UCSF Center for Translational & Policy Research on Personalized Medicine

Launched in 2008, the Center for Translational and Policy Research on Personalized Medicine (TRANSPERS) at the University of California, San Francisco is a first-of-its-kind research center dedicated to developing evidence-based information for patients, providers, industry, researchers and policymakers to objectively assess how personalized medicine can be most beneficial and efficient in improving health outcomes. 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 the TRANSPERS Center is coverage, reimbursement, and policy decisions by payers. Since 2007, we have been working with our Payer Advisory Board comprised of private payers and thought leaders. The Advisory Board includes senior executives from the top largest national private health plans and leading regional plans as well as thought leaders with industry, government, and Medicare perspectives. Our work on coverage and reimbursement policy decisions by payers has been funded by several grants from NIH and several foundation grants.

TRANSPERS Payer Advisory Board Members

Anthem: John Whitney, MD, Vice President Medical Policy and Clinical Pharmacy Policy

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

Beacon Laboratory Benefit Solutions: Trisha Brown, MS, LCGC, Vice President, Product and Business Development

Blue Cross Blue Shield Association: Erick Lin, MD, PhD, MBA, Medical Director

Blue Shield of CA: Terry Gilliland, MD, Senior Vice President and Chief Health Officer

CIGNA: Julie Kessel, MD, Senior Medical Director Coverage Policy

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

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

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

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

Independence Blue Cross: Virginia Calega, MD, Vice President Medical Management & Policy

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

Oklahoma Health Care Authority (Medicaid): Alison Martinez, PhD, Geneticist.

UnitedHealth Group: Jen Malin, MD, Senior Medical Director, Oncology & Genetics

Reimbursement Expert: Bruce Quinn, MD, PhD, MBA, (former regional Medicare Medical Director for the California Part B program).

The focus of our work with the Advisory Board

Our work addresses two critical gaps for translation of personalized medicine into practice and policy:

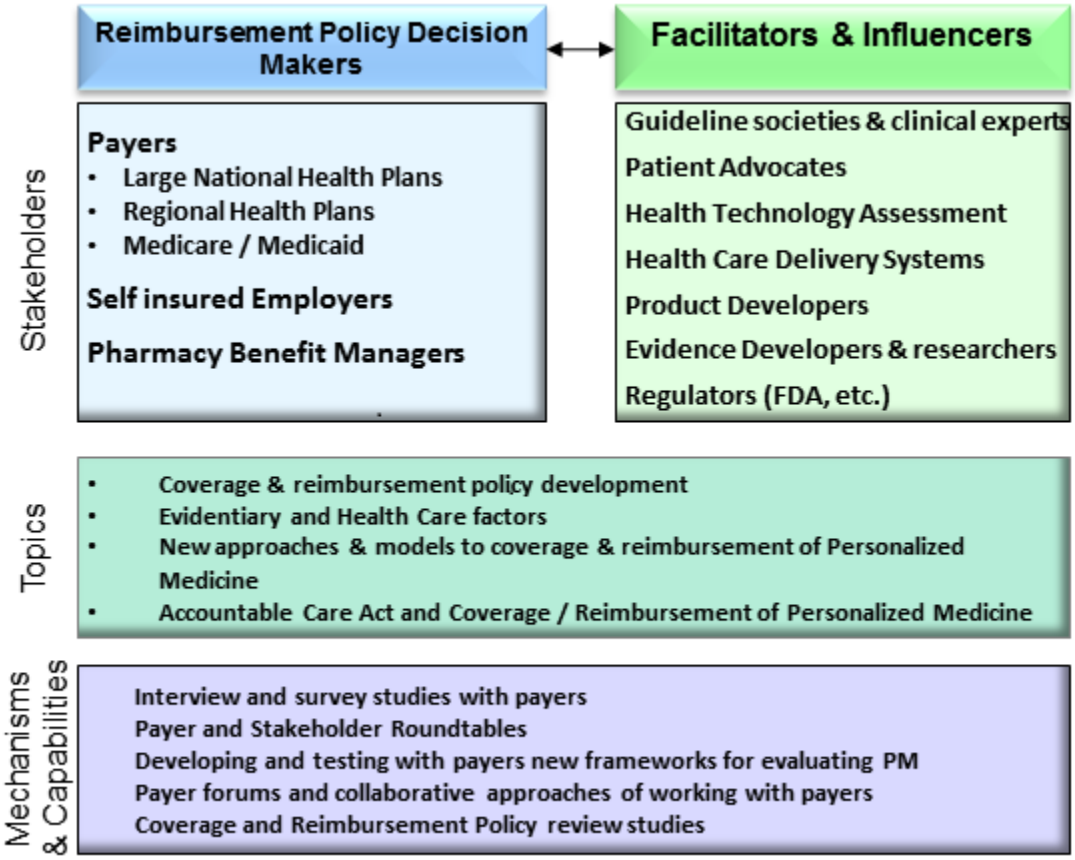
- Lack of an evidence base on translating personalized medicine into policy and adoption decisions
- Lack of forums bringing together the multiple stakeholders needed to formulate, recommend, and implement relevant guidelines and policies

We are developing, testing, and implementing evidence-based approaches to addressing these challenges:

- Analyzing how payers make policy decisions, particularly how they use evidence on healthcare system factors in conjunction with clinical evidence
- Identifying gaps in the evidence base for personalized medicine and how to address them
- Developing approaches and mechanisms to working with payers to develop data sources such as using claims data to examine use of personalized medicine
- Examining the development and timing of payer policies on key examples of personalized medicine, including genomic clinical sequencing
- Developing a predictive model on what factors result in a successful adoption of new technologies

Disclaimer: The TRANSPERS Center conducts independent, objective research and does not endorse or recommend any specific commercial products, companies, or organizations.

Our approach and Conceptual Framework



Our work with the Board has influenced the conversation about payer coverage issues through presentations to a range of organizations including:

- Government agencies (e.g., NIH, CDC, PCORI)
- Professional organizations (e.g., BIO, American Diabetes Association, Association of Clinical Oncology, National Business Group on Health, AdvaMed, National Association of Cancer Executives, American College of Medical Genetics, National Society of Genetic Counselors, Association of Molecular Pathologists)
- Industry (e.g., Illumina, Eli Lilly, AstraZeneca)
- Venture capital firms (e.g., Kleiner, Perkins, Caulfield, & Byers; Mohr Davidow Ventures; Burrill Inc; RockHealth)
- And conferences/symposia (e.g., National Academy of Medicine, Mayo Clinic, Harvard Partners, Personalized Medicine World Conference, MedTech, Stanford MEDX, ASCO Annual Meeting).

Key activities and accomplishments (in reverse chronological order)

Advisory Board Meeting. Topic: Current Coverage of NGS Tests in National Coverage Decision, 2018.

In this web meeting, the Board members reviewed TRANSPERS's latest work and shared their respective perspectives on the recent National Coverage Determination (NCD) by CMS for cancer NGS tests. Board members also participated in an online survey prior to the meeting on the importance of this NCD and how it impacts their plans for coverage of cancer NGS tests.

Study to explore payer coverage policies and clinical adoption and reimbursement on Whole Exome Sequencing in the diagnosis of prenatal congenital abnormalities and pediatric developmental disorders in conjunction with the NIH Clinical Sequencing Evidence-Generating Research Consortium, 2017-2021.

TRANSPERS is conducting a series of clinical and reimbursement stakeholder interviews to identify the clinical adoption and reimbursement decision making process for whole exome sequencing in two patient populations: prenatal congenital abnormalities and pediatric developmental disorders. TRANSPERS researchers will also conduct a longitudinal analysis of payer coverage policies over the course of the study.

Study to explore perspectives on barriers to clinical adoption and reimbursement for Expanded Carrier Screening, 2017-2018

TRANSPERS is conducting a series of clinical stakeholder interviews to identify known barriers to the clinical adoption of expanded carrier screening for over 175 conditions that could be passed on from parents to their children. TRANSPERS researchers will also interview reimbursement stakeholders to identify barriers and solutions to the reimbursement of these expanded carrier screening tests.

Advisory Board Meeting. Topic: Pressing issues in Precision Medicine and Coverage / Reimbursement, 2017.

In this web meeting, the Board members reviewed TRANSPERS latest work and shared their respective interest and priorities related to Precision Medicine. The discussion of payers' challenges and priorities helped TRANSPERS strategic direction, as well as research plans for 2017.

Study to explore perspectives on benefits, risks and coverage for hereditary cancer risk panels, 2015-2016

Conducted within an R01 Grant from NHGRI, this study focused on exploring views of clinical experts and payers on benefits and risks of multi-gene, multi-cancer hereditary risk panels. Further, we analyzed study findings in the context of the Precision Medicine Initiative, and how our results, as well as the overall payer experience with hereditary cancer genetic testing, may inform the Initiative. Manuscript "Payer Coverage for Hereditary Cancer Panels: Barriers, Opportunities, and Implications for the Precision Medicine Initiative" (Trosman et al, JNCCN 2017)

Developing UCSF Coverage Policy Registry and conducting coverage policy analyses – funded in part by NIH supplemental grant, 2015 - present

Informed by a Registry Working group, and collaborating with Tufts University and American Institutes for Research, we developed the first iteration of the UCSF Payer Coverage Policy Registry, focused on genomic technologies. We conducted systematic policy analyses for illustrative tests, including Non-Invasive Prenatal Tests (NIPT) and genetic sequencing panels. Five papers have been published in peer-reviewed journals.

Advisory Board Meeting. Topic: Precision Oncology, November 2014

Board members and guest participants gathered in Chicago to explore a spectrum of precision oncology topics, including adoption and reimbursement 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 represented 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 grant examines the issues of adoption of Whole Genome Sequencing and Next Generation Sequencing (Tumor Sequencing) in coverage / reimbursement policy and in the health care system. As part of the grant, we conducted several studies with private payers, including interviews with the Advisory Board. The program is linked to the MedSeq Project: Integration of Whole Genome Sequencing into Clinical Medicine (PI: Robert Green, Harvard)

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

TRANSPERS collaborators, Scientific Advisory Board members, and Payer Advisory Board 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. TRANSPERS was joined by the UCSF community. Dr. Robert Green from Harvard 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 a 'case study" for payer interviews. We interviewed our Advisory Board to gather their views on potential benefits of NGTS, and factors of coverage and reimbursement. ASCO 2014 Annual Meeting poster. Published in Journal of NCCN (Trosman et al, 2015)

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

This study allowed developing a deeper understanding of the challenges of 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 Board 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 Board 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) guidelines 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 Board Roundtable (WebEx), October 2009

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

Advisory Board 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 Board.

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

We reviewed seven HTA frameworks used in payers' policy decisions on personalized medicine and interviewed seventeen senior executives from six major national and five leading regional health plans. 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 (Trosman, 2011).

Advisory Board 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 6 major national health plans 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 Board.

Advisory Board 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 Peer-reviewed Publications

1. Phillips KA, Trosman JR, Deverka PA, Quinn B, Tunis S, Neumann PJ, Chambers JD, Garrison LP, Douglas MP, Weldon CB. Insurance Coverage for Genomic Tests. Science. 2018;360(6386):278-279.
2. Phillips KA, Deverka PA, Douglas MP, Hooker G. Genetic Test Availability and Spending. Where Are We Now? Where Are We Going? Health Affairs. 2018;37(5):710-716.
3. Trosman JR, Weldon CB, Gradishar WJ, Benson AB, Cristofanilli M, Kurian AW, Ford JM, Balch A, Watkins J, Phillips KA. Measuring the Value of Multigene Clinical Sequencing: Evolution of Payer Frameworks and a Path Forward. Value in Health. *Published online Aug 3, 2018.*
4. Douglas MP, Parker SL, Trosman JR, Slavotinek AM, Phillips KA. Private Payer Coverage Policies for Exome Sequencing (ES) in Pediatric Patients: Trends Over Time and Analysis of Evidence Cited. Genet Med. *Published online July 12, 2108.*
5. Phillips KA. Evolving Payer Coverage Policies on Genomic Sequencing Tests: Beginning of the End or End of the Beginning? JAMA. 2018; *Published online April 16, 2018.*
6. Trosman JR, Weldon CB, Douglas MP, Kurian AW, Kelley RK, Deverka PA, Phillips KA. Payer Coverage for Hereditary Cancer Panels: Barriers, Opportunities, and Implications for the Precision Medicine Initiative. J Natl Compr Canc Netw. 2017;15(2):219-228.
7. Phillips KA, Deverka PA, Trosman JR, Douglas MP, Chambers JD, Weldon CB, Dervan AP. Payer Coverage Policies for Multigene Tests. Nature Biotechnol. 2017;35(7):614-617.
8. Dervan AP, Deverka PA, Trosman JR, Weldon CB, Douglas MP, Phillips KA. Payer decision making for next-generation sequencing-based genetic tests: insights from cell-free DNA prenatal screening. Genet Med. 2017;19(5):559-567.
9. Clain E, Trosman JR, Douglas MP, Weldon CB, Phillips KA. Emergence of New BRCA1/2 Tests and Gene Panels: Availability & Payer Coverage Policies. Nature Biotechnology. 2015;33(9):900-2.
10. Trosman JT, Weldon CB, Kelley RK, Phillips KA. Challenges of coverage policy development for next-generation tumor sequencing panels: experts and payers weigh in. J Natl Compr Canc Netw. 2015 Mar;13(3):311-8.
11. 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
12. Phillips KA, Trosman JR, et al. Genomic Sequencing: Assessing The Health Care System, Policy, And Big-Data Implications. Health Affairs.2014;33(7):1246-1253.
13. 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;16(3):251-257.
14. Trosman JR, Weldon CB, Schink JC, Gradishar WJ, and Benson AB. What do providers, payers and patients need from comparative effectiveness research on diagnostics? The case of HER2/Neu testing in breast cancer. Journal of Comparative Effectiveness Research 2013;2(4):461-477.
15. Weldon CB, Trosman JR, Gradishar WJ, Benson AB, Schink JC. Barriers to the Use of Personalized Medicine in Breast Cancer. Journal of Oncology Practice. 2012;8(4):24e-31e.
16. 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;13(12):1045-50.
17. 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.
18. 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.
19. 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;49(6):e1-8.
20. 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.

21. 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;9(1):13-25.

22. 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. 2010;6(5): 238-242.

23. 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.

24. 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.

25. 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.

26. Phillips KA. Closing the Evidence Gap in the Use of Emerging Testing Technologies in Clinical Practice. JAMA. 2008;300(21):2542-4.

Selected Research Reports

1. Trosman JR, Weldon CB, Examining Factors and Challenges to Coverage and Reimbursement of Next Generation Tumor Sequencing. Report to Life Technologies / Thermo Fisher. June 2013.

2. Trosman JR, Phillips KA. Assessment of Molecular Diagnostics for Coverage and Reimbursement: Examining Payer Decision-making Using Two Example Tests in Rheumatoid Arthritis and Coronary Artery Disease. Report to Kleiner, Perkins, Caufield and Byers, and Mohr Davidow Ventures. July 2012.

3. Trosman JR, Weldon CB. Examining factors of adoption and reimbursement for blood-based colorectal cancer screening tests. Report to Abbott Molecular. February 2012.

4. Trosman JR, Phillips KA. Building capacity for real-world evidence development to support payer decisions. Report to the UCSF TRANSPERS Evidence and Reimbursement Policy Advisory Board. August 2010.

5. Trosman JR, Weldon CB, Phillips KA. Examining the Case for Healthcare Value of a Standardized BCR-ABL Transcript Monitoring Test in Chronic Myeloid Leukemia in the United States. White paper and report to Novartis AG. July 2010.

6. Trosman JR. Policies for Gene Expression Profile Tests for Breast Cancer Recurrence: Private Payer Approaches and Insights. Report to the UCSF TRANSPERS Evidence and Reimbursement Policy Advisory Board. January 2009.

7. Trosman JR. Payer policies for quality and utilization management of HER2 testing in breast cancer. Report to the UCSF TRANSPERS Evidence and Reimbursement Policy Advisory Board. June 2008.