phgfoundation
making science work for health

Beyond the horizon: Connecting science and health

Celebrating 15 years of public health genomics

New thinking for health in the post-genomic era

Public health genomics has come of age. Government reports such as *Building On Our Inheritance* and *Innovation, Health and Wealth*, together with the growth in genomics and translational research show how UK public policy is embracing the translation agenda.

> *If we are serious about improving health, we must act on what we know modern biology has to offer and not focus only on the social and environmental determinants of disease*
>
> **Ron Zimmern**
> **Chairman, PHG Foundation**

When we started our work 15 years ago, genetics research had yet to filter into the consciousness of policy makers and the general public. However, the Human Genome Project was gaining significant momentum, challenging us all to change the way we think about health and healthcare.

The time was ripe to take stock of what genomics and molecular biology had to offer the practice of public health; and to consider the capacity building necessary to prepare the NHS and wider society for the opportunities that would be presented by the emerging science of genomics.

Preparing for the paradigm-shift

It was in this context that in 1997, as Director of Public Health for Cambridge and Huntingdon, Ron Zimmern established the Public Health Genetics Unit (PHGU); made possible with funding from the Regional Health Authority. This was in no small way due to the support of Keith Peters, Regius Professor of Physic, and Richard Himsworth, NHS Regional Director of R&D at the time. PHGU was set up explicitly to serve as a focus for population-based enquiry about the potential impact of genetics and biomedical research on the provision of healthcare in the UK, and to promote policy action to support the translation of research into practice.

As the PHGU team began to work with the NHS and policy makers in the UK, totally independently across the Atlantic, Muin Khoury was thinking along similar lines, founding the Office of Genetics and Disease Prevention at the US Centers for Disease Control.

Much has happened since. The science has developed in ways and at a speed that we could not have imagined when we started. The narrower concentration on heritable and inherited disorders that we call genetics has broadened into genomics and genomic science. Our emphasis on the wider policy aspects has not waned over the years - together with our US collaborators we have pursued a shared commitment to an enterprise that is now recognised internationally as the field of public health genomics.

An independent voice

The PHG Foundation is the successor to the PHGU, and has been an independent non-profit since 2007. Our mission is to be alert to scientific advances, to re-think the status quo and mobilise effective responses in healthcare systems so that as a society we can turn our investment in biomedical research into real improvements in population health.

Today, in the richer nations at least, policy makers do not need prompting to see the significance of genomics or to pay attention to the translation agenda. But public health professionals on the whole still fight shy of embracing genomic and molecular science as opportunities for global health improvement, while NHS and health services worldwide are inadequately prepared.

The road ahead

Of course building momentum to turn scientific discoveries into practical healthcare applications is crucial, but if we limit our thinking narrowly in terms of translational research we may miss important opportunities for achieving improvements in population health and efficiencies in healthcare.

At the PHG Foundation we want to understand how genes and environment interact to cause disease, and how we can use genomic science to improve the effectiveness of public health practices and develop new interventions.

The burden of common conditions such as cancer, diabetes and heart disease is increasing in richer countries and in the developing world, and the costs of applying public health interventions across whole populations will be immense. Whilst personalised disease prevention is still a long way off, the science is now sufficiently developed to offer the prospect of being able to stratify populations according to disease risk, and ultimately to target our public health interventions where they will make the biggest difference.

The economic, logistical and health benefits of being able to target those individuals with the highest risk are obvious.

> *The group (PHG) has assumed a global leadership role in assessing and integrating genome-based knowledge for the benefit of population health in the UK and around the world.*
>
> **Dr Muin Khoury**
> **National Office of Public Health Genomics, USA**

Genetic science can change the way we diagnose and manage disease. Getting genomics into everyday practice across the health system represents a formidable challenge, but the UK NHS is well placed to respond.

Hilary Burton
Director, PHG Foundation

A new era for population health

In the post-genomic age, advances in science and technology and our increasing understanding of biological systems are not the only drivers we need to be concerned with. Shifts in social attitudes, structures and dynamics; the era of 'big data' and infrastructure science; the changing epidemiology of disease, especially in emerging economies; and globalisation are all issues which require us to rethink the way we will organise and deliver healthcare in the future.

The PHG Foundation will work to resolve the major disparities in provision of new technologies across the UK; and to bring attention to the opportunities, challenges, risks and distractions that scientific advances present for our health systems and society as a whole.

We will promote the role of genomics in public health practice at a global level, and advocate for the relevant and responsible application of genomics knowledge and technologies for the benefit of populations in both the developed and developing world.

The PHG Foundation as a policy think tank will be using all we have learned over the past 15 years to address some of the wider challenges inherent in making science work for health in the 21st century.

Hilary Burton
Director

Technology watching

Deciphering the DNA sequence of the entire human genome opened the door to a new molecular pathology that would shed light not just on heritable diseases, but also on the genetic contribution to common complex conditions such as coronary heart disease, diabetes and cancer

Genomics research offers exciting opportunities for better diagnosis, treatments and disease prevention – taking genomics beyond the realm of clinical genetics into the territory of population health.

As the millennium approached, the huge interest in basic research was not being matched by a strategic approach to the translation of findings into practice. It was time to engage health policy leaders in the UK in thinking about the policies and infrastructure needed to realise the benefits of society's investment in biomedical research.

In 2000 we worked with the Nuffield Trust as part of their *Policy Future for UK Health* programme, imagining alternative futures for healthcare. Using scenario planning techniques we worked with a wide range of stakeholders to generate policy recommendations for developing the science research base; planning health services; workforce education; financing new technologies in healthcare; and information, privacy and regulatory frameworks.

Published in a seminal report, *Genetics and Health* (2000), practically all of those recommendations are reflected in today's health policy discourse.

Tackling the barriers

Since 2000 we have continued our systematic 'technology watching' across the breadth of genome-based biomedical research. By spotting those innovations with most potential for early practical implementation, we inform the critical decisions of policy makers and service providers as they tackle the barriers to innovation in the NHS and other healthcare systems.

The PHG Foundation works to provide strategies for health systems of the future, enlightened by what we learn from studying the environment, individual technologies and their use in particular applications or disease categories; and by thinking about how we manage the complexities, ethical challenges, uncertainties and risks associated with the adoption and diffusion of new genomic technologies in healthcare.

The PHG Foundation has a strong and consistent track record of work on the application of genetic and genomic research to healthcare and provides a vital contribution to policy development.

Dr Mark Bale
Department of Health

NIPD – a paradigm shift in prenatal care?

Sometimes scientific innovation delivers a truly game-changing opportunity. In the late 1990s, Professor Dennis Lo made a breakthrough with the discovery of cell-free fetal DNA and RNA in the blood plasma of pregnant women.

These short fetal nucleic acids are present from just a few weeks into pregnancy, but (unlike fetal cells) are cleared entirely from the mother's blood within hours of delivery. This discovery had the potential to create a paradigm shift in prenatal diagnosis – if the fetal DNA could be isolated, then genetic analysis of the fetus could be achieved much earlier from a simple maternal blood sample instead of using more invasive techniques which carry a risk of miscarriage. Ten years later, this research was sufficiently advanced to make non-invasive prenatal diagnosis (NIPD) a real prospect for clinical application.

The potential value of the new technique was immediately clear, but the route to clinical implementation was less so – at the PHG Foundation we recognised that the impact on current antenatal screening and testing services would be significant. The technology is very effective in confirming the sex of a fetus, crucial for families with sex-linked genetic disorders. It could also be used to identify the blood group of the fetus – important for identifying pregnancies at risk of problems due to blood group incompatibility between mother and baby – and to diagnose some specific serious genetic diseases.

This is no 'niche' technique for geneticists. NIPD could be used to detect conditions such as Down's syndrome, currently part of the antenatal screening programme for all 900,000 pregnancies in England and Wales each year, meaning that eventually it could be used in mainstream NHS antenatal services.

In 2008 we brought together a wide range of interested stakeholders to examine the issues. We produced the first comprehensive reviews of the technology and its current and future applications in the UK, including an assessment of the ethical, legal and social implications. The Government is now making substantial investment in clinical trials, such as the UK RAPID programme, and leading professional bodies such as the National Screening Committee and the Royal College of Obstetricians and Gynaecologists have published their policy positions and practice guidelines.

Science may be more agile than health systems, or indeed society – but by anticipating key developments in NIPD our work has meant that the undoubted benefits of this ground-breaking new technique will be available to women sooner.

Congratulations on the excellent report on cell free fetal nucleic acids for non-invasive prenatal diagnosis. It is a welcome overview and will assist us in developing our policy framework in this controversial area.

Professor Peter O'Leary
Department of Health,
Western Australia

Change and adapt: **Genomics** in the mainstream

Genomic science has altered the possibilities for understanding diseases, making diagnoses and providing effective clinical management. Progress has been transformative for managing patients with inherited disorders and we believe that genomics will improve the treatment of common diseases too - but in both cases, access to high quality services will be crucial

In 2000 UK Secretary of State for Health Alan Milburn was one of the very first politicians to acknowledge the vital role that genomics would play in modern medicine. He challenged the NHS to 'change and adapt' its services to respond to the opportunities of genomics. Helping the NHS to achieve that transformation is one of our core ambitions.

Too often concepts of translation or implementation are built on the notion that a product (for example a genetic test or a new drug treatment) emerges from scientific research and just 'needs to be taken up' in clinical practice. In contrast we take an holistic approach to look at how the introduction of new knowledge, technologies and capabilities impacts on whole areas of clinical practice – unpicking the complexities of modern health systems and tackling issues of capacity, funding, organisation, service quality, ethics and clinical competencies.

Healthcare for inherited diseases

Over the last ten years, we have been able to draw some important generic conclusions from our detailed studies of services for conditions such as inherited metabolic disorders, learning disability, genetic eye diseases and inherited cardiovascular disease.

There are important new clinical applications for genomics in all areas; but although services with appropriate expertise and capacity are provided in a small number of centres (usually associated with substantial research activity) our studies have shown that there is not one single area of clinical medicine in which these high quality, specialised services are available across the NHS as a whole.

Professionals in specialist genetics services must take on a leadership role, whilst hands-on care for diagnosis and management of people with possible inherited disease increasingly will be undertaken within the relevant clinical specialty. There is a real need for development of sub-specialities (with all their training implications) in all areas looking after inherited disease.

> *This report provides the best and most recent picture of IMD services to date.*
>
> **Strategic Advisory Committee Report 03/08**
> (about *Metabolic Pathways: Networks of Care* 2005)

Inherited diseases: Listening to professional concerns and meeting patients' needs

It is now possible to test for mutations that may, for example, underlie sudden cardiac death in a young person, or indicate the likely cause of serious visual impairment. We can identify those who may be at risk and encourage other family members to be tested. But NHS provision is very uneven.

In one study we found that the numbers of patients able to access specialised services for inherited eye conditions such as retinitis pigmentosa varied seven-fold between geographical regions with the best and worst service provision.

Listening to the concerns of stakeholders is crucial. By working with multidisciplinary stakeholder groups including patients, health service providers and researchers, we have been able to explore questions such as what do patients and their families need, what would be the best way of meeting those needs given the 'state-of-the-science', are services across the UK currently meeting these needs, and can everyone access high quality services irrespective of where they live?

Our studies have demonstrated just how important genomics has become outside the traditional domain of clinical genetics. Building on earlier work and using case studies from cardiac medicine and ophthalmology we presented recommendations for change to a meeting of representatives of 15 clinical specialties at the Royal College of Physicians in June 2011.

Crucially, their endorsement has prompted widespread acceptance that it will be vital to embed genetics at specialist and generalist levels in the clinic and in development of new NHS commissioning systems in England.

Our assessment of the problems and recommendations for action in key policy areas were published in an influential report *Genomics in Medicine* in 2012.

> *Since the PHG Foundation has become involved ...the momentum has changed in such a way that a previously static process is now moving to its ultimate objectives – the improvement of patient care nationally.*
>
> **Dr Elijah Behr MD**
> **St George's University of London.**
> (about *Heart to Heart* 2008)

Tackling the big public health problems

Common conditions such as cancer, heart disease and diabetes affect many people in the UK and worldwide and constitute a major source of ill-health and premature death. Policy makers, researchers and clinicians hope that genomics will have an impact here too.

The common chronic disorders such as heart disease or cancer have multiple underlying factors. Epidemiologists have long ago shown that our environment or lifestyle such as exposure to tobacco smoke, diet high in saturated fat or low levels of physical activity may act as causal factors in these diseases. Current public health interventions focus on moderating societal and individual behaviours in relation to these factors.

Genomic research is throwing light on patterns of genetic variation and their links with disease susceptibility, and how they interact with the environment to increase or decrease risk of disease. In 2003 the Genetics White Paper expressed the hope that people would have the option to be tested for predisposition to common diseases and that those at higher risk would have access to appropriate 'preventive and monitoring' services. This aspiration was somewhat tempered in the 2009 House of Lords report on Genomic Medicine.

Expectations remain that the knowledge obtained from research at this level will lead to new treatments. However, at present it is fair to say that genomic science has not yet delivered evidence that will lead to modifications in public health programmes – stopping smoking, a healthy diet and exercise are still and will continue to be the best options.

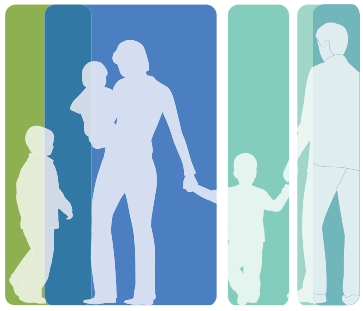
However we believe that over time evidence will emerge that these same programmes, specifically directed at groups categorised according to disease risk profiles, may lead to a more efficient and effective route for the prevention of disease.

> *The Department of Health welcomes this report, which we will use in our work with Specialised Services Commissioners and cardiac networks to support the NHS in the further development and delivery of service improvements for patients.*
>
> **Dr Huon Gray**
> **Department of Health, UK**
> (about *Heart to Heart* 2008)

Progressing a stratified approach

Until recently, much of the emerging science in this area has involved the identification of 'single gene subsets' of disease, such as those rare mutations that can underlie familial forms of colorectal cancer, diabetes or heart disease. Identifying affected individuals is an important form of 'high-risk' disease prevention.

In the last four years, however, through our role in the major European project on genetic variants associated with breast, prostate and ovarian cancer ('COGS'), we have shown how these variants may be used to stratify risk for the population and increase the utility and cost effectiveness of preventive population screening programmes whilst also reducing harm from over diagnosis.



We plan to use this proof of principle for stratified prevention to engage the public health community with the need to incorporate genomic approaches into their programmes. However, whilst risk stratification will be possible, its introduction into prevention programmes will be immensely complex.

Dilemmas of the genomic era

What are the public health implications of adding new knowledge about genetic information to the health risk equation? What are the challenges for service delivery systems and the health information landscape? What about cost effectiveness, benefit and harm? And how do we prepare for the ethical and social consequences?

Through COGS we are approaching a new era of stratified prevention. The age based screening of today will be replaced by a risk based identification of individuals that will benefit from future screening programs. The international workshops hosted by PHG are a landmark in the pathway from science to policy. New knowledge is only the beginning - implementing new screening routines in a complex and diverse world, in a way that is fair, acceptable, practical and cost effective will present the next set of challenges.

Professor Per Hall
Karolinska Institutet, Sweden

The PHG Foundation and researchers from the University of Cambridge have been investigating these questions as collaborators in a large multicentre research initiative, COGS (Collaborative Oncological Gene-environment Study).

Using modelling techniques we looked at how we can use knowledge from nearly 70 variants known to be associated with breast cancer to categorise populations into lower, medium and higher risk groups. We wanted to know whether this could be used to fine-tune the mammography screening programme, so that women with higher risk could be offered earlier or more frequent screening, and those with lower risk could benefit from a less intensive offer.

We found that under certain conditions such a programme could increase the number of breast cancers detected. And, of course would be a more cost-effective option.

Although the increased risk conferred by each susceptibility variant was low, our findings confirmed (even to sceptics) that examining many variants together provided a wide enough distribution of risk in the population to be useful.

We are also exploring how such a programme would be put into practice. Stratification of risk in interventions such as the UK Breast Screening Programme brings an additional layer of complexity – as one of the experts in our multidisciplinary workshops commented: "*this is when it starts to get difficult*".

So, with the COGS initiative, we are offering answers to some tricky dilemmas.

Both professionals and public require greater genetic knowledge: so that those offered stratified prevention understand the programme sufficiently to give informed consent, and that health professionals are knowledgeable and able to provide appropriate support. Above all, we must avoid confusing people with messages about variation in risk so much that they lose trust in screening programmes and decide not to attend at all.

Testing technologies: **Appraising** innovations

As we develop more genome-based tools for diagnosis and healthcare, what are the opportunities, how can we be sure they are adding value and how do we appraise the risks?

Our growing knowledge of the genetic contribution to common diseases, coupled with access to cheaper, faster and more accurate technologies is driving the need to evaluate new tests and to understand the implications for healthcare.

The last decade has seen rapid growth in the number of genetic tests coming onto the market. In the early days there was no corresponding development of processes and systems to evaluate them – methods for establishing their validity and utility in clinical practice were not keeping pace.

The PHG Foundation has made a significant contribution to the development of genetic test evaluation frameworks and processes both in the UK and internationally.

We played a major role in the development and introduction of the UK Genetic Testing Network's Gene Dossier framework for genetic test evaluation, which is used to approve new genetic tests that are recommended for adoption by the NHS. We ran a diagnostic summit with the Royal College of Pathologists making recommendations about the evaluation and regulation of diagnostic biomarkers; hosted an OECD expert working group on this topic in 2006; and participated in a number of Eurogentest working groups, developing policies for genetic test evaluation within Europe.

We continue to provide public health and epidemiological expertise for the NHS in this area and to contribute to UK and European policy on genetic test evaluation.

Looking ahead we see that next generation sequencing technologies will have major implications for the understanding, treatment and prevention of disease and the organisation of health services.

Concepts and models for the evaluation of genetic tests

In most cases the first clinical application of new genomic knowledge about the relationship between a specific genotype[1] and defined phenotype[2] is the development of a genetic test to identify the presence or absence of the genotype. The test results should provide information which doctors use in making decisions about the care of the patient and their family.

We promoted to policy makers the concept, now widely accepted, that it is necessary to distinguish a test from an assay. An assay is a method to analyse or quantify a substance in a sample. The term genetic test should be regarded as shorthand to describe an assay to detect 'a particular genetic variant (or set of variants) for a particular disease in a particular population and for a particular purpose'. This concept is now central to genetic test evaluation frameworks being implemented in the UK and internationally.

A clinical test (of which a genetic test may be an example) may have a variety of different purposes including: making or excluding a diagnosis, guiding and monitoring treatment, population screening and risk stratification. The extent to which a test or intervention meets the objectives for which it was designed is the formal definition of effectiveness.

Therefore, defining the purpose of a test is a necessary requirement without which the effectiveness of a particular biomarker cannot be evaluated.

In synthesising conceptual thinking with existing frameworks like the well-established ACCE (Analytical validity, Clinical validity, Clinical utility and Ethical, legal and social implications) methodology initially developed by colleagues in the US, PHG has been instrumental in establishing new models for evaluating novel genetic tests.

Recently we led work which draws the distinction between two components of clinical validity - scientific validity and test performance – and which has been incorporated into the final draft of the European Regulation on *in vitro* devices.

[1] genotype: an individual's genetic 'make up' or constitution

[2] phenotype: disease or physiological trait arising from underlying genetic factors

> *The report and its recommendations have been certainly taken up where labs have been able to get funding and in most cytogenetic labs.*
>
> **Professor Peter Lunt**
> **UKGTN**
> (about *Evaluation of Array CGH* 2006)

Advocacy in action

New biomedical technologies have a disruptive impact on health systems. Decision-makers need knowledge, evidence and neutral spaces where they can consider the opportunities, challenges and risks presented by scientific advances, and reconcile their often competing interests

Over the last 15 years we have enjoyed working with policy makers and health professionals on both cross-cutting policy issues and projects that have led to improvements in health services.

As an independent non-profit organisation with multidisciplinary expertise we bring people from our networks of professional colleagues and patient groups together. They help us ensure our policy recommendations reflect ethical, legal and social issues, and the input of service users as well as the clinical and scientific agenda.

In 2000 we were invited to brief the Secretary of State for Health about the implications of genetic science for health and health services and our policy recommendations, outlined in our report *Genetics and Health*. The following year, the UK Government went on to announce its major investment in genetics, including increased funding for genetics clinics and laboratories and pledges to establish Genetics Knowledge Parks and to publish policy commitments in a Government White Paper. More recently, our work was widely mentioned in the 2010 report from the House of Lords Select Committee on Genomic Medicine.

Taking a stand

Throughout 2003-4, the PHG Foundation closely followed the Human Tissue Bill's progress through Parliament. The main driver for the Bill was to right the wrongs that were so apparent from the Bristol and Alder Hey retention of body parts cases, but it seemed that the proposed legislation would go much further than simply addressing unauthorised tissue holdings. We were concerned that the resulting Act would have a detrimental effect on genetic testing for medical purposes.

As it turned out, this fear was shared by others. The British Society for Human Genetics saw the threat as significant stating: "*In its original draft form (the Human Tissue Bill) could have made many elements of our clinical and laboratory practice impossible*". Shortly after the Bill was published we produced a critique and hosted a conference that brought together the Wellcome Trust, the Medical Research Council and other key policy makers to address its deficits.

Our analysis and evidence (set out in *The Human Tissue Act 2004: An assessment of the Act and its implications for the specialties of clinical and laboratory genetics*) together with our briefings to policy makers have been widely recognised as being influential in ensuring that the eventual inspection and licensing regime was responsive and proportionate.

Next generation sequencing: Too much information?

Recent rapid developments in DNA sequencing technologies have dramatically cut both the cost and the time required to sequence a human genome. Soon it will be easier and cheaper to sequence an entire genome than to extract and test sections for specific mutations.

Our report *Next steps in the sequence*, published in 2011, was the first comprehensive examination of the issues involved in implementing whole genome sequencing technologies in the NHS. But already on the horizon is the next generation of genomic diagnostic technologies – whole genome sequencing plus array–based molecular karyotypes, tailored multiple gene arrays, and massively parallel (exome) sequencing.

Around the world next generation sequencing (NGS) is being used by a large number of researchers. Although there is some work being done on the ethical issues involved, there is very little on the use of NGS in a clinical rather than a research context.

It is clear that when NGS is eventually used in health services, the scale of genetic information generated by NGS technologies will dwarf that currently provided by existing diagnostic techniques. One of the principal concerns is what we do with that information, particularly incidental, unsolicited findings from test results. We simply do not know what ethical, legal, social and practical issues will arise when NGS is introduced into the clinical setting.

In the case of stratified medicine (referred to variously as stratified, personalised, or precision medicine), using NGS offers the prospect of being able to categorise patient populations into biological sub-groups to deliver more personalised medical care and disease prevention programmes. There is thought to be huge potential for increasing patient benefit and improving healthcare effectiveness and business performance in the UK's biotechnology sector.

Again we do not yet understand the organisational, ethical, social and regulatory barriers and drivers which will affect adoption and implementation into mainstream clinical practice.

In two new projects for 2013, the PHG Foundation will address these questions and work with a wide range of stakeholders to provide knowledge, data and recommendations for policy action.

A **global** outlook

Genomic technologies can, and should, be used to improve the lot of people worldwide. Policy makers in today's high growth economies have a unique opportunity to make the best use of biomedical innovation. Even in low resource settings there are programmes that can be put in place now that would make a big difference to population health and wellbeing

Modern biology has a lot to offer population health programmes, which conventionally emphasise the role of social and environmental factors in causing disease and overlook the potential of genomic advances for tackling some of the world's major health issues.

The PHG Foundation is committed to promoting effective and equitable access to new health technologies both in the UK and beyond. Recent international commissions include one from the Hong Kong Hospital Authority to review genetic services and to make recommendations for genomic medicine in the territory.

In emerging health economies, we believe that getting basic genetics services into front line healthcare is just as important as building sophisticated infrastructure such as biobanks and big research institutions, and the two should go side-by-side. We are working with the World Health Organisation on a Grand Challenges project which aims to inform policy and research priorities by identifying the top ten opportunities for using genomics for public health in developing countries.

Our key message is that we should apply what we already know and that there are programmes that can be put in place right now. Work such as our Born Healthy project, which aims to reduce the burden of birth defects in low and middle income countries, is a reflection on how we can best use our experience in public health genomics to enable this to happen.

In such complex areas it can be quite difficult for policy makers to know where to start but the learning is by no means one way. We have the privilege to work with some of the world's leading experts and local health champions who are really focused on making a difference to the people they serve. They inspire us and teach us so much about the needs of their local communities, and help us to understand the contribution that genomics can make to improving global health.

The Born Healthy project

Each year around five million babies, most of them in developing countries, are born with congenital disorders. As health programmes aimed at tackling infectious disease take effect, congenital disorders become the leading cause of mortality and morbidity in childhood.

Many conditions (like sickle cell disease and thalassemias) have underlying genetic causes but environmental factors can worsen them. As many as 70% of cases can be prevented or significantly ameliorated by better services and simple, affordable interventions in ante- and postnatal care, yet congenital disorders remain a neglected issue.

In 2010, the World Health Assembly exhorted its member states to redress "*the limited focus to date on preventing and managing birth defects, especially in low and middle income countries*". They highlighted the fact that solutions are already available and within reach of these nations, and others are possible given the necessary resources but noted the lack of political commitment, technical guidance and managerial action.

At the PHG Foundation we were already working on our pioneering *Health Needs Assessment Toolkit for Congenital Disorders*. Three years in the making, during which time it was piloted in Latin America, the toolkit was made freely available to the world in 2012 and is already making an impact; most notably in Brazil where it is being used to develop preconception services in the Porto Alegre region.

Ethical questions in a local context

The toolkit contains essential, country specific information on disease epidemiology, the impact on communities and effective measures to reduce the burden of disease. It also goes beyond the technical, spurring users into considering the sensitive ethical, legal and social issues that are relevant to their situation, for example around prenatal testing or the rights of people with disabilities.

We have no doubt that such questions can only be addressed by policy makers and health professionals in their own national and social contexts – but we hope that the data we provide and the suggestions we make in the toolkit enable them to initiate appropriate dialogue with governments and action for their populations.

> *The Toolkit is helping us get to the heart of how to review existing services and prioritise the implementation of new services in order to improve population health in the region.*
>
> **Dr Anita Kar**
> **University of Pune, India**

Trading **knowledge** and experience

The PHG Foundation supports capacity building in public health genomics by providing opportunities for networking, teaching and learning

Rarely a day goes by without the announcement of some new advance in genomics related to healthcare. In such a complex, knowledge-driven environment, we can only make real progress through sharing our experience.

People, connections and relationships are vital to the PHG Foundation's mission. We could not do what we do without the support of the many academics, health professionals, policy makers and other experts who are willing to share their knowledge and expertise with us. In return, it is only right that we create opportunities for knowledge exchange, learning and developing the collective capacity for action.

PHG Foundation staff serve on national committees and working groups, including: The NICE Diagnostics Advisory Committee, The Human Genomics Strategy Group, UK Genetic Testing Network, Genetic Alliance UK, Ethics Group National DNA Database.

Building networks and collaborations

In 2002, government funding enabled us to create the Cambridge Genetics Knowledge Park with partners from Cambridge University, the University of East Anglia and the local health and biomedical research communities. That initiative also helped us to establish, in partnership with the MRC Biostatistics Unit, the first UK coordinating centre for HuGENet, an international collaboration which aims to assess the epidemiological evidence for associations between human genomic variation and population health.

Just three years later, with interest in public health genomics gaining momentum, the PHG Foundation, with colleagues from the US, secured funding from the Rockefeller Foundation to bring people together from across the globe to create the GRaPH-Int network. The principal goal of the network was to promote the translation of genome-based science into improvements in population health.

That first meeting resulted in the 'Bellagio statement' which set out a shared definition and vision for public health genomics. The statement emphasises the importance of addressing the gap in translation between scientific advances and health service application and the need to evaluate and integrate knowledge across a broad range of disciplines, using this knowledge to address the organisational and policy barriers to implementation.

We value the PHG Foundation's role in bringing together all those with an interest in innovation and health to play a role in shaping the future.

Dr Richard Henfrey
Illumina

The PHG Foundation is an affiliate of: Cambridge Institute of Public Health, NIHR Cambridge Biomedical Research Centre, Eastern Academic Health Science Network, Cambridge Network, One Nucleus, The Humanitarian Centre, Charity Comms.

A strategy for education

An invitation from the Department of Health and the Wellcome Trust provided us with the opportunity to revisit some of the key themes in *Genetics and Health*; namely the need for an NHS workforce suitably equipped to practise in the post-genomic era. This work, published in in our 2002 report *Addressing Genetics: Delivering Health -Genetics Education for Health Professionals* was echoed in the 2003 Genetics White Paper, with three initiatives in particular coming to fruition: the creation of a new National Genetics Education and Development Centre in Birmingham, GPs with Special Interest in Genomics and several service development pilots.

Reaching out

As well as thinking strategically about genetics education, we deliver it, in the UK and internationally. Staged four times between 2000 and 2006 our popular Genetics and Health Policy courses created a cadre of senior professionals with the knowledge and confidence to take a leadership role on genetics in their own field. We co-produced public health genomics courses with Hong Kong University in 2007 and VU University in Amsterdam in 2011. In the UK, we contribute speakers and learning materials for third party genomics education programmes and have regular commitments to Masters' and undergraduate medical teaching at the University of Cambridge.

My time at the PHG Foundation has been incredibly rewarding. ...Working as part of the interdisciplinary team provided me with transferable skills and a great insight into the knowledge brokering and the science consulting profession...

Alex Oldman intern 2011 -2012

Welcoming in

Young graduates and more experienced professionals who are interested in the interface between medicine, genomics, biomedical science and bioethics recognise that the PHG Foundation offers a unique learning experience.

The Foundation is an accredited training location for Specialist Registrars on the UK's public health training programme and we regularly host trainees who have chosen to add public health genomics to their portfolio.

As well as welcoming students, trainees, visiting academics and health professionals from institutions across the UK and further afield, we supervise student projects for the Cambridge School of Clinical Medicine and the Judge Business School, and regularly support visiting fellows from Cambridge's Centre for Science and Policy.

Having hosted very successful internships for the Economic and Social Research Council and the Leonardo da Vinci Foundation, we launched our own paid internship scheme which welcomed its first incumbent in 2011.

We feel privileged to be able to build relationships with our visitors, who make a tremendous contribution to our own learning whilst they are with us and, we hope, take away some knowledge of genomics into their future careers.

Delivering the potential of genomic medicine

We have come a long way but our health systems have not kept pace with the new possibilities offered by advances in genomics research. So what are the PHG Foundation's main achievements, and what should we do next?

As we reflect on what the PHG Foundation has achieved so far, two things stand out.

Firstly, our work is acknowledged as having a pivotal role in establishing the role of genomics in mainstream medicine and public health practice. Although there is much more to be done, there is increasing recognition that genomics is not just about rare inherited diseases (important though these are), but is meaningful for us all.

Secondly, our argument that effective clinical translation of science requires more than just translational research is being heeded, at least in the UK, where recent government strategies are focusing on the need for effective implementation of innovations within health systems.

It is gratifying to see many of the recommendations in our key publications *Genetics in Health* (2000), *Genomic Medicine* (2010) and *Genetics in Mainstream Medicine* (2011) are reflected by the UK government advisory body the Human Genomics Strategy Group in their recent report *Building on Our Inheritance: Genomic Technology in Healthcare*.

Where next?

For us, the drive towards personalised medicine is hugely interesting, particularly the potential for using genomic information to improve on current methods for stratification – for example grouping patients according to their likely outcome or response to treatments; or populations according to risk profiles for targeting prevention.

These offer the prospect of 'stratified prevention' which will improve efficiency and effectiveness – and minimise potential harms - of public health programmes. It also means there will be important conceptual, regulatory and practical issues that will have major implications for the way we structure healthcare.

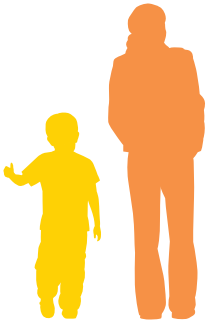
The lack of progress in implementing the science we already know is an on-going concern. The rate of scientific advancement is such that in continuing our mission of 'making science work for health' we will have to watch and 'horizon scan' the scientific environment for new developments and then to prioritise the areas where we can make greatest impact. Our guiding objectives are still to do all we can to see that everyone benefits from high quality genetics services, in the UK and beyond.

We would like to thank all our trustees, staff, associates, funders and supporters for their vital contribution to our work over the last 15 years. If you would like to be involved in or support our future work please contact us at ***contact@phgfoundation.org***

Since 1997 we have...

published over **30 reports** addressing implications of new genomic technologies

seen our online tutorials get an average of **600 views** a day

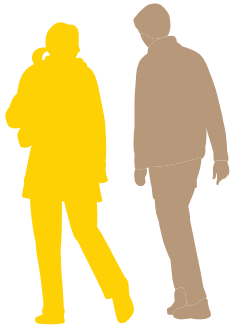


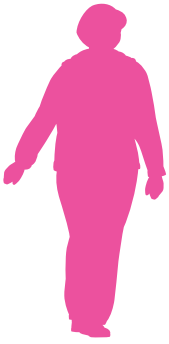
responded to **over 40 consultations** on subjects from innovation and emerging biotechnologies to the ethics of personalised medicine

had around **200 papers** published in leading **health and science journals**

supported the creation of **6 international networks**

received around **100,000** unique visits to our website each year

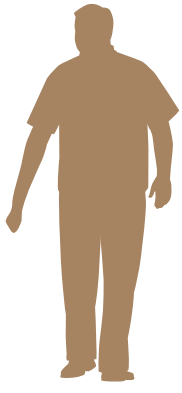




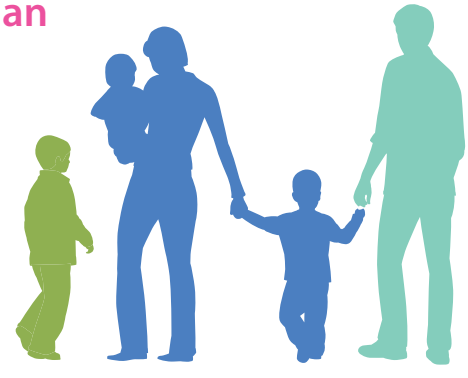
gained over **3,000 subscribers** to our monthly news round-up

given more than **£800,000** in donations and grants

run **2 internships** since the launch in 2011 of our formal intern scheme



welcomed almost **100 visitors with an interest in public health genomics** from across the globe



Our thanks go to Illumina for sponsoring our 15th anniversary events.

phg foundation
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