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Personalised medicine

Personalized medicine in context: social science perspectives

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In the 1990s, the scientific and popular press heralded the emergence of a new paradigm in drug discovery and development called pharmacogenomics (pgmx). As well as capturing the interest of scientists, policymakers and journalists, the field of personalized medicine has also been of immense interest to social scientists who research new innovations in health and biomedicine. This article reviews existing social science research on pgmx. It considers work on mapping industry involvement in pgmx; the dynamics of clinical adoption and the challenges of pgmx testing becoming a standard healthcare service; and patient and public perspectives on pgmx. In conclusion, the article reflects on the future research agenda.

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Introduction

In the 1990s, the scientific and popular press heralded the emergence of a new paradigm in drug discovery and development called pharmacogenomics (pgmx). This science would produce a new generation of 'personalized medicines' utilizing information about individuals' genotypes to make more effective and safer drugs. As well as capturing the interest of scientists, policymakers and journalists, the field of personalized medicine has also been of immense interest to social scientists who research new innovations in health and biomedicine. Social science has mapped industry involvement in pgmx and 'personalized medicine' since the 1990s, identifying the visions that have guided development in this field and reflected on the broader social and economic contexts in which pgmx has appeared. The clinical adoption and the challenges of pgmx testing becoming a standard healthcare service have also been documented by careful examination of clinicians' own practices, and social science has also explored public perspectives on pgmx and the potential implications of patient stratification. The purpose of this article is to review this research and its contribution to an understanding of personalized medicine. It will summarize some of the most important findings to date, and reflect on the future research agenda.

Personalized medicine as a vision

One of the key roles of social science research has been to map the construction of scientific fields of inquiry over time and the means by which these fields attract their supporters. Central to this undertaking has been the study of language not for its own sake but for understanding its practical significance. Hedgecoe argues that the adoption of the term pgmx did not describe an area of research distinct to that of pharmacogenetics (pgx) which had been in existence for 40 years, but served as a rhetorical device to gain support and investment by linking it to the Human Genome Project [1]. This is not to deny that important technical changes had taken place such as the development of SNP databases and

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chips to genotype individuals to identify genetic variation. However, it is of note that the term pgmx only first appeared with the announcement of an alliance between Genset and Abbot Pharmaceuticals in 1997 and so became associated more closely with the commercial potential of the study of the role of genetic variability in drug response. The two terms pgx and pgmx have continued to be used and their exact meanings disputed and debated by scientists and others [2].

The potential contribution of pgmx was described as producing 'a new generation of personalized medicines' – drugs aimed at the individual as opposed to the 'average person' [3]. Since that time, 'personalized medicine' (in the singular now) has proven to be a highly popular term that easily conveys to a range of audiences what genomics has to offer medicine and healthcare in the 21st century. However, clinicians had used the term personalized medicine since the early 1950s to describe a patient-centered practice that focused on the 'art' of clinical judgment and was often hostile to technology in medicine [4]. The term personalized medicine has also been controversial: some claim that it promises more than can be delivered because individualized therapy can only be truly realized in a biopsychosocial paradigm while pgmx is a biomechanistic concept concerned with the stratification of patient populations [5]. Recently, certain actors have preferred other expressions such as stratified medicine as a more accurate description of how drugs are targeted at groups as opposed to individuals [6].

Building on this interest in language, social scientific analysis of emerging biotechnologies has also proceeded with understanding that the visions of social actors such as scientists can shape technological outcomes by attracting allies and their resources to support work to realize these visions. Therefore the study of visions has been central to a thorough examination of how a technology is constructed and then translated into everyday use. This approach has been adopted by social scientists in relation to pgmx [7,8]. Smart and Martin show that there were multiple and potentially competing pathways for pgmx to develop, which included: (i) discovering new 'pgmx' drugs aimed at genomic subpopulations; (ii) the identification at later clinical development stages of 'good responders' for new drugs; (iii) use of efficacy data in the marketing of both new and existing drugs; (iv) preprescription screening to identify patients at risk of ADRs; and (v) preprescription screening to identify 'good responders' [8]. Smart and Martin's study investigated the level of support from the biotech and pharma industry for each of these 'visions' to assess their prospects, interviewing industry leaders and analyzing published data on publicly announced collaborations. They conclude that there was significant interest in the potential of pgmx to aid in new drug discovery and development (i, ii), but there were barriers to applying pgmx in relation to already licensed drugs. However, there were some exceptions, most notably the HIV/AIDS drug Abacavir (Ziagen™) developed by GlaxoSmithKline; it was also clear that some specialist diagnostic developers saw opportunities to develop and market diagnostic tests for existing drugs.

Recent analysis of FDA data by one of the authors (RT) indicates that just over 10% of the 385 drugs licensed in the period 1998–2011 had pgmx biomarker data included in their labels at the time of their approval. Only three drugs – Herceptin®, Xalkori® and Zelboraf® – were approved by the FDA as 'combination products' of codeveloped drugs and companion diagnostics. Of the drugs listed by the FDA as having pgmx biomarker data in their labels the majority are already licensed drugs for which these data are included in the main to improve their safer use by clinicians and patients. Therefore, the evidence is that significant headway has been made on preprescription screening on drug safety grounds. Where drugs have been approved with biomarker data to guide their use by clinicians, the majority have been cancer therapies. The wider application of pgmx to other therapeutic areas is for now unclear.

Personalized medicine in clinical practice

Social science research has followed personalized medicine into clinical practice to document how preprescription testing is mobilized to identify patients who are likely to respond well to particular drugs and those that are at increased risk of adverse drug responses [10,11]. At present, this approach is almost exclusively limited to secondary care where the increased complexity, cost and toxicity of therapies makes a trial-and-error model of prescribing inappropriate. Oncology is of particular note as a clinical specialism in which pharmacogenetic approaches to medicines and patient bodies have become fairly well routinized. As noted above, 42% ($n = 36$) of the current 117 biomarker associations identified in FDA-approved drugs pertain to this therapeutic area. Within this field, the breast cancer drug Herceptin® has repeatedly been drawn on as an example of the highly successful integration of personalized medicine into routine clinical use. Herceptin is only effective in the 25–35% of breast cancer patients whose tumors over-express the human epidermal growth receptor 2 (HER2) protein as a result of gene amplification. Given this, preprescription testing of the breast tumor for HER2+ status can determine whether Herceptin is an appropriate therapy option. Notwithstanding the debate as to whether Herceptin ought to be considered pgmx drug at all (because it is targeted at the tumor not the genotype of the patient), its adoption is noteworthy for several reasons. For example, the media played a central part in debates about the extension of Herceptin's license for the treatment of early stage breast cancer [12,13]. Moreover, by funding HER2 tests before Herceptin's approval, Roche gained widespread professional support from oncology