The past decade has been an important time for human genetics, and many have asserted that the wealth of knowledge offered by the human genome portends a time of rapid change in medicine. Genome-based medicine includes amongst its scope the use of genetic tests to diagnose, predict and determine susceptibility to a disease, as well as the evaluation of drug response through genetic tests (pharmacogenomics). More than four years after the completion of the Human Genome Project however, researchers continue to express both excitement and scepticism concerning the opportunities for a near-term derived application in either preventive or curative fields.

One of the most significant promises is that the unravelling of the genetic origins of common diseases will lead to individualised medicine, in which prevention and treatment strategies are personalised on the basis of the results of predictive genetic tests. According to some enthusiastic claims, the integration of genome-based knowledge into health care has the potential to change primary, secondary and tertiary prevention.1 The possibility to provide early detection for those individuals more susceptible to complex diseases because of their genetic make-up, might in fact, theoretically result in individualised primary (for example, chemoprevention or prophylactic surgery interventions) and secondary prevention (for example, assiduous monitoring) programmes. Actually some emerging tests support this promise: mutations in BRCA1 and BRCA2 genes can be used to identify women with a higher lifetime risk of breast and ovarian cancer, thus eligible to prophylactic surgery or assiduous breast magnetic resonance imaging screening; similarly, genotyping of HER-2 expressions identifies women with metastatic breast cancer eligible for trastuzumab drug treatment.

Nonetheless, due to the progressive release of results from large population-based studies and meta-analyses in genetic epidemiology, this great optimism has been counterbalanced by the realisation that most gene variants associated with common complex diseases have only modest effects (relative risk of 1.5) that increase only in the presence of well known environmental risk factors. The example of BRCA genes, in fact, represents a rare mutation accounting only for a small minority of breast cancer cases, while most genetic contributors to breast cancer risk have only a small effect. With many genes each contributing a small effect to disease aetiology, the question of their clinical


Assessment of genomics as a priority for public health

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Summary: Advances in genetic technology are increasing the availability of genetic tests for common complex diseases and the evaluation of drug responses. Ensuring the appropriate use of these tests is an important challenge for health policy makers at this time. This requires that systematic, evidence-based technology assessments and economic evaluations are used to guide their incorporation into clinical practice and prevention. The next decade will provide the opportunity to establish infrastructures and educate health providers to enable genome-based technologies to be translated into evidence-based guidelines and policies.

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utility in disease prevention management is no doubt pertinent, and an emphasis on genetic contributors to disease might also result in the neglect of environmental risk factors.

Additionally, among the sceptics concern has been raised over the ethical, legal and social implications of genomic medicine, such as the protection of privacy and autonomy, stigmatisation, discrimination and the psychological burden of genetic testing.5 As the possibilities for investigating many gene variants (genome profiling) in the same individual become a reality, these concerns will probably require a different approach from that applied to predictive genetic testing for monogenic diseases due to the low predictive value of multiple genetic testing.

From this premise, it is evident that the extent of the contribution of genomics to population health over the next fifty years remains uncertain. Undoubtedly, increased understanding will lead to measurable improvements in human health, but the time scale and extent of final impact remain unknown. At least in the preventive field, according to a more realistic forecast, genomics will help facilitate the integration of traditional community-based activities with individually targeted preventive strategies.5 So, the pressing challenge of genome-related technologies at the moment is to devise an efficient strategy to distinguish between innovative and clinically useful advances and false leads. Last but not least, the pace of this transformation will be limited not only by the pace of discovery and the proofs of effectiveness, but also by the need to educate practicing physicians and health-care professionals more generally in order to ensure the appropriate use of genome-based knowledge.

Public health genomics

The integration of genomics into public health research, practice and policy will be one of the most important challenges for health care systems in the future. Thus far health care systems and industries are not prepared for this conceptual change and all stakeholders are struggling to transfer emerging knowledge into clinical and technological applications. Public Health Genomics (PHG) is an emerging multidisciplinary scientific approach which aims to integrate genome-based knowledge in a responsible and effective way into public health. According to the statement of an expert group that discussed public health genomics concepts in Bellagio, Italy, in 2005, it can be defined as: ‘the responsible and effective translation of genome-based knowledge and technologies for the benefit of population health’. The working group in Bellagio soon after established an international forum to address public health genomics challenges, known as the Genome Based International Network (GRAPH Int). This includes participants from the National Office of Public Health Genomics in the US Centres for Disease Control (CDC), as well European partners.

In Europe, being aware of the future possible benefits of genomics for population health, in 2005 the European Commission made a call in the work plan 2005 of the public health programme for a networking exercise, aiming to identify ‘public health issues linked to current national practices in applying genetic testing and on that basis contribute to developing best practice in applying genetic testing’. The Institute of Public Health North Rhine-Westphalia (lögöd) in Bielefeld, Germany, as lead partner, together with the PHG Foundation in Cambridge, UK, and the German Centre for Public Health Genomics (DZPHG) at the University of Applied Sciences in Bielefeld, Germany, applied to develop a ‘Public Health Genomics European Network’ (PHGEN) and subsequently received funding.4 PHGEN was officially established in February 2006 and involves experts as collaborating partners from the fields of public health and epidemiology, human genetics and molecular biology, social sciences, ethics, medicine, economics, political sciences and law. It is envisaged that PHGEN, together with its spin-offs, will serve the European Commission as an ‘early detection unit’ for horizon scanning, fact finding, and monitoring of the integration of genome-based knowledge and technologies into public health.

The proper evaluation of genome technologies

The development of efficient research strategies to investigate health outcomes associated with genetic testing is a crucial factor in ensuring appropriate test use. According to the ‘evidence-based medicine’ concept, every medical intervention should be recommended if: high-quality evidence shows that it results in improving health outcomes; it delivers a net benefit; and is cost-effective. Subsequently, evidence-based guidelines should be developed for using genetic information to profile disease risk or guide a pharmacological treatment. At this point it is clear that the proper evaluation of genome-based technologies within the Health Technology Assessment (HTA) framework is one of the most important challenges for health service researchers and health policy makers to consider at this time.

Genetic tests for more than 1,300 diseases and conditions are currently available in clinical practice, while many more are being developed in research settings. Moreover, a number of companies in the US and UK offer genomic profiles consisting of chips for the concurrent detection of multiple gene variants associated with an increased risk to a particular condition, such as the Oxidative Stress Profile and Obesity Susceptibility Profile. The same can be said for pharmacogenomic tests, whose clinical implementation seems to be driven in some instances more by intensive pharmaceutical company campaigns rather than by evidence on clinical utility and cost-effectiveness.

Clearly, there is a strong need to distinguish useful genetic tests from those that are useless or even potentially dangerous. One approach is the ACCE framework developed by Haddow and Palomaki in 2004,5 and subsequently updated by the PHG Foundation and Eurogentest. That model takes its name from the four components of a genetic test evaluated: analytic validity (A), clinical validity (C), clinical utility (U) and ethical, legal and social issues (E). Unfortunately, this approach is infeasible in some instances because of the lack of data on which such evaluations, especially those concerning clinical utility, depend. In fact, as described in the methodology of the US Preventive Task Force,6 definitive evidence of effectiveness requires randomised clinical trials that evaluate all relevant outcomes of testing, as well as the effects of any associated intervention. While these types of study design are often unfeasible or unethical for many genetic conditions, nonetheless some HTA reports on genetic tests have now been released from both AETMIS (Agence d’Évaluation des Technologies et des Modes d’Intervention et Santé) in Quebec, Canada, and EGAPP (Evaluation of Genomic Applications in Practice and Prevention) inside the CDC. Additionally, genomic technologies will influence not only health outcomes but also the delivery and costs of health care.
In this era of increasing concern about health care costs, it will be impossible to consider the implications of genomic medicines without also considering their economic implications. The use of genetic information to guide interventions should be justified only if data demonstrate improved outcomes, reduced costs, or preferably both. Thus the need for a strong evidence base of efficacy, effectiveness and cost-effectiveness will be an essential element if resources are not to be wasted, particularly where health services are publicly funded. Although some cost-effectiveness evaluations have been published in the last few years on genetic and pharmacogenetic tests, there remains an urgent need from health service researchers for a rigorous and systematic evaluation of genome technologies. This requires new collaborations between public health providers, geneticists, economists and policy-makers.

The policy response and education of health care providers

At this point it should be clear that it is difficult to predict to what extent these advances will lead to effective and affordable clinical and public health interventions. Policy should therefore ensure that expertise is harnessed in all pertinent fields, first beginning with public health professionals, to prepare the ground and enable society and citizens to be equipped and respond responsibly. To make this happen, the provision of education and training for health providers in the public health genomics field and related disciplines is needed. Some research indicates that health care providers are poorly prepared to integrate genetics into practice, while other surveys suggest that 90% of US public health schools teach health policy but only 15% genetics. In order to achieve this goal, there needs to be additional development in infrastructures for training courses in genetics, health care and health economics, targeted as appropriate at health care providers, geneticists and economists.

In conclusion, an unfortunate feature of the genomic revolution has been a tendency to hype up the scope and timing of the integration of genome technologies into health care. This situation, together with its commercial potential, has manifested itself in the widespread use of genetic testing for susceptibility to complex disorders, or for drug responses, with little evidence of efficacy, effectiveness and cost-effectiveness. Since a shared methodology for the proper evaluation of genomic tests does not as yet exist, health service research should work hard to identify universal criteria against which to evaluate genetic tests. This should also take into account the acceptability and the potential for harm of the testing process itself. So, public health professionals and policy-makers in the next decade would do well to clarify the conditions under which the genomic revolution, already underway in medicine, will result in public health benefits.

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