NHS South West
NHS Genomic Medicine Centre

100,000 Genomes Project
South West GMC
Rare Disease Recruitment

July, 2016

Contents

South West GMC Team

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Highlights in this newsletter

- **Thank you** to everyone involved for their efforts over the past few months.
- Welcome to North Devon District Hospital who have now recruited their first participant!
- The GMC has the next Quarterly review on 2nd August so all efforts are being made to increase recruitment for July and make as many bookings as possible for August.Launch Event held on June 28th (see **section 1**)
- Clarifications on information needed for recruitment, to be supplied by referring clinician: (1) Diagnostic category (2) Family structure (see **section 4**)
- Please note that to avoid confusion with the (real) GMC, the office email address has been changed to:

  rde-tr.SWGMC@nhs.net
- Some clarification on which sample types may be used (stored DNA, saliva etc) (see **section 4**)
- Update on special consent categories: Adults lacking capacity; deceased adults; fetal samples (see **section 5**)
- Some **results** should be available very soon (see **section 6**)
- Appointments of Genomics Champions (see **section 7**)
- Recruitment team: introduction of 'Error log' – please take note (see **section 9**)
- Clinical Genetics: please note changes in eligibility for familial breast and bowel cancer: proband only recruitment is now possible for these categories **(see section 11)**

1. Launch Event

This was held at the Rougemont Hotel on Tuesday June 28th, to mark the recruitment of the first 100 families to the project.

Main speakers were introduced by Rosie Benneyworth, Managing Director of SW Academic Health Science Network: Prof Sue Hill, Chief Scientific Officer of NHS England, and Prof Sian Ellard, head of the SouthWest Genomic Medicine Centre gave national and regional overviews of the project, respectively.

Website

www.swgmc.org

Representatives from two families gave talks about the impact that rare disease has had on them and about their involvement in the project. Maria Scholey (pictured with her son Aidan and other family members below) spoke movingly about Aidan and his involvement with the project.

A panel discussion about the future of genetic testing took place. Panel members were Professor Heather Skirton, Professor in Health Genetics at Plymouth University, Dr Susan Kelly, Associate Professor of Medical Sociology at Exeter University and Dr Charles Shaw-Smith, Consultant Clinical Geneticist and SW GMC Rare Disease Lead. The discussion was chaired by Dr Leigh Jackson, SW GMC Education & Training Lead. A lively floor debate followed the initial presentations.

The pictures show Aidan Scholey with mum Maria (left) and (L-R) Rosie Benneyworth, Sian Ellard and Charles Shaw-Smith at the event.

The event was covered by the Exeter Express and Echo- pictures and text available here:
http://www.exeterexpressandecho.co.uk/families-offered-hope-through-gene-testing-in-exeter/story-29457101-detail/story.html

2.Local Delivery Partners

The local delivery partners are the partner Trusts within the SoutWest Genomic Medicine Centre. There are seven: Exeter, Plymouth, Truro, Torbay, Barnstaple, Taunton and Yeovil. The process of 'onboarding' of a Trust is quite technical; in practice six of the seven centres are now open for recruitment, and ready to receive referrals, with recruitment team members available in each; Yeovil to follow soon. The first patient was recruited in Barnstaple recently. Thanks to Amanda Skinner for her enthusiastic contribution.

3.Recruitment

- **Recruitment to date**

Heartfelt thanks to all of you from the team for your continued support. Despite best efforts, recruitment has been significantly lower than the trajectory in the last four months and we are currently at about 80% of the total overall trajectory. This has largely due to a large number of people not attending appointments.

New disorders open for recruitment in July 2016

Congenital malformations
Syndromic cleft lip/cleft palate
Familial non-syndromic cleft lip/cleft palate
Familial hemifacial microsomia
Radial dysplasia

Endocrine disorders
Disorders of sex development
Early onset familial premature ovarian failure

Disorders of growth
Silver-Russell syndrome

Dermatology
Lymphoedema distichiasis
Milroy disease

Hearing disorders
Autosomal dominant deafness
Ear malformations with hearing impairment

Paediatric gastroenterology
Gastrointestinal epithelial barrier disorders
Infantile enterocolitis and monogenic inflammatory bowel disease

Metabolic disorders
Undiagnosed metabolic disorders
Congenital disorders of glycosylation

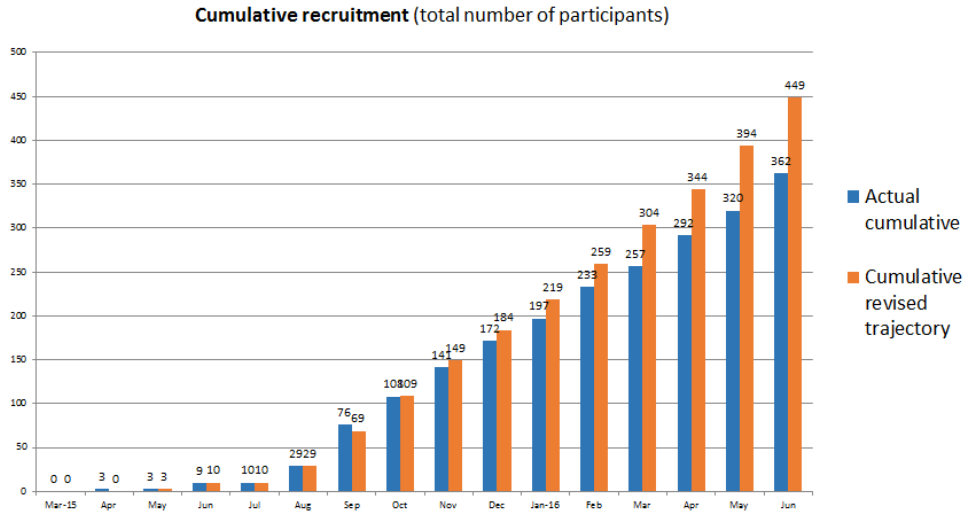
Neurology and neurodevelopmental disorders
Neurotransmitter disorders
Structural basal ganglia disorders

Renal and urinary tract disorders
Unexplained kidney failure in young people

Rheumatological disorders
Kyphoscoliotic Ehlers-Danlos syndrome

Skeletal disorders
Unexplained skeletal dysplasias

Ultra-rare disorders
Neonatal or paediatric intensive care unit admission with a likely monogenic diagnosis

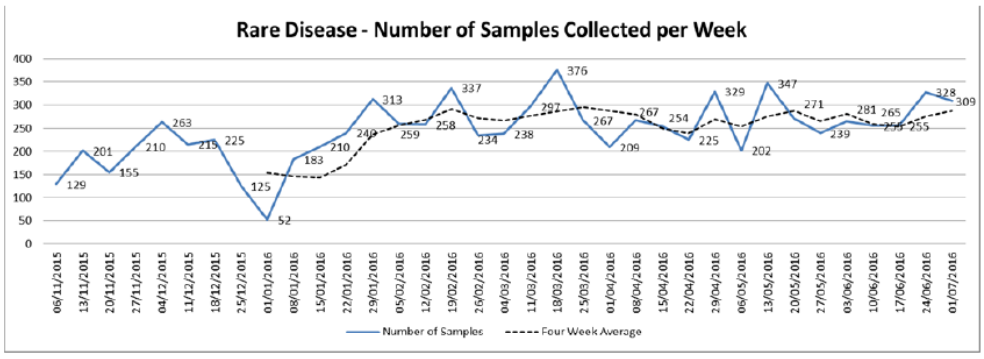


The project office now has additional admin support and is calling to confirm all appointments. A huge effort has been made by all and 85 participants are confirmed for July to date, allowing the gap between actual recruitment and the trajectory to be closed.

Approximately half of referrals to date have been from the Peninsula Clinical Genetics Service, with the paediatric, renal, endocrinology, immunology, neurology and dermatology specialities in Exeter contributing a significant amount.

The current monthly referral rate will need to double to 30 to ensure we have enough participants to meet our year-end target. If you have any suitable patients sitting in your in tray, the project office are waiting to hear from you (see below for reminder on how to recruit a patient)
Work continues to engage clinicians outside of Exeter and the Community Paediatrics team at Truro have already made a significant contribution to the project. Interested clinicians in any hospital are encouraged to contact the project office in advance to find out more by emailing rde-tr.gmc@nhs.net.

The graph below shows recruitment across the whole country, up to Friday 8th July. Up until 1 July a total of 10,422 Rare Disease samples had been collected.



If you have any suitable patients sitting in your intray, Steve is waiting to hear from you (see below for reminder on how to recruit a patient).

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Recruitment team

Paediatric Research Nurses, Exeter
Su Wilkins
Caroline Harrill
Sue Ward

Paediatric Research Nurses, Truro
Nina Worrin

Clinical Research Nurse, Barnstaple
Amanda Skinner

Genetic Counsellors, Exeter
Anne Searle
Heather Chalinor
Gemma Corbett

Genetic Counsellors, Plymouth
Matilda Bradford
Nicol Lambord

Specialist Registrars
Lettie Rawlins (Clinical Genetics, Exeter)
Rhian Clissold (Renal Medicine, Exeter)
Harriet Aughey (Paediatrics, Truro)

Genomics Champions

Dr Lucy Leeman, SpR in Immunology, Derriford Hospital

Dr Siying Lin, SpR in Ophthalmology, Torbay Hospital

Dr Kashyap Patel, Wellcome Trust Research Fellow in Diabetes and Endocrinology Royal Devon and Exeter Hospital.

a. How to recruit a patient

We have tried to make this as simple as possible. An example, the version for paediatricians, is shown.

Please note that these documents have been updated recently. New versions are obtainable from the GMC website www.swgmc.org

The easiest way to recruit a patient/family is from clinic, but phoning on receipt of a negative molecular test is also an effective option.

Ask for help if needed!

Genomics england

NHS South West NHS Genomic Medicine Centre

100 000 Genomes Project recruitment for paediatricians

This is for a 'trio' family structure, with affected child and unaffected parents. If family structure differs, please contact for advice.

Step 1: Check eligibility

A comprehensive list of eligibility criteria is available via the link below:
http://www.genomicsengland.co.uk/library-and-resources/
(See under "Eligibility statements"/"Rare disease eligibility statements")

Some examples of eligible disorders:
Intellectual disability; Congenital Heart Disease; Congenital anaemias; Non-syndromic hearing loss; Craniosynostosis syndromes

Step 2: Discuss with the family in clinic or by telephone

1. Purpose of study is to try to obtain a molecular genetic diagnosis [NB there must be a diagnostic question]
2. Blood samples are needed from the affected individual and unaffected parent(s) or other affected family members
3. Family members will be offered opportunity to consent to 'secondary' findings
4. Data will be made available in anonymized form to research/commercial bodies (non-negotiable)

Step 3: Notify GMC office (Steve Johnson, Project Manager)

Please email the following information to: rde-tr.GMC@nhs.net

1. Name and NHS number of affected individual, or name and date of birth
2. Names and dates of birth of other individuals who would be recruited (typically the parents)
3. The diagnostic category (Intellectual disability etc)
4. An email address (preferred but not essential) or postal address for the family

The project office will then contact family re consent/sampling appointment

Step 4: Clinical data entry

Once the consent/sampling process has been completed, the recruiting consultant will be asked to complete an online phenotype data entry form. This will include growth parameters, systems examination and dysmorphology. (Help with this will be available)

Please contact us if you have any questions about any aspect of the project:
charles.shaw-smith@nhs.net T: 5737
sian.ellard@nhs.net T: 8259
rde-tr.GMC@nhs.net T: 8177 (Project office)

b. New clinical disorders for recruitment/changes to eligibility criteria

New disorders are open for recruitment in July. Please see the panel previous page for details.

Please check if you are unsure whether or not a condition is possible

Thanks to the following for commitment to the project:

All members of Peninsula Regional Clinical Genetics Service

Richard Tomlinson, Eleanor Thomas, and all members of the Community Paediatrics team, RDE, Exeter

Coralie Bingham, Rhian Clissold, Renal Medicine, RDE, Exeter

Claire Bethune, Lucy Leeman, Andrew Whyte, Immunology and Allergy, Derriford Hospital, Plymouth

Vijay Baidya and Andrew Hattersley, Diabetes and Endocrinology, RDE, Exeter

Nick Gutowski, Neurology, RDE, Exeter

Elizabeth Househam, Neurology, Derriford Hospital, Plymouth

Carolyn Charman, Naomi Goldstraw, Dermatology, RDE, Exeter

Kayal Vijayakumar, Germaine Pierre, Bristol Children's Hospital

for recruitment. This is best done by re-visiting the website, as the list of eligible conditions is constantly being updated. See: http://www.genomicsengland.co.uk/library-and-resources/ and navigate to Rare Disease Eligibility Statements

Additional changes to the rare disease programme

Unaffected relatives can be recruited using telephone consent. DNA samples can be submitted without omics. Stored DNA samples or DNA extracted from blood posted to Exeter can be submitted without omics.

Probands from devolved nations

Potential probands can now be resident in England, Scotland, Northern Ireland or Wales as long as they are under the care of the NHS in England.

4. Note to clinicians: information needed by the project office at recruitment

Information needed at recruitment

Information on how to recruit a patient is given in section 3 above. This hasn't changed significantly since the inception of the project.

Please could we ask if recruiting clinicians could be specific in the information provided concerning

1. Diagnostic category
2. Number of individuals in the family to be recruited?

The diagnostic category should tally exactly with one of the eligible conditions specified. These are available here:
http://www.genomicsengland.co.uk/information-for-gmc-staff/rare-disease-documents/
Please click on "Rare Disease Eligibility Statements" and usually easiest is to search for specific disease category using <Ctrl+F> - works for me, anyway. If you're not sure just email Steve or myself and we'll be glad to help.

Concerning number of individuals to recruit from a given family, often this will be a trio (affected individuals plus both unaffected parents). Where more than one individual in the family is affected, usually the requirement is to recruit as many affected individuals as possible. Additional affected family members should please be identified and specified unambiguously by the recruiting clinician. The project office cannot do this! (though are able to help facilitate contact with such individuals as required). It's a slightly complicated area, please check with us if unsure. Further information also available here:
http://www.genomicsengland.co.uk/information-for-gmc-staff/rare-disease-documents/
Please click on "Guidelines for family pedigree selection".

Which samples may be used?

There are reasons why it may not be possible to obtain a blood

sample for recruitment in the usual way. The following explanatory notes explain the hierarchy of preference.

(1) Preferred option: all blood samples, including those required for '-omics' analysis are obtained at the recruitment appointment
(2) Especially where children are concerned, it may be difficult to obtain all the samples needed- in this scenario, the EDTA sample for DNA extraction takes priority
(3) If a blood sample is not possible, then it is acceptable to use a stored DNA sample if the alternative is not to recruit the family to the project.
(4) Deceased individuals: a stored DNA sample may be used for an unaffected individual, if necessary
(5) Saliva samples: the project is at the time of writing not officially sanctioning the collection of saliva samples, though this may change in the future.

If unsure, please ask. Steve, Sian or I will be happy to help.

5.Update on special consent categories

The question of recruitment of patients in 'special categories' has come up a few times recently, and I will attempt to clarify:

1. Adults lacking capacity. These patients are recruitable. Information sheets and consent forms are on the 100,000 Genomes Project website (category R7, "For a personal consultee regarding a patient with a rare genetic disorder", see http://www.genomicsengland.co.uk/taking-part/patient-information-sheets-and-consent-forms/). For further information, there is also some brief and to the point general Department of Health guidance available at http://arec.org.uk/wp-content/themes/grandeur/documents/dh_083133consultee-guidance.pdf.

2. Deceased adults. These indivuals are also recruitable. Information sheets and consent forms are available on the 100,000 Genomes Project website as above (category R8, "For the nominated representatives, relatives or friends of a deceased adult with a rare genetic disease").

3. Fetal samples: discussions are taking place about recruitment of families where such samples exist, but the study is not currently recruiting such families. Please await further updates.

6. Feedback of results from the 100 000 Genomes Project

Prof Sue Hill mentioned in her talk at the launch event (see section 1) that there is currently an initiative within Genomics England to start to make some results available, and more recently we were updated that "the plan is to select cases from each GMC and release results by the end of August." These cases will be selected by Genomics England.

I have been supplied with a list of 9 cases by Genomics England, and completed phenotype data entry on these. We wait in hope for some results!

7. Appointment of Genomics Champions

Genomics Champions

Three 'Genomics Champions' have recently been appointed. These Health Education England funded appointments will help drive engagement with the project and genomic education in their own specialties They are:

Dr Lucy Leeman, an SpR in Immunology at Derriford Hospital in Plymouth
Dr Siying Lin, an StR in Ophthalmology at Torbay Hospital in Torquay
Dr Kashyap Patel, a Wellcome Trust Rsearch Fellow in Diabetes and Endocrinology at the Royal Devon and Exeter Hospital.

Dr Kash Patel Dr Lucy Leeman Dr Siying Lin

We are very excited to have them on board from August and hope to make further appointments in the near future.

Further appointments were made very recently and will be introduced in the next newsletter.

8. Presentations around the Peninsula

There have been quite a few presentations about the project around the Peninsula in the last weeks, with more to follow.

Dr Charles Shaw-Smith discussed the project at the medical staff round on 9th June at Derriford Hospital in Plymouth (hosted by Dr Simon Dunlop). There were over 30 attendees and each feedback form rated the talk as either above average or excellent. There was good discussion about both the project and the educational opportunities provided by the fully-funded Master's course (see below).

Professor Sian Ellard gave a talk at the South West fetal medicine study day in Plymouth on the 10th June to around 80 attendees and Dr Charles Shaw-Smith spoke at a renal meeting in Exeter on the 16th June.

Dr Charles Shaw-Smith also presented at the medical round at the Royal Cornwall Hospital in Truro on the 7th July. This was again well attended and generated discussion about the role of genomics in the NHS going forwards. This meeting was hosted by Dr Sanjeev Gupta.

9. Masters in Genomic Medicine

The University of Exeter is delivering a Master's course in Genomic Medicine. Health Education England are funding NHS healthcare staff to complete individual CPPD modules, PgCert, PgDip or the full Master's qualification completely fee-free for the student. Registration is now open and more information can be found at: http://www.exeter.ac.uk/postgraduate/taught/medicine/genomicmsc/ The link for HEE funding details and application is: https://www.genomicseducation.hee.nhs.uk/taught-courses/

For any further information regarding the modules, application or funding please contact: leighjackson@nhs.net

10. Recruitment team

Joining the recruitment team

The team is open to new members, especially in Torquay and Barnstaple. Team members should be up to date on the following:

1. Good Clinical Practice training- usually offered as part of Trust mandatory training
2. Completion of online consent training provided by Health Education England- the module can be completed in around an hour
3. Face-to-face consent training specifically for 100 000 Genomes Project, provided to date by Charles Shaw-Smith, Rare Disease Lead.

New members this month:

Amanda Skinner, Research Nurse, Barnstaple.

Error log

In discusison with other members of the team, and taking into account feedback received, we wanted to put in place a system that will allow some cross-referencing/communication between members of the recruitment team.

In the first instance, we would like to collect data on any aspect of

the recruitment appointment that has not gone according to plan. Possible examples might include:

- Patient/family arrived at wrong location for appointment
- Non-availability of clinic rooms for an appointment
- Incorrect consent forms supplied in recruitment packs
- Failure or recruitment team to be notified of a child with significant behavioural or learning difficulties, making blood sampling impossible with available resources
- Any expression of dissatisfaction/complaint about the project by the family at the recruitment appointment

We have tried to devise as simple a system as possible to monitor these issues: please send an email to rde-tr.SWGMC@nhs.net and put "**Error log**" in the subject header. These reports will be catalogued by Ana Juett and reviewed by the project team on a monthly basis.

Many of you have been proactive about feeding back difficulties which you have encountered, and we acknowledge and are grateful for this – we now wish to try to put in place a system to capture problems more systematically.

We will provide feedback about problems which have arisen and solutions which have been implemented. Thank you to the recruitment team very much for assistance with this.

11. Clinical Genetics

Please note that there have been some interesting changes to recruitment criteria for heritable cancer syndromes.

Breast cancer: please note eligibility for proband only recruitment in box below:

Level 3 Title	Breast and endocrine (23190.14)
Level 4 Title	Familial breast cancer (23191.14)
Eligibility Statement	**Familial breast cancer inclusion criteria (23193.14)** Multiplex cases: Proband is affected by invasive breast cancer (age <50) - 3 family members (FDR, SDR, TDR) affected by invasive breast cancer (average age of BCs <60) - Samples available and to be collected from >= 2 affected relatives Proband only recruitment: - Proband is affected by breast cancer (age <50) or ovarian cancer (any age). - Manchester Score of family >22 - Cases of ovarian cancer (any age) and breast cancer (<40) have been confirmed. - Ovarian cancers demonstrated to be invasive epithelial; mucinous and borderline tumours non-eligible (where histology available) - Family is not eligible for recruitment to the multiplex families breast cancer eligibility. - Samples to be supplied from: proband only. Unaffected individuals should not be recruited in this disorder. **Familial breast cancer exclusion criteria (23194.14)** **Prior genetic testing guidance (22556.14)** - Results should have been reviewed for all genetic tests undertaken, including disease-relevant genes in exome sequencing data. The patient is not eligible if they have a molecular diagnosis for their condition. - Genetic testing should continue according to routine local practice for this phenotype regardless of recruitment to the project; results of these tests must be submitted via the 'Genetic investigations' section of the data capture tool to allow comparison of WGS with current standard testing. PLEASE NOTE: The sensitivity of WGS compared to current diagnostic genetic testing has not yet been established.

Colorectal cancer: please note eligibility for proband only recruitment in box below:

Level 3 Title	GI tract (23208.14)
Level 4 Title	Familial colon cancer (23209.14)
Eligibility Statement	**Familial colon cancer inclusion criteria (23211.14)** PREFERABLY: proband is affected by colorectal cancer (age <50) Additional 3 family members (FDR, SDR, TDR) affected by colorectal cancer (average age <60) Samples to be supplied from proband AND ≥2 affected relatives OR proband is affected by colorectal or Lynch-related cancer (age <50) Additional 2 family members (FDR or SDR of each other) affected by colorectal or Lynch-related cancer (average age <60). If proband's tumour is colorectal cancer, the tumour must exhibit microsatellite instability. Cancer diagnosis confirmed in ≥ 2 family members Proband has ≤1 living affected family members (ie ineligible for multiplex CRC) Samples to be supplied from: proband only (Lynch-related tumours: Colorectal cancer Endometrial cancer Ovarian cancer Pancreatic cancer Ureter cancer Benign skin tumours Sebaceous adenoma Sebaceous epithilioma Keratoacanthoma Skin cancers Sebaceous carcinoma Transitional cell cancer of renal pelvis Gastric cancer Hepatobiliary tract cancer

12.Thank you!

Thank you to all clinicians who have recruited to the project, and to all members of the recruitment team for their work.