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# Accuracy of glomerular filtration rate (GFR) estimation using creatinine and cystatin C and albuminuria for monitoring disease progression in patients with stage 3 chronic kidney disease: the eGFR-C study

Submission date 26/09/2013	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered [X] Protocol
Registration date 08/10/2013	<b>Overall study status</b> Completed	<ul><li>[_] Statistical analysis plan</li><li>[X] Results</li></ul>
Last Edited 29/07/2024	<b>Condition category</b> Urological and Genital Diseases	Individual participant data

### Plain English summary of protocol

http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/renal/egfr-c/participants /index.aspx

#### **Study website** http://www.birmingham.ac.uk/egfr-c

# **Contact information**

**Type(s)** Scientific

**Contact name** Mr Ryan Ottridge

### Contact details

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### Additional identifiers

EudraCT/CTIS number

#### **IRAS number**

ClinicalTrials.gov number NCT02433002

Secondary identifying numbers HTA 11/103/01, UKCRN ID 15268

# Study information

#### Scientific Title

Accuracy of glomerular filtration rate (GFR) estimation using creatinine and cystatin C and albuminuria for monitoring disease progression in patients with stage 3 chronic kidney disease - prospective longitudinal study in a multi-ethnic population: the eGFR-C study

Acronym eGFR-C

#### **Study objectives**

The eGFR-C study will assess the accuracy of current and alternative tests of kidney function against a reference test in people with moderate (stage 3) chronic kidney disease (CKD).

More details can be found at: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=15268 More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1110301 Protocol can be found at: https://www.birmingham.ac.uk/egfrc/documents (version 4.0 02.02.17)

#### Ethics approval required

Old ethics approval format

Ethics approval(s) South East Coast Surrey REC, 09/10/2013, ref 13/LO/1349

**Study design** Observational prospective longitudinal cohort study

**Primary study design** Observational

**Secondary study design** Cohort study

**Study setting(s)** Hospital

Study type(s) Screening

Participant information sheet

Patient information can be found at http://www.birmingham.ac.uk/research/activity/mds/trials /bctu/trials/renal/egfr-c/participants/sheet.aspx

#### Health condition(s) or problem(s) studied

Topic: Renal and Urogenital; Subtopic: Renal and Urogenital (all Subtopics); Disease: Renal

#### Interventions

Main study: 1300 patients. Biological variability study: In a sub-study 20 participants will undergo the reference test four times over four weeks and then exit the study.

Iohexol GFR tests, 1300 participants will undergo baseline (month 0) and final (month 36) reference GFR, estimated GFR (eGFR) and urinary albumin-to-creatinine ratio (ACR) tests. Additionally they will provide ACR and eGFR tests at 6-monthly intervals. A subset of the cohort (n=375) will receive annual reference GFR tests.

Participants will be recruited from hospital clinics and GP practices at six major UK centres.

Participants will undergo reference GFR testing at study entry with a second follow-up reference test three years later. The reference test involves injecting a small amount of iohexol into a vein and taking blood samples over the next 4 hours to see how quickly the iohexol disappears from the blood stream as a result of glomerular filtration. The rate at which iohexol disappears is equivalent to the level of kidney function. Blood tests for monitoring kidney function, including testing for creatinine and cystatin C, and measurement of urinary albumin will be done every six months during the study period. Iohexol measured GFR will be accepted as the reference (gold standard) measure of kidney function against which each GFR-estimating equations will be compared. The alternative estimated measures of GFR, derived from measuring substances (creatinine and cystatin C) in the blood, will be compared against the reference test. An important outcome is how much the reference test changes over the three years of the study, and how well the surrogate measures reflect this change. We will also collect accurate test cost data for subsequent cost-effectiveness analysis (e.g. do the relative costs of the tests justify any change in practice due to improved performance of one test compared to another?).

Follow-up length: 36 months

#### Intervention Type

Other

#### Phase

Not Applicable

#### Primary outcome measure

1. To estimate and compare the accuracy and precision of GFR-estimating equations based on the Modification of Diet in Renal Disease (MDRD) equation and three Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations using either creatinine or cystatin C or a combination of both in people with stage 3 CKD.

2. To estimate the accuracy and precision of the GFR-estimating equations according to ethnic group (particularly Caucasians, African-Caribbean and South-Asian), and baseline diabetes and proteinuria.

Percentage error in eGFR compared to reference GFR. Values will be computed (primary outcome measures 1 and 2) using baseline data for each of the four eGFR equations, and the proportions within 30% (P30) of the reference standard quoted and compared as a measure of

accuracy and precision.

3. To evaluate and compare how accurately these GFR-estimating equations reflect change in GFR over three years. Difference in rate of change in eGFR compared to rate of change in reference GFR. Rates of change will be estimated using linear regression and the change per annum and percentage change per annum compared to baseline values will be computed. Large error will be defined as differing by more than 3 mL/min/1.73 m^2/year or by 5 percent points per annum.

#### Secondary outcome measures

1. To establish which GFR-estimating equation, together with ACR, or ACR alone, most accurately predicts those people that have progressive loss of kidney function (CKD progression). Progressive loss of kidney function defined as decline in GFR of more than 10 mL /min/1.73 m^2/3 years or increase in albuminuria category as defined by Kidney Disease: Improving Global Outcomes (KDIGO).

2. To compare the effectiveness and costs of monitoring strategies for identifying people that have progressive loss of kidney function (CKD progression) utilising different GFR-estimating equations and test schedules, accounting for differences in risk of progression. Measured using Cost per quality-adjusted life-year (QALY).

#### Sub-study of patterns of disease progression

To estimate and model disease progression (decline in GFR or increase in ACR) according to ethnic group (particularly Caucasians, African-Caribbean and South-Asian), and baseline diabetes and proteinuria. Difference in rate of change in eGFR compared to rate of change in reference GFR based on measurements made every 12 months.

Additional study of intra-individual biological variation Within-individual (CVI) variation and the critical difference (reference change value, RCV) for

reference GFR and the estimated GFR equations.

#### Overall study start date

01/02/2014

#### **Completion date**

30/06/2020

# Eligibility

#### Key inclusion criteria

1. Male and female, aged 18 years or over

2. Patients with stage 3 CKD (GFR 30-59 mL/min/1.73 m2) as defined internationally, diagnosed using Modification of Diet in Renal Disease/Chronic Kidney Disease Epidemiology Collaboration (MDRD/CKD EPI) eGFR (at least two consecutive test results in this range at least 90 days apart, with the most recent test in the last 12 months)

3. Written informed consent

#### Participant type(s)

Patient

#### **Age group** Adult

#### Lower age limit

18 Years

**Sex** Both

**Target number of participants** Planned Sample Size: 1320; UK Sample Size: 1320

### Key exclusion criteria

1. History of untoward reactions to iodinated contrast media or allergy to topical iodine 2. Episode of acute kidney injury in previous 6 months (as defined by the Acute Kidney Injury

Network criteria)

3. Amputation of whole or part limb

4. Pregnant or breastfeeding

5. Known alcohol or drug abuse

6. Any clinical condition with an expected survival of less than study duration

7. Inability to comply with study schedule and follow-up

8. Inability to provide informed consent e.g. due to cognitive impairment

### Date of first enrolment

01/02/2014

Date of final enrolment 31/07/2015

# Locations

#### **Countries of recruitment** England

United Kingdom

**Study participating centre Birmingham Clinical Trials Unit** Public Health Building University of Birmingham Birmingham United Kingdom B15 2TT

# Sponsor information

#### **Organisation** University of Birmingham (UK)

#### Sponsor details

Edgbaston Birmingham England United Kingdom B15 2TT

**Sponsor type** University/education

Website http://www.birmingham.ac.uk

ROR https://ror.org/03angcq70

### Funder(s)

#### **Funder type** Government

**Funder Name** NIHR Health Technology Assessment Programme - HTA (UK)

# **Results and Publications**

### Publication and dissemination plan

There will be three different sets of results:

1. A substudy (BVS – biological variability), which has been submitted for publication in 2019.

2. The first primary outcome, accuracy of eGFRs, will be submitted for publication in 2020.

3. The second primary outcome, comparison of eGFRs for monitoring disease progression (over the 3 years of study follow up) will be submitted for publication in 2021.

### Intention to publish date

30/06/2021

#### Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

#### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		14/01/2014		Yes	No

Results article	01/08/2019	10/08/2020	Yes	No
HRA research summary		28/06/2023	No	No
<u>Results article</u>	01/07/2024	29/07/2024	Yes	No