

## POLICY

# Global implementation of genomic medicine: We are not alone

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Around the world, innovative genomic-medicine programs capitalize on singular capabilities arising from local health care systems, cultural or political milieus, and unusual selected risk alleles or disease burdens. Such individual efforts might benefit from the sharing of approaches and lessons learned in other locales. The U.S. National Human Genome Research Institute and the National Academy of Medicine recently brought together 25 of these groups to compare projects, to examine the current state of implementation and desired near-term capabilities, and to identify opportunities for collaboration that promote the responsible practice of genomic medicine. Efforts to coalesce these groups around concrete but compelling signature projects should accelerate the responsible implementation of genomic medicine in efforts to improve clinical care worldwide.

The growing number of advances in human genomic research that are directly relevant to disease diagnosis, treatment, and prevention coupled with the declining cost of genome sequencing has promoted the use of genomic technologies in routine clinical care (1). Among the many challenges to widespread implementation of genomic medicine, what looms largest is the lack of evidence to demonstrate improved clinical or economic outcomes (2). Other needs include standardization and quality assurance of genomic data produced by clinical laboratories, a clinical-informatics infrastructure for managing genomic information, education for health professionals and patients in using the information, and policies for data sharing that permit ongoing capture of generalizable clinical experiences in what has been termed “evidence-generating medicine” (3). A host of ongoing efforts exist worldwide to establish national implementation strategies for genomic medicine (table S1) (4), but many such efforts are being conducted in relative isolation. Sharing of strategies, data, and standards could minimize wasteful duplication and speed progress in identifying genomics-based interventions and translating them to the clinic.

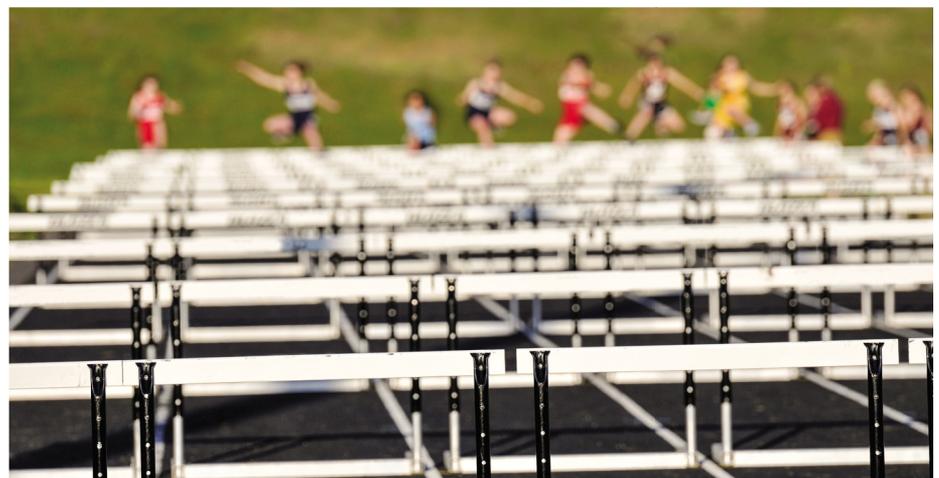
To assess the current global state of the art (2), the U.S. National Human Genome Research Institute and the U.S. National Academy of Medicine convened 90 leaders in genomic medicine from the United States and 25 other countries on five continents for a Global Leaders in Genomic Medicine symposium in 2014 (table S1). Although the organizers attempted to identify and invite every nation working on the implementa-

tion of genomic medicine, participation was somewhat restricted by the lack of systematic information on such efforts and limited travel funding [see full list of participating countries at [www.genome.gov/27555775](http://www.genome.gov/27555775)]. Here we summarize efforts described by the participants, with an emphasis on (i) regions with singular capabilities because of the structures of their health care systems, cultural or political readiness for implementation, or unusual disease burdens or risk-allele frequencies; (ii) the current state of implementation in the various countries and capabilities desired over the next 3 to 5 years; and (iii) opportunities for collaboration to promote the responsible implementation of genomic medicine.

## INTERNATIONAL LANDSCAPE

Early efforts at genomic-medicine collaborations include the European Association for Predictive, Preventive, and Personalised Medicine (EPMA), the European Commission's EuroBioForum and observatory, and the Genomic Medicine Alliance (table S1) (5), which have spearheaded promising projects such as the application of genome sequencing in pharmacogenomics and the development of online pharmacogenomic resources. Related efforts include the International Rare Disease Research Consortium (IRDiRC), which is developing new diagnostic strategies and therapies for rare diseases; the Global Alliance for Genomics and Health (GA4GH), which promotes responsible sharing of genomic data for research (6); and EuroGentest (table S1), which is drafting professional guidelines for diagnostic DNA sequencing.

In an informal poll of participants prior



**Teamwork: Clearing of hurdles to the clinical translation of genomic medicine demands a unified focus.**

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**Table 1. Haves and have nots.** Selected current and desired genomic medicine capabilities across participating countries and regions (number surveyed = 25).

Capability	Today (%)			Desired in 3 to 5 years (%)		
	Not at all	Specialized centers	Widely available	Not at all	Specialized centers	Widely available
Pharmacogenomics	23	66	11	17	29	56
Germline sequencing	23	66	11	11	72	17
Tumor sequencing	17	72	11	11	60	29
Newborn sequencing	64	36	0	11	72	17
Maternal-fetal DNA sequencing	29	65	6	11	66	23
Rare disease diagnosis	23	71	6	6	77	17
Microbial pathogen identification	17	72	11	11	36	53
RNA profiling	50	50	0	11	66	23
Metabolomics	53	47	0	11	78	11
Proteomics	64	36	0	29	60	11
Systematic family history	17	36	46	6	23	71
Genetic counselors	23	47	30	6	17	77
EMRs	23	47	30	6	0	94
Clinical-decision support	33	33	33	6	0	94

to the symposium, nearly all sites reported some genomic medicine capabilities, such as using genotyping or genome or exome sequencing for disease prediction, diagnosis, prevention, and treatment as well as family counseling (Table 1). More than 70% of respondents reported the availability, in specialized centers only, of clinical genomic sequencing resources for targeted cancer treatment, rare disease diagnosis, and microbial pathogen identification, while ~10% reported these capabilities to be widely available. Conversely, more than half reported the lack of any capabilities for newborn genomic sequencing or RNA,

metabolomics, or proteomic profiling. Over the next 3 to 5 years, participants hope to see substantial gains in the availability of clinical genomic resources, particularly for pharmacogenomics, pathogen identification, genetic counseling, electronic medical records (EMRs), and clinical-decision support. Several other technologies, including newborn sequencing, rare disease diagnosis, and RNA profiling, were projected to become available, within 3 to 5 years, in specialized centers where no capability currently exists. The barriers to global implementation of genomic medicine worldwide (Table 2) are similar to those

identified in a 2012 survey that examined U.S. genomic medicine-implementation efforts (2), reinforcing the notion that the global genomic-medicine community shares important challenges and goals.

The most common implementation efforts involve cancer genomics, large-scale exome or whole-genome sequencing, and pharmacogenomics, while several current projects focus on particular geographical priorities (table S2). National efforts to build infrastructures for genome sequencing and other genomic and information technologies are under way in nearly all countries represented at the symposium.

**Table 2. Genomic medicine: Barriers to implementation.**

Lack of evidence of the effectiveness of genomic interventions and related codependent technologies* as well as expertise and training programs in genetics, genomics, informatics, and statistics
High cost and lack of reimbursement for tests and codependent technologies
Need for evidentiary thresholds for genomic testing; quality-control standards for genome technologies; and databases with genomic variants linked to clinical phenotypes
Lack of consensus on what investments are needed in research and health care capacity for effective, sustainable implementation
Limited access to educational information and reliable standardized genotyping or sequencing platforms
Lack of bioinformatics and EMR infrastructure to order, receive, act on, and follow up results and assess the impact of clinical interventions
Concerns over consent and privacy
Need to align genomic research with the future burden of disease and health needs of patients and populations and the development of genomic tests with the development of effective co-dependent technologies
Need to consider ethical and legal aspects of the ownership of genomic information and manage competing interests in a fair and transparent manner

\*A codependent health technology is one that depends on a second technology to achieve or enhance the intended effect, such as a diagnostic test used to determine a patient subgroup that is most likely to respond to a new medication. [www.health.gov.au/internet/hta/publishing.nsf/Content/co-1]

Perhaps the largest such effort is the UK project to sequence 100,000 whole genomes by 2017 through the creation of Genomics England (table S1) (7). This project builds on a national strategy to link the National Health Service (NHS) EMRs to genomic-medicine research and development (table S1), focusing initially on NHS patients with cancer and rare and infectious diseases. The sequenced genomes will be analyzed to enhance each patient's clinical care as well as to create a research dataset linked to EMRs. Genomics England also aims to train the wider health care community in using the technology and will build secure data linkages to the NHS to ensure that the effort leads to improvements in patient care. Pilot studies of 2,000 patients with rare inherited diseases will be completed in 2015, and pilot studies of 3,000 patients with lung, breast, and colon cancer began in late 2014. The main study will involve the sequencing of 30,000 whole genomes per year in these three emphasis areas through 2017 and should produce a rich infrastructure of next-generation genome sequencing centers, a sample pipeline and biorepository, and large-scale data resources for producing new diagnostics and therapies.

Belgium is also building a national genome-sequencing pipeline, the Belgian medical genomics initiative (BeMGI) (table

S1)—a comprehensive network of scientists and clinicians intended to boost research, translate genomics to clinical care, and prepare the next generation of researchers and clinicians to use genomic technologies. Current efforts are devoted to collecting and sharing variant-frequency data and translating next-generation genome sequencing techniques to clinical practice (for example, in diagnosing rare or novel diseases). Similarly, the Estonian government recently approved a pilot program for personal medicine, which involves the sequencing of 5,000 Estonian genomes and the development of an Estonian-specific genotyping array, coupled with automated decision support and training of physicians to use the results in everyday practice. This comprehensive approach will be pilot tested in 50,000 individuals within the Estonian Biobank (8) and linked with Estonia's rich national EMR system, through which all residents of Estonia can access their personal medical information via a smartcard-based national identity card. If successful, the resulting array-based test will then be offered to all Estonian residents ages 35 to 65 years, yielding a database of up to 500,000 individuals, each with a longitudinal EMR, genotype, and prescription data for use in disease-risk assessment and drug-response prediction as well as in biomedical research.

Israel's Clalit health system has established a national laboratory that provides all medical institutes in Israel with sequencing-based panels that assess somatic tissue and germline genomic changes for cancer disease risks and treatment responses. It is also testing extensively for founder mutations in various disease states and is developing models of primary care in which patients will be routinely tested with broad genomic panels by staff trained to interpret genomic results.

In Australia, newly developing comprehensive cancer centers are integrating genomics-based cancer research, patient care, and education while giving patients access to the latest experimental protocols and drugs. Several other countries, such as Korea and Kuwait, are pursuing more limited genome-sequencing programs, some in close collaboration with the private sector to build capacity and expertise. These and many other participating nations expressed their willingness to deposit their resulting sequence and phenotype data in widely accessible databases such as ClinVar (9) or db-GaP (table S1). Such sharing will not only facilitate the interpretation of human-genomic variation globally but also give external visibility to these nations' emerging programs and better integrate their scientists into the international genomics research community.

Canada's Genomics and Personalized Health competition (GAPH) is a somewhat different approach to building national genomics capacity and assessing the cost-effectiveness and impact of genomic technologies on patient outcomes (table S1). Seventeen projects have been funded to support genomic-medicine implementation and related research in health administration, health technology, and comparative effectiveness. Close involvement of the private sector is an important and innovative component and is reflected in the participation of 19 biotechnology-oriented companies in the project teams. Private-sector involvement is also critical to Kuwait's Genatak sequencing initiative in which patients themselves pay for their whole-genome sequencing (table S1). Japan is implementing a program somewhat similar to Canada's GAPH in its Implementation of Genomic Medicine project to establish a network of genomics-focused biobanks, build a comprehensive genomic-variation database, and perform studies to assess clinical efficacy and utility of genomic information in clinical practice.

A third approach—the use of highly focused pilot programs to build capac-

**Table 3. Opportunities for international collaborations.****Evidence generation**

- Catalog ongoing evidence-generating projects
- Assess availability of data and specimens
- Define standards for evidence
- Establish standards for genetic and genomic tests
- Encourage development of professional practice guidelines
- Identify countries/systems willing to enable access to patient data
- Develop systems to capture outcomes from EMRs and other clinical systems

**Health information technology**

- Define key elements that should be stored in EMR
- Identify and share existing IT solutions that are more robust and generalizable (clinical decision support, variant databases, informatics pipelines)
- Develop global resource for actionable clinical variants
- Define and link necessary federated databases needed to implement genomic medicine
- Collect and aggregate gene and variant data [for example, Exome Aggregation Consortium (ExAC), ClinVar]
- Develop controlled vocabulary for phenotypes (ontology); identify available ontologies
- Establish clearinghouse of genomic medicine implementation guidelines

**Education/workforce development**

- Genomics professionals
  - Collect data on genomic professional workforce and training in different countries
  - Summarize existing workforce surveys and conduct new ones as needed
  - Share competencies and training paradigms
  - Compare training paradigms for geneticists and identify best practices
  - Examine extending current capabilities by telemedicine and other remote approaches
- Other health professionals
  - Examine curricula and determine where genetics competency training can be accommodated
  - Define necessary genomic competencies for trainees at completion of training, which may differ across regions/countries
  - Deploy new educational tools, such as distance learning
  - Develop region/country-specific teaching materials, perhaps on common templates
- Public
  - Adapt existing products and activities, such as DNA Day, to specific cultures
  - Extend to students at secondary school level
  - Engage patient support groups to sponsor programs, develop and distribute educational materials
  - Provide clearinghouse for accumulated educational resources
  - Consider novel educational paradigms

**Pharmacogenomics**

- Promote improved quality-of-evidence base for pharmacogenomics implementation
- Prioritize for study and implementation inexpensive drugs with risk of treatment failure or severe adverse drug reactions likely to be limited to genetically defined subset
- Develop and pilot large-scale implementation project around successful programs such as global eradication of genetically mediated SJS/TEN

**Policy**

- Data sharing and regulatory issues
  - Map current activities and issues being addressed
  - Perform gap analysis
  - Establish “network of networks” in policy development to share information
- Costs and benefits
  - Identify burdens of disease and points in care pathway where genomic tools would integrate and have the greatest impact on outcomes
  - Improve capacity for conducting convincing economic, feasibility, and sustainability analyses
  - Perform economic, feasibility, and sustainability analyses from perspective of different stakeholders, such as payers, delivery systems, national health services
  - Engage payers and payment decision processes
  - Work in and learn from systems with one or a few centralized payers

ity and demonstrate effectiveness before full-scale implementation—capitalizes on disproportionate disease burdens or singular capabilities within a given country. For example, Luxembourg's Centre for systems biomedicine is leveraging local expertise in neurobiology, pathway analysis, and community-driven annotation (10, 11) to create an interactive map that charts the genetic and molecular underpinnings of Parkinson's disease (12). This map will be integrated with genome sequence data to facilitate early diagnosis and molecular stratification of patients. Singapore's Personalized Omic Lattice for Advanced Research and Improving Stratification (POLARIS) project takes advantage of local expertise and interest in genomics and ophthalmology in launching a pilot effort of transforming growth factor- $\beta$ -induced (*TGFBI*) sequencing to assess genetic risk for stromal corneal dystrophies (13). This effort will be followed by the implementation of a 90-gene panel that targets gastrointestinal cancers—diseases of high burden in Singapore—in a systematic effort to develop a nationwide framework for genetic and genomic testing.

Thailand's Ministry of Public Health and Ramathibodi Hospital are focusing on a condition that occurs at unusually high frequency locally and was recently shown to have strong genetic determinants. Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is a devastating and often fatal cutaneous reaction to medications that is largely mediated by high-risk HLA alleles. Thailand has one of the highest rates of SJS/TEN in the world, mainly attributable to a high frequency of these risk alleles and use of causative drugs. Ramathibodi hospital has launched a "pharmacogenetics card" that can be carried in a wallet and provides a patient's HLA variant information, which predicts the risk of contracting SJS/TEN from specific drugs. Initial cost-effectiveness studies have been sufficiently convincing that the Thai government has agreed to provide the testing as standard of care (14). Singapore has come to the same conclusion: Asian patients who are being considered for carbamazepine treatment are offered *HLA-B\*15:02* screening (15, 16).

These three briefly described approaches—population-wide genomic sequencing and EMR integration, coordinated nationwide genomic medicine research programs, and localized efforts that focus on unusual capabilities or needs—demonstrate that no country has a monopoly on the im-

plementation of genomic medicine. Quite the contrary, implementation is expanding globally in diverse and highly innovative ways. Yet here again, as noted in early U.S. genomic medicine implementation programs (2), many of these efforts are being conducted with little interaction or collaboration. Given the rapid growth of the genomics-based biotechnology sector (17) and the pressure on university-based researchers to commercialize their work (18), some degree of competition is to be expected. Still, willingness to share effective tools and strategies through consortia such as the Electronic MEDical Records and GENomics (eMERGE) network (19), the Pharmacogenomics KnowledgeBase (PharmGKB), the Implementing GeNomics In pracTice (IGNITE) network, and the GAPH, IRDiRC, and GA4GH efforts described above demonstrate the possibilities for synergistic global interactions (table S1). Indeed, the international collaborations GA4GH, IRDiRC, and GAPH, which focus predominantly on research, illustrate the potential power of such alliances and the readiness of the genomics community to form them. Given the critical need for clinical-evidence generation and evaluation of genomic medicine interventions as well as the value of harnessing information from diverse populations to capture the immensity of human genomic variation, international collaborative projects in clinical implementation are an obvious solution.

#### MULTINATIONAL TEAMWORK

Several areas in particular could benefit substantially from multinational collaborations in genomic-medicine implementation (Table 3). Even when taking into account cultural differences as well as variations in public perception, governance structures, health care systems, resources, infrastructure, allele frequencies, and prevalent diseases, there is much to be learned and the potential for unnecessary duplication is so great that some degree of coordination and sharing of results is critical. Systematic mapping of ongoing implementation projects worldwide and an inventory of available evidence and evidence-generation projects will help to define gaps and reveal how a particular group can best interact with existing efforts.

**Evidence generation.** Studies designed to determine the value of genomic medicine for patients, clinicians, and health care systems are among the most expensive of the potential international collaborations, and

considerable work is ongoing, as detailed above. Despite differences in health care delivery systems, research in a variety of disciplines has demonstrated the value and relevance of data accumulated in diverse settings (20, 21). International collaborations have amply shown the speed with which multinational consortia can answer questions that few countries can tackle on their own, as demonstrated for survival after myocardial infarction (22), the global burden of disease (23), and HIV/AIDS (24). As many genomic-medicine implementation projects are already in progress, a critical first step is to catalog ongoing evidence-generating projects and the genomics-based interventions that they can be used to evaluate. Such a catalog should include the availability of these projects' specimens and data, including patient data, for additional research. Registries such as the Australia and New Zealand clinical trials registry, the E.U. Clinical Trials Register, and ClinicalTrials.gov (table S1) (25) could conceivably be adapted to receive and provide information about evidence-generation projects in genomic medicine.

To fill gaps in evidence identified by surveying the cataloged projects, a key next step is to identify countries and health care systems willing to enable access to patient data, within appropriate constraints of policy, privacy, and consent. Differences across systems—including but not limited to language—also must be evaluated to find those most scientifically advantageous for combined analysis. Systems will then be needed to capture relevant outcomes from EMRs and other clinical systems and settings as well as to analyze and interpret the findings. Funding for these efforts is needed, but to the degree that studies can be embedded in ongoing clinical care, costs of evidence generation might be reduced substantially (26–28).

Another important step is to define standards for what constitutes sufficient evidence to implement a genomic medicine intervention, which likely will vary depending on whether a gene, genetic variant, or genetic test is under consideration and whether it would be used for risk prediction, diagnosis, treatment, or an understanding of pathogenesis. Also needed are additional standards for performance of genetic tests, with emphasis on interpretation and clinical decision support, and standards for incorporating genomic information into EMRs. Once a sufficient body of evidence is avail-

able, professional organizations and policy-makers will need to develop professional practice guidelines suitable to a specific setting or country. For example, the National Health and Medical Research Councils of Australia and New Zealand are developing a framework and principles to facilitate the translation of genomic-based tests from discovery to health care (table S1).

**Health information technology.** With the possible exception of imaging, few areas of medicine are as dependent on information technology (IT) as genomics, given the vastness of genome sequence data. Although sequence data can and likely should be stored and manipulated outside EMRs (29), extracting even the clinically relevant genomic variants found in a single patient is a challenging task. Because of the rapid evolution of knowledge about clinically relevant variants and the changing clinical situation of an individual patient, a dynamic approach is needed for presenting variant information only when it can potentially make a difference in that individual's care (30). In addition, genome sequence data should ideally be retrievable for use later in a patient's clinical course and throughout their lifetime and should be accessible to other specialists and care systems as needed.

A critical first step is to define the key data elements that should be stored in the EMR, so that construction of IT systems can accommodate them. Truly global resources for actionable clinical genomic variants are urgently needed and could build on current efforts such as the Clinical Genome Resource (ClinGen) (table S1) (31), which includes the ClinVar database of the U.S. National Center for Biotechnology Information (9). Other federated databases necessary to interpret variants and implement genomic medicine, such as the international Exome Aggregation Consortium (ExAC) dataset (table S1) and the Sanger Institute's Database of Chromosomal Imbalance and PHenotype in humans using Ensembl Resources (DECIPHER) (32), are needed, as is the aggregation of worldwide genomic-variant data and agreed-upon strategies to create relevant reference genome sequences where needed to underpin these resources. Use of available and widely accepted controlled vocabularies (ontologies) for phenotypes and avoidance of proliferation of local or regional ontologies will be essential to the interpretation of variants and sharing of information. The Innovative Medicine initiative project ETRIKS, funded jointly by

the European Union and industry, aims to create and run an open, sustainable research informatics and analytics platform for sharing data and supporting translational research in personalized medicine (table S1).

**Education and workforce development.** Educational needs will vary by target group (Table 3). Assessment of the currently available genomic professional workforce and estimates of workforce needs—although likely to show shortages at almost every level in almost every country—will help to prioritize educational programs that can then be tailored to the settings in which genomics-based care will be delivered, such as through routine primary care, specialized genetic clinics, or pharmacists or other allied health personnel. Competencies need to be defined and appropriate educational programs developed for health care professionals at multiple levels within a given system (see National Coalition for Health Professional Education in Genetics, table S1) (33). Integration of genomics into health-professional curricula is becoming increasingly necessary, and, although translation for language and cultural appropriateness will be needed, global sharing, rather than reinventing, of effective training paradigms and best practices is a worthwhile endeavor. Online tools help to facilitate rapid implementation and global distribution (for example, Coursera and EuroGenTest clinical utility gene cards, table S1). Educational materials for patients, policy-makers, and regulatory agents should also be built from new and available resources, translated and customized for specific cultures and target audiences, (34), and dispersed through an information clearinghouse.

**Pharmacogenomics.** Several pharmacogenomic applications have already been widely implemented in the United States and elsewhere (1, 35, 36) and could represent an “early win” ripe for transnational sharing of best practices and lessons learned. Effective international collaborations have been formed to study the genomics of adverse drug reactions (37, 38), but actual implementation efforts have been more isolated. The Pharmacogenomics for Every Nation Initiative (PGENI) is a notable exception, promoting integration of pharmacogenomics into public health decision-making by using population-specific allele-frequency data for nationally tailored drug selection in developing nations (table S1). Also being used clinically are guidelines from the Pharmacogenomics research network's Clinical

Pharmacogenetics Implementation Consortium (CPIC) (table S1), which provides recommendations on drug selection and dosing on the basis of an individual's genotypic data.

Collaborative implementation efforts in pharmacogenomics could promote the generation of an improved evidence base that focuses on inexpensive drugs characterized by treatment failure, such as clopidogrel (39), or severe adverse reactions, such as abacavir (40), likely to be limited to a genetically defined subset of patients. The pharmacogenomics card for avoidance of SJS/TEN being implemented in Thailand is an elegantly simple and practical approach for reducing the incidence of one of the most feared adverse drug reactions. Wider implementation of this approach in neighboring countries that have similar health systems and ancestries, with an ultimate aim of global eradication of genetically related SJS/TEN, appears to be an achievable goal around which an international genomic-medicine collaborative could coalesce.

Application of whole-genome sequencing in pharmacogenomics eventually could fully define an individual's personalized pharmacogenomics profile (41). Customizing such an approach in a targeted sequencing effort of the several hundred pharmacogenes involved in drug metabolism and transport or a smaller subset of clinically actionable pharmacogenes would reduce costs and make this application more immediately affordable than more comprehensive sequencing efforts (42).

**Policy and regulatory issues.** Multiple international initiatives are addressing policy needs to facilitate data sharing in genomic research, particularly the Canadian-led Public Population Project in genomics and Society (P<sup>3</sup>G) (43) and Global Alliance for Genomics and Health (GA4GH) (table S1) (14). Such efforts are quite relevant to genomic-medicine implementation and, as with the evidence realm, an assessment of current activities along with a gap analysis are important initial steps. Harmonizing national ethical guidelines and regulatory frameworks as feasible is essential for successful international collaborations, as is a complete understanding of regional laws that govern genomics research, privacy, and confidentiality. To evaluate costs, risks, and benefits of genomic interventions, one must identify diseases for which genomic tools would have the greatest impact on patient and population outcomes—such as cancers,

metabolic disorders, anti-HIV therapy, or well-defined genetic disorders such as cystic fibrosis. By integrating economic assessments into translational research, scientists and clinicians can determine the utility and relative value of genomic interventions and use the data to inform clinical decision-makers and policy-makers. Expanding single-country studies of cost-effectiveness to multiple health care systems, through multinational collaborations, may help to identify key structural components that promote favorable cost-benefit ratios (44).

## COMING TOGETHER

The wealth of international programs actively engaged in genomic-medicine implementation and the potential for synergy and collaboration among them present exciting opportunities for speeding knowledge generation and improving patient care. Especially in this online age, none of these projects should have to labor in isolation. Several organizations are already showing the power of the international genomics community to form effective collaborations around research, although most are closer to the generation of new knowledge than to implementation of that knowledge for improving patient care. Engaging and building on the ongoing work of these groups will be critical in furthering the effort without wasteful duplication. Coalescing these groups around concrete but compelling signature projects may have a galvanizing effect that will facilitate similar programs in the future.

To explore these possibilities, several participating investigators and countries have formed a Global Genomic Medicine Collaborative (G2MC; [www.iom.edu/G2MC](http://www.iom.edu/G2MC)) hosted by the U.S. National Academy of Medicine as part of its Roundtable on Translating Genomic-Based Research for Health (table S1). Goals of the G2MC are to serve as a nexus for genomic medicine activities globally, develop opportunities for global genomic-medicine implementation and outcomes research, and capture and disseminate best practices across the global community.

Recognizing that this initial survey has likely failed to capture many relevant projects and interested countries, the authors invite scientists and policy-makers who represent their governments' genomic medicine-implementation efforts to join this collaborative by making their interests known to the authors (in particular, G.S.G., G.P.P., and J.E.L.W.). Genomic medicine has

the potential to dramatically change the way medical professionals deliver health care. As we work toward realizing our common interests in the appropriate implementation of genomic medicine, it is indeed encouraging to know that none of us need to tackle these challenges alone.

## SUPPLEMENTARY MATERIALS

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Table S1. Genomics programs worldwide: URLs

Table S2. Specialized genomic medicine-implementation projects in participating countries and regions

## REFERENCES AND NOTES

- J. J. McCarthy, H. L. McLeod, G. S. Ginsburg, Genomic medicine: A decade of successes, challenges, and opportunities. *Sci. Transl. Med.* **5**, 189sr4 (2013).
- T. A. Manolio, R. L. Chisholm, B. Ozenberger, D. M. Roden, M. S. Williams, R. Wilson, D. Bick, E. P. Bottinger, M. H. Brilliant, C. Eng, K. A. Frazer, B. Korf, D. H. Ledbetter, J. R. Lupski, C. Marsh, D. Mrazek, M. F. Murray, P. H. O'Donnell, D. J. Rader, M. V. Relling, A. R. Shuldiner, D. Valle, R. Weinsilb, E. D. Green, G. S. Ginsburg, Implementing genomic medicine in the clinic: The future is here. *Genet. Med.* **15**, 258–267 (2013).
- P. J. Embi, P. R. Payne, Evidence generating medicine: Redefining the research-practice relationship to complete the evidence cycle. *Med. Care* **51** (suppl. 3), S87–S91 (2013).
- B. Simone, W. Mazzucco, M. R. Gualano, A. Agodi, D. Coviello, F. Dagna Bricarelli, B. Dallapiccola, E. Di Maria, A. Federici, M. Genuardi, L. Varesco, W. Ricciardi, S. Boccia-GENISAP Network, The policy of public health genomics in Italy. *Health Policy* **110**, 214–219 (2013).
- D. N. Cooper, A. Brand, V. Dolzan, P. Fortina, F. Innocenti, M. T. Lee, M. Macek, F. Al-Mulla, B. Prainsack, A. Squassina, E. Vayena, A. Vozikis, C. M. S. Williams, G. P. Patrinos, Bridging genomics research between developed and developing countries: The Genomic medicine alliance. *Pers. Med.* **11**, 615–623 (2014).
- E. C. Hayden, Geneticists push for global data-sharing. *Nature* **498**, 16–17 (2013).
- Select Committee on Science and Technology, House of Lords, Second Report—Genomic Medicine (London, The Stationery Office, HL Paper 107-I, 2009), p.104.
- L. Leitsalu, T. Haller, T. Esko, M. L. Tammesoo, H. Alavere, H. Snieder, M. Perola, P. C. Ng, R. Mägi, L. Milani, K. Fischer, A. Metspalu, Cohort Profile: Estonian Biobank of the Estonian Genome Center, University of Tartu. *Int. J. Epidemiol.* **11**, (2014). 10.1093/ije/dyt268
- M. J. Landrum, J. M. Lee, G. R. Riley, W. Jang, W. S. Rubinstein, D. M. Church, D. R. Maglott, ClinVar: Public archive of relationships among sequence variation and human phenotype. *Nucleic Acids Res.* **42** (D1), D980–D985 (2014).
- I. Thiele, N. Swainston, R. M. Fleming, A. Hoppe, S. Sahoo, M. K. Aurich, H. Haraldsdottir, M. L. Mo, O. Rolfsson, M. D. Stobbe, S. G. Thorleifsson, R. Agren, C. Bölling, S. Borel, A. K. Chavali, P. Dobson, W. B. Dunn, L. Endler, D. Hala, M. Hucka, D. Hull, D. Jameson, N. Jamshidi, J. J. Jonsson, N. Juty, S. Keating, I. Nookaew, N. Le Novère, N. Malys, A. Mazein, J. A. Papin, N. D. Price, E. Selkov, Sr, M. I. Sigurdsson, E. Simeonidis, N. Sonnenschein, K. Smallbone, A. Sorokin, J. H. van Beek, D. Weichart, I. Goryanin, J. Nielsen, H. V. Westerhoff, D. B. Kell, P. Mendes, B. Ø. Palsson, A community-driven global reconstruction of human metabolism. *Nat. Biotechnol.* **31**, 419–425 (2013).
- I. Thiele, B. Ø. Palsson, Reconstruction annotation jamborees: A community approach to systems biology. *Mol. Syst. Biol.* **6**, 361 (2010).
- K. A. Fujita, M. Ostaszewski, Y. Matsuoka, S. Ghosh, E. Glaab, C. Trefois, I. Crespo, T. M. Perumal, W. Jurkowski, P. M. Antony, N. Diederich, M. Buttini, A. Kodama, V. P. Satagopam, S. Eifes, A. Del Sol, R. Schneider, H. Kitano, R. Balling, Integrating pathways of Parkinson's disease in a molecular interaction map. *Mol. Neurobiol.* **49**, 88–102 (2014).
- R. Lakshminarayanan, E. N. Vithana, S. M. Chai, S. S. Chaurasia, P. Saraswathi, A. Venkatraman, C. Rojare, D. Venkataraman, D. Tan, T. Aung, R. W. Beuerman, J. S. Mehta, A novel mutation in transforming growth factor-beta induced protein (TGFB1p) reveals secondary structure perturbation in lattice corneal dystrophy. *Br. J. Ophthalmol.* **95**, 1457–1462 (2011).
- W. Rattanavipapong, T. Koopittakajorn, N. Praditsithikorn, S. Mahasirimongkol, Y. Teerawattananon, Economic evaluation of HLA-B\*15:02 screening for carbamazepine-induced severe adverse drug reactions in Thailand. *Epilepsia* **54**, 1628–1638 (2013).
- D. Dong, C. Sung, E. A. Finkelstein, Cost-effectiveness of HLA-B\*15:02 genotyping in adult patients with newly diagnosed epilepsy in Singapore. *Neurology* **79**, 1259–1267 (2012).
- D. S. Toh, L. L. Tan, D. C. Aw, S. M. Pang, S. H. Lim, T. Thirumoorthy, H. Y. Lee, Y. K. Tay, S. K. Tan, A. Vasudevan, A. Laateef, Y. Y. Chong, Y. C. Chan, C. Loke, C. L. Chan, E. S. Koay, E. C. Ren, E. J. Lee, C. Sung, Building pharmacogenetics into a pharmacovigilance program in Singapore: Using serious skin rash as a pilot study. *Pharmacogenomics J.* **14**, 316–321 (2014).
- I. R. Wiechers, N. C. Perin, R. Cook-Deegan, The emergence of commercial genomics: Analysis of the rise of a biotechnology subsector during the Human Genome Project, 1990 to 2004. *Genome Med.* **5**, 83 (2013).
- T. Caulfield, S. H. Harmon, Y. Joly, Open science versus commercialization: A modern research conflict? *Genome Med.* **4**, 17 (2012).
- O. Gottesman, H. Kuivaniemi, G. Tromp, W. A. Faucett, R. Li, T. A. Manolio, S. C. Sanderson, J. Kannry, R. Zinberg, M. A. Basford, M. Brilliant, D. J. Carey, R. L. Chisholm, C. G. Chute, J. J. Connolly, D. Crosslin, J. C. Denny, C. J. Gallego, J. L. Haines, H. Hakonarson, J. Harley, G. P. Jarvik, I. Kohane, I. J. Kullo, E. B. Larson, C. McCarty, M. D. Ritchie, D. M. Roden, M. E. Smith, E. P. Bottinger, M. S. Williams, MERGE Network, The Electronic Medical Records and Genomics (eMERGE) Network: Past, present, and future. *Genet. Med.* **15**, 761–771 (2013).
- A. Sommer, Preventing blindness and saving lives: The centenary of vitamin A. *JAMA Ophthalmol.* **132**, 115–117 (2014).
- R. J. Berry, Z. Li, J. D. Erickson, S. Li, C. A. Moore, H. Wang, J. Mulinare, P. Zhao, L. Y. Wong, J. Gindler, S. X. Hong, A. Correa, Collaborative Project for Neural Tube Defect Prevention, Prevention of neural-tube defects with folic acid in China. China-U.S. *N. Engl. J. Med.* **341**, 1485–1490 (1999).
- Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. *Lancet* **2**, 349–360 (1988).
- C. J. Murray, M. Ezzati, A. D. Flaxman, S. Lim, R. Lozano, C. Michaud, M. Naghavi, J. A. Salomon, K. Shibuya, T. Vos, A. D. Lopez, GBD 2010: A multi-investigator collaboration for global comparative descriptive epidemiology. *Lancet* **380**, 2055–2058 (2012).
- D. Avila, K. N. Althoff, C. Mugglin, K. Wools-Kaloustian, M. Koller, F. Dabis, D. Nash, T. Gspöner, S. Sungkanuparph, C. McGowan, M. May, D. Cooper, C. Chimbete, M. Wolff, A. Collier, H. McManus, M. A. Davies, D. Costagliola, B.

- Crabtree-Ramirez, R. Chaiwarith, A. Cescon, M. Cornell, L. Diero, P. Phanuphak, A. Sawadogo, J. Ehmer, S. P. Eholie, P. C. Li, M. P. Fox, N. R. Gandhi, E. González, C. K. Lee, C. J. Hoffmann, A. Kambugu, O. Keiser, R. Ditangco, H. Prozesky, F. Lampe, N. Kumarasamy, M. Kitahata, E. Lugina, R. Lyamuya, S. Vonthanak, V. Fink, A. d'Arminio Monforte, P. M. Luz, Y. M. Chen, A. Minga, J. Casabona, A. Mwango, B. Y. Choi, M. L. Newell, E. A. Bukusi, K. Ngonyani, T. P. Merati, J. Otieno, M. B. Bosco, S. Phiri, O. T. Ng, K. Anastos, J. Rockstroh, I. Santos, S. Oka, G. Somi, C. Stephan, R. Teira, D. Wabwire, G. Wandeler, A. Boulle, P. Reiss, R. Wood, B. H. Chi, C. Williams, J. A. Sterne, M. Eggerle, DEA and ART Cohort Collaborations, Immunodeficiency at the start of combination antiretroviral therapy in low-, middle-, and high-income countries. *J. Acquir. Immune Defic. Syndr.* **65**, e8–e16 (2014).
25. D. A. Zarin, T. Tse, R. J. Williams, R. M. Califf, N. C. Ide, The ClinicalTrials.gov results database—Update and key issues. *N. Engl. J. Med.* **364**, 852–860 (2011).
26. M. S. Lauer, Time for a creative transformation of epidemiology in the United States. *JAMA* **308**, 1804–1805 (2012).
27. G. Ginsburg, Medical genomics: Gather and use genetic data in health care. *Nature* **508**, 451–453 (2014).
28. T. B. Ferguson Jr., E. D. Peterson, L. P. Coombs, M. C. Eiken, M. L. Carey, F. L. Grover, E. R. DeLong, Society of Thoracic Surgeons and the National Cardiac Database, Use of continuous quality improvement to increase use of process measures in patients undergoing coronary artery bypass graft surgery: A randomized controlled trial. *JAMA* **290**, 49–56 (2003).
29. J. Starren, M. S. Williams, E. P. Bottinger, Crossing the omic chasm: A time for omic ancillary systems. *JAMA* **309**, 1237–1238 (2013).
30. C. L. Overby, I. Kohane, J. L. Kannry, M. S. Williams, J. Starren, E. Bottinger, O. Gottesman, J. C. Denny, C. Weng, P. Tarczy-Hornoch, G. Hripsak, Opportunities for genomic clinical decision support interventions. *Genet. Med.* **15**, 817–823 (2013).
31. E. M. Ramos, C. Din-Lovinescu, J. S. Berg, L. D. Brooks, A. Duncanson, M. Dunn, P. Good, T. J. Hubbard, G. P. Jarvik, C. O'Donnell, S. T. Sherry, N. Aronson, L. G. Biesecker, B. Blumberg, N. Calonge, H. M. Colhoun, R. S. Epstein, P. Flicek, E. S. Gordon, E. D. Green, R. C. Green, M. Hurles, K. Kawamoto, W. Knaus, D. H. Ledbetter, H. P. Levy, E. Lyon, D. Maglott, H. L. McLeod, N. Rahman, G. Randhawa, C. Wicklund, T. A. Manolio, R. L. Chisholm, M. S. Williams, Characterizing genetic variants for clinical action. *Am. J. Med. Genet. C. Semin. Med. Genet.* **166C**, 93–104 (2014).
32. H. V. Firth, S. M. Richards, A. P. Bevan, S. Clayton, M. Corpas, D. Rajan, S. Van Vooren, Y. Moreau, R. M. Pettett, N. P. Carter, DECIPHER: Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources. *Am. J. Hum. Genet.* **84**, 524–533 (2009).
33. B. R. Korf, A. B. Berry, M. Limson, A. J. Marian, M. F. Murray, P. P. O'Rourke, E. R. Passamani, M. V. Relling, J. Tooker, G. J. Tsongalis, L. L. Rodriguez, Framework for development of physician competencies in genomic medicine: Report of the competencies working group of the inter-society coordinating committee for physician education in genomics. *Genet. Med.* **16**, 804–809 (2014).
34. T. A. Reydon, K. Kampourakis, G. P. Patrinos, Genetics, genomics and society: The responsibilities of scientists for science communication and education. *Pers. Med.* **9**, 633–643 (2012).
35. D. F. Carr, A. Alfirevic, M. Pirmohamed, Pharmacogenomics: Current State-of-the-Art. *Genes (Basel)* **5**, 430–443 (2014).
36. C. Sukasem, A. Puangpetch, S. Medhasi, W. Tassaneeyakul, Pharmacogenomics of drug-induced hypersensitivity reactions: Challenges, opportunities and clinical implementation. *Asian Pac. J. Allergy Immunol.* **32**, 111–123 (2014).
37. A. L. Holden, J. L. Contreras, S. John, M. R. Nelson, The international serious adverse events consortium. *Nat. Rev. Drug Discov.* **13**, 795–796 (2014).
38. M. Pirmohamed, G. Burnside, N. Eriksson, A. L. Jorgensen, C. H. Toh, T. Nicholson, P. Kesteven, C. Christersson, B. Wahlström, C. Staffberg, J. E. Zhang, J. B. Leathart, H. Kohnke, A. H. Maitland-van der Zee, P. R. Williamson, A. K. Daly, P. Avery, F. Kamali, M. Wadelius, EU-PACT Group, A randomized trial of genotype-guided dosing of warfarin. *N. Engl. J. Med.* **369**, 2294–2303 (2013).
39. J. M. Pulley, J. C. Denny, J. F. Peterson, G. R. Bernard, C. L. Vnencak-Jones, A. H. Ramirez, J. T. Delaney, E. Bowton, K. Brothers, K. Johnson, D. C. Crawford, J. Schildcrout, D. R. Masys, H. H. Dilks, R. A. Wilke, E. W. Clayton, E. Shultz, M. Laposata, J. McPherson, J. N. Jirjis, D. M. Roden, Operational implementation of prospective genotyping for personalized medicine: The design of the Vanderbilt PREDICT project. *Clin. Pharmacol. Ther.* **92**, 87–95 (2012).
40. M. A. Martin, D. L. Kroetz, Abacavir pharmacogenetics—From initial reports to standard of care. *Pharmacotherapy* **33**, 765–775 (2013).
41. C. Mizzi, B. Peters, C. Mitropoulou, K. Mitropoulos, T. Katsila, M. R. Agarwal, R. H. van Schaik, R. Drmanac, J. Borg, G. P. Patrinos, Personalized pharmacogenomics profiling using whole-genome sequencing. *Pharmacogenomics* **15**, 1223–1234 (2014).
42. K. Kampourakis, E. Vayena, C. Mitropoulou, R. H. van Schaik, D. N. Cooper, J. Borg, G. P. Patrinos, Key challenges for next-generation pharmacogenomics: Science & Society series on Science and Drugs. *EMBO Rep.* **15**, 472–476 (2014).
43. B. M. Knoppers, I. Fortier, D. Legault, P. Burton, The Public Population Project in Genomics (P3G): A proof of concept? *Eur. J. Hum. Genet.* **16**, 664–665 (2008).
44. S. R. Snyder, C. Mitropoulou, G. P. Patrinos, M. S. Williams, Economic evaluation of pharmacogenomics: A value-based approach to pragmatic decision making in the face of complexity. *Public Health Genomics* **17**, 256–264 (2014).

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