

# Withdrawal of renin-angiotensin system inhibitors' effect on estimated glomerular filtration rate in adults with advanced kidney disease: the STOP-ACEi RCT

Sunil Bhandari,<sup>1\*</sup> Samir Mehta,<sup>2</sup> Arif Khwaja,<sup>3</sup>  
John Cleland,<sup>4</sup> Natalie Ives,<sup>2</sup> Elizabeth Brettell,<sup>2</sup>  
Marie Chadburn<sup>2</sup> and Paul Cockwell<sup>5</sup>  
for the STOP-ACEi Trial Investigators

<sup>1</sup>Department of Renal Medicine, Hull University Teaching Hospitals NHS Trust, and Hull York Medical School, East Yorkshire, UK

<sup>2</sup>Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, UK

<sup>3</sup>Sheffield Kidney Institute, Sheffield, UK

<sup>4</sup>National Heart & Lung Institute, Imperial College London, London, UK

<sup>5</sup>Department of Renal Medicine, Queen Elizabeth Hospital, Birmingham, UK

\*Corresponding author [sunil.bhandari@nhs.net](mailto:sunil.bhandari@nhs.net)

## Disclosure of interests

**Full disclosure of interests:** Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at (<https://doi.org/10.3310/TTMC6210>).

**Primary conflicts of interest:** The authors have no conflicts of interest related to this trial and all other potential conflicts of interest are detailed in each individual ICMJE form submitted.

Published March 2024  
DOI: 10.3310/TTMC6210

## Plain language summary

Withdrawal of renin-angiotensin system inhibitors' effect on estimated glomerular filtration rate in adults with advanced kidney disease: the STOP-ACEi RCT

Efficacy and Mechanism Evaluation 2024; Vol. 11: No. 5  
DOI: 10.3310/TTMC6210

NIHR Journals Library [www.journalslibrary.nihr.ac.uk](http://www.journalslibrary.nihr.ac.uk)

## Plain language summary

Drugs called angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, together known as renin-angiotensin system inhibitors, are used to treat high blood pressure, slow worsening kidney function and lower the risk of kidney failure (known as end-stage kidney disease which requires treatment with dialysis or kidney transplantation) in patients with early chronic kidney disease. However, we did not know if patients treated with renin-angiotensin system inhibitors and who have progressed to more advanced chronic kidney disease (stage 4 or 5) should stop or continue renin-angiotensin system inhibitors.

To determine whether stopping renin-angiotensin system inhibitors in people with advanced chronic kidney disease leads to an improvement or stabilisation of kidney function required a study comparing the outcomes of people who had had these drugs stopped with a group who continued these drugs (the STOP-angiotensin-converting enzyme inhibitors trial). We recruited 411 participants with advanced chronic kidney disease who were receiving renin-angiotensin system inhibitors from 37 kidney units in the UK, and randomly (like flipping a coin) allocated them to either stop or continue renin-angiotensin system inhibitors.

We then compared kidney function between the two groups at 3 years. We also assessed whether stopping or continuing renin-angiotensin system inhibitors had an influence on the development of end-stage kidney disease or need for kidney replacement therapy, the number of hospitalisations, blood pressure, quality of life and physical function. We collected data on safety outcomes including death and heart-related events (such as heart attacks).

The results of the trial showed no difference in kidney function at 3 years. The number of participants requiring dialysis, or a kidney transplant was also similar, as was the quality of life and physical function between the groups. Deaths and the number of heart events were similar in both groups.

This research suggests that there is no benefit in stopping renin-angiotensin system inhibitors in patients with advanced chronic kidney disease.

# Efficacy and Mechanism Evaluation

ISSN 2050-4373 (Online)

A list of Journals Library editors can be found on the [NIHR Journals Library website](#)

*Efficacy and Mechanism Evaluation* (EME) was launched in 2014 and is indexed by Europe PMC, DOAJ, Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and NCBI Bookshelf.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) ([www.publicationethics.org/](http://www.publicationethics.org/)).

Editorial contact: [journals.library@nihr.ac.uk](mailto:journals.library@nihr.ac.uk)

The full EME archive is freely available to view online at [www.journalslibrary.nihr.ac.uk/eme](http://www.journalslibrary.nihr.ac.uk/eme).

## Criteria for inclusion in the *Efficacy and Mechanism Evaluation* journal

Reports are published in *Efficacy and Mechanism Evaluation* (EME) if (1) they have resulted from work for the EME programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

## EME programme

The Efficacy and Mechanism Evaluation (EME) programme funds ambitious studies evaluating interventions that have the potential to make a step-change in the promotion of health, treatment of disease and improvement of rehabilitation or long-term care. Within these studies, EME supports research to improve the understanding of the mechanisms of both diseases and treatments.

The programme supports translational research into a wide range of new or repurposed interventions. These may include diagnostic or prognostic tests and decision-making tools, therapeutics or psychological treatments, medical devices, and public health initiatives delivered in the NHS.

The EME programme supports clinical trials and studies with other robust designs, which test the efficacy of interventions, and which may use clinical or well-validated surrogate outcomes. It only supports studies in humans and where there is adequate proof of concept. The programme encourages hypothesis-driven mechanistic studies, integrated within the efficacy study, that explore the mechanisms of action of the intervention or the disease, the cause of differing responses, or improve the understanding of adverse effects. It funds similar mechanistic studies linked to studies funded by any NIHR programme.

The EME programme is funded by the Medical Research Council (MRC) and the National Institute for Health and Care Research (NIHR), with contributions from the Chief Scientist Office (CSO) in Scotland and National Institute for Social Care and Health Research (NISCHR) in Wales and the Health and Social Care Research and Development (HSC R&D), Public Health Agency in Northern Ireland.

## This report

The research reported in this issue of the journal was funded by the EME programme as award number 11/30/07. The contractual start date was in February 2014. The final report began editorial review in November 2022 and was accepted for publication in May 2023. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The EME editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research. The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the MRC, the EME programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the EME programme or the Department of Health and Social Care.

Copyright © 2024 Bhandari *et al.* This work was produced by Bhandari *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This is an Open Access publication distributed under the terms of the Creative Commons Attribution CC BY 4.0 licence, which permits unrestricted use, distribution, reproduction and adaptation in any medium and for any purpose provided that it is properly attributed. See: <https://creativecommons.org/licenses/by/4.0/>. For attribution the title, original author(s), the publication source – NIHR Journals Library, and the DOI of the publication must be cited.

Published by the NIHR Journals Library ([www.journalslibrary.nihr.ac.uk](http://www.journalslibrary.nihr.ac.uk)), produced by Newgen Digitalworks Pvt Ltd, Chennai, India ([www.newgen.co](http://www.newgen.co)).

