Ethical Perspective

Pharmacogenetics and public policy: expert views in Europe and North America

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The new genetics is stimulating the development of genetic testing of patients to help choose the best drug, adjust doses and avoid side effects. Proponents say that this personalized medicine will revolutionize drug development and healthcare. In a series of group meetings, 48 leading experts from regulatory agencies, industry, academia and consumer interests gave their opinions on the public policy priorities. Most believed that pharmacogenetics would have a clear impact on care within 15 years and that a public policy response was needed. The establishment of a good clinical evidence base should be a priority, together with addressing the needs of drug response gene minorities. A total of 72% also believed that postmarketing surveillance systems should be collecting DNA from patients experiencing moderate or severe adverse events.

Introduction

Pharmacogenetics, the study of genetically determined variability in drug response, is resulting in a new wave of clinical applications, with two recent cancer treatments linked to genetic testing of malignant cells (Herceptin® and Glivec®). Pharmacogenetic applications or products will also involve genetic tests of somatic genes of patients to help choose the most appropriate drug for each individual, to select an optimal dose or to identify those at risk from atypical adverse drug reactions. Recent advances in molecular genetics and the falling costs of genetic testing have provided a great deal of momentum to this field.

In the optimistic days of the race to map the human genome, a number of leading experts argued that pharmacogenetics would revolutionize drug marketing and prescribing [1,2]. Instead of hoping for the best, a genetic test would indicate the best therapeutic choices for each patient. Pharmaceutical companies could accelerate drug development, and promising compounds previously dropped because of adverse events could be marketed for patients who could safely take them. It was also suggested that pharmacogenetics and the wider genetic revolution would undermine socialized healthcare systems [3].

The prospect of a prescribing revolution necessitates a consideration of public policy responses to this technology. The project reported here aimed to explore and measure expert opinion on public policy priorities for pharmacogenetics. In the light of critiques of precision of genetic testing for complex traits [4], the project paid special attention to clinical evaluation of pharmacogenetic products to support evidence-based clinical practice in the future [5].

Methods

Interviews and focus groups were held with leading European and North American experts in the field. The data presented are from self-completed questionnaires administered to those who attended the five main stage focus group meetings held in 2001 and 2002. Of the 52 attendees, 48 completed the questionnaire after participating in over six hours of group discussions on the policy implications of pharmacogenetics. Respondents included 10 industry representatives, 7 senior regulators, 14 academics (including clinical pharmacologists, geneticists and clinicians), 3 non-academic clinicians, and 14 people representing consumer interests, ethics or social science perspectives. There were 27 European respondents and 21 from the US or Canada. Experts participating included:

- Drs J Woodcock, L Lesco and S Guttman from the US Food & Drug Administration
- Prof NA Holtzman, Chair of the US Secretary's Task Force on Genetic Testing
- Dr M Papaluca Amati of the European Agency for the Evaluation of Medicinal Products
- Dr A M Carty of GlaxoSmithKline
- Dr R Shah of the UK Medicines Control Agency
- S Terry of the Genetic Alliance International

A full list of those attending the focus groups is available from the authors.
Analysis used anonymized data to explore group responses. There were no statistically significant differences in responses between experts by ‘discipline’, for the items presented here.

Results

Table 1 shows the proportions of participants who agreed with each policy statement on pharmacogenetics. There was strong support for the idea that pharmacogenetics will have an impact on more than 15% of hospital patients within 15 years. Few experts also believed that it was ‘too early to make important policy decisions on pharmacogenetics’, with only 19% agreeing with this view.

Very few experts believed that current market mechanisms and public sector programs were sufficient to foster the development of pharmacogenetics. Some commentators have voiced concerns about the potential for pharmacogenetics to make explicit the existence of many ‘genetic minorities’ with uncommon drug response genes. There was very little support for the view that the market would take care of these groups, without public policy action.

Intellectual property rights on genetic sequences have been identified as a potential hurdle in the development of pharmacogenetics but respondents were split evenly on the impact of these rights. A majority did believe that confidentiality and data privacy procedures pose a threat to progress in developing pharmacogenetics. Agreement with this was significantly stronger in North American participants.

Current laboratory or test device regulations concentrate on analytic validity, i.e., whether the test accurately identifies the target DNA sequence. Regulations, especially in Europe, have required little evidence of ‘clinical validity’ (that the test identifies the patient targeted clinical problem, e.g., being a ‘slow metabolizer’) and no evidence of ‘clinical utility’ (that the test result will lead to improved care or health). In our expert groups, 100% of respondents believed that clinical utility evaluation should be required, and the great majority believed that this should be achieved through statutory or formal health system mechanisms and not left to voluntary or market mechanisms.

Clinical trials of new drugs are generally too small to reveal less common adverse events and postmarketing surveillance is the main means of studying these. 72% of respondents believed that genetic material should be collected in such schemes, from all patients experiencing moderate or severe (adverse) drug events.

### Table 1. Percentage of experts agreeing with each statement about pharmacogenetics (48 responded of 52 attending five focus groups).

<table>
<thead>
<tr>
<th>Statement</th>
<th>% Agreeing with statement</th>
</tr>
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<tbody>
<tr>
<td>Pharmacogenetic tests will impact on the care of more than 15% of hospital patients within 15 years</td>
<td>70</td>
</tr>
<tr>
<td>It is too early in the development of pharmacogenetics for any important policy decisions to be made</td>
<td>19</td>
</tr>
<tr>
<td>Market mechanisms and existing public sector research programs are sufficient to ensure that pharmacogenetics will develop and make a major contribution to clinical care</td>
<td>11</td>
</tr>
<tr>
<td>The market will take care of pharmacogenetically defined minorities</td>
<td>6</td>
</tr>
<tr>
<td>Exclusive patents/intellectual property rights on gene sequencing relating to pharmacogenetic tests pose a threat to progress in this area</td>
<td>47</td>
</tr>
<tr>
<td>Confidentiality and data privacy are significant barriers to pharmacogenetic testing</td>
<td>62</td>
</tr>
<tr>
<td>Pharmacogenetic tests will require evaluation for their utility in clinical decision making</td>
<td>100</td>
</tr>
<tr>
<td>Requirements for pharmacogenetic test clinical evaluation should be:</td>
<td></td>
</tr>
<tr>
<td>• Statutory</td>
<td>86</td>
</tr>
<tr>
<td>• Health system based evaluation of tests</td>
<td>77</td>
</tr>
<tr>
<td>• Voluntary</td>
<td>19</td>
</tr>
<tr>
<td>• Left to the market</td>
<td>5</td>
</tr>
<tr>
<td>Genetic material should be collected on all patients experiencing moderate or severe (adverse) drug reactions</td>
<td>72</td>
</tr>
<tr>
<td>Current systems of information and dissemination are sufficient to equip healthcare professionals to employ pharmacogenetics appropriately</td>
<td>6</td>
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</table>
North America comparisons showed that North American participants were, however, significantly less likely to support this view. Pharmacogenetics will add greatly to the growing complexity of prescribing, and very few of those responding believed that current information and dissemination systems to healthcare professionals would be adequate to handle pharmacogenetic products.

Discussion and conclusions
The recent rapid evolution of new genetic technologies has resulted in greatly intensified activity in pharmacogenetics. The resulting scientific and policy issues are highly complex and, thus, this survey of the views of 48 of the leading opinion formers in the field, both in Europe and North America, provides a powerful pointer for policy development.

Experts seem agreed that pharmacogenetics will make a significant impact on care within the next decade and a half, and that a public policy response is needed now. There was very strong support for the establishment of a clinically relevant evidence base for pharmacogenetics tests and test-drug combinations, as a key aim of policy. Public policy was also seen as needed to protect ‘pharmacogenetic minorities’. There was also agreement that current privacy and confidentiality procedures could stifle the development of pharmacogenetics and delay its benefits in making prescribing safer and more effective. Possibly the most controversial view was that postmarketing surveillance systems should be investigating genetic factors involved in adverse events, especially for the more severe events.

Bibliography

For the Wellcome project summary and full reports see http://www.phpc.cam.ac.uk/epg/IPP.html