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## Public health and genomics

New genomic technologies that underpin the increasing personalisation of medicine in clinical care are also important within public health practice. Powerful new tools, including significant advances in the management of data, now enable an increased understanding of disease risk and pathology, the personalisation of prevention and improvements in healthcare derived from more accurate diagnosis, as well as health protection through pathogen sequencing. All those working in public health need to identify the opportunities for genomic medicine that affect their area of practice.



### Understanding disease risk

The epidemiological tools of the last century focused on external disease risk whether arising from the environment (e.g. poor housing or unclean water) or from unhealthy lifestyles (e.g. smoking, lack of exercise or poor nutrition). New technologies to characterise an individual's genetic makeup can show that for most diseases genetic and environmental factors act in combination. For rare disease, the predominant influence is usually a single (but rare) change with large effect size in the DNA sequence whereas for more common, chronic diseases there may be hundreds of changes (variants) in the DNA sequence, each having a very small effect.

### Rare genetic disease

Rare diseases, 80% of which are genetic in origin, collectively affect 1 in 17 people in the UK population and therefore make up a proportion of the clinical caseload in all specialties. The burden of disease is also compounded in a number of ways: for individuals – they are often multisystem, long term and chronic diseases; for their families - there may be multiple inherited cases; and for the health system – they are rare, and may be hard for the non-specialist practitioner to initially recognise (leading to delays) and, when referred, they may require more complex diagnostic tests (including genetic tests) and specialist management.

Advances in genetic knowledge and sequencing mean that we can now predict with accuracy individuals who may experience inherited disease with a potential to prevent disease at individual and population level. From a public health point of view, it is important that practitioners are aware that healthcare needs arising from inherited conditions will be significant in each clinical specialty and recognise the need for equitable population access to high quality diagnostic, preventive and management services for people with (or at risk of) these complex conditions.



### Example 1: Antenatal testing

At a population level, recent technological advances in DNA testing have enabled antenatal testing using non-invasive techniques based on measuring tiny quantities of fetal DNA in the mother's serum. Used in the context of the national screening programme this means that cases of fetal anomalies such as Down's Syndrome can be diagnosed without exposure (as previously) to the significant risk of miscarriage arising from an invasive test such as amniocentesis.

### Example 2: Familial hypercholesterolaemia

Familial hypercholesterolaemia is a common inherited condition affecting about 120,000 people in the UK. It is often clinically undetected but the lifelong exposure to high cholesterol levels lead to premature atherosclerosis and associated cardiovascular morbidity. Guidelines recommend that adults with cholesterol over 7.5 mmol/l should receive DNA testing. Where an FH mutation is found cascade testing to family members allows individuals to be unambiguously identified as affected (and treated from an early age) or given the 'all clear' (although a healthy lifestyle is still advisable for all).

### Example 3: Abnormalities of cardiac rhythm

Abnormalities of cardiac rhythm such as long QT syndrome may come to light as sudden cardiac death (or near death) in a family which should prompt genetic testing. For those who possess the harmful genotype advice can be given about avoidance of specific triggers for arrhythmia and/or suitable drug treatment, or implantable cardioverter defibrillator.

One way that disease prevention may be achieved at population level is through screening. These may be at various stages in the life course including preconception (e.g. sickle cell carrier screening) or prenatal, where the aim is to enable couples at risk of having offspring with serious medical conditions to take alternative actions such as preimplantation genetic diagnosis or testing and termination of affected pregnancies. These have been vastly enabled by new non-invasive technologies (see Example 1). In the neonatal period, recent expansion in newborn screening using tandem mass spectrometry now enables early diagnosis of rare inherited metabolic conditions, such as phenylketonuria, where early treatment can save life and considerably reduce morbidity and disability in affected babies.

In later life, prevention may be achieved for an individual and for the family by accurate diagnosis followed by cascade testing (testing of first degree relatives of confirmed cases) to identify relatives who might also be at risk (see Example 2). Some of the relevant conditions appear as rare disease subsets of more common complex diseases (e.g. familial hypercholesterolaemia and some inherited forms of breast, ovarian or colorectal cancer). Genetic diseases present throughout the entire range of clinical medicine and it is important that they are recognised and diagnosed accurately so that preventive management and optimum treatment can be put in place (see Example 3).

In the past, genetic tests were expensive and time-consuming, and were usually offered as single gene tests as determined by genetics specialists. Increasingly, new technologies allow for these single genes related to the suspected condition to be gathered together into multiple 'panels' of genes and tested in parallel, at vastly reduced time and expense. In whole genome sequencing (WGS) information from the entire genome potentially becomes available in addition to that strictly required for the clinical test. This leads to the possibility of identifying people at risk of serious inherited disease (outwith the reason for their consultation) but from a public health point of view raises the question of utility at population level, harm arising from false positives and overall cost effectiveness. The NHS UK Genetic Testing Network undertakes evaluations of new genetic tests for inherited diseases and provides information on these on its website. The NHS Directory of Genetic Tests can also be accessed.

### Example 4 : Breast cancer screening

In breast cancer, modelling showed that personalised mammographic screening based on age and polygenic risk score could target screening more efficiently and improve the balance of benefit and harm for women.

### Genetics of common complex diseases

Most common diseases including cardiovascular disease, cancer, diabetes and conditions such as obesity are complex in aetiology, caused by a combination of environmental risk factors and an underlying genetic susceptibility. In most common chronic disease areas studies of how disease occurs within families and large genome wide association studies (GWAS) have enabled quantification of the relative contribution of each. For example, genes are thought to be responsible for 40-70% of the differences in body mass index between individuals within populations. There is thus potential that stratifying the population according to risk could lead to fine-tuning of preventive interventions (see Example 4).

More commonly, however, the knowledge of which genetic variants are associated with disease has been more informative in providing insights into disease mechanisms. For example, in obesity many of the changes are in genes that are active (expressed) in the central nervous system, suggesting that factors to do with appetite control are important in obesity. Greater understanding of pathways involved in disease mechanisms can also lead to potential targets for drug development.

### Pharmacogenomics and treatment

Important also in the provision of high quality healthcare is the increasing use of genomic diagnostic support to guide drug treatment. This may be related to the underlying molecular pathology of disease or by understanding the variability in individual responses to medicines. Variability may include efficacy to a given drug, which may alter drug choice and / or dose. This information can also predict susceptibility to adverse drug reactions, including those at the more severe end of the spectrum, such as warfarin toxicity. With the development of WGS it is anticipated that testing for relevant genetic variants that influence both drug efficacy and drug safety will increasingly be available at the time of prescribing and will be used to aid both drug and dosage selection.



### Example 5 : Pathogen whole genome sequencing

Pathogen whole genome sequencing was used to detect and resolve an outbreak of MRSA (methicillin resistant *Staphylococcus aureus*) infections on a special care baby unit. Once the outbreak was confirmed the probable source of the infection was also identified enabling control measures to end the outbreak to be put in place.

### Pathogens

One of the most important roles for genome sequencing is when applied to the genome of pathogens rather than of humans. This has found multiple uses in the area of infectious disease management at individual and population level. Relatively cheap sequencing enables rapid identification and characterisation, identification of key virulence factors, antibiotic resistance profiling, and detection, mapping and analysis of outbreaks. Pathogen sequencing will have an increasingly important role in health protection practice facilitating more efficient and effective management of disease outbreaks (see Example 5).

### Further information and resources

PHG Foundation

[www.phgfoundation.org](http://www.phgfoundation.org)

*(Reports and policy documents related to the application of genomics to improve population health, and educational material on public health genomics)*

HEE Genomics Education Programme  
Health Education England

Information on genomics education including HEE sponsored MSc., Diploma, PG Certificate and CPPD genomics courses  
0121 695 2374

[genomicseducation@wm.hee.nhs.uk](mailto:genomicseducation@wm.hee.nhs.uk)

[www.genomicseducation.hee.nhs.uk](http://www.genomicseducation.hee.nhs.uk)

Online module, St George's, University of London, The Genomics Era: the future of genetics in medicine

[www.futurelearn.com/courses/the-genomics-era](http://www.futurelearn.com/courses/the-genomics-era)

UK Genetic Testing Network (UK GTN)

0203 350 4999

[ukgtn@nwlcsu](mailto:ukgtn@nwlcsu)

[ukgtn.nhs.uk](http://ukgtn.nhs.uk)

UK Pharmacogenetics and Stratified Medicine network

[www.uk-pgx-stratmed.co.uk](http://www.uk-pgx-stratmed.co.uk)

Burton H, Jackson C, Abubakar I. The impact of genetics on public health practice. *British Medical Bulletin*; 112: 37-46 2014 doi: 10.1093/bmb/ldu032.

Ethical, legal, social and organisational implications

Making the most of genomics to achieve improvements in population health requires attention to health systems, as well as the potential for testing to be used outside that system by individuals wishing to find out more about their own health. With their wide responsibilities across healthcare, health promotion and health protection, public health practitioners are ideally placed to ensure optimum use of these new technologies for the benefit of society. There are a number of important challenges that will require a whole organisation strategy:

- Impact of genomics on current healthcare services, resources and patient pathways (including equity of access to genomic tests)
- Commissioning high quality services that meet rapidly evolving needs
- Developing skills and expertise in genomics across the entire health professional workforce including public health
- Ensuring that systems are in place for genomic and related clinical data collection, storage and sharing
- Responsible policies for responding to unexpected findings and using secondary findings effectively
- Developing and ensuring public and patient confidence in genomic developments and services

The future

The last two decades have seen unprecedented investment in life sciences in the UK. Advanced technologies are now available to sequence the entire genome at a cost of a few thousand pounds in as little as 24 hours, and it is envisaged that this cost will fall considerably over the next few years. More recently, the Government has signalled its confidence in the power of genomic science to produce major health benefits for the population through its investment in the 100,000 Genomes Project. The skills of the public health professional in population health and healthcare services will be essential in the realisation of this ambition for the maximum benefit for patients.

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