Center for Translational and Policy Research on Personalized Medicine
NEWS

NEWSLETTER
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Upcoming TRANSPERS Center Events

February 5, 2009
Kickoff Center Symposium
OPEN TO THE PUBLIC!
3-4PM
Fisher Family Hall
Jewish Community Center, San Francisco

February 5-6, 2009
Investigator and
Center Board Meetings

TRANSPERS Center, UCSF
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San Francisco, CA 94143
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TRANSPERS Center Launches at UCSF

National Cancer Institute awards over $5 million for first-of-its-kind research center

The University of California, San Francisco is pleased to announce the launch of the Center for Translational and Policy Research on Personalized Medicine. Known as the TRANSPERS Center, it is a first-of-its-kind research center dedicated to developing evidence-based information to assess how personalized medicine can be most beneficial and efficient in improving health outcomes.

"Our Center is being created at a critical time," said Kathryn Phillips, who is the founder and director of the TRANSPERS Center. "Personalized medicine – health care targeting medical interventions to patients based on their genetics – is already being used, and the pace of adoption is expected to accelerate. But there is little research being done on the translation of genomics into clinical practice and health policy. That will be the focus of the Center."

The TRANSPERS Center is primarily funded by a $5 million grant from the National Cancer Institute (NCI) – the first major NCI grant focused on health policy issues related to personalized medicine and pharmacogenomics – along with grants from the Blue Shield Foundation of California, the Aetna Foundation, and the Department of Veterans Affairs. The goal of the TRANSPERS Center is to provide evidence-based information that will be useful to patients, clinicians, industry, providers, researchers and policymakers in applying personalized medicine technologies to clinical care.

To achieve this goal, the TRANSPERS Center brings together a broad spectrum of stakeholders from government and groups representing patients, providers and payers, as well as scientists and academics from several leading universities, to examine key questions related to personalized medicine in clinical care, including:

-Who has access to the newest technologies?
-How do patients and providers make decisions about personalized tests or drugs?
-How can policies be designed to encourage the most effective use of technologies?

These questions will be examined in the context of several specific study areas, including HER2 testing for breast cancer, gene expression profiling for breast cancer recurrence and Lynch Syndrome as a risk factor for colorectal cancer.

For more information on the TRANSPERS Center and its areas of research, contact Christina Hosenfeld, Program Manager, at TRANSPERSInfo@ucsf.edu.

TRANSPERS Center Highlights

- $8M in funding
- Funded by the National Cancer Institute, Blue Shield of California Foundation, Aetna Foundation, and Department of Veterans Affairs
- Located in the Department of Clinical Pharmacy; includes several other UCSF schools, departments and institutes, as well as institutions worldwide
- Cuts across basic, clinical and social science with emphasis on translating research to practice – "T2" research
- Research projects focus on: utilization of, preferences for, economics and cost-effectiveness of, and evidence for personalized medicine
- Initial topics include: HER2/neu testing for Herceptin®, gene expression profiling for predicting risk of breast cancer recurrence and Lynch Syndrome Screening

TRANSPERS Center Studies: Initial Findings

NEWS FLASH: Be sure to watch for Dr. Phillips' commentary, "Closing the Evidence Gap in the Use of Emerging Testing Technologies in Clinical Practice" (in press, JAMA). Using the well-known example of HER2 testing, her manuscript discusses the need to build an evidence base to support decision making in using new testing technologies in clinical practice. Dr. Phillips concludes by providing four potential solutions to close this "evidence gap."

What do we know about HER2 testing in practice?

HER2 testing for breast cancer is one of the best known examples of personalized medicine. Center investigators, using literature and available data, examined what is known about the "who," the "what" and the "where" of HER2 testing and found key gaps in knowledge and opportunities to expand the evidence base.

Key Findings

- Little evidence is available to determine whether all eligible patients are tested; how many are retested to confirm results; how many with negative HER2 test results still receive Herceptin; and cost-effectiveness of testing strategies.
- Up to 66% of eligible patients had no documentation of testing in claims records.
- Up to 20% of patients receiving Herceptin were either not tested or had no documentation of a positive test (and thus no known benefit from therapy).
- 20% of HER2 results may be incorrect.
- There is no information on access to testing and treatment for underserved patients.

Implications

- There are variations in testing practices and key gaps in knowledge.
- It is critical to build an evidence base to address these gaps, given the increasing use of high-cost targeted therapies, the growth of new testing technologies and personalized medicine, and the urgent need to translate basic research findings into practice and policy.

Leveraging Findings – Next Steps for Center Research

- Center investigators are developing an evidence base that supports informed decision-making on emerging testing technologies in clinical practice.

TRANSPERS Center investigators explore HER2/Herceptin policies, perceptions among payers

With so little information in the literature on HER2 testing and Herceptin utilization, Center investigators conducted interviews with key individuals at five health plans about practices and policies for HER2/neu testing and Herceptin utilization.

Key Findings

- Variable levels of concern and multiple policies.
- Several payers have already implemented prior authorization for Herceptin.
- Tracking Herceptin utilization relative to the test is a challenge due to insufficient detail of HER2 test information submitted in claims to payers.
- Among payers concerned about accuracy issues, strategies include (1) covering a repeat, "second opinion" HER2 test, (2) physician and patient education and awareness of this issue, (3) improved communication between the lab and physician regarding test results, and (4) establishing differential coverage for testing by labs based on their accreditation.
- Some payers are working toward making this accreditation information from the College of American Pathologists available from an accreditation body or via lab self-disclosure.

Implications

- In the future, better evidence may be available for tracking HER2 tests and Herceptin utilization.

Leveraging Findings – Next Steps for Center Research

- Center investigators are examining claims data and medical records to track and analyze utilization.

Ongoing TRANSPERS Center Studies

TRANSPERS Center researchers discuss ongoing studies:

Claims Data and HER2 Testing/Gene Expression Profiling for Breast Cancer

Following up on our studies of HER2 testing and Herceptin utilization, TRANSPERS Center investigators at UCSF and Harvard will examine the appropriateness of personalized-medicine based treatment decisions among women with breast cancer using Aetna claims and medical record data. Specifically, we are examining the clinical utility of two key technologies: (1) HER2/neu testing and trastuzumab (Herceptin) therapy, and (2) gene expression profiling and chemotherapy. Results will be available in 2009.

A Delicate Balance: The Risks and Benefits of Genetic Tests after the Death of a Newborn Baby from Codeine Overdose

In 2006 a breastfed infant died from morphine overdose because the mother was positive for a mutation in the CYP2D6 gene, which caused rapid metabolism of codeine into morphine. We have compiled newspaper stories, broadcasts and articles from health/parenting magazines to review the reporting of this death and the 2007 FDA warning that ensued. Currently, we are working on writing a review paper that uses this case study to discuss the greater dilemma of evidence-based decision-making versus informed decisions of individuals, which will continue to be an issue as genetics plays a greater role in our understanding of diseases and medicine.

A Model for Translating Personalized Medicine to Patients: Self-Insured Employers and Pharmacy Benefits Managers

One model for translation is currently coming from Self-Insured Employers (SIE) and Pharmacy Benefits Managers (PBM). Medco, a major PBM, is conducting studies of genetic testing for both Warfarin dosing and Tamoxifen prescribing, using data from their SIE clients. Medco believes its large database of customers and prescriptions can address gaps in the evidence needed to move these strategies to the clinic. We are examining this model of translation and asking: Why are SIEs and PBMs examining personalized medicine? What are the challenges to these studies? How might the results be used? How might the findings suggest a model for translation?

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Report Watch

TRANSPERS Center investigators have identified key reports and findings on personalized medicine. Following are some of the latest items of interest:

President's Council of Advisors on Science and Technology (PCAST) Report: **Priorities of Personalized Medicine**

This long awaited report from PCAST highlights the potential and role of genomics-based molecular diagnostics in accelerating the progress of personalized medicine. Policy actions in the areas of technology and tools, regulation, and reimbursements were specifically identified in the corresponding recommendations.
http://www.ostp.gov/galleries/PCAST/pcast_report_v2.pdf

Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) Report: **Realizing the Potential of Pharmacogenomics: Opportunities and Challenges**

http://www4.od.nih.gov/oba/SACGHS/reports/SACGHS_PGx_Report.pdf

Agency for Healthcare Research and Quality (AHRQ) Report: **Infrastructure to Monitor Utilization and Outcomes of Gene-based Applications: An Assessment**

http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=nr&ProcessID=63

Institute of Medicine (IOM) Report: **Diffusion and Use of Genomic Innovations in Health and Medicine: Workshop Summary**

http://www.nap.edu/catalog.php?record_id=12148

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Status:

EGAPP has released the following reports.
http://www.egappreviews.org/workingrp/reports.htm

- Impact of Gene Expression Profiling Tests on Breast Cancer Outcomes
  The Johns Hopkins University Evidence Based Practice Center | January 2008
- *Hereditary Nonpolyposis Colorectal Cancer: Diagnostic Strategies and Their Implications*
  Tufts New England Medical Center Evidence Based Practice Center | May 2007
- Testing for Cytochrome P450 Polymorphisms (CYP450) in Adults with Non-Psychotic Depression Prior to Treatment with Selective Serotonin Reuptake Inhibitors (SSRIs)
  Duke University AHRQ Evidence-based Practice Center | January 2007
- Genomic Tests for Ovarian Cancer Detection and Management
  Duke University AHRQ Evidence-based Practice Center | October 2006

Personalized Medicine in the News

"Rep. Kennedy Revives Obama's Personalized Medicine Bill for Next Congress; Adds Incentives." *GenomeWeb News*, September 10, 2008
A bill in this year's US Congress that aimed to advance personalized medicine and pharmacogenomics will be replaced in the upcoming 111th Congress by another bill that includes a new tax incentive for personalized medicine research. (http://www.genomeweb.com/issues/news/149316-1.html)

"Genetic-Testing Guidance." *The Wall Street Journal*, July 13, 2008
A new federal law and many state laws prohibit employers and health insurers from discriminating on the basis of genetic tests.
(http://online.wsj.com/public/article/SB121591245002648885.html)

"Pricey Drugs Put Squeeze on Doctors." *The Wall Street Journal,* July 8, 2008
American doctors rarely used to let costs factor into their treatment decisions – but rising prices are dramatically changing that ethos in the field of oncology.
(http://online.wsj.com/public/article/SB121548254807634713.html)

"In Costly Cancer Drug, Hope and a Dilemma." *The New York Times*, July 6, 2008
Despite the cost of Avastin, studies show that the drug prolongs life by only a few months – yet it remains one of the most popular cancer drugs in the world. (http://www.nytimes.com/2008/07/06/health/06avastin.html)

"Results from Gene ID Studies Could Lead to New Dxs for Genomic Health." *Pharmacogenomics Reporter*, June 11, 2008
Studies could lead to the development of two new diagnostics tests, expanding the indication of Genomic Health's Oncotype DX technology. (http://www.pgxreporter.com/issues/6_24/features/147495-1.html)

"ASCO Presenter Urges KRAS Testing for All Colorectal Cancer Patients Before Erbitux Treatment." *GenomeWeb News*, June 2, 2008
Clinical trial shows patients with metastatic colorectal cancer whose tumor carries the wild-type version of the KRAS gene are much more likely to benefit from Erbitux.
(http://www.genomeweb.com/issues/news/147303-1.html)

"Monogram's Herceptin Response Test May Rival IHC, FISH Dxs, Preliminary Data Say." *Pharmacogenomics Reporter,* May 21, 2008
Disclosure of preliminary results on Monogram's test is meant to position the test as a potential rival to the two top players in the HER2 breast cancer diagnostics market. (http://www.pgxreporter.com/issues/6_21/features/147058-1.html)

"ImClone's Gene Test Battle." *Forbes*, May 16, 2008
A simple gene test could allow doctors to predict in advance which patients will likely benefit from Erbitux.
(http://www.forbes.com/2008/05/15/imclone-erbitux-genetics-biz-healthcare-cz_rl_0516imclone.html)

"Comparative Effectiveness Research Best Way to Assure Effective Treatment, Panel Says." The Commonwealth Fund, Washington Health Policy Week in Review Newsletter, April 4, 2008
Private health care professionals and industry academics believe comparative effectiveness is the best way to avoid wasteful treatments and ensure people get the best care.
(http://www.commonwealthfund.org/healthpolicyweek/healthpolicyweek_show.htm?doc_id=676791#doc676796)

Ongoing TRANSPERS Center Studies, **continued from Page 3**

Evidence Frameworks for Evaluating Personalized Medicine: Summarizing the Options, Advantages & Limitations
Various groups have used a multitude of frameworks for evaluating new technologies and, specifically, personalized medicine. To assist decision-makers in their ability to find and understand the evidence, we are preparing a report on evidence frameworks for personalized medicine. This report will identify the players in evidence evaluation and the content of frameworks, and provide recommendations for using these frameworks in decision-making.

Expenditures and Medicare Formulary Coverage for Top-Selling Biotechnology Drugs
The utilization of biotechnology drugs ("biologics") has grown dramatically, yet little is known about expenditures and formulary coverage for these often-costly drugs. The objectives of this study are to examine the recent trends in the expenditures of top selling biologics and to understand the formulary coverage for these drugs under the Medicare Prescription Drug Plan. Despite increasing sales of the top biotechnology drugs, preliminary results show variation in coverage by drug, state and plan type.

We are obtaining more recent data to examine specifics of formulary coverage including cost-sharing tiers, whether prior authorization is required, and whether step therapy applies.