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The Personalized Medicine Coalition

Goals and Strategies

Edward Abrahams,[1] *Geoffrey S. Ginsburg*[2] and *Mike Silver*[3]

1 Personalized Medicine Coalition, Washington, DC, USA
2 Duke University, Institute for Genome Sciences & Policy, Durham, North Carolina, USA
3 Feinstein Kean Healthcare, Cambridge, Massachusetts, USA

Abstract

The concept of personalized medicine – that medical care can be tailored to the genomic and molecular profile of the individual – has repercussions that extend far beyond the technology that makes it possible. The adoption of personalized medicine will require changes in healthcare infrastructure, diagnostics and therapeutics business models, reimbursement policy from government and private payers, and a different approach to regulatory oversight. Personalized medicine will shift medical practices upstream from the reactive treatment of disease, to proactive healthcare management including screening, early treatment, and prevention, and will alter the roles of both physician and patient. It will create a greater reliance on electronic medical records and decision support systems in an industry that has a long history of resistance to information technology.

Personalized medicine requires a systems approach to implementation. But in a healthcare economy that is highly decentralized and market driven, it is incumbent upon the stakeholders themselves to advocate for a consistent set of policies and legislation that pave the way for the adoption of personalized medicine. To address this need, the Personalized Medicine Coalition (PMC) was formed as a nonprofit umbrella organization of pharmaceutical, biotechnology, diagnostic, and information technology companies, healthcare providers and payers, patient advocacy groups, industry policy organizations, major academic institutions, and government agencies. The PMC provides a structure for achieving consensus positions among these stakeholders on crucial public policy issues, a role which will be vital to translating personalized medicine into widespread clinical practice.

In this article, we outline the goals of the PMC, and the strategies it will take to foster communication, debate, and consensus on issues such as genetic discrimination, the reimbursement structures for pharmacogenomic drugs and diagnostics, regulation, physician training and medical school curricula, and public education.

1. The Transition to Personalized Medicine

History may mark this period as the beginning of a new era in the practice of medicine, in which knowledge of an individual's genetic and molecular profile guides preventative care and the selection of therapies that convey maximum effectiveness and safety. A small but growing number of molecular tests are emerging that support the diagnosis and classification of disease, predict future disease risk, or predict the response to drug therapy (table I). The area in which these applications are the most advanced, and which may be characterized as the front end of 'personalized medicine', is cancer.[1,2]

Industrial, academic, and government research related to personalized medicine (including pharmacogenomics and molecular diagnostics) continues to be strong. Although some have argued that pharmacogenomic research activity is tapering off, measured by the number of corporate collaborations or the reinvention of pharmacogenomic companies as 'product' companies, there remains a core group of over 30 biotechnology firms conducting disease-gene association studies and developing or marketing products and services for personalized medicine.[3] The contraction of pharmacogenomics in the biotechnology sector has been offset by increased in-house investment in pharmacogenomics at about 30 major pharmaceutical companies.[3]

Table I. Examples of personalized medicine therapies

Variable target	Therapy/prevention	Disease	Patient selection
Current clinical practice[a]			
BCR-ABL; c-KIT	Imatinib	Cancer/chronic myelogenous leukemia	Efficacy
BRCA1/2	Surveillance, tamoxifen; prophylactic surgery	Breast and ovarian cancer	Prevention; efficacy
CYP2D6/CYP2D19	~25% of prescribed drugs	Various diseases	Efficacy; safety
Estrogen receptor	Tamoxifen	Breast cancer	Efficacy
HER2/neu receptor (ERBB2)	Trastuzumab	Breast cancer	Efficacy
PML-RARα	All trans retinoic acid	Acute myelocytic leukemia	Efficacy
CDKN2A (p16) gene	Surveillance	Melanoma	Prevention
TPMT	Mercaptopurine	Acute lymphocytic leukemia	Safety
Transcriptional profile – 21 genes	Chemotherapy protocols	Breast cancer	Efficacy
Emerging			
Alpha-adducin	ACE inhibitors	Hypertension	Safety
CETP	HMG-CoA reductase inhibitors	Atherosclerosis	Efficacy
CYP2C9/VKORC1	Warfarin	Coagulation disorders	Safety
Transcriptional profiles	Chemotherapy protocols	Non-Hodgkin lymphoma/diffuse large B cell	Efficacy
Transcriptional profiles	Chemotherapy protocols	Acute myeloid/lymphoblastic leukemia	Efficacy and relapse

a Includes recently introduced marketed products.

BCR-ABL = breakpoint cluster region – Abelson; ***BRCA1/2*** = breast cancer susceptibility gene 1 or 2; **CETP** = cholesteryl ester transfer protein; **c-KIT** = tyrosine kinase receptor; **CYP** = cytochrome P450 enzyme; **HER2** = human epidermal growth factor receptor 2; **HMG-CoA** = 3-hydroxy-3-methylglutaryl coenzyme A; **PML-RARα** = promyelocytic leukemia retinoic acid receptor alpha; **TPMT** = thiopurine-*S*-methyltransferase; **VKORC1** = vitamin K epoxide reductase complex 1.

The pipeline of early stage discoveries leading to personalized medicine is also strong. An informal survey of major announcements for genetic and molecular tests that classify disease, predict susceptibility, or predict response to drug therapy indicates about 10–12 new discoveries or developments per month,[4] while the number of PubMed citations per year for pharmacogenomics has increased from 191 to 598 between the years 2000 and 2004.

While we can say that the era of personalized medicine may have begun, we must be cautious not to assume that its widespread practice is imminent. There remain scientific and technical issues to overcome, and because the implementation of personalized medicine will require some degree of re-engineering the healthcare system, the transition is likely to be impeded if left solely to market forces and the current fragmented policy landscape.

The highly decentralized and market-driven healthcare system in the US has both helped and hindered the dissemination of innovative medical technologies. New devices, drugs, and procedures receive rapid uptake in the healthcare market when they can demonstrate improved outcomes. However, if new technology involves restructuring the system itself, such as in the implementation of electronic medical records (EMRs), there is little chance of adoption without progressive government policy, or the establishment of standards set by a consortium of stakeholders.

In this article we examine the role that the Personalized Medicine Coalition (PMC) will take in promoting supportive government policy, aligning the interests of competing stakeholders, and educating the public and policymakers such that decisions on any one issue are made with full consideration of its system-wide impact.

2. Catalyzing and Responding to Change Through a Broad-Based Coalition

Major policy initiatives related to personalized medicine already exist at the Centers for Disease Control and Prevention (CDC),[5] the National Institutes of Health,[6] the US Food and Drug Administration (FDA)[7] and in the UK, the National Health Service.[8] Other nonprofit organizations, such as the Genetic

Alliance, have assembled patient advocacy groups to promote research in genetic disease and the adoption of personalized medicine approaches. Centers have been established worldwide to study the ethical, legal, and social impact of personalized medicine, including the Duke Institute for Genome Sciences and Policy[9] and the Genetics and Public Policy Center at Johns Hopkins University.[10] The Wellcome Trust has supported analysis of case studies to identify factors influencing the adoption of personalized medicine[3] and to determine the current state and future strategy of genetics education for the healthcare professions in the UK.[11] Despite the growing number of organizations weighing in on personalized medicine, a comprehensive set of policies has yet to emerge.

The PMC was established to foster a better understanding of personalized medicine, and to provide a neutral meeting ground for generating consensus and coherent policy among all the relevant stakeholders. The organization is without precedent in that its mission is supported by a broadly diverse membership from industry, government, academia, and other nonprofit healthcare-related groups (see figure 1) that represents all sides of almost every issue, yet has come together to identify ways to align objectives. As an accessible network of experts, the PMC also provides a resource to legislators and the media to help build a foundation of law and public opinion based on accurate information.

The PMC directive is to "debate, educate and communicate". This role is critical because personalized medicine will require the concerted effort and a mutual understanding among various interest groups. Each group of stakeholders must become familiar with issues that are not in its 'regular' area of expertise, in order to agree on a coherent set of policies that will facilitate adoption of personalized medicine.

An important objective of the PMC is to draw on its collective expertise to anticipate and find solutions to deal with the impact of change on the healthcare provider, the patient, and the companies that deliver personalized medicine products.

2.1 The Changing Role of the Healthcare Provider

As molecular diagnostics and personalized medicine approaches become more prevalent, the ability to predict outcomes, or detect disease at its earliest stages, will require substantial changes, and even a culture shift, in clinical practice. The PMC anticipates that the following will occur.

- The paradigm for medical care will change from reactive treatment to pro-active prevention and early intervention. Medical care will move upstream from 'disease treatment' to 'healthcare management'.
- Providers must become proficient in the application of a very large number of molecular tests, which will be used increasingly to help diagnose disease, predict progression, and select treatments. Clinical decisions will depend less on trial-and-error, and more on predictive evidence.
- Physicians will take on the role of information manager rather than repository of medical knowledge, and will have a significantly greater reliance on information technology for clinical decision support.
- A 'new' model for the healthcare provider organization will evolve based on improving quality of care and outcomes, not on short-term cost cutting.
- The physician will have to be trained or have access to a support system to deal with new ethical and legal issues/quandaries that arise from genetic testing.

Patient management will become heavily reliant on *information systems*. The evidence that physicians act on will not always be presented by the patient as visible symptoms, but as information accumulated in a database. It will be beyond the capacity of most providers to keep abreast (outside of a narrow specialty) of the molecular diagnostic tests that are available and their predictive utility, yet they will have to understand the tests' benefits, risks, and clinical interpretation.[12] Clinical decision support systems, EMRs, and computerized physician order entry (CPOE) systems will become a critical part of clinicians' daily practice, helping them manage volumes of knowledge and data that could not have been imagined a generation ago.

Medical education and training will play a central role in preparing the next generation of clinicians to manage information related to patient care and to function effectively within a network

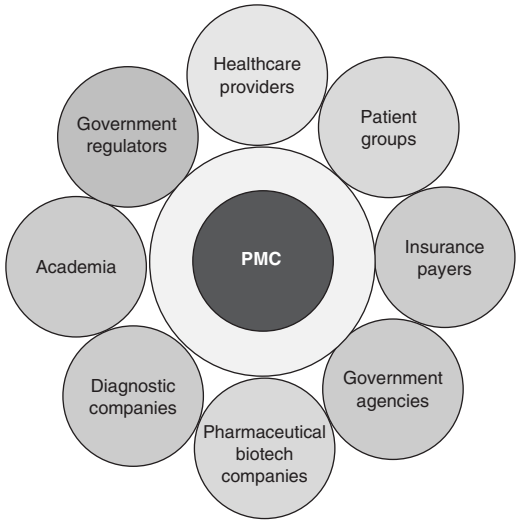

Fig. 1. The Personalized Medicine Coalition (PMC) promotes and facilitates communication among all personalized medicine stakeholders.

of providers, including genetic specialists, diagnostic laboratories, and pharmacists. Pharmacogenetic testing and treatment will create a host of new decision points – which test should be administered, how to interpret and use the results in treatment decisions, and how to deal with ethical issues such as a patient refusing to take a test, or demanding a therapy not indicated by the results. Most clinicians today are not trained in genetic counseling and treatment decisions related to predictive tests. Proper training will be critical to ensuring standards of care and ethics that facilitate personalized medicine.

The National Cancer Institute conducted a survey of physician use of genetic testing to gauge the level of preparedness in the healthcare workforce to take on personalized medicine.[13] According to the survey, about 31% of physicians report having ordered a cancer susceptibility test within the previous 12 months, or directed the patient for testing during 1999–2000. Interestingly, the factor that most strongly correlated with physicians' use of genetic testing was patient inquiry. Most of the physicians (87%) referred patients to other providers rather than administer the test themselves. About 50% of physicians felt unqualified to recommend cancer susceptibility testing.

With the current trickle of genetic tests likely to grow into a flood within the next few years, genomic knowledge may be lurching far ahead of conventional medical practice.[14] A growing number of patient inquiries and the potential for malpractice cases involving the omission or misinterpretation of genetic tests are likely to highlight the need for proper medical training and education in personalized medicine. The well trained physician will become key to the smooth transition to personalized medicine.

The PMC seeks to facilitate this transition through:

- the support of professional educational programs;
- workshops on ethical, legal, and clinical decisions that physicians and healthcare workers will face in their practice;
- advocacy of standards in clinical decision support systems, CPOE systems, and EMRs.

2.2 The Changing Role of the Patient

As a result of personalized medicine, the patient is expected to take on a more active role in their own healthcare. The PMC anticipates several changes.

- There will be greater knowledge of one's own genetic predispositions, resulting in more specific, actionable lifestyle and nutrition recommendations for reducing the risk of disease.
- Treatment decisions will be improved by an educated patient.
- Medical records may become more patient-centered rather than physician- or institution-centered, providing greater control and access to the individual.
- Prevalence of genetic information will affect every aspect of the individual's life, beyond the bounds of the healthcare system.

Through events and publications, the PMC will support education that improves the public's understanding of personalized medicine, so that the patient can become an active participant in the new paradigm of proactive healthcare. Through communications efforts and policy statements, the PMC will continue to support legislative initiatives that protect the individual from the misuse of genetic information, while making that information more easily accessible to the patient and their healthcare providers.

2.3 New Business Strategies for the Pharmaceutical Industry

The pharmaceutical industry has long been plagued by risk in drug development. With much of the 'low hanging fruit' in pharmaceutical therapies already developed, the stakes are even higher. For every 5000 compounds that enter preclinical testing, only one will make it to regulatory approval (based on drugs approved from 1994 to 1998).[15] Even after approval, the exposure of the drug to a large population of consumers may reveal severe adverse effects undetected in clinical trials, which could lead to the withdrawal of the drug and significant financial loss. The introduction of new technologies has done little to mitigate this risk. Personalized medicine promises to reduce some of that risk in the clinical trial stage by enabling the selection of high-responder populations and omission of patients susceptible to adverse reactions. But the PMC anticipates that changes brought about by personalized medicine may introduce other risks.

- The economics of drug development and commercialization will remain uncertain as the industry makes the transition away from blockbusters toward personalized medicine and 'niche-busters'.
- Regulatory mandates (e.g. toward drug/diagnostic combination products) could disrupt development budgets and market plans.
- The 'personalization' of drugs may affect product lifecycle and the impact of generic competition. There is also the possibility of third parties introducing diagnostic tests that restrict a product's market.
- Direct-to-consumer advertising will play an important role in extending markets to early and pre-symptomatic individuals. But the focus might shift to consumer education, while debate continues on the nature of advertising genetic tests to consumers, particularly for rare conditions.[16]

Pharmaceutical companies will continue to sail into uncharted waters as personalized medicine reshapes the business environment. Pharmacogenomic development will not be appropriate for

all drugs, and companies will need the tools and, if necessary, the incentives to make better choices as to which products should fall into the category of personalized medicine.

The PMC provides industry with a resource to help map out business risks, and the opportunity to initiate a dialog with government and industry partners to minimize those risks. The resources available to industry participants include facilitated panel discussions, workshops and conferences, and commissioned studies on the economics of personalized medicine development and commercialization.

3. Personalized Medicine Coalition Goals and Strategy

Personalized medicine will provide many positive benefits to patients, but unlike most previous innovative technologies, its introduction is potentially disruptive to the healthcare system and the traditional roles of physician and patient. In order to facilitate the adoption and smooth transition to personalized medicine, the PMC has established a set of goals:

- provide opinion leadership with respect to the evolving discussion of public policy issues that affect personalized medicine;
- help educate the public, policymakers, media, government officials, and private sector healthcare leaders about the public and personal health benefits of personalized medicine;
- serve as a forum for identifying and informing others of those public policies that may impede the ability to deliver the promise of personalized medicine;
- create a structure for achieving consensus positions on crucial public policy issues[1] and support changes needed to further the public interest in personalized medicine.

In the coming months and years, the PMC will consider a number of key public policy issues critical to the adoption of personalized medicine. These issues include, but are not limited to:

- the implementation of supportive information technology, such as EMRs and clinical decision support systems;
- insurance payer reimbursement;
- regulation of drug and diagnostic products;
- economic analysis;
- ethical, legal and social issues;
- healthcare workforce education;
- public education and acceptance of personalized medicine.

3.1 Electronic Medical Records and Clinical Decision Support

Information technology will play a critical role in facilitating the adoption and use of the molecular diagnostics and personalized medicine approaches. In addition, well designed systems will enable data from the clinic to be combined with research data from the laboratory, to provide valuable information leading to the discovery of disease-gene associations. However, there are many hurdles to the use of supportive information technology, including a reluctance to move away from paper-based systems,[17] and patients' concerns about confidentiality and the control of ownership of their medical data. Current systems are variable in quality and their ability to facilitate, rather than impede, medical practices,[18,19] and much of the technology still needs to be developed. Because personalized medicine will require collaborative databases merging data from multiple sources (physicians, pharmacists, specialists, diagnostic laboratories, and researchers), the systems must also account for the way independent healthcare providers expect to use and share information.

Recognizing that the healthcare system lags behind other industries in its utilization of information technology, President Bush proposed that the Federal Government spend $US125 million in the 2006 budget to prototype EMRs.[20] Recent developments suggest that momentum is building toward the nationwide adoption of EMRs in the US, including the introduction of bipartisan legislation calling for a national EMR system,[21] and an initiative by the Centers for Medicare and Medicaid Services (a Federal agency within the US Department of Health and Human Services) to subsidize the installation of EMR systems in physician offices.[22] But implementation in hospitals and physician's offices will take several years, and privacy protection and the role of patients and physicians in controlling access to the records has yet to be defined. A uniform set of standards for data structure, transfer, and protection will also be a prerequisite for progress, as this will make the large investment in technology more palatable to healthcare providers.

The PMC includes among its membership major information technology firms dedicated to finding solutions to the technology challenges in healthcare, specifically solutions amenable to personalized medicine. Implementation of EMRs, CPOEs, and clinical decision support systems will be an essential component of personalized medicine, which requires repositories of knowl-

1 The structure for achieving a consensus begins with a draft statement introduced by PMC members or the executive director. The draft is presented to the Public Policy Committee, which reviews the statement and issues a document to the membership. The document would include context, background, pros and cons, and a recommended statement/position. Revisions may be made by the PMC membership or executive director, and sent back to the Public Policy Committee for endorsement by a two-thirds majority vote. Final approval is made by a two-thirds majority vote from the PMC Board of Directors.

edge that are vastly larger than could ever be kept in the head of one physician, or even in one institution. The PMC provides a network of relationships between information technology firms, physicians, healthcare organizations, insurers, patients, and other stakeholders to better define issues of systems design, cost savings, privacy, and information access.

3.2 Insurance Reimbursement

Current attention given by insurers to genetic and molecular diagnostics is limited, and a large number of such tests are simply not covered. In one report,[23] it was found that 84% of insurers never considered the possibility of covering *BRCA* gene testing, which indicates whether the patient is susceptible to breast cancer based on a particular genetic variation. Only 4% of insurers surveyed decided to cover the test, despite the fact that preventive treatment options were available.

Insurers are likely to consider coverage of molecular diagnostic tests as they become more prevalent, and their use starts to drive consumption of other expensive resources, such as drug therapy, surgery, or the further testing of family members. Until then, many new tests will simply be paid out-of-pocket by the patient.

Short-term economic considerations have pushed insurers to ignore the value of the longer term implications of disease predispositions. There may be little incentive to support the use of susceptibility tests and preventative care when insurers are faced with rapid subscriber turnover. In contrast, if short-term value can be demonstrated in targeting therapies to patients, such as immediate improvements in safety and efficacy, then a reimbursement decision is usually triggered. A case in point, while insurance companies have largely avoided testing for breast cancer susceptibility using breast cancer susceptibility gene (BRCA) diagnostics, human epidermal growth factor receptor 2 (HER2)/neu testing for the treatment efficacy of trastuzumab is widely covered.

Insurer focus on unit cost and short-term budget impact is also evident in restrictive drug formularies and therapeutic substitution. The targeting of drugs based on genetic and other molecular tests will require greater complexity and sophistication of formularies, which in turn will play an important role in driving the utilization of pharmacogenomic drugs. It will be critical for formularies to take into account the full economic and health benefits to both the patient and society of personalized diagnostic/drug combinations, which may have higher unit costs, but could provide savings in doctor visits, length of hospital stay, or other medical procedures.

Insurers exert a strong influence on the selection of diagnostic tests through reimbursement and, therefore, play a critical role in the adoption of personalized medicine. *In vitro* tests represent <5% of total hospital costs but leverage up to 70% of critical healthcare decisions, according to a study by the Lewin Group.[24]

The PMC encourages insurers to implement healthcare payment policies that support patient access to molecular diagnostic tests. According to the PMC, financial incentives need to be aligned to ensure that there are no barriers to providing clinicians and patients with the best information that technology has to offer, and treatments that provide benefit to the patient, while reducing the overall cost of their care.

The PMC will remain vigilant about molecular test and pharmacogenomic drug reimbursement issues. Through discussions among the Centers for Medicare and Medicaid Services, private insurers, lawmakers, healthcare providers, and other key constituencies, the PMC will help generate consensus toward reimbursement policy supportive of personalized medicine.

3.3 Regulation

The regulatory system can tip the balance between innovation and stagnation in the pharmaceutical and diagnostics industries. It is fortunate that the FDA has taken a leadership role in establishing new ground rules for submitting pharmacogenomic data. The PMC applauds the FDA's issuance of their guidance on pharmacogenomic data submissions.[7] The FDA has shown the positive effect that open dialog among stakeholders, and proactive policy development, can have on the advancement of personalized medicine; their actions serve as a template for other policy efforts supported by the PMC. The PMC sees three main opportunities from the guidance.

1. It is clear that genomic technologies are driving or contributing to much of current biomedical discovery and development in industry and academia. Thus, a better understanding of FDA expectations and attitudes in this arena is very helpful to innovators who must carry their products through the regulatory system. In particular, the PMC supports the FDA on the introduction of the voluntary submissions process. This process allows product sponsors to have broad technical discussions with FDA experts about research data without undue concern that the submitted data will be used for regulatory decision-making. Such a concept is extremely important for progress in this highly complex technology, and is of broad applicability to other emergent and related areas of regulation, such as biomarkers. Several PMC members have already submitted data according to the spirit of this guidance, and others are expected to follow.

2. It is a major step towards the creation of a clear regulatory environment for pharmacogenomics and personalized medicine approaches. Regulatory clarity and standards are essential for

innovation to take place and new products to move expeditiously from laboratory bench to patient bedside.

3. The PMC is looking forward to additional guidance documents and protocols from the FDA in the coming months. Expected protocols include one on the subject of the co-development of pharmacogenomic diagnostics and therapeutics (a concept document was published in April[25]), and another on the use of microarrays in DNA analysis. Together, the three guidances will constitute an excellent foundation for the establishment of a technically sound but flexible regulatory environment for the development of important new personalized medicines, and a notable landmark in global regulation.

The response from industry to the FDA policies has been very positive. The FDA reported an increasing number of new drug applications (NDAs) and investigational new drugs (INDs) that included pharmacogenomic data since it began a dialog with industry to formulate the guidance on pharmacogenomic data submissions.[26] It is anticipated that those numbers will continue to grow now that the final guidance has been issued.

The PMC encourages the FDA to: support globally harmonized regulatory guidances in genomics; consider incentive systems for products targeting small 'orphan' genomic populations; define post-approval surveillance guidelines in the age of genetic/molecular screening;[27] and develop guidelines for actions required when new genetic/genomic information emerges for drugs already on the market.[28]

Another open issue is whether the FDA will consider the regulation of genetic tests, which are currently considered 'clinical services' and, therefore, covered under the Clinical Laboratory Improvement Amendments (CLIA). CLIA provisions do not regulate clinical validity or utility of the tests, which may become more of a necessity as the tests become closely linked to therapeutic decisions.[29]

3.4 Economic and Industry Analysis

Many advocates of personalized medicine have based their support not only on anticipated improvement in quality of care, but also on projections of cost savings in clinical development and healthcare delivery.[30,31] However, discussions of healthcare delivery and cost are often conducted using broad generalizations, and formal analyses of cost effectiveness[32-34] and implementation[3] are scarce. Concerns over rising healthcare costs are growing, so it is essential to critically evaluate personalized medicine and not take all the benefits as a given. Sound policy must be based on accurate data. One of the objectives of the PMC is to commission studies to evaluate the impact of personalized medicine on the cost and speed of drug and diagnostic development, and on the cost and quality of healthcare.

Important questions for pharmaceutical and diagnostic companies are: 'what are the financial benefits and risks of segmenting markets, shifting from blockbuster drugs to drugs based on genetic 'niche' markets?'; 'Are claims of the potential of pharmacogenomics to minimize serious adverse reactions justified?'; 'Under what conditions of regulatory and competitive environments, and inherent properties of drug and disease, does it make sense to pursue pharmacogenomic markets of various types?' and 'What proportion of the overall pharmaceutical market might turn out to be pharmacogenomic?'

For the healthcare payer, the overriding concern of increasing healthcare costs will focus attention on the economic impact of molecular diagnostics and pharmacogenomic therapies. The questions faced by payers include: 'What are the economic trade-offs between reimbursement for preventive medical care, and healthcare dollars saved in the long run, and how is that equation affected by subscriber turnover?'; 'How frequent (and severe) must a serious adverse effect be before a genetic test for the entire treated population is justified?' and 'Does it make sense to pay for a genetic screen for efficacy of a drug when positive responders are above a certain percentage of the population?'

The first commissioned study by the PMC will examine the contention that personalized medicine has the potential to lead to systemwide healthcare cost savings in addition to providing better healthcare. This two-part project will study current thinking on the subject and then determine what empirical evidence is necessary in order to demonstrate that more widespread use of personalized medicine products will save payers money in the long term.

3.5 Ethical, Legal, and Social Issues

The ethical, legal, and social issues in personalized medicine have been addressed by several organizations, including the Nuffield Council on Bioethics,[35] and in numerous publications.[36-40] The PMC has no intention of duplicating such efforts, but rather will serve as a clearinghouse of information from various sources. The PMC will benefit from the debate of ethical, legal, and social issues in its evaluation of policies such as those related to equitable distribution of benefits, product marketing, prevention of discrimination through employment and insurance, informed consent, and new ethical and legal issues that the physician must face in the administration of personalized medicine.

The starting point for all PMC policy is that genetic information, including family history, deserves strong and enforceable protections against misuse in employment and insurance. Policies consistent with this premise will ensure individuals will make full

use of diagnostic screens and counseling services to improve their healthcare, and increase participation in clinical trials that explore the genetic origins of disease. However, the issue of confidentiality of genetic information is more complex than is often represented. For example, asymmetric access to information may put some parts of the insurance industry at risk.

One study examined the effects of genetic testing for Alzheimer disease on the choices that people make in insurance coverage.[41] Insurers are concerned that when people have knowledge of their risk of disease from genetic tests (e.g. on apolipoprotein E, ε4 or the recently discovered link to ubiquitin-1), they may purchase more insurance coverage at lower rates to protect themselves. This behavior is termed 'adverse selection' – and consists essentially of tricking the system to take advantage of information not available to the insurer. According to the study results, people who discovered they have increased risk of Alzheimer disease made no significant changes in healthcare, life, or disability insurance, but were six times more likely to make changes in long-term insurance coverage.

In the long run, a viable insurance industry is in the interest of consumers as well. Policymakers will need to create safeguards and incentives that preserve consumer protection from discrimination (addressed by the Health Insurance Portability and Accountability Act and the Genetic Information Non-Discrimination Act) while at the same time addressing industry concerns.[42,43] This cannot be done without establishing a neutral meeting ground. Through discussion forums, workshops, and formal procedures for reaching consensus on public policy among its members, the PMC provides the environment for representatives on all sides of an ethical, legal, or social issue to devise solutions that strike a balance between their objectives.

3.6 Healthcare Workforce Education

Personalized medicine will create significant challenges for healthcare professionals unaccustomed to using genetics in their clinical decision-making. It is also likely to bring about confusion among consumers who will struggle with concepts such as molecular profiles, predictive power, risk, and the growing complexity of treatment choices. The PMC will support and sponsor educational initiatives for healthcare professionals, policy makers, and the general public as a way to help to build an informed set of stakeholders, who will then contribute more productively to policy debate or be better prepared to implement personalized diagnostics and treatments.

A growing number of genetic tests, biomarkers, and pharmacogenomic drugs are expected to make the transition from the research laboratory to market, and it will become necessary for physicians and other healthcare providers who are not normally trained in genetics to develop expertise in personalized medicine.[44] Physicians, nurses, pharmacists, and other caregivers will be seriously challenged to keep up with new diagnostic and treatment protocols. Decisions will have to be made about whether to administer a test, regulatory obligations must be adhered to, new legal minefields avoided, and ethical quandaries addressed.

Healthcare professionals will also be called on to use personalized medicine to improve disease management. Physicians will be expected to use and maintain databases that will tell them when and how to follow up with patients based on their susceptibility to various diseases, or predicted response to certain drugs. Medical schools will need to produce active participants in the paradigm shift in medical practice from disease treatment to healthcare management.

The current state of medical school curricula in personalized medicine (including genetics, genomics, and pharmacogenomics) will need to advance. Comprehensive genomic education programs have been implemented at a few medical schools such as the Tel Aviv University School of Medicine and the University of California San Francisco.[45] The Harvard Medical School – Partners Healthcare Center for Genetics and Genomics is also supporting genomic curricula at the Harvard Medical School and medical colleges in the Boston area, and Duke University is engaged in building curricula around genomic science and its impact on all aspects of life, human health, and social policy. An international survey of medical school curricula is currently underway,[45] but the results may well show a significant gap between the anticipated need and current availability of genetics training for physicians.

Pharmacists will also have to prepare for the next generation of pharmacogenomic drugs, particularly as they take on a more advisory role in the administration of molecular diagnostic tests. In the UK, an initiative has been established by the Royal Pharmaceutical Society to examine standards of care, the pharmacists' role in personalized medicine, and educational requirements as part of a wider campaign to improve genetics education among the healthcare professions.[46] The US pharmacy industry could benefit from similar efforts.

In the area of public health, the CDC has recognized that a better understanding of human genetic variants known to interact with environmental factors will be critical in developing new guidelines for environmental and lifestyle interventions. The need for a public health workforce capable of interpreting and using genomics has led the agency to establish three Centers for Genomics and Public Health,[47] charged with developing genomics educational programs for public health workers.

The National Coalition for Health Professional Education in Genetics (NCHPEG) is a notable example of an interdisciplinary

coalition developing competencies in genetics essential for all healthcare professionals.

The PMC will support professional educational programs in personalized medicine, usually in partnership with educational institutions, government agencies, and organizations such as those mentioned above.

3.7 Public Education

Most Americans have a positive attitude toward the use of genetic data in their treatment, as indicated by a recent US survey funded by the National Institutes of Health.[48] Eighty percent of respondents were somewhat or very likely to take part in genetic research. Those with more education were more willing to participate. However, the survey also found that most Americans do not fully grasp how pharmacogenomics works or how it might affect them.

Another survey by the CDC indicated that there is limited public awareness even of the most commonly used genetic tests.[49] In that study, about 41% of people in the US were aware that genetic tests are available that can determine an individual's risk of developing cancer. However, it is clear that patients exert a significant influence over the decision to apply a genetic test in their treatment[50] and so educational initiatives directed at the general public, or to specific patient populations, will be critical to the adoption of personalized medicine. The PMC will help to establish or sponsor educational programs and communication initiatives to raise the level of knowledge and awareness of personalized medicine among the general public. Such initiatives will be necessary in the context of increasingly prominent direct-to-consumer advertising for genetic testing.

4. Conclusion

The adoption of personalized medicine will not be propelled by science alone. The value proposition of 'the right drug for the right patient at the right time' will remain an overstatement until concerted action is taken to prepare a receptive healthcare environment. The first steps will involve quantifying and presenting the benefits of personalized medicine in terms of healthcare outcomes and economics, and developing a coherent set of public policies. The membership of the PMC (figure 2), representing many of the

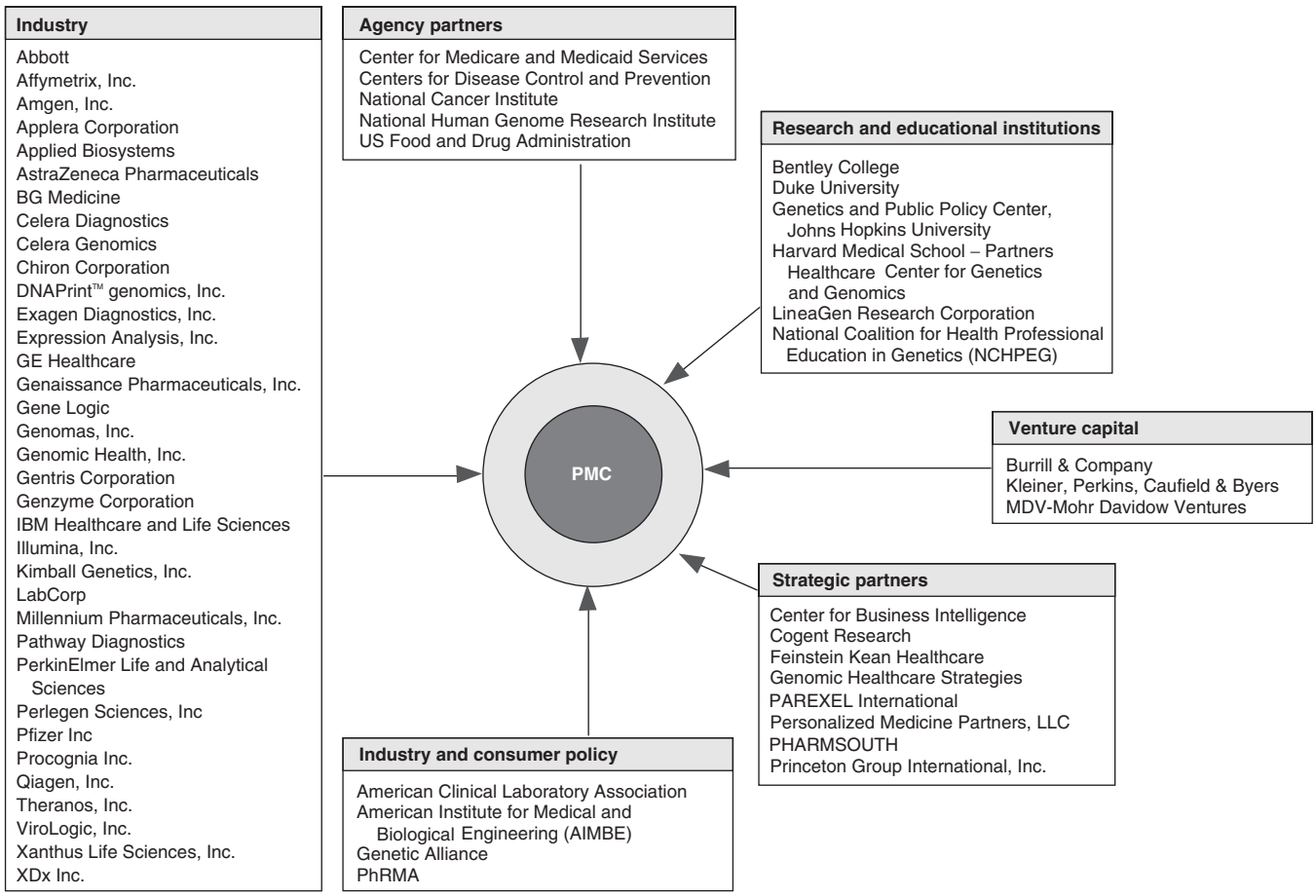

Fig. 2. Personalized Medicine Coalition (PMC) membership, as at September 2005.

stakeholders in personalized medicine, and who encompass academic, industrial, patient, and healthcare provider constituencies, has come together to mold a friendlier landscape for the advancement of personalized medicine through education and advocacy in the public sphere, with particular attention to developing supportive policies and regulations. The PMC is examining and communicating the benefits of personalized medicine by sponsoring studies and surveys, by promoting national events that convene thought leaders, and by advocating policies that will help the effort to reshape medical practice. The PMC believes that all of the key stakeholders have a role to play in this effort. Our success will be measured by how well we promote dialog and understanding among disparate groups and help create a new policy paradigm that keeps pace with increasing scientific knowledge of the molecular foundations of illness and health.

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Correspondence and offprints: Dr *Edward Abrahams*, Personalized Medicine Coalition, 1401 H Street, NW Suite 200, Washington, DC 20005, USA.
E-mail: eabrahams@personalizedmedicinecoalition.org