

Guide to the Newborn Screening Cost-Benefit Model for Adding Severe Combined Immunodeficiency (SCID)

John D. Thompson and Mike Glass, Washington State Department of Health
206-418-5531 and 206-418-5470

Introduction

Severe combined immunodeficiency (SCID) is a deadly immune system disorder and is a candidate for adding to the mandatory newborn screening panel. One of the SBOH criteria for prospective conditions is evaluating the benefits and the costs of adding screening. Newborn screening staff researched the primary literature, reports from states already screening for SCID and consulted with expert immunologists while preparing the following cost-benefit analysis. The accompanying spreadsheet is the medical model for comparing the status quo, or a “No Screening Model” (upper section) with the SCID “Newborn Screening Model” (lower section). The model predicts a benefit-cost ratio of 4.93, meaning that for every dollar of costs to screen newborns for SCID, there will be almost \$5 worth of benefits.

Model Parameters

This narrative describes the estimates for the parameters in the models. First, we chose numbers for the base case: if we had several estimates from the published data, we either used an average or the middle value. Following the base case is a sensitivity analysis that varies the parameters to give what we judge to be very conservative and moderately liberal estimates of the benefit-cost ratio. Note: the spreadsheet calculates the percentages and estimates, which have in some instances been rounded for simplicity. Subsequent calculations are unaffected by this rounding, so sometimes the numbers appear to not match perfectly.

- **Birthrate.** This analysis is for a hypothetical birth cohort of **90,000 babies** (cells B10 and B37) which is the average number of babies expected to be screened per year in Washington State between 2013 and 2018. This number is based on estimates published in the *November 2011 Components of April 1 Population Change* by the Washington State Office of Financial Management, Forecasting Division (OFM 2011).
- **Prevalence.** The prevalence used was **1 SCID case per 49,827 births** (cells D10 and D28) which is the prevalence found among 1,345,341 babies tested for SCID by four newborn screening programs (Baker 2011, Caggana 2011, Comeau 2011, Lorey 2012). This predicts 1.81 babies born with SCID in Washington each year.
- **Percent of babies with SCID with a positive family history of SCID.** These babies will be treated early in the “No Screening Model” because of a positive family history of SCID (mostly an older affected sibling). The estimate for this parameter (**20.3%** - cell G5) was the middle value of three reported in the literature (Chan 2011, also Hague 1994 and Myers 2002). These babies are assumed to derive the same benefits of early treatment that babies screened at birth would enjoy (better survival rate and lower treatment costs).
- **Sensitivity.** The sensitivity, or the ability of the screen to correctly identify babies with SCID, is estimated at **93.8%** (cell G25). This is a conservative estimate as there have been no known cases of SCID missed by newborn screening programs (zero false negatives). The estimate used is the mid-point of the 95% binomial confidence interval calculated from 27 reported cases (Baker 2011, Caggana 2011, Comeau 2011, Lorey

2012) with no false negatives (27 screening successes for the 27 cases). This sensitivity value predicts 1.69 true positives identified early and 0.11 false negatives (missed cases of SCID) per year.

- **Specificity.** The specificity, or the ability of the screen to correctly identify babies who do not have SCID, is estimated at **99.983%** (cell G47). The value used is the average of specificities from Wisconsin and Massachusetts (Baker 2011 and Comeau 2011). The specificity from New York was not used because the program changed cutoffs twice post implementation to reduce the number of false positives. Data from California did not include false positives; therefore no specificity calculation was possible. This specificity value predicts 15.2 false positives per year: these are babies who need diagnostic testing called flow cytometry, and sometimes clinical follow-up for other forms of immune deficiency (they do not have SCID).
- **Mortality of cases identified early.** The numbers used for mortality (**8.6%** - cells J3 and J23) is data compiled from Duke University and the two transplant centers in the UK regarding survival rates of babies with SCID. This estimate is the percent survival of 81 babies with SCID who received early transplants prior to 28 days of age (Myers 2002) or had an older sibling diagnosed with SCID (Brown 2011). This percentage is used in both models and predicts 0.03 deaths in the “No Screening Model” and 0.15 deaths in the “Screening Model” among the babies treated early. Recent publications from Duke University reported a 6.1% mortality rate for 48 babies with treatment prior to 3.5 months of life (Buckley 2012 and Buckley 2010).
- **Mortality of cases identified late.** The numbers used for mortality (**37.5%** - cells J13 and J32) is data compiled from Duke University and the two transplant centers in the UK regarding survival rates of babies with SCID. This estimate is the percent survival of 144 babies with SCID who received transplants after 28 days of age (Myers 2002) or were probands, meaning the first in their family diagnosed with SCID (Brown 2011). This percentage is used in both models and predicts 0.54 deaths in the “No Screening Model” and 0.04 deaths in the “Screening Model” among the babies who were treated later. Recent data from Duke University show a mortality rate for 118 babies treated after 3.5 months of life of 31.4% (Buckley 2010).
- **Monetary value of a life.** The value of one life saved is estimated at **\$ 7.7 million** (cell Q35). This is the average of estimates used by three Federal Agencies in 2010 (Appelbaum 2011): Environmental Protection Agency (\$9.1 million), Food and Drug Administration (\$7.9 million) and the Transportation Department (\$6.1 million).
- **Difference in treatment costs: early v. late treatment.** The cost difference between early v. late treatment is estimated at **\$ 350,000/baby** (cell H18 subtract cell H8). This data comes from Dr. Rebecca Buckley’s data on cost of treatments of the two cohorts (Buckley 2012).

The next step is to evaluate the differences between the models to quantify the benefits of screening. This is done by combining the mortality estimates and assigning a dollar value to deaths avoided and the difference in treatment costs.

- **Deaths averted.** The total number of deaths for each model are compared; there are 0.57 deaths (cell Q2) predicted in the “No Screening Model” and 0.19 deaths (cell Q22) in the “Newborn Screening Model.” The “No Screening Model” has three times the mortality rate of the “Newborn Screening Model.” The difference between the two models is **0.38 deaths averted** (cell Q34). This means that approximately one baby every three years will not die because of early treatment afforded by newborn screening.
- **Value of lives saved.** The value of lives saved by newborn screening is the number of deaths averted multiplied by the monetary value of a life. The model estimates yearly benefits of **\$ 2.9 million** (cell Q36) for saving lives of babies with SCID.

- **Shift in treatment costs.** The early and late treatment costs for each model are calculated and combined to determine the costs of treatment in each model (**No Screening = \$ 685,000**, cell Q6; **NBS = \$ 220,000**, cell Q26). The annual treatment costs saved by screening (**\$ 465,000**, cell Q37) are the difference between these totals.
- **Total benefits.** The total benefits (**\$ 3.4 million**, cell Q38) are the sum of the value of lives saved and the treatment cost saved by screening.

Costs are estimated next.

- **Cost of screening.** The estimated costs of TREC analysis are **\$ 7.10 per baby** (cell B40).
- **Costs of clinical care and diagnostic testing for false positives.** Only the false positive babies are counted for diagnostic testing costs because the babies with SCID will have clinical evaluation and diagnostic flow cytometry testing regardless. Based on discussion during the advisory committee meeting, we looked carefully into potential costs for babies that have abnormal TREC screening but do not have SCID. We consulted with Dr. Skoda-Smith and the team of immunologists for treatment and cost estimates, which included additional diagnostic testing, clinic visits and prophylactic antibiotics. The false positives fall into three categories with the following estimated costs (data not included on spreadsheet):
 - Transient: 0.77 babies/year costing \$3,370/baby (1 year follow-up).
 - Idiopathic: 2.42 babies/year costing \$8,570/baby (5 year follow-up).
 - Other: 3.45 babies/year costing \$8,570/baby (5 year follow-up).

Please note: Ideally, we would also include the benefits to the babies of early identification for these infants. However, we lack sufficient data to adequately estimate their value. The benefits include: not administering live virus vaccinations (the live virus can cause dangerous infections in babies with impaired immune systems), avoiding resource-intensive diagnostic odysseys, and preventing infections that could range from chronic to severe, even life threatening.

- **Total costs for SCID newborn screening.** The birthrate multiplied by cost per baby is **\$ 639,000** (cell Q41).
- **Total costs for clinical care and diagnostic testing of false positives.** The total cost per year for the false positive cases outlined above is **\$52,900** (cell H42)
- **Total costs of Newborn Screening Model.** The annual costs of NBS for SCID are estimated to be **\$ 692,000** (cellQ43).

Finally, the ratio of benefits to cost is calculated. Any ratio greater than 1 signifies that the benefits outweigh the costs.

- **Benefit/Cost Ratio.** \$ 3.2 million of benefits divided by \$ 692,000 of costs yields a benefit/cost ratio of **4.93** (cell Q47).

After completing the base case benefit-cost ratio, we performed a sensitivity analysis to evaluate how the benefit-cost ratio changes when estimates for the parameters are varied.

- **Sensitivity Analysis.** Table 1 contains three estimates for each parameter, the best guess estimate used in the base case followed by conservative and liberal estimates. Only one parameter was changed at a time to generate unique benefit/cost ratios for each of the scenarios. The only exception is that the parameters for

mortality of early versus late identification were varied together to achieve a larger difference between the conservative and liberal estimates.

Table 1

Parameter	Base Case	Conservative Estimate	Liberal Estimate	B/C Ratio Swing
Prevalence	~1:49,000	~1:71,000	~1:37,000	3.45 to 6.68
% early ID – family history of SCID	20.3%	28.9%	17.9%	4.35 to 5.09
Sensitivity	93.8%	86.7%	100%	4.51 to 5.35
Specificity	99.983%	99.886%	99.986	3.44 to 5.00
Mortality – early ID	8.6%	10.0%	4.8%	3.04 to 8.89
Mortality – late ID	37.5%	26.0%	60.4%	
Monetary value of a life	\$ 7.7 million	\$ 6.1 million	\$ 9.1 million	4.05 to 5.71
Δ in treatment costs: early v. late tx	\$ 350,000	\$ 0	\$ 475,000	4.26 to 5.17

- **Break Even Points.** Table 2 contains the break-even point for each parameter. This is what the estimate would need to be, holding all other parameters constant, to reduce the favorable benefit/cost ratio to 1 (meaning it is no longer beneficial).

Table 2

Parameter	Base Case	Break-Even Point
Prevalence	~1:49,000	1:245,000
% early ID – family history of SCID	20.3%	78.9%
Sensitivity	93.8%	35.1%
Specificity	99.983%	99.112%
Mortality – early ID	8.6%	35.2%
Mortality – late ID	37.5%	10.9%
Monetary value of a life	\$ 7.7 million	\$ 600,000
Δ in treatment costs: early v. late tx	\$ 350,000	- \$ 1,700,000 (early tx would need to cost more than late tx)
Cost of NBS (per baby)	\$ 7.10	\$37.40

Conclusion

Early identification of babies with SCID is critical to their health. The mortality rate is greatly reduced with early treatment and medical costs are dramatically lower compared to babies treated after becoming symptomatic (the last baby born with SCID in California prior to starting screening generated more than \$4 million in medical bills) (Puck 2012). This analysis used data from the first four newborn screening programs to begin testing for SCID to predict the medical outcomes for a hypothetical birth cohort of Washington babies. We used data from the primary literature and expert opinion to quantify the costs and benefits of treatment for babies with early and late treatment. The benefit-cost ratio was 4.93, meaning that for every dollar of costs to provide SCID screening, there

will be \$4.93 worth of benefits. The sensitivity analysis showed that the model is robust because the benefit-cost ratio did not change much when more conservative or liberal estimates for parameters were made in the model.

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