BlueCross BlueShield Association

An Association of Independent Blue Cross and Blue Shield Plans

Translating Actionable Variants into Evidence-based Practice: The View from TEC

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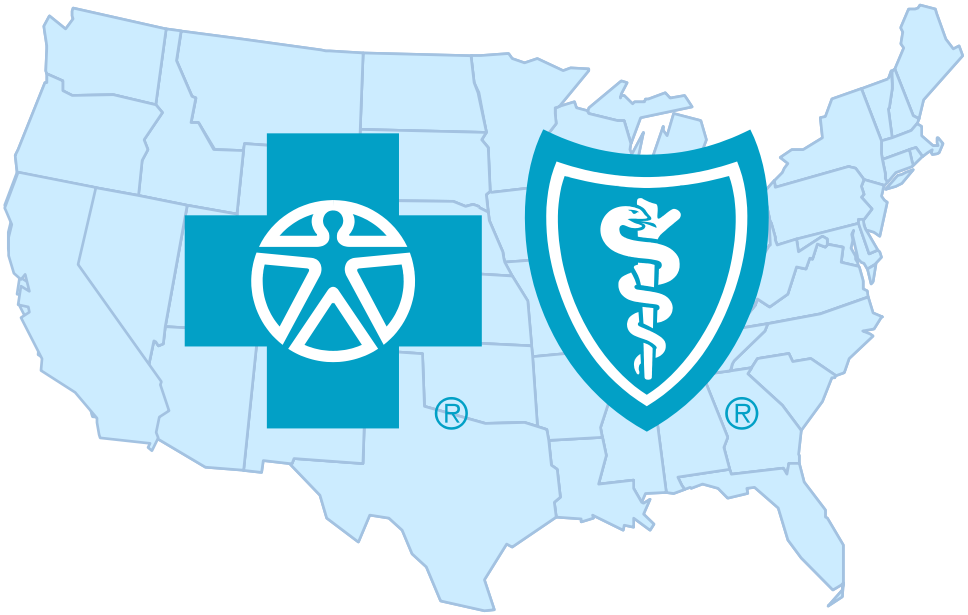
Overview

- BCBSA Technology Evaluation Center
- Evaluating Evidence
- Value and Affordability

Blue Plans Cover Every Community in the Nation



- 39 Blue Cross and/or Blue Shield Plans
- 99 million members
- Contract with 90% of hospitals, 80% of doctors
- 5-million member FEP Program – Largest private health insurance product in world
- Largest processor of Medicare claims in the nation
- 1985 Technology Evaluation Center (TEC)

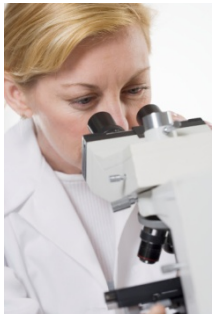
Technology Evaluation Center (TEC)

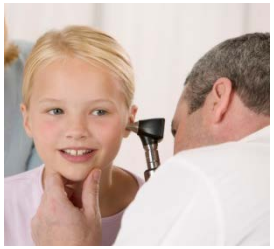
- Rigorous assessment of clinical evidence, systematic review with quality appraisal: Does this technology improve health?
- Independent, expert Medical Advisory Panel
- TEC Assessments 3-year inventory at ***(www.bcbs.com/tec)***
- Medical Policy Reference Manual (MPRM): a confidential and proprietary inventory of approximately 350 evidence-based policies, updated annually, that is offered to support Blue Plans' operations*
- Dedicated professional staff
- Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center ***(www.ahrq.gov)***
- AHRQ Comparative Effectiveness Research EPC cancer and infectious disease

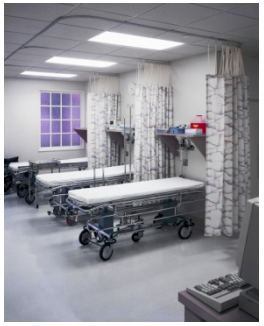
*Note: Each Plan, acting independently, may adopt the MPRM, in whole or in part, modify it, or reject it, in making that Plan's own medical policy decisions.

Technology Assessment Supports Health Plans and Other Stakeholders in Developing Evidence-based Policies

Tec







Medical Policy

- Based on scientific evidence
- Costs and coverage NOT considered

Coverage Policy

- Determined by purchasers of health plan products
- Cost effectiveness considered

Payment Policy

- Contract between health plans and medical professionals and providers

TEC Focus on Genomics 1997-2007

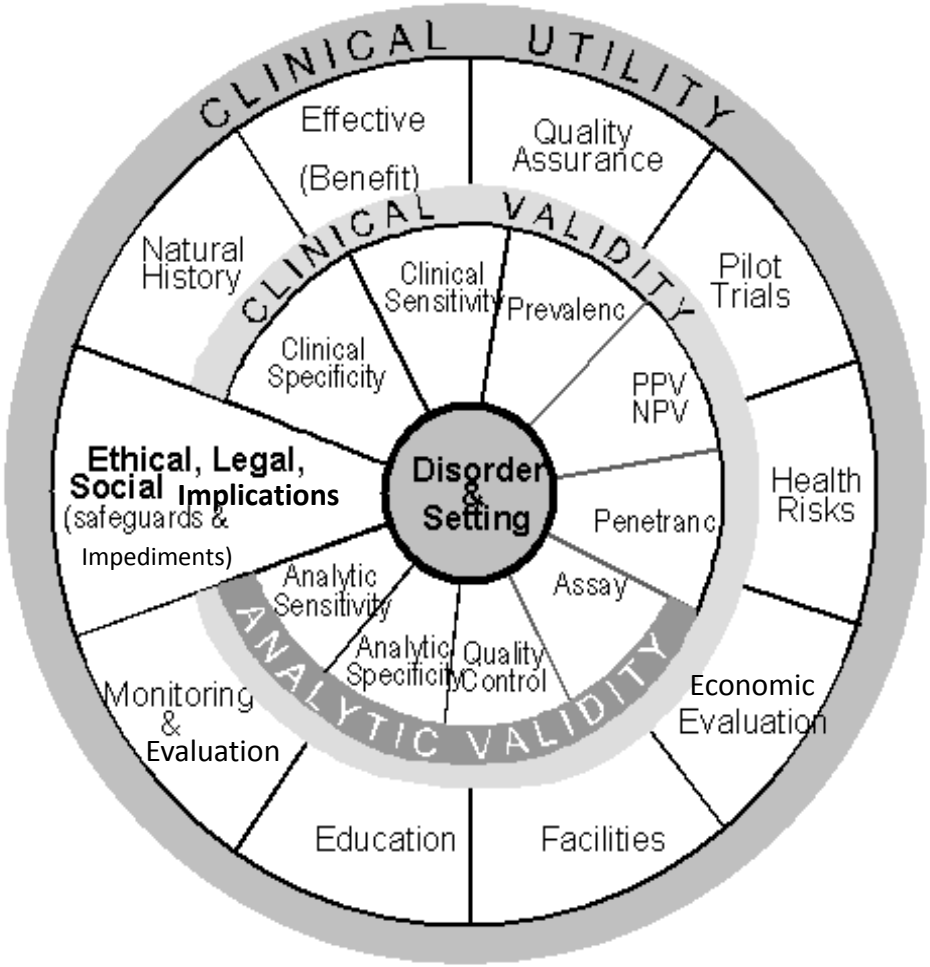
- Gene Expression Profiling for Breast Cancer - Update (2007)
- Pharmacogenomics of Cancer (2007)
- Cardiovascular Pharmacogenetics (2007)
- Use of GeneSearch Breast Lymph Node Assay (2007)
- Pharmacogenomics of EGFR-Targeted Therapy (2007)
- Fecal DNA for Colon Cancer Screening (2006)
- Gene Expression Profiling for Breast Cancer (2005)
- Genotyping for Cytochrome P450 Polymorphisms (2004)
- HFE Gene Mutations and Hereditary Hemochromatosis (2001)
- Alzheimer's Disease: ApoE Epsilon 4 Allele (1999)
- Inherited Susceptibility to Colorectal Cancer (1998)
- Inherited BRCA1 or BRCA2 Mutations (1997)
- Germline Mutations of the *RET* Proto-Oncogene in Medullary Carcinoma of the Thyroid (1997)

TEC Focus on Genomics 2008-2010

- EGFR mutations and tyrosine kinase inhibitor therapy in advanced non-small-cell lung cancer (2010)
- Gene Expression Profiling in Women with Lymph-Node-Positive Breast Cancer (2010)
- Genetic Testing for Familial Hypertrophic Cardiomyopathy (in press)
- Pharmacogenetic Testing to Predict Serious Toxicity from 5-Fluorouracil (2009)
- Special Report: Molecular karyotyping by aCGH (2008)
- Special Report: Genetics of Prostate Cancer (2008)
- *KRAS* testing for anti-EGFR treatment in colorectal cancer (2008)
- Pharmacogenomics-Based Treatment of *Helicobacter Pylori* (2008)
- CYP2D6 Pharmacogenomics of Tamoxifen Treatment (2008)
- Genetic Testing for Long QT Syndrome (2008)

Framework for Evaluating Evidence

The ACCE evaluation process for genetic testing



From the CDC National Office of Public Health Genomics
http://www.cdc.gov/genomics/gtesting/ACCE/index.htm

Diagnostic Model a Continuum for Efficacy

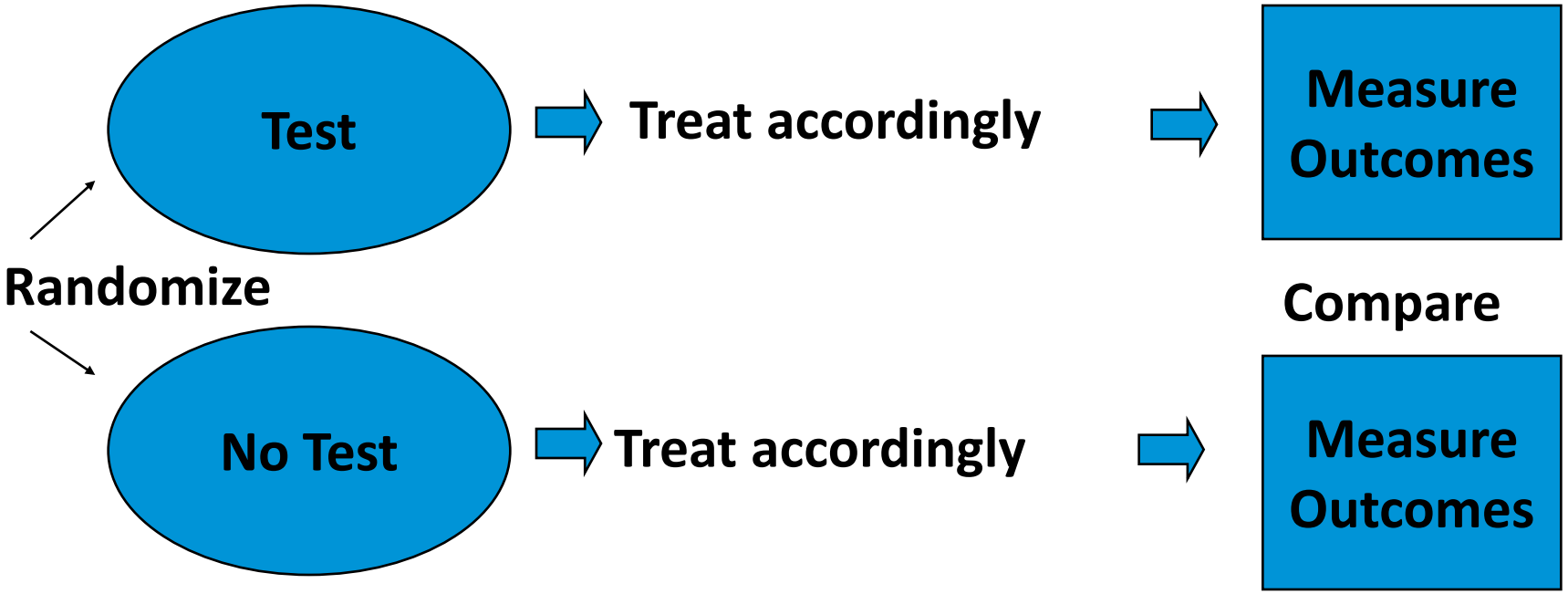
Paraphrased

- Level 1: Technical efficacy — Pretty Picture
- Level 2: Diagnostic accuracy efficacy — Improved Accuracy
- Level 3: Diagnostic thinking efficacy — Improved Diagnosis
- Level 4: Therapeutic efficacy — Improved Treatment
- Level 5: Patient outcome efficacy — Improved Health
- Level 6: Societal efficacy — Improved Efficiency

Fryback & Thornbury (1991) Med Dec Making, 11:88-94

Source: ***(www.bcbs.com/tec)***

Ideal … Direct Evidence



Indirect Evidence: Genetic test long QT syndrome

(http://www.bcbs.com/blueresources/tec/vols/22/22_09.pdf)

Family history

Suspect LQTS

Performance

LQT test vs. clinical criteria

No true gold standard

LQT test more "sensitive" in 2 series @ n >500

→

Change Management

LQT-positive start beta-blockers

LQT-negative for all known mutations ↓likelihood LQTS

↓LQTS if LQT-negative for known family mutation

→

Improve Outcomes *(Qualitative Conclusions)*

Potential catastrophe untreated

Observational evidence LQTS population

Beta-blocker low- risk intervention

"Prospective-Retrospective" Methodologic Framework (Simon et al.)

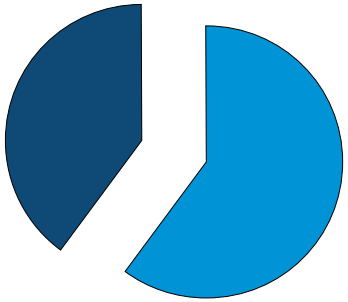
- *Simon RM et al. Use of archived specimens in evaluation of prognostic and predictive biomarkers. J Natl Cancer Inst 2009;101:1446-52.*

- Studies that use a prospectively designed protocol to investigate a candidate predictive marker using archived specimens from a completed prospectively designed RCT that was conducted for a different purpose

- Typically, the purpose of the original trial would be to test therapeutic efficacy (e.g., tamoxifen vs. no tamoxifen or adjuvant chemotherapy vs. no adjuvant chemotherapy)

- Existing tumor samples could be used to determine whether the candidate marker predicted improved survival (or poorer survival, or no effect) with the treatment of interest

Direct evidence for diagnostics: Genotyping for warfarin dose



VKORC1 and CYP2C9 genetic variants account for one-third to one-half of the variability in stable warfarin dose (in European Caucasians)

Need different starting warfarin dose – how different?

Genotyping

Personalized warfarin dose

??????

Other enzymes

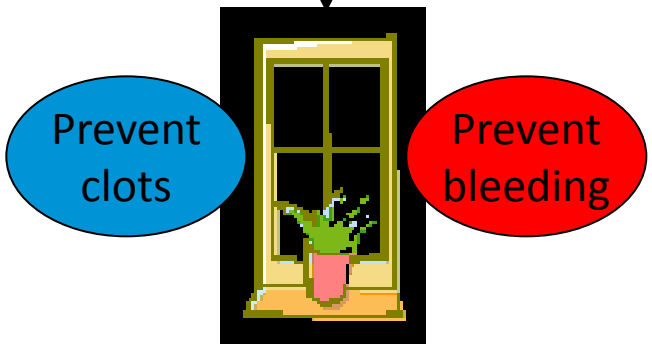
Co-existing disease

Clotting factor genetic variant

Age

Diet

Other drug interactions

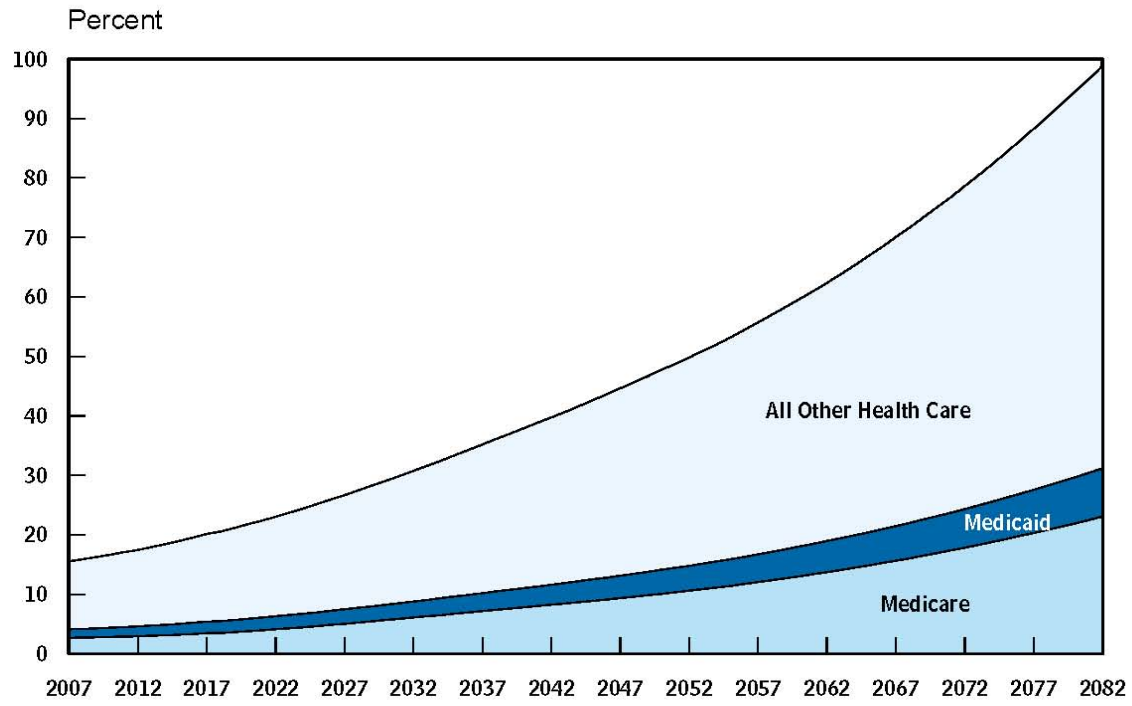


Value and Affordability

- Clinical effectiveness is cornerstone of Plan medical and coverage policy
- New technologies may bring small benefit at high cost
- Cost effectiveness and affordability are pressing issues
- But no clear cost-effectiveness threshold: can you afford everything that is a “good buy”?

Projected Spending on Healthcare as Percentage GDP

Spending on Health Care as a Percentage of Gross Domestic Product Under an Assumption That Excess Cost Growth Continues at Historical Averages



Source: Congressional Budget Office, 2007 (15).

Summary

- TEC process is evidence based and independent. Genomics is high priority and we seek to complement and collaborate with other organizations.
- Diagnostic technologies raise common questions, whether for diagnostic, prognostic, or predictive use. Critical are when direct or indirect evidence of clinical utility is sufficient and how to be pragmatic and creative in developing good evidence.
- Effectiveness and affordability are pressing issues. All stakeholders need to exercise stewardship for a sustainable healthcare system.