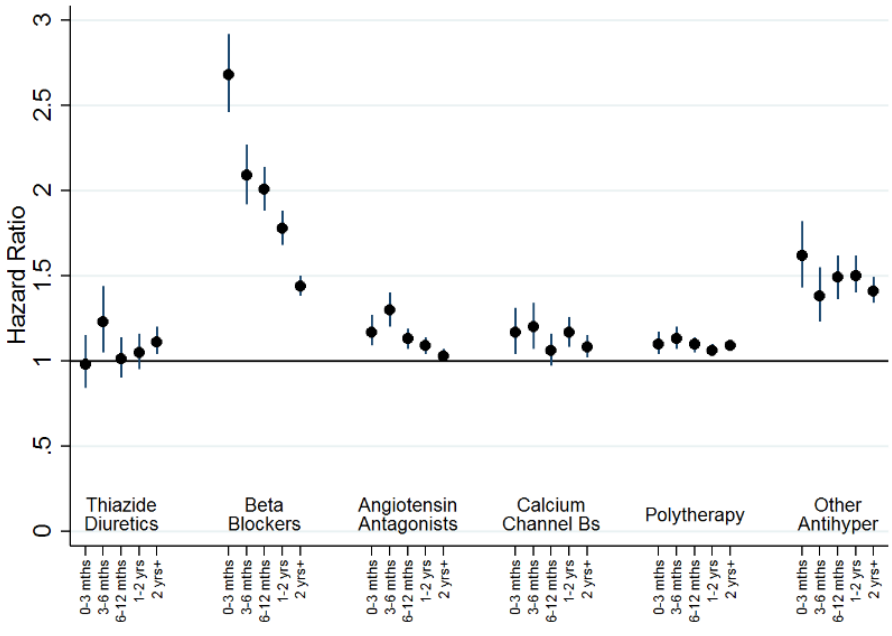
Two cohorts of patients treated with antihypertensives: one without a previous history of mood disorder (n=538,730) and one with a previous history of mood disorder (n=262,278), identified from Scottish prescribing (2009-2016) and hospital admission (1981-2016) records. Both cohorts were matched by age, sex and area deprivation to untreated comparator groups. Associations between treatment with antihypertensives and major depressive disorder or bipolar disorder episodes were assessed using data on over 6 million person-years of follow-up.

## WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

For people with no history of mood disorder, being treated with most antihypertensive classes was associated with an increased risk of new-onset major depressive disorder (see figure), and a reduced risk of bipolar disorder. These associations were stronger in the early stages of antihypertensive treatment and for beta-blockers. Antihypertensives, and particularly angiotensin antagonists, might be repurposed to treat bipolar disorder, but not depression. The mechanism of these effects are complex and likely to include health-seeking behaviour, psychosocial factors and individual variation on genetic or biological pathways.

Findings for people with an already established mood disorder were similar. In this group, all classes of antihypertensives were associated with increased risk of depressive episodes (but not bipolar episodes).

**Hazard Ratio for new-onset depression by antihypertensive class over time (0 to 3 mths, 3 to 6 mths, 6-12 mths, 1 to yrs, and 2 yrs).**



## WHAT IMPACT COULD THE FINDINGS HAVE?

- Patients receiving antihypertensive treatments, particularly propranolol, should be monitored for risk of new-onset major depression.
- Antihypertensive treatments are unlikely to be useful overall as repurposed treatments for depression.
- The potential for angiotensin antagonists as new treatments for bipolar disorder should be studied in more detail.
- Lower long-term risk of depression among people who have not received antihypertensive treatments may indicate an unmet care need.

## HOW WILL THE OUTCOMES BE DISSEMINATED?

- This work has been submitted for publication to *PLOS Medicine.*
- Professor Daniel Smith presented interim findings at the NHS Research Scotland Annual Meeting, Perth, Sept 2018.
- Further presentations of the results are planned at local and national meetings.

## CONCLUSION

We found little evidence to support the idea that antihypertensive medications might be usefully repurposed as treatments for depression. Tentatively, we conclude that some classes of antihypertensive - and angiotensin antagonists in particular - may offer some protection against BD, but this finding awaits replication and further study.

## RESEARCH TEAM & CONTACT

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### Additional Information

The project ended on 31st January 2019 and received £300k of funding from the Chief Scientist Office.