

Institution: University of Sheffield		
Unit of Assessment: A-02 Public Health, Health Services and Primary Care		
Title of case study: Changing national policy to expand the newborn bloodspot screening programme and to deliver economic benefits		
Period when the underpinning research was undertaken: 2012–2016		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Alice Bessey	RA in Health Economic Modelling	2011–present
Jim Bonham	Honorary Professor	2000–present
James Chilcott	Prof of Healthcare Operational Research	1996–present
Jo Cooke	Programme Manager & Honorary Professor	1997–2009 and 2020–present (honorary position 2009-2020)
Simon Dixon	Professor of Health Economics	1994–present
Jo Leaviss	Systematic Reviewer	2010–present
Sue Mawson	Professor of Health Services Research	2012–present
Suzy Paisley	Senior Research Fellow	2001–present
Abdullah Pandor	Senior Research Fellow	2001–present
Phil Shackley	Reader in Health Economics	2006–present
Anthea Sutton	Information Specialist	2014–present
Ruth Wong	Information Specialist	2010–present
Period when the claimed impact occurred: 2014–2020		
Is this case study continued from a case study submitted in 2014? N		
1. Summary of the impact (indicative maximum 100 words)		
<p>Identifying rare but serious diseases at birth is crucial to early treatment and the ability to save lives. Our research showed the potential health and economic benefits of expanding the newborn bloodspot screening programme in the UK. This was pivotal to the decision in 2014, by the UK Newborn Screening Committee, to include four additional conditions into the newborn screening programme. This changed screening for all babies since implementation began in 2015. To date, 112 newborn babies and their families have benefited from early detection helping to prevent severe disability and save lives.</p>		
2. Underpinning research (indicative maximum 500 words)		
<p>Newborn screening seeks to identify babies who have rare but serious conditions, to enable early treatment and improve health outcomes. In England, all babies have been screened a few days after birth using blood obtained from a heel prick to test for phenylketonuria, congenital hypothyroidism, sickle cell disorders, cystic fibrosis and medium-chain acyl-CoA dehydrogenase deficiency (MCADD).</p>		

The UK National Screening Committee (NSC) places a high priority on ensuring screening programmes are not associated with harm to otherwise healthy people, such as the increased stress and anxiety for families associated with false positives. Whilst some qualitative research existed into the problem, there had been very little research into the potential health economic impact of this issue. Simon Dixon and Phil Shackley from the School of Health and Related Research (SchHARR) together with the Sheffield Children's Hospital NHS Foundation Trust (SCH NHS FT) undertook research to establish how important it was to parents to avoid false positive results within screening programmes for inborn errors of the metabolism. The results suggested that there is widespread parental support for extended screening in the UK and that the number of false positives is a relatively small issue [R1]. The study was funded by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care for South Yorkshire (NIHR CLAHRC SY) in 2012.

In 2012, an evaluative pilot was established to consider expanding the screening programme to include five further inborn errors of the metabolism. This evaluation was undertaken by the NIHR CLAHRC SY with the support of newborn screening laboratories throughout the UK and led by Professor Jim Bonham. Babies born between July 2012 and July 2013 were tested for these five additional disorders: maple syrup urine disease (MSUD), homocystinuria (HCU) (pyridoxine unresponsive), glutaric aciduria type 1 (GA1), isovaleric acidaemia (IVA) and long chain hydroxy-acyl CoA dehydrogenase deficiency (LCHADD).

A separate economic evaluation based upon this pilot was undertaken by SchHARR, led by Jim Chilcott and Simon Dixon to estimate the cost-effectiveness of screening for the five additional disorders, particularly taking account of the costs associated with false and true positive cases.

Our study revealed that screening for the five additional disorders is cost saving when compared to the costs incurred when patients are not screened, and instead present clinically. The results from our deterministic analysis and probability sensitivity analysis suggest that screening for all five conditions is cost-saving with screening associated with lower total costs and higher total quality adjusted life years (QALY) compared to no screening. The incremental net benefit for all five conditions, at a threshold of £25,000 per QALY, was between £0.46 for IVA and £5.94 for GA1. Reports from these studies were presented to the UK NSC in 2013 [S1]. An updated paper which includes data since the expansion of the programme was published in 2020 [R2].

Further research undertaken by Jim Chilcott and Alice Bessey since 2015 includes an economic evaluation of further expansion of the screening programme to include Severe Combined Immune Deficiency (SCID) funded by Public Health England (PHE) on behalf of the UK NSC [R3] and an assessment of screening for childhood Cerebral Adrenoleukodystrophy (cCALD) funded through The Leukodystrophy Charity (Alex TLC, formerly ALD-Life) [R4].

3. References to the research (indicative maximum of six references)

- R1. Dixon, S., Shackley, P., Bonham, J., & Ibbotson, R. (2011).** Putting a value on the avoidance of false positive results when screening for inherited metabolic disease in the newborn. *Journal of Inherited Metabolic Disease*, 35(1), 169–176.
<https://doi.org/10.1007/s10545-011-9354-0>
- R2. Bessey, A., Chilcott, J., Pandor, A., & Paisley, S. (2020).** The Cost-Effectiveness of Expanding the UK Newborn Bloodspot Screening Programme to Include Five Additional Inborn Errors of Metabolism. *International Journal of Neonatal Screening*, 6(4), 93.
<https://doi.org/10.3390/ijns6040093>

R3. Bessey, A., Chilcott, J., Leaviss, J., de la Cruz, C., & Wong, R. (2019). A Cost-Effectiveness Analysis of Newborn Screening for Severe Combined Immunodeficiency in the UK. *International Journal of Neonatal Screening*, 5(3), 28.
<https://doi.org/10.3390/ijns5030028>

R4. Bessey, A., Chilcott, J. B., Leaviss, J., & Sutton, A. (2018). Economic impact of screening for X-linked Adrenoleukodystrophy within a newborn blood spot screening programme. *Orphanet Journal of Rare Diseases*, 13(1), 179.
<https://doi.org/10.1186/s13023-018-0921-4>

4. Details of the impact (indicative maximum 750 words)

Newborn bloodspot screening identifies babies who may have rare but serious conditions. Most babies screened will not have any of the conditions but for the small number who do, the benefits of screening are enormous. Early treatment can improve health, prevent severe disability and save lives.

Our research has contributed to the expansion of the Newborn Bloodspot Screening Programme in the UK from screening for five metabolic disorders to nine. It has also directly informed the establishment of the PHE SCID screening evaluation. Children born since 2015 in England and Wales, since 2017 in Scotland, and since 2020 in Northern Ireland have benefited from this screening programme when having the heelprick blood test.

Changing national policy

Previously, all babies in England were screened for five metabolic conditions. Our evaluation of the pilot and economic evaluation reports on screening for five further metabolic conditions were submitted to the UK NSC in 2013. This directly informed the decision by the UK NSC to include four additional conditions, MSUD, HCU, IVA and GA1 into the newborn screening programme but exclude LCHADD [S1].

On 9 May 2014, the UK NSC announced the expansion of the newborn screening programme to screen for MSUD, HCU, IVA and GA1. The recommendations and roll-out received national coverage on the BBC News [S2]. On 5 January 2015, PHE announced the roll-out of the expansion in England. Professor Anne Mackie, Director of Programmes for the NHS Screening Programmes, part of Public Health England, said, “*screening for these rare disorders has the potential to benefit around 30 children in England each year. The early identification of these conditions can prevent death and significantly improve the quality of life for those living with these conditions*” [S3].

National rollout began in January 2015 in England and Wales. The change in policy will have affected the approximately 700,000 children born annually in England and Wales. The screening roll-out began in Scotland March 2017, with the roll out announced for Northern Ireland in March 2020 [S3].

Improving health outcomes

Data collected since the expansion of the programme between 2014-2018 showed that 112 screen positive babies have been detected. The benefits of the expanded newborn screening programme are continuing year on year [S4]:

PHE NBS Annual Report	MSUD, IVA, GA1, HCU	
	No. tested	No. of screen positives
2017-2018, (p15) UK total	755,704	38
2016-2017, (p13) UK total	701,260	31
2015-2016, (p13) UK total	705,808	26
2014-2015, (p13) UK total	461,445	17
2013-2014, (pp11-12) UK total	-	-

A package of multimedia information and resources to support parents and professionals has been produced, including examples of babies and families who have been affected by the screening programme. Baby Habul was the first baby to be detected for MSUD since the NBS programme started. Dr Chakrapani, Birmingham Children's Hospital NHS FT said, "*children who are not treated promptly would often go on to develop learning difficulties and developmental problems which fortunately in this case we have managed to avoid*" [S5].

Cost savings to NHS

Although actual screened incidence rates in England since 2014 have been lower than predicted [S4], based upon the international evidence, screening is still estimated to improve quality-adjusted life years (QALYs) and provide cost-saving to the NHS for all conditions apart from IVA. With discounted lifetime cost savings of £0.15, £1.44, £0.83 per baby screened for MSUD, HCU, and GA1 respectively and a small increase of £0.01 per baby screened for IVA. The new incidence rates for IVA results in an incremental cost-effectiveness ratio of £776 per QALY still well within the threshold used in the UK [R2].

Informing national policy on SCID screening

Our report and evidence review on the cost-effectiveness of screening for SCID was submitted to the UK NSC in March 2017. In December 2017, PHE recommended an evaluation of testing babies for SCID. In 2019, PHE announced that the two-year evaluation would commence in 2020 (delayed to 2021) [S6]. Jim Chilcott and Alice Bessey are contributing to the PHE Oversight Board for the design and implementation of the pilot.

Influencing international beneficiaries

Informing the newborn screening programme in Spain: The Servicio Canario de la Salud (SCS) Health Technology Agency (HTA) unit in the Canary Islands have used our model as the basis for their cost-effectiveness analysis of SCID screening for Spain. Alice Bessey and Jim Chilcott contributed to their HTA report to the Spanish Ministry of Health [S7].

International influence of our research has been ongoing through Professor Jim Bonham, the current President of the International Society of Neonatal Screening (ISNS) [S8]. The development of newborn screening in Bangladesh has been influenced by our research. Dr Das indicates that in 2016 prior to approaching our team for advice there was no systematic screening for any condition and it was not in the remit of the government and the Ministry of Health and Welfare. Since 2016, Dr Das states "*I have managed to get the attention on the importance of NBS and a number of high-profile healthcare stakeholders from Bangladesh have*

actually visited Sheffield. This has resulted in ongoing piloting at the ministry of health for CHT (congenital hypothyroidism) screening in Bangladesh” [S9].

Recognising the potential for newborn screening to benefit children in low- and middle-income countries Prof Bonham has recently helped launch and Chair an initiative, 'A Global Taskforce on Newborn Screening'. A webinar organised by the organisation attracted almost 2,000 registrants from 113 countries around the world [S10].

5. Sources to corroborate the impact (indicative maximum of 10 references)

- S1. Current UK NSC recommendations for newborn screening for MSUD, IVA, GA1, HCU are available at: <https://legacyscreening.phe.org.uk/screening-recommendations.php>. The UK NSC recommendations refer to the 'Last external review - Expanded Newborn Bloodspot Report: Screening Study July 2012 to July 2013, Report to National Screening Committee', published by the National Institute for Health Research, 21 Nov 2013. Page 4 (para xii) references SchARR and the health economics analysis.
- S2. BBC News coverage: 'Newborn babies to be tested' <http://www.bbc.co.uk/news/health-27341507> (9 May 2014); 'Baby screening: Life-saving scheme expanded' <http://www.bbc.co.uk/news/health-30657478> (5 Jan 2015).
- S3. Combined: Newborn screening programme national announcements of roll-out by Public Health England 2015 (<http://bit.ly/393JQQw>), Commissioning for Scotland's Health 2017 (<http://bit.ly/3lGhoJw>) and Northern Ireland direct government services 2020 (<http://bit.ly/2QvPwfQ>).
- S4. Newborn bloodspot screening: data collection and performance analysis report. Annual reports on data collected by the newborn bloodspot screening programme from 2013-2014 to 2017-2018 at: <https://bit.ly/30UZadG>.
- S5. NIHR Expanded Newborn Screening: website provides an information resource for parents and professionals – with links to audio-video materials, leaflets and other press coverage: <http://www.expandedscreening.org/site>. Baby Habul's video: <http://bit.ly/3sicyVA>.
- S6. Combined recommendation and pilot for NBS for SCID: UK NSC 2017 recommendation on SCID (<http://bit.ly/3tEoZLA>) and PHE evaluation update - screening for SCID 2019 (<http://bit.ly/397Ah3f>).
- S7. Report to Spanish Ministry of Health. *Neonatal screening for severe combined immunodeficiency: cost-effectiveness analysis*. Health Technology Evaluation Report (SESCS). 2019. Available at: <https://bit.ly/3ttX1C6>.
- S8. International Society for Neonatal Screening (ISNS) website: <https://www.isns-neoscreening.org>
- S9. Barisal Biotechnology UK Ltd. Founder and Chief Scientific Officer. Factual statement. 22 Dec 2020.
- S10. The International Federation of Clinical Chemistry and Laboratory Medicine. Taskforce on Global Newborn Screening (<https://bit.ly/38NpCdG>). Link to webinar, 04 Nov 2020: <https://bit.ly/3lrzfnl>.