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Capacity building for assessing new technologies: approaches to examining personalized medicine in practice

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Abstract

This article focuses on the overarching question: how can we use existing data to develop the capacity to improve the evidence base on personalized medicine technologies and particularly regarding their utilization and clinical utility? We focus on data from health payers who are key stakeholders in capacity building, as they need data to guide decisions and they develop data as part of operations. Broadly defined, health payers include insurance carriers, third party payers, health-plan sponsors and organized delivery systems. Data from health payers have not yet been widely used to assess personalized medicine. Now, with an increasing number of personalized technologies covered and reimbursed by health payers, and an increasing number of emerging technologies that will require policy decisions, there is a great opportunity to develop the evidence base using payer data and by engaging with these stakeholders. Here, we describe data that are available from, and are being developed by, health payers and assess how these data can be further developed to increase the capacity for future research, using three examples. The examples suggest that payer data can be used to examine clinical utility and approaches can be developed that simultaneously address the characteristics of personalized medicine, real world data and organizations. These examples can now help us to elucidate how to best examine clinical utility in actual practice and build evaluation approaches that can be applied to future technologies.

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Keywords

cancer; data development; evidence development; health payer; organized delivery system; personalized medicine; pharmacy benefits manager

An important component of appropriately translating personalized medicine technologies into clinical practice and policy is developing the evidence regarding their clinical application [1]. While evidence is needed along all the stages of the translation continuum, it is particularly in the later stages, such as implementation, dissemination, outcomes and policy, that there are major gaps in the evidence base [2]. One key focus has been on the lack of evidence on clinical utility for genomic technologies, which will be incorporated into personalized medicine strategies together with characteristics of the patient, such as physiological or behavioral and characteristics of the environment. We define clinical utility as the balance of benefits and harms associated with a personalized medicine intervention in practice, including improvements in measurable clinical outcomes and the added value in clinical management and decision-making [3,4]. In response to a need for such evidence in this regard, funding has been dedicated for translational research [101] and groups are forming to address these gaps [102]. It is likely that multiple approaches are going to be needed to develop the evidence on personalized medicine so that it is useful for informing decisions about clinical practice and policy [5].

This article addresses the overarching question: how can we use existing data to develop capacity to improve the evidence on personalized medicine technologies, such as genomic testing, and particularly regarding their utilization and clinical utility? This is important for at least two reasons. First, it is helpful to focus on the several personalized medicine technologies that have emerged into practice and policy. Despite the fact that some technologies are now well-established (e.g., HER2 testing for trastuzumab [Herceptin®; Genentech, CA, USA]) there is still little known about their use in clinical practice and their clinical utility [1,6–11]. It is because these technologies are now the standard of care that we have an opportunity to better understand their use in actual practice and to examine the associated health outcomes. These examples can now help us to elucidate how best to examine utilization and clinical utility in actual practice, and build evaluation approaches that can be applied to future technologies.

Second, we agree with others who suggest that we need to engage key stakeholders who can help facilitate this research [5,12,13]. Although there are several key stakeholders in evidence development for personalized medicine, we focus here on the health payer. Broadly defined, health payers are “entities that finance or reimburse healthcare and may include insurance carriers, other third party payers, or health plan sponsors” [103]. This definition includes groups that are less prominent in the discussions of evidence development: self-insured employers, pharmacy benefits managers and other similar payer organizations. Payers are critical because of their dual role as users of evidence and creators of data. In the former role, payers need evidence to develop policy and make decisions about what to include in formularies and plans. In the latter role, payers develop data, such as for claims as part of regular operations. Health payer data can now be used to describe the actual use of established and emerging personalized medicine technologies and, in doing so, can help build approaches to examining future technologies.

Responding to the aforementioned overarching question will require the description of data that are available from, and being developed by, health payers and assessing how this data can be further developed to increase the capacity for future research. In this article, we highlight the key findings about the process of researching personalized medicine

technologies using payer data and engaging these stakeholders in research. We describe three examples – data from two large commercial private payers, data collected by pharmacy benefits managers and the data from organized delivery systems. The examples illustrate a range of approaches to capacity development and are based primarily on research conducted by members of the University of California San Francisco (UCSF; CA, USA) Center for Translational and Policy Research on Personalized Medicine (TRANSPERS) [104]. Box 1 provides selected definitions of terms we use in this paper.

Conceptual framework for understanding healthcare utilization

Studies that examine utilization are a step to improving the evidence on clinical utility in actual practice because they can identify factors that are associated with use and because they can examine how the use is associated with benefits and harms. Our underlying conceptual framework for understanding healthcare utilization and clinical utility is derived from the Behavioral Health Model. The Behavioral Health Model has been widely used to empirically examine differences in treatment utilization and health outcomes [14–19]. The model asserts that an individual's use of healthcare services is a function of his/her predisposition to use services (predisposing characteristics), need for healthcare (need characteristics) and factors that impede or promote the use of healthcare services (enabling characteristics). Applying the Behavioral Health Model to the example of personalized medicine helps to elucidate what data are thus needed to fully examine clinical utility. The model is not only useful for examining existing data but also for capacity building, because it can help define an ideal list of variables that would predict healthcare use and outcomes. Data on all variables may not be currently available but could be developed for the future.

Table 1 describes the types of measures that are needed to predict the use of personalized medicine technologies and to examine the health outcomes associated with and/or without use. Table 1 lists example measures for each of the three main classifications of the Behavioral Health Model, which predict healthcare utilization.

Examples to describe health payer data & capacity development

Developing evidence using commercial health plan data

Commercial health plans are health insurance companies that provide, or pay the costs of, medical care [105,106]. These plans typically have data in the form of administrative claims, which are submitted for the purpose of billing and reimbursement for the covered services. These claims data may also be linked to the medical record data of the plan enrollees. Although these data have limitations [20], they can be used to examine the utilization and, to a lesser extent, clinical utility of personalized medicine. In this article, we describe data from commercial health plans, how we obtain data and what is needed to develop the capacity of these data.

We use the specific example of HER2/neu testing for treatment with trastuzumab therapy and gene-expression profiling (OncotypeDX, Genomic Health, CA, USA) for breast cancer treatment decisions. HER2/neu is a test carried out on a tumor using one or a combination of diagnostics [21]. The OncotypeDX test is a unique diagnostic that examines the expression of 21 genes and offers information that can be used for prognosis of recurrence risk as well as to predict the likelihood that a patient will benefit from chemotherapy [4]. Describing who uses personalized medicine for treatment decisions is a necessary first step in addressing the clinical utility of the relevant diagnostics and targeted treatments.

We have used two approaches to work with commercial health plans to examine utilization of personalized medicine for breast cancer because the health plans differ in how they allow

access to and work with researchers. One approach is the use of a data intermediary, the only means by which researchers can access data from some plans. In this model, the intermediary obtains the claims and medical record data, maintains the data in-house, and provides a data analysis service with our scientific guidance [107]. However, a restricted de-identified dataset can also be arranged that is analyzed directly by the study investigators. The second approach is direct collaboration. In this working model, we directly collaborated with the plan's associated foundation, which uses a vendor to abstract data from medical records but releases the de-identified claims and medical record data to us for analysis [22]. Two key differences in the approaches are the time and cost to obtain the data for research purposes. Obtaining data via an intermediary takes longer and costs more than directly working with the health plan foundation. However, one advantage of using an intermediary is that data are believed to be initially of higher quality (e.g., with fewer missing variables), which means our team spends less time in the intermediate stages of data acquisition (e.g., reviewing variables and coding).

Although the methods for obtaining data differ, the general sources of data needed to examine these two clinical scenarios are similar. Both studies require the use of administrative data and medical records review. Applying the Behavioral Model of Health, there are two personalized medicine examples that require data on:

- Outcome variables (utilization of HER2, trastuzumab, gene-expression profiling or adjuvant chemotherapy);
- Predisposing factors (age or race/ethnicity);
- Need (comorbidity, results of tests indicating the genetic status, clinical characteristics, e.g., cancer stage, tumor size, menopause status and estrogen- and progesterone-receptor status);
- Enabling factors (type of health plan and household income).

Table 2 shows the data we obtained and the source of these data. Table 2 shows that multiple data sources are required to capture all of the relevant predictors and outcome variables. In some cases, multiple data sources are also used to ensure the accuracy of individual measures (e.g., use of HER2 tests).

The use of administrative data is relatively straightforward as these are typically coded as part of regular operations; however, the use of medical records requires the development of specific tools for abstracting the needed data. A medical record abstraction tool to collect detailed clinical information that is not available in claims is developed, and then medical record abstractors collect the data we need. We then create a unique database linking the medical record data to the health plan's administrative claims data (containing the information about enrollee age, enrollment, health plan types and the services and procedures rendered), and the health plan's proprietary data (enrollee race/ethnicity and household income).

There are key advantages for evidence development using health plan data. First, health plans have a wealth of data and can be a key contributor to the development of an evidence base for studying emerging technologies. Second, large commercial health plans serve and represent a significant proportion of the insured population. The potential of obtaining critical clinical information from medical records is valuable. There are also key challenges to overcome for future evidence development. In our experience, working with health plan data requires time and innovative data triangulation. No single data source is sufficient for developing the evidence base for studying the utilization of emerging personalized medicine technologies. For example, claims data often lack specific billing codes to identify the use of genomic testing and lack information on health outcomes and genomic information (e.g.,

test results). Medical record review is often costly and hard to implement. Still, our general template for both administrative data analysis and medical records review can be applied to other plan data and this work contributes to developing approaches to collecting data into the future, which we discuss in our 'Conclusion' section.

Pharmacy benefits manager's approach to evidence development

A pharmacy benefits manager (PBM) manages and administers the pharmacy benefit of group health-plan sponsors and offer clients services, such as drug formulary development, manufacturer rebate negotiation and collection, specialty pharmaceutical distribution and mail-order prescription delivery options [23,24]. A major client type is the self-insured employer (SIE), an arrangement in which the employer assumes direct financial responsibility for the costs of enrollees' healthcare claims [108].

Medco (NJ, USA) is one of the top three PBMs in the USA (along with CVS Caremark [RI, USA] and Express Scripts [MO, USA]). Since 2007, Medco has conducted two studies on personalized medicine: a study on CYP2C9/VKORC1 testing for warfarin and a study on CYP2D6 testing for tamoxifen treatment decisions [109]. The overarching objective of these studies is to develop pharmacogenetics data (the use of genetic or genomic information to guide drug treatment decisions). A key feature of the Medco studies is that evidence is being developed prospectively, with existing Medco claims data being primarily used to help identify potential study participants.

Although there are examples of payer initiated prospective studies [110], there are no other examples that we could find where a PBM has worked with its client SIE to conduct prospective research. We are particularly interested in this model because there has been uncertainty about who will lead evidence development in this field and because PBMs are relatively new players in personalized medicine who are now creating a niche of their own in this regard (more recently, CVS Caremark via Generation Health [NJ, USA] has also started their own evidence development for personalized medicine) [111]. The Medco study thus represents a novel approach to evidence development.

We used focused interviews with Medco executives to describe the role of the PBM and the role of participants in the study as it relates to evidence development. Interview topics included why these groups participate, what challenges were identified and what roles these two groups believe they have or could have for building an evidence base.

We learned three main lessons about the approach by Medco. First, prospective studies require willingness and interest of key stakeholders. The Medco experience suggests that many SIEs are very interested in participating generally because of the potential clinical benefit for their employees and the potential to create cost savings by utilizing personalized medicine. In addition, there is an interest to contribute to the field more broadly as SIEs and Medco both reported that, through these studies, they can contribute to evidence at higher levels such as to inform the US FDA. However, some SIEs were concerned that the informed consent and necessary communication to their employees cause anxiety, which becomes a barrier for study participation.

Second, successful patient recruitment requires novel communication mechanisms and carefully thought out roles for SIEs and Medco. Our interviews suggest that SIEs play a role in facilitating patient recruitment; although employers stay at arms length from actual recruitment to protect employee privacy (study recruitment is performed by Medco, and the decision to participate is between the patient and physician), employers provide a means of communication via the intranet, workplace town halls and targeted mailings. These mechanisms are believed to be effective vehicles for employee education and for allaying

concerns, including privacy and future use of study results. Still, Medco reports barriers to patient recruitment in the studies, potentially owing to patients' privacy concerns or lack of understanding the tests. For this and other evidence development efforts to be successful, it is critical to understand and address patients' interests and concerns.

Last, the primary study aim, which is to evaluate novel use of diagnostics, was believed to facilitate the research. Medco felt that a study on diagnostics was less risky than a study of new drugs. Furthermore, the diagnostics being examined are developed and used in some clinical practice but are not widespread. Indeed, some interviewees told us that they are less interested in earlier stages of product development and more in studies of areas that are almost ready for adoption but not quite there yet. It is possible that the Medco studies are facilitated by an interest in studies that will more immediately help with real world coverage decisions [25].

Developing evidence using organized delivery systems: the Veterans Health Administration & Cancer Care Ontario

Organized delivery systems are characterized by patient-care teams, defined patient populations, aligned financial and payment incentives, partnership between medicine and management, information technology, and accountability [26,27]. Members of the TRANSPERS team are working with two organized delivery systems to examine data on personalized medicine and develop capacity for future research: the San Francisco Veterans Affairs Medical Center (SFVAMC; CA, USA) service and Cancer Care Ontario (CCO; ON, Canada). A research team at the SFVAMC is building a unique database to study the utilization of genomic services for nonpolyposis hereditary colon cancer and a team in Ontario, Canada is building capacity via a project to examine HER2 testing in the context of trastuzumab treatment and subsequent monitoring. In both studies, our research teams are developing unique databases that build on the particular data strengths of organized delivery systems, such as the multiple administrative and outcomes databases available. Below, we describe the two organizations and the process of working with each of them in turn, and then focus on their shared key strengths and challenges.

The Veterans Health Administration (VHA; NC, USA) consists of over 1400 sites, including medical centers, community-based outpatient clinics, community living centers, vet centers and other facilities [112]. It is organized around 21 regional veterans integrated service networks (VISNs), which use shared resources to provide care to over 5.5 million veterans each year [28]. VHA national offices work closely with the veterans integrated service networks to ensure safety, privacy and quality of care, and to support quality research and policy to improve the health of the nation's veterans. A system of academic affiliates links VHA medical centers to academic institutions where many VHA health professionals maintain joint appointments. Through these affiliations, the VHA is the largest provider of graduate medical education in the USA. In addition, the VHA's automated information system allows providers to access and enter all patient information through a unified electronic medical record. The VHA is one of the largest integrated health systems in the world. Furthermore, the VHA serves predominantly persons of lower income and education and, thus, may have strong policy implications for the underserved population.

In order to maintain the highest standards of data security, the VHA data are accessed only within the VHA system and behind the VHA firewall according to approved protocols. Obtaining these data through the VHA requires local and national review, and approval of the credentials and qualifications of the research team members who will access the data and accomplish the linkages. Obtaining data also requires local and national approval of the research protocol and then, during the course of the research, there is ongoing monitoring of

the work at the national level to ensure that the data are accessed according to the approved protocol.

The VHA Office of Research and Development, Health Services Research and Development Service, supports the VA Information Resource Center (VIREC) to assist investigators with the complex data security and scientific considerations critical to working with VHA administrative and clinical data [113]. The administrative data files are accessed from a secure site in Austin (TX, USA). The clinical and facility level data are obtained through the VHA Office of Patient Care Services. To develop capacity within the VHA involves linking national data from a number of sources including: administrative data, cancer registry data, oncology facility data and electronic medical record. The administrative datasets include information on inpatient and outpatient care, care provided by non-VA facilities, as well as pharmacy, pathology and laboratory services. Examples of the measures that are being developed in the study of nonpolyposis hereditary colon cancer are given in Table 3.

Cancer Care Ontario is a second example of an organized delivery system. CCO is the provincial agency responsible for cancer services and advising the provincial government with regard to cancer care as specified in legislation [29]. CCO directs and oversees close to CA\$700 million in public healthcare dollars to hospitals and cancer care providers, and is responsible for planning and implementing cancer care services to over 11.5 million residents in the province. The cancer-care system is organized into regional cancer programs corresponding with the 14 local health integration networks in Ontario. The regional cancer programs are designed to ensure that cancer care is of a consistently high quality for all patients who reside in the province. CCO is also responsible for maintaining the Ontario Cancer Registry (OCR), which provides research infrastructure [114].

The data from CCO included the pathology reports (which contained information on estrogen receptor/progesterone receptor testing and HER2 testing) and information on herceptin treatment through the New Drug Funding Program. In order to evaluate practice patterns and resource use, researchers at the Institute for Clinical Evaluative Sciences (ICES; ON, Canada) linked this information to other administrative databases [115]. In this way, the CCO example is also similar to the commercial health plan described earlier in that ICES serves as an intermediary, required to access the data itself. The requirement to link to ICES administrative databases in order to evaluate patterns of treatment and monitoring is one challenge in working with these data.

The CCO/ICES data we obtain and develop, like the studies we are conducting with commercial health plan data, will document 'real world' utilization patterns of testing for HER2 overexpression in incident cases of early-stage breast cancer in Ontario, including which patients receive testing, what test is used, and test sequencing when confirmatory testing is performed. Again, in this example, developing capacity via the example of HER2 testing requires linking several databases. No electronic database currently exists which combines information on HER2 overexpression testing and trastuzumab therapy in Ontario prior to 2008; electronic documentation of tumor pathology, including staging, is also lacking. Examples of the measures that are being developed with the CCO/ICES data are given in Table 3.

In addition to the requirements that must be met for the VHA and CCO in order to obtain data, there are other key challenges to overcome in using and developing organized delivery system data. Both the VHA and CCO examples require linking multiple databases because of a lack of coding for genomic services in the administrative data. While the challenge is similar to the commercial health plan studies previously described (e.g., HER2 status needs to be coded using a case-by-case pathology record review), the organized delivery system

data are potentially more comprehensive than commercial health plan data. For example, there is greater availability of predictive variables (e.g., provider characteristics, specific test type, test result, test sequencing and treatment regimen) within the organized delivery systems. Even for the organized delivery systems; however, services provided outside the system are unlikely to be captured.

Overall findings about building capacity to examine personalized medicine

Few studies have used payer data to examine the utilization or clinical utility of personalized medicine [1,22,30,31]. The lack of studies may characterize a field that is still emerging in clinical practice or it may be that more research is needed to identify what data are available to assess utilization and clinical utility, and how those data can be further developed. From our perspective, established personalized medicine technologies such as HER2 testing, *KRAS* mutation testing and gene-expression profiling in breast cancer provide the opportunity to move forward on developing capacity. We highlight selected insights based on our work with payers that will be helpful to others interested in building capacity to assess new technologies for personalized medicine.

First, payer data is available to assess utilization but it is necessary to combine data from multiple sources, such as administrative claims, pathology reports and medical records. This finding is consistent with an Agency for Research on Health Care Quality report that examined a wide range of data sources (not only payer data) available to monitor or examine utilization of gene-based tests, which concluded that no single data source is sufficient for such purposes [20]. Key reasons for needing multiple data sources include the fact that personalized medicine diagnostics are often coded with nonspecific identifiers in claims databases and that health outcomes are not typically found in administrative claims databases. Medical records reviews can be used but it is expensive and time consuming. Unique coding for novel diagnostics such as the *OncotypeDx* test may help to identify test use in administrative claims but will still not solve the problems associated with lack of health outcomes data. Thus, opportunities to develop prospective datasets, such as in the Medco example, or to build unique comprehensive databases, such as in the VHA and CCO, are important initiatives to developing the capacity to access new technologies in the future.

Data are more limited for examining clinical utility than for examining utilization. Even when current data sources, such as administrative claims, medical records and pathology reports, are combined and health benefits can be evaluated, clinical utility, broadly defined, is difficult to ascertain. For example, none of the data described above specifically elucidate provider or patient preferences or behavior, which are important to the clinical utility of an intervention. Data on the therapeutic objectives (e.g., the reason for the selection of a treatment, such as prevention or improvement of quality of life) are limited as are data on whether patient preferences influenced treatment decisions. These data are particularly relevant to an example like the *OncotypeDX* test for breast cancer treatment decisions, where preferences for treatment are likely to play an important role because many women will receive test results that do not specifically determine a particular treatment decision [32].

These examples also highlight advantages to examining utilization and clinical utility across a range of payers and approaches. In the commercial health plan and organized delivery system examples, retrospective analysis is used to examine utilization and to a lesser extent clinical utility for technologies that are widely used and widely covered by insurers. Since the technologies are used in practice and covered by insurers, commercial health plan data are expected to be, and are, despite challenges, a feasible source for addressing utilization. The Medco example differently illustrates a prospective approach, which is used to examine

promising personalized medicine approaches that are not yet widely applied because of lack of clinical utility data. Medco has seen an opportunity to use its existing client population to advance clinical utility studies for these emerging examples. Moreover, as a pharmacy benefits manager, Medco has seen an opportunity to develop studies that are consistent with its business by focusing on pharmacogenetics.

There are other advantages gained when building capacity using prospective approaches, such as the Medco studies, and investing in infrastructure, such as the VHA and CCO. One advantage is that these approaches have the potential to improve the quality of data, for example, by improving the way data on tests are collected or entered into computer systems. Currently, quality is highly dependent on the source of data and, as suggested, already can vary from one source to the next, which has implications for research. Another advantage is the potential to expand capacity using electronic health records, which are rapidly emerging as an important piece of US health reform and are expected to be an 'inevitable next step' for improving healthcare [116]. For example, via electronic health records, data could be improved on exactly the types of variables needed for examining clinical utility, such as demographics, decisions (e.g., preferences for treatment), behaviors (e.g., adherence) and outcomes.

Finally, throughout this article, we have emphasized the point that the examples discussed illustrate capacity development, which is guided by using specific examples of existing personalized medicine technologies. Although we have not provided the results of our utilization or clinical utility analyses here, it is by conducting such analyses that we can learn the strengths and weaknesses of different data and approaches to examine utilization and clinical utility. It is our perspective that the lessons in how to develop data are as important as the findings of our data analysis. For example, one key finding from the commercial health plan study is that some women with positive HER2 tests do not receive the recommended therapy [22]. There are several possible reasons why women do not receive trastuzumab, including contraindications to the drug treatment (e.g., cardiac disease), but drug use may also be associated with nonclinical factors, such as provider characteristics. The result is noted here because the capacity to further elucidate why these women are not receiving the expected therapy requires the capacity of the data to be expanded in order to potentially include a more extensive review of medical records or to examine associations by linking to additional data sources, such as the American Medical Association (IL, USA). Again, the result may also be driven by provider or patient behavior, such as treatment objectives or preferences, which are not currently captured in databases. Identifying what data can be collected and used in the future is critical to building capacity.

Future perspective

A major objective of the UCSF TRANSPERS is to develop data and approaches to address important questions about the use of personalized medicine technologies in clinical practice. We recognize that a number of US and international research groups have related objectives [112,117–121]. Sharing our collective experience will facilitate more rapid understanding of research questions such as who has access to and who benefits from new technologies. This article described approaches for research with and on various health payers and highlights the advantages and challenges of using payer data. We acknowledge that payer data are only one type of data needed to examine utilization and clinical utility in populations and that other data should be developed to overcome its specific limitations [20]. However, these data have not been widely used to date for addressing questions on personalized medicine.

There are some incentives to payers to build capacity for personalized medicine and we propose that these be considered as future research develops. First, our examples typically

illustrate high-cost diagnostics (e.g., *OncotypeDX*) and drugs (e.g., trastuzumab, cetuximab or panitumumab), which payers arguably have incentive to monitor for utilization. Going forward, capacity development should not only include better tracking for the clinical utility of high-cost diagnostic and treatment interventions but also interventions aimed at prevention, which need to be examined with longitudinal data. Second, incentives to build capacity may depend on the characteristics of the payer organization. In our examples, the Medco studies were part of a business strategy and the capacity development within the VHA is partly a result of its linkage to multiple academic affiliates. Other payers may have less incentive to develop data for research but equally important data to contribute. Mechanisms for obtaining data from payers that do not typically participate in research should be developed.

In our experience, payers are willing to advance objective and transparent evidence development together with health services researchers. From our perspective, research with payers increases our understanding of the current context and helps identify key gaps in what is known. Our experience suggests that working with payers is feasible but also costly, particularly when working with intermediaries who sell data for research. However, our experience highlights the important role of public funding for studies that use these data so that studies are both peer reviewed and approved by Institutional Review Boards. We speculate that payers would welcome health researchers to conduct objective research to both inform and support their policy decisions. As payer capacity to examine personalized medicine is built, one particular policy area to watch is the Genetic Information Nondiscrimination Act (GINA), which was passed to protect Americans from both insurance and employment discrimination on the basis of genetics [33]. It is unclear how payers might apply GINA in the context of capacity development on genomic tests, such as those for personalized medicine. Testing data that are required prior to drug treatment (e.g., HER2 for trastuzumab) are likely to be collected as they are now, but information about risk, such as BRCA or Lynch Syndrome screening, may be variably available in health-plan data. As experts, we can develop data so that it can address the important utilization and clinical utility questions, while at the same time protecting the patients' privacy. The focus of this article was to describe the process of research using payer data and developing capacity. Detailed information about the specific projects noted here is beyond the scope of this article. Table 4 provides selected resources for more information about the research and groups described in this perspective for those interested in learning more about these and related projects.

Going forward, researchers can continue to provide payers with guidance on how to develop the evidence base, such as developing a data infrastructure for examining the clinical application of personalized medicine [22], developing a framework for evaluation [7,8] or providing a neutral place for discussion. We recognize that obtaining and analyzing data will remain challenging with regards to protecting patient information. However, challenges with regard to the time and costs to health services researchers may decrease as collaborative approaches develop between payers and health services researchers. We know that there will continue to be competing perspectives and interests and that payers too are constrained by their resources. Still, initiatives that build health system capacity, such as via infrastructure development, are likely to be valuable for evidence-based medicine. Studies that engage key stakeholders such as payers will continue to be important for creating solutions to fill the current gaps in the evidence base [122].

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Box 1. Glossary of selected terms**Evidence**

- Refers to any information needed for making decisions about personalized medicine technologies, including clinical and nonclinical (e.g., costs) evidence but also primary and secondary data, and published and gray literature

Translation continuum

- A framework proposed by Khoury and others [11] for, “the continuum of multidisciplinary translation research” that builds on previous efforts and includes four phases:
 - Phase 1 translation (T1) research seeks to move a basic genome-based discovery into a candidate health application (e.g., genetic test/intervention);
 - Phase 2 translation (T2) research assesses the value of a genomic application for health practice leading to the development of evidence-based guidelines;
 - Phase 3 translation (T3) research attempts to move evidence-based guidelines into health practice, through delivery, dissemination and diffusion research;
 - Phase 4 translation (T4) research seeks to evaluate the ‘real world’ health outcomes of a genomic application in practice

Clinical utility

- The balance of benefits and harms associated with a personalized medicine intervention in practice including improvements in measurable clinical outcomes and the added value in clinical management and decision-making [3,4]

Health payers

- Entities that finance or reimburse healthcare and may include insurance carriers, other third party payers or health plan sponsors [103]

Pharmacy benefits managers

- Manages and administers the pharmacy benefit of group health plan sponsors and offer clients services such as drug formulary development, manufacturer rebate negotiation and collection, specialty pharmaceutical distribution and mail-order prescription delivery options [23,24]

Organized delivery systems

- Characterized by patient-care teams, defined patient populations, aligned financial and payment incentives, partnership between medicine and management, information technology and accountability [27]

Executive summary

- The lack of evidence on clinical utility is a frequently cited challenge to translating personalized medicine to clinical practice and policy.
- This article addresses the overarching question: how can we use existing data to develop capacity to improve the evidence on personalized medicine technologies, such as genomic testing and particularly regarding evidence on their utilization and clinical utility? We focus on data from private payers.

Conceptual framework for understanding utilization & clinical utility

- Studies that examine utilization are a step to improving the evidence on clinical utility in actual practice because they can identify factors that are associated with use and because they can examine how use is associated with benefits and harms.
- The Behavioral Health Model, which has been widely used to empirically examine differences in treatment utilization and health outcomes, is useful for identifying key data that are needed to assess personalized medicine technologies.

Developing evidence using commercial health plan data

- Commercial health data is useful for examining utilization and, to a lesser extent, clinical utility, but requires linking administrative data with medical records, which can be time consuming and costly.

Pharmacy benefits manager's approach to evidence development

- Medco, a pharmacy benefits manager is developing data on personalized medicine by advancing prospective clinical studies and engaging its clients in research.

Developing evidence using organized delivery systems

- Organized delivery systems such as the Veterans Health Administration (NC, USA) and Cancer Care Ontario (ON, Canada) are well positioned to develop capacity for examining personalized medicine because of the multiple related databases they use, but these data still need to be carefully developed to examine utilization and clinical utility.

Overall findings about building capacity

- Analyzing existing data tells us not only about the utilization and to a lesser degree clinical utility of technologies but also about how to build capacity for future studies.
- Payers are interested in capacity building and are engaging in various approaches to develop evidence, including retrospective analyses, prospective studies and improvements to health system data infrastructure.
- Unique datasets, in particular that combine administrative data and medical records, need to be developed to examine personalized medicine but more specific coding for technologies and further development of electronic health records may facilitate future analyses and build capacity.

Future perspective

- There are advantages to using multiple approaches and sources to analyze and develop data, and we should be encouraged by an increasing number of groups now examining these issues, by increased funding for translation research and by interest in unique collaborations. Now and in the future, these are critical components to the translation of personalized medicine.

Table 1
Examples of measures for the Behavioral Health Model applied to personalized medicine

Behavioral model classification	Example measures
Health outcomes	Recurrence, morbidity and mortality
Utilization	Use of personalized medicine tests Use of personalized medicine treatments Use of other treatments
Predisposing	Age Race/ethnicity
Needs	Comorbidity Results of tests indicating the genetic status Clinical characteristics
Enabling	Type of health plan Household income

Table 2
Examples of measures for the Behavioral Health Model applied to personalized medicine for breast cancer using commercial health plan data

Example measures	Health plan data sources
<i>Utilization variables</i>	
HER2 tests	Administrative claims or medical record [†]
Trastuzumab	Administrative claims or medical record [†]
Gene-expression profiling	Administrative claims or medical record [†]
Adjuvant chemotherapy	Administrative claims or medical record [†]
<i>Predisposing factors</i>	
Age	Administrative data
Race/ethnicity (white, African–American, Hispanic or other)	Health plan proprietary data or medical record
<i>Needs</i>	
Comorbidity	Administrative claims
Results of tests indicating the genetic status	Medical record
Clinical characteristics (cancer stage, tumor size, menopause status and estrogen- and progesterone-receptor status)	Medical record
<i>Enabling factors</i>	
Type of health plan	Administrative claims data
Household income	Health plan proprietary data

[†]Primary data source.

Table 3
Examples of measures for the Behavioral Health Model applied to available data from organized delivery systems

Example measures	VHA data sources [†]	CCO data sources [‡]
Outcome variables		
Documentation of family history	Administrative data or EMR [§]	NA
Genetic counseling	Administrative data or EMR [§]	NA
Molecular analysis	Administrative claims or EMR [§]	Pathology reports
Genetic testing	Administrative claims or EMR [§]	Pathology reports
Predisposing		
Patient sociodemographic characteristics (age, gender, marital status and race/ethnicity)	Race/ethnicity from VHA cancer registry, other variables from the administrative data	Administrative
Needs		
Comorbidity	Administrative	Administrative
Cancer diagnosis	Administrative	Cancer registry
Cancer treatment	Administrative, EMR, cancer registry	NDFP, Administrative
Cancer stage	Cancer registry	Cancer registry, pathology reports
Psychosocial problems	EMR	NR
Enabling factors		
Insurance status	Administrative	NR
Distance of residence from VHA	Administrative	NR
Environmental factors		
Provider characteristics (e.g., speciality)	The American Medical Association Master file	Administrative
Facility characteristics (e.g., availability of cancer treatment, specialists or psychosocial services, and academic affiliation)	Administrative	Administrative

[†]VHA data sources include: multiple administrative databases, registry databases, EMRs and other data that will be linked.

[‡]CCO data sources include: CCO pathology data, Ontario Cancer Registry, NDRP and Institute for Clinical Evaluative Sciences administrative data.

[§]Primary data source.

CCO: Cancer Care Ontario; EMR: Electronic medical record; NA: Not available; NDRP: New drug funding program; NR: Not relevant; VHA: Veterans Health Administration.

Table 4
Selected links to projects and organizations discussed

Project/organization	Ref.
The Center for Translational and Policy Research on Personalized Medicine (CA, USA)	[123]
Utilization of personalized medicine for breast cancer studies using commercial health plan data [†]	[124]
Medco pharmacogenetic studies [‡] (NJ, USA)	[125]
Veterans Health Administration (NC, USA)	[126]
Cancer Care Ontario (ON, Canada)	[127]
The Center for Genomics and Public Health [§] (WA, USA)	[128]
Evaluation of Genomics Applications in Practice and Prevention [§]	[129]
Center for Personalized Health Care [§] (OH, USA)	[118]
Partners HealthCare Center for Personalized Genetic Medicine [§] (MA, USA)	[119]
Duke Institute for Genome Sciences and Technology [§] (NC, USA)	[120]
PHG Foundation [§] (Cambridge, UK)	[121]

[†] Preliminary results from this study were presented at the 2009 American Society for Clinical Oncology meeting. Complete analysis of this study is forthcoming.

[‡] For general information about the Medco pharmacogenomics programs and links to studies.

[§] Selected groups conducting related research to develop the evidence base.