Objective: The NHS newborn bloodspot screening programme screens all babies in England for five rare conditions. This study assessed the economics of expanding the screening programme to include five new inborn errors of the metabolism; HCU, MSUD, GA1, IVA, and LCHADD.

Methods: A decision analytic model (Figure 1) was used to estimate cost-effectiveness. Model parameters included:

- **Prevalence:** Data from studies reporting incidence with and without screening were synthesised using a Bayesian meta-analysis with a fixed effect logit model, with bias adjustment for potential ascertainment and over detection.
- **Sensitivity and specificity of the MSMS device in screening** are estimated from systematic review data using a logit model within a Bayesian synthesis.
- **Survival and morbidity estimates for the screened and unscreened populations** were derived from published case series.
- **Quality adjusted life years (QALYS)** were estimated from the extended EQ-5D+H(C) which includes a cognitive dimension in order to capture the impact of neurological impairment and developmental delay which are known sequelae of the five conditions.
- **Costs** related to the marginal cost of the expanded screening programme, management cost of the conditions, and costs associated with the sequelae of the conditions were estimated from the pilot study of the expanded screening, case reports from the pilot, expert elicitation, published guidelines and estimates from the literature.

Costs and QALYs were multiplied by survival and morbidity estimates to give lifetime estimates for the screened and unscreened populations. A probabilistic sensitivity analysis (PSA) was conducted.

Results:

- **Cost-effectiveness**
  - The determinsitic analysis (Table 1) and PSA suggest that screening for all five conditions is cost-saving with screening associated with lower total costs and higher total QALYs compared to not screening. The incremental net benefit (INB), at a threshold of £25,000 per QALY, was between £0.46 for IVA and £5.94 for GA1. However, the PSA showed that an INB below zero was possible for all conditions.

Prevalence of the five inborn errors of the metabolism

For MSUD, HCU and LCHADD the model estimates the prevalence to be virtually equivalent in the screened and unscreened populations. For IVA and GA1 the results suggest that the screened prevalence is much higher than the clinical prevalence. Table 2 presents the cases detected and over detected (i.e. otherwise asymptomatic without screening) for a 5 year England and Wales birth population.

Conclusions: Screening for MSUD, HCU, IVA, GA1 and LCHADD are each estimated to dominate no screening. However these results are subject to a number of methodological weaknesses including:

- **The methods used to calculate quality of life estimates**
- **The assumptions used for treatment costings**
- **Estimating true condition prevalence for treatment**
- **The issues with the identification of isolated LCHADD rather than the spectrum of conditions known as MTP.**

The uncertainties around which are not captured within the model.

Table 1: Costs and effects of screening compared to no screening

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cost</th>
<th>QALYs</th>
<th>Cost</th>
<th>QALYs</th>
<th>Incremental compared to no screening</th>
<th>Cost</th>
<th>INB*</th>
<th>Cost effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSUD</td>
<td>£7.58</td>
<td>41.7934</td>
<td>£7.30</td>
<td>41.7934</td>
<td>-£0.28</td>
<td>0.000069</td>
<td>£2.00</td>
<td>Dominating</td>
</tr>
<tr>
<td>HCU</td>
<td>£6.31</td>
<td>41.79146</td>
<td>£6.98</td>
<td>41.79156</td>
<td>-£3.33</td>
<td>0.000105</td>
<td>£5.94</td>
<td>Dominating</td>
</tr>
<tr>
<td>IVA</td>
<td>£1.31</td>
<td>41.79356</td>
<td>£1.20</td>
<td>41.79358</td>
<td>-£0.10</td>
<td>0.000014</td>
<td>£0.46</td>
<td>Dominating</td>
</tr>
<tr>
<td>GA1</td>
<td>£2.87</td>
<td>41.7944</td>
<td>£2.72</td>
<td>41.7945</td>
<td>-£0.15</td>
<td>0.00012</td>
<td>£3.14</td>
<td>Dominating</td>
</tr>
<tr>
<td>LCHADD</td>
<td>£3.94</td>
<td>41.7934</td>
<td>£1.54</td>
<td>41.7935</td>
<td>-£2.40</td>
<td>0.000114</td>
<td>£5.25</td>
<td>Dominating</td>
</tr>
</tbody>
</table>

*INB: Incremental net benefit calculated at a threshold of £25,000 per QALY

Table 2: Estimated incidence and over detection with screening

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence Mean</th>
<th>95% CI</th>
<th>Projected over detection Mean</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSUD*</td>
<td>26.82 (21.97, 31.81)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HCU</td>
<td>26.93 (19.48, 34.81)</td>
<td>0.67 (0.00, 1.39)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>IVA</td>
<td>30.14 (25.27, 35.51)</td>
<td>19.15 (10.92, 26.34)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>GA1</td>
<td>37.27 (31.81, 42.51)</td>
<td>20.27 (9.76, 29.40)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LCHADD</td>
<td>23.6 (19.10, 28.78)</td>
<td>3.61 (0.00, 11.35)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Unable to estimate over-detection from screening due to ambiguities in the evidence base regarding prevalence in the clinical and screened population.

References:


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