UK National Screening Committee

Background to an in-service evaluation (ISE)

Dr David Elliman: Clinical Advisor to the Newborn Blood Spot Screening Programme

Background - 1

Inherited disorder of immune system resulting in increased susceptibility to infection with death by one year if untreated

Estimated incidence in UK c.1 in 40,000 (higher in some ethnic groups, reflecting frequency of consanguinuity)

If treated early, ie younger siblings of cases, by HSCT, prognosis is better – predominantly related to infection status

Screening based on TRECs (T-cell receptor excision circles), using current day 5 newborn blood spot

Screening in a number of countries, e.g. USA, with favourable outcomes

Background - 2

Review and modelling for UKNSC by ScHARR in 2017, suggested that probably cost effective in UK -

71% probability at £20,000 threshold and 99% at £30,000

But some issues that need further elucidation

In-service evaluation (ISE) was recommended by UKNSC

SCID in-service evaluation
Issues to be addressed - 1

The key uncertainties highlighted by sensitivity analysis of the ScHARR cost effectiveness work were:

- The cost of the TREC test
- The incidence of SCID
- Post HSCT mortality rates in the early diagnosed population
- The length of stay in hospital of the early diagnosed SCID patients
- The proportion detected by family history in the absence of screening

SCID in-service evaluation
Issues to be addressed – 2a

Other issues to be addressed:

- The effect of the screening programme on the participant families
- The benefits and harms to those with non-SCID immunological problems
  - these are much more commonly found after screening than SCID
- The capacity of NHS services

SCID and Bacillus Calmette-Guerin (BCG) vaccination

BCG is a live vaccine

Most effective against severe disease – TBM and BCGosis

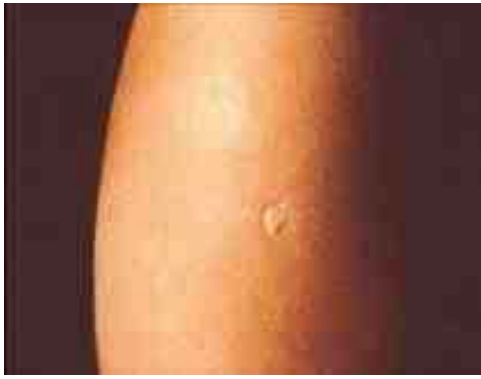
Contraindicated in immunosuppressed individuals, in whom it can cause serious morbidity and sometimes mortality

Policy for use varies around the world from nil to multiple doses

In UK, now primarily given as part of a targeted neonatal programme

Countries screening for SCID have different policies

JCVI recommended delaying BCG until SCID screening result available



SCID In-Service Evaluation
Issues to be addressed – 2b

Other issues to be addressed:

- The effect of the screening programme on the participant families
- The benefits and costs to those with non-SCID immunological problems
- The capacity of NHS services
- The effect on the BCG programme (and, to a lesser extent, rotavirus)

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Pre-evaluation preparation

Prof Jim Bonham: Laboratory Advisor to the Newborn Blood Spot Screening Programme

Policy, governance and money

Clarity about the Questions to be answered by the ISE

Identifying the stakeholders – patients and parents, public, professionals, policy makers + NHSE managers, those who will undertake the work e.g. scientists, clinicians, economists, statisticians, midwives etc., those with overseas experience

Creating a governance structure – planning, reporting, co-ordination and scrutiny, e.g. overarching board: patient/public/professional information group; clinical group; laboratory group; data management group; diagnostic review group

Management, administrative & IT support

Publication policy for use during the study with acceptance by those involved

Plan of the design of report writing – an outline of the structure, data and those to be involved – consider outline report for an International audience

Funding – agreed in advance, procurement and contracting support (e.g. equipment purchase, SLAs and contracts) – these all take longer than envisaged

Preparative activity

Updated literature search to inform strategy including recent grey literature sources

Case definition **and** long term follow-up arrangements

Design of the study - power calculations, duration, multi site study?, one or more methodologies, possible implications for other related aspects of health care and existing services etc.

Due diligence when securing commercial aspects – kits/equipment etc – i.e. market research

Communications - within the ISE, within the organisation, with individual Trusts involved, wider public, policy makers, politicians etc. The role of including dedicated websites to maintain contact and co-ordination

Logistics, training and awareness

Pre-screening information design and content

Training – midwives (sample takers), lab staff, clinicians

Wider awareness – GPs, HVs, professionals in unscreened areas, QA teams

Comms teams announcements centrally and in participating sites – liaison needed

Policies on participation e.g. born and resident only or also 'movers in'

Sample collection and transport

Screening laboratory aspects (1)

- Choosing the labs/sites who will participate – principles and what may be allowable
- Contractual arrangements - SLAs etc.
- Staffing requirements and recruitment
- Choice of methods to be assessed - available options
- IT and equipment purchase
- Contingency planning in the event of disruption
- Timescales

Screening laboratory aspects (2)

- Gaining access to retrospective samples including 'normals' and positive cases, taking into account ethical aspects of their use, anonymisation etc. and the approvals needed
- Validation/verification of the assays
- Choice of cut-off value
- Implementation of any IT modifications
- QC/EQA

Screening laboratory aspects (3)

- Accreditation
- Turn around times, weekend working etc.
- Arrangements for testing of screen positives by the alternate method(s) being evaluated

Clinical and reporting aspects

- Referral routes for screen positive patients
- Initial referral guidelines
- Confirmatory testing
- Results reporting for normal results for parents and child health systems - IT implications
- Definition of data reporting requirements – items to report, frequency, route of reporting, units etc.

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Progress and learning

Liz Robinson: Newborn Blood Spot Programme Manager, NHSE

Progress and learning

- Exceptionally complex to plan
- Taking a leap of faith – trusting the team/evidence
- Engage the right stakeholders and keeping them engaged
- Understand the evolution
- Be prepared to challenge your standards

Key support

- Internal support from within our own NBS team
- Support from the wider NHSE support teams (i.e. IT, Business, Commercial, communication, commissioning, SQAS, D&A)
- External key stakeholders
- Drawing on the right expertise at key points and during certain phases of the ISE

Having a flexible approach

ISE is an opportunity to learn as we go along, to collect evidence

Making alterations and changes as the project progresses:

- Treatment of duplicates
- Extending the evaluation
- Additional pathway for preterm babies
- Altering/adjusting cut off values
- Supporting labs during periods where testing for SCID had to pause
- Changes with data requirements (i.e. labs/immunology/expectations)
- Evolving governance to reflect organisational change
- Monitoring of the diagnostic pathway
- Introducing new technologies

Challenges/considerations (1)

Resources/Time

Burn out/motivation

Pandemic

Getting the ‘buy in’

Reorganisations

Considering the impact on other clinical programmes and pathways – BCG/Rotavirus

Brexit

Changes in the commercial markets

Challenges/considerations (2)

Sample takers – communication, keeping updated

Diagnostic pathway

Immunology teams

Detecting other conditions from the test

Impact on preterm pathway

ISE means in our case 2/3 of England

Data collection/mission creep

Completion/next steps

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Post-evaluation: what next?

Dr Jane Scarlett: Clinical Advisor to the Newborn Blood Spot Screening Programme

Process and timescales

Final report goes to UK National Screening Committee (NSC) – quarterly meeting

NSC consider report and make recommendation

Recommendation goes to ministers who decide whether to implement

Ministerial decision goes to NHSE to implement – implementation timescale could be long

Producing a final report

Process of producing report starts well before end of evaluation

Tension between documenting all of the learning from the evaluation and producing a focused report to answer the NSC questions

Process for sign-off of report across different organisations

Public information vs restricted document

Confidential information and small numbers

Data chasing – difficult to obtain data in a timely way

How to manage emerging international research over the timescale of the evaluation

Issues to consider following end of the evaluation

Continuity of service in evaluation sites.

Communication to all stakeholders.

Impact across screening pathway and on related services.

Incorporating ongoing research and technology changes.

Data collection and storage.

Public and stakeholder expectations following NSC recommendation.

If the recommendation is to screen

Consider impact of full roll-out across all stakeholders

Plan technical, data and workforce aspects of roll-out

May be some difficult logistic issues to resolve, e.g. labs participating in the evaluation did not require any building work to carry out screening. Timescales for work needed may be long.

Consider one roll-out date or staged roll-out as services are ready in each area.

Clear communication to all stakeholders.

If the recommendation is not to screen

Actions may depend on whether this is a ‘final’ negative or whether further questions remain.

Stopping screening in the evaluation sites would need careful planning.

Decision may attract more publicity than decision to implement, press campaign needed.

Process to manage repeat samples from those screened before end date.

Impact on full pathway and on other related services.

Consider how to manage changes to technology and emerging research internationally.

Clear communication to all stakeholders.

Further research following evaluation

Some questions cannot be answered within timescale of evaluation, and longer follow-up will be needed for:

- Outcomes for SCID babies
- Outcomes for Non-SCID TCLs
- Performance of laboratory tests as these develop and as greater numbers are screened
- Long term impacts of false positives – 5 year follow up for utilities

Process to ensure these are reported and considered needs to be established, regardless of NSC recommendation and ministerial decision

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For any questions please email:

screeninginformation@dhsc.gov.uk