POLICY FORUM: HEALTH CARE DELIVERY

Building Population Genetics Resources Using the U.K. NHS

Robin Fears and George Poste

Genomics is revolutionizing the study of biology and will transform pharmaceutical industry R&D, medical practice, and public health (*1*). The union of genomics research with clinical genetics promises new routes to the understanding of complex disorders such as cancer, diabetes, asthma, cardiovascular and cerebrovascular disease, and psychiatric and neurological conditions—all major causes of mortality and morbidity in industrialized and, increasingly, in developing countries (*2*).

However, innovation is as much an imperative at the level of institutional organization and culture as in the formal generation of novel products and services. Although less emphasized, it is vital that all health care constituencies work together to ensure timely and orderly adoption of scientific advances.

The economics of R&D and of health care provision are already under considerable scrutiny in the United Kingdom Transfer of research findings into clinical practice to create a knowledge-based health service can be a slow and haphazard process (*3*). The U.K. National Health Service (NHS) has an obligation to act as a research resource for the development of initiatives that will improve the quality of care. We contend that to fulfill this prerogative, new public-private partnerships will be needed.

As health care systems begin to embrace population-based medicine, developing robust tools for patient segmentation based on genetic epidemiology and for the elucidation of individual disease risk profiles to optimize diagnosis and care, it is evident that the NHS is a substantial but underused research resource. It has much to offer in developing new clinical R&D initiatives in population genetics and epidemiology, technology assessment, and the coordination of clinical trials and outcomes research. Here we focus on the unparalleled opportunity afforded by the NHS in population genetics research.

The New NHS as a Research Resource

Historically, the structure of the NHS has facilitated academic research in clinical genetics, generating family material for gene mapping, pedigree analysis, and related research (*4*). This role was weakened in the early 1990s by the internal market reforms of the NHS, which led to organizational fragmentation and disparate priorities by creating autonomous geographic zones and independent health authorities, with minimal imposition of demands for uniform clinical standards. The recent Government White Paper's objective of abolishing the internal market (*5*) is an encouraging sign that the continuation of academic genetics research is feasible. But much more is possible.

The NHS is a high-quality health care system that provides a comprehensive service to everyone in the United Kingdom (59 million people). It also provides a research resource, assembled over 50 years, comprising detailed patient records and archived tissue samples for constructing disease libraries. The NHS is probably the largest single source of medical information and well-characterized biological samples in Europe and encompasses substantial subpopulations of important ethnic groups. In addition, it represents a significant research resource in terms of clinical expertise and infrastructure. NHS records provide a large longitudinal population database that is of great potential value for genetic epidemiology, for the clinical analysis of risk traits, and for correlating genotype-to-phenotype patterns of disease progression and treatment outcomes (*6*). The potential biases created by the selective study of small family pedigrees or isolated populations justify an ambitious strategy to define the risks associated with particular genomic profiles in larger outbred populations.

The possibilities for a single national effort in the United States have been outlined by Welch and Burke (*7*) and would build on data already available, for example, from the National Center for Health Statistics. Such an effort will require the resolution of difficult ethical questions, such as: What constitutes informed consent for obtaining and storing patients' DNA? Can previously collected blood samples be used to address new genetic questions? Should research subjects expect notification when risk markers are identified? How many markers can be profiled without compromising the anonymity of DNA data? Although significant, these ethical issues must be balanced by the parallel ethical questions raised by the validity of making potentially premature clinical decisions using genetic data without accurate risk estimates derived from large population cohorts (*7*).

How, then, might a strategy to use the NHS as a research resource be moved forward? We believe that it will require appropriate scientific and clinical skills, matched with large-scale computational infrastructure capable of handling large subsets of clinical data, as well as transparent and coherent policies for addressing the ethical, legal, social, and political issues arising from the use of clinical information.

Large-Scale Health Informatics

As discussed elsewhere (*1*), there are considerable challenges to be faced in the development of new informatics tools, building expertise in database hyperlinking, analytical algorithms, the assembly of databanks for genetic association studies, and the use of sophisticated encryption methods to ensure protection of individual privacy and confidentiality. The response to these challenges can be mounted only if there is a coherent policy for information technologies in the NHS as a whole. The recently published *Information for Health* strategy (*8*), establishing the time frame for the generation of "cradle-to-grave" electronic records, is an important advance in the capture and transfer of data. The content, structure, and use of such databases will need to comply with the 1998 Data Protection Act (the U.K. implementation of the European Data Protection Directive) in order to prevent unnecessary, and now illegal, identification of individual patients without their specific consent (*8*).

Uses of Medical Information

The ethical and legal complexities raised by genomics have evoked substantial debate. Although by no means unique to genetic medicine, the issues relating to potential discrimination based on genetic profiling, new aspects of informed consent, the retrospective use of archived tissue samples, and the adequacy of protections for privacy and confidentiality have galvanized public concerns about the pace and scale of technological change.

The debate on the acceptable uses of information must address the issues of medical privacy at large rather than treat genetic information as a discrete category, so that genetic information is not itself stigmatized. It seems preferable to act on

The authors are with SmithKline Beecham, New Frontiers Science Park, Harlow, Essex CM19 5AW, UK. E-mail: robin_b_fears@sbphrd.com

the misuse of information rather than to promulgate further laws to protect privacy, which if poorly drafted, as in the case of considerable state law in the United States, may constrain research (*9*). In the United Kingdom, the Human Genetics Advisory Commission and the Advisory Committee on Genetic Testing, both nonstatutory bodies reporting to government, have taken a leading role in crafting recommendations for what is appropriate with regard to the use of genetic information for nonmedical purposes, such as in life insurance. This transparent science-driven approach serves as a basis for discussing the issues in the community at large and provides a model for other public policy analyses of controversial topics.

What can be learned from the plans to establish a database of the medical records of the population of Iceland (*10*)? It is important to understand the concerns expressed about privacy and informed consent, and the apprehension that a commercial company, put into a monopoly position, might impede academic research or propagate commercial abuses. The privacy and consent issues can be debated and resolved. What is more worrying is that even though it is agreed that the database concept is exciting, and it has public support in Iceland, commercial companies are being stereotyped and demonized by some academics as insensitive to human rights and having scant interest in improving the quality of life. One lesson from this is that biomedical companies must do much more to build transparent and accountable policy relationships with the various constituencies involved in genetics research and health service delivery if they are to avoid similar adversarial relationships.

We envisage a precompetitive public-private consortium requiring a fusion of technologies (particularly biomedical, informatics, and communications disciplines), involving multiple companies, universities, medical research charities, and government. The challenge of very-high-cost new technologies has forced other industry sectors to explore the value of precompetitive consortia, both to generate innovation and to unify standards. Prominent examples of this trend are the computing, automobile, aerospace, and materials science sectors. We suggest that the time has come when the escalating cost of life sciences research requires analogous activities in health care. The challenge, however, is to go beyond the concept of company consortia and accountability to build public involvement and to ensure that while the resulting databases are sufficiently protected, access is available to all the potential users (including patient groups). Because of the magnitude of this collaboration, it is important to begin now to consider how to create such a strategic resource, without preempting what must be a wide-ranging debate on the best ways to achieve shared policy goals.

In the coming years, the impact of advances in genetics on the practice of clinical medicine will be profound (*11*). Action is also urgently needed to ensure that the pace of progress in genomics, informatics, and epidemiology does not outstrip the competency of health care professionals. This risk is real; reform of the medical teaching curriculum and continuing medical education to enhance knowledge of these subjects is an urgent priority.

Health Care Delivery: Rationing or Rational?

We believe that the United Kingdom has an unrivaled opportunity to use the NHS as a research resource if the enthusiasm can be generated to establish a "third way" paradigm (*12*) for clinical research that responds to the rapid expansion of new knowledge and technological advances and adapts to the changing environment for health services delivery (*13*). The U.S. Centers for Disease Control and Prevention initiative to create HUGE Net (*14*) to develop and disseminate population-based epidemiological information on the human genome illustrates the importance that this subject has already been accorded in the United States.

The NHS recognizes that supporting R&D is one of its main priorities (*15*), but it is time to extend the debate on priorities to establish how the NHS as a whole, rather than the R&D directorate alone, can contribute to R&D. There is much to be done to convince policymakers of the value of genomics R&D for the delivery of quality health care and that the NHS is an unmatched but underleveraged vehicle that can put the United Kingdom in the vanguard of rational care based on molecular medicine. The alternative bleak prospect is progressive rationing of increasingly constrained health care resources.

There is also a great need (*9*) to initiate public debate to increase awareness of the potential benefits of genomics and molecular medicine, to provide robust protections against misuse of information, and to establish clear priorities for care delivery. Public-private partnership is essential for the generation of new products and services in a cost-effective manner. Failure to seize this opportunity may condemn health services to rationed rather than rational health care. The challenge now lies in forging the relationships for this partnership, for improved training, and for consideration of the ethical and social issues, in order to ensure that the potential value of genetic epidemiology is realized to produce better health and quality of life.

Reference and Notes

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