Antihypertensive drugs and COVID-19

To the Editor

Professor Hippisley-Cox and colleagues took on a daunting task in linking and analysing electronic medical records with test results for SARS-CoV-2 and admissions to intensive care units in the UK. They deserve great credit for linking wrangling and analysing this data set. As the authors state randomised trials are underway and these should guide use of ACE inhibitors/angiotensin receptor blockers (ACEI/ARB) as therapy for COVID-19. Their data provide reassurance that continuation of treatment is safe, but I think we need to be cautious in accepting their conclusion that ACEI/ARB may be protective against infection with SARS-CoV-2.

First, the unadjusted relative risk estimates for severe COVID-19 with ACEI and ARB seem to be elevated. If so, the crude risk of developing severe disease was higher in users than non-users of these drugs. As the authors recognise, there is a strong confounding effect of treatment indication. A cluster of conditions, including hypertension, diabetes and heart failure, are indications for treatment with ACEI/ARB and are also believed to be associated with study endpoints—admission to hospital or intensive care unit with COVID-19. The authors have performed extensive adjustments and sensitivity analyses. To see such adjustments flip a risk-elevating relationship to a significant protective effect is unusual. In a smaller study published while this paper was in preparation, Fosbøl and colleagues calculated an unadjusted HR for severe COVID-19 (analogous to the present study) with community use of ACEI/ARB of 2.34 (1.97–2.77). Adjusted only for age and sex the HR estimate was 1.32 (1.10–1.58). Adjusted further for various comorbid states and medications the HR was 1.15 (0.95–1.41), seeming to rule out a substantial protective effect.

Second, Hippisley-Cox and colleagues have included negative control exposures in their main analyses in the form of HR estimates for COVID-19 in users of thiazides and calcium channel blocking (CCB) drugs. The apparent ‘protective’ effect of thiazides they saw is similar to that with ACEI/ARB and the effect of CCB is smaller but significant. I think it is unlikely that all three drug classes have a protective effect, and this association may be a product of the adjustment model than a causal effect. It would be helpful to have a table of the unadjusted, age and sex adjusted and fully adjusted HR estimates for each of the main antihypertensive drug classes to better understand how these risk estimates differ and how statistical adjustment for confounding changes them.

David Henry

Correspondence to Professor David Henry, Institute for Evidence-Based Healthcare, Bond University, Robina, Q1 4229, Australia; dhenny@bond.edu.au

Contributors DH is the sole author of the letter.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

This article is made freely available for use in accordance with BMJ’s website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.

To cite Henry D. Heart Epub ahead of print: [please include Day Month Year]. doi:10.1136/heartjnl-2020-318313

http://dx.doi.org/10.1136/heartjnl-2020-318314
Heart 2020;0:1.
doi:10.1136/heartjnl-2020-318313

ORCID iD

David Henry http://orcid.org/0000-0003-2934-2242

REFERENCES
