Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Screening on X-ALD in the Netherlands

An ethical perspective

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Phased extension NL NBS with 14 conditions

Phase I-2017	Phase II-2019	Phase III-2020/22
• *Alfa-thalassemia (HbH-disease)* • *Beta thalassemia major (TM)*	• Carnitine palmitoyltransferase deficiency type 1 (CPT1) • Methylmalonic acidemia (MMA) • Methyl-acetoacetyl-CoA thiolase deficiency; ketothiolase deficiency (BKT) • Propionic acidemia (PA)	• Carnitine-acylcarnitine translocase deficiency (CACT) • Carnitine palmitoyltransferase deficiency type 2 (CPT2) • Galactokinase deficiency (GALK) • Guanidinoacetate methyltransferase deficiency (GAMT) • Mucopolysaccharidosis type 1 (MPS I) • Organic cation transporter 2 (OCTN 2) • Severe combined immune deficiency (SCID) • **X-linked adrenoleukodystrophy (X-ALD)**

NBS on X-ALD-> Health Council advice

Pre test selection on boys

Test *only male* newborns primarily on cerebral variant

Health Council advice

SCREENING

X-ALD positive male newborns

Carrier status mother

Carrier status sister(s)

DIAGNOSTICS

Female carriers:
-> 80% develops untreatable and late onset variant (adrenomyeloneuropathy)

Follow up in University hospital referral centre

NBS on X-ALD -> Health Council advice

Wilson & Jungner:

->There should be a recognisable latent or early symptomatic stadium of disease

->There should be a broad accepted treatment for the disease

Elaborated in NL NBS as…

-Screening should benefit the newborn

-There should be direct health gain or improved diagnostics/care for the newborn

Screening is performed for:

-> *Early onset* severe conditions

-> Only *treatable* conditions

Ethical considerations and implications…

Early knowledge on an untreatable condition impairs the right on an ‘open future’

Early knowledge on an untreatable condition leads to loss of golden years

Proposed X-ALD test procedure reveals two ethical dilemmas

Secondary findings

Avoid testing girls

First ethical dilemma-secondary findings

Through screening and referral to a University hospital referral centre of X-ALD positive boys we find:

female carriers-mother/sister(s) of the X-ALD positive boy

80% of female carriers develops *untreatable* and *late onset X-ALD* variant (adrenomyeloneuropathie)

But:

Health gain male newborns by screening outweighs the disadvantages of finding carriers in the diagnostic phase.

So:

Provide good support to families with carriers in University hospital referral centre

THE ETHICAL DILEMMA

Second ethical dilemma-avoid testing girls

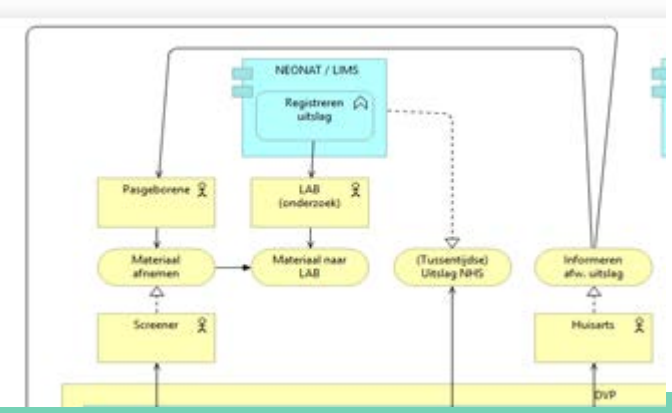
Screen only male newborns on X-ALD-> avoid screening female newborns on X-ALD

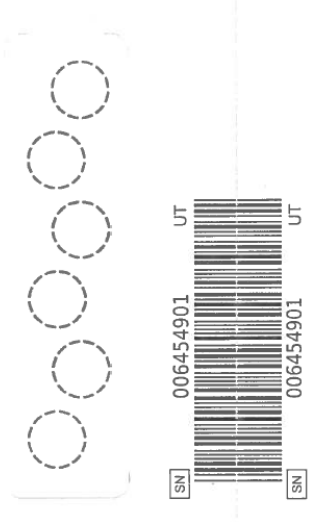
Practical challenge to stratify between boys and girls in the screening laboratory-logistics.

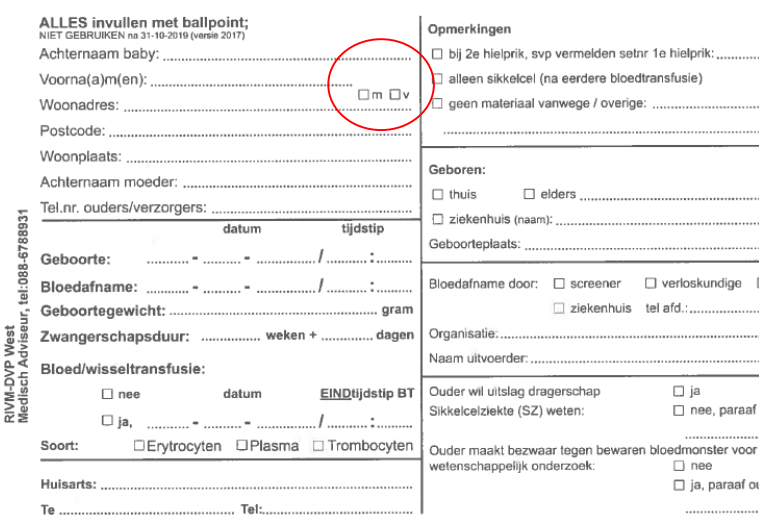
Current situation:

All newborns are screened for all 19 conditions in NBS programme

-> sex registered on heelprick-card, not in the laboratory



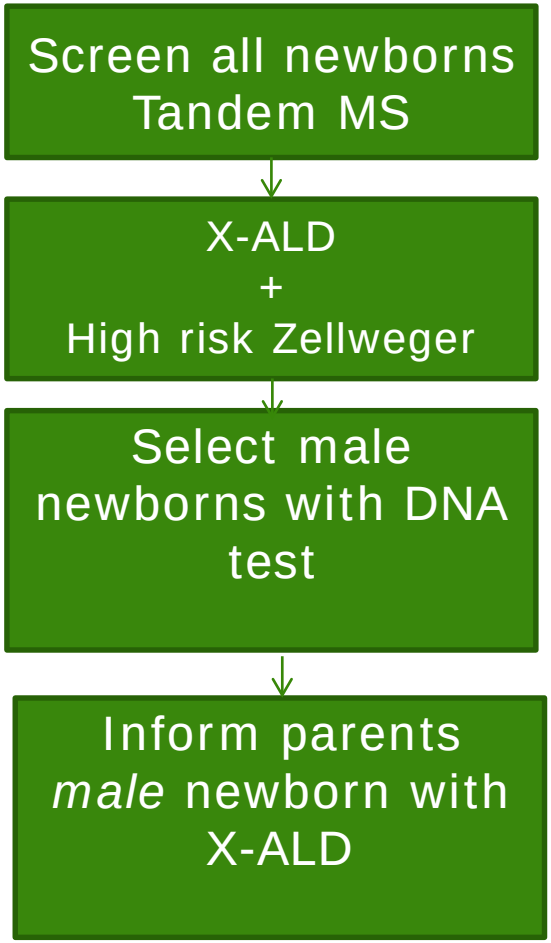





Plan A
Plan B

Alternative for dilemma – avoid testing girls

Post screening selection on boys



Conclusion

But: this testing procedure generates information on screen positive girls

Caregivers cannot share this information with the parents-> creating an ethical dilemma

So:

The preferable route is selection on sex before start first tier testing on screening on X-ALD

And:

Every solution comes with a price…..

Next steps forward to screening on X-ALD in the Netherlands…

1. Decision of MoH on start implementation for X-ALD screening

2. Research on a manner to robustly select the sex of the male newborns before start first tier testing on X-ALD

3. Start pilot screening on X-ALD in the Netherlands
   - is it possible to reliably select the male newborns in the screening laboratory before testing?
   - is it possible to inform the parents in an accurately manner about possible secondary findings?
   - is it possible to have a good follow up in the University hospital referral centre for families with X-ALD carrier?

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