February 11 DRAFT

# Costs and Cost-Effectiveness: Terms & NBS Applications

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Presentation to

Discretionary Advisory Committee on Heritable Disorders in Newborns and Children

Rockville, MD

February 12, 2015

National Center on Birth Defects and Developmental Disabilities

Office of the Director

# Acknowledgments


- Lisa Prosser, University of Michigan
- Alex Kemper, Duke University
- Yao Ding, Association of Public Health Laboratories
- John Thompson, Washington Department of Health
- Anne Comeau, New England Newborn Screening Program
- Scott Shone, New Jersey Department of Health

# Glossary

- **Cost – resources used up or foregone**
  - Direct cost – resources used up due to disease (or injury)
  - Indirect costs – foregone production due to disability or death
- **Cost analysis – partial economic evaluation**
  - Cost-of-illness analysis – direct and indirect costs of disease
  - Costing analysis – incremental cost of program or intervention
- **Cost-effectiveness analysis**
  - Full economic evaluation in which costs and health are counted separately
- **Cost-benefit analysis**
  - Full economic evaluation in which health and other outcomes are valued in money terms

# What's a Cost?

- Economic cost – value of resources used up or foregone (opportunity or resource cost)
- Financial or accounting cost – who pays what
  - Example of difference: evidence reviews
- Variable and fixed costs
  - Fixed costs do not vary with output (e.g., number of tests)
  - Variable costs increase with output
- Marginal cost – change in total cost when you do more of the same thing, e.g., test twice as many specimens
- Incremental cost – change in total cost when you do something different, e.g., add a new lab test

# How to Estimate Costs for Health Care?

- **Direct**
  - Micro-costing
    - Calculate quantities of labor time, equipment, supplies, etc.
    - Apply unit costs to calculate total costs
  - Cost accounting data
- **Indirect (used for clinical services)**
  - Charges
    - Hospital charges may be 2-5 times higher than actual cost
    - Cost-to-charge ratios can be used to estimate average cost, but costs may be underestimated because of exclusion of professional fees
  - Fee schedule – Medicare or state-specific Medicaid
  - Average payment – claims data

# Incremental Costs in Dried Blood Spot NBS

- **Costs to public health departments**
  - Laboratory testing
    - Staff costs
    - Equipment and reagents
    - Space and utilities
  - Short-term follow-up and tracking
- **Downstream costs to health care systems and families**
  - Clinical follow-up from screening through diagnosis
  - Long-term management
    - Target conditions – difference in treatment following early diagnosis
    - Secondary conditions or ambiguous diagnoses
- **Cost of NBS expansion is more than laboratory costs**

# Laboratory Testing Cost using Flow-injection MS/MS for Lysosomal Storage Disorders

- State X has 100,000 births per year, 1.2 screens per infant
- Cost to purchase 3 MS/MS instruments and ancillary equipment ~$1.2 million
  - Annual cost of depreciation $160,000
  - Annual maintenance cost $150,000
  - Annual cost of lab upgrades $20,000
- Labor cost for 3 FTEs including fringe and indirects
  - Annual cost $340,000
- Reagents cost $1 per test per LSD
- Incremental cost to screen for 1 LSD is $7.90 per infant
- Incremental cost to screen each additional LSD is $1.20 per infant

# Costs of Diagnostic Testing for MPS I

- **Between 8 and 45 per 100,000 infants screen positive for MPS I and referred for diagnostic testing**
- **Confirm low or undetectable enzyme activity**
  - Alpha-L-iduronidase enzyme activity assay in white blood cells
  - Urinary excretion of glycosaminoglycan (GAG)
  - Cost between $200 and $600 per specimen tested
  - Total cost of $2,400 to $27,000 for 100,000 infants screened
- **Diagnostic molecular testing**
  - Cost between $1,000 and $2,800 per *IDUA* gene sequencing test
  - Total expected cost between $2,000 and $8,000.
- **Total cost $4,500 to $36,000, or $0.05-0.35 per infant**

APHL. Public Health System Impact Assessment: Fact Sheet for MPS I Screening

# Cost to WA Department of Health to add SCID

- Washington has 86,600 births with 2 screens per infant
- Cost of TREC assays (TREC amplification and a control gene, *beta-actin*) calculated by WA Department of Health to be $8.08 per infant
  - Other screening laboratories report ~$6 per specimen
- NBS short-term follow-up costs $50 per positive screen
  - No additional clinical cost because no additional visits needed
- 0.029% of all infants referred for confirmatory flow cytometry testing cost $250 each
  - Including phlebotomy and clinical interpretation
- Total screening cost estimated to be $8.17 per infant
  - NBS fee raised by $8.17 when SCID was added

# Cost to States to Add a Condition Varies

- Average variable cost of laboratory testing may be higher with lower testing volume
- States may attribute share of fixed costs to new tests
- States may pay for cost of confirmatory and diagnostic testing
- States may offer contracts to specialty centers
- SCID example: Florida Department of Health
  - Cost per infant calculated to be $16.67
  - Includes staff time, equipment, reagents, "colocation", and referral center contracts

Kubiak C, et al. Fiscal implications of newborn screening in the diagnosis of severe combined immunodeficiency. J Allergy Clin Immunol Pract. 2014;2(6):697-702.

# Economic Cost of Screening for a Disorder

- Incremental cost of screening
- Incremental costs of confirmatory and diagnostic testing
  - Cost per test multiplied by number of infants tested with NBS minus number of infants tested without NBS
- Incremental costs of treatment

**TABLE 2** Projected Costs and Health Benefits for Newborn-Screened and Clinically Identified Newborn Cohorts

| | Clinical Identification (SE) | Newborn Screening Program (SE) | Difference With Screening |
|---|---|---|---|
| Population, *n* | | | |
| Size of population | 100 000 | 100 000 | |
| Children diagnosed with MCADD | 5.88 (0.01) | 8.40 (0.01) | 2.52 |
| False-positive screen results | NA | 20 (0.02) | 20 |
| Costs, $[a] | | | |
| Screening | NA | 710 251 | 710 251 |
| Treatment[b] | 630 704 (10 639) | 919 231 (12 243) | 288 527 |
| Total | 630 704 (10 639) | 1 629 482 (12 250) | 998 778 |

Prosser LA, Kong CY, Rusinak D, Waisbren SL. Projected costs, risks, and benefits of expanded newborn screening for MCADD. Pediatrics. 2010;125(2):e286-294.

# Value for Money

- **Is newborn screening for condition X**
  - Cost-effective?
  - Cost-saving?
  - Cost-beneficial?
  - Positive ROI?
- **Terms matter**
  - Each is associated with specific method
  - Choice of methods depends on purpose of analysis and stakeholder preferences

# Economic Evaluation Methods

- **Cost-effectiveness analysis (CEA)**
  - Which approach costs less per unit of health gained?
  - CEA using quality-adjusted life years (QALYs) also called cost-utility analysis (CUA)
- **Cost-benefit analysis (CBA)**
  - Is the monetary value of benefits to society greater than total cost?
- **Budget impact analysis (BIA)**
  - Expected net change in financial expenditures for a health care system over a given timeframe – budget holder perspective
  - Can also be used to assess financial return on investment (ROI)

Sullivan SD, Mauskopf JA, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. Value Health. 2014;17(1):5-14.

# CEA or CBA: Which Method to Use?

- **Cost-effectiveness analysis is favored by experts in medical decision making**
  - Journals and academics often prefer use of QALYs
  - Focus is on medical costs and impact on health care sector
  - Doesn't require one to put an explicit dollar value on life
- **Legislators and policy makers may prefer cost-benefit analysis**
  - All outcomes expressed in dollars, easy to understand
  - Allows for comparison across multiple sectors
  - Essential for interventions whose primary benefits accrue to other sectors, e.g., home visiting, childhool lead prevention

# Value is in the Eyes of the Stakeholder

- **For some, only health outcomes matter**
  - Medicare coverage decisions based on "medical necessity"
- **Others are interested in budget impact**
  - Affordability – direct outlays
  - Net cost savings and return on investment (ROI)
- **Affordability or value?**
  - If an intervention is "affordable" in terms of overall costs and no major change in infrastructure is required, decision may be driven by perceived benefits alone
  - If intervention is perceived as difficult or expensive, consideration of cost-effectiveness or cost-benefit may play a role

# Affordability vs. Value

- A low-cost intervention may be seen as affordable but a more expensive intervention may be cost-effective
- Example: lung cancer screening and HCV treatment
  - Cost of lung cancer low-dose CT screening about $100 per visit
  - Cost of sofosbuvir-based treatment of chronic hepatitis C virus infection is about $84,000
  - We know which intervention is more expensive, but what about value for money? We'll come back to this question later


Black WC, et al. Cost-effectiveness of CT screening in the National Lung Screening Trial. N Engl J Med. 2014;371(19):1793-802.

Liu S, et al. Sofosbuvir-based treatment regimens for chronic, genotype 1 hepatitis C virus infection in U.S. incarcerated populations: a cost-effectiveness analysis. Ann Intern Med. 2014;161(8):546-53.

Carroll AE. Can I interrupt your repeating a Medicare press release to talk about cost-effectiveness? TheIncidentalEconomist.com , February 7, 2015

# How Can Decision Makers Use Economic Evaluations?

- **Consider health outcomes and costs as separate criteria, i.e., traditional approach**
- **Assess balance of costs and outcomes, e.g., net benefit or cost-effectiveness ratio**
  - Use economic findings to inform decision to approve an intervention
    - Decision rule – yes/no decision or deferral of final decision
    - Cost-effectiveness or net benefit as one among many decision criteria
  - Use economic findings to guide prioritization or implementation by providers of recommended services
- **Use findings to identify gaps in knowledge and prioritize research**

# How Do Other Federal Advisory Committees Use Economic Information?

- **US Preventive Services Task Force**
  - No explicit use
- **Community Guide**
  - Existing economic estimates reviewed by CDC economists after a decision is made to recommend a service
  - Intended to help stakeholders with prioritization of implementation
- **Advisory Committee on Immunization Practices (ACIP)**
  - Required input for decisions on adding vaccines to schedules
  - Nominators for vaccines must provide economic analysis
  - Reviewed by CDC economists and Committee members

# US Vaccine Policy: Advisory Committee for Immunization Practices


- Disease burden
- Vaccine safety
- Vaccine effectiveness
- Cost-effectiveness
- Impact on providers

Source: Lisa Prosser

# Pre-2009 Influenza Vaccination Mean C/E Ratios, $/QALY

| | Low Risk | High Risk |
|---|---|---|
| 6-23 m | $15,000 | CS |
| 24-59 m | $29,000 | <$1,000 |
| 5-18 y | $120,000 | $10,000 |
| 19-49 y | $26,000 | CS |
| 50-65 y | $7,000 | CS |
| 65+ y | CS | CS |

CS = Cost saving

Source: Lisa Prosser

# Is an Ounce of Prevention Worth a Pound of Cure?

- **Yes, but not necessarily *cheaper* (cost-saving)**
  - Sometimes prevention reduces total direct costs of care
    - Traditional childhood vaccines
    - Folic acid fortification
    - Smoking cessation
  - Most preventive services cost more than they save in medical costs
- **Is early detection of disease worth the extra cost compared to current standard of care?**
  - Cost-effective – Compares favorably to other ways to improve health
  - Cost-beneficial – Monetary value of health improvements exceeds the societal cost, i.e., positive net benefit

**Grosse SD**. Does newborn screening save money? The difference between cost-effective and cost-saving interventions. *Journal of Pediatrics*. 2005; 146(2):168–170.

# From Partial to Full Economic Evaluation

- **A full economic evaluation requires a sequence of partial analyses**
  - Systematic evidence review
    - Screening test characteristics (analytic and clinical validity)
    - Health outcomes (clinical utility)
  - Costing analysis – cost of screening and diagnosis
  - COI (incidence-based analysis) –costs of treatment with and without early identification
- **Decision analytic modeling**
  - Tto project net direct costs and health outcomes
  - Sensitivity analyses to model uncertainty
  - Highlight gaps in data and need for more research

Prosser LA, Grosse SD, Kemper AR, Tarini BA, Perrin JM. Decision modeling, economic evaluation and newborn screening: challenges and opportunities. *Genet Medi* 2012;14(703-12.

# Effectiveness First, then Cost-Effectiveness

- Without sufficient evidence to quantify effectiveness, it may be misleading to assess cost-effectiveness
- Evidence of effectiveness is often incomplete
- Or, estimates of effectiveness may vary
  - Mammography – What fraction of breast cancer deaths are avoided: 15-20% or 35-40%?
  - Newborn screening for CAH – What is the infant mortality rate without NBS: 2% or 12%?

Grosse SD. Economic analyses of genetic tests in personalized medicine: clinical utility first, then cost-utility. *Genet Med.* 2014;16(3):225-227.

# Framing a Full Economic Evaluation

- Assuming evidence of effectiveness
- Define the audience
  - Legislators, payers, hospitals, health department?
- Select analytic perspective and time frame
  - Societal, long-term
  - Health care, long-term
  - Health care payer or health department, short-term
- Define intervention options to be evaluated
- Select costs and health outcomes to be modeled

# Framing an Economic Evaluation for a Candidate Condition for Newborn Screening

- **Decision analysis without costs**
  - Epidemiology and test characteristics
    - Incremental cases detected, by level of severity
  - Assuming better outcomes with early diagnosis and treatment
    - Quantify health outcomes with and without screening
      - Cases of disease or disability avoided
      - Life-years saved or quality-adjusted life-years (QALYs)
- **Add costs to decision analysis**
  - Calculate total costs for each strategy being compared
  - Calculate incremental costs
  - Estimate net costs, benefits, or incremental cost-outcomes ratios

# Cost-Effectiveness Analysis (CEA)

- Method for comparing net cost per health outcome
- For each pair of options (e.g., screening vs. no screening, two different screening algorithms)
  - Assess total outcomes and costs
  - Exclude dominated options that cost more and less effective (i.e., one option is cost-saving)
  - Calculate incremental cost-effectiveness ratio (ICER) for two strategies that are non-dominated

$$Cost - effectiveness\ ratio = \frac{intervention\ costs\ - costs\ averted}{change\ in\ health\ outcome}$$

# How to Interpret Cost-Effectiveness Ratios?

- **Decision rules**
  - Single threshold, e.g., if <$50,000 per QALY, intervention is cost-effective – arbitrary value (Neumann et al. 2014; Grosse 2008)
  - Range of values, e.g., $50,000-$250,000 per QALY as lower and upper bounds for cost-effectiveness
- **Comparison with other coverage decisions**
  - Revealed willingness of decision makers to pay for health
  - A "league table" of ICERs for other clinical preventive services or public health programs (usually <$250,000 per QALY)
  - Funded services may have very wide range of ICERs
  - Treatments for rare diseases often >$1 miillion per QALY

Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness--the curious resilience of the $50,000-per-QALY threshold. *N Engl J Med*. 2014;371:796-7.

Grosse SD. Assessing cost-effectiveness in healthcare: history of the $50,000 per QALY threshold. *Expert Rev Pharmacoecon Outcomes Res*. 2008; 8:165-78

# Rare Disorders: Revealed Willingness to Pay

- **Orphan drugs to treat rare disorders often cost more than $250,000 per person per year**
  - Cystic fibrosis – New "breakthrough" drug targeted to 4% of patients with a specific *CFTR* mutation costs $300,000 per year
  - Pompe disease – ERT cost varies with body weight
    - In US average cost is said to be $300,000 per year
    - In Europe, ICER estimated at $1.3 million per QALY
  - Hemophilia A (congenital Factor VIII deficiency)
    - Mean cost of treatment about $150,000 per year in 2008
    - ~7% develop an antibody inhibitor that requires a recombinant bypassing agent, at an average cost of ~$500,000 per patient

Guh S, Grosse SD, McAlister S, Kessler CM, Soucie JM. Health care expenditures for Medicaid insured people with hemophilia in the United States, 2008. *Haemophilia*. 2012;18(2): 276–283.

Kanters TA, Hoogenboom-Plug I, et al. Cost-effectiveness of enzyme replacement therapy with alglucosidase alfa in classic-infantile patients with Pompe disease. *Orphanet J Rare Dis*. 2014 ;9:75.

# Cost-Effectiveness and Coverage Decisions

- Medicare will soon cover CT screening for lung cancer in ever smokers (history of at least 30 pack-years, current smokers or quit within past 15 years)
- CEA of National Lung Screening Trial, ages 55-74
  - Current smokers $43,000 per QALY
  - Former smokers $615,000 per QALY
- Sofosbuvir for chronic HCV infection is controversial
- CEA of 12 week course of sofosbuvir-based 3-drug treatment of prisoners with genotype 1 HCV infection
  - <1.5 years remaining sentence $25,700 per QALY

Black WC, et al. Cost-effectiveness of CT screening in the National Lung Screening Trial. N Engl J Med. 2014;371(19):1793-802.

Liu S, et al. Sofosbuvir-based treatment regimens for chronic, genotype 1 hepatitis C virus infection in U.S. incarcerated populations: a cost-effectiveness analysis. Ann Intern Med. 2014;161(8):546-53.

# Cost-Benefit Analysis (CBA)

- **All costs and benefits are in the same metric (dollars)**
  - All health outcomes must be assigned dollar values, controversial
- **Outcome measures: net benefit and benefit-cost ratio**
  - Economists prefer net benefit (net present value or NPV)
  - Benefit-cost ratio is less reliable because cost denominator can be calculated in different ways

net benefit of intervention = benefits – costs

benefit-cost ratio = benefits / costs

# Two Approaches to Valuation in CBA

- **Traditional CBA approach**
  - 'Human capital' valuation of ill-health or premature death in terms of foregone earnings and household services
  - Present value at birth (3% discount rate) of $1.1-1.3 million
  - Indirect cost, does not reflect intangible costs
- **CBA in regulatory policy analyses**
  - 'Willingness-to-pay' (WTP) to reduce risk of ill-health
  - WTP to avoid death is called Value of a Statistical Life (VSL)
    - Includes intangible value of life and spillover benefits to others
    - Typically $6-9 million per death avoided or delayed
    - Based on statistical analyses of occupational deaths and earnings

# Washington State's Use of CBA & CEA in NBS

- Washington state law requires cost-benefit analysis for new regulations, including additions to NBS panel
- Since 2002 Washington Department of Health (WDOH) has developed spreadsheet economic models prior to each NBS expansion
  - Cost-benefit analysis
    - Calculates dollar value of deaths averted using estimate of Value of Statistical Life ($7.7 million used in 2012 SCID analysis)
  - Cost-effectiveness analysis (for some conditions)
    - Direct cost per life-year saved

Grosse SD. Cost effectiveness as a criterion for newborn screening policy decisions. In: Baily MA, Murray TH (eds). *Ethics and Newborn Genetic Screening: New Technologies, New Challenges*. Baltimore: Johns Hopkins University Press. 2009: 58–88.

Grosse SD, Thompson JD, Glass M. The use of economic evaluation to inform newborn screening policy decisions: The Washington state experience. Draft manuscript.

# CEA/CBA Model of NBS for SCID

- Collaboration of WDOH, APHL, and CDC based on adaptation of WDOH SCID cost-benefit model
- Model components
  - Screening costs
  - Reduction in mortality
  - Cost offset from early treatment
  - Net cost per life-year saved
  - Economic benefit using VSL (WTP) valulation of averted deaths

Ding Y, et al. A model of the economic impact of universal newborn screening for severe combined immune deficiency in Washington state. Draft manuscript.

# Cost Offset of NBS for SCID

- **Early diagnosis is associated with lower treatment costs**
  - Mean cost at Duke University Medical Center $100,000 for early HCT vs. $450,000 for late HCT (Buckley 2012)
  - Mean hospital charges at 3 referral hospitals (Kubiak et al. 2014)
    - $366,000 for early HCT vs $1.43 million for late HCT
    - Applying national cost-to-charge ratio of 0.345 for SCID, mean costs of $126,000 vs. $494,000
  - Modell et al. (2014) assume mean cost of $320,000 for early HCT and $2 million for late HCT
  - Chan (2014) assumes average treatment costs with and without NBS at approximately $120,000 and $1.2 million.


Buckley RH. The long quest for neonatal screening for severe combined immunodeficiency. *J Allergy Clin Immunol*. 2012';29 :597-604

Kubiak C. et al. Fiscal implications of newborn screening in the diagnosis of severe combined immunodeficiency. *J Allergy Clin Immunol Pract*. 2014; 2:697-702.

Modell V, Knaus M, Modell F. An analysis and decision tool to measure cost benefit of newborn screening for severe combined immunodeficiency (SCID) and related T-cell lymphopenia. *Immunol Res*. 2014; 60:145-52.

K. Chan, A global economic evaluation simulation model of cost-savings In newborn screening for severe combined immunodeficiency,.9th International Society for Neonatal Screening European Regional Meeting 2014, Birmingham, UK.

# Cost-Effectiveness of NBS for SCID in Washington

- **Base case estimate is $32,970 per life-year saved**
  - 1.49 SCID cases detected per year
  - 0.34 annual deaths avoided
  - 30.34 discounted life years per infant death avoided
  - Net direct cost of $343,070 per year
    - Cost of screening: $756,961
    - Cost offset: $413,888
- **Sensitivity analyses**
  - NBS would be cost-saving if the difference in treatment cost per infant with SCID exceeds $637,300
  - One-way sensitivity analyses show ICER <$65,000 per LY saved under all plausible assumptions

# Net Benefit of NBS for SCID in Washington

- **WTP of $9 million per death averted**
  - Based on average VSL used in recent CBAs by Federal regulatory agencies (Office of Management and Budget, 2014)
  - Value of death averted: $3,086,424
- **Calculations of net benefit**
  - Base case
    - Net benefit: $2,743,351
    - Benefit-cost ratio: 4.62
  - WTP of $7 million
    - Net benefit: $2,057,459
    - Benefit-cost ratio: 3.72
  - WTP of $1.2 million – BCR of 1.09, essentially break-even

Office of Management and Budget. 2013 Report to Congress on the Benefits and Costs of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities. Washington, DC (May 2014).

# Lessons Learned

- **Modeling cost-effectiveness or cost-benefit of expanding NBS is resource intensive**
  - CDC CEA of screening for CCHD took two years
  - APHL CEA of screening for SCID has taken 9 months to adapt an existing model
  - SCID and CCHD models were conducted after conditions had been added to the RUSP
    - Previously published systematic reviews were available
  - Other costing or cost-effectiveness analyses had been published
- **Economic evaluations of screening for candidate disorders may be even more challenging**