Ref: 1718/FOI/011

Mr Sam Smith
request-410881-
a300febc@whatdotheyknow.com

04 July 2017

Dear Mr Smith,

Freedom of Information (FOI) Act request

We are writing in response to your request for information, under the FOI Act, dated 07 June 2017. Thank you for your enquiry. You requested the following information relating to REC reference 15/SC/0693 - *Using machine learning to improve prediction of AKI & deterioration*:

a) any minute/note of the meeting at which that approval was granted,

b) the papers on which that approval was made (we'd expect names etc. to be redacted),

c) Any conditions placed on that approval, or undertakings given in advance, that are not covered in either a, b, or the published information given at the link above.

Our response is as follows:

a) Please find attached the minutes of the Proportionate Review Sub-Committee meeting of the South Central Oxford C Research Ethics Committee (REC) meeting on 10 November 2015 where this study was reviewed. Please note personal identifiable information has been redacted in line with Freedom of Information Act (FOIA) section 40(2) data protection as the release of the information would breach the principles of the Data Protection Act. Please also note an unrelated REC study was reviewed at the meeting and this minute has been redacted as it does not relate to your request.

b) Please find attached the following papers which were reviewed and approved at the above meeting:

   i. Covering letter from Google DeepMind dated 27 October 2015 with personal identifiable information redacted under FOIA section 40(2).

   ii. Confirmation of insurance letter from Marsh Ltd dated 21 May 2015 with personal identifiable information redacted under FOIA section 40(2).

   iii. Confirmation of sponsor letter from Google DeepMind dated 28 October 2015 with personal identifiable information redacted under FOIA section 40(2).

   iv. NHS REC form 15/SC/0693 with personal identifiable information redacted under FOIA section 40(2).

   v. A further paper, the study protocol, was reviewed at the meeting however this has not been released.

FOIA Section 43(2) exemption; commercial interests, has been applied to a number of question detailed in the NHS REC form (iv) and the study protocol (v). Information referenced in the document is commercially sensitive as the release of the information *'would, or would be likely to, prejudice the commercial interests of any person'*. The relevant information redacted from the application form and detailed in the protocol relates to the research methodology which, if shared, could potentially lead to the replication by a competitor organisation which would prejudice the commercial interest of Google DeepMind.

We have considered the test of prejudice and believe the release could impact on the third parties commercial activity. The environment in which the third party operates in is competitive therefore disclosure of the information could undermine the third parties ability to utilise its own research and would provide its competitors with an unfair advantage thus leading to harm to its commercial interests. In this commercially competitive area of research and development any competitor seeking to develop a similar research methodology will be given a significant opportunity if the information is shared. This information has been provided in confidence to inform the Research Ethics Committee review.

We have considered the public interest test which, within the duty of confidence, assumes that information should be withheld unless the public interest in disclosure outweighs the public interest in maintaining the duty of confidence. This test was applied in this specific case and there was found to be no overriding public interest in the disclosure of the information.

c) Please find attached the REC favourable opinion letter which details the conditions of the favourable opinion with personal identifiable information redacted under FOIA section 40(2).

We hope that this information is helpful to you, but should you require further clarification, please let us know.

If you are unhappy about the way in which your request has been handled, the HRA has an internal complaints procedure through which you can raise any concerns. Further details of this procedure may be obtained by contacting the Complaints Manager via hra.foi@nhs.net. If you are dissatisfied with the outcome of the complaints procedure, you can apply to the Information Commissioner's Office (ICO), who will consider whether we, as a public authority, have complied with its obligations under the Act, and can require the HRA to remedy any problems. You can find out more about how to do this, and about the Act in general, on their website www.ico.org.uk. Complaints should be sent to:

> FOI Complaints Resolution – Information Commissioner's Office
> Wycliffe House, Water Lane, Wilmslow, Cheshire SK9 5AF

Yours sincerely

Stephen Tebbutt

Stephen Tebbutt
Head of Corporate Governance

Direct Line +44 (0)20 7972 2487

NHS

South Central - Oxford C Research Ethics Committee

Minutes of the Proportionate Review Sub-Committee meeting of the *South Central - Oxford C Research Ethics Committee* held on *10 November 2015* at *12:00 pm* in *correspondence*

Present:

Name	Profession	Capacity
Dr Lee Potiphar	Clinical Trials Manager	Expert
Professor David Scott	Pharmacist	Expert (Meeting Chair)
Mrs Vivienne Laurie	Barrister	Lay Plus

Also in attendance:

Name	Position (or reason for attending)
Mrs Maeve Ip Groot Bluemink	REC Manager (Minutes)

1. DECLARATIONS OF INTEREST

There were no declarations of interest.

2. NEW APPLICATIONS FOR ETHICAL REVIEW

2.1	15/SC/0693	**Using machine learning to improve prediction of acute kidney injury and general patient deterioration.**
	Chief Investigator:	▮▮▮▮▮▮▮▮▮▮▮▮
	Type of review:	*Other*
	Sponsor:	*Google DeepMind*
	Lead reviewer:	*Mrs Vivienne Laurie*

The PR Committee reviewed the above study.

Summary of Application

Acute kidney injury (AKI) is a sudden and recent reduction in a person's kidney function. In the UK 1 in 5 emergency admissions into hospital are associated with AKI, with up to 100,000 deaths each year in hospital associated with acute kidney injury. Up to 30% could be prevented with the right care. For this reason, the UK Dept of Health have said that an automated system ('national algorithm') must be put in place to alert doctors to cases of AKI.

By combining real-time and historic electronic data that hospitals store about their patients (such as laboratory information), DeepMind have created a system which generates such alerts at the Royal Free London NHS Trust. However, it appears that the national algorithm can miss cases of AKI, can misclassify their severity, and can label some as having AKI when they don't. The problem is not with the tool which DeepMind have made, but with the algorithm itself.

We think we can overcome these problems, and create a system which works better.

By combining classical statistical methodology and cutting-edge machine learning algorithms (e.g. 'unsupervised and semi-supervised learning'), this research project will create improved techniques of data analysis and prediction of who may get AKI, more accurately identify cases when they occur, and better alert doctors to their presence.

The PR Sub-Committee confirmed the study raised no material ethical issues under the following headings:

Social or scientific value; scientific design and conduct of the study, Recruitment arrangements and access to health information, and fair participant selection, Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future), Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity, Informed consent process and the adequacy and completeness of participant information, Suitability of the applicant and supporting staff, Independent review, Suitability of supporting information, Other general comments and Suitability of research summary.

Ethical issues raised, noted and resolved in discussion:

The PR Sub-Committee agreed that this was a well presented study with no material ethical issues.

<u>Decision</u>

The PR Sub-Committee gave a favourable opinion of the application.
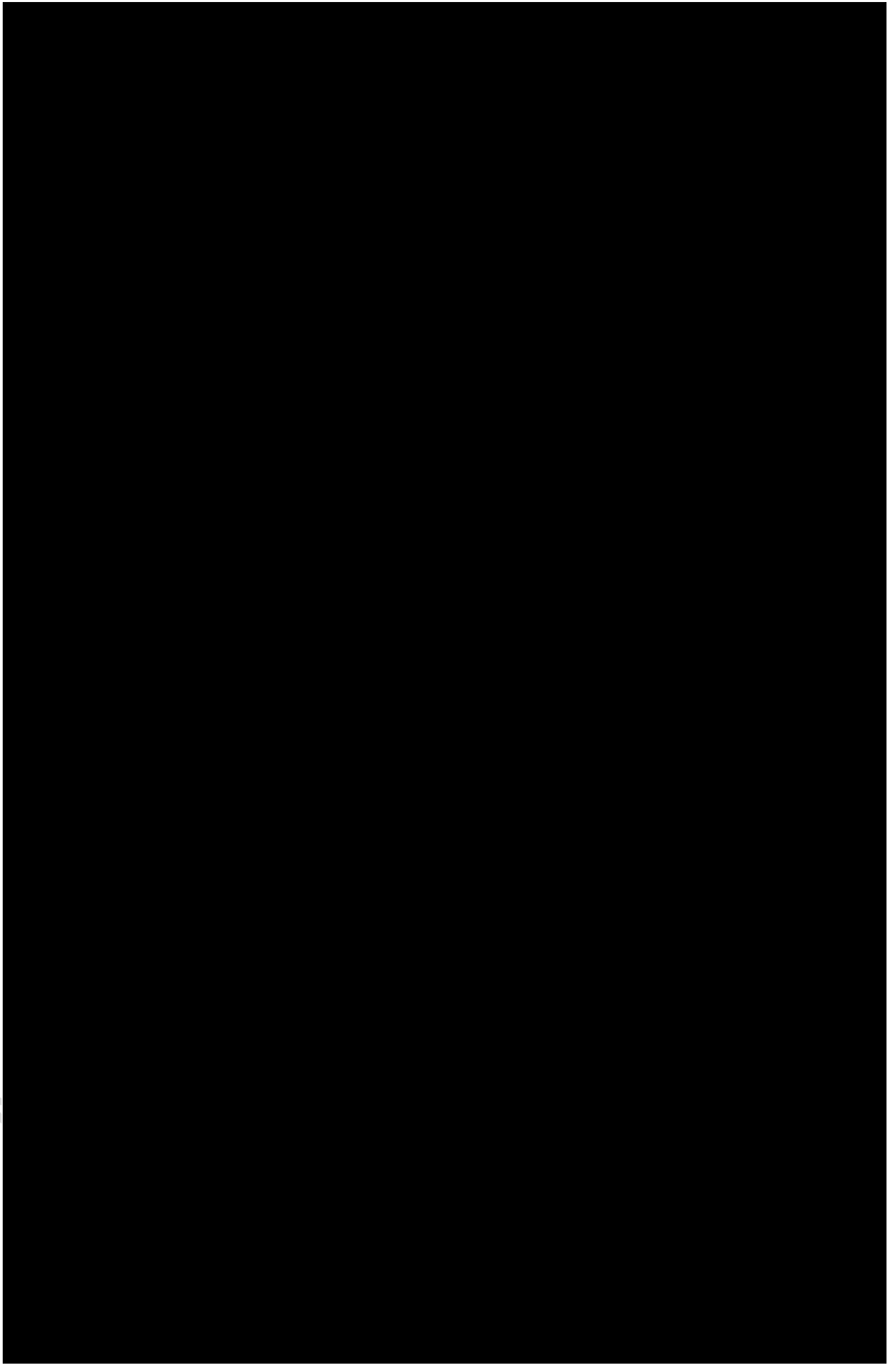
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Signed – Chair *Date*

………………………………………………… ……………………………..
Signed – REC Manager *Date*

Google DeepMind

October 27, 2015

NHS Research Ethics Committee
℅ NHS Health Research Authority
Submitted electronically via IRAS
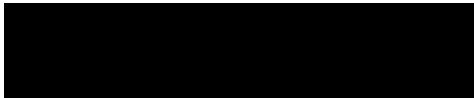
To whom it concerns,

Please find enclosed for your consideration our ethics application: *using machine learning to improve prediction of acute kidney injury and general patient deterioration*.

Our mission at DeepMind is to Solve Intelligence. We combine the best techniques from machine learning and systems neuroscience to build powerful general‑purpose learning algorithms. We firmly believe that machine learning algorithms, when applied to health data as outlined in this application, will enable us to improve our understanding of health data as well prediction, diagnosis and management of acute kidney injury.

Should you have any further questions, need any clarification of the points outlined in this application, or require further documentation from us please do not hesitate to contact me.

Yours Faithfully,

21st May 2015

To whom it may concern

Dear Sirs,

CONFIRMATION OF INSURANCE – Google Inc

As requested by the above client, we are writing to confirm that we act as Insurance Brokers to the client and that we have arranged insurance(s) on its behalf as detailed below:

PUBLIC LIABILITY

INSURER: ACE European Group Ltd

POLICY NUMBER: UKCANC68939

PERIOD OF INSURANCE: *1st June 2015 to 31st May 2016 (both dates inclusive)*

LIMIT OF INDEMNITY: USD5,000,000 any one occurrence

EMPLOYERS LIABILITY

INSURER: ACE European Group Ltd

POLICY NUMBER: UKCANC68939

PERIOD OF INSURANCE: *1st June 2015 to 31st May 2016 (both dates inclusive)*

LIMIT OF INDEMNITY: GBP10,000,000 any one occurrence

MARSH & McLENNAN COMPANIES

We have placed the insurance which is the subject of this letter after consultation with the client and based upon the client's instructions only. Terms of coverage, including limits and deductibles, are based upon information furnished to us by the client, which information we have not independently verified.

This letter is issued as a matter of information only and confers no right upon you other than those provided by the policy. This letter does not amend, extend or alter the coverage afforded by the policies described herein. Notwithstanding any requirement, term or condition of any contract or other document with respect to which this letter may be issued or pertain, the insurance afforded by the policy (policies) described herein is subject to all terms, conditions, limitations, exclusions and cancellation provisions and may also be subject to warranties. Limits shown may have been reduced by paid claims.

We express no view and assume no liability with respect to the solvency or future ability to pay of any of the insurance companies which have issued the insurance(s).

We assume no obligation to advise yourselves of any developments regarding the insurance(s) subsequent to the date hereof. This letter is given on the condition that you forever waive any liability against us based upon the placement of the insurance(s) and/or the statements made herein with the exception only of wilful default, recklessness or fraud.

This letter may not be reproduced by you or used for any other purpose without our prior written consent.

This letter shall be governed by and shall be construed in accordance with English law.

Yours faithfully,

For Marsh Ltd

Google DeepMind

October 28, 2015

NHS Research Ethics Committee
℅ NHS Health Research Authority
Submitted electronically via IRAS

To whom it concerns,

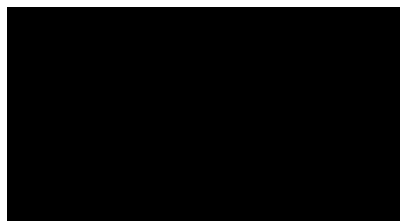**Re ethics application:** *Using machine learning to improve prediction of acute kidney injury and general patient deterioration*.

I can hereby confirm that Google DeepMind will take responsibility for the above named research study.

Please find enclosed documents showing confirmation of insurance to cover these activities.

Should you require any further information please do not hesitate to contact us.

Yours Faithfully,

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
Using machine learning to improve prediction of AKI & deterioration.

1. Is your project research?

◉ Yes   ◯ No

2. Select one category from the list below:

◯ Clinical trial of an investigational medicinal product

◯ Clinical investigation or other study of a medical device

◯ Combined trial of an investigational medicinal product and an investigational medical device

◯ Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

◯ Basic science study involving procedures with human participants

◯ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

◯ Study involving qualitative methods only

◯ Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

◉ Study limited to working with data (specific project only)

◯ Research tissue bank

◯ Research database

If your work does not fit any of these categories, select the option below:

◯ Other study

2a. Please answer the following question(s):

a) Will you be processing identifiable data at any stage of the research (including in the identification of participants)?   ◯ Yes   ◉ No

b) Please confirm that you will be processing only anonymised or pseudonymised data:

◉ Yes, only anonymised or pseudonmyised data   ◯ No

3. In which countries of the UK will the research sites be located?(Tick all that apply)

☑ England
☐ Scotland
☐ Wales
☐ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

◉ England

○ Scotland

○ Wales

○ Northern Ireland

○ This study does not involve the NHS

4. Which review bodies are you applying to?

☐ HRA Approval
☐ NHS/HSC Research and Development offices
☐ Social Care Research Ethics Committee
☑ Research Ethics Committee
☐ Confidentiality Advisory Group (CAG)
☐ National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D offices, the CI must create Site-Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

5. Will any research sites in this study be NHS organisations?

○ Yes   ◉ No

6. Do you plan to include any participants who are children?

◉ Yes   ○ No

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes   ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes   ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes   ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes   ◉ No

Integrated Research Application System
Application Form for Study limited to working with data (specific project only)

NHS
Health Research Authority

Application to NHS/HSC Research Ethics Committee

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Using machine learning to improve prediction of AKI & deterioration.

Please complete these details after you have booked the REC application for review.

REC Name:
South Central - Oxford C Research Ethics Committee

REC Reference Number:
15/SC/0693

Submission date:
28/10/2015

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Using machine learning to improve prediction of acute kidney injury and general patient deterioration.

A3-1. Chief Investigator:

Title Forename/Initials Surname

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* This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.

A copy of a <u>current CV</u> (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

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A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	2015/10-DM-01
Sponsor's/protocol number:	2015/10-DM-01
Protocol Version:	1.2
Protocol Date:	26/10/2015
Funder's reference number:	NA
Project website:	

Additional reference number(s):

Ref.Number Description	Reference Number

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

A5-2. Is this application linked to a previous study or another current application?

○ Yes   ◉ No

Please give brief details and reference numbers.

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2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK*

Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.

Acute kidney injury (AKI) is a sudden and recent reduction in a person's kidney function. In the UK 1 in 5 emergency admissions into hospital are associated with AKI, with up to 100,000 deaths each year in hospital associated with acute kidney injury. Up to 30% could be prevented with the right care. For this reason, the UK Dept of Health have said that an automated system ('national algorithm') must be put in place to alert doctors to cases of AKI.

By combining real-time and historic electronic data that hospitals store about their patients (such as laboratory information), DeepMind have created a system which generates such alerts at the Royal Free London NHS Trust. However, it appears that the national algorithm can miss cases of AKI, can misclassify their severity, and can label some as having AKI when they don't. The problem is not with the tool which DeepMind have made, but with the algorithm itself.

We think we can overcome these problems, and create a system which works better.

By combining classical statistical methodology and cutting-edge machine learning algorithms (e.g. 'unsupervised and semi-supervised learning'), this research project will create improved techniques of data analysis and prediction of who may get AKI, more accurately identify cases when they occur, and better alert doctors to their presence.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, R&D office or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

We do not foresee any major ethical, legal or management issues.

A6-3. Proportionate review of REC application *The initial project filter has identified that your study <u>may</u> be suitable for proportionate review by a REC sub-committee. Please consult the current guidance notes from NRES and indicate whether you wish to apply through the proportionate review service or, taking into account your answer to A6-2, you consider there are ethical issues that require consideration at a full REC meeting.*

⦿ Yes - proportionate review   ◯ No - review by full REC meeting

Further comments (optional):

We do not believe there to be any material ethical issues inherent in this research proposal.

Note: This question only applies to the REC application.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

☐ Case series/ case note review

☐ Case control

☐ Cohort observation

☐ Controlled trial without randomisation

☐ Cross-sectional study

☑ Database analysis

☐ Epidemiology

☐ Feasibility/ pilot study

☐ Laboratory study

☐ Metanalysis

☐ Qualitative research

☐ Questionnaire, interview or observation study

☐ Randomised controlled trial

☐ Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

To develop improved computer algorithms that can analyse routinely collected electronic patient record data to more accurately predict, diagnose and risk-stratify acute kidney injury.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

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A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Patients with complex long-term medical conditions are frequently admitted to hospital with either a deterioration of these chronic conditions or other acute medical problems. These acute admissions are often complicated by Acute Kidney Injury (AKI - which is a sudden decline in kidney function). Indeed, 1 in 5 emergency admissions will suffer AKI. AKI makes the patient sicker, prolongs the length of time a patient stays in hospital, and increases the risk of dying in hospital. It is estimated by the National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) that approximately 30% of AKI cases could be prevented. Furthermore, early detection and treatment of AKI may improve outcomes.

A national algorithm for the detection of AKI has been endorsed by NHS England, and its implementation has been mandated by a Patient Safety Alert and reinforced in the NHS's 'Five-Year Forward Review'. However there remain

major limitations with the national algorithm:

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If these proposed improvements to the national algorithm are found to be successful, we are confident that this new algorithm could provide benefits to patients and the NHS by reducing complications associated with acute kidney injury.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

All patients with blood tests processed by the Royal Free London NHS Foundation Trust laboratories including:
• Inpatients
• Emergency Department Patients
• Outpatients
• GP Patients.

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

• Patients where test data are not available electronically. (eg. point-of-care testing recorded on paper notes only).
• Patients who have not had any test performed.
• Patients who have explicitly dissented to the use or sharing of their data, even in anonymised form for research purposes and have informed The Royal Free Hospital NHS Trust of this.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

DeepMind acting as a data processor, under existing information sharing agreements with the responsible care organisations (in this case Royal Free Hospitals NHS Trust), and providing existing services on identifiable patient

data, will identify and anonymise the relevant records.

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INCENTIVES AND PAYMENTS

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

◯ Yes   ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

◉ Yes   ◯ No

If yes, please give details including the amount of any monetary payment or the basis on which this will be calculated:
Yes, the Chief Investigator and some co-investigators are paid employees of Google / Alphabet Inc. The company is also funding the research. However, this is not considered a conflict of interest. Rather, this is the norm for any commercial company involved in research to improve patient outcomes (for instance, drug companies performing drug trials).

NOTIFICATION OF OTHER PROFESSIONALS

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

◯ Yes   ◉ No

Please give details, or justify if not registering the research.
No appropriate public database exists for work such as this. However, any future trials of intervention, such as CTIMPs or those involving randomisation would be appropriately registered.

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

☑ Peer reviewed scientific journals
☑ Internal report
☑ Conference presentation
☑ Publication on website

☑ Other publication

☐ Submission to regulatory authorities

☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators

☐ No plans to report or disseminate the results

☑ Other (please specify)

Through the publication and implementation of any new and improved detection algorithms for acute kidney injury and/or generalised patient deterioration.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

☐ Independent external review

☑ Review within a company

☐ Review within a multi−centre research group

☑ Review within the Chief Investigator's institution or host organisation

☑ Review within the research team

☐ Review by educational supervisor

☑ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
This project has been developed using a cross-disciplinary team drawn from University College London, clinicians at UCLH & Royal Free Hospitals, and from within DeepMind.

This team includes world-leading experts in patient deterioration, medical epidemiology, statistics and machine learning research.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

☐ Review by independent statistician commissioned by funder or sponsor

☐ Other review by independent statistician

☑ Review by company statistician

☐ Review by a statistician within the Chief Investigator's institution

☑ Review by a statistician within the research team or multi−centre group

☐ Review by educational supervisor

☐ Other review by individual with relevant statistical expertise

☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

Title   Forename/Initials   Surname

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Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Sensitivity and specificity of novel predictive algorithms for the detection of AKI, as compared to the Nationally AKI Algorithm.

A58. What are the secondary outcome measures? *(if any)*

Sensitivity and specificity of novel predictive algorithms for general patient deterioration.

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:
Total international sample size (including UK): ██████████
Total in European Economic Area:

Further details:

██
██████████
██

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

Traditional statistical methods for sample size calculation are not helpful in determining the sample size for machine learning research.

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A61. Will participants be allocated to groups at random?

◯ Yes   ⦿ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Using statistics and systems that can learn to classify, predict and stratify from a wide array of structured and unstructured data, we aim to improve the early detection, prediction and stratification of AKI and patient deterioration.

The technical details of these techniques are outlined in brief below and expanded upon in the study protocol.

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(For details of references, please see full study protocol document.)

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

Title Forename/Initials Surname

████████████████████████

Title Forename/Initials Surname

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Title Forename/Initials Surname

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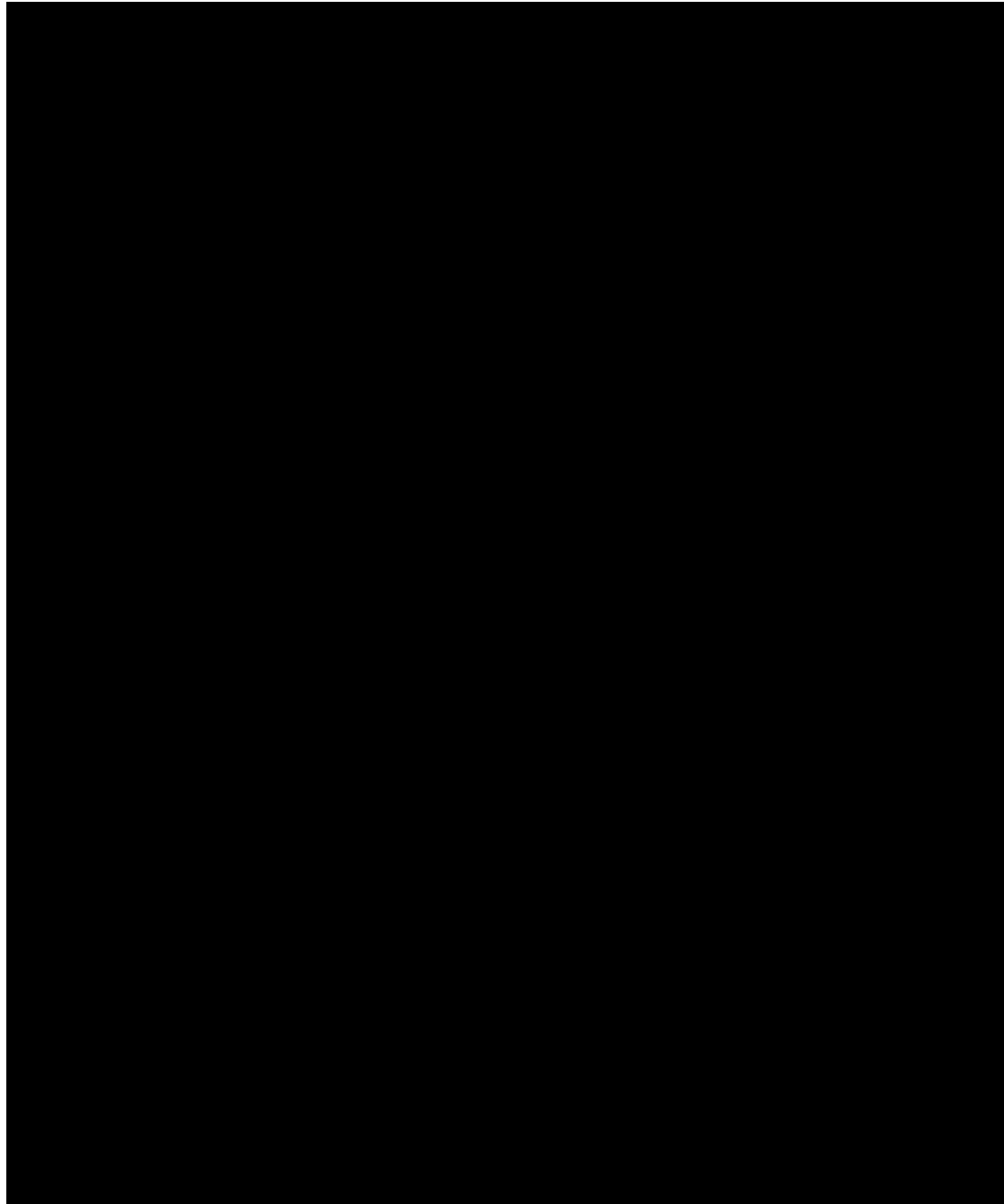
A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status: ○ NHS or HSC care organisation   Commercial status: Commercial

          ○ Academic

          ○ Pharmaceutical industry

          ○ Medical device industry

          ○ Local Authority

          ○ Other social care provider (including voluntary sector or private
          organisation)

          ⦿ Other

If Other, please specify: Commercial Research Organisation

Contact person

Name of organisation Google DeepMind
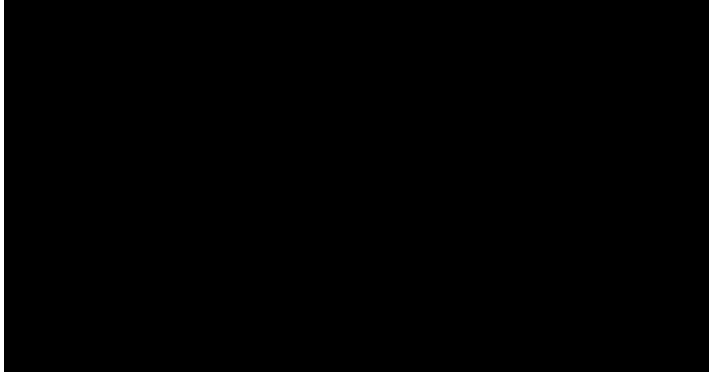
Is the sponsor based outside the UK?

◯ Yes　◉ No

Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.

A65. Has external funding for the research been secured?

☐ Funding secured from one or more funders

☐ External funding application to one or more funders in progress

☑ No application for external funding will be made

What type of research project is this?

◉ Standalone project

◯ Project that is part of a programme grant

◯ Project that is part of a Centre grant

◯ Project that is part of a fellowship/ personal award/ research training award

◯ Other

Other – please state:

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

◯ Yes　◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/12/2015

Planned end date: 01/12/2017

Total duration:

Years: 2 Months: 0 Days: 1

A71-2. Where will the research take place? *(Tick as appropriate)*

☑ England

☐ Scotland

☐ Wales

☐ Northern Ireland

☐ Other countries in European Economic Area

Total UK sites in study 1

Does this trial involve countries outside the EU?

○ Yes   ◉ No

A72. Which organisations in the UK will host the research? *Please indicate the type of organisation by ticking the box and give approximate numbers if known:*

☐ NHS organisations in England

☐ NHS organisations in Wales

☐ NHS organisations in Scotland

☐ HSC organisations in Northern Ireland

☐ GP practices in England

☐ GP practices in Wales

☐ GP practices in Scotland

☐ GP practices in Northern Ireland

☐ Joint health and social care agencies (eg community mental health teams)

☐ Local authorities

☐ Phase 1 trial units

☐ Prison establishments

☐ Probation areas

☑ Independent (private or voluntary sector) organisations   1

☐ Educational establishments

☐ Independent research units

☐ Other (give details)

Total UK sites in study: 1

PART B: Section 7 - Children

1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.

All ages. Acute kidney injury may affect patients of all ages. Since this is a database study with no direct patient contact, concerned only with routinely collected data the inclusion of patients under the age of 16 presented no major ethical issues in the study design.

2. Indicate whether any children under 16 will be recruited as controls and give further details.

Not applicable - this is a database study with no patient recruitment.

3-2. Please describe the arrangements for seeking informed consent from a person with parental responsibility and/or from children able to give consent for themselves.

Not applicable - informed consent is not sought from patients under or over the age of 16 as this is a database study performed on anonymised data.

4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.

 Not applicable.

Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Research site	Investigator/ Collaborator/ Contact
Institution name Google UK Ltd Department name DeepMind Street address Seven Pancras Square Town/city Kings Cross, London Post Code N1C 4AG	███████████████████
Institution name Department name Street address Town/city Post Code	Title First name/ Initials Surname
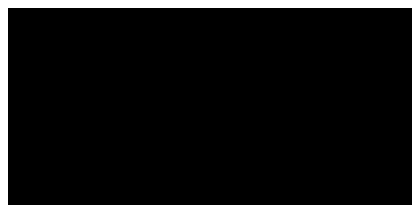
PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.

9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.

11. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication(Not applicable for R&D Forms)

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

○ Chief Investigator

◉ Sponsor

⚪ Study co-ordinator

⚪ Student

⚪ Other – please give details

⚪ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by ▓▓▓▓▓▓▓▓ on 05/11/2015 11:16.

Job Title/Post: ▓▓▓▓▓▓▓▓▓▓▓▓▓▓▓

Organisation: Google DeepMind

Email: ▓▓▓▓▓▓▓▓▓▓▓▓▓▓▓

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

   Please note: *The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.*

6. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

7. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by ▮▮▮▮▮▮▮▮▮ on 05/11/2015 11:23.

Job Title/Post: ▮▮▮▮▮▮▮▮▮

Organisation: Google DeepMind

Email: ▮▮▮▮▮▮▮▮▮

South Central - Oxford C Research Ethics Committee

Level 3, Block B
Whitefriars Building
Lewins Mead
Bristol
BS1 2NT

Telephone: 0117 342 1383

10 November 2015

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Dear ██████████████

Study title:	**Using machine learning to improve prediction of acute kidney injury and general patient deterioration.**
REC reference:	**15/SC/0693**
Protocol number:	**2015/10-DM-01**
IRAS project ID:	**193991**

The Proportionate Review Sub-committee of the South Central - Oxford C Research Ethics Committee reviewed the above application on 10 November 2015.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager Maeve Groot Bluemink, nrescommittee.southcentral-oxfordc@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Ethical opinion

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the

study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion").

Approved documents

The documents reviewed and approved were:

Document	Version	Date
Covering letter on headed paper [Cover Letter]	1.0	27 October 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		21 May 2015
IRAS Checklist XML [Checklist_05112015]		05 November 2015
Letter from sponsor		28 October 2015
REC Application Form [REC_Form_05112015]		05 November 2015
Research protocol or project proposal [Study Protocol]	1.2	26 October 2015
Summary CV for Chief Investigator (CI) ▓▓▓▓▓▓▓▓▓		26 October 2015

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at
http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

15/SC/0693	Please quote this number on all correspondence

Yours sincerely

Pp Professor Nigel Wellman
Chair

Email: nrescommittee.southcentral-oxfordc@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

                           "After ethical review – guidance for researchers"

Copy to: ███████████

South Central - Oxford C Research Ethics Committee

Attendance at PRS Sub-Committee of the REC meeting on 10 November 2015

Committee Members:

Name	Profession	Present	Notes
Mrs Vivienne Laurie	Barrister	Yes	
Dr Lee Potiphar	Clinical Trials Manager	Yes	
Professor David Scott (Chair)	Pharmacist	Yes	

Also in attendance:

Name	Position (or reason for attending)
Miss Maeve Groot Bluemink	REC Manager