"The Public Health Call" performed by the author is available at <http://jech.bmj.com/supplemental>.

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Research in genomics

Assessing the social meaning, value and implications of research in genomics

Blanca Lumbreras, Miquel Porta, Ildefonso Hernández-Aguado

Genomic discoveries need to be translated to clinical and public health practice

Many health professionals and citizens believe that science is on the cusp of generating a major revolution in medicine as a result of advances in genomics, proteomics and other “-omics” disciplines. However, it has long been clear that other approaches, such as those typical of epidemiology, are essential to fulfil the promise of genomics for clinical and public health practice,¹ and should be part of the research agenda. The main objective is the translation of genomic discoveries to clinical and public health practice. However, moving too rapidly to the clinics with immature technologies could jeopardise the promising future of this research, as Ioannidis remarks in the Research Agenda section in this issue.²

As knowledge of the human genome has progressed,³ health professionals and the general population have been pledged dramatic improvements in health.⁴ Unfortunately, although such discoveries are occurring at a fast pace, the impact that they will have on public health is unclear; there is ample evidence that many research results have been “lost in translation”.⁵ There has also been some disappointment and impatience that diagnostic tests derived from the human genome have not been applied immediately to clinical diagnosis. However, Ioannidis and Ransohoff, among others,^{6–8} have already stressed the need to obtain more robust information regarding several methodological concerns before applying these novel insights

to clinical and public health practice. The principles of valid study design and sample size, for instance, must not be forgotten in any drive to generate novel data.⁹ As Ioannidis describes, genetic association studies of complex phenotypes have typically failed to discover susceptibility loci or to replicate other results. This lack of reproducibility is often ascribed to small samples; in other words, large sample size, rigorous p value thresholds, and replication in multiple independent datasets are necessary, though not sufficient, for reliable results. Ioannidis and others think that a possible solution lies in the organisation of biobanks, which systematically store biological material and information from a large number of people, and “represent the new generation of cohorts” for discovery and characterisation of genes associated with common diseases.² There is no doubt that biobanks are a key part of this area of research. Nevertheless, their role could be more effective if their samples were linked to well-designed epidemiological and population-based studies, as recently illustrated by Frayling *et al.*¹⁰ This move is essential to avoid important problems, such as selection bias.³

Further to the various methodological points raised by Ioannidis in his article, it might be worth considering the health, industrial, regulatory and social context, in line with other Research Agendas published so far.^{11 12} Virtues such as clear

thinking, good will and hard work may not be enough to push forward the highly relevant agenda suggested by Ioannidis. The fact is that commercial and social influences abound. And while these influences have several positive aspects, they often apply pressure to speed up marketing, take “shortcuts”, exaggerate promises,¹³ or circumvent regulatory approval.^{14 15} Commercial actors are very prominent in many stock exchanges. For example, biotechnology companies such as Illumina, Cephalon or Celgene, among others, are among the 25 technological businesses with the highest growth. Yet, references to “external actors” are frequently absent from academic reviews on the successes and failures of -omics technologies. Such omission probably reflects the fact that the technological, industrial, civilian and political forces that shape the evolution of health research have seldom been studied.^{3 16} More realistic, “feet on the ground” analyses would perhaps help to achieve the “transparent and comprehensive availability of information” that Ioannidis and others rightly request.^{2 17} Failure to disclose the interests of an author is the main reason for a rather symbolic reprimand of *The Wall Street Journal* to *The New England Journal of Medicine*.¹⁸

Another process threatening translation of “omics” to clinical and public health practice is the reduction or breaking up of biotechnology research into independent sections.³ Research is typically conducted by different scientists and funded separately: the discovery phase relies on basic scientists, testing depends on manufacturers, application on laboratories, and the final evaluation rests largely on clinicians. However, as Ioannidis states,² even though there is a clear need to develop systematic procedures in order to achieve analytical and clinical validity of the derived devices, an increase in integration, coordination and collaboration seems to be required to meet the growing demands for rapid improvements in healthcare.³ In addition

to the requirement of more integrated and cooperative work between researchers from different areas, we also need a continuous and multidirectional exchange of knowledge and information among researchers, consumers, professional groups, industry, policy makers and public agencies.¹⁹ The main objective of this collaboration should be the integration of genome-based knowledge and technologies into the clinical and public health research agenda, thus forming the scientific basis for developing sound policies and effective interventions. This approach should overcome critical gaps in translating research results into population benefits.

Until recently, the field of genetics was largely confined to rare disorders caused by specific genetic alterations in single genes in each individual. However, since most chronic diseases are aetiologically heterogeneous, future medical care and disease prevention may eventually be partly based on genetic risk profiles.²⁰ Ioannidis argues that if we want genomic profiling to have an important role in future health care practice, epidemiological studies should collect information about both the genome and environmental exposures. Nevertheless, some authors²¹ have proposed a rationale for prioritising genomic research on the basis of public health goals. They argue that the highest priority for genomic research should be given to diseases with the strongest evidence of genetic aetiology, a high public health impact, and limited ability to modify exposures. They suggest that for modifiable causes of disease, genomic research should have a lower public health priority, because a population approach to prevention will achieve a greater public health benefit than interventions targeted at high-risk groups on the basis of genotypes. According to these proposals, the research agenda should formulate policies that will evaluate the effectiveness of genomic discoveries by assessing the health impact on the population of the new developments.²²

In fact, there is a strong demand for studies confirming the usefulness of the new genomic devices, with definitive and measurable clinical endpoints, such as sense of well-being and established medical outcomes. We are all aware of the difficulties detailed by Ioannidis in carrying out a clinical trial, and few genomic profiles are likely to be assessed in randomised clinical trials. Thus, careful thought needs to be given to the level of evidence that justifies clinical use of genomic profiling, taking into account the strength of the observational data, the

clinical benefit and the potential to harm.²⁰

A research agenda with a population perspective should make public education about genomics a priority. There is a huge need for development and evaluation of health education approaches for groups with low biological literacy. Testing strategies to communicate the complexity of gene-environment interactions and genomic risk may be especially fertile ground.²³ Nevertheless, despite the increased recognition of the importance of genetic and genomic education, the proportion of public funds that is devoted to educational research efforts is presently too small compared with that devoted to basic research. Patients have increasing opportunities to obtain information about health care products and services from sources outside the traditional health care setting, such as the printed press, television and the internet. This advertising, however, is more problematic when these products are characterised by complex information, a complicated social context and lack of clinical value.¹⁵ Clinicians will also have to correct consumers' false impressions of genomics; however, it may prove difficult to modify consumers' inaccurate expectations. Several studies²⁴⁻²⁵ have revealed that physicians may not have the skills necessary to critically analyse and communicate genomic information and meaning, suggesting that some are not prepared for the present flood of new consumers interested in genetic testing.²⁶ Thus, public health professionals also have a crucial role in educating other health professionals and stakeholders in evaluating the value and implications of integrating genomics into health promotion and disease prevention programs.²⁷

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