Expansion of a National Newborn Bloodspot Screening Program with Fourteen Conditions

Preparations in the Netherlands

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Program and process in the Netherlands

- Netherlands
  - Approximately 175,000 newborns annually
- National program currently 19 conditions
  - Voluntary, informed consent
  - 99.3% participation
  - Five screening laboratories
- Policy process
  - Ministry
  - Health Council
  - RIVM

Expansion of a National Newborn Bloodspot Screening Program with Fourteen Conditions | 12-09-2017
Policy advice & decision on expansion

- Expansion with 14 conditions in three phases
  - Primary program, Ministry decided on phased time frame

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Available in English from [https://www.gezondheidsraad.nl/sites/default/files/201508e_neonatalscreeningnewrecommendations.pdf](https://www.gezondheidsraad.nl/sites/default/files/201508e_neonatalscreeningnewrecommendations.pdf)
Implementation

● Feasibility study\(^1\)
  - Primary process
  - Organization and responsibility
  - Quality assurance
  - Communication and education
  - Information tools
  - Monitoring and evaluation

● Additional details required
  - Stakeholder involvement through experts groups

Principles for screening

● **Whether** to screen: framework screening criteria
  – Wilson & Jungner principles

● **How** to screen: Checklist based on international examples:2,3
  – Australia; Canada; Denmark; UK; USA

● Additional details required
  – Test method
  – Disease variants and Dutch prevalence
  – Treatment consensus

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3. English translation of checklist available via marleen.jansen@rivm.nl
Stakeholder involvement

- Eight multidisciplinary expert groups for eleven conditions
  - Background document
    - Scientific publications
    - Grey literature, international examples
  - Agenda meeting
    - Test, disease variants, treatment consensus
  - Outcome
    - Advice on current status and types of further research needed
  - Member check through summary of the minutes, advice, checklist
  - Evaluation of process

CACT; CPT1; CPT2 | GALK | GAMT | BKT | MMA; PA | MPS I | OCTN 2 | X-ALD
Advice for conditions and further research

- Retrospective studies: Dutch prevalence, cut-offs
- Post analytical tool with CLIR database: potentially applicable to multiple conditions

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GAMT

● Prevalence
  - Unknown in Netherlands, estimated at 1:250,000

● Test method
  - Off-label MS/MS
  - In-house
  - LC MS/MS

● Logistics
  - In-house: central lab or all labs
  - Analysis within 24 hours

● Advice
  → Retrospective studies: Dutch prevalence, cut-offs
  → Prospective pilot study
OCTN-2

● Prevalence
  – Unknown in Netherlands, estimated 1:20,000 – 1:200,000

● Disease variants
  – Broad spectrum: life threatening to apparent healthy
  – Genotype-phenotype relation unclear
  – Asymptomatic mothers

● Test method
  – Available MS/MS: C0 carnitine

● Logistics
  – Assess time point for reliable heel prick

● Advice
  → Retrospective studies: Dutch prevalence, cut-offs
  → Prospective pilot study
Estimated time frame

2017
- Preparation
  - Feasibility study

2018
- Expansion NBS
  - Lab technology
  - Standard values
  - Algorithm

2019
- Logistics
- Pilot studies
- Additional studies

2020

2021

Phase 1
- Decision Minister

Phase 2

Phase 3
- Tender laboratoria
Acknowledgements

- RIVM CvB
  - Eugènie Dekkers
  - Marie-Louise Heijnen
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  - Arjan Lock
  - Herma Vermeulen
- RIVM GZB
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  - Wouter Visser
  - Annemieke de Vries
- RIVM IDS
  - Rose Maasse
  - Peter Schielen

Experts participated groups
Extra slide – Topics on checklist

A. Test parameters
   I. Which analytes or parameters are tested, and about what disorders does the test provide information? If a test involves multiple steps, answer for each tier.
   II. If screening will inevitably identify carriers, it must be clear (i) how to deal with this information, and (ii) the consequences of this must be weighed

B. Analytical and clinical validity of the screening test
   I. A simple, rapid, specific, precise, accurate and safe test must be available, which can be performed on dried blood spots.
   II. The distribution of the biomarker in the target population must be known
   III. The test is acceptable for the target population.

C. Follow-up in the case of positive test result
   I. There must be an agreed policy for a positive screening result
   II. The benefit for individuals must outweigh the drawbacks (caused by the test)
   III. There must be an agreed policy for secondary findings and variants, discovered in the screening
   IV. The follow-up costs of the screening programme in the case of secondary findings/variants are reasonable in relation to costs on healthcare in general (value for money)
Extra slide – Participants in expert groups

- Pediatrician
- Clinical geneticist
- Clinical biochemist
- NBS Advisory committee member
- Medical ethicist
- Laboratory expert
- Scientific consultant
- Policy expert
- Evaluation consultant
- Patient advocate
- Program coordination