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The Impact of Genomics on Public Health Practice: The Case for Change

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Genetics · Genomics · Health policy · Personalised medicine · Public health · Translation

Abstract
Public health practice will not be able in the 21st century to ignore the impact of genomics, cell and molecular biology. It will need to take into consideration issues that include, among others: the complementary nature of social and biological models of disease, genetic exceptionalism, the readiness of public and patient to respond to genomic information, the relationship between individuals and populations, and concepts of population stratification. Health systems will need to adapt their practice and organisation to include new sequencing technologies, bioinformatic expertise and proper evaluation of genetic and molecular tests. Links with the commercial sector will increase in importance. The impact on developing countries cannot be ignored and will require special attention.

The views expressed in this paper are those of the authors and do not reflect the opinions or positions of the Centers for Disease Control and Prevention.

Introduction

Public health genomics has almost reached the age of 15. It started in 1997, the year the Office of Public Health Genomics was established at the Centers for Disease Control and Prevention in the USA; and entirely independently, the Public Health Genetics Unit was established in Cambridge, UK. The first conference on Genomics and Public Health was held in Atlanta in 1998. It was followed by 3 other such meetings in the USA over the following 12 years. In 2005, the Rockefeller Foundation funded a 5-day working meeting in Bellagio, Italy, attended by 18 experts from the UK, France, Germany, the USA, and Canada, where the international status of the field was confirmed [1, 2]. The meeting resulted in 3 outcomes. It led first, to an agreed definition of public health genomics as 'the responsible and effective translation of genome-based knowledge and technologies for the benefit of population health'; second, to the development of a conceptual framework for the practice of public health genomics; and third, to the establishment of an international network in public health genomics [2].

During these first 15 years, much effort has been spent in trying to understand how the knowledge gained from the human genome project and scientific advances in genomic medicine can contribute to population health. The public health genomics movement worked with geneticists and honed its own knowledge of genetic science and

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epidemiology. The human genome was its concern; public health was the context in which it approached its learning about the genome. These activities have proved extremely fruitful and have resulted in a number of initiatives that have been documented elsewhere [3–5]. While the field of genomics has not led to major impact on health practice during that time, foundational initiatives have developed in many countries that allow for the responsible and effective translation of the accelerating discoveries in the next few years into policy and practice.

The field of public health genomics has now matured. Our concern in this paper is to address appropriate changes in public health practice, even during times of economic downturn, to take into account both the knowledge and technologies that have emerged from genomic science and the new emerging social context that embraces individual autonomy and health literacy in the information age. These trends have been at the heart of the growing discourse around *personalised medicine*, the idea that medicines and other health technologies including the prediction of individual risk may be 'customised to each person's specific genetic, physiological or psychological characteristics' [6]. But for the most part they have been ignored by public health professionals. The purpose of this paper is to discuss why change will be necessary for public health practice in the 21st century.

The Schism between Genomic Science and Public Health Practice

There are 6 issues that highlight the current divide between genomic sciences and public health practice.

Social and Biological Models: A False Dichotomy

Genomic science has given greater emphasis to the importance of molecular and cellular mechanisms in health and disease. Practitioners of public health have tended to embrace social models of disease as their guiding principle, and to play down and, at times, avoid the part played by biological factors as health determinants. A false antithesis between social and biological models can be detrimental to population health. New biological knowledge should be integrated with the social and environmental models to improve health both at the individual and population levels.

Genetic Exceptionalism

The public health community needs to reject *genetic exceptionalism*, the view that genetic information and tests are special and must be more strictly regulated than other types of medical information. All medical information is sensitive, and genomic information is no more or no less sensitive than any other, except in selected rare Mendelian disorders. It is not the fact that DNA, RNA or chromosomes were used in testing for these disorders. The ethical, legal and social consequences or genetic testing flow from having made the diagnosis and not from the technology used to do so.

Availability of Genomic Information to the Public

Advances in genomics will undoubtedly contribute even more to the already exponential growth of scientific information on health and disease. Genome-wide association studies, data from biobanks and the advent of whole genome sequencing will, in time, all require new means of data analysis and interpretation. These new sources of information will themselves feed into the evidence base for clinical and public health practice. Bioinformatics will emerge as a key population health scientific discipline [7]. The establishment of systems for the analysis, synthesis and dissemination of these data will become an essential element for the public health system. Making genomic information available in a credible and transparent manner to citizens in a form that they can understand, and to medical practitioners by way of an evidence base, will be central to empowering citizens and healthcare systems to use this information for improving health and preventing disease across the lifespan. This honest broker role for public health in genomics is discussed in greater detail elsewhere [8].

Patient Autonomy

Patient autonomy has highlighted a stark contrast between public health and clinical practice. For the clinician, patient autonomy is ingrained as a fundamental tenet of medical ethics that is universally accepted. By contrast, the practice of public health continues to be paternalistic. Health promoters offer advice to the citizen, which if not taken up results in disapproval and implications of irresponsibility. Advice and imparting information is regarded as insufficient of itself; behaviour change is demanded so that healthy outcomes can be the end result. Our concern is not that either autonomy or paternalism should prevail, but that there is incoherence between the practice of clinical and public health medicine. Public health must examine its own activities and decide how its practice might change to reflect the greater autonomy now accorded to both patient and citizen.

Table 1. The Nuffield Council intervention ladder

Eliminate choice
Restrict choice
Guide choice through disincentives
Guide choices through incentives
Guide choices through changing the default policy
Enable choice
Provide information

Individuals versus Populations: Ethical Implications

There is an implicit shift from conceptualising a population as being an entity in itself to that of being a set of individuals. Interventions instead of being directed at the population as a whole (for example, providing clean water and clean air, fiscal measures such as alcohol or tobacco tax or the prohibition of certain advertisements) are now at times directed specifically at individuals. To the extent that such population programmes act on individuals, they do so only indirectly. By contrast, health promotional advice is now often directed specifically at the individual citizen with the aim, not just of providing her with information, but of altering her behaviour.

This shift has profound ethical implications. The Nuffield Council for Bioethics in the UK [9] has stated clearly their view that 'the central issue in public health is the extent to which it is acceptable for the state to establish policies that will influence population health'.

There can be little controversy that the classical interventions aimed at the entire population, the *health protection* elements of public health practice, are entirely legitimate activities for states and governments. What is less certain is the extent to which the state may attempt directly to change the behaviours of its citizens in order to improve their health.

The Nuffield Council has set out an intervention ladder that we reproduce in table 1, setting out the range of actions that may be undertaken [10]. Of relevance to this debate is the literature on *nudging* [11], the view that such activities might 'increase the chances that people act in ways that, on reflection, they would have chosen themselves', and how it is to be distinguished from *shoving*, so increasing 'the chances that people act in ways preferred by the shover but not the shoved' [12]. The citizen's autonomy was the reason why the Nuffield Council was concerned to open up this debate; but from the perspective of public health genomics, the insight provided by genomics, showing that what may be the correct advice for one may not be so for another citizen, provides a further impetus.

One Size Does Not Fit All

Classic epidemiological thinking has, in a similar way, been based on an implicit assumption of population homogeneity. Comparisons are made between a group of individuals who are exposed to a risk factor under study to a group of individuals who are not exposed to the risk factor. Smokers are at increased risk of lung cancer; consumption of a high-fat diet leads to an increased risk of heart disease. The insights of genetic epidemiology now turn some of these questions on their head. The genetic basis of why certain exposed individuals do not develop lung cancer or heart disease is now increasingly relevant, both as scientific and as policy directed questions.

Populations are, of course, not homogenous. Risks of any particular disease are not distributed evenly among individuals. But the variation can no longer be treated as random as it had been in the era of classical epidemiology, and regarded as due only to stochastic factors. Geoffrey Rose showed clearly the differences between population and high risk prevention [13], but his categorization of populations into a high risk group and the remainder may now be further developed. The standard Gaussian curve showing the distribution of risk across a population may be segmented into different groups, each with a different risk profile. It may therefore be feasible, effective and appropriate to attempt to more precisely delineate the details of the intervention across different strata of the population. An example of this is provided in the context of mammographic screening and the prevention of mortality from breast cancer [14]. Epidemiologic thinking can now integrate routinely the evaluation of why risk factors (e.g. smoking and diet) and interventions (e.g. vaccines and medical screening) can affect subsets of the population differently based on genetic susceptibility and how the emerging information can be used to improve health and prevent disease.

Three underlying themes can be discerned from the above observations:

(1) the relationships between autonomy and paternalism and between individual and collectivist activities in public health and health care;

(2) the relationship between the state, the population, individual citizens and corporate entities (fig. 1);

(3) the extent to which it is desirable for public health programmes to seek to change directly the behaviour of individuals in order to improve their health.

All 3 will require greater scrutiny and study in the years ahead. A full analysis is outside the scope of this paper, but we believe that detailed examination of these questions with the involvement of political philosophers should be as a fundamental component of academic public health study over the coming years.

The other observation that we make is that in the 21st century public health may, in a very significant way, be regarded as one which is dominated by the individual citizen rather than by the entire population. This places the individual requirement for information as a means of improving population health at the heart of public health practice. To the extent that the 19th century might have had the sanitary engineer as its key public health worker, and the 20th century the social engineer in the guise of the health promoter, we suggest that in the 21st century the information engineer may be the dominant force in public health practice. The analysis and synthesis of scientific and medical data and its dissemination to the individual citizen may prove to be the key to empowering individuals and to improving their health.

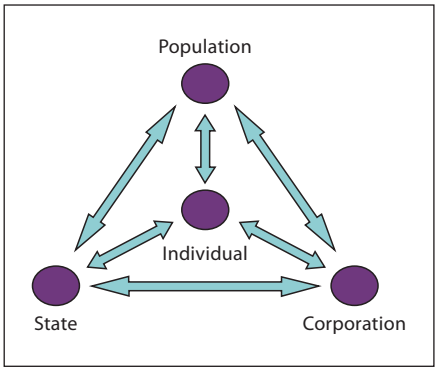

Fig. 1. Genomic information and the relationship between individuals, state, population and corporate entities.

Table 2. Implications for public health practice

1	The organisation of health systems and the delivery of health care
2	The establishment of new information systems and capacity building in bioinformatics
3	The use of evidence and the appropriate translation of scientific advances into clinical and public health practice
4	The role of commerce and industry in health care
5	The implications for low and middle income countries

Implications for Public Health Practice

The insights from genomic science and the growing status of individual autonomy have a number of practical implications that merit further consideration. These are set out in table 2 and discussed below.

Health Service Organisation

The organisation of health services differs greatly between countries, as do the means by which they are funded. A common theme, however, is that all countries are experiencing an increasing gap between what can be done from a technical perspective to improve population health and the amount of funding available. This discrepancy is in part due to innovation and scientific advances, but it is also the consequence of demographic changes and the rise in patient expectation. Whether we work in state funded systems (such as in the UK) or in more pluralistic service environments (such as in the USA), all public health professionals will have an interest in making our health systems more efficient, more effective and more equitable.

The much greater understanding that we will gain from genetic, molecular and cellular mechanisms of disease will be crucial to this endeavour. The training, education and the development of capacity in the health service workforce should be a priority. Genetic knowledge and an appreciation of risk and risk prediction and its implications for patients must be seen as key concepts in all medical specialties including the practice of family medicine and all the pathology specialties [15]. Nurses and the professions allied to medicine must also be included [16].

A second priority is to think strategically about how health systems need to be changed to meet the needs of genomic science in the context of the growing burden of chronic disease. The rethinking of how laboratory services should be provided within a hospital that take into account new technologies such as whole genome sequencing will be an important question for hospital managers and policy makers to consider [17, 18].

Bioinformatics and New Information Systems

The need to make sense of, and to synthesise and disseminate, medical information will be a key task for the 21st century. The discipline of bioinformatics is confined

by and large to the scientific community, but in the future, it will have to expand into the health sector and align itself with pathology services in order to help make sense of the data that will emerge from whole genome sequencing and allied techniques [7]. The establishment of credible and accessible databases and information systems that summarise the evidence for the effectiveness of diagnostic and predictive tests and therapeutic interventions will also be a key task for 21st century health care practice. Public health must play an energetic role in developing, implementing and disseminating such information systems.

Evidence-Based Translation

An important priority for public health practice today in genomics is to serve as an honest broker of evidence-based processes to inform providers, the public and policy makers whether the deployment of a particular technology for a particular intended use can have a net positive health impact on the population [8]. Such a process can mitigate against 'premature translation' of new technologies into practice while at the same ensuring that such technologies are not 'lost in translation' [8]. Processes for evidence-based evaluation exist around the world, but until recently, none have been specific to genomic medicine. In response to the emerging challenges of genomic tests, in 2005, the Centers for Disease Control and Prevention set up an independent multidisciplinary panel to address specifically the issue of genetic applications in clinical practice and disease prevention. The Evaluation of Genomic Applications for Practice and Prevention (EGAPP) working group systematically reviews and updates evidence of validity and utility of genomic applications and makes recommendations for appropriate use. The EGAPP working group has established methods for reviewing the evidence for different types of genomic tests, including those for screening, early detection, risk assessment and prognosis, and pharmacogenomics [19, 20].

Role of the Commercial Sector

The organisation of health care across different countries, as we have already pointed out, is extremely diverse, and some, unlike the UK, already have significant private and commercial involvement. The private sector has a large role not only in health care, but also in the development of novel interventions (both diagnostic and therapeutic). Genomics has already had huge influence on the pharmaceutical industry and has given significant impetus to pharmacogenetic considerations both in the prescribing of existing drugs and in the development of new drugs and their companion diagnostics [21].

But it is in the context of diagnostic and predictive tests that we think genomics will have the greatest novel impact. The use of genetic information in the diagnosis of inherited and heritable disorders has already provided significant clinical benefit, and there is growing evidence of its utility in determining prognosis and the assessment of treatment in cancer patients [22]. In time, genomic science will be used for a variety of complex disorders, such as cardiovascular disease [23]. The policy background and the evaluation and regulation of genomic applications are both, however, much less mature than we would wish [24]. A balance must be found that will adequately protect the public yet allow innovation to flourish.

The approach that we most favour is to provide in a transparent fashion a publically accessible evidence base that can be available to citizens, patients and physicians alike. In the UK, the National Genetic Testing Network with its set of *gene dossiers* has been in place since 2002 [25]; while recently the National Institutes of Health announced their intention to establish a Genetic Testing Registry [26]. In the field of cancer, the Centers for Disease Control and Prevention and the National Cancer Institute have developed a knowledge base that spans epidemiologic finding of gene-cancer associations and evaluation of genomic and genetic tests proposed for cancer care and prevention [27]. Although these initiatives are to be greatly welcomed, in no country is there yet in place the necessary systems and activities for the proper evaluation of diagnostics in the same way that we have for pharmaceuticals. This is a policy gap that needs to be filled.

The intellectual property regime and its impact on the development of diagnostics is another area that falls within the ambit of public health genomics [28]. Time does not permit discussion of this important matter. Suffice it to note that it is an area of active consideration by patent lawyers and that at the time of writing the validity of the BRCA patents owned by Myriad, for example, is under forensic consideration by the US courts. Another area that requires specific consideration is the issue of direct-to-consumer tests. Different views predominate [29, 30]. The trends that we have discussed earlier in this paper suggest that our citizens may in the future always require such interventions from either the profession or the state. Patients may demand that they be given the choice to make decisions about their own health, including what tests they may or may not take [31].

Developing Countries

Advances in genomic science will not just affect developed nations, but impact on low and medium income countries (LMICs). Equity demands that they should not be deprived of the benefits of genomic medicine. Two epidemiological facts should guide our actions. First, as infectious diseases become less burdensome and infant mortality falls, so the proportion of infant deaths due to heritable and inherited disorders and to birth defect will rise. Second, over a longer period, cardiovascular disease, diabetes and cancer will be a major cause of morbidity and mortality. The burden of these disorders will be much greater in LMICs than in developed countries. Genomic sciences including human and pathogen genomics must be used to help not just with the reduction in infectious diseases, but also in the management and prevention of birth defects and of common chronic disease. Robust health systems and services using leapfrogging technologies must be established as must research capacity with links between academic institutions in LMICs and established centres in the developed world. The priorities for action are set out in table 3. We must consider the global context and the implications of public health genomics for developing nations. The World Health Organization has initiated an ongoing global consultation process in 2011 to explore the role of genomics on health in LMICs [32].

Table 3. Priorities for action in public health genomics for developing countries

Infectious diseases
AIDS
Influenza
Tropical diseases
Birth defects
Single gene disorders
Haemoglobinopathies
Chromosomal disorders
Down syndrome
Congenital defects
Neural tube defects
Congenital heart disease
Cleft lip and palate
Mixed disorders
Congenital hypothyroidism
Foetal alcohol syndrome
Chronic diseases
Cardiovascular disease and stroke
Diabetes and obesity
Cancer
Respiratory disease

Conclusion: Moving Forward

These are issues that have been at the forefront of our thinking over the previous 2 years. Many of these concepts were presented to and debated at a workshop in the UK in May 2010. This meeting was seen by many of us as the sequel to the Bellagio meeting in 2005, and many who attended the Bellagio meeting were also at the Ickworth meeting [33]. The issues that we have raised above and at Ickworth are there for debate and discussion, but at the heart is our view that public health practice in the 21st century can no longer ignore the knowledge derived from genetic, cell and molecular biology. Major roles await for public health in educating consumers, empowering individual autonomy, eschewing genetic exceptionalism, and providing an honest broker role for evaluating evidence of genomic approaches to health services delivery. The realization that 'one size does not fit all' will increasingly push public health practitioners to regard biological and social models of disease as complementary paradigms that are equally essential to their efforts to improve the health of individuals and populations.

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