November 2021

Academy of Medical Royal Colleges

Genomics
Generic syllabus

Contents

Background

Healthcare is evolving. New generation genomic technologies are facilitating cheaper, faster access to the genome which, in turn, is transforming how we diagnose and treat disease. However, if healthcare is increasingly to be underpinned by genomics, it is essential that the workforce is prepared. While the integration of genomic medicine across healthcare will not be uniform (with some specialties likely to adopt and incorporate genomic medicine into their clinical practice sooner than others), if we are to future-proof our workforce, it will be essential that all healthcare practitioners acquire the fundamental genomic building blocks. We have therefore developed a genomic syllabus, detailing these fundamental building blocks, which we hope will be useful across the medical specialties to inform specialty-specific curricula, develop educational resources and to map professional exams.

Syllabus development

The Academy of Medical Royal Colleges (the Academy) Clinical Genomic Leads group was established in 2018 to 'oversee the work related to championing and supporting the NHS to embed the use of genomic medicine into clinical practice in the NHS'. The work was funded by the Genomics Education Programme within Health Education England, and the group includes genomic representation from 30 Royal Colleges/professional organisations and 17 specialties[1] (Appendix 1).

The programme includes three work packages:

1. Syllabus development
2. Workforce, networks and genomic champions
3. Genomic resource creation.

The focus of this document is on work package 1, syllabus development.

The purpose of a genomics-based syllabus is to ensure that genomics is represented, appropriately and relevantly, in each of the healthcare specialties. While there is general acknowledgement within the Academy Clinical Genomics Leads' working group that genomics should be represented cross-curricula there is a realisation that this process entails many challenges. It is beyond the scope of the Academy syllabus development exercise to address these challenges but it is hoped that an appreciation of the barriers can, in time, facilitate the adoption and implementation of genomic medicine:

— Genomic needs are different across the specialties. While a good understanding of the fundamentals of genomics is essential for all practising clinicians, it is likely that specific capabilities for individual specialties will need to be developed.

— Engagement. For many specialists and royal colleges, the relevance of genomics is not yet apparent. While individual clinicians recognise that genomics is driving many areas of research, they are not yet witnessing the impact of genomics on the immediate management of their patient.

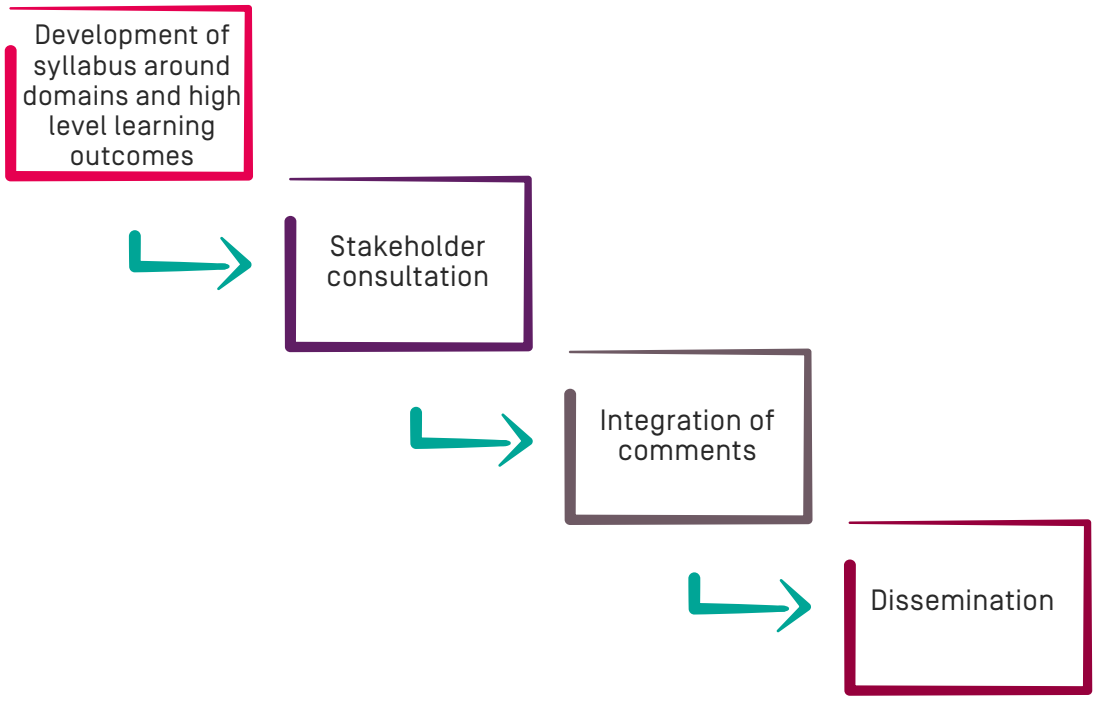
1. The remit and membership of the Clinical Leads group has recently been updated. The group is now known as the Genomics Professional Partnerships Group (GPPG).

- Availability of cases. If genomics is to be integrated into curricula, it is essential that junior doctors are exposed to patients where genomics is actively being employed in their diagnosis and management. While this access is currently limited, it is likely that, with the launch and establishment of the Genomic Medicine Service Alliances (GMSAs) and the concurrent integration of genomics into mainstream practice, trainees will increasingly use genomics in their daily practice.
- Access to appropriate training resources. If an understanding of genomics is mandated through curricula, it is essential that an appropriate number and range of training resources, mapped to the curricular capabilities, have been developed and are appropriately signposted.
- Availability of appropriate mentors. Junior doctors in training are supervised by consultants, in the role of both educational and clinical supervisors. However, many senior clinicians have no greater exposure or knowledge of genomics than their juniors resulting in a lack of appropriately trained mentors.
- Curricula have just been updated and so there is limited appetite to make any substantial amendments/additions for several years.
- There are many demands to include subjects in curricula; genomics is not the only subject.

Syllabus methodology

The approach to the development of the Academy genomic syllabus is summarised in Figure 1 below.

Figure 1. Approach to genomic syllabus development



Development of syllabus around domains and high-level learning outcomes

The generic syllabus has been developed to be applicable across the healthcare specialties. It was developed by considering how genomics will be used practically for patient care, and the knowledge and skills required to deliver this. This approach was informed by the General Medical Council (GMC) document Excellence by design: standard for postgraduate curricula and utilises high level learning outcomes with accompanying

descriptors for each. The GMC has reviewed the genomics curriculum and stated in July 2021 that they are *"supportive of this work that provides learning about genomics for all the medical specialties as part of the generic professional capabilities for doctors."*

The syllabus is divided into three domains, designed to develop the knowledge, skills and attitudes of the medical workforce. The first, knowledge, covers the basic science concepts that form the foundation to the clinical application of genomics. Domain II focuses on the application of this basic science to clinical practice and outlines the skills a doctor should develop to effectively consent for/request a genomic test and interpret/communicate a genomic result. Finally, it was deemed essential that all healthcare practitioners should have an appreciation (and for some clinicians participate) in the evolving NHS genomic infrastructure (domain III). High level outcomes, mapping to each of these domains, are listed below.

Domain I. Knowledge

- Describe and differentiate DNA, genes and chromosomes
- Evaluate the genetic basis of disease
- Evaluate disease-causing genomic variation in the context of normal genomic variation
- Determine the inheritance of single gene disorders
- Describe the genetic contribution to common complex disease
- The evolution of genomic technologies

Domain II. Skills

- Assess when genetic testing is indicated and when it is not appropriate or helpful
- Choose a genetic test that is appropriate for a given clinical scenario
- Effectively obtain consent while respecting the unique ethical and confidentiality implications of genomic medicine
- Critically appraise a genomic report
- Read and interpret genomic test results confidently
- Communicate a genomic result
- Implement and practice personalised medicine

Domain III. Attitudes

- Describe how genomic medicine is delivered through the NHS UK-wide.

How to use the syllabus

This syllabus is available to all doctors on the Academy website.

Please note:

- The Academy recognises that genomics will be variably relevant across healthcare and that some specialties will adopt genomic medicine sooner and to a greater extent than others. This is a generic syllabus that has been developed to be useful across the specialties. It is not the expectation that every doctor from every specialty develop each of the competencies, rather it is a starting point to inform the development of specialty specific curricula and "Rough Guides" within the royal colleges; to act as a reference for individual clinicians to chart their own progress and to align educational resources and specialty examinations.
- It is not within the scope of the syllabus to include assessment criteria as these will be determined by the specialty and the representative royal college, based upon the specialty specific curricula.
- The UK NHS Genomic Medicine Service is supported by a specialist Clinical Genetics Service. Referral to or communication with the Clinical Genetics Service is specified for some of the sub-domains. However, it is likely that Clinical Geneticists, Genomic Counsellors and Clinical Scientists will be closely involved across the domains, especially during initial implementation of genomic medicine.

Together with the Genomics Education Programme at HEE, there will be invitation and monitoring of ongoing feedback of the syllabus with evaluation, iteration and improvement of the syllabus on a regular basis.

	High level learning outcomes	Healthcare practitioners working with genomics should be able to:
I	KNOWLEDGE: Fundamental Principles of Genomics	
1	Describe and differentiate DNA, genes and chromosomes	a. Conceptualise genes as heritable units that are constructed from DNA and are packaged in chromosomes. b. Describe that the (approximate) 20,000 genes are packaged into 23 pairs of chromosomes (46,XX in females and 46,XY in males). c. Describe the difference between the genome and epigenome (including imprinting).
2	Evaluate the genetic basis of disease	a. Describe the different types of single nucleotide variation (synonymous missense, splice, stop gain, frameshift etc). b. Apply the concepts of loss of function and gain of function variants (gain of natural function and gain of novel function). c. Describe the different types of copy number variation (trisomy, monosomy, microdeletions, microduplications, translocations, etc). d. Distinguish between constitutional and somatic variation and their respective roles in the development of disease/cancer. e. Describe the genomic landscape of disease, appreciating that specific disease mechanisms are responsible for specific disease i.e. loss of function variants cause some diseases whereas gain of function variants cause others. f. Describe genomic mosaicism and its implications for disease.
3	Evaluate disease causing genomic variation in the context of normal genomic variation	a. Describe the extent of normal genomic variation and recognise that more variants in genes are not pathogenic and do not require clinical action. b. Describe differences in normal genomic variation due to ancestry. c. Locate databases of normal variation (i.e. gnomAD) and use these in the context of their limitations due to lack of population diversity. d. Describe the make-up of normal genomic variation, including sequence and copy number variation. e. Evaluate genomic variation linked to drug response.

	High level learning outcomes	Healthcare practitioners working with genomics should be able to:
I	KNOWLEDGE: Fundamental Principles of Genomics	
4	Determine the inheritance of single gene disorders	a. Describe the salient features of autosomal dominant and autosomal recessive inheritance patterns in single gene disorders (and understand that autosomal recessive disorders are more common if parents are consanguineous). b. Identify inheritance patterns where expert input may be required i.e. X-linked recessive, X-linked dominant and mitochondrial inheritance. c. Describe the concepts of incomplete penetrance and variable expressivity in single gene disorders.
5	Describe the genetic contribution to common complex disease	a. Describe the contribution of multiple, differing penetrant genomic factors to common complex disease. b. Describe the genomic factors that influence the development of cancer. c. Evaluate the benefits and limitations of polygenic risk scores. d. Employ polygenic risk scores in risk stratification and access to surveillance options. e. Describe the complex interactions of genetics and environment in common complex disorders.
6	The evolution of genomic technologies	a. Understand the difference between single gene testing, gene panel testing, (clinical) exome sequencing and genome sequencing.
II	SKILLS: the application of genomic knowledge to clinical practice	
1	Assess when genetic testing is indicated, and when it is not appropriate or helpful	b. Take an accurate family history and identify those affected by or at risk of genetic conditions. c. Assess a pedigree to establish the likely mode of inheritance of a genetic condition. d. Understand probability around recurrence or offspring risk of a genetic condition. e. Stratify patients who would benefit from a referral to specialist genomic services e.g. difficult to interpret genomic variant or a patient seems highly likely to have a genetic basis for disease but routine analysis of data has not identified a diagnosis.

	High level learning outcomes	Healthcare practitioners working with genomics should be able to:
II	SKILLS: the application of genomic knowledge to clinical practice	
2	Choose a genetic test that is appropriate for a given clinical scenario	a. Appreciate the different applications of chromosome tests (e.g. karyotype and array comparative genomic hybridisation (array CGH)) and DNA sequencing tests for the detection of copy number and single nucleotide variants respectively. b. Appreciate that the time frame around results will be determined by the clinical presentation ie prenatal testing will need to be expedited. c. Determine when additional tests may be required in certain circumstances (e.g. Multiplex Ligation Probe Amplification (MLPA), Fluorescent In Situ Hybridisation (Fish) etc).** d. Appreciate the limitations of each of the tests and when to seek input from specialist genomic services.** e. Evaluate the strengths and weaknesses of the different next generation sequencing approaches e.g. gene panel, exome and genome sequencing. f. Choose whether to undertake a trio/quad or singleton approach to sequencing in the context of robust parental phenotyping. g. Request the correct tube for sample collection for each of the different genomic tests.
3	Effectively obtain consent while respecting the unique ethical and confidentiality implications of genomic medicine	a. Provide information to patients around options for genomic testing and discuss the benefits and risks in a non-directive way, respecting patient autonomy. b. Consent for a genomic test, ensuring that the individual understands the nature, purpose and possible outcomes of the test (clearly causative, no alteration identified, uncertain finding, incidental finding), thereby asserting their right to self-determination. c. Explain that a genomic test result may have implications for other family members. d. Appreciate the different approach to consent that needs to be taken in the diagnostic and pre-symptomatic context.

**Discussion with the Clinical Scientists/Clinical Geneticists may be needed

	High level learning outcomes	Healthcare practitioners working with genomics should be able to:
II	SKILLS: the application of genomic knowledge to clinical practice	
3	Effectively obtain consent while respecting the unique ethical and confidentiality implications of genomic medicine	e. Understand guidelines around confidentiality in genomic medicine. f. Understand the Code on Genetic Testing and Insurance agreed between HM Government and the Association of British Insurers on the role of genetic testing in insurance. g. Understand that making pseudonomised data available to researchers may result in a more accurate clinical result.
4	Critically appraise the genomic report	a. Assess the patient details included on the form to ensure that they are correct; the report is the most recent and that the laboratory is a UK accredited diagnostic laboratory. b. Understand that genomic medicine is rapidly evolving and, as such, previous genomic test reports should be re-visited on review of patients. c. Interpret the genomic result in the context of the patient's phenotype and family history. d. Assess whether the most appropriate test been undertaken for the patient given their clinical presentation.**
5	Read and interpret genomic test results confidently	a. Describe the different classifications of genomic variation and determine which variants are clinically actionable and which are not. b. Recognise that all results should be interpreted in the context of normal genomic variation. c. Recognise that all results should be interpreted in the context of phenotype. d. Differentiate between genetic results identifying constitutional and somatic mutations, and their different implications for the patient and their family. e. Apply an evidence-based approach to genomic reports, recognising the incidence of false negative/positive results and that a negative genomic report does not mean that a patient does not have a genomic diagnosis.

**Discussion with the Clinical Scientists/Clinical Geneticists may be needed

	High level learning outcomes	Healthcare practitioners working with genomics should be able to:
II	SKILLS: the application of genomic knowledge to clinical practice	
6	Communicate a genomic result	a. Communicate a genomic test result clearly to patients in terms that are easy to understand. b. Communicate effectively with patients when there is uncertainty around a genomic test, result or risk and discuss next steps to clarify. c. Communicate and manage identification of incidental findings (unexpected results unrelated to the test indication). d. Recognise and communicate that a genomic test result may have implications, beyond the patient (recognising transgenerational implications if the patient is a fetus). Testing of other family members may be appropriate. e. Discuss the implications of a genomic test result on reproductive options, where relevant. f. Identify where a patient or family might benefit from psychosocial support through referral to the genomic counselling service.
7	Implement and practice personalised medicine including the integration of pharmacogenomics into patient care	a. Evaluate and implement personalised treatment options based upon constitutional and/or somatic genomic data. b. Evaluate and implement pharmaceutical treatment options based upon an individual's underlying genomic data.
III	ATTITUDES: Implementation of Genomic Medicine within the NHS	
1	Describe how genomic medicine is delivered through the NHS UK-wide	a. Describe how to request genomic testing within the NHS. b. Navigate to up-to-date information about available genomic tests. c. Evaluate the role of the multi-disciplinary team (MDT) in genomic results interpretation and management decisions and ensure that variants are appropriately prioritised for discussion at the MDT meetings. d. Recognise the educational importance of the MDT. e. Describe the structure and role of the regional Genomic Medicine Service Alliances (GMSAs) and Genomic Laboratory Hubs (GLHs).

Appendix 1
Genomics Professional Partnerships Group representation

Academy of Medical Royal Colleges, including representation from:
- Academy Patient Lay Committee
- Academy Trainee Doctors Group
- Academy Foundation Programme Committee

British Society for Genetic Medicine
Chartered Society of Physiotherapy
Faculty of Dental Surgeons
Faculty of Intensive Care Medicine
Faculty of Pharmaceutical Medicine
Faculty of Public Health
Faculty of Sports and Exercise Medicine
Genomics England
Health Education England
Joint Royal Colleges of Physicians Training Board
Medical Schools Council
NHE Education for Scotland
NHS England
Public Health Genomics Foundation
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians
Royal College of Physicians of Edinburgh
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of Edinburgh
Royal College of Surgeons of England
Royal Pharmaceutical Society
Scottish Genetics Consortium
Wales Medical Genomics Service

Academy of Medical Royal Colleges
10 Dallington Street
London
EC1V 0DB
United Kingdom

Website: aomrc.org.uk
Registered Charity Number: 1056565