WHITE PAPER

# Cost-Effectiveness Analysis of Newborn Screening for Severe Combined Immunodeficiency (SCID)

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*Early detection of severe combined immunodeficiency (SCID) followed by prompt treatment is critical for affected babies to live healthy lives. Newborn screening (NBS) for SCID using the T-cell receptor excision circle (TREC) test has been being performed in California for two years and around 1 million babies have been screened there. The test has demonstrated high specificity and sensitivity in the early identification of the affected babies. While the essential medical benefit of identifying SCID infants early rather than late has been proven in several studies, less salient is the potential cost benefit of screening.*

*We created a calculation model to examine cost-scenarios and used data applying to the UK in trialing the usability of the model. We estimated the overall program cost of screening by adding together the key component costs, including treatment of the SCID-affected infants. We then compared the total cost of newborn screening with the cost of clinical care in a situation where screening is not performed, and quantified the potential cost-benefits that screening offers.*

*In the UK, SCID infants who are treated early have almost 10-fold lower total clinical care costs compared with those treated later, i.e. £78,540 vs. £744,200. Applied to a population with an annual birth rate of 813,000 (www.ons.gov.uk), the annual cost of clinical care without and with screening would be £9.17M and £970k, respectively.*

*NBS for SCID combined with early treatment costs approximately £3 less per screened infant than the cost spread per infant if there is no screening at all. Although here using data for the UK, it is suggested that the model is also relevant for other health care systems, and that the cost-benefits of SCID screening are universal. In addition to saving lives, newborn screening for SCID supports a reduction in overall healthcare costs.*

## INTRODUCTION

Newborns affected with severe combined immunodeficiency (SCID) are prone to infections and will invariably die unless successfully treated with bone marrow transplantation (BMT). Early detection of SCID followed by prompt BMT treatment is critical for affected babies to live healthy lives (Chan *et al.* 2011, Brown *et al.* 2011). Newborn screening (NBS) for SCID using the T-cell receptor excision circle (TREC) test enables early detection of SCID cases (Chan and Puck, 2005). The test has demonstrated high specificity and sensitivity in identifying the affected babies. (Kwan *et al.* 2013)

Currently more than half of the babies born in the U.S. are screened for SCID. A recent publication by Kwan *et al.* (2013) reported the results of the first two years of SCID NBS in California. After screening close to one million babies, 50 infants had been identified positive for T cell lymphopenias of which 15 infants with a severe immunodeficiency were treated by BMT. Thus, the incidence rates of SCID and T cell lymphopenias were 1/66,000 and 1/20,000, respectively. Vogel and colleagues (2014) from New York published a similar article presenting results of the two first years of screening in that state. The incidence rates for SCID and clinically significant conditions for New York were 1/50,000 and 1/5,000, respectively. Outside the U.S. other countries are interested in implementing SCID screening. However, there are reservations due to the lack of knowledge of costs associated with the implementation and sustainability of the program.

In this paper our aim was to find out whether health economy assessment (HEA) -related assumptions already made in the U.S. could be generalized to apply in other regions. We created a calculation model to estimate the costs of SCID screening and treatment, and to compare cost-scenarios with and without an NBS program for SCID. We used data based on the UK health care system in trialing the usability of the model.

## METHODOLOGY

It is commonly agreed that the benefit of screening is quite salient but the cost-savings may be less apparent. So, to assist stakeholders considering SCID screening, we estimated the overall program cost of screening by adding together the key component costs, including treatment of the SCID-affected infants. We then compared the total cost of newborn screening with the cost of clinical care in a situation where screening is not performed, and quantified the potential cost-benefits.

The general parameters for the model, including the annual birth rate and the incidence rates of SCID and T-cell lymphopenias, are shown in Table 1. The number of births is an estimate of the current birth rate for the UK. The incidence rates are those reported for the established and large-scale screening program in California. (Kwan *et al.* 2013). Although not specifically UK figures these rates were chosen because we considered them to be the most reliable estimates available.

The essential testing parameters; the sensitivity and specificity of the 1st tier test, the 2nd tier testing rate, and the need for confirmatory testing; were extracted from literature. (Kwan *et al.* 2013) The testing parameters and the associated costs are presented in Tables 2 and 3 respectively.

Clinical care of SCID patients in the UK has been in the hands of the governmental-support healthcare system. The data used (Table 4) was extracted from UK National Health Service sources and studies conducted in the UK. (Myers *et al.* 2002, Gaspar *et al.* 2013).

| **Table 1** | **General parameters** |
|---|---|
| Number of births | 813,000 |
| SCID Incidence rate | 1/66,000 |
| TCL Incidence rate | 1/20,000 |
| **SCID cases / year** | **12.3** |
| **TCL cases / year** | **40.7** |

| **Table 2*** | **Testing parameters** |
|---|---|
| Sensitivity | 99.9% |
| Specificity | 99.99% |
| 2nd tier test rate | 1% |
| Confirmation | 1/6250 |

* Based on Kwan et al. 2013.

| **Table 3** | **Testing costs [£]** |
|---|---|
| Price / screening test | 7 |
| Price / confirmatory test | 250 |
| Screening test cost | 5,691,000 |
| 2nd tier testing | 56,910 |
| Confirmation | 32,520 |
| **Total cost of screening** | **5,780,430** |

| **Table 4*** | **Clinical care costs of one SCID infant [£]** | | | | | |
|---|---|---|---|---|---|---|
| **Clinical care of a SCID patient** | **Unit** | **Cost per unit [£]** | **No screening** | | **Screening** | |
| | | | Units | Total | Units | Total |
| Inpatient days, screening | day | 150 | - | | 30 | 4,500 |
| Inpatient ICU days, no screening | day | 750 | 120 | 90,000 | - | |
| Out-patient (home care), screening | visit | 30 | - | | 8 | 240 |
| Out-patient (home care), no screening | visit | 100 | 4 | 400 | - | |
| BMT early | transplant | 50,000 | - | | 1 | 50,000 |
| BMT late 1st | transplant | 300,000 | 1 | 300,000 | - | |
| BMT late 2nd | transplant | 200,000 | 0.8^ | 160,000 | - | |
| Post-BMT care, no screening | day | 750 | 180 | 135,000 | - | |
| Post-BMT care, screening | day | 150 | - | | 60 | 9,000 |
| IVIG | dose | 300 | 36 | 10,800 | 36 | 10,800 |
| Loss of productivity# | GDP loss/ worker/month | 4,000 | 12 | 48,000 | 1 | 4,000 |
| **Total cost of clinical care per a SCID patient** | | | | **744,200** | | **78,540** |

** The estimated costs of clinical care were extracted from National Health Service sources (UK) and medical literature (Gaspar et al. 2013; Myers et al. 2002).*

*^ 0.8 represents the probability of a SCID patient obtaining a second transplant based on medical literature.*

*# The loss of productivity represents the average lost contribution to society through work (or Gross Domestic Product (GDP)) by one parent due to care-taking.*

Considering the total savings in SCID management, Table 5 is based on the costs of clinical care per a SCID patient (from Table 4), the UK incidence figure of 12.3 cases per year (from Table 1), and the total cost of screening (from Table 3)

The essential outcome measures of the assessment are then as follows:

*Cost / Infant, without screening*
The sum of the medical care costs of all treated SCID infants divided by the total number of annual births. The medical care costs include the inpatient and outpatient costs for identified SCID patients, BMT, post-BMT care, and IVIG treatment as presented in Table 4. In addition to treatment costs, we also included the loss of work productivity of parents of the SCID patients to take the societal perspective into consideration.

*Cost / Infant, with screening*
The overall cost of the population-wide NBS program for SCID as well as the medical care costs of the infants diagnosed positive after identification through screening.

*Cost-saving due to screening*
The total cost of treatment without screening subtracted by the total cost of screening and treatment.

***Cost-saving due to screening / SCID Infant*** is the total cost-saving due to screening divided by the number of identified SCID infants.

Values for these essential outcome measures are presented in Table 6.

| **Table 5** | **Total cost of SCID management [£]** |
|---|---|
| SCID treatment without NBS Program | 9,167,191 |
| NBS Program and early SCID treatment | 6,747,900 |
| Difference, £ | 2,419,291 |

| **Table 6** | **Outcome measures [£]** |
|---|---|
| Cost/Infant, without screening | 11.28 |
| Cost/Infant, with screening | 8.30 |
| Cost-saving due to screening | 2,419,291 |
| Cost-saving due to screening/ SCID Infant | 196,400 |

## MAJOR FINDINGS

The essential medical benefit of identifying SCID infants early rather than late has been proven in several studies. SCID patients identified late have a compromised immune system, resulting in less positive BMT outcome (Chan *et al.*, 2011; Brown *et al.*, 2011). Added to the outcome benefits of early detection, our model illustrates cost benefits; screening for SCID is less expensive than not screening at all.

The overall costs are steered by the general parameters and testing-related parameters presented in Tables 1 and 2. The actual cost-savings and -benefits, though, are driven by the fact that early-diagnosed SCID infants require less-intensive clinical care for a shorter period of time compared to the late-diagnosed cases. Apart from reducing the survival rate, transplants performed later will often also associate with higher health care costs due to the prolonged hospitalization, and increased need for medications to treat possible infections. There will also be an attendant higher loss of productivity of the parents due to longer times spent away from work. A comparison of the clinical care costs with and without screening is shown in Table 4. The SCID infants who are treated early - early treatment being possible because of early identification via newborn screening and timely diagnosis - have almost 10-fold lower total clinical care costs; *i.e.* £78,540 vs. £744,200. Furthermore, the annual cost of clinical care without and with screening in our example population of 813,000 annual births with a SCID incidence rate of 1/66,000 would be £9.17M and £970,000, respectively. The numbers of SCID cases reported by Gaspar (2011) suggests that the incidence figure in the UK may actually be higher than the one used in our study. If this is the case the reduction in treatment costs, here estimated at more than £8M annually, and also the total savings reported below, would be greater.

The main factors driving the higher cost of late identification are the duration and intensity of hospitalization, cost of BMT, and the loss of productivity. All this is quite aside from the fact that the SCID babies identified via screening would also have higher probability of successful treatment and recovery.

The cost of screening program was based on an estimated cost of £7.00 per infant screened, which included the actual test and also the screening infrastructure. The total cost of a SCID screening program in the example population would be ~£5.8M. Furthermore, the screening program cost together with the early treatment cost (~£967,500) sums to about £6.75M, which is still £2.4M lower that the cost of treatment without screening (Tables 5 & 6). Hence, the benefit of identifying 12 SCID patients via screening could result in annual cost-savings of £2.4M and, at the same time, those same 12 infants could live healthy lives.

## CONCLUSION

Screening for SCID is an important, life-saving public health intervention. In the model introduced here, using a SCID incidence rate of 1/66,000, NBS for SCID combined with early treatment generates a cost of £8.30 per infant screened. This is approximately £3 less per screened infant than the cost spread per infant if there is no screening at all. The significant difference is due to the fact that in the absence of screening, infants with SCID are often identified after frequent visits to the doctor's office and lengthened hospitalization periods. Thus, infants identified late produce remarkably higher medical care costs and greater loss of work productivity of parents taking care of their child with SCID. Overall, in addition to saving lives, newborn screening for SCID can also be beneficial in terms of reduced overall costs.

In this paper we suggest a model that can be used to calculate cost-scenarios related to SCID screening. The model is applied here using data from the UK health care system but we believe the model is generalizable to other health care systems as well, assuming that the specific characteristics of the country/ region are taken into consideration. Furthermore, we believe our conclusions about the cost-benefits of SCID screening are universal and can therefore be generalized for countries considering the implementation of NBS for SCID.

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