Comparison of international evidence review processes for evaluating changes to the newborn blood spot test

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Plan of talk

• The newborn blood spot test
• Rationale
• Methods
• Results
• Conclusion
The Newborn Blood Spot Test

- First 10 days of life
- Spot of blood from baby's heel
- Tandem Mass Spectrometry
- Can test for >100 rare conditions
- Informed choice issues
Rationale

- Prevalence typically 1/100,000
- Randomised Controlled Trials are Impossible/Unaffordable
- How are we measuring the benefits and harms of screening in the absence of RCT evidence?
Rationale

• Randomised Controlled Trials are Impossible/Unaffordable
• Prevalence typically 1/100,000
• How Are we measuring the benefits and harms of screening in the absence of RCT evidence?
Methods

1. Describe pathways to key benefits and harms
2. Extract all previous blood spot reviews from policy making organisations in 15 countries (identified in previous systematic review)
3. Score each review for 3 key elements of the pathway:
   1. Test Accuracy
   2. Benefit of Early Treatment
   3. Overdiagnosis
# Methods: Inclusion criteria

<table>
<thead>
<tr>
<th>Included</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>• National policy making organisation</td>
<td>• Regional</td>
</tr>
<tr>
<td></td>
<td>• Other groups e.g. clinical societies</td>
</tr>
<tr>
<td>• Starting or stopping screening</td>
<td>• Changes to screening</td>
</tr>
<tr>
<td>• Conditions on the newborn blood spot test</td>
<td>• Other conditions</td>
</tr>
<tr>
<td>• Any review methods: systematic review, expert working group, unclear methods</td>
<td></td>
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<tr>
<td>• All dates</td>
<td></td>
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</tbody>
</table>
# Methods: Scoring system

<table>
<thead>
<tr>
<th>Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not investigated at all</td>
</tr>
<tr>
<td>1</td>
<td>Considered in some way (mentioned in at least one document once).</td>
</tr>
<tr>
<td>2</td>
<td>Measured in some way (at least one study or source cited, AND at least some numerical estimate given)</td>
</tr>
<tr>
<td>3</td>
<td>Investigated using systematic methods of collecting evidence (score if detail two elements of systematic review)</td>
</tr>
<tr>
<td>4</td>
<td>Mention any element of external validity OR internal validity</td>
</tr>
<tr>
<td>5</td>
<td>Assessed using formal quality assessment</td>
</tr>
</tbody>
</table>
Key Pathways
Population sieve test

TP
FP
TN
FN
Indeterminate

Sort test

TP
TN
Indeterminate
Incidental findings

Earlier treatment
Overdiagnosis

Direct harm from test
Harm
Potential harm from false reassurance
Direct harm from test
Harm
Harm
Harm from false positive
Harm from overdiagnosis

Mortality benefit
Morbidity benefit
No benefit.
Results

• 130 documents including 243 reviews across 14 countries

Australasia: 2
Australia: 4
Belgium: 8
Canada: 5
Denmark: 3
Finland: 6
France: 8
Germany: 13

Italy: 4
Japan: 4
Netherlands: 5
New Zealand: 8
Spain: 25
Sweden: 0
United Kingdom: 8
USA: 26
Results

• 103 different conditions reviewed
• Most reviewed conditions
  – Medium-chain acyl-CoA dehydrogenase MCAD (n=9)
  – Cystic Fibrosis (n=9)
• Countries recommend between 5 (Finland) and 34 (USA +26 secondary) conditions
Results

- 24% (n=58) systematic reviews

- Recommend screening
  - Yes 57% (n=139)
  - No 34% (n=82)
  - No recommendation 9% (n=22)
Results: All recommendations

- Test
- Early detection
- Overdiagnosis

- Prevention and detection of disease

- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
- 80%
- 90%
- 100%

- Test: 90%
- Early detection: 70%
- Overdiagnosis: 80%
Results: Systematic Reviews

Test

Early detection

Overdiagnosis

- 5
- 4
- 3
- 2
- 1
- 0
Limitations

- Reliance on published records (not doing or not recording?)
- Largely ‘grey’ literature
- Language translation
Conclusion

- Key elements of patient benefit/harm are not being considered/published in evaluating whether to add or remove conditions from the newborn blood spot test
Next Steps

• Evaluate predictors of decision of whether to recommend screening

• Develop evidence review methods/standards for evaluating screening when RCT impossible
Thank you!

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