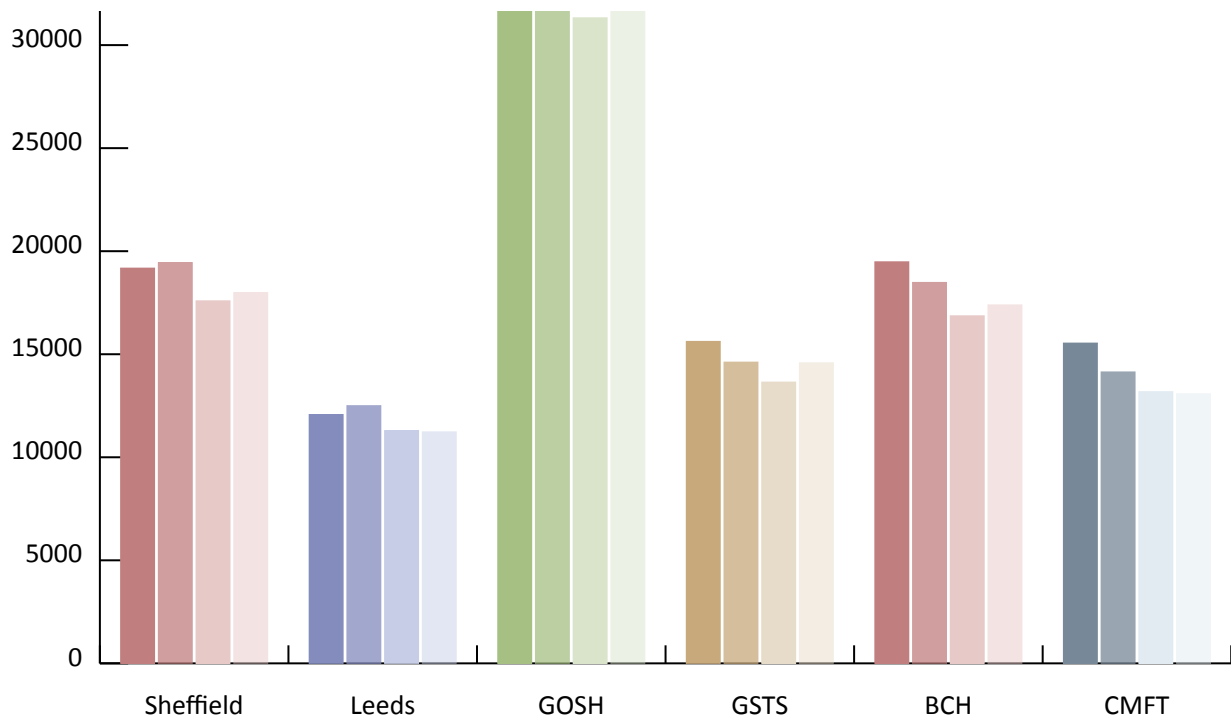




WELCOME to the revised edition of the 9th Expanded Newborn Screening newsletter. The main focus of this newsletter will be to report on the results which we found during the 12 month pilot. This is an amendment to the newsletter issued earlier in August which provides updated information on the number of births. Once again, we would like to say a huge well done and thank you to everyone who has contributed to make the pilot a success. As always, we hope you enjoy the newsletter!

The Number of Births

In the previous edition of the newsletter we made a mistake in the reporting of the number of births at Guy's St Thomas in the 1st quarter of the pilot. This has only come to light whilst reviewing the data at the end of the study. The quantity of cards processed by the lab was recorded rather than the actual number of births. Sometimes, when processing bloodspot sample cards in the lab, a 2nd card will need to be used for the same baby (for example if a poor sample was given initially). During the first quarter at Guy's St Thomas, the number of cards was errantly recorded rather than the number of births. As such, there is reduction from 16,599 (previously depicted) to 15, 622. The graph below includes the updated figures.



Before the pilot commenced we predicted that there would be approximately 430,000 births. Our predictions came in pretty close with a total of 437, 187 births seen in the year period. See the graph for the breakdown by site.

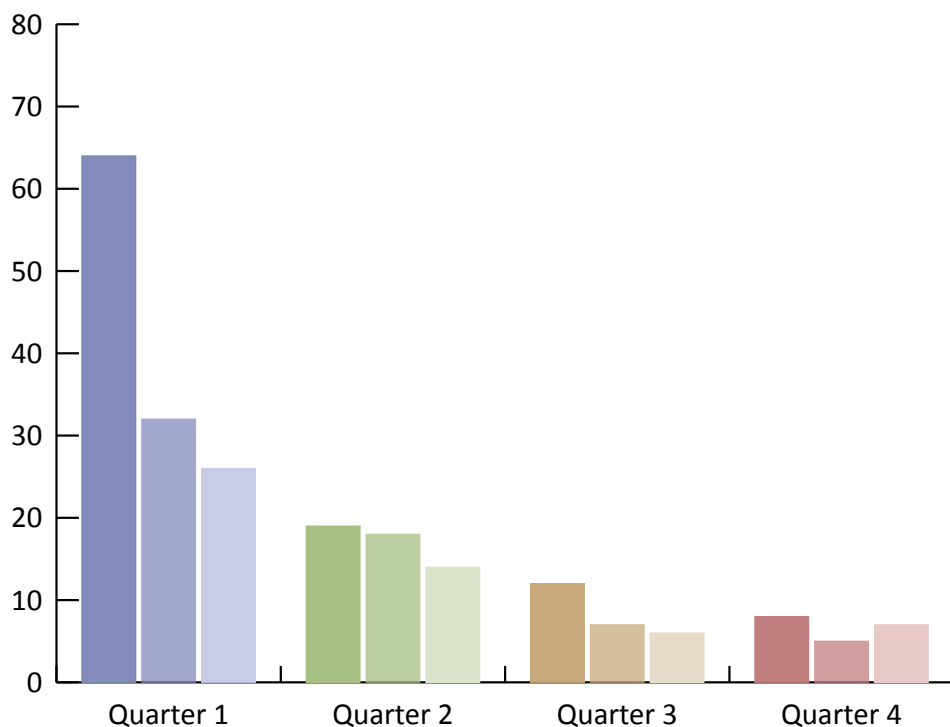
(Abbreviations: GOSH: Great Ormond Street Hospital, GSTS: Guy's St Thomas', BCH = Birmingham Children's Hospital, CMFT = Central Manchester Foundation Trust)



We want your feedback and comments! We want this newsletter to be useful and interesting to you. Please provide feedback and any information that you would like including in the newsletter via the website: <http://tinyurl.com/cjwg8nh>

The Number of Declines

Over the year pilot, a tiny 0.05% (218 parents) declined screening for their baby. The majority (122, 56%) of the declines came in the first quarter which suggested that there may have been a few teething problems. As acceptability increased and people became more familiar with the process, the number of declines has decreased over time. In the final quarter there was just 20 declines across all six sites. See the graph right for overall number of declines by month and the table below for percentage decline rate by site.



	1st Quarter			2nd Quarter			3rd Quarter			4th Quarter			Total		
	No. of Births	No. of Declines	% Declines	No. of Births	No. of Declines	% Declines	No. of Births	No. of Declines	% Declines	No. of Births	No. of Declines	% Declines	Total No. of Births	Total No. of Declines	Total % Declines
SCH	19178	38	0.20	19446	12	0.06	17591	10	0.06	17992	5	0.03	74207	65	0.09
Leeds	12075	3	0.02	12505	2	0.02	11293	0	0.00	11232	0	0.00	47105	5	0.01
GOSH	33970	36	0.11	32061	12	0.04	31325	8	0.03	31875	6	0.02	129231	62	0.05
GSTS	16599	4	0.02	14617	3	0.02	13648	0	0.00	14585	1	0.01	59449	8	0.01
BCH	19485	23	0.12	18484	9	0.05	16864	1	0.01	17395	4	0.02	72228	37	0.05
CMFT	15540	18	0.12	14141	13	0.09	13182	6	0.05	13081	4	0.03	55944	41	0.07
Total	116847	122	0.10	111254	51	0.05	103903	25	0.02	106160	20	0.02	438164	218	0.05

Leeds and GSTS have the joint lowest number of declines averaging just 0.01% over the course of the pilot. Sheffield had the highest number of declines with an average of 0.09%, however, the comparatively high percentage (when considering other sites) is a result of the large number of declines seen in the first month. By the end of the pilot period, the number of declines in Sheffield was comparable with other sites with the decline rate being between 0.01 and 0.3% across the sites.

The Final Number of Cases

Condition	Screen Positives	True Positives	False Positives
GA1	4	4	0
HCU	3	2	1
IVA	18	4	14
LCHADD	3	1	2
MSUD	2	1	1
Total	30	12	18

During the 12 month pilot, we saw a total of 30 screen positive cases. This resulted in 12 true positive cases and 18 false positive cases. At least one true positive was identified for each of the five conditions, the most common being IVA and GA1. See the table to the left for complete details of the number of cases.

How Did We Do Compared With What We Predicted?

Prior to the pilot commencing, we made predictions on the number of cases that we might see. The table to the right shows what these were. For most of the conditions, there were fewer false positives than predicted. The exception to this is IVA where there were twice as many false positives than predicted. The number of true positive cases of GA1 was as predicted, whilst the number of true positives cases of IVA were one more than expected. For the remaining three conditions, the number of cases was lower than expected. Prior to the pilot, 4 true positive cases of MSUD were predicted, whereas in fact only one was seen.

Condition	Screen Positives	True Positives	False Positives
GA1	10	4	6
HCU	8	3	5
IVA	10	3	7
LCHADD	5	2	3
MSUD	8	4	4
Total	41	16	25

Prior to the pilot, 4 true positive cases of MSUD were predicted, whereas in fact only one was seen.

Condition	Predicted PPV (%)	PPV from pilot (%)
GA1	40	100
HCU	38	50
IVA	30	22
LCHADD	40	33
MSUD	50	50
Total	39	40

And What About the Positive Predictive Value?

The Positive Predictive Value or PPV is the proportion of screen positives that result in true positive cases. A low PPV indicates a high rate of false positives and is to be avoided. The table left shows the PPV that we predicted before the pilot commenced and the actual numbers seen. The overall PPV, taking into consideration the five conditions, was pretty much as expected. Whilst the number of cases seen of MSUD was

lower, the proportion of true and false positives was as expected and therefore the predicted PPV of 50% was correct. Due to number of false positive cases seen in IVA, the actual PPV observed during the pilot was even lower than anticipated. A PPV of 22% would suggest that there may need to be some improvement in the screening methodology for IVA. During the pilot, no false positive cases of GA1 were seen – all of the screen positives turned out to be true positives. As such the PPV GA1 is reported is 100%!

A Word of Caution...

The Expanded Newborn Screening Pilot has gone to plan and we are confident in reporting the above results. However, all of the conditions which are screened for as part of the pilot are very rare. Due to the very low numbers (30 screen positives in 437, 946 screened) and the relatively short pilot, it is difficult to be sure that the statistics definitely represent what might happen over a longer period of time and therefore it is likely that there will be some variability in the number of cases and PPVs. For example, from the pilot we are reporting a perfect PPV (100%) for GA1. However, if there had been just one false positive case of GA1 during the pilot then the PPV would have reduced to 80%

A Request for Help Please:

In order to understand any problems that those might have encountered or recommendations for improvements in the future, we have requested the professionals involved in the project complete a short questionnaire. There are 3 different questionnaires available relating to clinicians and allied healthcare professionals, laboratory staff, and midwives / health visitors. If you would like to provide feedback on the pilot and have not received a questionnaire, please contact Clare.Gibson@sch.nhs.uk or Jason.Sowter@sch.nhs.uk

Time to Say Goodbye

Dr Clare Gibson has been working as the Expanded Newborn Screening Project Manager since June 2012. She will be leaving us in September for pastures new in Edmonton, Canada. Whilst working on the Expanded Newborn Screening Project, she has undertaken various roles within the programme including data collection, report writing, ethics and research governance, collaborating to assist in the development of the expanded screening films and writing this newsletter! We wish her the best of luck for the future.



What's Going On?

Whilst the pilot has completed, the Expanded Newborn Screening Group are still busy at work. This next section explains the activities which are currently being undertaken.

Preparation of the Report for the National Screening Committee:

Data collected during the pilot will be used to prepare a short report for the National Screening Committee (NSC). It will be presented at the committee late November after which the committee will have time to review the information provided and make a decision as to whether to recommend continuation of the expanded screening to ministers. The report will include an update on the 21 criteria used by the committee along with lessons learned from running the pilot which may be useful in implementation in the future.

Continuation of Screening:

Whilst the timeframe for recruitment to the research is completed, screening for each of the 5 conditions will continue to 31st March 2014. During this time we will continue to collect information from the labs on the number of births, cases (screen positive, true positive and false positive), and declines. This information will be useful as the greater time period over which we are able to collect data, the more confidence that we will have in our results.

Data Collection on Clinically Identified Cases:

It has been requested that labs provide information on any clinically identified cases of the conditions. This data collection will continue for at least 5 years after the pilot to enable identification of any false negative cases. False negatives are cases which have not been picked up by screening and therefore the result is reported as negative (i.e. that baby does not have that condition) where in fact they are positive (they do have the condition). Identification of false negative cases may suggest that there is a need for changing the cut-offs used for an analyte or making another change to a screening protocol. It is therefore important that we continue to collect this data.

Communication:

The website (www.expandedscreening.org) will continue to be updated. Ideas for further films and further development of the website are currently being considered. The newsletter will continue to be distributed with information on the ongoing work.

Health Economics Evaluation:

The inclusion period for the research study had to complete in July in order to enable sufficient data to be collected for the Health Economics evaluation. Preliminary results from the evaluation will be included in the report to the NSC. A small team at the School of Health and Related Research, University of Sheffield led by Jim Chilcott are undertaking this work. They are in the process of building a model which will compare the cost of identification and treatment of cases identified through screening compared with the cost of treatment of cases where they present clinically. To develop this model, Jim's team are reviewing information available in the literature and consulting with experts to generate a picture of what a case of each condition may look like. They then assign costs to each activity. When the data is input from the pilot, the model will provide this information.

Improving the Assays:

While the laboratory assays used in testing have proved acceptable, Rachel Carling and Rodney Pollitt are investigating causes of residual variation. They hope that by looking critically at internal standards, instrumentation and methodological approach, that laboratory to laboratory variation can be reduced further and this may be important if future national roll-out is agreed. This work is continuing.

Update of the Evidence:

Prior to the start of the pilot, Hilary Burton and Sowmiya Moorthie of the PhG Foundation completed a review of evidence in relation to the five conditions which are included in the Expanded Newborn Screening Programme. They are currently completing a systematic review to check for any new research publications since the previous review published 2010 and will provide an update for inclusion in the NSC report.

Communication Study:

As previously reported, Louise Moody will be leading a qualitative study looking at the communication of screen positive and confirmatory results. Louise and her team will shortly commence interviews with clinicians and parents of screen positive cases. They will provide a report including recommendations for the future.

The Expanded Newborn Screening project is supported by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care for South Yorkshire (NIHR CLAHRC SY). The views and opinions expressed are those of the authors, and not necessarily those of the NHS, the NIHR or the Department of Health. CLAHRC SY would also like to acknowledge the participation and resources of our partner organisations. Further details can be found at www.clahrc-sy.nihr.ac.uk.

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