OECD

An International Perspective on Pharmacogenetics

17 – 19 October, 2005

Pharmacogenetics and Evidence-Based Medicine

Or:

“Out of the Research Lab and Into the Clinic”

Mitchell Sugarman

Outline

- EBM and technology assessment
- Confounding issues
- Reimbursement
- Cost effectiveness
- Patient perspectives
- Final thoughts

Is evidence-based medicine different when applied to pharmacogenetics?

Is evidence-based medicine really needed?
(phenotype versus genotype)

Steps in Technology Assessment

- Identify and rank assessment topics
- Specify the assessment problem
- Collect evidence
- Interpret evidence
- Formulate findings/recommendations
- Disseminate findings/recommendations
- Modify as new evidence becomes available

Examples

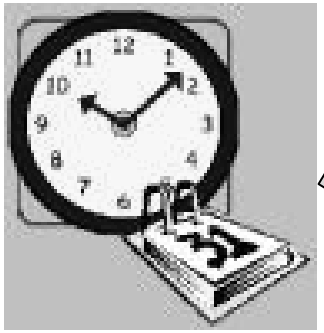
- BCBSA TEC
- INAHTA
- ECRI
- Hayes
- Cochran Library
- NICE
- MCAC (Medicare and NCD process)

BCBSA/KP Technology Evaluation Center (TEC)

- Does the technology have appropriate regulatory approval (if required)?
- Does the scientific evidence permit conclusions about the technology's effect on health outcomes?
- Does the technology improve health outcomes?
- Is the technology as beneficial as any established alternatives?
- Is the improvement attainable outside the investigational setting?

How Can One Body of Evidence Yield Different Conclusions?

Timing



Problem Formulation

Evidence

Analytical Methods

Clinical Expertise

= "The Answer"

Confounding Issues

- Legal challenges
- Media events
- Ethical issues
- Cost issues
- “Only alternative is death”
- Legislation

Some Interesting Cases

- Fetal surgery for diaphragmatic hernia
- HDC-AuBMT for breast cancer
- Ceredase for Gaucher’s disease
- Non-ionic contrast media for imaging

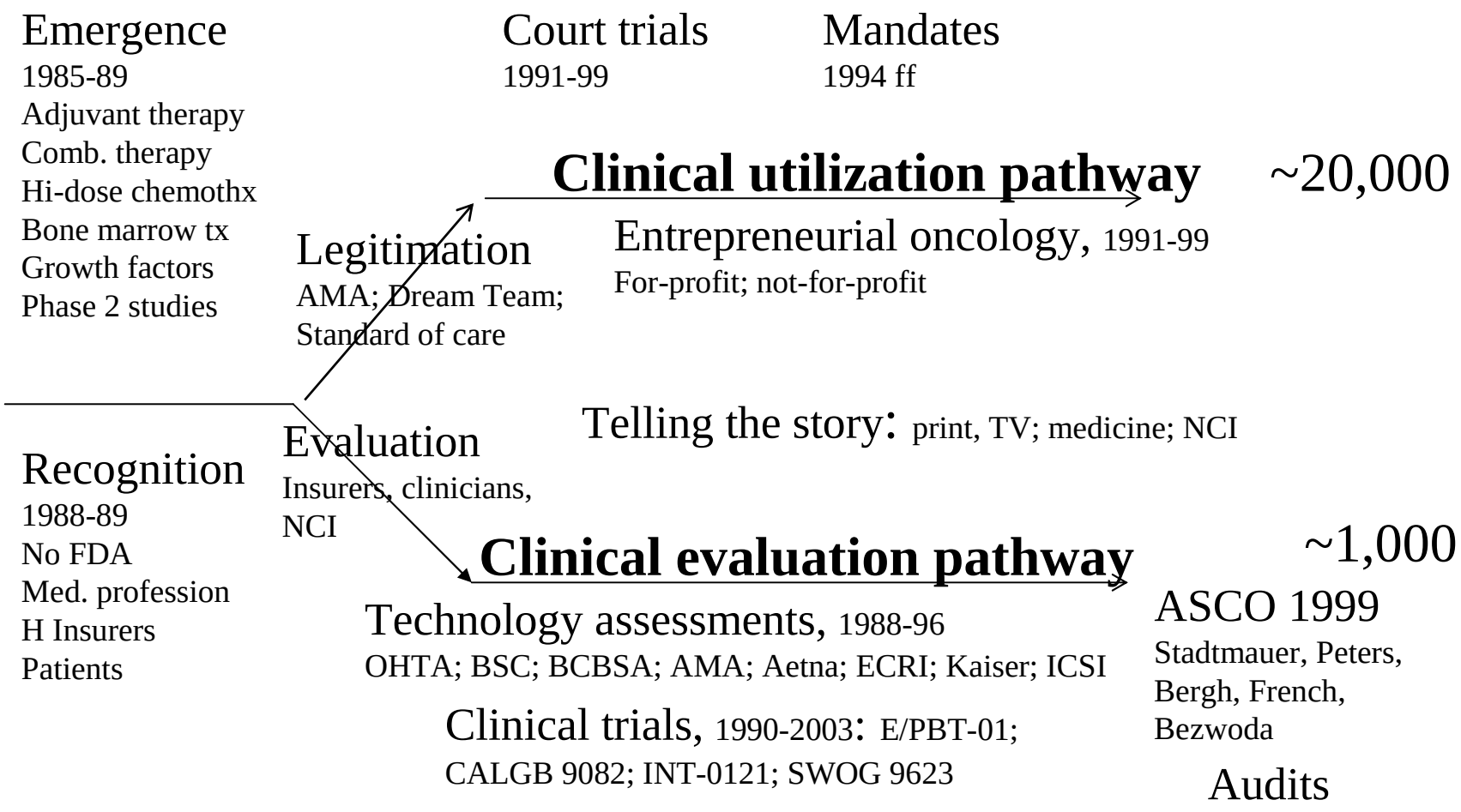
Fetal surgery for diaphragmatic hernia

- Natural outcomes of condition
- 11 Cases; 9 SABs, 2 successes
- Publication in Scientific Journal
- Publication in Lay Press
- “Kaiser Permanente Won’t Save My Baby!!”

The HDC/AuBMT Procedure

- Provide standard chemotherapy with FDA-approved drugs (to ascertain responsiveness)
- Aspirate/rescue bone marrow a/o stem cells
- Administer HDC (2X-10X standard dose)
- Re-infuse bone marrow a/o stem cells
- Add growth factor
- Wait and watch

The HDC/ABMT Natural Experiment



BMT for Breast Cancer

- Evidence?
- “Woman’s” Issue
- Patient Perceptions
- Nalene Fox case against Health Net
- Reimbursement
- Expense
- Difficulty enrolling clinical trials
- Response Technologies
- ASCO
- Reimbursement Stopped

3 C’s of Reimbursement

- CODING
  - What was done?
  - Why was it done?
- COVERAGE
  - Will it be paid for?
- COMPENSATION
  - Who pays?
  - How much?

Value-Based Pricing

Diagnostic Test Value =

sensitivity & specificity & applicability

Consider: PET

Reimbursement versus Approval:

FDA (regulator)

- Safety
- Efficacy
  - "Does it do what it says it does?"
- Substantially equivalent or comparison to placebo
- Intermediate, short-term outcomes

Medicare (payer)

- Experience relevant to members (65+)
- Effectiveness
  - "Is what it does important?" (cost effectiveness)
- Comparisons to standard of care
- Longer-term, health outcomes
- Operational impact

Predicted Clinical Restenosis Rates

Diabetes

Adapted from Ho KKL et al. AAC 1998

Vessel Diamete	10 mm	15 mm	20 mm	25 mm	30 mm
ř2.5 mm	23%	26%	29%	31%	34%
3.0 mm	15%	17%	20%	22%	24%
3.5 mm	10%	11%	13%	15%	16%
4.0 mm	6%	7%	8%	9%	10%

No diabetes

2.5 mm	18%	20%	22%	25%	27%
3.0 mm	11%	13%	15%	17%	18%
3.5 mm	7%	8%	9%	11%	12%
4.0 mm	4%	5%	5%	7%	7%

Patient Perceptions

- Two Drugs: 1=$ 2=$$$
- Drug 1: 1 in 2,000 patients will experience complication
- Drug 2: 1 in 2,700 patients will experience complication

Patient Perceptions

- 26% less likely to experience complication (RRR)
- Reduce risk by .00013 (from 1 in 2,000 to 1 in 2,700) (ARR)
- Almost 8,000 people treated to avoid one event (NNT)

The up-front costs of pharmacogenetics will be significant.

This bitter pill will only be swallowed if evidence of cost effectiveness exists.

The time to measure health economics is during the clinical trial.