Original Investigation

The Use of Economic Evaluation to Inform
Newborn Screening Policy Decisions:
The Washington State Experience

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Policy Points:

- Newborn screening not only saves lives but can also yield net societal economic benefit, in addition to benefits such as improved quality of life to affected individuals and families.
- Calculations of net economic benefit from newborn screening include the monetary equivalent of avoided deaths and reductions in costs of care for complications associated with late-diagnosed individuals minus the additional costs of screening, diagnosis, and treatment associated with prompt diagnosis.
- Since 2001 the Washington State Department of Health has successfully implemented an approach to conducting evidence-based economic evaluations of disorders proposed for addition to the state-mandated newborn screening panel.

Context: Economic evaluations can inform policy decisions on the expansion of newborn screening panels. This article documents the use of cost-benefit models in Washington State as part of the rule-making process that resulted in the implementation of screening for medium-chain acyl-CoA dehydrogenase (MCAD) deficiency and 4 other metabolic disorders in 2004, cystic fibrosis (CF)

in 2006, 15 other metabolic disorders in 2008, and severe combined immune deficiency (SCID) in 2014.

Methods: We reviewed Washington State Department of Health internal reports and spreadsheet models of expected net societal benefit of adding disorders to the state newborn screening panel. We summarize the assumptions and findings for 2 models (MCAD and CF) and discuss them in relation to findings in the peer-reviewed literature.

Findings: The MCAD model projected a benefit-cost ratio of 3.4 to 1 based on assumptions of a 20.0 percentage point reduction in infant mortality and a 13.9 percentage point reduction in serious developmental disability. The CF model projected a benefit-cost ratio of 4.0-5.4 to 1 for a discount rate of 3%-4% and a plausible range of 1-2 percentage point reductions in deaths up to age 10 years.

Conclusions: The Washington State cost-benefit models of newborn screening were broadly consistent with peer-reviewed literature, and their findings of net benefit appear to be robust to uncertainty in parameters. Public health newborn screening programs can develop their own capacity to project expected costs and benefits of expansion of newborn screening panels, although it would be most efficient if this capacity were shared among programs.

Keywords: neonatal screening, economics, cost-benefit analysis, cystic fibrosis, MCAD deficiency.

NEWBORN SCREENING (NBS) IS A SYSTEM IN WHICH INFANTS are tested after birth and then undergo further testing if they screen positive, followed by diagnostic evaluations and referral for services. NBS encompasses both laboratory testing for various disorders using dried blood spots (DBS) collected on filter paper cards and point-of-care testing for hearing loss and critical congenital heart defects. State NBS programs began in 1963 with the Guthrie test for phenylketonuria (PKU), a preventable cause of intellectual disability.¹

In many countries NBS is a national program, but in countries with federal governments such as the United States and Canada, state, provincial, or regional governments carry out NBS and decide which conditions should be screened under public health authority. The processes and criteria used by US states to decide which conditions to add to screening panels vary,²⁻⁷ as in other countries.^{8,9} The Wilson-Jungner screening criteria published in 1968 and inspired by the PKU experience¹⁰ have been widely used. Other criteria have been published by various

groups.^{7,11,12} Common themes are benefit to the newborn, feasibility of screening, and the availability of diagnostic and therapeutic services.⁷ Questions of cost and the balance of cost and benefits are discussed later.

To assure a common minimum screening panel, the US Department of Health and Human Services (HHS) commissioned the American College of Medical Genetics to establish an expert group to recommend screening criteria and a panel.¹³ The resulting panel of 29 primary conditions was endorsed in 2005 by the HHS Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC).^{13,14} That panel formed the basis for the HHS-endorsed Recommended Uniform Screening Panel (RUSP) that states are encouraged to adopt.

The ACHDNC subsequently established an evidence-based process for recommending disorders to be added to the RUSP.^{15,16} Recommendations are based primarily on evidence of the “magnitude and certainty of net benefit” (clinical effectiveness), along with feasibility and readiness of states to adopt screening. In particular, emphasis is placed on benefit to affected infants in terms of reduced risk of death in early childhood or of severe morbidity. Five additional conditions had been added to the RUSP as of February 16, 2016: severe combined immune deficiency (SCID) in 2010, critical congenital heart disease (CCHD) in 2011, Pompe disease in 2015, and mucopolysaccharidosis type I (MPS I) and X-linked adrenoleukodystrophy (X-ALD) in 2016, for a current total of 34 disorders.^{17,18}

This article has 5 purposes. One is to describe the process used in Washington State (Washington) since 2001 to decide on expansions to the NBS panel. The second is to document how economic evaluation modeling informed Washington NBS policy decisions from 2002 through 2012 (Table 1). A third objective is to summarize spreadsheet models and internal reports prepared by the Washington Department of Health (WDOH) for 2 conditions: medium-chain acyl-CoA dehydrogenase (MCAD) deficiency¹⁹ and cystic fibrosis (CF),²⁰ as well as a 2011-2012 WDOH model for SCID, the internal report for which is available online²¹ (a separate article describes an updated version of that model²²). A fourth purpose is to critique the assumptions in the MCAD and CF models relative to published cost-effectiveness analyses, the epidemiologic literature on those conditions, and the cost-benefit valuation methods. The final purpose is to draw lessons for the development of economic evaluations for other disorders proposed for addition to NBS panels.

Table 1. Prospective Economic Assessments of Newborn Screening Expansions Conducted by the Washington State Department of Health, 2002-2012

Conditions	Years of Economic Analysis	Year Screening Implemented	Health Benefits Modeled	Value of Statistical Life Used and Range (Millions US\$)
5 metabolic diseases ^a	2002-2003	2004	Mortality, developmental disabilities	4 (1-16)
Cystic fibrosis (CF)	2002-2005	2006	Mortality	4 (no range)
15 metabolic diseases ^b	2007-2008	2008	Mortality, developmental disabilities	4.4 (1-7)
Severe combined immune deficiency (SCID)	2011-2012	2014	Mortality	7.7 (6.1-9.1)

^aConditions included: biotinidase deficiency, galactosemia, homocystinuria, maple syrup urine disease, and medium-chain acyl-CoA dehydrogenase (MCAD) deficiency.

^bConditions included: isovaleric acidemia (IVA), very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency, long-chain L-3-hydroxy acyl-CoA dehydrogenase (LCHAD) deficiency, trifunctional protein (TFP) deficiency, glutaric acidemia type 1 (GA-1), methylmalonic acidemia – mutase deficient (MUT), methylmalonic acidemia – Cbl A,B (CblA,B), propionic acidemia (PROP), 3-hydroxy-3-methylglutaric aciduria (HMG), beta-ketothiolase (BKT) deficiency, citrullinemia (CIT), argininosuccinic acidemia (ASA), holocarboxylase synthetase deficiency (HCS) (multiple carboxylase deficiency (MCD), carnitine uptake deficiency (CUD), and tyrosinemia type 1 (TYR-1).

Economic Evaluations and NBS Policy Decisions

Economic evaluations of health interventions are of 2 general types.^{23,24} Cost-effectiveness analyses (CEAs) estimate the net costs of interventions and the numbers of outcomes achieved. For policies with both improved health outcomes and higher total costs, analysts calculate incremental cost-effectiveness ratios (ICERs). The definition of incremental cost is crucial. Only new costs are included in CEAs, unlike in cost accounting; the cost of existing screening infrastructure, including equipment already being used, is not apportioned to new tests. ICERs can be compared with those of other policies or interventions or some threshold value (eg, \$50,000 per life-year or quality-adjusted life-year) to inform decision makers who decide whether the additional value of health gains justifies the additional cost. We exclude partial economic evaluations that calculate costs relative to intermediate outcomes such as number of cases detected but that can be described as CEAs, since they provide no information about improvements in health or the value of NBS.

Cost-benefit analyses (CBAs), or benefit-cost analyses, express costs of both health and nonhealth outcomes in common monetary values, reporting estimates of net benefit in absolute terms as well as relative benefit-cost ratios. Two approaches can be used to assign monetary values to health benefits in CBAs.²⁵ The “human capital” approach values health in terms of impact on economic production by valuing years of productive life lost by individual productivity.²⁶ The approach used in regulatory CBAs values lives lost by a measure of society’s “willingness to pay” (WTP) to reduce the risk of adverse health outcomes such as premature death. WTP estimates based on “revealed preferences” used in US regulatory CBAs include the value of a statistical life (VSL), which is estimated through regression analysis as the increase in pay required to induce workers to work in relatively dangerous jobs divided by the absolute difference in mortality risk.²⁷ For example, if a difference in mortality risk of 1 in 100,000 is associated with a difference in annual earnings of \$70, the undiscounted VSL is \$70 divided by 0.00001, ie, \$7 million. Recent empirical US VSL estimates are in the range of \$8 million–\$11 million.²⁷ VSL estimates exceed the present value of expected future productivity, which at birth is approximately \$1 million.²⁸

One of the Wilson-Jungner criteria, “[t]he costs of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole,”¹⁰ suggests that economic assessments of both costs and benefits should inform policy decisions. However, this criterion can be understood as a weighing of separate criteria of costs of screening and the expected gains in health.²⁹⁻³¹ Even experts who do support the use of economic evaluation to quantify the balance of costs and benefits disagree whether this should be a required criterion¹² or just one factor to be considered along with criteria such as values of justice and equity.^{11,32}

Although the cost of testing is almost always listed as a criterion, no consensus exists regarding the net balance of costs and benefits.³³ In a sample of 22 European NBS policy decisions, costs were almost always considered, but in only 4 cases were CEAs conducted.^{34,35} Similarly, US NBS policy decisions typically consider the cost of testing^{4,13} but not cost-effectiveness or cost-benefit.²⁹ The ACHDNC is directed by the US Congress to consider “cost” for a disorder proposed for the RUSP,³⁶ which can encompass costs incurred by the public health and clinical systems, including short-term follow-up and data systems to track children and assess long-term outcomes. Although the ACHDNC evidence review process for candidate disorders includes peer-reviewed economic analyses,¹⁵ cost-effectiveness is not used by the ACHDNC in deciding which disorders to recommend.¹⁶ Also, economic analyses are rarely available for candidate disorders.³⁷ The secretary of HHS in approving the addition of CCHD to the RUSP in early 2012 charged the Centers for Disease Control and Prevention (CDC) with assessing cost-effectiveness of NBS for CCHD to inform subsequent state decisions.³⁸

Washington State NBS Policy Process and Economic Evaluations

The Revised Code of Washington (RCW) makes the Department of Health responsible for ensuring that required screening of all newborns is done. A separate part of statutory law authorizes the Department to “require a reasonable charge” for screening services (RCW 43.20B.020). The RCW gives the State Board of Health the responsibility to determine which disorders are to be included in the screening (RCW 70.83.020) and to “adopt rules and regulations necessary to carry out the intent of this chapter” (RCW 70.83.050), which the Board does under

Chapter 246–650 of the Washington Administrative Code (WAC). The Board defines the processes and criteria for making decisions and invites requests to consider adding a condition to the required NBS panel. If the Board decides to review a condition, it convenes an ad hoc NBS advisory committee to consider the merits and to make a recommendation. The Board decides whether to add the condition to the state panel in which case it amends the administrative code to list the new condition.

In 2001, the Board established 5 criteria to assess candidate disorders: prevention potential and medical rationale; treatment available; public health rationale; available technology; and cost-benefit/cost-effectiveness. If there is sufficient evidence that a condition satisfies the first 4 criteria, the Department is asked to conduct an internal economic evaluation to allow the Board to determine if the fifth criterion is also satisfied. The economic analyses are conducted to inform the Board's decision-making process and to satisfy the Washington Administrative Procedure Act, which states,

[b]efore adopting a rule . . . an agency shall: determine that the probable benefits of the rule are greater than its probable costs, taking into account both the qualitative and quantitative benefits and costs and the specific directives of the statute being implemented. [Revised Code of Washington (RCW) 34.05.328 Section (1)(b)]

The law does not require demonstration of positive net economic benefit based on quantitative benefits and costs, only that those benefits and costs be assessed. Likewise, there is no requirement that the analyses be disseminated outside of the agency responsible for making a regulatory decision.

The 2-step approach taken in Washington, ie, first evaluate feasibility and clinical benefit, and only then assess cost-benefit, is logical.²⁹ Without evidence of the effectiveness or clinical utility of an intervention, no conclusion can be made regarding cost-effectiveness, cost-utility, or cost-benefit.³⁹

Between 2002 and 2012 WDOH staff created CBAs of all conditions that received preliminary approval by the Board based on meeting the first 4 criteria. All of the analyses indicated positive net benefit for the conditions being evaluated. All of the conditions were ultimately approved by the Board for addition to the screening panel (see Table 1), and the Board considered the economic analyses to be persuasive (Maxine Hayes, MD, written communication, December 15, 2015).

All of the economic models assessed benefits of expanded NBS in terms of avoided direct medical costs and avoided deaths; the latter were valued using VSL estimates, which have varied over time (see Table 1). For those conditions for which prevention of developmental disability is an important benefit of early detection, the economic models included both direct medical and education costs (the difference in expected lifetime cost of schooling for children with and without a disabling condition) and the indirect cost of foregone productivity due to disability.

MCAD Deficiency and Other Metabolic Disorders

During 2001 and 2002, the advisory committee assessed 8 disorders detectable through laboratory tests and concluded that 5 had sufficient evidence to merit full economic evaluations: biotinidase deficiency, galactosemia, homocystinuria, maple syrup urine disease, and MCAD deficiency. A WDOH staff economist created spreadsheet models of costs and benefits for all 5 conditions and found net benefit for each. Each of the 5 conditions was recommended by the advisory committee in April 2002. The Board requested revisions to the economic analyses, which were finalized in July 2003; in August 2003 the Board approved the addition of the 5 disorders. Screening began during the first half of 2004 after the necessary infrastructure had been put in place. The MCAD model is summarized in Table 2.

Summary of MCAD Model. The costs attributed to NBS for MCAD deficiency were projected to amount to roughly \$9.9 million over 10 years, of which approximately \$8.7 million was the cost of the laboratory screening using tandem mass spectrometry (MS/MS) of 827,000 infants (present value of \$10.54 per infant, with an undiscounted cost of \$12 per infant screened). The other major cost of \$848,635 reflected the cost of additional hospitalizations for observation.

The entire cost of introducing MS/MS technology was assigned to MCAD deficiency. That is because the adoption of the technology was justified on the basis of its being able to detect cases of MCAD deficiency; other conditions with lower frequency were added because they could be identified at little extra cost using the same testing platform. Consequently, the incremental cost of screening for other disorders using MS/MS was estimated to be much lower than for MCAD deficiency.

Table 2. Key Assumptions and Findings for the MCAD Model

Variables	
Number of newborns screened in 10 years	827,000
Number of newborns with MCAD detected in 10 years	n = 35.1
Difference in survival with NBS	20.0 percentage points, n = 7.0
Difference in severe disability with NBS	13.9 percentage points, n = 4.9
Hospitalization for clinical identification without NBS	71%
Total costs (present value for a 10-year program)	
MCAD screening	\$8,727,769
Hospitalization for periods of fasting ^a	\$848,635
Clinical program (including confirmatory testing)	\$314,307
Total benefits (present value for a 10-year program)	
Avoided mortality	\$28,057,737
Reduced hospital-based cost of clinical identification	\$328,599
Avoided developmental disabilities	\$4,217,432
Net benefits (present value for a 10-year program)	\$22,713,057
Benefit-cost ratio	3.4
Cost per life-year saved	\$48,168

Abbreviations: MCAD, medium-chain acyl-CoA dehydrogenase; NBS, newborn screening.

^aCost was estimated based on a 72-year life span and hospitalization once every 3 years.

The WDOH MCAD cost-benefit model¹⁹ modeled 4 benefits: reductions in mortality, disability, morbidity, and unnecessary hospitalizations prior to diagnosis. Specifically, the model assumed that in the absence of NBS 20.4% of infants would die, most without a diagnosis, compared with 0.4% with screening, a 98% reduction in mortality (reduction of 20.0 percentage points). In the base model, avoided deaths were valued at \$4 million based on a midpoint of VSL estimates reported in studies published in the 1980s and 1990s.¹⁹ Similarly, it assumed that 14.2% of children would experience a serious developmental disability such as either cerebral palsy or intellectual disability compared with 0.3% with

screening (reduction of 13.9 percentage points). Finally, NBS would avoid for 71% of children an unnecessary hospitalization averaging 4 days in addition to \$12,000 in clinical costs incurred prior to diagnosis, offset by the cost of additional hospitalizations of diagnosed infants for observation and treatment (see Table 2). These assumptions are discussed further below.

Per-child lifetime costs for developmental disabilities were taken from a CDC-sponsored modeling study.^{40,41} In that study, roughly 70% of per-child costs were due to lost earnings resulting from disability, with the remainder attributed to lost earnings from premature mortality, special education services, and medical costs. No cost was assigned in the MCAD model to milder complications, in order to be conservative.

The MCAD model projected aggregate economic benefits over a 10-year period of \$32.6 million associated with the expected identification of roughly 35 infants with MCAD deficiency. The expected benefits are composed of approximately \$28.1 million for averted deaths, \$4.2 million for avoided developmental disabilities, and \$329,000 for the reduced cost of clinical identification through unneeded hospitalizations. The net benefit was estimated to be \$22.7 million, and the benefit-cost ratio was 3.4 to 1. The model also calculated a net cost-effectiveness ratio as \$48,000 per life-year saved.

In 2006 WDOH considered 16 additional metabolic disorders detectable using MS/MS, which had been included as primary targets in the 2005 panel recommended by the ACHDNC. In 2007 the advisory committee concluded that there was sufficient evidence of benefit of reduced mortality for 15 disorders. WDOH NBS program staff developed a simplified cost-benefit model for each of the 15 recommended metabolic disorders as well as for the one that had not been recommended. The incremental costs associated with adding these conditions were minimal, since the cost of MS/MS screening had already been accounted for. Fourteen of the 15 recommended conditions were added in June 2008, and the remaining one, tyrosinemia type 1, was added in September 2008.

Critique of MCAD Model. This assessment draws heavily on 2 book chapters that critically reviewed CEAs of screening for MCAD deficiency published prior to 2009, one with a focus on economic evaluation methods and one with a focus on epidemiology.^{42,43} The major determinant of net benefit in the model was the number of premature deaths

avoided. The mortality assumption in the WDOH MCAD model was consistent with the information available at the time the model was developed, including a CEA of MCAD screening published by Wisconsin's program.⁴⁴ The 20.4% mortality estimate in the model is similar to those in other published analyses of MCAD deficiency, with a modal range of 16%-22%.⁴³ Subsequently published empirical estimates from population-based studies in Australia and the Netherlands suggest the true risk of death may be 15% or less.^{45,46}

The WDOH estimate of the prevalence of serious disability in untreated MCAD deficiency, 14.2%, is similar to the 15% sum of the frequencies of cerebral palsy and severe developmental delay assumed by Carroll and Downs.⁴⁷ However, the assumed reduction in serious disability with early detection of MCAD deficiency is substantially higher relative to other CEAs,⁴² including a 5% frequency of severe disability previously assumed by Insinga and colleagues.⁴⁴ Furthermore, subsequent population-based studies also indicate a low frequency of serious disability in unscreened MCAD deficiency.^{48,49} In Australia, none of 28 unscreened children with MCAD deficiency born between 1994 and 2002 had intellectual disability when assessed at age 6 years, and just one (4%) had a mild disability.⁵⁰ In the Netherlands, the prevalence of serious disability in a population-based cohort of children with MCAD deficiency born between 1985 and 2003 was 4%.⁵¹

Nonetheless, the cost assigned to developmental disabilities in the WDOH model may have been conservative. The study from which the average costs were taken modeled the average cost for all children with intellectual disability, most of whom had mild disability.^{40,41} Children with severe disability could incur substantially higher average costs. Also, the cost estimates did not include the spillover effect on lost earnings for parental caregivers.⁵²

The WDOH estimate of the avoided cost of clinical identification of roughly \$12,000 per child with MCAD deficiency as a result of NBS⁴² was almost identical to that in a subsequent Dutch study.⁵¹ Other economic analyses have sometimes assumed unrealistic estimates of avoided medical costs of screening for MCAD deficiency. In particular, Carroll and Downs assumed a per-child cost of approximately \$300,000 associated with late-diagnosed MCAD deficiency.⁴⁷ The authors cited the unpublished WDOH report, which actually estimated \$300,000 as the aggregate cost for 25 children.⁴² That mistaken inference led Carroll and Downs to calculate that screening for MCAD deficiency would be

cost-saving (negative total cost).⁴⁷ Subsequent CEA studies of screening for MCAD deficiency have estimated positive net costs.^{51,53-59}

The MCAD model conservatively assumed that infants diagnosed with MCAD deficiency would typically undergo hospitalization in the case of symptoms such as vomiting or high fever that could provoke a metabolic crisis. The net increase in hospitalization cost following screening was projected to be almost \$15,000 per child with MCAD. The Wisconsin model assumed similar costs of medical monitoring,⁴⁴ but other CEAs have generally either assumed a lower cost of medical monitoring or left that out of the model.⁴² That difference could help account for the relatively high ICER in the WDOH model compared with those in the majority of published CEAs. An Australian CEA of MS/MS screening found higher hospitalization costs with screening based on 4 years of screening experience, but MCAD results were not reported separately.⁵⁵

A long-term follow-up study in New York State found that almost one-half of infants with fatty-acid oxidation disorders, of which MCAD deficiency is the most common, underwent acute care visits, and the average length of stay was 46 days⁶⁰; similar studies have also found high rates of hospitalization for infants and young children with these disorders.⁶¹ Those findings suggest that published cost-effectiveness findings on MCAD deficiency and similar conditions may have understated the downstream health care costs associated with implementation of screening; further research is needed to retrospectively assess the economic impact of MS/MS screening for disorders such as MCAD deficiency.

The screening cost estimate in the MCAD model, which included the costs of MS/MS screening for 2 other disorders as well, was \$12 per infant, which is similar to other US estimates for MS/MS testing of multiple disorders of \$10-\$16 per birth.⁴² If one subtracts costs for homocystinuria and maple syrup urine disease and adjusts for the fact that 2 specimens were analyzed for each newborn, the cost per sample to test for MCAD deficiency alone was under \$5 per test, which is similar to the roughly \$4 per specimen cost to screen for MCAD deficiency that had been estimated for Wisconsin.⁴⁴

Cystic Fibrosis

In 2004 a CDC-led writing group produced an evidence review that considered NBS for CF to be “justified.”⁶² The evidence included

long-term outcomes from 2 randomized controlled trials of NBS for CF, as well as observational studies from regions that conducted screening for CF beginning in the early 1980s. The CDC recommendation statement was accompanied by an endorsement from the Cystic Fibrosis Foundation, which had cosponsored the 2003 meeting at which evidence was presented and subsequently published.⁶³ The most influential findings came from long-term follow-up of a population-based screening trial in Wisconsin that enrolled infants from 1985 to 1994, which demonstrated evidence of long-term nutritional and cognitive benefits.⁶⁴⁻⁶⁶

CF was subsequently included as one of 29 conditions in the proposed NBS panel that was endorsed in early 2005 by the ACHDNC¹³ and formed the basis for the RUSP. The Washington advisory committee requested an economic analysis, and WDOH staff, including a WDOH staff economist and an MPA-level analyst in the NBS program (JDT), adapted a decision tree model previously developed in 2002. The Board reviewed the analysis and approved the addition of CF to the panel in October 2005; screening began in March 2006.

Summary of CF Model. The CF model projected that the primary quantifiable benefit of screening would be reduced child mortality.²⁰ The base-case model assumed that screening would reduce the cumulative risk of death to age 10 among children with CF from 6% to 4%, a 33% or 2 percentage point reduction; a sensitivity analysis modeled a more conservative 1 percentage point reduction (Table 3). The model used a value of a statistical life-year (VSLY) estimate of \$117,647 to value each life-year saved. This was calculated by taking a VSL of \$4 million and dividing by the undiscounted life expectancy of 34 years for an infant with CF. The value of averted mortality was projected to be roughly \$1.1 million for an annual birth cohort of 25 infants with CF.

The model assumed 2 other benefits: reduced hospitalizations and avoided “diagnostic odysseys,” ie, repeated examinations and acute care visits to treat symptoms prior to a definitive diagnosis being realized. First, the model assumed a roughly 25% reduction in hospitalization, saving 1 hospitalization per child with CF during the first 10 years of life. Second, the model assumed a modest reduction of excessive follow-up visits of less than \$1,000 per infant with CF.

The cost of screening and diagnostic testing was modeled for 2 different testing strategies: (1) persistent elevation of the pancreatic enzyme precursor immunoreactive trypsinogen (IRT) at 2 different times (IRT/IRT) and (2) a single elevation of IRT followed by DNA analysis

Table 3. Key Assumptions and Findings for the CF Model with IRT/IRT Protocol^a

Variables	Base Case	Sensitivity Analysis
Number of newborns screened in 1 year	79,058	79,058
Number of newborns with CF	25	25
Screening cost per infant	\$3.68	\$3.68
Reduction in child mortality with NBS to 10 years of age	2 percentage points	1 percentage point
Discount rate	4%	3%
Total costs (of screening tests, sweat tests, office visits, and genetic counseling) in 1 year	\$326,956	\$326,956
Total benefits		
Avoided costs of “diagnosis odysseys”	\$22,352	\$22,352
Avoided costs of hospitalization	\$667,958	\$667,958
Discounted life-years saved	9.2	5.2
Avoided mortality	\$1,082,352	\$611,764
Net benefits for 1 year of screening	\$1,445,706	\$974,758
Benefit-cost ratio	5.4	4.0

Abbreviations: CF, cystic fibrosis; IRT, immunoreactive trypsinogen; NBS, newborn screening.

^aIRT/IRT protocol requires obtaining a second dried blood spot specimen at approximately 2 weeks of age to measure IRT again.

for common CF mutations. The IRT/IRT strategy was projected to be less costly, in part because Washington is one of 14 states that either mandates or recommends the routine collection of a second specimen from infants at roughly 2 weeks of age.⁶⁷ Washington is also one of 10 states that chose CF screening strategies that do not include DNA testing.⁶⁸

The screening strategy chosen by Washington was projected to result in total costs of \$326,956 for a single-year birth cohort, and to save 9.2 life-years using a 4% discount rate. The base case benefit-cost ratio

was calculated to be roughly 5.4 to 1. Sensitivity analyses conducted by WDOH show that with a conservative 1 percentage point difference in mortality and a discount rate of 3% rather than 4%, the benefit-cost ratio would still be favorable, 4.0 to 1 (see Table 3).

Critique of CF Model. This assessment draws on a recently published review of CEAs of CF NBS published prior to 2015.⁶⁹ The WDOH prepared its CF model prior to the first publication, in 2005, of a CEA of CF NBS that modeled health outcomes. The 2005 study hypothesized that NBS would delay the onset and progression of CF respiratory symptoms by an average of 6 months, thereby resulting in better lung function and health-related quality of life.⁷⁰ In contrast, the WDOH CF model was based on more conservative epidemiologic assumptions that were consistent with published evidence summarized in the 2004 CDC evidence review.⁶²

Two subsequent CEAs from the Netherlands both assumed a 1.5 percentage point reduction in mortality to age 5 years,^{71,72} similar to the WDOH base model assumption of a 2 percentage point reduction to age 10 years and consistent with published findings.^{69,73} An individual-level analysis of data from the Cystic Fibrosis Foundation CF Patient Registry found a similar survival advantage for infants whose diagnosis was reported during the first month of life,⁷⁴ and a state-level analysis found a 1.7 percentage point difference in mortality through age 9 years in states with and without CF NBS implemented prior to 1996.⁷³

The WDOH assumption of avoided “diagnostic odyssey” costs was conservative (low) relative to 2 published estimates from the United Kingdom⁷⁰ and the Netherlands.⁷¹ The model was less conservative in its assumption of avoided hospitalization costs, although within the range of published estimates. The WDOH assumption was based on a French study that found one-third fewer hospitalizations among young children with CF in a region with CF NBS than in a nearby region.⁷⁵ That finding was consistent with previous Australian and UK findings⁶² as well as with a subsequent UK study.⁷⁶ However, the Wisconsin randomized trial found no difference in hospitalization costs with NBS.⁷⁷ A partial economic analysis of CF screening in Wisconsin assumed no difference in hospitalization costs,⁷⁸ as did the two Dutch CEAs.^{71,72} At the other end of the spectrum, a recent Canadian CEA of screening for CF assumed 85% lower hospitalization costs with NBS.⁷⁹ If the WDOH model had conservatively assumed no reduction in hospitalizations from

CF screening, the benefit-cost ratios would still have been favorable, 3.5 and 1.5, respectively (results not reported).

The WDOH CF model was very conservative in its valuation of deaths averted. If the model had multiplied projected deaths by a VSL of \$4 million, the mortality benefit for each cohort would have been \$2 million rather than \$1.1 million calculated using a VSLY estimate of \$118,000 based on undiscounted life expectancy multiplied by life-years saved that were discounted at 4% per year. If the same discount rate had been used to calculate both VSLY and life-years saved, the estimate of mortality benefit would have been substantially larger.

Severe Combined Immune Deficiency

SCID is a rare disorder that without treatment is usually lethal in the first 2 years of life as a result of recurrent severe infections. The primary treatment, hematopoietic (or stem) cell transplant, is usually effective in reconstituting the immune system and avoiding premature mortality if initiated in early infancy.⁸⁰ Even before NBS for SCID using a molecular T-cell receptor excision circle (TREC) assay was demonstrated to be feasible, preliminary calculations showed that screening for SCID was likely to be cost-effective despite a low prevalence and high cost of treatment.^{81,82} A CEA published in 2011 confirmed that screening using that assay would likely be cost-effective by conventional criteria.⁸³

WDOH staff (primarily JDT) completed a cost-benefit model of testing for SCID during 2011 and 2012. The SCID cost-benefit model demonstrated positive net benefit as a result of the lower mortality rate for infants with SCID who receive early identification and treatment and the lower cost associated with early transplantation.²¹ After the economic model was reviewed by the advisory committee and revised to incorporate the impact of false-positive screening tests, the Board approved addition of SCID in June 2012. The legislature approved an NBS fee increase during the 2013 session, allowing screening to be implemented in January 2014.

Discussion

In the United States, cost-benefit and cost-effectiveness are not explicit criteria for NBS policy decisions at the federal level.^{13,14,16,29,37} To our

knowledge, only 2 states, Arizona and Washington, require a CBA of the addition of new conditions to the state NBS panel.^{29,84} Other states may require “fiscal notes” in special cases, eg, legislation for NBS for critical congenital heart defects in North Carolina.^{85,86}

Washington appears to be the only state that routinely does its own formal cost-benefit modeling of proposed NBS expansions. Until now the Washington experience has not been documented or evaluated in the peer-reviewed literature. The models appear to be robust relative to similar models published in the peer-reviewed literature, particularly in light of the information that was available at the time the models were prepared.

Economic evaluation of an intervention such as screening requires a counterfactual scenario in which outcomes in unscreened cohorts are assessed holding constant factors such as access to the same treatments as in screened cohorts.⁶⁹ A major challenge to accurate estimation of the benefits of NBS is the lack of reliable, population-based data on the frequency of adverse health outcomes in unscreened cohorts of children with rare conditions who received effective treatments once they were diagnosed. Clinical case series are often biased sources of information on the occurrence of outcomes among unscreened children because of ascertainment, referral, selection, and spectrum biases.⁴² Historical data on the “natural history” of disorders can also be misleading because they conflate the effects of late diagnosis with lack of treatment.

The scarcity of reliable population-based data for model parameters is particularly problematic for less prevalent NBS disorders. For example, the 2003 biotinidase deficiency model assumed a 50% death rate in the absence of screening, and the economic value of avoided deaths accounted for most of the projected economic benefit of screening.²⁹ However, no epidemiologic data were available. One subsequently published US economic evaluation of screening for biotinidase deficiency assumed no excess deaths in the absence of screening,⁴⁷ which was likewise unsupported by data.

The assessment of developmental or neurocognitive outcomes in cohorts of screened and unscreened children can be particularly challenging because of the need for standardized measures. Furthermore, the economic valuation of developmental outcomes is difficult because of the lack of specific cost estimates. For example, the least robust aspect of the MCAD model was its estimates of benefits of avoided developmental disability.

The valuation methods used in the WDOH CBA models are consistent with usual practice but may nonetheless undervalue the benefits of investment in child health. First, research studies of various types consistently find that parents report being willing to pay more to reduce health risks for their children than for themselves.^{87,88} A stated preference study that assessed WTP to reduce fatal medication errors estimated VSL to be roughly \$14 million for a child aged 4 years and roughly \$4 million for adults aged 20 to 45 years.⁸⁷ Also, valuations of the prevention of developmental disabilities resulting from delayed diagnosis and treatment of metabolic conditions may exceed the expected loss of earnings for individuals with developmental disabilities.

Conclusion

The limited use of economic evaluation methods to inform US public health policy decisions has been widely noted.⁸⁹⁻⁹¹ A survey of US local and state health department stakeholders identified several reasons for the limited use of economic evaluations.⁹⁰ These include lack of economic modeling capacity within health departments, challenges in communicating results to policymakers and other stakeholders, and uncertain demand for economic calculations to guide policy decisions. However, the contrast between the United States and other countries may be more apparent than real. A recent review concluded that the United States is not less likely than Canada to consider economic evaluation in informing health policy decisions,⁹² and European countries in general have not used cost-effectiveness as a criterion for NBS expansions.^{34,35}

This article advances the understanding of the use of economic evaluation in US NBS policymaking by documenting and critically evaluating the experience of one state health department. The Washington experience demonstrates that an economic evaluation is feasible, at least for assessing and valuing avoided deaths. Few health departments have the resources to undertake rigorous economic studies on their own. It would be more efficient if economic evaluation models were developed centrally and then customized to project expected costs and benefits in specific states. Also, economic evaluation is an iterative process; ideally estimates should be periodically reassessed and updated based on new evidence and programmatic experience.

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