UCSF Center for Translational & Policy Research on Personalized Medicine

Launched in 2008 and based at the University of California San Francisco, TRANSPERS brings together a broad spectrum of experts from across the world — from academia, government, and groups representing patients, providers, and payers — to examine critical issues that impact the translation of personalized medicine into practice and policy. Using an evidence-based approach, we launch projects and establish working groups to explore key areas, including healthcare utilization, patient preferences, costs and cost-effectiveness, evidence development and evaluation, patient diversity, decision-making (patient, provider, payer, and government), and policy. The TRANSPERS Center is funded by grants from the National Institutes of Health (NIH) and several foundations.

TRANSPERS PROGRAM ON EVIDENCE AND REIMBURSEMENT FOR PERSONALIZED MEDICINE

A major focus of our work is healthcare coverage, reimbursement, and policy decisions by payers. Since 2007, TRANSPERS has convened an Evidence and Reimbursement Policy Advisory Council comprised of private payers and thought leaders. This unique advisory group includes senior executives from the seven largest commercial US health plans and leading regional plans as well as thought leaders from industry and government. Our work on coverage and reimbursement policy decisions by payers has been funded by several grants from NIH and several foundation grants, including Blue Shield of California Foundation and Aetna Foundation.

Evidence and Reimbursement Advisory Council Members (as of 2015)

Anthem: Alan Rosenberg, MD, Vice President

Aetna: Joanne Armstrong, MD, MPH, Senior Medical Director, Health of Genetics, Women's Health

CIGNA: Jacob Asher, MD, Chief Medical Officer, Northern California Region, CIGNA HealthCare of CA

Kaiser Permanente: Patrick Courneya, MD, Executive Vice President and Chief Medical Officer

Highmark: Donald Fischer, MD, Chief Medical Officer

CAMBIA Health Solutions / Regence: Csaba Mera, MD, FAAP, FRCPSC, Deputy Chief Medical Officer; Executive Medical Director, Regence BlueCross BlueShield of Oregon

Health Care Service Corporation: Kim Reed, MD, Vice President

Health Net: David Haddad, MD, MBA, Vice President & Senior Medical Director, Medical Management

Humana: Bryan Loy, MD, Vice President- Oncology, Laboratory, and Personalized Medicine

UnitedHealth Group: Lewis Sandy, MD, Executive Vice President

Premera Blue Cross: John Watkins, PharmD, MPH, BCPS, Pharmacy Manager

(Also)

Bruce Quinn, MD, PhD, MBA, Foley Hoag LLP (former regional Medicare Medical Director for the California Part B program)

The focus of our work with the Advisory Council

Our work addresses two critical gaps in the translation of personalized medicine into healthcare practice and policy:

- The need for an **evidence base** on personalized medicine to enable policy decisions.

- The need for a **forum** that brings together the necessary stakeholders to formulate, recommend, and implement relevant guidelines and policies.

An evidence-based approach
Through our collaborative efforts, we address a range of important challenges using evidence-based approaches. These include:

- **Identify** gaps in the personalized medicine evidence base and how to address them
- **Analyze** how payers make policy decisions and the implications for comparative effectiveness research
- **Examine** how personalized medicine is affected by the Affordable Health Care Act and how it is integrated into new healthcare models
- **Develop** approaches to work with payers that seek to harness data on the use of personalized medicine
- **Create** and test, together with payers, a framework for evaluating healthcare system factors for policy decisions
- **Assess** the development and timing of payer policies on key examples of personalized medicine, including genomic sequencing
- **Generate** a predictive model of the factors that lead to the successful adoption of new technologies in healthcare

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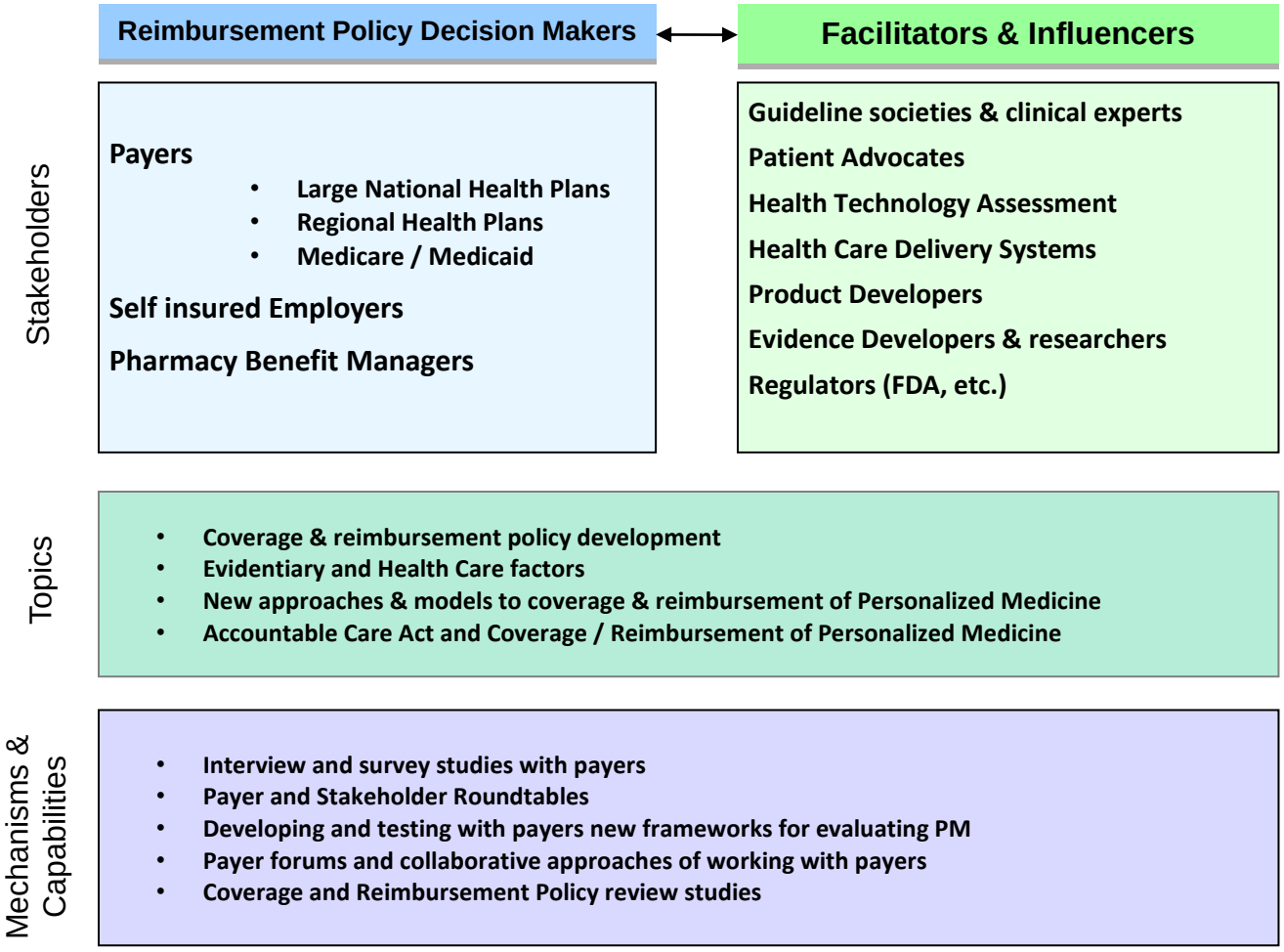
Our Approach and Conceptual Framework



Key activities and accomplishments (in reverse chronological order)

NIH supplemental grant to develop genetic testing reimbursement registry. 2015 -current

- This project will a collaboration with Tufts university and will develop a comprehensive registry of public and private payer coverage policies for new and emerging sequencing tests, as well as illustrative examples of existing molecular tests for comparative analyses. Specifically, we will systematically assess coverage and reimbursement of sequencing tests as they move into clinical care, using insights developed from an analysis of coverage policies for established tests already in clinical use and a multi-stakeholder technical working group.

Advisory Council Meeting. Topic: Precision Oncology. November 2014

- Council members and guest participants will gather in Chicago to explore a spectrum of precision oncology topics, including adoption and reimbursement aspects of genetic cancer risk panels, adoption and physician readiness for tumor sequencing, transformation of oncology clinical trials as a new standard of care, precision oncology in the community setting and the impact of new evidence assessment and FDA regulatory frameworks on reimbursement for precision oncology. Guests represent NCCN, Northwestern University, Stanford, Dana Farber and ACCC.

NIH Grant to examine benefit / risk tradeoffs of Whole Genome Sequencing and Next Generation Tumor Sequencing in care and reimbursement – 2012 - current

- The program examines the issues and approaches of adoption of Whole Genome Sequencing and Next Generation Sequencing (Tumor Sequencing) in coverage / reimbursement policy and in the health care system in light of the

Affordable Care Act and other health care changes. As part of the program, we will conduct several studies with private payers, including interviews with the Evidence and Reimbursement Advisory Council.

- The program is linked to the MedSeq Project: Integration of Whole Genome Sequencing into Clinical Medicine (principal investigator, Robert Green, Harvard Medical School).

Advisory Council Meeting (part of TRANSPERS Symposium on Sequencing), Sept 2013

- TRANSPERS collaborators, Scientific Advisory Board members, and Evidence and Reimbursement Council members gathered from across the US and internationally for a symposium on "Benefit-Risk Tradeoffs for Whole Genome Sequencing". The symposium continued TRANSPERS work on the key issues of coverage and reimbursement, with our Evidence and Reimbursement Council. TRANSPERS was joined by the UCSF community. Dr. Robert Green from Harvard Medical School presented preliminary results from the MedSeq Study which seeks to develop a process to integrate genomic sequencing into clinical medicine.

Study of considerations for coverage of Next Generation Tumor Sequencing by private payers. 2013

- The study included interviews with clinical and technical experts to identify features and potential benefits of next generation tumor sequencing (NGTS), based on which we developed a 'case study" for payer interviews. We then interviewed private payers on our Advisory Council to gather their views on potential benefits of NGTS, and factors of coverage and reimbursement. ASCO 2014 Annual Meeting poster. Paper in press at JNCCN.

Study of evidence and coverage of molecular diagnostics in cardiovascular disease and rheumatoid arthritis, December 2011 – October 2012.

- This unique study allowed developing a deeper understanding of the challenges and approaches to assessment and coverage of personalized medicine technologies, and keeping this understanding in pace with continued development of personalized medicine. We used case studies of two emerging molecular diagnostic tests addressing different diseases, with different utility and patient / physician bases. Comparing and contrasting the two tests allowed us to explore in more depth the concepts of clinical utility, evidence requirements and coverage considerations.

Developed collaborative study with a health plan – Advisory Council member, Oct 2010 – May 2011.

- Developed a collaborative research approach and data sources for a project examining utilization and physician adoption of personalized medicine in colorectal cancer with Humana. The study includes analyses of health plan data to determine utilization patterns, methods studies to analyze new data sources, and a survey of Humana network physicians on adoption of personalized medicine for colorectal cancer treatment.

Advisory Council Roundtable (WebEx), March 2011

- Discussed the results of the TRANSPERS study which examined utilization of gene expression profile testing in the population of a large health plan. The study was published in Breast Cancer Research and Treatment.

Examining the role of evidence in Payer Decisions: Focus on medical guidelines: ongoing

- Payers have suggested that medical guidelines such as the National Comprehensive Cancer Network (NCCN) have an important role in policy development (e.g. coverage, utilization management)
- Studies are ongoing that examine how evidence on personalized medicine and biomarkers is developed and used by professional organizations (e.g. NCCN) as part of technology adoption and a study of the evidence on biomarkers for colorectal cancer treatment available for guideline development.

Study of Breast Cancer Testing Strategies and the utilization of targeted therapies, 2008-2009

- The study examined Aetna's claims data for its 392 members diagnosed with breast cancer in 2006-2007. The study found that HER2 tests are widely used, with discrepancies in HER2 classification of HER2 status based on different testing strategies. We did not find evidence of overuse of Herceptin by HER2-negative woman. We found modest adoption of GEP, and GEP score was associated with the use of adjuvant therapy.

Advisory Council Roundtable (WebEx), October 2009

- The Roundtable discussed the results of the TA Frameworks study, its implications for payers and recommendations on further research.

Advisory Council Roundtable, June 2010

- The Roundtable discussed the results of the study on building capacity for real world evidence development, implications for research and opportunities for payers to participate in evidence development. The Roundtable determined concrete next steps in building TRANSPERS capacity for real world evidence development.

Study "Building capacity for real world evidence development on new technologies to support payer decisions: current capabilities and future opportunities. July 2010

- The study explored opportunities to use existing data sets that payers have or utilize for developing evidence on medical technologies via research collaborations. The study involved literature research and interviews with twenty six individuals from the twelve payer organizations on the Advisory Council.

Study of Technology Assessment (TA) Frameworks and their role in payers' policy decisions on Personalized Medicine, December 2009.

- We reviewed seven TA frameworks used in payers' policy decisions on personalized medicine and interviewed seventeen senior executives from six major national (Aetna, HCSC, Humana, Kaiser Permanente, UnitedHealthcare, WellPoint) and five leading regional health plans (BCBS of TN, BS of CA, Highmark, Premera and Regence).
- We found differences in how the external TA frameworks analyze clinical evidence and healthcare system factors for a genomic technology. We identified common shortcomings of the frameworks in supporting payers' decision needs. Published in AJMC, May 2011

Advisory Council Roundtable, February 2009

- The Roundtable discussed the variations in payers' policies and decisions, the need to define heuristics for decision-making in personalized medicine, and potential benefits of an industry-wide evidence assessment framework.

Study of factors influencing coverage and reimbursement decisions on Personalized Medicine – the case of GEP testing, January 2009

- We interviewed senior executives from Aetna, HCSC, Humana, Kaiser Permanente, UnitedHealthcare, and WellPoint. Their online policies for Oncotype Dx were reviewed. The study found that payers use the intersection of clinical evidence and market factors in their policy decisions on personalized medicine, and that market factors may influence the level of evidence sufficient for a coverage decision. Published in JOP, September 2010.

Study of payers' policies around HER2 utilization and accuracy issues, May 2008

- We interviewed senior executives from Aetna, HCSC, UnitedHealthcare, Kaiser Permanente and WellPoint on issues of HER22 test utilization and accuracy. We also reviewed their online policies on HER2 testing and Herceptin. We found that payers had varying levels of concern for these issues and varying policies, with variations related to different requirements for evidence and influence of market factors. Provided findings to the Advisory Council.

Advisory Council Roundtable, November 2007

- Participants included several national and regional plans (Aetna, HCSC, Kaiser Permanente, Blue Shield of California, Harvard Pilgrim), and academic experts and thought leaders (Steve Pearson, Kathy Behrens, others).
- The Roundtable identified key challenges in making evidence-based decisions on personalized medicine: determining the level of evidence sufficient for coverage; decisions for diagnostics with evolving evidence; and the role of cost-effectiveness in decisions. Participants made recommendations for research in these areas.

Selected Publications

1. Trosman JT, Weldon CB, Kelley RK, Phillips KA. Challenges of coverage policy development for next-generation tumor sequencing panels: experts and payers weigh in. In press by J Natl Compr Canc Network.
2. Schink JC, Trosman JR, Weldon CB, Kalliopi P. Siziopikou, Gregory J. Tsongalis, Alfred W. Rademaker, Jyoti D. Patel, Al B. Benson III, Edith A. Perez, William J. Gradishar. Biomarker Testing for Breast, Lung, and Gastroesophageal Cancers at NCI Designated Cancer Centers. J Natl Cancer Inst (2014) 106(10): dju256
3. Phillips KA, Trosman JR, et al. Genomic Sequencing: Assessing The Health Care System, Policy, And Big-Data Implications. Health Affairs, 33, no.7 (2014):1246-1253.

4. Phillips KA, Ann Sakowski J, Trosman J, Douglas MP, Liang SY, Neumann P. The economic value of personalized medicine tests: what we know and what we need to know. Genet Med. 2013 Nov 14. doi: 10.1038/gim.2013. PMID: 24232413
5. Wang G, Beattie M, Ponce NA, Phillips KA. Eligibility criteria in private and public coverage policies for BRCA genetic testing and genetic counseling. Genet Med. 2011 Dec;13(12):1045-50.
6. Odierna DH, Afable-Munsuz A, Ikediobi O, Beattie M, Knight S, Ko M, Wilson A, Ponce NA. Early developments in gene-expression profiling of breast tumors: potential for increasing black-white patient disparities in breast cancer outcomes? Per Med. 2011;8(6):669-79. PMCID: 3242007.
7. Haas JS, Liang SY, Hassett MJ, Shiboski S, Elkin EB, Phillips KA. Gene expression profile testing for breast cancer and the use of chemotherapy, serious adverse effects, and costs of care. Breast Cancer Res Treat. 2011;130(2):619-26.
8. Ferrusi IL, Leighl NB, Kulin NA, Marshall DA. Do Economic Evaluations of Targeted Therapy Provide Support for Decision Makers? Journal of Oncology Practice. 2011;7(3S):36s-45s. PMCID: PMC3092467.
9. Kelley RK, Wang G, Venook AP. Biomarker use in colorectal cancer therapy. J Natl Compr Canc Netw. 2011;9(11):1293-302. PMCID: Freely avail: http://www.medscape.org/viewarticle/752677.
10. Haas JS, Phillips KA, Liang SY, Hassett MJ, Keohane C, Elkin EB, Armstrong J, Toscano, M. Genomic Testing and Therapies for Breast Cancer in Clinical Practice. Journal of Oncology Practice. 2011;7(3S):e1s-e7s.
11. Liang SY, Phillips KA, Wang G, Keohane C, Armstrong J, Morris WM, Haas JS. Tradeoffs of using administrative claims and medical records to identify the use of personalized medicine for patients with breast cancer. Medical Care. 2011 Jun;49(6):e1-8.
12. Trosman JR, Van Bebber SL, Phillips KA. Health Technology Assessment and Private Payers' Coverage of Personalized Medicine. American Journal of Managed Care. 2011;17(5 Spec No.):SP53-SP60.
13. Kelley RK, Van Bebber SL, Phillips KA, Venook AP. Personalized medicine and oncology practice guidelines: a case study of contemporary biomarkers in colorectal cancer. Journal of the National Comprehensive Cancer Network. 2011 Jan;9(1):13-25.
14. Trosman JR, Van Bebber SL, Phillips KA. Coverage Policy Development for Personalized Medicine: Private Payer Perspective on Developing Policy for the 21-Gene Assay. Journal of Oncology Practice. September 2010;6(5): 238-242.
15. Van Bebber SL, Trosman JR, Liang SY, Wang G, Marshall DA, Knight S & Phillips KA. Capacity building for assessing new technologies: approaches to examining personalized medicine in practice. Personalized Medicine 2010 7(4): 427–439.
16. Wang G, Van Bebber S, Phillips KA., A successful adoption of personalized medicine: example of KRAS genetic testing. Accepted for poster presentation at 15th Annual International Meeting of International Society for Pharmacoeconomics and Outcomes Research (ISPOR), May 2010, Atlanta GA.
17. Van Bebber S. Trosman J, Phillips KA. When and How Are Evidence Reviews on Personalized Medicine Used for Health Plan Policy Decisions? Accepted for poster presentation at 15th Annual International Meeting of International Society for Pharmacoeconomics and Outcomes Research (ISPOR), May 2010, Atlanta GA.
18. Phillips KA, Marshall DA, Haas JS, Elkin EB, Liang SY, Hassett MJ, Ferrusi I, Brock JE, Van Bebber SL. Clinical Practice Patterns and Cost Effectiveness of Human Epidermal Growth Receptor 2 Testing Strategies in Breast Cancer Patients. Cancer. 2009;115(22):5166-74.
19. Phillips KA, Liang S, Van Bebber S, CANPERS Research Group. Challenges to the translation of genomic information into clinical practice and health policy: Utilization, preferences and economic value. Curr Opin Mol Ther. 2008;10(3):260-6. PMCID: 2910510.
20. Phillips KA. Closing the Evidence Gap in the Use of Emerging Testing Technologies in Clinical Practice. JAMA. 2008;300(21):2542-4.