Epithelium-off corneal cross-linking surgery compared with standard care in 10- to 16-year-olds with progressive keratoconus: the KERALINK RCT

Daniel FP Larkin,^{1*} Kashfia Chowdhury,² Caroline J Doré,² Catey Bunce,¹ Jennifer M Burr,³ Emilia Caverly,² Lisa French,² Dimitra Kopsini,² Anne Klepacz,⁴ Mathew Raynor,⁵ Matthew Edwards⁵ and Stephen J Tuft¹

Declared competing interests of authors: none

Published October 2021 DOI: 10.3310/eme08150

Plain English summary

The KERALINK RCT

Efficacy and Mechanism Evaluation 2021; Vol. 8: No. 15

DOI: 10.3310/eme08150

NIHR Journals Library www.journalslibrary.nihr.ac.uk

¹National Institute for Health Research Biomedical Research Centre, Moorfields Eye Hospital, London, UK

²Comprehensive Clinical Trials Unit, Institute of Clinical Trials and Methodology, University College London, London, UK

³School of Medicine, University of St Andrews, St Andrews, UK

⁴Keratoconus Support and Self-Help Association (known as The Keratoconus Group), London, UK

⁵Department of Ophthalmology, Royal Hallamshire Hospital, Sheffield, UK

^{*}Corresponding author f.larkin@ucl.ac.uk

Plain English summary

Reratoconus is a long-term disorder causing increasing steepening and thinning of the cornea, the clear front wall of the eye. It leads to progressive distortion of vision. In most cases keratoconus starts during the teenage years and stops progressing when people are about 30 years old. It is often more severe if it starts in childhood. It can progress quite quickly to a stage that good vision cannot be achieved by standard care (wearing glasses and contact lenses) and a transplant operation becomes necessary. Recently, a new surgical intervention involving the removal of the surface layer of the cornea ('epithelium-off'), the administration of eye drops and the application of ultraviolet light has become available. The procedure can be performed under local anaesthesia in most patients. It is called corneal cross-linking. It is believed to stop keratoconus progression by increasing the stiffness of the cornea, but previous research has been of poor quality.

KERALINK was a high-quality randomised trial to see if the new treatment really works. Young people with confirmed keratoconus progression in one or both eyes were randomly allocated to the new treatment in addition to standard care, or to standard care alone. In total, 60 young people aged 10–16 years participated (30 allocated to the new treatment and 30 allocated to standard care alone).

Participants were followed up for 18 months. The primary outcome was the degree of distortion of the cornea at 18 months. Other outcomes included vision, need for glasses and contact lenses, quality of life, and safety. We found significantly less distortion in eyes receiving the new treatment. This shows that the new treatment is effective in preventing disease progression. Participants allocated to the new treatment group also had better vision and were less likely to need to wear glasses or contact lenses, and there were no treatment-related complications.

Efficacy and Mechanism Evaluation

ISSN 2050-4365 (Print)

ISSN 2050-4373 (Online)

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

Editorial contact: journals.library@nihr.ac.uk

The full EME archive is freely available to view online at www.journalslibrary.nihr.ac.uk/eme. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

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 man 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 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 project number NIHR131734. The contractual start date was in October 2015. The final report began editorial review in November 2020 and was accepted for publication in May 2021. 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, NETSCC, 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, NETSCC, the EME programme or the Department of Health and Social Care.

Copyright © 2021 Larkin et al. This work was produced by Larkin 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 adaption 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), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).

NIHR Journals Library Editor-in-Chief

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

NIHR Journals Library Editors

Professor John Powell Chair of HTA and EME Editorial Board and Editor-in-Chief of HTA and EME journals. Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK, and Professor of Digital Health Care, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Professor Andrée Le May Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals) and Editor-in-Chief of HS&DR, PGfAR, PHR journals

Professor Matthias Beck Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Dr Peter Davidson Consultant Advisor, Wessex Institute, University of Southampton, UK

Ms Tara Lamont Senior Scientific Adviser (Evidence Use), Wessex Institute, University of Southampton, UK

Dr Catriona McDaid Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

Professor William McGuire Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads Emeritus Professor of Wellbeing Research, University of Winchester, UK

Professor James Raftery Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

Professor Jonathan Ross Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

Professor Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Please visit the website for a list of editors: www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: journals.library@nihr.ac.uk