Genetic Technologies: Cost-Effectiveness Determinants and Data Needs

David L. Veenstra, PharmD, PhD

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Department of Clinical Pharmacy
UC San Francisco
davidv@itsa.ucsf.edu

Overview

- Cost-effectiveness analysis and decision making in healthcare
- Economic evaluations of genetic technologies
  - Methods
  - Data needs
- Examples of cost effectiveness analyses of genetic technologies

Cost-effectiveness analysis (CEA)

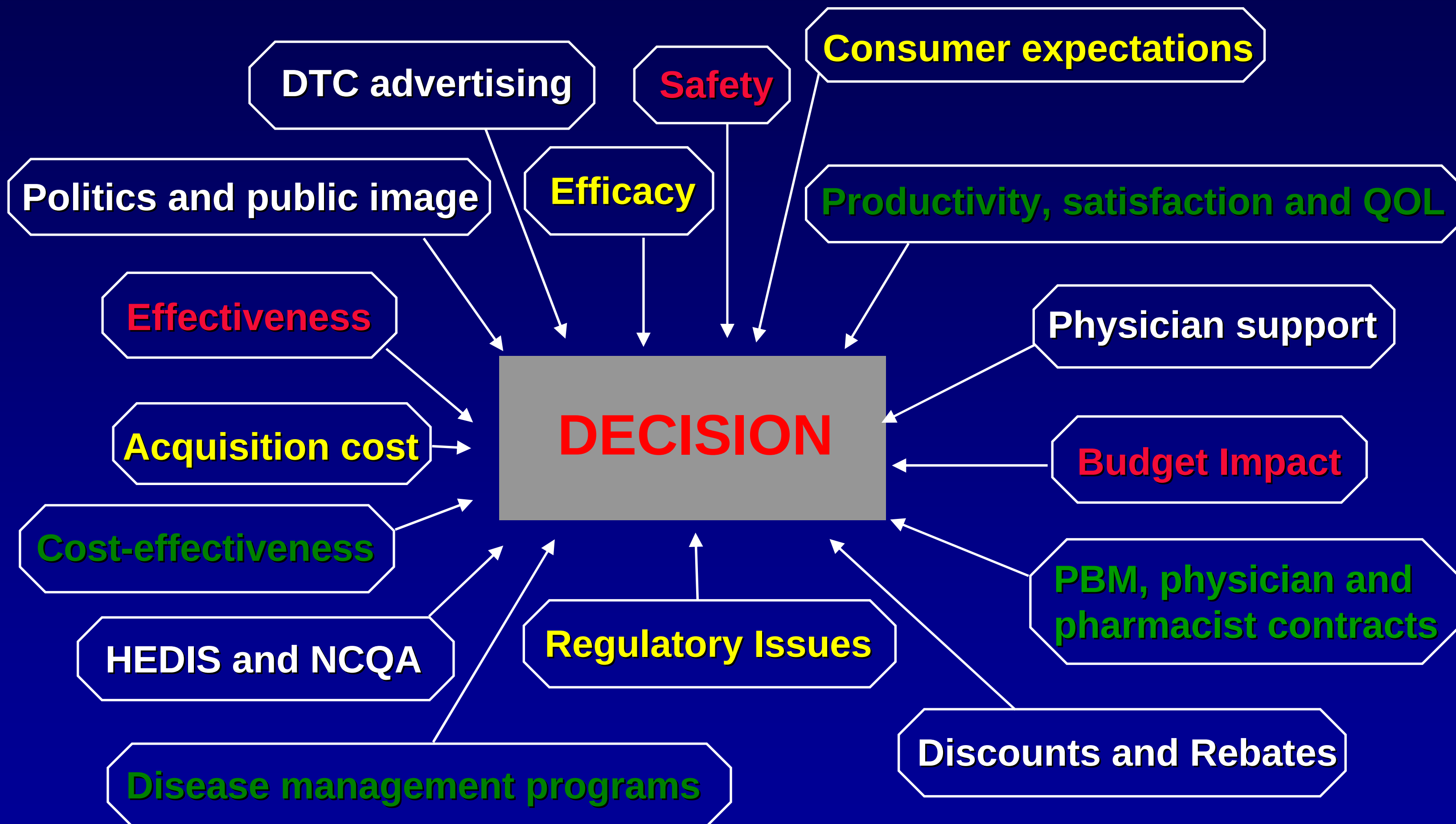
- A quantitative framework for evaluating the complex and often conflicting factors involved in the evaluation of health care technologies
- Can evaluate many types of costs and benefits
- Allows comparison of multiple strategies
- Provides decision makers with ‘real-time’ data for decision making

Types of Economic Evaluation in Healthcare

Study design	**Costs measured?**	**Effects measured?**
Cost-minimization	yes	no
Cost-consequences	yes	clinical outcomes
Cost-benefit	yes	economic outcomes ($)
Cost-effectiveness	yes	clinical outcomes
Cost-utility	yes	Quality-adjusted life-years (QALYs)

What information does CEA provide to health plans?

Just one of the factors in reimbursement decisions!

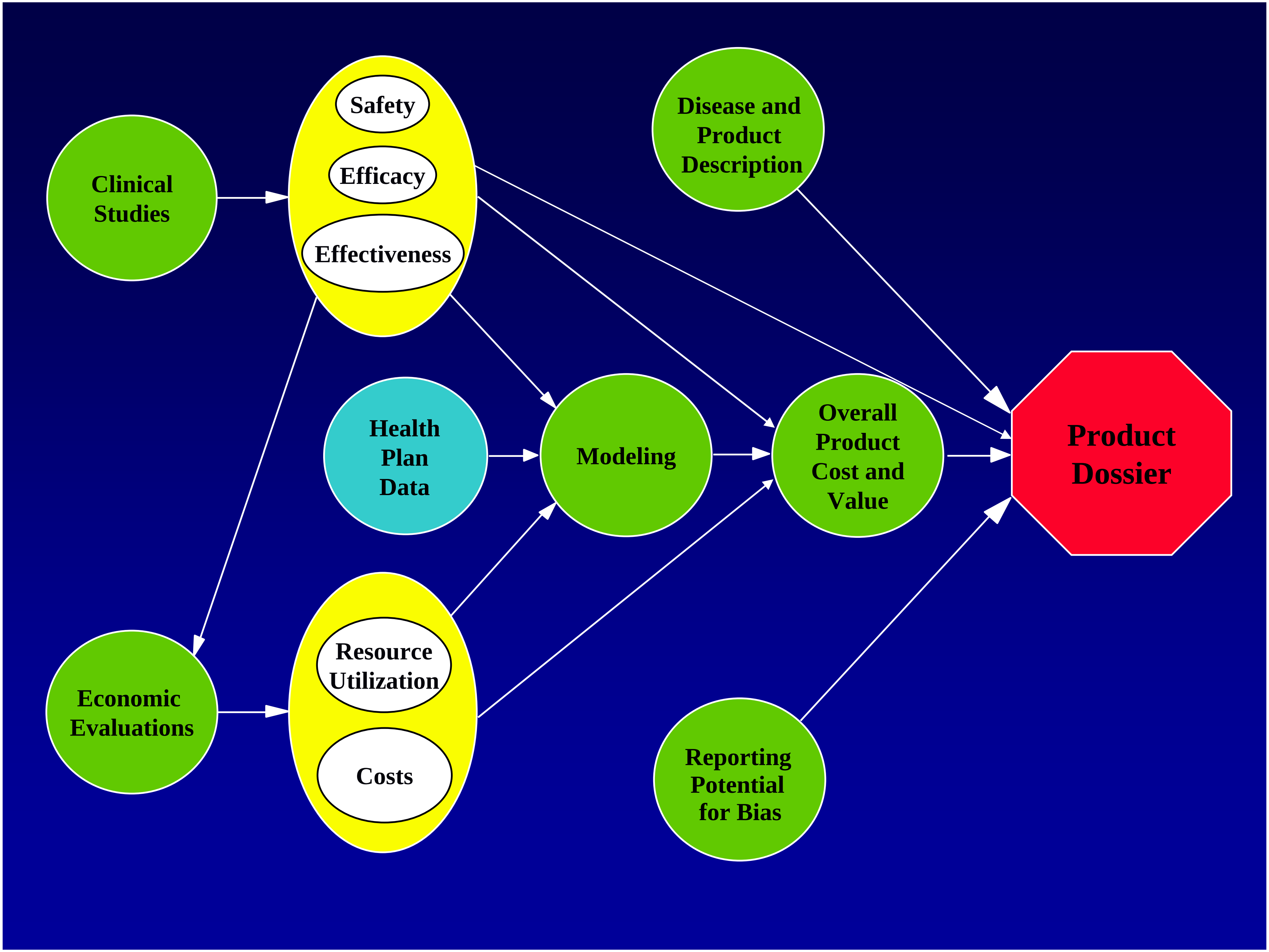


Is Cost Effectiveness Information Used in Reimbursement Decisions in the U.S.?

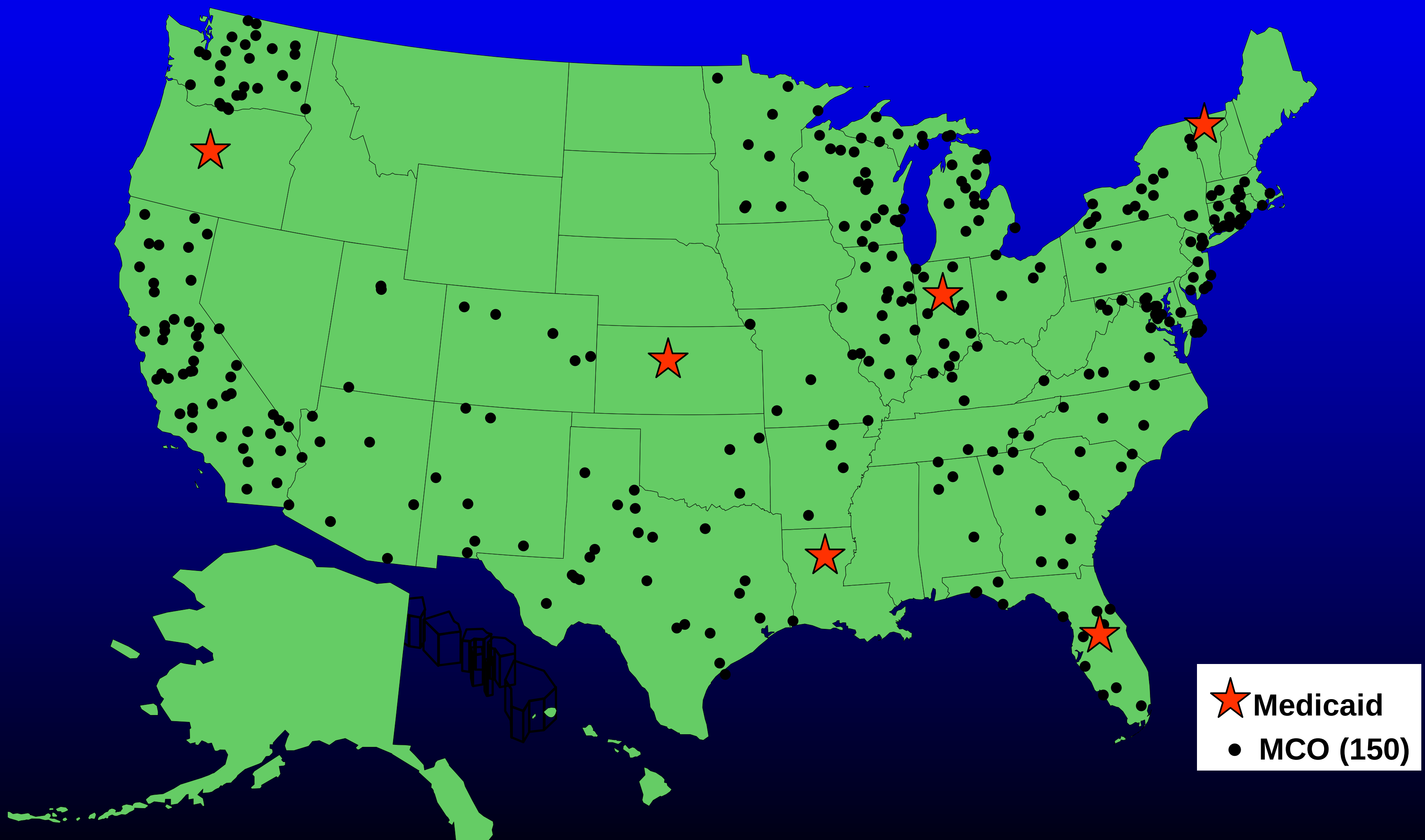
Academy of Managed Care Pharmacy Format

- **Approved by the AMCP Board of Directors in October 2000.**
  - **Specific unsolicited request for drug information to support formulary evaluation by health plans and PBMs.**
  - **Goals**
    - **Improve access to all available drug information at the time of formulary consideration.**
    - **Improve transparency of information.**
    - **Improve consistency with which the information is received.**
      - **Level the playing field for manufacturers.**

Fry RN, Avey SG, Sullivan SD. Value Health. 2003;6:505-21.


Clinical Studies
Safety
Efficacy
Effectiveness
Disease and Product Description
Health Plan Data
Modeling
Overall Product Cost and Value
Product Dossier
Economic Evaluations
Resource Utilization
Costs
Reporting Potential for Bias

States Requiring Health Outcomes Data for MCO or Medicaid Reimbursement



When is CEA most used?

1. When several similar products available, which one is most cost-effective?
   - E.g., statin drugs for high cholesterol
   - Guides selection of technology

2. For expensive and novel technologies, is the price reasonable?
   - E.g., Enteracept for rheumatoid arthritis
   - Guides access to technology

Genetic technologies: Do payers care?

- ‘Biotechnology’ drugs are of concern
- Genetic tests generally not on the radar screen yet - limited budget impact
- Genetic tests for disease predisposition
- Genetic tests for drug response (pharmacogenomics)

When will payers get more involved?

- When use of tests increases
  - tests for more common diseases or drugs
- When tests drive consumption of expensive resources
  - drugs, surgeries
- When regulatory authorities are more involved
  - e.g., FDA labeling changes

A framework for evaluating the cost-effectiveness of genetic technologies

1. How severe and frequent are the outcomes of interest?

- Pharmacogenomics
  - Dose selection (safety) ->

    Does the drug have a narrow therapeutic index, and is there significant inter-patient variability?
  - Drug selection (efficacy) ->

    Are the drugs expensive or used chronically?
- Pathogenomics
  - Disease risk ->

    What are the mortality and quality of life impacts of the disease?

    Is the disease expensive to treat?

Higashi and Veenstra, Am J Manag Care. 2003 Jul;9(7):493-500

Veenstra et al, AAPS PharmSci. 2000;2(3):E29

2. What is the alternative?

- Pharmacogenomics
  - Many drugs are already individualized, e.g., blood pressure, lipid levels, blood glucose
  - When there are readily available, inexpensive, and validated means of monitoring drug response, pharmacogenomics may offer little incremental benefit.
- Pathogenomics
  - Are there alternative screening strategies?
  - Are there other markers for risk?

3. What is the Strength of the Genotype-Phenotype Association? ("Effectiveness")

- Genotype -> Phenotype
- Example:
  - 50% of patients with mutation get an ADR
  - avoiding drug in **all** patients with mutation
  - half of the patients (the "false positives") would unnecessarily be deprived of medication.
- High penetrance = more cost-effective

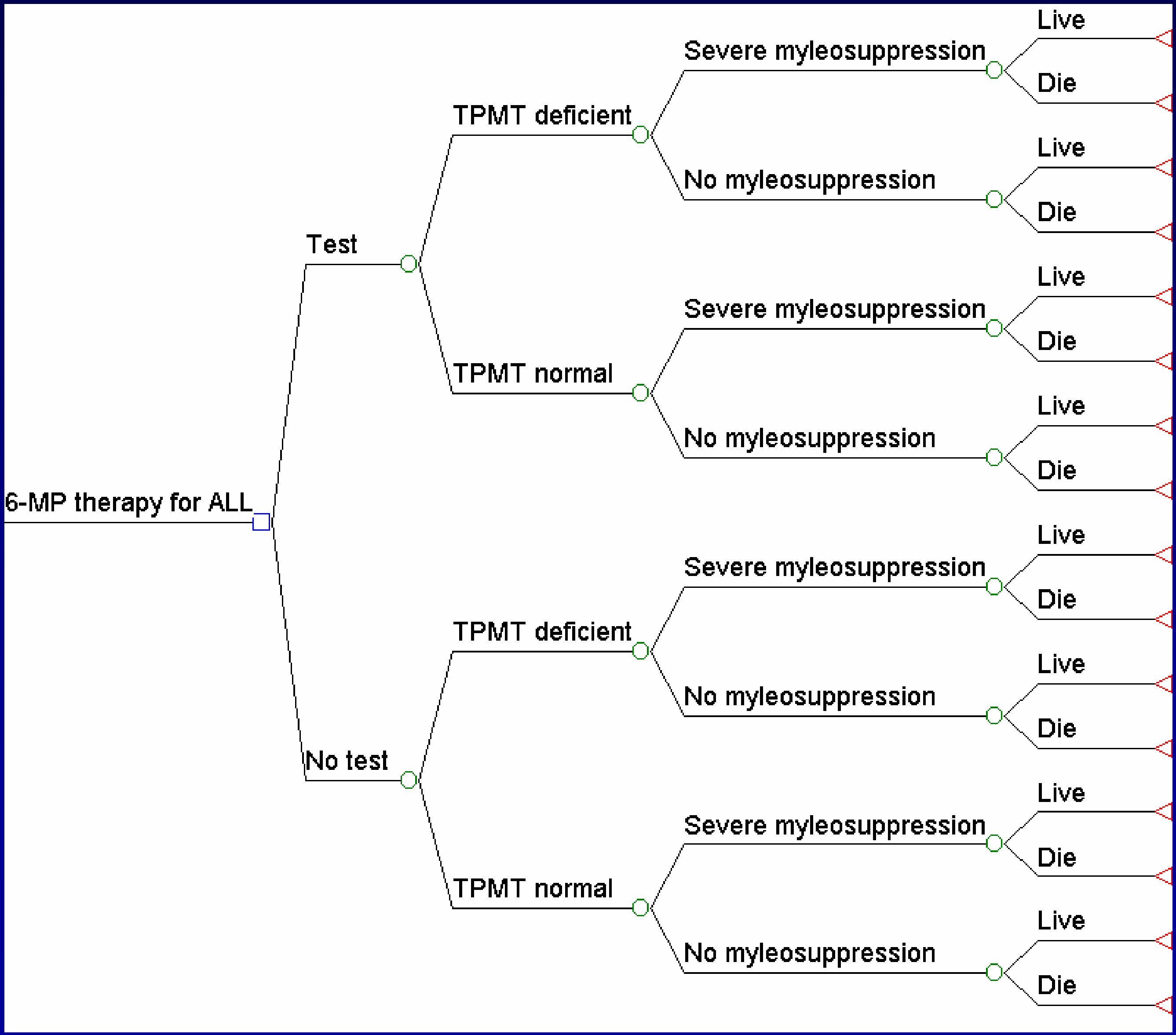
4. What does the test include?

- Induced costs
  - additional clinic visits
  - genetic counseling
- Additional use of information
  - used throughout the lifetime of the patient
  - used for other diseases or drugs
- Time costs
  - For pharmacogenomics, turn-around time may be critical
- Direct cost
  - Can vary substantially

5. What is the prevalence of the genetic variant?

- Genetic testing is essentially a screening strategy
- Thus, the frequency of the variant allele in the population being tested will be a critical factor
- Example:
  - prevalence of a genotype is 0.5%,
  - 200 patients must be tested to identify 1 patient with a variant allele, on average
- Sensitivity enhanced by methods used in CEA
  - e.g., calculating an incremental cost effectiveness ratio

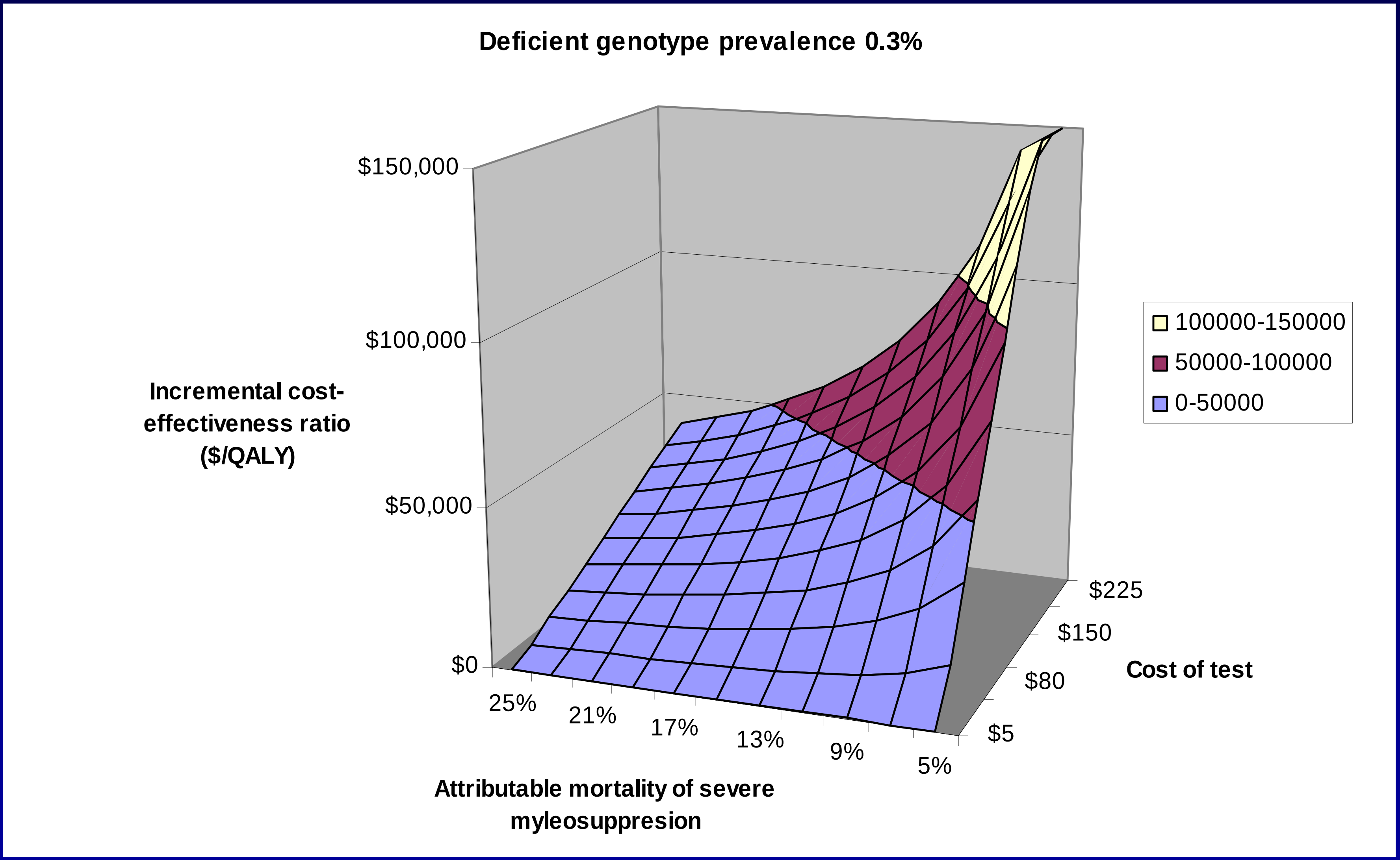
Genotyping children with ALL



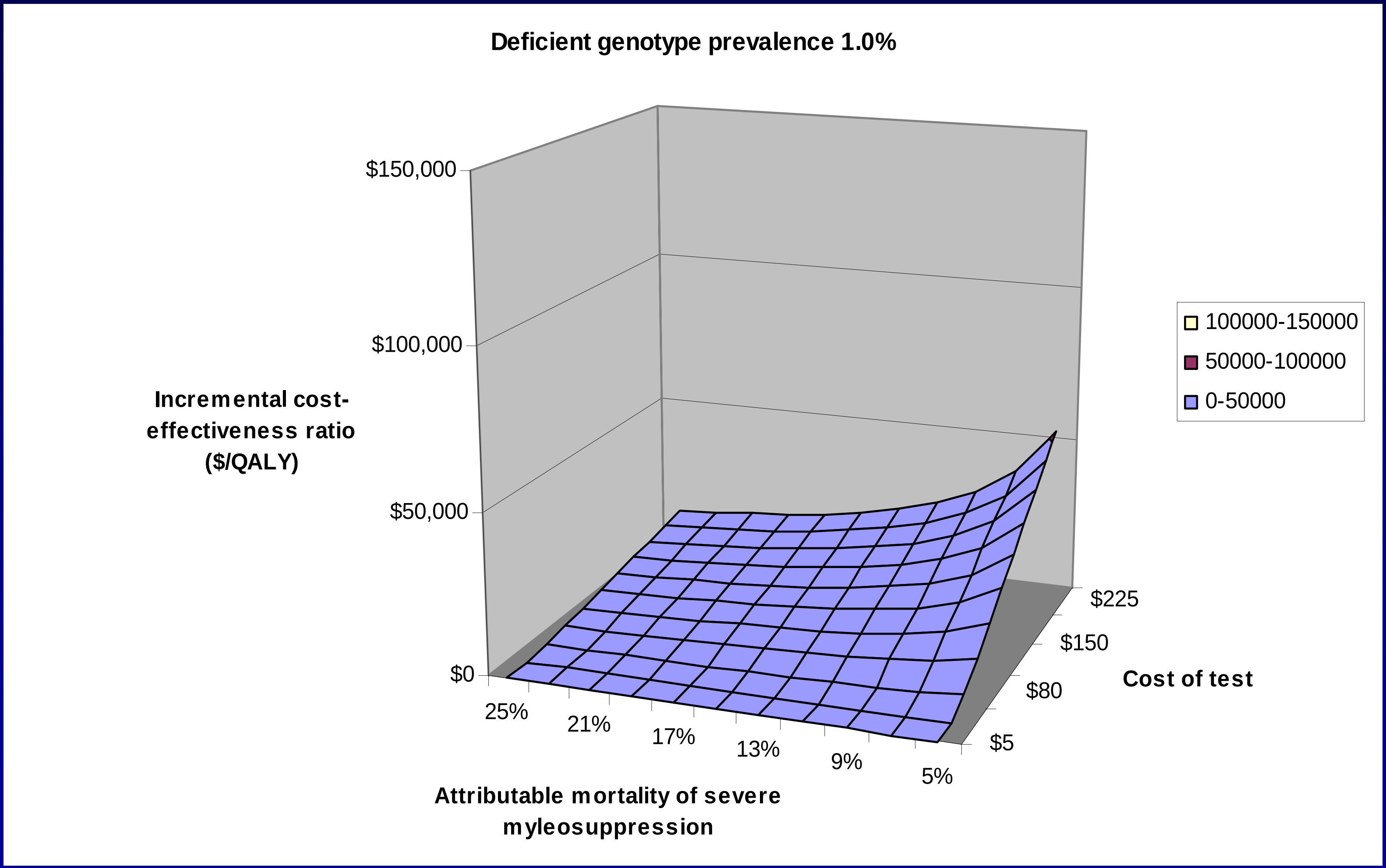
Hypothetical Analysis

- Varied the following parameters:
  - cost of the test ($5 to $250)
  - mortality due to severe myleosuppression (5% to 25%)
  - prevalence of patients with a TPMT deficient genotype (0.3%, 0.5%, and 1.0%)
- These 3 parameters are representative of 3 of the dimensions that affect the cost-effectiveness of genetic testing:
  - economic (cost of test)
  - genetic (genotype prevalence)
  - clinical (mortality of myleosuppression)

Genotype prevalence 0.3%



Genotype prevalence 1.0%



Newborn Screening: MCADD

- Medium-chain Acyl-CoA dehydrogenase deficiency (MCADD) screening at birth [1/15,000 births]
- Cost-utility analysis using modeling techniques
- Cost of test: an additional $4
- Screening vs. No Screening (2001 birth cohort, 4M births)
  - Longer and better life: 990 QALYs
  - Higher overall cost: $5.5 M
  - But 'cost-effective' at $5,600 per QALY

Venditti et al, Pediatrics. 2003 Nov;112(5):1005-15.

Cancer Screening: HNPCC

- Hereditary nonpolyposis colorectal cancer (HNPCC)
- Bethesda guidelines
  - Family hx. followed by MSI and germline testing
- When only patients offered testing:
  - $42,210 per QALY
- When siblings and children offered testing:
  - $7,556 per QALY
- Bethesda guidelines are cost effective, especially when relatives are included

Ramsey et al, Genet Med. 2003;5:353-63.

Ramsey et al, Ann Intern Med. 2001;135:577-88.

Systematic review of CEA's of pharmacogenomics

- Ten studies met the inclusion criteria for a CEA of PGx (out of 253 citations identified).
- Studies examined:
  - thromboembolic disease (n=4)
  - chronic hepatitis C virus (n=2)
  - Thiopurine s-Methyltransferase Polymorphisms (TPMT) (n=2)
  - Helicobacter pylori infection associated with Duodenal Ulcer (n=1)
  - HIV (n=1)
- Eight studies found genotyping to be relatively cost-effective, while two studies found it to be less cost-effective than other options

Phillips, Van Bebber, and Veenstra, Working paper.

Pharmacogenomics: TPMT and autoimmune rheumatic diseases

- TPMT inactivates Azathioprine (AZA)
- 10-15% of patients have serious ADR from AZA
- Results
  - The usual dosing strategy cost $677 Cdn per patient,
  - Whereas the genotype directed dosing strategy cost $663 Cdn per patient.
- NNT to avoid 1 ADR over 6 months: 20
- TPMT testing to guide AZA dosing may be not only cost-effective, but cost saving.

Marra et al, J Rheumatol. 2002;29:2507-12.

Unique challenges of CEA of genetic technologies

- The data needs for evaluating genetic technologies are extensive
- The interaction among these components are complex
- A better understanding of the clinical, economic, and patient outcomes is needed
  - cost issues surrounding testing
  - cost of disease and/or adverse drug reactions
  - impact of patient preferences (quality of life)

How do we address these challenges?

- Use decision-analytic and disease modeling techniques to:
  - build a framework for addressing these complex decisions
  - incorporate data from a multitude of sources
  - evaluate uncertainty in the decision and drivers of CE
- Evaluate economic costs
  - testing
  - clinical outcomes
- Evaluate patient outcomes
  - preferences
    - attitudes -> preferences -> quality of life
- Evaluate clinical outcomes
  - association studies!
  - then, intervention studies

Next steps

- Establishing guidelines and policies for reimbursement of genetic tests and services
- Evidence for effectiveness of tests
  - efficacy of intervention
  - decreased morbidity, increased life expectancy, improved quality of life
- Evidence of cost-effectiveness
  - Prevalence of variant genotypes
  - Cost of test, interventions
  - Patient perspective

Future Issues

- Who will be responsible for decisions?
  - Pharmacy and Therapeutics Committees
  - Medical services
- Will testing be <u>required</u> before certain interventions?
  - 'Prior authorization'
  - Formulary structure
- Will results be a part of the medical or billing records?

Summary

- Reimbursement decisions about genetic technologies are very complex
- Cost-effectiveness analysis can assist decision making by
  - providing a quantitative framework for the decision
  - highlighting data needs
  - identifying the important clinical, economic, and patient parameters
- Significant additional studies in this area are needed