

Public health

in an era of genome-based and personalised medicine

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CENTER FOR BIOETHICS



Acknowledgements

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The meeting was co-organised by four partners: the PHG Foundation (Cambridge, UK), the Centre for Bioethics (Indiana University, USA), the Centre of Genomics and Policy (McGill University, Canada) and the Telethon Institute for Child Health Research (University of Western Australia). A full list of delegates is provided at the end of this report.

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Foreword by Dr Tikki Pang (Pangestu)
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Genomics is increasingly seen as one of several sources of information and technologies in the tool kit of clinical and public health practitioners. The information and the technologies developed in the field of genomics have great potential for making clinical and public health practice more effective, efficient and equitable. An increased understanding of human genomics and genomics of disease-causing pathogens and their vectors would allow health interventions to be informed more and more on the biologic characteristics of the sub-population or disease of interest, thereby potentially increasing effectiveness and reducing adverse effects.

The publication of this Report is both important and timely. The last decade has seen rapid advances in genomics technologies and information, particularly in our understanding of genetic variation within and between populations, and the identification of common genetic variants that predispose to common complex diseases. These advances have led to large media and public interest, particularly in genetic testing, with often exaggerated and unrealistic expectations of immediate clinical and public health applications.

A decade after the announcement of the first draft of the human genome sequence catapulted genomics and the potential of genomics medicine into public attention, the path from basic science to health interventions has proven to be longer and less predictable than first anticipated. This is partly due to the complexity of human biology, and the demand for resources and technology innovation to advance our genomics understanding. Also, insufficient emphasis has been placed on the translation of scientific discoveries into tangible health interventions, especially in resource-poor settings.

Genomics is relevant and important to all countries and populations, as it has the potential to help tackle morbidity and mortality due to major communicable and non-communicable disease in all regions of the world. The last decade has, however, exposed a large gap between developed and developing countries in their capacity to carry out biomedical research and in their ability to benefit from advances in biomedicine. For example, human genetics research is largely being done in developed countries with a focus on populations of Western European origin and on public health needs of developed countries. The history and diversity of human genetic variation, and the diversity and influence of environmental determinants on disease, make it necessary for research to be carried out in populations all over the world for it to be relevant and valid to all of us.

Similar to other health interventions, there is a set of minimum conditions necessary for genomics interventions to be implemented and utilized. These include: well-functioning health systems; access to health services; an evidence-based infrastructure that evaluates, regulates, sets guidelines, and compares cost-effectiveness of interventions; and an understanding of how local contexts influence relevance, uptake and acceptance of interventions. For genomics-based interventions, much work still needs to be done to meet these conditions. This Report will help clinicians, public health practitioners and relevant decision-makers frame and focus their strategies and approaches in an era of rapid advances in genomics.

WHO stands committed to facilitate the evaluation and equitable implementation of interventions utilizing genomics information and technologies by promoting international partnerships and cooperation strategies.

Table of Contents

1	Introduction	4
2	Process	6
3	Potential for genomics to improve population health	7
3.1	What do we mean by public and population health?	7
3.2	Lack of clarity about what genomics can achieve	7
3.3	Where does the potential for public health genomics lie?.....	9
3.4	Establishing clinical utility.....	10
3.5	Distinguishing between gains for populations and individuals	11
3.6	Managing expectations	12
4	Genomics and research	13
4.1	What should the research priorities be?	13
4.2	Research infrastructure	13
4.3	The proper scope of public health genomics research	15
4.4	Ethical issues in research	16
5	The Translation agenda	17
6	Delivering genomics within health care systems and services.....	20
6.1	Integrating multiple datasets	20
6.2	The effectiveness of different types of public health interventions.....	21
6.3	Creating effective health systems and services	22
6.4	Motivating behaviour change.....	23
7	Commercialisation and the role of industry	24
7.1	The impact of commercialisation.....	24
7.2	Direct-to-consumer testing	25
8	Global public health	27
8.1	To what extent is public health genomics relevant to LMIC?	27
8.2	Future proofing health systems and services in LMIC.....	28
8.3	Building research capacity in low and middle income countries	28
9	Conclusion	30
10	Recommendations.....	32
	List of delegates.....	34

1 Introduction

Genomics and molecular biology have developed at an ever increasing pace over the last decade. Building on the achievements of the Human Genome Project, and aided by advances in sequencing and information technology, groundbreaking discoveries in genomics and molecular biology are reported almost daily in the scientific and popular literature, suggesting multiple opportunities for improving the health of populations.

Against this background, a multidisciplinary expert meeting was held in Bellagio, Italy in 2005 to assess the potential implications of these developments for population health. The goal of the Bellagio meeting was to *'explore the possibility of establishing an international network to promote the goals of public health genomics, to share knowledge and resources, and to ensure equitable access to the benefits of genome-based knowledge by all, including those in the developing world'*.¹ The focus of this meeting was to ground these developments firmly within an analytical structure that could take account of social, regulatory and legal frameworks and add momentum to the growing public health genomics movement.

Five years on, the consensus and commitments achieved by this meeting have stood the test of time. These were:

- (1) to agree a formal definition of *public health genomics as the responsible and effective translation of genome-based science and technologies for the benefit of human health*;
- (2) to articulate a model of knowledge generation, integration and application known as 'The Enterprise', as a tool to describe its practice; and
- (3) to establish an international forum, the Genome-based Research and Population Health International Network (GRAPHInt), to promote the practice of public health genomics.

Over these last five years, GRAPHInt² and the public health genomics community have driven and supported multiple multicentre projects that have led to the publication of numerous peer-reviewed papers and reports, the establishment of the Public Health Genomics Journal, as well as grant funding to researchers.

One of the motivations for convening this present meeting was the feeling that the time was now right for there to be a detailed discussion about how public health should engage with this new scientific agenda, and of the fundamental issues that might be raised for public health practitioners. For example, how should we regard the tension between the collectivist principles that have formed the basis of traditional public health practice as against the individualism that appears to inform the practice of genomic and personalised medicine?

1 Genome-based Research and Population Health: Report of an expert workshop held at the Rockefeller Foundation Study and Conference Centre, Bellagio, Italy, 14-20 April 2005 (2005) Public Health Genetics Unit, Institute for Public Health Genetics, Centers for Disease Control and Prevention (CDC).

2 <http://www.graphint.org/ver2/>

A strong consensus had also emerged since Bellagio around certain principles which have grown out of the practice of *public health genomics*. These principles operate at a number of levels (both conceptual and operational) and have helped to create a coherent and consistent approach. These include:

- (i) **The explicit rejection of genetic exceptionalism:** rejection of the view that genetic and genomic samples and information *per se* demand special protection. Instead, the ethical and regulatory justification for using genetic and genomic samples and data should be no greater (nor less) than that of other sensitive medical information, and that where regulation is needed it should be proportionate and informed by the extent of the predictability and sensitivity of the information;
- (ii) **An emphasis upon the importance of translation supported by a strong evidence base:** in both the developed and Low and Middle Income Countries (LMIC), those concerned with public health genomics have noted a systemic failure to capitalise upon advances in biomedical sciences, through deficiencies in the translation process. This is manifested most notably in the lack of explicit mechanisms to determine the clinical validity or utility of a particular product or intervention, which impacts upon the translation of a scientific idea into the product itself. The reasons can be seen at many levels, with lack of the necessary expertise and workforce, of funding, and of political will all playing their part;
- (iii) **Understanding the limits of personalised medicine:** personalised medicine can be conceptualised at a number of levels and is subject to many, often inconsistent, definitions. Our own preference is for the term to be used in its most general form, namely for any medical purpose - predictive, diagnostic or therapeutic - to designate care that is tailored to the individual or stratified by the population subgroup. The use of genomic data to distinguish one individual or population subgroup from another represents an important emerging tool to assist health care providers in this task. Another emerging consensus is that *public health genomics* should focus primarily upon populations rather than individuals, and in so far as it will affect individuals and the practice of clinical medicine, the role of the discipline is to influence the development and reorganisation of health systems and services to take advantage of medical and clinical advances in the genomic era. This role includes assuring a robust evidence base for the use of genomic applications in both medicine and public health, and development of both evaluation and knowledge transfer strategies that support evidence-based practice.

With this ethical and operational infrastructure for public health genomics firmly established, the Ickworth meeting was convened to reflect upon how genome-based and personalised medicine might impact upon the agenda for public health. The scope of this meeting included both economically developed countries and LMIC, where the tangible benefits offered by these technologies to population health, may be less apparent than in the developed world.

2 Process

Building on the success of the Bellagio initiative, a meeting of 27 international experts from diverse disciplines was convened to set out the future direction and challenges for public health in an era of genome-based and personalised medicine. The meeting, held at Ickworth House, Suffolk, UK on 10-14 May 2010, was co-organised by four partners: the PHG Foundation (Cambridge, UK), the Centre for Bioethics (Indiana University, USA), the Centre of Genomics and Policy (McGill University, Canada) and the Telethon Institute for Child Health Research (University of Western Australia). It included experts representing a range of disciplines from Argentina, Australia, Canada, France, Italy, the Netherlands, Switzerland, the UK and the USA.

The steering group identified eight key topics for discussion, which were elaborated further in a proposal paper circulated to delegates in advance of the meeting. These topics were:

- (i) Post-genomic science and personalised medicine
- (ii) The socio-political and philosophical context
- (iii) Delivery of health services and the organisation of health systems
- (iv) Health information
- (v) Evidence, translation, knowledge transfer and brokering
- (vi) Public-private mix and the role of commerce and industry
- (vii) Perspectives from developing countries
- (viii) Perspectives from policy makers

On the basis of individual knowledge and expertise, each delegate was asked to contribute either a short presentation (supported by a short summary paper included in the briefing paper supplied to delegates) or to chair a session. Two final sessions were dedicated to developing practical recommendations to direct policy development and research priorities over the next decade.

3 Potential for genomics to improve population health

3.1 What do we mean by public and population health?

As a starting point for our discussions, we adopted a broad definition of public health:

*‘The science and art of preventing disease, prolonging life and promoting health through the organised efforts and informed choices of society, organisations, public and private, communities and individuals’.*³

In so conceptualising public health, the discipline of *public health genomics* concerns itself with how genome-based science and technologies will impact upon the science and art described above.

In practice, the scope of ‘public health’ varies between countries. In many countries in the developed world, for example, although there are common elements, there is variation in the extent to which public health practitioners are responsible for the direct provision of health care services. Thus in the UK, the three strands of health protection, health improvement and service improvement are combined such that public health practice includes conventional community-based public health programmes services, such as immunisation and health promotion, as well as issues concerning the organisation and development of primary care and hospital-based health services. In other contexts, such as the USA, public health physicians have no role in directly influencing the provision of clinical services,⁴ whilst in some LMIC, the practice of public health may be curtailed to such an extent that it is effectively limited to assuring basic sanitation and infection control.

By ‘public health’ we mean ‘the public’s health’ which can be influenced via a variety of different routes including programmes that operate at both population and individual levels.

3.2 Lack of clarity about what genomics can achieve

Although genomics has potential for improving population health, the exact ways in which it can deliver on this potential are unclear for a number of reasons:

Complexity of human biological systems

Research suggests that human biology is more complex than was perhaps anticipated, which suggests that a clearer understanding of what genomics can achieve will only become possible after more research.

3 C.-E. A. Winslow. *The Untilled Fields of Public Health*, Science, n.s. 51 (1920), p. 23; see http://www.en.wikipedia.org/wiki/Public_health

4 LM Beskow, W Burke, JF Merz, PA Barr, S Terry, VB Penchaszadeh, LO Gostin, M Gwinn, MJ Khoury. Informed consent for population-based research involving genetics. *JAMA* 2001, 286(18):2315-21.

Confusion between indirect and direct translation of genomic science

There has been a failure to distinguish carefully between the power of genomic science to provide insights into biological mechanisms at a molecular and cellular level (which it is hoped in due time will lead *indirectly* to new technologies, medicines, diagnostics and services) from those gained from discoveries about gene-disease association that may be used *directly* in the prediction and prevention of disease.

Failure to deliver interventions

The focus for some of the research methodologies adopted widely in genomics research has not been as successful in leading directly to effective clinical interventions as had been hoped. For example, genomics research initially focused upon candidate-gene association studies, but when these failed to substantially advance genomics knowledge, other approaches were adopted, such as genome-wide association studies (GWAS). Although GWAS have identified hundreds of common genetic variants that are associated with numerous diseases, individually these variants have only a small effect on the overall burden of disease and even in combination contribute little by way of effective risk prediction.⁵ Thus despite considerable research effort, much of the heritable component of disease remains unexplained.⁶

Failure to use existing knowledge and expertise effectively

The experience in many countries is that existing genetics knowledge has not been utilised in an effective manner. Only a small number of developments have already made a tangible impact on health, such as new diagnostic tests and targeted therapeutics (e.g. Herceptin). For example, even where the genetic basis for particular single gene disorders has been well characterised, and genetic tests developed which would allow testing of one family member to be cascaded through an extended family, this knowledge has often not been implemented to improve the health of those families.

The context for adopting new technologies

The experience of translating genomic advances varies quite widely between countries, particularly between the developed and LMIC. But even within countries, the prevailing research infrastructures, research capacities, the availability of a competent workforce, funding and competing priorities are not adequately co-ordinated in producing an effective translational mechanism to bring genomic science into clinical and public health practice. For example, in no developed country are there mechanisms and activities to provide data for the clinical validity and utility of genetic tests in a systematic manner. Nor are there systems for determining the manpower requirements of groups such as genetic epidemiologists, biostatisticians and bioinformaticians and for putting in place an appropriate manpower plan.

5 ACJW Janssens, CW van Duijn (2008) Genome-based prediction of common diseases: advances and prospects. *Human Molecular Genetics* Vol 17, Issue 2.

6 B Maher. The case of the missing heritability. *Nature* 2008, 456:18-21.

The multidimensional use of the label ‘genomics’

The term ‘genomics’ has been applied to numerous technological advances and research methods, but covers developments that are qualitatively different from each other. Whilst some such advances are the result of intensive investment in basic science or technology (such as the development of novel technologies used for high throughput genome sequencing), others describe existing technologies applied in new settings (such as the characterisation of the microbiome, or transcriptomics) or even novel processes of data collection (such as population biobanks or GWAS). The disparate nature of these advances makes it difficult to characterise the implications which might arise, and simply describing them all as ‘genomics’ can lead to exaggeration, confusion and unwarranted genetic exceptionalism.

Ultimately, these contextual factors have resulted in profound variations in the extent to which genomics advances have been implemented, particularly between developed and LMIC.

For multiple reasons the current implementation of genomic knowledge and benefits is both ineffectively and inequitably distributed, and realisation of its potential has been uneven.

3.3 Where does the potential for public health genomics lie?

Lack of consensus reflects the current state of genomic evidence

Amongst the delegates, there was a spectrum of opinion as to the potential for developments in genomics to deliver significant health benefits for public health, particularly in the short and medium term.⁷ Those who were most sceptical were resistant to the view that genomic data could be used directly to provide risk stratification strategies that would be effective for either individuals or populations within this timeframe. Their opinion was that pharmacogenetic interventions (thought by some to provide the greatest promise) would be of little public health value and they also argued that genomics advances had limited application within LMIC. However, the more optimistic believed that the likely benefits to public health were much more imminent and that in particular there would be value in pursuing further the potential for using genetic variants in combination with each other and with other environmental determinants. But even the optimists were wary of the hype and over-optimism concerning direct benefits in the shorter term. Despite this caveat, all agreed that there were some specific areas where genetics is already being used to substantially improve health, particularly in the area of inherited diseases.

⁷ By short and medium term, we mean up to five and ten years respectively.

Better understanding of basic science leading to more effective interventions

Whilst acknowledging these difficulties, there was, by contrast, much greater consensus in relation to the value of genomic research as a basis for understanding disease mechanisms, and to the possibility that this would, in the longer term, lead to effective and useful clinical and public health interventions. The contribution of different genetic variants to the phenotypic development of disease, together with other advances in post-genomic science (such as comparative genomics, systems biology and epigenetics), have the potential to elucidate how genes and environment interact and together contribute to disease. Notwithstanding the lack of consensus about timescales, these insights will eventually open the way to better treatments by identifying a plethora of new drug targets. New treatments should thus be more effective and have the potential to result in less frequent adverse drug reactions. In addition the development of more effective diagnostics for inherited diseases will improve their management, as well as allow more effective cascade testing at all stages of the lifespan. Screening programmes could potentially also be improved by stratifying the population by genetic risk and targeting preventive measures towards those in the highest risk groups.

Although there was general agreement about the importance of genomic research as the basis for understanding disease mechanisms, there was little consensus as to the extent to which this might in the short term lead to interventions that would directly improve population health.

3.4 Establishing clinical utility

The translation of advances in biomedical sciences and genomics is hampered by the lack of an infrastructure to systematically collect, publicise and evaluate evidence of clinical utility of genomic tests. This deficiency is particularly evident in the context of diagnostic tests. Although it was agreed that it would be desirable to have evidence in place, there was less consensus about who should be responsible for generating, collecting, monitoring and updating this evidence. We discussed whether a positive obligation to provide evidence should be placed upon relevant stakeholders (such as the pharmaceutical and biotechnological industries), as well as the extent of that obligation and any commercial incentives for collection (such as continued protection through patents or licences).

The deficiency in both generating and collecting relevant data needs to be clearly distinguished from two other separate and related questions; first, who should be responsible for the evaluation and analysis of those data; and second, who should determine and set the standards against which the evaluators might pronounce on the utility of a particular test or otherwise. Although different views were expressed about the need for statutory regulation of genetic tests, there was consensus that the most important issue was to ensure transparency of information so that physicians, patients and citizens could all have access to the evidence base.

Although not fully developed, a number of initiatives to systematically collect data on clinical validity and utility are underway in various countries.⁸ While these tend to be limited in scale, in part because of a paucity of relevant data and lack of funding, it is clear that there is a developing consensus amongst policy makers, funders and service providers that robust evidence of clinical validity and utility, where it exists, should be publically available.

3.5 Distinguishing between gains for populations and individuals

The original scope of epidemiological studies was to provide an understanding of the general determinants of disease and, by so doing, enable hypotheses concerning disease mechanisms to be generated and then tested. They also enabled differences in disease incidence between populations to be understood and provided the scientific basis for public health interventions at a population level. However, the extent to which these population measures apply to individuals cannot be determined through epidemiological studies. For example, the determination through epidemiological research that smoking raised the chance of lung cancer in all populations, and was a potential causal element in the pathogenesis of that disease, does not imply that in each and every individual, smoking would invariably lead to the development of the cancer. There were many smokers who did not develop the disease, and some non-smokers who did. The recent use of population-based studies of genetic risk factors as a means of absolute risk prediction at an individual level may be empirically and philosophically flawed and is an area that requires future research effort.

It follows that, since our understanding of disease processes operates largely at the level of subpopulations rather than individuals, the term *stratified medicine* may be more appropriate than *personalised medicine* when attempting to show that interventions, whether predictive or therapeutic, may work more effectively on some individuals or groups than on others.

8 Existing schemes include those provided by the UKGTN (http://www.ukgtn.nhs.uk/gtn/Information/Services/Gene+Dossiers/Gene_Dossier_evaluation_process) and GAPPNet (<http://www.sph.umich.edu/gappnet/>). Additional pilot schemes include resources developed by Labtestsonline (<http://www.labtestsonline.org/>). The announcement of plans for a Genetic Testing Registry by the National Institutes of Health (<http://www.ncbi.nlm.nih.gov/gtr/>) is also a welcome development.

3.6 Managing expectations

The rapid pace of advances in genomics has bred an understandable impatience for realising the benefits to human health. A realistic assessment of the potential harms and benefits of genomics is made more elusive by the 'hype' which tends to surround the topic. In part this is a legacy from the Human Genome Project which was built upon promises to unlock past biological secrets enabling great strides in health care. However the current infrastructure for funding and mechanisms for reviewing potential research seems to have entrenched this approach resulting in primacy being given to those research projects that promise tangible and short-term health benefits. These pressures to deliver are likely to be even greater in the future given the economic downturn.

The expectations generated by genomics have been overestimated in the short and medium term. Realistic expectations for what genomics will achieve in the next decade or so are likely to include the identification of specific genetic tests that are useful in clinical care (of which the most promising are in inherited disorders, cancer care, and pharmacogenetics). In the longer term, a better understanding of disease aetiology and pathogenesis has the potential to deliver improved health outcomes for both individuals and populations.

4 Genomics and research

4.1 What should the research priorities be?

Past investments in genomic research have not generated the evidence that will be necessary to transform profoundly and immediately the practice of health care. The meeting recognised shortcomings in existing research strategies, where most of the emphasis and funding have been directed at basic research, and little attention has been paid to either providing an evidence base for the translation of that research or facilitating uptake into improved health care. It also noted that other areas of research were being pursued, such as investment in high-throughput genome sequencing, without a clear view of how outputs from this work could be translated effectively into better health care. A strongly expressed sentiment was that health outcomes should drive the use of new tests and interventions in health services, rather than the availability of novel technologies.

Medical research funding should be directed purposively and pragmatically at those areas of clinical and public health practice where the medical and clinical impact will be the greatest. Our expectation is that some benefits are likely to arise from genomic medicine particularly in the medium and longer term through the more effective identification and management of single gene disorders and application of promising pharmacogenetic tests. Some funding should also be used to provide the evidence for the utility of genome-based knowledge in addressing the common complex diseases, such as cancer, heart disease, diabetes and mental health. Engagement across a broad spectrum of stakeholders from the scientific community and community organisations is likely to improve priority setting and aid the selection of realistic clinical scenarios for research.

4.2 Research infrastructure

The need for better descriptive tools

Common complex diseases are characterised by a multitude of interacting genetic and environmental factors to cause a specific disease phenotype. One recurring theme that emerged was the need for improved analytical tools to accurately and reproducibly describe and measure phenotypes and environmental exposures, including the social determinants of health. The failure to better characterise disease and its various sub-categories, and to develop effective metrics for established non-genetic contributors to disease, was a serious impediment that will invariably lower the effectiveness of research strategies because of disease misclassification.

The need for better integration of environmental and genetic factors

Effective integration of genomic data and phenotypic data is a prerequisite to understanding the significance of genetic variation. This integration is likely to involve the increased use of large population databases, as well as the need to amalgamate smaller amounts of phenotypic and genotypic data from multiple fragmented sources. In particular, the importance of gene-environment interactions in common complex diseases suggests that the development of phenotypic or gene expression biomarkers that reflect gene-environment interactions and correlate with disease risk may be key. Other interactions may also be important in understanding disease development, such as the way in which gene expression is moderated (epigenetics) as well as understanding more about ways in which host DNA can be mediated by external forces (nutrigenomics, infectomics, toxigenomics). The lack of appropriate bioinformatics tools and the failure to develop medical bioinformatics capacity through workforce planning and development were seen to be significant impediments to such integration.

Increased use of population biobanks

The establishment of biobanks were seen by most to be an important element of infrastructure provision. The prospective collection of genotype and phenotype data from large cohorts, both community and disease-based, over an extended period is a comparatively new development. In future years, these will provide a valuable epidemiological resource of scientific information with potential to yield important insights into genotype/phenotype correlation, and constitute an effective tool for population health planning, promotion and prevention. Whether these insights will actually result, and ultimately lead to improved health outcomes, has been questioned by some who argue that the sums spent on biobanks might be better used on more narrowly defined, clinically relevant research proposals.

Transparency and data sharing

Many of the large biobank projects encourage the sharing of data wherever possible, and also provide for appropriate safeguards to be in place to maximise the privacy and confidentiality of participants, and for cultural norms to be taken into account when data sharing occurs across different countries and jurisdictions. However, protections are not uniform. In addition, recent informatics developments increase the potential to re-identify participants, heightening the need to provide realistic assessments to participants of the extent to which their identity can be effectively protected⁹ and personal details remain completely confidential. Despite these caveats, wherever possible it was regarded as important to make data available for sharing to qualified investigators (subject to appropriate governance structures being in place), although it was acknowledged that some issues remain unresolved, such as the extent of public involvement in biobanks and how best to accommodate cultural variations in data sharing.

⁹ N Homer, S Szlinger, A Redman *et al.* (2008) Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. *PLoS Genetics* 4(8): e1000167.

Evidence of clinical validity and clinical utility

Currently effective translation of research findings is hampered or curtailed by the systematic failure to collect an evidence base around clinical validity and clinical utility of genetic information. This evidence gap is relevant to a host of genetic applications, from assessing the significance of genetic variants in GWAS, to the use of genetic tests in population screening programmes or the sale of predictive genetic tests on a direct-to-consumer basis. The recent initiatives by the National Institutes of Health (USA) to set up a voluntary genetic testing registry, and the Royal College of Pathologists (UK) to set up a pathology formulary for diagnostic tests, provide the starting point for collecting useful data on clinical validity and clinical utility. However, some experts have pointed out that these schemes will be ineffective because they are not mandatory. They also do not resolve wider questions about optimal form of incentives for research.

Incentivising research

The meeting failed to reach a consensus as to the best strategy for incentivising research and development by investigators, institutions, governments and others. It recognised that in some contexts the patent system provided a stable environment for generating novel research findings, whilst optimising transparency. Others felt that the patent system tended to distort research priorities and stultify researchers and funders. There was however some agreement with the view that the patent system as it now functioned was not fit for purpose for the diagnostics industry, and were this to be the main instrument for incentivising the development of diagnostics there would have to be significant changes.

4.3 The proper scope of public health genomics research

Public health genomics research is likely to become increasingly international and collaborative over time for several reasons. First, as GWAS reveal rarer or less penetrant genetic variants, larger cohorts will be needed to achieve statistical significance, and to assess meaningful gene-gene and gene-environment interactions. Second, integration of numerous datasets from different countries representing multiple gene variants and environmental factors may add to the richness of the findings. Up to now, the majority of genomic research has been done in populations of European ancestry. In part, this bias has been dictated by the manufacturers of the arrays that are in routine use, who have selected single nucleotide polymorphisms (SNP's) that are common in these populations. Increasingly however, there is a realisation that a shared evolutionary history and the breadth of global human genetic and environmental variation impose an obligation to ensure that basic genomics research and translational research are carried out worldwide. This is necessary to ensure that the research outputs are relevant and clinically valid for us all.

4.4 Ethical issues in research

Many of the ethical issues raised by public health genomics research are familiar from other settings. In most economically developed countries, regulatory safeguards are in place to ensure that the risks of proceeding with research are reasonable in relation to the likely benefits. Research participants should be appraised of these issues and additional institutional controls may be in place (such as Institutional Review Boards and Research Ethics committees) to ensure that the balance of risks and benefits is appropriate.

However, a number of specific issues arise: the longitudinal collection of gene/environment data highlights the need for realistic assessment of procedures for obtaining informed consent, expectations for protection of participants from re-identification, and clarity about the extent to which research findings are fed back to study participants. Policies may need to be tailored to the type of research methodology used: for example the justifications for feedback may be different in pharmacogenetic research (where individual drug response data may be used to tailor ongoing drug treatment) to the feedback of incidental findings following the prospective use of whole genome sequencing in a research setting. Appropriate measures for assuring accountability need to be considered. Finally, we note that unlike traditional clinical trials involving individual participants, public health genomic research implicates communities and populations.

Specific ethical concerns relating to informed consent, the protection of privacy, and accountability arise from large-scale studies seeking to understand disease aetiology, particularly those studies of common complex diseases that incorporate large amounts of genomic, clinical and environmental data.

5 The translation agenda

A major challenge is to bridge the gap that currently exists between genome-based discovery and the realisation of clinical and public health benefit. A measure of the optimal translation agenda might be the ease with which novel genome-based discoveries may be implemented by health services and made available to the public. This is influenced by a host of different factors, such as the availability of research funding, research capacity and expertise, the prevailing regulatory climate, and competing resources. A range of possible situations currently exist, of which those at the opposite ends of the spectrum represent dysfunctional situations differing in the potential harms they pose (Table 1 adapted from Muin Khoury).¹⁰ Neither is desirable, and both approaches reduce the potential for effective and cost efficient use of novel research findings for patient benefit.

Table 1: Comparison of two alternative (dysfunctional) models of translation

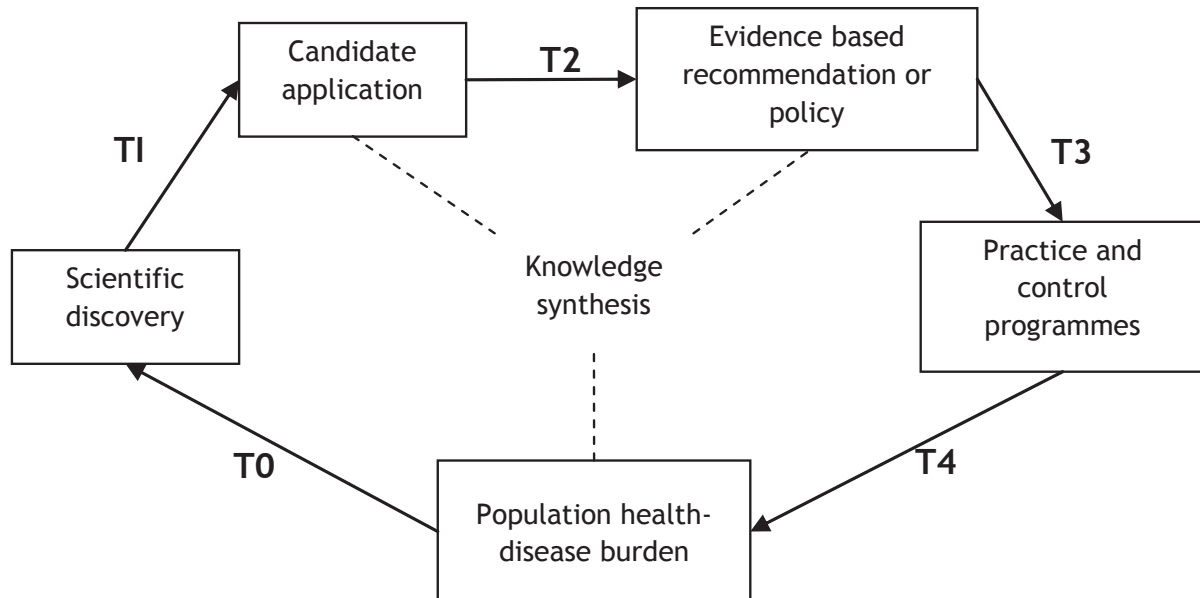
'Premature Translation'	'Lost in translation'
Rapid implementation of novel tests	Promising discoveries are rarely translated into practice
Lack of evidence about clinical validity and/or clinical utility	Requirements for evidence of clinical validity and clinical utility are so onerous that they are rarely satisfied
No information about clinical utility	Valid useful tests where clinical utility is assured
Potential for increased health benefit	Diminished health benefit overall because few tests reach the market
Potentially harmful	Diminished overall potential for harm
Potentially useless tests reach the market	No useless tests reach the market
Use likely to be mediated by experts and public curiosity	Use likely to be mediated by medical professionals
Researchers may be encouraged by their work being made accessible	Researchers may be disenchanted because discoveries rarely reach the public
Many tests are implemented	Few tests are implemented
Lack of professional and public engagement	Lack of professional and public engagement
Commercial engagement if markets grow	Lack of commercial engagement
Increased commercial investment	Dwindling public and private investment
Innovation stimulated	Innovation stifled

¹⁰ MJ Khoury, M Gwinn, JPA Ioannidis. The Emergence of Translational Epidemiology: From Scientific Discovery to Population Health Impact. *American Journal of Epidemiology* (2010) 172(5):517-524.

The translation of genomic research into interventions has been categorised into four phases (T1 to T4). This is set out diagrammatically in Figure 1 below. In higher income countries a well developed infrastructure exists to support the translation of novel drug targets from animal to human subjects. This phase of translation (T1) is managed through the clinical trial system, and is relatively generously funded because drug development has a well-defined route, and for the minority of blockbuster drugs that make it to market, the patent system guarantees a financial reward.

With novel genomic discoveries however, the process is less well defined. Although the T1 phase is relatively well funded, subsequent phases of translation (T2-T4) lack the necessary infrastructure and funding for effective implementation. This is particularly the case for translational research that does not result in a marketable product, such as new models of service delivery that emphasise cost-savings. There is also a lack of political will for translation at these levels. Finally, the application of new knowledge to reduce the population health-disease burden can also result in new understanding that can feed back into basic scientific understanding (T0). There was very strong support for developing outcomes driven research that focuses upon the evaluation of public health programmes (T3) and that builds capacity, growth and development through population-based research.

Figure 1: Knowledge Synthesis - the Engine of Translational Research



There should be greater investment in the later stages of translation of public health genomics. Investing in infrastructures for translational research will have multiple benefits and is likely to:

- *build capacity*
- *shape the organisation of health systems and services*
- *result in more effective public health programmes which incorporate more accurate measures of environmental and social determinants of health (as well as genetic factors)*
- *make a powerful contribution to the effective evaluation of new and existing public health interventions.*

6 Delivering genomics within health care systems and services

Increased affluence has resulted in global increases in the incidence of lifestyle and complex diseases. Despite this convergence, there are also increasingly divergent health outcomes both within and between developed and LMIC. All countries, even those with rapidly growing populations, seem likely to have rapidly aging populations that are increasingly subject to complex diseases such as cancer, heart disease and diabetes. In part, this is the product of increasing urbanisation, as the majority of the world's population now lives within an urban rather than a rural environment.¹¹ Pressures from climate change and diminishing resources such as water and food will exacerbate this health burden and are likely to result in even greater inequality. In developed countries it seems likely that one of the biggest burdens of disease in the future may arise from poor mental health, a disease category that is currently even more intractable to cheap and effective interventions at the population level than common complex diseases.¹²

6.1 Integrating multiple datasets

Set against this bleak backdrop, some may question the role for public health genomics. The scientific evidence is clear in showing that most traits and diseases arise through a combination of genetic, environmental and social factors. We have already noted the role of effective translational research in helping to generate robust outcome data by combining the findings from different types of research activity and datasets. The future may allow populations to be segmented according to genetic predisposition to disease, and by so doing enable standard public health interventions, be they screening programmes, health promotional advice or therapeutic interventions, to be targeted more efficiently and effectively. Genomics and related molecular tools may also stimulate drug discovery and novel approaches to prevention, through a better understanding of disease biology.

The effective translation of genomic advances into better health care will inevitably require access to and integration of multiple databases, which is likely to raise logistical and ethical considerations. Once new technologies have been implemented into health care services, confidentiality, privacy and autonomy interests will need to be respected, and where appropriate protected. Thus the introduction of these technologies could highlight tensions between an approach that prioritises individual autonomy (as a means of managing confidentiality and privacy), and one which accords wider obligations to the family unit, the community or even the nation as a whole (the public interest issue), a view which is predominant in some LMIC. These considerations based on existing ethical paradigms might limit how genomic information about one person can be used for the benefit of another (including the sharing of family history information). Whether or not it will be possible or desirable for the primacy of individual autonomy to be replaced by a more balanced approach which takes into account the public interest (when considering the conduct of research) and the needs of other family members (in the context of inherited disorders) remains to be seen.

11 UNFPA (2008) State of World Population 2007. Unleashing the Potential of Urban Growth.

12 Young Australians: their health and wellbeing 2007 AIHW <http://www.aihw.gov.au/publications/index.cfm/title/10451>; and AD Lopez, CCJL Murray (1998) The global burden of disease, 1990-2020. *Nature Medicine* 6(11):1241-1243.

Currently, the most effective public health interventions may be to capitalise on our existing knowledge of genetics and inherited disorders and utilise proven models (such as newborn screening, cancer and disease registries and newborn disease registries) to make better use of limited health care resources and systems.

6.2 The effectiveness of different types of public health interventions

As public health evolves from a 20th century model into one that takes account of 21st century advances in scientific understanding, we will need to update and strengthen the methodological framework for public health interventions as well as develop a more rigorous approach to ranking competing health care interventions. Public health comprises a range of interventions which act variously upon individuals and upon populations. There was considerable discussion of a hierarchical model proposed by Thomas Frieden which ranks public health interventions according to their differential impact upon populations and individuals,¹³ suggesting that those interventions which act at population or societal level have the greatest potential impact. Widespread adoption of this methodological framework by policy makers would have implications for the translation of genomic interventions since most of these act at the level of the subpopulation, the family or the individual rather than at the entire population.

The meeting concluded that an integrated approach which took into account interventions at all these levels was necessary to optimise health gains for the population. It was agreed that environmental and social factors continue to be of the greatest importance in the determination of health and disease in populations. Nevertheless public health practice in the 21st century can no longer ignore the knowledge derived from genomics, cell and molecular biology; and biological and social models of disease must be regarded as complementary paradigms by public health practitioners in their efforts to improve population health. Ethical considerations demanded that where effective interventions existed, patients should not be deprived of these just by virtue of the fact that they had a rare form of disease. However, it was necessary to be mindful of the costs and benefits of competing interventions in order to prioritise services; comparative effectiveness research has recently emerged as a helpful tool.

13 TF Frieden (2010) A Framework for Public Health Action: The Health Impact Pyramid, *Am J Public Health* 100(4):590-595.

6.3 Creating effective health systems and services

Within health care systems, genomic tools are already used in the prevention, diagnosis and treatment of disease. To ensure effective and efficient development will however require modification to the organisation of health care services. In some clinical areas this may build on the considerable expertise in specialist genetics services, which will be well-placed to show substantial leadership. The role of new genomic technologies in clinical specialties such as cancer, haematology and infectious diseases must be explored including, in all cases, consideration of how the necessary massive expansion of bioinformatics support can be developed and sustained. Any strategy should explicitly address how clinical and laboratory personnel can be trained and employed, so to retain expertise and competence whilst enabling increases in capacity. This may involve reconfiguration of laboratories, clinical services and their supporting systems.

The potential for genomics to improve public health systems was thought to be relatively modest in the short term. However the possibility that in the medium and longer term, genomics might play a more substantive role in public health systems suggests that a strategic review needs to be taken now to assess what infrastructure might be needed to prepare for future developments. This could run in parallel with the work on health systems, with experience being shared in the two areas. For both, effective change management will also require engagement with health care professionals and the public.

Developments in genomic medicine require a strategic response. This response (encompassing clinical and laboratory services) should anticipate an increase in service requirement and must incorporate elements of workforce development, service development and reconfiguration. Bioinformatics elements currently constitute a substantial gap.

6.4 Motivating behaviour change

The application of genomics within public health services is likely to involve some interventions or treatments being offered to those identified at higher risk of disease as a result of a screening programme. If the intended benefit of screening includes motivating individuals to change their behaviour, then evidence from health psychology suggests that genetic information is of limited usefulness. However if the diagnostic information provided to individuals includes DNA results, then limited evidence suggests that individuals may be more amenable to biological solutions (medication) and may be more compliant with treatment than with non-biological interventions (such as behavioural or psychological treatment). These findings raise the possibility of a limited role for genetic risk prediction in motivating behaviour (for example, when compliance with drug therapy is the goal), but also raise a concern that genetic risk information could motivate the use of unproven therapies and therefore lead to iatrogenic harm. There is also an emerging literature on reflective and impulsive models of behaviour, and evidence that public health initiatives may be most effective when they capitalise on impulsive cognition by imposing environmental changes.

Evidence from health psychology research suggests that simply providing individuals with information about their genetic risks of disease may be of limited usefulness. More traditional public health approaches which involve changing the environment to reduce exposure to risks or to force individuals to change their behaviour may be more effective.

7 Commercialisation and the role of industry

7.1 The impact of commercialisation

Multiple sources of funding

Scientific research is funded through multiple sources, often through a combination of support from commercial, public and voluntary (charitable or philanthropic) organisations. The process of translating basic science into better health care for the population may be prohibitively expensive for a single provider to accomplish alone. Even where scientific advances have been initially funded in the public sector, private investment is often needed to bring the findings to market. Yet the involvement of private investors can come at a cost. It may influence the type of research, distort the process by restricting the direction of research, prevent collaboration, and restrict the sharing of the raw data generated by the research. It also might prevent the results of the research being disseminated effectively or cause publication bias. Most importantly, it may serve to reduce public trust in the research process. Some evidence suggests that potential participants may be less willing to engage in research if this is privately funded (as they perceive themselves to be more exposed to potential exploitation).

In much of the commercial world, the patent system provides a relatively stable mechanism for investors to realise some returns whilst ensuring that the technical details of scientific breakthroughs remain in the public domain. Thus it arguably provides a structured equilibrium where risks are shared between the manufacturer and the paying user of the product. This serves the pharmaceutical industry well, where new chemical entities are developed, but has inherent challenges for the diagnostics industry, where multiple new technologies can be designed to measure or characterise the same biomarker, and where the inventive step is often not the characterisation of the biomarker but either the showing of a strong relationship between the biomarker and the disease, or the combination of multiple biomarkers in an algorithm with industrial applicability. Attempts to patent the biomarker itself instead of the technology have often failed, and the patenting of genes and genetic tests is currently being challenged by the judiciary in the USA.¹⁴

Outside of the commercial sector, some elements of international scientific collaboration and public health depend upon the equitable distribution of public goods, such as information. This is not governed by competitive markets, unless public funds are used specifically to create these resources.

Incentives for the development of diagnostics

Given this context, it seems clear that market forces alone are insufficient to provide the necessary incentives for the proper validation of diagnostic tests, with existing regulatory and financial conditions providing limited incentives for investment. In the field of genetic and genomic testing, there are likely to be low margins, high volume and competition between technology platforms. This is in stark contrast to the traditional model for therapeutics in which high margins and high risks demand blockbuster financing with a reasonable expectation of financial gains through pricing and licensing. Public funding may therefore be needed for the development of diagnostic tests, particularly those ultimately to be used for public health population screening programmes.

¹⁴ *Association for Molecular Pathology et al. v. United States Patent and Trademark Office et al.* (2010)

Sustained investment from public, private and philanthropic funders is likely to be necessary to realise the potential of public health genomics.

Benefits of commercialisation

Even if many aspects of genomic science cannot (yet) deliver tangible health benefits, it was agreed that enhanced investment in biotechnology could yield real economic and commercial benefits through technological development, including job creation and increased GDP. The importance of investment in these developments could therefore be justified on economic considerations alone, even if in the short term health benefits were minimal. What was necessary, however, was to be transparent about the nature of the benefits of genome-based research, with care taken to be explicit about whether benefits in the short, medium and long term were primarily health, scientific or economic in nature.

Commercialisation can generate independent benefits, such as increased employment or capacity, irrespective of prospective health gains. This could justify continued investment in genomics where health benefits are likely to arise in the medium or long term.

7.2 Direct-to-consumer testing

The last few years has seen an increase in the number and type of genetic tests available direct-to-consumer via the internet, from multiple providers. In order to obtain personalised information, consumers typically purchase a testing kit from a provider, consisting of a swab for collecting a buccal cell sample and preservative. Upon receipt, the provider analyses the sample and provides an interpretation of the findings to the consumer via email. Some services also involve retention of the sample or data as part of a research cohort, or the periodic updating of risk assessments to take account of new research findings.

These services pose a novel set of challenges. The scope of the services offered are not confined to tests for which there is established clinical validity or utility or which are clinically actionable. Some providers offer a mix of ancestry and predictive health testing within the same package; others purposively offer a relationship testing service. Where services claim to offer predictive genetic testing for serious health problems, the evidence base on which they rely differs substantially and in most instances, appears to be insufficient to make clinically meaningful risk predictions. This means that consumers who access tests from more than one provider may be given conflicting results and advice, which may itself change over time as new research is added. However, due to the global nature of this market, the judicial reach of any country may be limited to either consumers or companies based within that country. Thus regulators may not be able to prevent these companies from offering services to consumers outside the jurisdiction.

There was considerable debate about the likely impact of direct-to-consumer genetic tests on public health services and systems. While some people believed that this fledgling market would have a limited effect on state health services, others took the view that some of the consumer genomics offerings could grow into a major industry in the future and that the resultant burden on health systems would be substantial. There was no consensus on the level of regulation that should be required for such tests, particularly where there is scant evidence of clinical validity or utility. However, it was agreed that, as a minimum, the provider should ensure transparency of information, so that potential consumers understand the limitations of such tests and are not misled by exaggerated claims.

Direct-to-consumer genetic tests lie at the confluence of genomics, market economies and public health. In order to protect the public there is a need for a high level of transparency to ensure that consumers can make an informed choice about the risks and benefits of proceeding with testing. Evidence as to the clinical utility of testing should be made available wherever possible to prospective consumers; where evidence is incomplete or absent this should also be made clear. Rigorous ethical standards for obtaining consent and safeguarding consent and confidentiality should be maintained.

8 Global public health

8.1 To what extent is public health genomics relevant to LMIC?

The relevance of public health genomics to the experience of LMIC proved to be one of the most contentious areas of discussion. The stark reality for many living in these countries is chronic ill health and disease that is overwhelmingly determined by economic and social conditions.

Pan American Health Organisation (PAHO) 2009 (data relating to the Americas)

- 230 million (46%) without health insurance
- 125 million (25%) without permanent access to basic health services (for a combination of economic and geographical reasons)
- 152 million live without access to drinking water and basic sanitation
- 17% of births occur without qualified professional care
- 680,000 children do not complete basic immunisations

A major challenge for public health genomics is to generate an evidence base to prove that a genomics approach is safe, effective and cost-effective. Although this challenge is not unique to LMIC, in these countries, the economic, social and political setting might result in low resources for households, poor health care systems and limited access to health care. In combination, these factors seem likely to demand low-cost solutions such as more effective use of family history information as well as innovative technological solutions. Indeed public health genomics technologies are already being used successfully for targeting infectious diseases, prevalent in LMIC.¹⁵ So the challenge for developing genomics-based technologies that are relevant to LMIC is to generate data that identifies when (if ever) genomic approaches (such as screening for inherited diseases, stratified risk prediction and personalised medicine) generate better health outcomes than modifying environmental or social determinants. This may require novel research processes, since in countries which prioritise the role of families, kinships and communities, the importance of individual choice or informed consent may be diminished.¹⁶ For some, the introduction of personalised medicine may appear somewhat esoteric in a world largely dominated by fears about harsh living conditions and uncertainties about the future.

In practice this might mean, in the short term at least, that the application of public health genomics is limited to a few key areas, such as the diagnosis, prevention and treatment of infectious diseases and the prenatal prevention of single gene disorders.

15 Examples include the MalariaGen Genomic Epidemiology project. <http://www.malariagen.net/network>

16 Nuffield Council on Bioethics (2002) The ethics of research related to healthcare in developing countries.

In the short term, public health programmes incorporating genomics in LMIC should, as in developed countries, focus upon applications where evidence of clinical utility is sufficient to establish substantial health outcome benefit. Examples include antenatal and newborn screening, as well as cascade testing for preventable inherited diseases.

8.2 Building robust health systems and services in LMIC

Despite reservations about the applicability of public health genomics in these settings, the concern was expressed that if basic and well validated genetic testing and screening programmes were not made accessible as part of universal publically funded health care services, a potential vacuum could be monopolised by private sector development resulting in worsening health inequalities.¹⁷ On the other hand, premature adoption of such technologies in the absence of cost-effective therapeutic interventions could result in ‘social misallocation of health resources’. However, there could be an advantage in adopting these technologies later than in developed countries. Pragmatic use of the most promising technologies by LMIC and applying them creatively within local settings could avoid repetition of the costly mistakes made by some developed countries, without setting up vast, expensive programmes.

That basic genetic services have a potential role, particularly in the context of maternal and child health services and the reduction of birth defects in LMIC is reasonably clear; but how these should be implemented, the priority that they should be afforded within health systems, and the extent to which they might take preference over funding for research were discussed at length. These matters are heavily dependent upon the environmental, social and economic context within individual countries.

8.3 Building research capacity in LMIC

African populations represent the ‘root and branch of genetic variability’ because of human evolutionary history. However genomic research has tended to concentrate upon populations of European ancestry, with the result that existing research strategies (such as current gene chips) are less accurate when applied to populations from Africa, requiring a bigger research cohort to achieve the same degree of accuracy of results. Differences in genetic history and environmental context, for example different diets or a sustained limitation on daily calorie intake, together with restricted access to health care or an unstable political context, compound difficulties in ensuring that research findings from the developed world are relevant to LMIC and vice versa.

One strategy is to purposively include LMIC when planning multicentre research, such that there is integration of research planning, effort, training and funding at all levels. This requires a more rigorous and sustained approach than has been traditional in the past, in which local capacity building is central. This approach will provide for future research capacity, foster a sense of ownership of the research and in the longer term help LMIC to conduct and apply such research independently.

¹⁷ World Health Organisation (2002) Genomics and World Health: Report of the Advisory Committee on World Health.

Increasingly, population-based genomic research should be based upon robust multidisciplinary partnerships between high and LMIC: these partnerships should be power-sharing, have local control and enable implementation of known benefits in LMIC as well as the participation of LMIC in outcomes orientated research. In order to build capacity, co-ordinated funding through agencies will be key.

9 Conclusion

The potential of genomics to improve human health has been overstated in the past, and this hype has contributed to a lack of clarity and transparency about what public health genomics is capable of delivering in the future. It was agreed that the most effective agenda for public health in an age of genomic and personalised medicine involves multiple strategies.

First, there is a need for a sustained drive to collect relevant evidence about the scientific and clinical validity and utility of genomics approaches, so that effective comparisons can be made with other public health interventions, and to make this available to citizen, patient and physician alike. The requirement for a sound evidence base also applies to other clinical and public health interventions, for which evidence may also be weak or non-existent.

The major challenge for public health genomics is to generate an evidence base to demonstrate when use of genomic information in public health can improve health outcomes in a safe, effective and cost-effective manner.

Second, there is a need to be pragmatic, and focus upon areas that can make a real difference to population health. In the short term this is likely to involve targeting single gene disorders, subsets of common complex disorders, or local circumstances in which the combination of genetic and environmental factors results in a large avoidable health burden, for which the evidence of scientific validity and clinical utility already exists. It was recognised that even where evidence of utility is lacking, that there may still be independent indirect benefits of investing in these technologies (such as increased knowledge of disease pathology and building technical expertise).

The implementation of evidence-based genomic applications could:

- 1. maximise health benefits and reduce disparities;***
- 2. reduce harms and unnecessary health care expenditures from premature and/or inappropriate use of gene/disease information;***
- 3. provide a means of evaluating public health interventions, and;***
- 4. deliberately foster capacity building, growth and development by convening and sponsoring population-based research (both through biobanking and the creation of large datasets and cohorts).***

Third, there is an obligation to ensure that these benefits reach the greatest number of people worldwide by establishing robust multidisciplinary partnerships between developed and LMIC.¹⁸ This approach would ensure coverage of the worlds' populations from a scientific perspective, satisfy ethical principles of distributive justice, and build capacity for future research and health service development. If the global impact of genomics is to be realised, this will require strong commitment and leadership at both national and international levels by national governments, multi-national organisations and non-governmental organisations. The ongoing revision of the Millennium Development Goals may be an opportunity for such priority setting. There will also need to be sustained investment in technologies and expertise by research and health care funders, who should be encouraged to work collaboratively and creatively towards more effective and evidence-based public health care systems.

Finally there is a need to understand and manage the tension between the long term promise that must eventually come from our increased scientific knowledge of the genome and molecular mechanisms at a cellular level, and the hype of associated premature interventions presented to health care funders and providers as well as individual citizens. Public health practice must engage with this new scientific agenda and give it considerable priority over the coming years.

18 Examples include the Human Heredity and Health in Africa (H3Africa) project: <http://www.nih.gov/news/health/jun2010/nhgri-22.htm>

10 Recommendations for future global public health practice

The following overarching recommendations were agreed and endorsed by the Workshop participants:

1. *Efforts to integrate genomics into public health research and practice should continue*

The integration of genomic sciences with population sciences, the social sciences and the humanities should be supported and enhanced to assess the contribution of genomics to population health, and to evaluate how this information can best be used to improve the health of populations;

2. *An appropriate research infrastructure for generating an evidence-base for genomic medicine needs to be established and maintained*

An infrastructure for population-based research that can systematically collect and evaluate relevant data to assess the impact of genetic variants (together with behaviour, diet and environment) on population health is urgently required, in the form of both cohort studies and population biobanks in developed and LMIC countries, as well as intervention studies that show health impact and clinical utility;

3. *Model public health genomics programmes and clinical services need to be developed, implemented, and evaluated*

These programmes and services should take critical account of the risks and benefits involved in implementing genomic applications, particularly in the short term, and should encompass the following objectives:

- To *formulate* an independent or ‘honest broker’ evaluation process which can discriminate between those genomic applications which can improve health, from those which are likely to result in potential harm and unnecessary healthcare expenditure through premature use;
- To *implement* those applications which have potential to improve health through public health tools and local and international collaborations, including clinical services, policy interventions and education, thus emphasising the importance of later stages of the translation process;
- To *develop* and *apply* tools for evaluating and documenting the health impact of those applications;

4. *International collaboration should be promoted*

These goals will be most effectively fostered through international collaboration via international organisations such as the World Health Organisation, and international networks such as the Genome-based Research and Population Health International Network (GRaPH-Int) as well as engagement with national governments and other multinational and/or non-governmental organisations;

5. *Appropriate genetic services and genome-based research should be fostered within LMIC*

There is a role for appropriately targeted genetic services, as well as genome-based research in LMIC, and these should be supported whilst taking careful account of contextual issues including social, environmental, political and economic factors;

6. *Programmes, research, and strategies in public health genomics should be informed by accepted ethical principles and practices*

Developments in public health genomics require that attention is focused on managing multiple ethical issues: methods of obtaining informed consent, engaging the public, protecting human participants, assuring responsible stewardship of resources, managing confidential information, and the commercialisation of genetic tests. Where ethically informed practices do not already exist, they should be developed.

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Telethon Institute for Child Health Research

www.childhealthresearch.com.au

The Telethon Institute for Child Health Research was founded in Western Australia in 1990 with the mission to improve and promote the health and wellbeing of all children.

Under the leadership of founding Director Professor Fiona Stanley AC, the Institute has pioneered a multidisciplinary approach in child health research that brings together scientists with a wide range of expertise to examine the most costly, common or debilitating diseases and issues affecting young people today. The Institute now has more than 450 staff and students. Our key research themes include Aboriginal child health, asthma, allergies and respiratory disease; children's cancer and leukaemia; healthy development; infectious disease; mental health, social and emotional wellbeing; and the early years.

The Telethon Institute for Child Health Research has a proven track record of translating research findings into actions that make a real difference to the lives of children everywhere. Our achievements including identifying the important role of folate in reducing neural tube defects such as spina bifida and ground-breaking findings into the way the immune system develops. The Institute has established powerful data-bases of de-identified information that tracks births and later health outcomes. It also has disability databases, a twins register, a cerebral palsy register and is home to the international Rett Syndrome database.



Centre of Genomics and Policy

www.genomicsandpolicy.org

Located at McGill the Centre of Genomics and Policy (CGP) is at the crossroads of the legal, medical and public policy fields. Within these fields, the CGP promotes prospective structuring and guidance for the orientation and application of research in genomic health sciences. The CGP's research covers five areas of genomics and policy: procreation and reproductive genetics, pediatric health, privacy, public health, and personalized medicine. These domains are approached using three guiding approaches: internationalization, policy development and knowledge transfer. First, CGP promotes internationalization by undertaking comparative analyses of policies and guidelines around the world. Secondly, CGP actively participates in the creation of international consortia with a view to promoting multidisciplinary policymaking. Finally, via the HumGen law and policy database (www.humgen.org), the CGP promotes knowledge transfer of its work.



PHG Foundation

www.phgfoundation.org

The PHG Foundation is an independent, non-profit organisation based in Cambridge, UK with the mission *making science work for health*. We identify the best opportunities for 21st century genomic and biomedical science to improve global health, and to promote the effective and equitable translation of scientific innovation into medical and public health policy and practice.

Originally founded in 1997 as the Public Health Genetics Unit, we were the first centre for public health genomics in the UK. A multi-disciplinary think-tank and policy development unit, we provide knowledge, evidence and ideas to inform debate on the potential and pitfalls of key biomedical developments, to facilitate the translation of those developments into better health care in the UK and other health systems (including in low and middle income countries). We also provide expert research, analysis, health services planning and consultancy services for governments, health systems, and other non-profit organisations.



INDIANA UNIVERSITY
CENTER FOR BIOETHICS

Indiana University Center for Bioethics

www.bioethics.iu.edu

The Indiana University Center for Bioethics (IUCB) was established in 2001 in the Indiana University School of Medicine with a mission to serve as a local, state, and national resource in bioethics research, education and policy. Among the IUCB's principal areas of emphasis are the ethical and policy issues in genomics and predictive health research. The IUCB has undertaken a number of research projects in this area, especially on biobanking, informed consent, secondary use of genetic information, risk perception, privacy, and genetic testing.

Many of IUCB's programs have been funded by the National Institutes of Health, the Lilly Endowment, the Indiana Humanities Council and the American Cancer Society. In addition to these, IUCB's Predictive Health Ethics Research (PredictER) program has been supported since 2007 by a generous grant from the Richard M. Fairbanks Foundation, Indianapolis. This has enabled the IUCB to build bioethics research capacity and collaborations with international researchers including those in the Ickworth Group.



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