NIHR Clinical Research Network - Cluster C

King's College London

Primary and Community Care Genomics Research

"The study of all the DNA in the genome together with the technologies that allow it to be sequenced, analysed and interpreted is collectively called genomics, or genomic medicine if applied to patients"

Annual Report of the Chief Medical Officer 2016
Generation Genome

1. Introduction and background

Within the NHS, there is an ongoing need to realise the full potential genomics has to offer the patient population. This potential begins within the primary care setting. The brief of the NIHR Clinical Research Network (CRN) is to ensure effective and efficient support for the delivery of high quality clinical research in the NHS. Genomics is a cross-cutting discipline recognised by the NIHR CRN as being of critical importance to the national research portfolio. Given the increasing role genomics plays in clinical research, and increasingly, within primary care, it is essential to develop a plan to improve capacity within NHS Primary Care to deliver genomics research and realise its potential.

Genomic science is developing apace; new technologies, and analytical techniques are driving significant changes in diagnostic accuracy and patient flows. As the role of genomic medicine is becoming more affordable, identifying biomarkers is increasingly of high importance in the development of new treatments and the selection of appropriate treatments for individual patients (precision medicine) and, hence, stratified medicine/genomics. Given the central role for genomics within clinical research, we aim to develop a plan to improve capacity for CRN genomics-led research within primary care and community settings. This is where most preventative and early diagnosis work occur and treatments are offered. The majority of research in this area is eligible for inclusion on the NIHR portfolio and a rich source of phenotypic data to link to genotypic data.

For relevant documents and literature - see appendix

2. Why have a Primary and Community Care (P&CC) focus?

The workload in P&CC settings continues to increase with more treatments and services moving to the sector from secondary care. GPs and other health professionals want to understand genetics and use genomic information in their daily practice to benefit patients. Traditionally, genomics has been the exclusive preserve of secondary and tertiary care. Despite this, a major part of the genomics initiative can be researched in a primary or community care setting where the need for an evidence base and clinical impact on patients has never been more pressing. Until recently the average GP would only encounter genomics in terms of pre-natal testing and rare diseases e.g. Huntington's disease - a small part of a GPs' workload. Increasingly however, GPs and their primary care teams are engaging with the emerging science of genomics in a number of areas.

1. Better prediction of overall disease risk e.g. familial breast cancer or familial hyperlipidaemia
2. Better stratification of an individual's genetic risk in general practice
3. Better treatment of existing disease through pharmacogenetics e.g. SSRI drugs and depression

4. Better prediction of adverse events e.g. codeine sensitivity determined by individual genes
5. Better identification of rare diseases in the community, for example linking with the 100K genomes project.
6. Better engagement with patients to promote use of their genomes for research, for example working with the BioResource.

3. Project aims

The main aim of this CRN initiative is to up-skill general practices and their primary care staff, to empower them and offer them appropriate tools and building blocks to facilitate research in primary community care, on the back of this genomics "wave". This can only benefit NIHR research, the NHS, its staff and ultimately the public. Additionally during the project we aim to strengthen links with relevant stakeholders for mutual benefit to allow cross fertilisation of ideas; input into our respective initiatives; prevention of duplication and to ensure that resources dedicated for genomics research are used to the best effect and represent value for money.

4. Governance

Project Lead: Professor Philip Evans, King's College London, Specialty Cluster Lead
Project Support: Joanne Ashcroft, Assistant Specialty Cluster Lead

The Genomics in Primary Care and Community settings project will use the expertise of the CRN Stratified Medicine Steering Group led by the University of Liverpool Specialty Cluster for high-level support; advice on the planned activities (to ensure planned work does not duplicate work within the Stratified Medicine workplan); and to identify areas for joint working and collaboration.

A Primary and Community Care sub-steering group will be established to oversee the workstream drawn from primary care and genomics professionals, patients and the public; including (but not limited to): King's College London; Royal College of General Practitioners, Pharmacogenetics & Stratified Medicine Network; Local NIHR CRNs, NIHR CRN Genetics Specialty (led by Dr Alex Henderson, University of Newcastle Specialty Cluster), Genomics England, INVOLVE and the PHG Foundation. Once established, terms of reference will be co-produced.

5. Partnership working

Initially we intend to work with relevant stakeholders such as NIHR BioResource; UK PGX Network; GEL; PHG Foundation, Health Education England (HEE Genomics Programme: Engaging Primary Care).

Patients and the public are at the heart of NIHR CRN work and their engagement will be central within the project. Communicating the aims of research and how results might be used has the potential to lead to greater public involvement in research using genetic data and to increase confidence in the work being undertaken. Initial engagement will include collaborating with INVOLVE and Genomics England through "*The Genomic Conversation Initiative*".

The NIHR BioResource is a panel of thousands of volunteers, both with and without health problems, who are willing to be approached to participate in research studies investigating the links between genes, the environment, health and disease. We are keen to explore how we might work together.

How we connect and make use of genomic 'big' data needs careful consideration. Key stakeholders for the CRN are the Clinical Practice Research Datalink (CPRD) as well as the GP software suppliers. Genomic information on its own, although useful, is only part of the story. Greater knowledge is gained when genetic information is linked to clinical outcomes. Thus, a major hurdle is to link genome databases to healthcare records, which need to be electronic for this to be done efficiently. Phenotypic data is routinely collected and available from primary care databases and can be "married" with genotypic data in the emerging era of genomics.

6. Scoping activities

The intention is to identify one or two stand-alone pieces of work which will add value to the delivery of genomic portfolio studies taking place in primary care and community settings. To aid the identification of suitable projects we are holding a workshop in London on 10 October 2017 in collaboration with the UK Pharmacogenetics & Stratified Medicine Network.

Workshop - Genomics in Primary and Community Care, London, 10 October 2017

- Exploring the potential of genomics research in primary care
- Practical aspects of genomics education in primary care
- Case studies outlining the implementation of genomic research in PC
- Group work to look at: barriers/incentives for genomic research in PC; set-up challenges; how we promote genomics research in this setting; what we can offer industry partners to encourage more genomics research in P&CC settings.

Other scoping activities will include….

- Exploring the current challenges and barriers to genomic research within P&CC settings. *Potential vehicles: surveys to professional groups and patients*
- Connecting with relevant stakeholders to gain an understanding of their initiatives to: 1) prevent duplication, especially around data issues and 2) aid collaboration and promotion. *Review of UK PGSM network roadmap and "next steps"*
- Identification of a cohort of genomics studies that have successfully recruited from PC&C settings.
  The intention is to identify researchers who are conducting genomics research in P&CC settings to target this community to gain insight into barriers and challenges and to highlight successful studies (potential to write some case-studies to promote work in this area).
- UK and International brief literature review to gain a more complete understanding of the area. *Potential Editorial in primary care peer-reviewed journal*
- Potential data linkage - the majority of the literature published on barriers to genomic research states the issues lie with lack of data access and the difficulty with the sharing of both medical records and genomic data itself. http://www.sciencedirect.com/science/article/pii/S2212066114000386
  Discuss with CPRD potential for data linkage and issues arising. We will link with work currently being undertaken by University of Leeds Cluster (MIDL)
- Work with the NIHR BioResource *We will explore whether we can link primary care more widely with the NIHR BioResource for mutual benefit.*

- Establish training needs for GPs and primary care staff. *Exploring with HEE issues specific to genomics research; especially in the area of consent*

7. Potential areas for a project/s

Actions and collaborations described above will help to define one or two stand-alone projects to aid the delivery of genomics work in PC&C settings. We have some initial ideas which we will put to and test with genomics professionals as to their value and worth.

- Promotion of family history recording software compatible with GP clinical software. This would be done in collaboration with Genomics England and NHS Digital. This would help facilitate CRN research by better identification of patients - it is important that P&CC datasets empower future precision medicine. *Inconsistency in primary care phenotypic data collection has been identified across GP practices and family history recording*
- Ensuring privacy and data protection in the context of primary care genomics research
- Collating and sharing examples of impact – how decisions are influenced and patients' outcomes improved when genomics information is used clinically. *Raising GP awareness of the potential harm of certain medications for some categories of patients would encourage closer monitoring and allow GPs to optimise treatment and help prevent adverse drug reactions*
- Assessing the possible incentivisation of GP practices to undertake genomics research
- Assessing how best to involve patients in primary care and citizens in the community in genomics research. We will explore this further with potential collaborators such as the NIHR BioResource - they might want to expand to recruit via PC and provide some people resource. The CRN could provide access to practices.

8. Structuring the project

We plan to use a similar method to structure the genomics work to that used in our imaging work plan, see: http://bit.ly/2eOzA5S for a report on our imaging work and how the subsequent imaging work plan was developed. However, as we plan smaller-scale more 'niche' projects than in our imaging work - some areas might be either out of project scope or already being dealt with by other organisations or within other genomic initiatives.

Areas for consideration

1. Workforce – objective to increase capacity and capability
2. Infrastructure – objective to improve efficiency of use of existing and emerging genomics systems in the NHS.
3. Industry – improve partnership with industry for genomics studies
4. Engagement – raising awareness and increasing genomics understanding of the workforce
5. Patient and Public Involvement

9. Next steps

- Workshop 10 October 2017
- Establish a sub-steering group (post 10 October 2017 workshop)
- Workshop report produced and agreed with collaborators (January 2018)
- Editorial in primary care journal e.g. BJGP (Early 2018)
- Review of current literature (end 2017)
- Cohort of P&CC setting portfolio studies identified (October 2017)
- Case studies produced (minimum of two by end 2017)
- A position statement on family history recording in general practice records (2018)

Appendix

Relevant documents and reports

- Genomic policy and strategy in UK
  - CMO report 2017 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/624628/CMO_annual_report_generation_genome.pdf
  - Genomic Medicine An Independent Response to the House of Lords Science and Technology Committee Report
  - Genetics and mainstream medicine Service development and integration
- Primary Care and Genomics
  - UK PGX Network Primary Care Workshop http://www.uk-pgx-stratmed.co.uk/index.php/spring-2017-workshop-videos
- Big data, genomics and electronic health records working with genomics
  - Data sharing to support UK clinical genetics and genomics services

Further reading

The Academy of Medical Sciences, 'Realising the Potential of Stratified Medicine'. 2013; available from the World Wide Web: https://acmedsci.ac.uk/viewFile/51e915f9f09fb.pdf

Genomic Alliance, UK, 'Genome Sequencing: what do cancer patients think? Patient Charter' 2016; available from the World Wide Web: http://www.geneticalliance.org.uk/media/2493/my-cancer-my-dna-patient-charter-edits-sept2016.pdf

House of Lords, Science and Technology Committee 2nd Report of Session 2008-09; 'Genomic Medicine, Volume I' 2009: available from the World Wide Web: https://www.publications.parliament.uk/pa/ld200809/ldselect/ldsctech/107/107i.pdf

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PHG Foundation, 'Data sharing to support UK clinical genetics and genomics services: Workshop report' 2015; available from the World Wide Web: http://www.phgfoundation.org/file/17089/

PHG Foundation, 'Genetics and mainstream medicine: Service development and integration' 2011; available from the World Wide Web: http://www.phgfoundation.org/file/7962/

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Roden DM, et al. Pharmacogenomics: challenges and opportunities. Ann Intern Med. 2006;145:749–757.

van Schaik T, et al. The need to redefine genomic data sharing: A focus on data accessibility. Applied & Translational Genomics. 2014;v3,i4:100-104

Vaught J, et al. Critical Issues in international biobanking. Clinical Chemistry. 2014;10:1373.