Webinars #6 - march 21st 2023

“ERN ITHACA Innovation in Newborn Screening across Europe “

Chaired by Pr Laurence FAIVRE,
Workgroup Teaching and Education

5pm-6.30

Co-funded by
the Health Programme
of the European Union

European Reference Networks

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Welcome – Technical points

- *We are please to be numerous **225***
- *Webinar being recorded*

- *Thank you for*
  - *Turn off your microphone and disconnect your camera*
  - *Raise your hand at the time of the questions and discussions*
  - *We will answer the questions sent in the registration form*
  - *A satisfaction survey will be sent to you : https://forms.office.com/e/SJsykbP04K*

- *Webinar#6 will be available on ITHACA's Website*

  https://ern-ithaca.eu/documentation/educational-resources/

Anne Hugon Project Manager ITHACA - anne.hugon@aphp.fr

Agenda

Welcome and Introduction

- Pr. Laurence Faivre, Centre de Génétique et Centre de Référence Anomalies du Développement et Syndromes Malformatifs, Dijon (France)

- Topic 1 - Presentation of 2 European NGS pilot projects in Europe
  - The UK 100.000 genome project in newborn screening

  Dr. David Bick, Newborn Genomes Programs at Genomics England, London
  - The Netherland pilot NGS extended newborn screening

  Dr. Marcel Nelen, Genome Diagnostics Center UMC, Utrecht (Netherlands)
- Topic 2 -Presentation of the newborn screening axis of the Screen4Care project
  - Pr. Alessandra Ferlini, Medical Genetics Unit, S.Anna University Hospital, Ferrara (Italy)

Discussion time

- Topic 3 - The Eurordis position statement harmonized newborn screening
  - Gulcin Gumus, Research & Policy Project Manager, EURORDIS, Barcelone (France)
- Topic 4 -The SeDeN project: a study of the acceptability of professionals and the population in France before setting up a pilot project
  - Dr. Camille Level, Study engineer in health economics at Dijon Bourgogne University Hospital, Dijon (France)

Discussion time

Conclusion with speakers and moderator

- Pr. Laurence Faivre, Centre de Génétique et Centre de Référence Anomalies du Développement et Syndromes Malformatifs, Dijon (France)

1.

Welcome and Introduction

- Pr. Laurence Faivre, Centre de Génétique et Centre de Référence Anomalies du Développement et Syndromes Malformatifs, Dijon (France)

Introduction - Advances in neonatal screening

Pr. Laurence Faivre, Centre de Génétique et Centre de Référence Anomalies du Développement et Syndromes Malformatifs, Dijon (France)

COLD SPRING HARBOR
Molecular Case Studies

PERSPECTIVE

2022: a pivotal year for diagnosis and treatment of rare genetic diseases

Stephen F. Kingsmore

Rady Children's Institute for Genomic Medicine, Rady Children's Hospital, San Diego, California 92123, USA; Keck Graduate Institute, Claremont Colleges, Claremont, California 91711, USA

Abstract The start of 2022 is an inflection point in the development of diagnostics and treatments for rare genetic diseases in prenatal, pediatric, and adult individuals—the theme of this special issue. Here I briefly review recent developments in two pivotal aspects of genetic disease diagnostics and treatments: education and equitable implementation.

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Advances in neonatal screening: Introduction

Kacper Rucinski asked a question .
31 July at 00:09 ·

What would cause more anxiety to you as a parent: to care for a child with SMA - OR to learn that your newborn baby has SMA, despite having no symptoms, and will have to undergo lifelong therapy, but otherwise may be healthy?

A person at today's meeting raised this question, also saying that one study of parents in cystic fibrosis found that having a child with CF, which is a lifelong severe disease, causes less anxiety for parents than learning about CF diagnosed through newborn screening.

(I was livid when responding but don't want to prejudice your answers).

[redacted] o be honest it even was a question. Obviously diagnosis at anytime would cause anxiety but had we had the option of knowing as a newborn now there are treatment options which could have quickly been started I would not have the same anxieties by far. The anxiety's of fighting for nearly 2 years to get a diagnosis that was quickly apparent to a neuromuscular specialist but took that long after starting symptoms for anyone to actually bloody listen to me to even get us in front of them, to what her futures holds, the anxiety's about how fast she would deteriorate the anxiety's caused by the constant fight for equipment and essentials to meet her needs. Nope I can hand on heart say diagnosis as a newborn would 1000% have saved me a lot of anxiety and I would've been able to fight for things to prevent the deterioration starting in the first place

[redacted] J otally relate to this. My daughter had to wait for a whole year to be diagnosed and that was the hardest year of my life. Not knowing what was wrong, how I can help her and what we can do to make sure she gets the support she needs. By the time she was diagnosed, she was 2 and a half nearly 3 and she wasn't meeting milestone at all. Having a child which is developmentally normal in some aspects and then physically behind is such a confusing place to be in. I remember even suggesting to them to maybe test for SMA! Because I was researching like crazy to find answers. Honestly more awareness needs to be made.

Like · Reply · 3 d 2

[redacted] I believe it is not a nice thing to learn your newborn looking perfectly healthy baby has a devastating disease, especially if test gives 2 copies of the SMN2 gene, but after that shock and after presymptomatic treatment, those parents and that kid will be eternally grateful.

[redacted] h **Sana Sheikh** exactly our story x I knew there was something wrong at 1 and she was diagnosed just before 3 but they wouldn't listen and kept sending us for physio 😢 I really hope the screening gets approved **Kacper Rucinski** wish I'd realised sooner this would come up as I would've been happy to speak or write about our experiences

[redacted] I culous question. Why would anyone want to know later about any kind of medical condition? We watched our son gradually regress and stop crawling about with no idea why and about a year until we got a correct diagnosis.

Like · Reply · 3 d 1

[redacted] Does this person know that there are efficient treatments for SMA, and the outcome is better the earlier you start?? If yes, it shouldn't be a question...
And you can always say no to newborn screening. That 0.000001% of parents, who think it is better not to know, can simply deny the newborn screening.

[redacted] I zed this is even a question! Receiving an SMA diagnosis is huge thing whenever it comes. However given that irreversible damage may have already happened before symptoms become obvious enough for Drs to believe that something is wrong, it's ethically questionable. Really the question should be re-framed as "would you prefer a lengthy and stressful diagnostic odyssey during which disease is relentlessly progressing and then treatment might start (or you may have already missed an age/weight-based funding restriction [I wonder if this is what motivated the question]) or would you prefer to skip all that and know what you need to now from the beginning?"

marfans

Adèle est tellement belle. Elle est née il y a un peu plus d'un mois, le 4 janvier 2035. J'étais submergée de joie, cela faisait si longtemps que je l'attendais.

Le lendemain de sa naissance, un médecin est venu nous annoncer que le test génomique de routine révélait une anomalie. Je l'ai vécu comme un choc. Mon tout petit bébé, atteint d'une maladie génétique ? Devant notre air paniqué, le médecin de la maternité a tout de suite tenu à nous rassurer : « le syndrome de Marfan est extrêmement bien soigné aujourd'hui ».

Il y a quelques jours, grâce à un parcours de soins 100 % pris en charge par la sécurité sociale, nous avons pu obtenir un rendez-vous avec un pédiatre spécialisé dans la maladie, dans un hôpital près de chez nous. Adèle était un peu inquiète, même si le médecin était doux. Elle a été auscultée et à l'issue du rendez-vous, le docteur nous a parlé de l'aorte ascendante, qui lui semblait déjà un peu large.

Un médicament révolutionnaire, le FibriCorrector, mis au point récemment par des chercheurs européens dans le cadre d'une collaboration internationale, lui a été prescrit. Il permet de stopper l'évolution des symptômes associés à la maladie et d'en empêcher l'apparition d'autres.

Nous avons en effet appris que le syndrome de Marfan, en plus du cœur, peut toucher les yeux, la peau, les articulations, les os... Heureusement ce petit médicament permet de soigner les différentes atteintes de syndrome. Enfin, il a vérifié nos génomes dans une base de données génomique internationale, et s'est aperçu que le mien présentait la même anomalie.

Il m'a conseillé de prendre rendez-vous avec la Consultation Marfan, pour que je me sois également prise en charge. Quelle chance immense de pouvoir bénéficier des avancées de la recherche !

Et si en 2035, grâce à vous, ce récit devenait une réalité ?

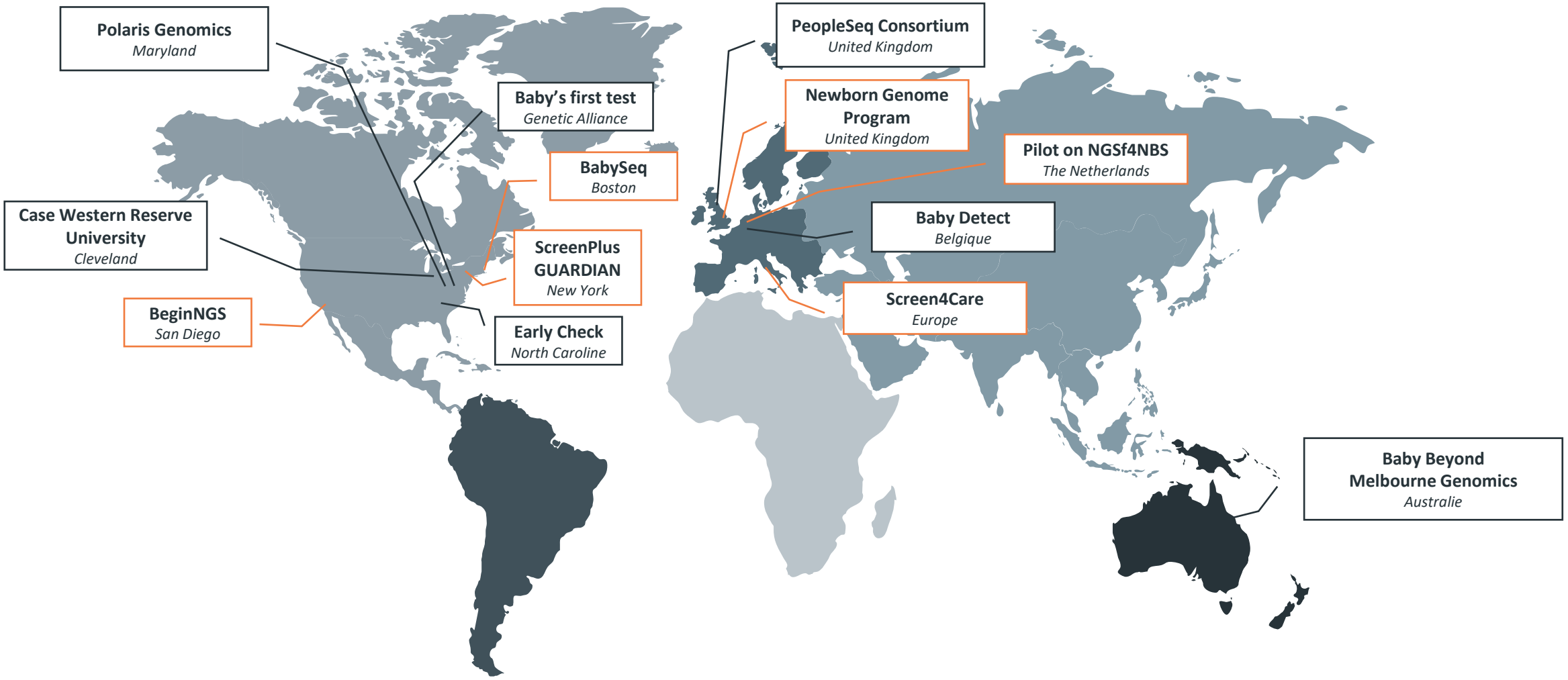
International Journal of *Neonatal Screening*
MDPI

Article

Parental Depression and Anxiety Associated with Newborn Bloodspot Screening for Rare and Variable-Onset Disorders

Natalie A. Boychuk [1], Niamh S. Mulrooney [1], Nicole R. Kelly [1], Aaron J. Goldenberg [2], Ellen J. Silver [1] and Melissa P. Wasserstein [1,*]

Advances in neonatal screening: Introduction



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Advances in neonatal screening: Introduction

Save the Date

ICoNS'23 Annual Meeting – 5 - 6 oct. 2023
The Royal Institution, London, UK

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2.

- Topic 1 - Presentation of 2 European NGS pilot projects in Europe
  - The UK 100.000 genome project in newborn screening

  Dr. David Bick, Newborn Genomes Programs at Genomics England, London

The UK 100,000 genome project in newborn screening

ERN ITHACA Innovation in Newborn Screening across Europe

21 March 2023

David Bick, MD, Principal Clinician, Newborn Genomes Programme

About Genomics England

Two core, linked functions:

To support an evolution in genomic healthcare

To accelerate genomic research

To do this, we:

- **Work with the NHS** to deliver and improve testing that helps doctors diagnose, treat, and prevent illnesses like cancer and rare diseases.
- Provide the health data and advanced technology **researchers** need to:
  - Make medical discoveries
  - Develop effective, targeted medicines for patients and their families

Key to both these activities: **turning science into healthcare together**

Background

Newborn Genomes Programme

Starting point 2019…

Current UK NHS Newborn Blood Spot (NBS) Screening Programme

Newborns can currently be screened for **nine conditions** via a bloodspot test.

There is a 97% uptake of newborns screening in the UK.

> "There is a clear potential for genomics in the testing for many of the conditions currently included in the blood spot test."
>
> Generation Genome

- Sickle cell disease
- Cystic fibrosis
- Congenital hypothyroidism
- Phenylketonuria
- Medium-chain acyl-CoA dehydrogenase deficiency
- Maple syrup urine disease
- Glutaric aciduria type 1
- Homocystinuria

NHS screening currently **only looks for these conditions**, rather than screening the baby's genome. **We are testing a broader approach.**

Our research study's focus

Three parts | All subject to ethics committee approval

** **Key point:** not just **how** each might be implemented, but **whether** they should be implemented.**

01 Evaluating the utility and feasibility of **screening newborns for a larger number of childhood-onset rare genetic conditions** in the NHS using whole genome sequencing

02 Understanding **how babies' genomic data could be used for discovery research,** focusing on developing new treatments and diagnostics for NHS patients

03 Exploring the potential risks, benefits, and broader implications of **storing a baby's genome over their lifetime**

Key numbers

Research study beginning **in 2023**

2022 — **2023** — 2024 — 2025

Aiming to find the **9** children born each day in the UK with a rare, treatable genetic disease – where early intervention is crucial

Expecting 1,000 **positive results** during the study

To find these children, we'll analyse

100,000+

newborn genomes for a specific set of childhood-onset, actionable conditions

How we work

Core in-house team

Expert working groups established, focusing on:

- Conditions the research study should screen for
- Recruitment
- Ethics
- Evaluation
- Education and training

- **NHS Steering Group** – designed to support and develop the research study
- **NHS England Newborn Genomes Programme Clinical Assurance Group** to support our 'choosing conditions' work
- **Co-design** with parents and healthcare professionals
- **Engagement programme** to work with stakeholders – including members of the public
- **Participant panel**

’All in offer’

Parents will be asked to sign up to their use of their babies’ genome and to be able to link to clinical data to allow:

1. Return of actionable findings to newborns’ families
2. Research on newborn screening
3. Research on broader healthcare questions (within NGRL acceptable uses)
4. Recontact to request follow up data related to newborn screening research or to offer opportunities to participate in other studies.
    - If further studies are related to specific conditions, it would only be possible where the baby has been identified through the screening analysis or has a confirmed diagnosis for that condition.
5. Use of any of the baby’s leftover sample for further research

Potential samples

Heel prick into DBS

Heel prick into capillary tube

Saliva via sponge

Cord blood

Choosing disorders for screening and the Wilson and Jungner screening criteria – a starting point….

- The condition sought should be an important health problem
- The natural history of the condition, including development from latent to declared disease, should be adequately understood
- There should be a recognisable latent or early symptomatic stage
- There should be a suitable test or examination
- The test should be acceptable to the population
- There should be an agreed policy on whom to treat as patients
- There should be an accepted treatment for patients with recognised disease
- Facilities for diagnosis and treatment should be available
- The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in reaction to possible expenditure on medical care as a whole
- Case-finding should be a continuing process and not a “once and for all” project

Conditions Framework workgroup results

- The working group established **four core principles** which each screened-for condition should meet
- The pilot will only screen for a **specific set of conditions, genes, and variants**

Four core principles

A

There is strong evidence that the genetic variant(s) causes the condition and can be reliably detected.

Where appropriate, there may be a confirmatory test that can establish whether the child has the condition.

B

A high proportion of individuals who have the genetic variant(s) would be expected to have symptoms that would have a debilitating impact on quality of life if left undiagnosed.

C

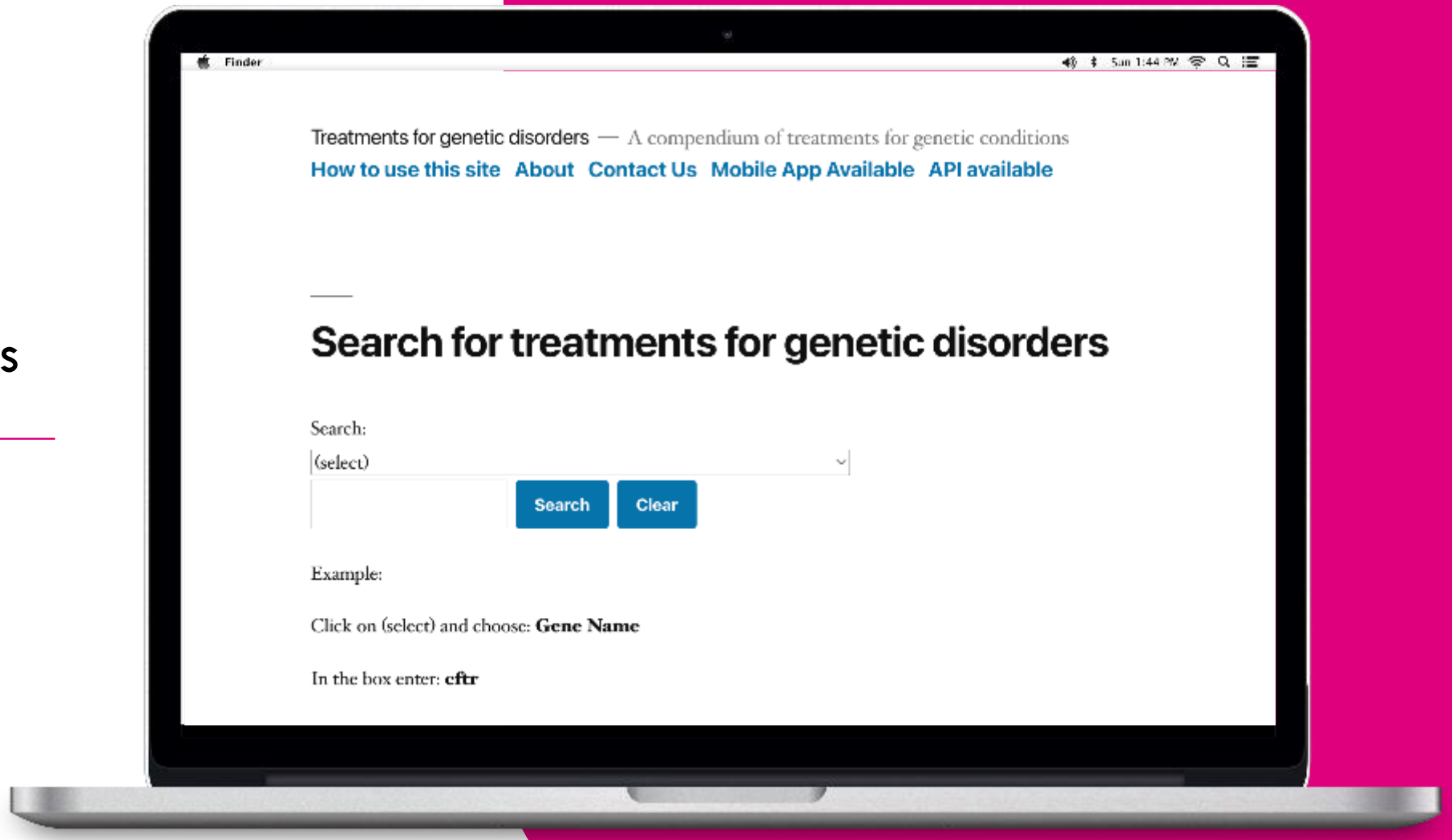
Early or pre-symptomatic intervention for the condition has been shown to lead to substantially improved outcomes in children, compared to intervention after the onset of symptoms.

D

Conditions screened for are only those for which the interventions are equitably accessible for all.

Website with information about treatable disorders

Rx-genes.com



An online compendium of treatable genetic disorders.

Bick D, Bick SL, Dimmock DP, Fowler TA, Caulfield MJ, Scott RH.
Am J Med Genet C Semin Med Genet. 2021 Mar;187(1):48-54.

Program will only include variants with high positive predictive value

Positive predictive value = (sensitivity x prevalence) / [(sensitivity x prevalence) + ((1 – specificity) x (1 – prevalence))]

Example disease

1 in 10,000 live births
Variant with sensitive 99.5% & specific 99.5% = 2% PPV
98 out of 100 times this is a FALSE POSITIVE!

Only pathogenic and like pathogenic variants will be reported

https://www.sciencedirect.com/science/article/pii/S1525157820300386

Care and treatment pathways

"Considering existing pressures in healthcare, the programme must understand the services and resources required to support children and families, and education and training needs for the workforce to provide high quality care."

* The above steps may not be needed for each condition, and the order of those steps may vary

Although the total number of screen-positive babies in the lifetime of the research study is expected to be 500 - 1,000. Each baby needs a structured care and treatment pathway in place before we begin.

Newborn Genomic Screening is starting worldwide

United States

BabySeq2 at Harvard – Massachusetts

BeginNGS at Rady Children's Hosp. - California

Newborn study at Columbia U – New York

ScreenPlus at Albert Einstein – New York

Newborn study at Geisinger – Pennsylvania

EarlyCheck2 at University of North Carolina - North Carolina

Perkin-Elmer – Commercial laboratory

Middle East

Newborn study – Qatar

Europe

Screen4Care – Consortium

Baby Detect – Belgium

Newborn Genomes Programme – England

Netherlands

Asia

Australia

Murdoch Children's Research Institute

University of Sydney

University of Adelaide

China

Newborn study at Children's Hospital of Zhejiang University

Newborn study at Beijing Children's Hospital

Newborn study by Beijing Genome Institute

Thank you

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www.genomicsengland.co.uk/newborns

@GenomicsEngland

The Genomics England newborns core team:

- **Nikki Agnes,** Delivery Manager
- **Dr David Bick,** Principal Clinician
- **David Bowen,** Enterprise Architect
- **James Calver,** Data Engineer
- **Katy D'Avella,** Content Designer
- **Dasha Deen,** Genome Data Scientist
- **Sally Donovan,** Delivery Manager
- **Ross Dudley,** Principal Service Designer
- **Frankie Edwards,** Senior Visual Communications Designer
- **Harriet Etheredge,** Ethics Lead
- **Mirabai Galati,** Design Researcher
- **Liz Gardner,** Mobilisation Operations Lead
- **Kate Harvey,** Engagement Manager
- **Edyta Jaworek,** Product Designer
- **Mathilde Leblond,** Senior Design Researcher
- **Alexandra Margarint,** Software Engineer
- **Christella Matoko,** Delivery Manager
- **Anna Need,** Senior Product Manager
- **David Phelan,** Delivery Manager
- **Amanda Pichini,** Clinical Lead for Genetic Counselling
- **Jonathan Roberts,** Clinical Content Developer
- **Tim Rogers,** Delivery Manager
- **Eni Rume,** Delivery Manager
- **Dr Richard Scott,** Chief Medical Officer
- **Sally Shillaker,** Clinical Content Developer
- **Katrina Stone,** Clinical Fellow in Genomics
- **Alice Tuff-Lacey,** Programme Lead
- **Chantal Wood,** Programme Manager
- **Joanna Ziff,** Delivery Manager

A long list of issues to resolve……

- How will we find enough positives for rare disorders to give evidence for/against adding a gene to newborn screening?
- Do we understand penetrance and expressivity of variants found in an asymptomatic newborn?
- Will we reanalyze genome if child develops a phenotype suggesting a genetic disorder?
- How long will families be followed to look for false negatives and study outcome of positives?
- Will genetic disorders where there is a clinical trial available in the UK be included?
- How will we handle an incidental finding? Example finding a hemizygous variant in treatable X-linked disorder a female which would suggest Turner syndrome.
- How will we ensure minority communities are well represented in the study?
- Will genes and variants be added during the program?

3.

- Topic 1 - Presentation of 2 European NGS pilot projects in Europe
  - The Netherland pilot NGS extended newborn screening,

A perspective on a molecular approach on newborn screening in the Netherlands

Dr. Marcel Nelen, Genome Diagnostics Center UMC, Utrecht (Netherlands)

A perspective on a molecular approach on newborn screening in the Netherlands

funded by ZonMW

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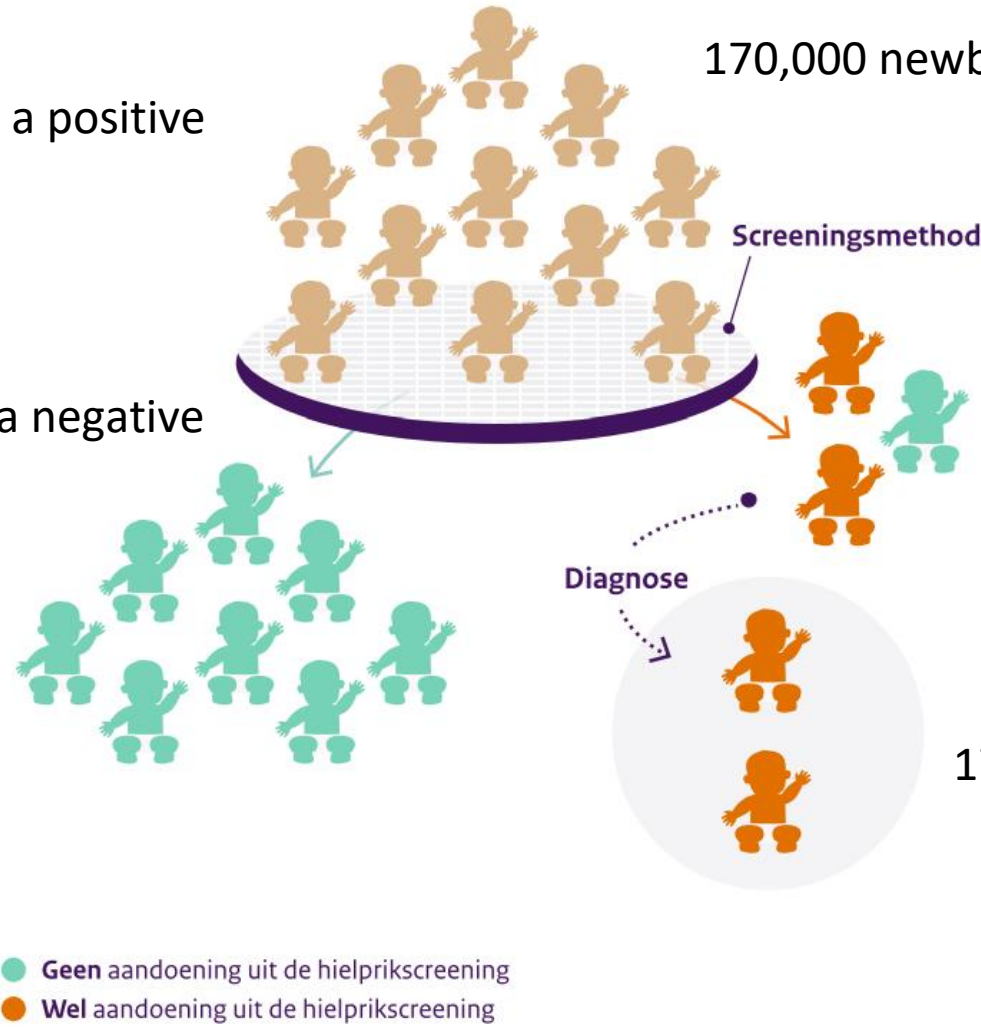
Radboudumc

The current heelstick works well

Sensitivity:
Affected with a positive test result
= 99%

Specificity:
Healthy with a negative test results
= 99.854%



170,000 newborns each year per jaar (>99%)

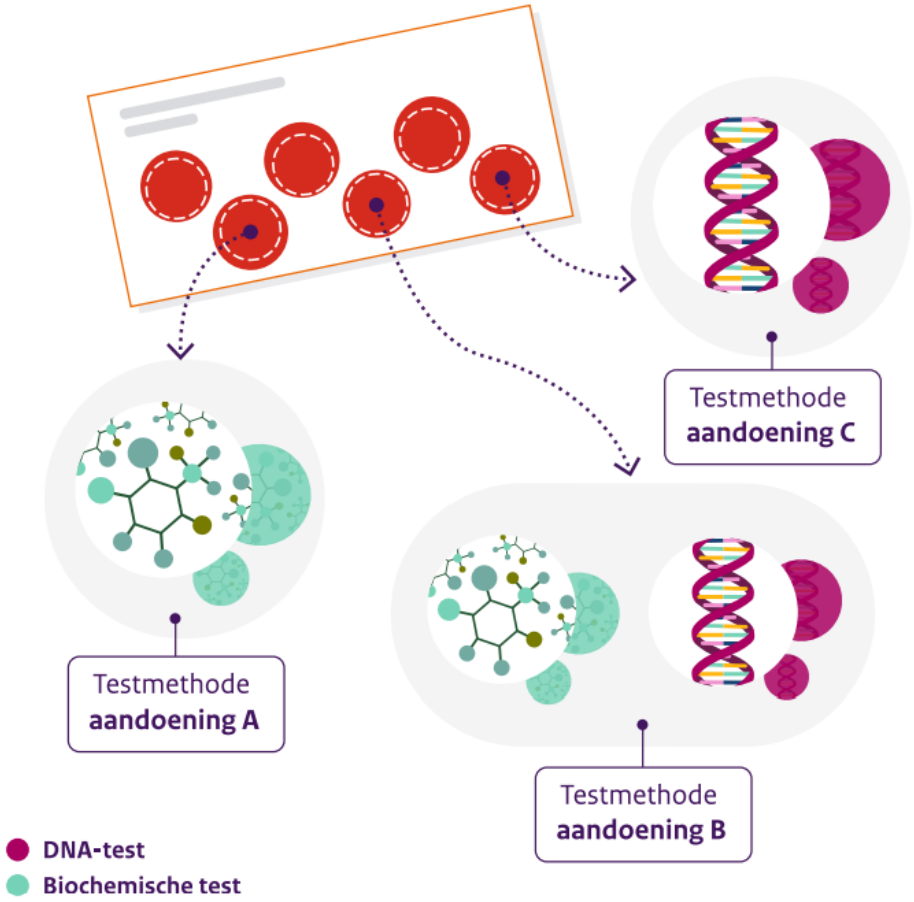
450 kids are referred

Positive predictive value:
Kids with a positive test result that are afected = 42%

175 kids get a diagnose

What does NGS add or improve?

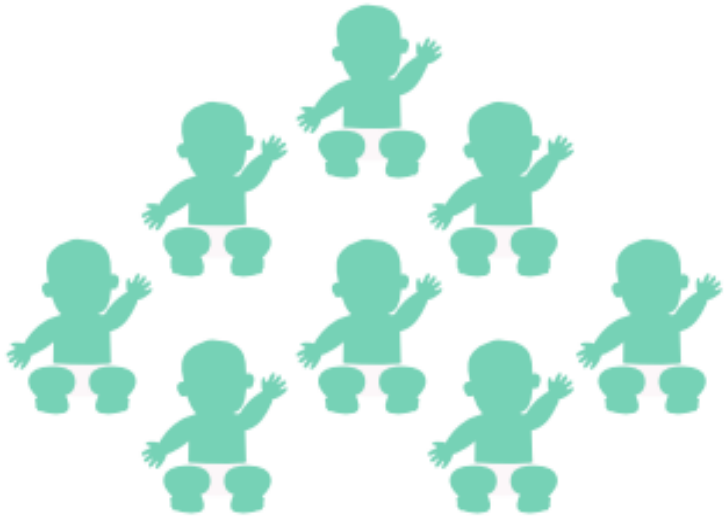
1) Diseases without markers in bloodspots can not be tested



2) DNA can replace multiple biochemical tests with one method

3) DNA can clarify unclear biochemical results

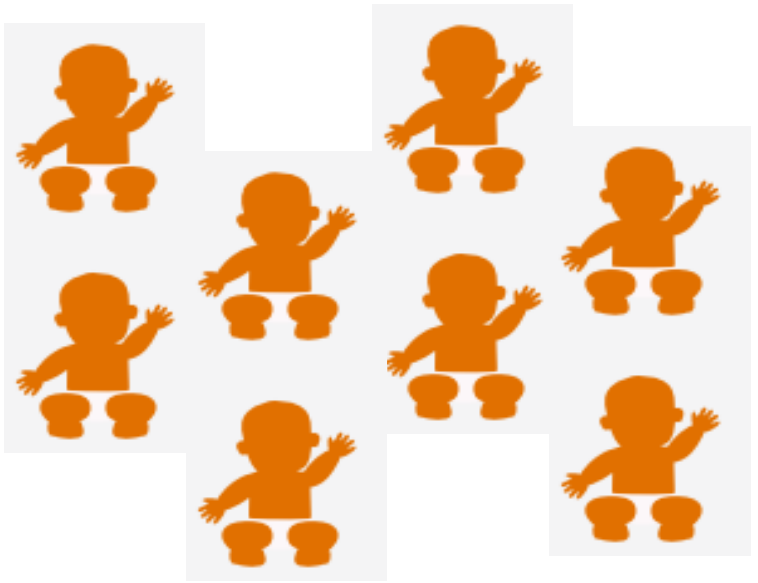
The datasets



healthy kids

~5000 healthy parents
= background population

~50 healthy individuals
= negative bloodspots



Affected kids

50 Affected kids
= positive bloodspots

Genes included

100 genes related to IEM

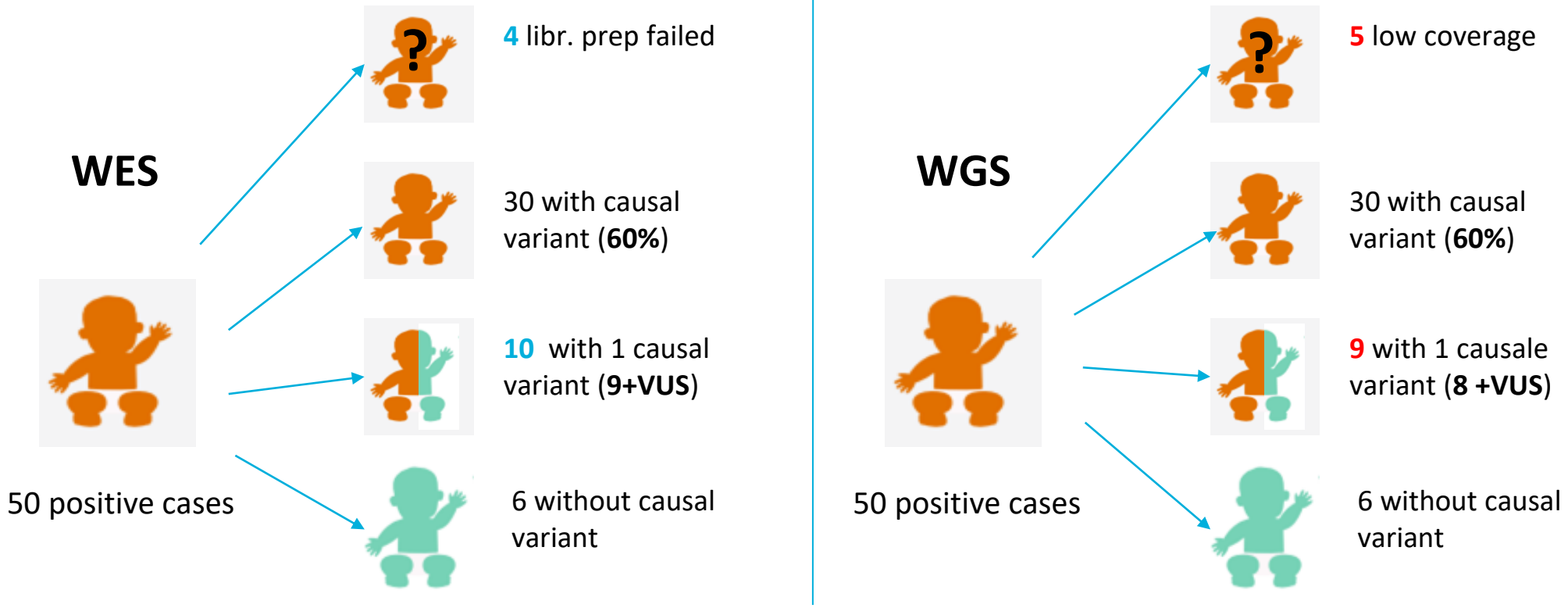
77 genes included not in the current heelstick criteria:

- **Treatebillity**
- Early-onset
- Symptoms

23 IEM genes in the current heelstick

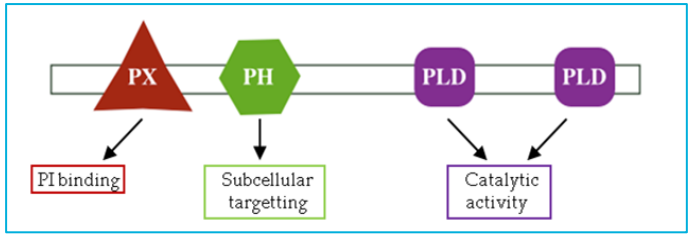
Aandoening	In hielprik sinds
Mucopolysaccharidosis type 1 (MPS I)	2021
Severe combined immunodeficiency (SCID)	2021
Galactokinase-deficiëntie (GALK)	2020
Propionacidemie (PA)	2019
Methylmalonacidemie (MMA)	2019
Carnitine-palmitoyltransferase-deficiëntie type 1 (CPT1)	2019
Alfa-thalassemie	2017
Bèta-thalassemie	2017
Taaislijmziekte of cystic fibrosis (CF)	2011
Sikkelcelziekte (SZ)	2007
Biotinidase-deficiëntie (BIO)	2007
Klassieke galactosemie (GAL)	2007
Medium-chain-acyl-CoA-dehydrogenase-deficiëntie (MCADD)	2007
Long-chain-hydroxyacyl-CoA-dehydrogenase-deficiëntie (LCHADD/MTPD)	2007
Very-long-chain-acylCoA-dehydrogenase-deficiëntie (VLCADD)	2007
3-methylcrotonyl-CoA-carboxylase-deficiëntie (3-MCCD)	2007
Glutaaracidurie type 1 (GA-1)	2007
HMG-CoA-lyase-deficiëntie (HMG)	2007
Isovaleriaan-acidurie (IVA)	2007
Maple syrup urine disease (MSUD)	2007
Multiple-CoA-carboxylase-deficiëntie (MCD)	2007
Tyrosinemie type 1 (TYR-1)	2007
Adrenogenitaal syndroom (AGS)	2000
Congenitale hypothyreoïdie (CH)	1981
Fenylketonurie (PKU)	1974

Results: positive bloodspots

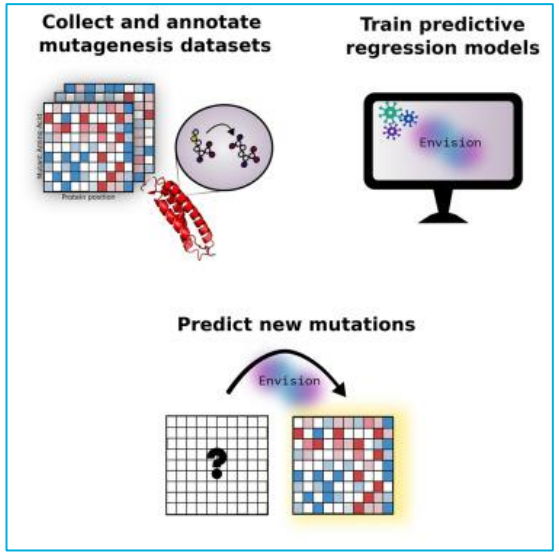


6 without causal variant: 3 homozygous (1 VUS, 1 in 5' UTR, 1 outside splice filter), 1 heterozygous (in 5' UTR), 2 sampling mistakes?

Variants are manally checked

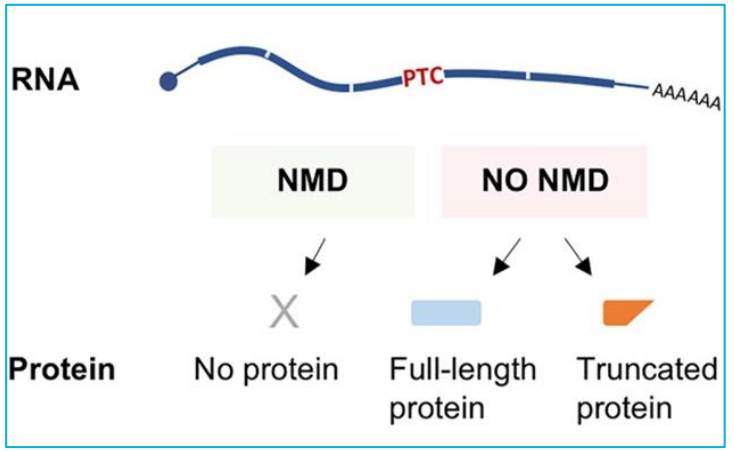


Is the inframe insertion/deletion in a proteindomain?



a damaging effect predicted in Alamut?

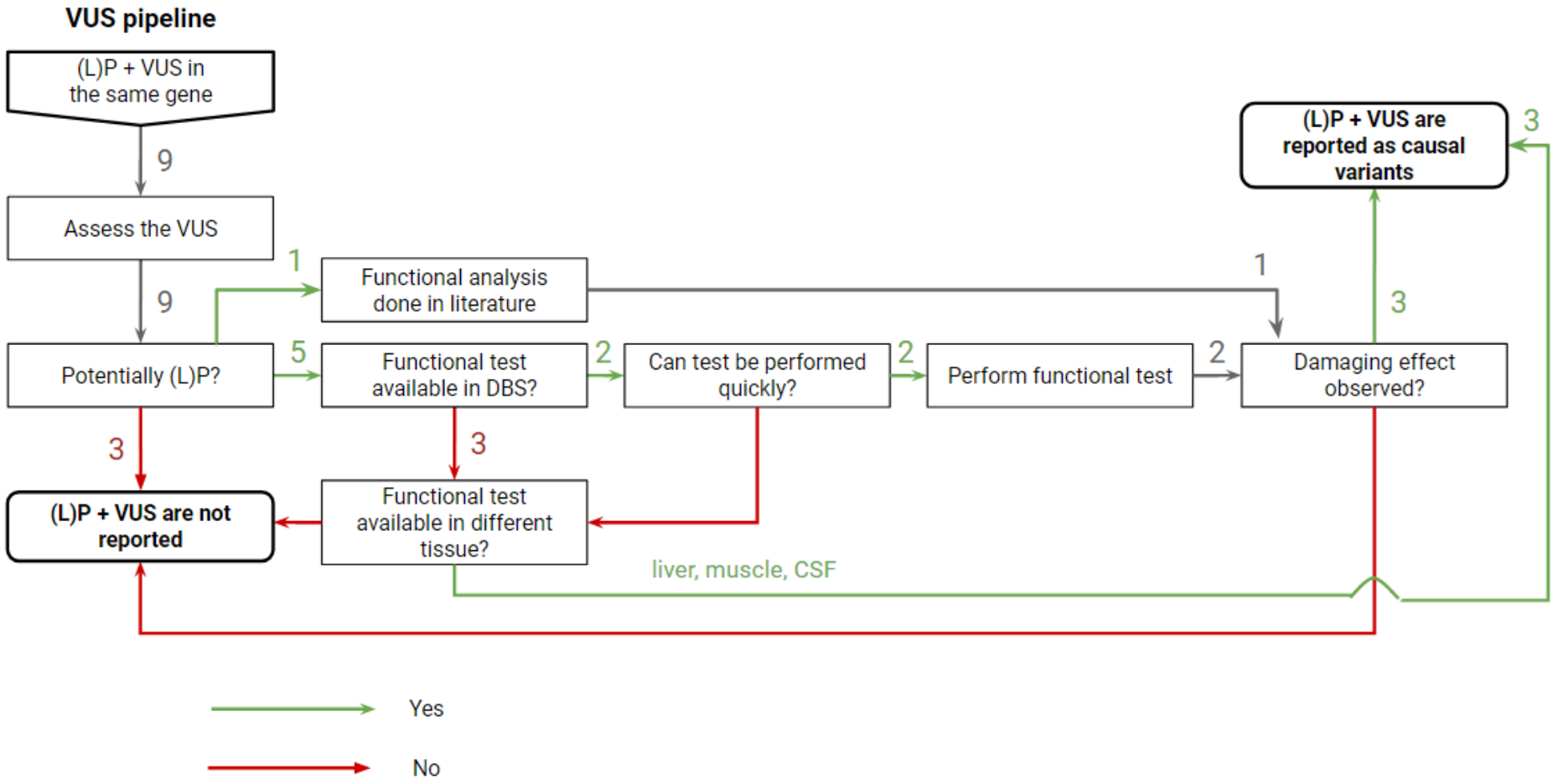
- Missense
- Splicing



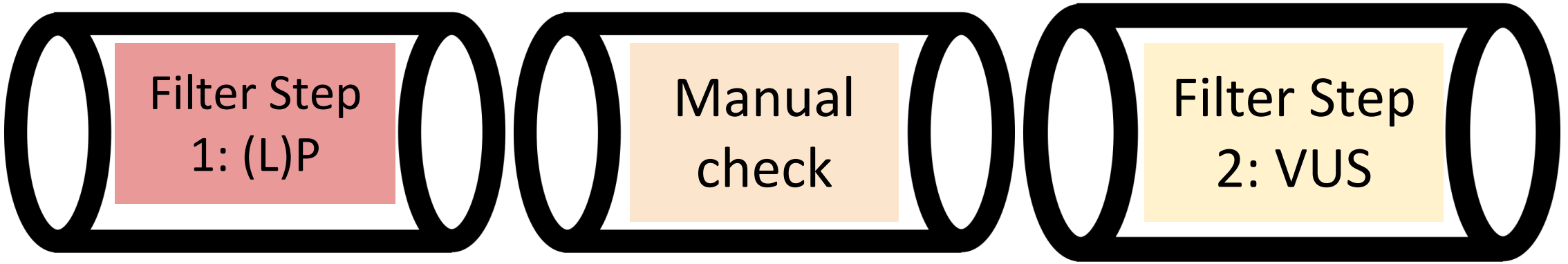
Is NMD used?

Is there *in vitro* functional prove?

Is a VUS pipeline useful?



Do we identify all positive cases?



31/50 positive results

- 30 kids with causal variants
- 1 carrier identified

+6/10 positive results

- 6 samples need resequencing
- 4 samples “missed”:
  - VUS in database
  - outside coding/splicing
  - Not truncating or pathogenic in database

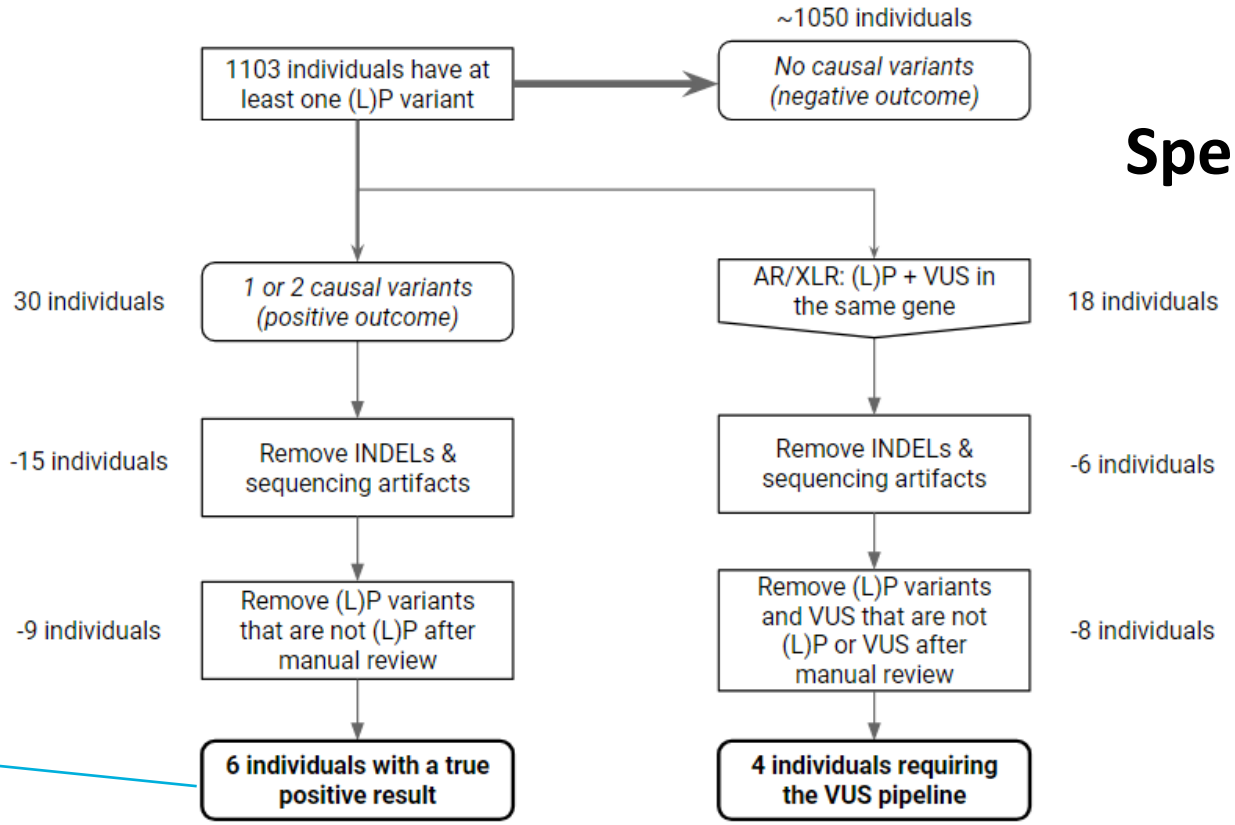
+6/9 positive results

3 “missed” samples with a VUS:

- benign prediction for two missense mutaties
- aminoacid deletion outside a protein domain

43 positive results, 6 “missed”

False positives in ~5000 healthy parent dataset



Specificity = 99.854%

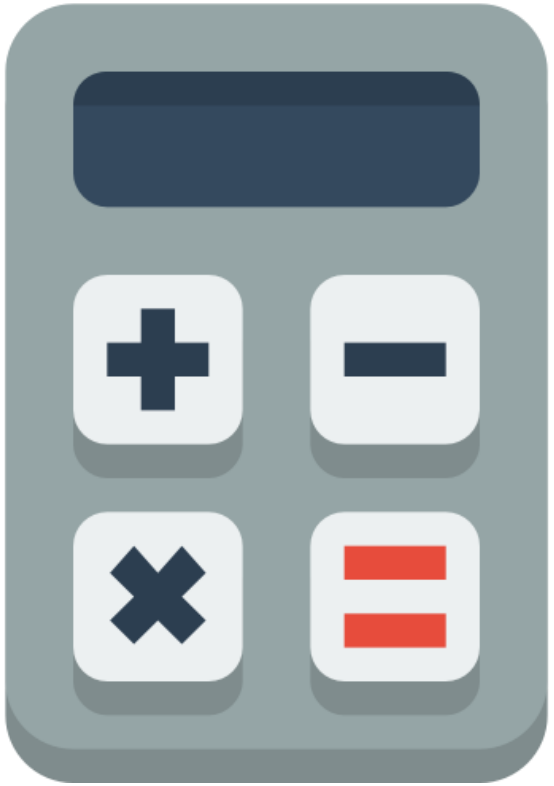
1 in ~830 kids ‘false-positive’

Results

3 false-positives from the 5000 cases dataset would have an IEM in the current NBS-diseases (0.06%)

66 cases are identified as false-positive for IEM within the current NBS-program (0.04%)

First-tier NBS with WES / WGS does not lead to more false-positives. However, it does have the risk of missing an IEM in the current NBS



Of the 7 “missed” cases, 3 diseases are found with the current heel prick program

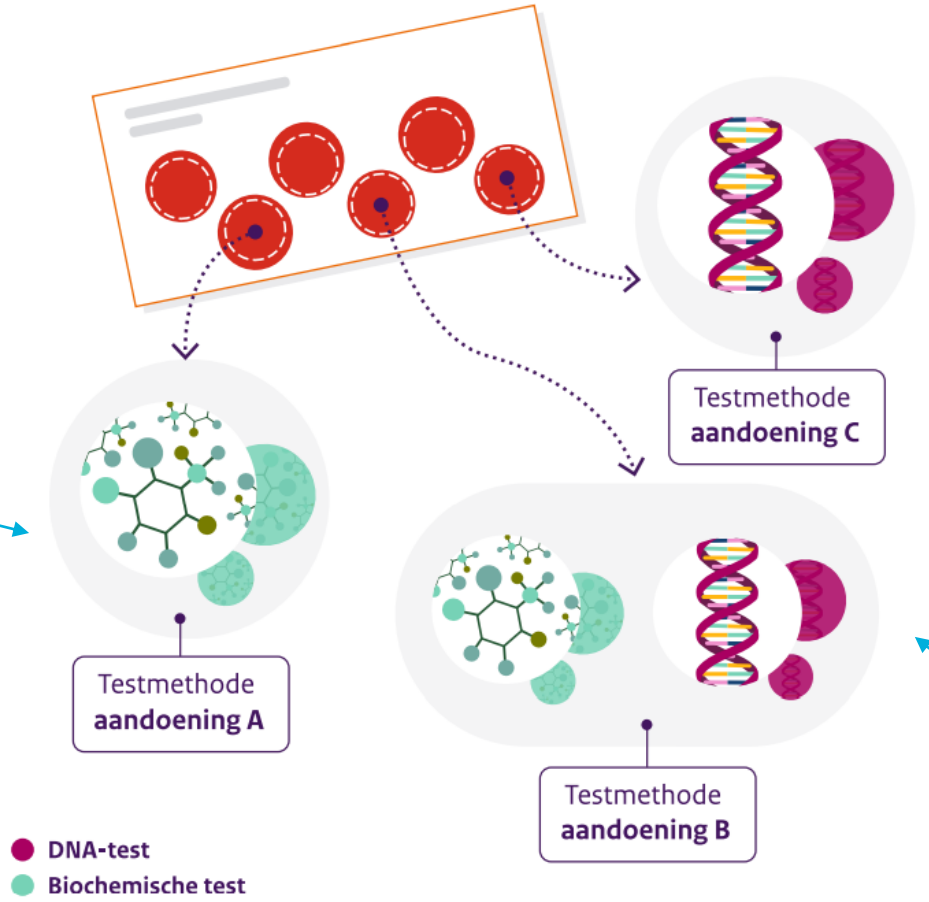
Of the 3 “missed” diseases, 2 diseases have low PPV: 6% and 23%

No false positives were found for these diseases in the 5000 parents dataset

Second-tier WES / WGS may improve the PPV for diseases in the current heel prick

Conclusion

For conditions with a well validated biochemical test, adding NGS is not necessary



For conditions without a biochemical marker, NGS has impact and can make an important contribution

For conditions with many unclear biochemical data, results can improve with NGS as a second-tier strategy

4.

- Topic 2 -Presentation of the newborn screening axis of the Screen4Care project
  - Pr. Alessandra Ferlini, Medical Genetics Unit, S.Anna University Hospital, Ferrara (Italy)

SCREEN 4CARE

Shortening the path to rare disease diagnosis by using newborn genetic screening and digital technologies

Alessandra Ferlini, MD-PhD
S4C Scientific Coordinator
Associate Professor in Medical Genetics
Head of the Medical Genetics Unit
University of Ferrara (UNIFE, Italy)

Nicolas Garnier, PhD
S4C Consortium Lead
Head of Patient Advocacy
Oncology & Rare Disease
Pfizer Global Product Development

Università degli Studi di Ferrara

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101034427.
The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

SCREEN 4CARE

Accelerating Diagnosis for Rare Disease Patients Through Genetic Newborn Screening and Artificial Intelligence

START DATE
1 OCTOBER 2021

DURATION
5 YEARS

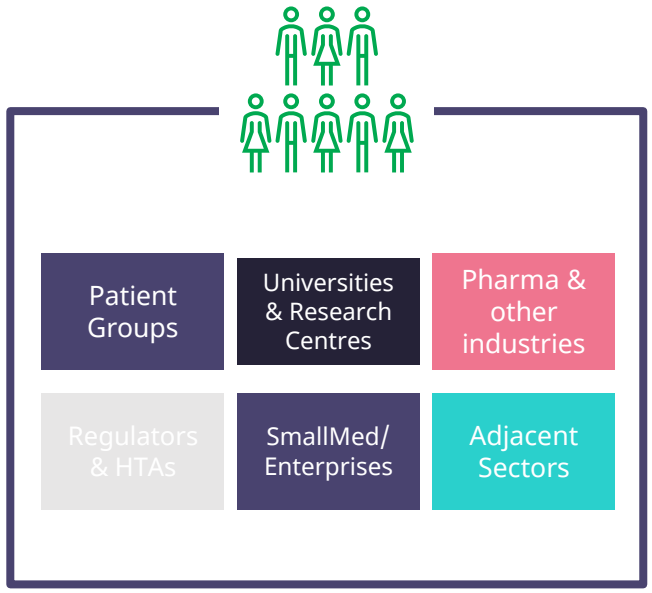
BUDGET
25 MIO €

14 COUNTRIES
35 PARTNERS

Public-Private Partnerships via the Innovative Medicines Initiative (IMI)

IMI brings over a decade of successful pre-competitive public-private partnerships (PPPs) in the life sciences, jointly funded by the European Union and European pharmaceutical industry

The partnership works to improve health by speeding up development and access to innovative medicines



Supports collaboration between the key players involved in health research from public and private sectors

Significant outputs from research and innovation that benefit from greater co-ordination and knowledge sharing

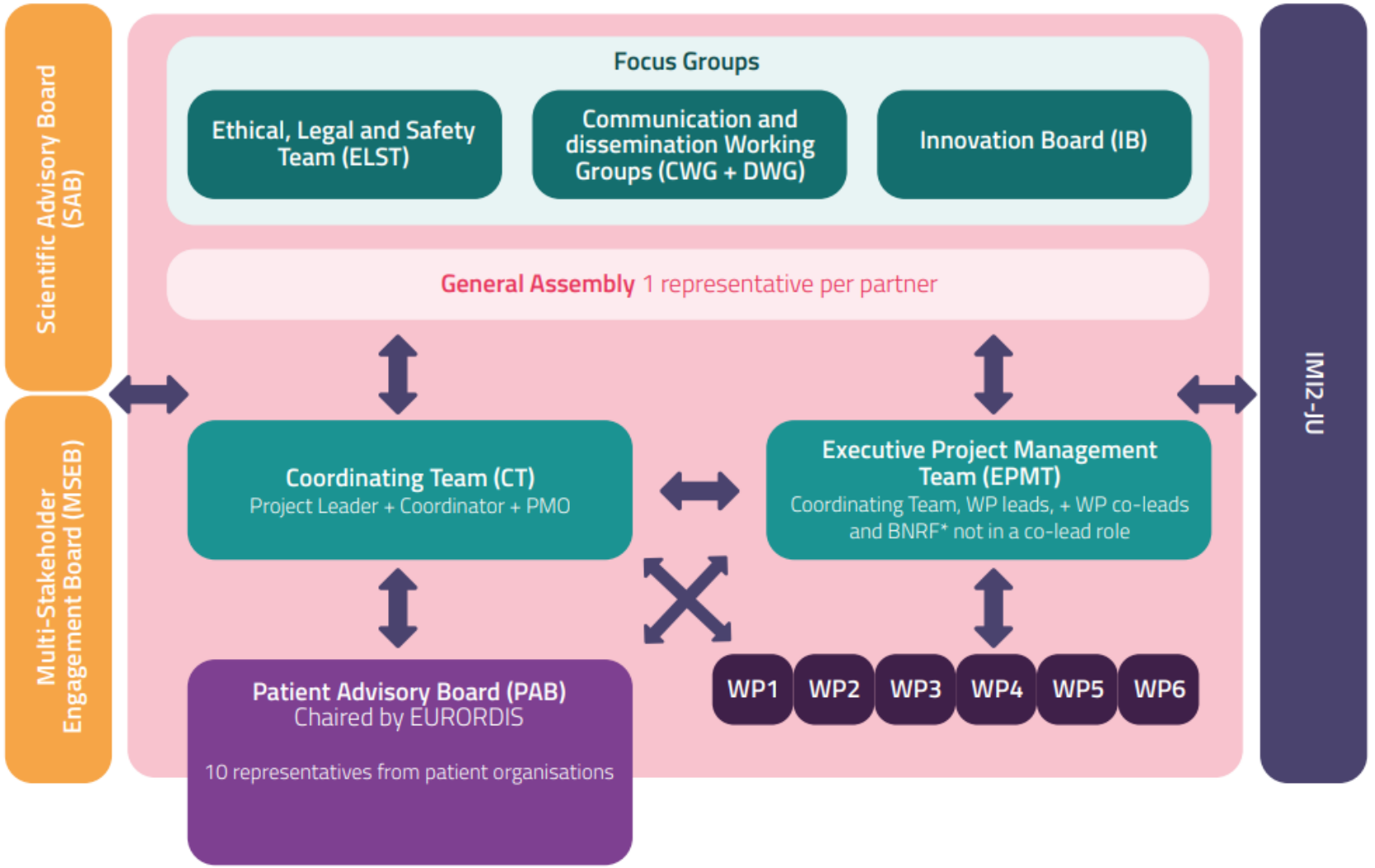
IMI projects receive funding from the Innovative Medicines Initiative Joint Undertaking (JU). The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

The Screen4Care Consortium

We are a fully integrated PPPP, aligned towards common goals and around shared deliverables

30.03.2023

S4C Governance



S4C VISION is to improve the lives of RD patients by 3 pillar aims:

1. **Federate the complex RD diagnosis / NBS EU ecosystem**

2. **Champion a sustainable genetic NBS framework for RD early diagnosis**

3. **Improve accuracy & speed of patient diagnosis using innovative digital tools**

6 interconnected work packages (WPs)

Multistakeholders, multidisciplinary boards, including Patient Organization, academia, SMEs, Public Health Decision Makers, Regulators, health technology assessment experts

WP1 - Understanding the business and regulatory framework for rare disease screening in Europe

Leaders: UBERN, Pfizer

1 Legal Readiness

- Data protection Impact Assessment
- Code of ethics
- Guidelines for device/in-vitro device regulation (CE)
- Business models
- Reimbursement environment

2 Data Readiness

- Ongoing RD initiatives in Europe
- Available data
- Accessibility and data readiness

3 Stakeholder engagement

- Patient and expert involvement
- Strategic recommendations

WP2 – Federated Machine Learning

WP3/4 – NBS & EHR screening

WP5 – Meta Symptom Checker and related apps

WP2 - Federated Metadata Repository and Machine Learning for Rare Diseases
Leaders: SDU, PFIZER

1 Federated Metadata Repository & ML

- Unified interface to RD data sources
- Ensures data becomes findable and useable
- Federated Algorithms allow training without transmitting data

2 Standardized Common Data Model

- Ensures interoperability and translation
- Based on established Standards to minimize translation effort
- Strong support through the CORD-MII network

3 Co-Creation and Adoptability

- Patient and expert involvement through co-creators
- Establishment of the ideal information flow
- Identification of adaptability risks

WP4 – EHR algorithms

WP5 – Meta Symptom Checker and related apps

WP3 – Innovative RDs gene-panels and WGS approach for genetic NBS
Leaders: UKB, SANOFI

Explore genetic testing methodologies to improve diagnostic yield in newborns and early symptomatic infants

1. **Stakeholder preference assessment on genetic NBS**
2. **Select treatable and actionable diseases for NBS**
3. **Pilot genetic NBS in 18.000 infants with follow-up**
4. **Explore WGS for early symptomatic followed upt infants**
5. **Evaluate impact of NBS on exposed families**
6. **Evaluate cost-effectiveness of genetic NBS for RDs**

Provide recommendations for genetic NBS of RDs

WP4 – Develop and repurpose pre-existing ML-algorithm to detect patients at risk having RD within EHRs
Leaders: UMG, PFIZER

WP1 – Framework readiness

WP2 – Federated Machine Learning/Ensuring interoperability

1 Algorithms

- Feasibility evaluations to ensure the data quality and plausibility of the utilization processes
- Repurpose algorithm
- Development and evaluation of different federated ML methods
- Evidenced- and feature-based approach

2 Pilot EHR/Effect on pilot participants

- 2 principles for EHR-based diagnosis: (i) defined disease selection (red flag RD), (ii) syndrome/ phenotype-based diagnosis group (proximal muscle weakness)
- Diagnostic follow-up
- Ethical assessment and preferences on pilot
- HTA model

3 Deep phenotyping

- MSOT-Imaging trial
- Ex vivo muscle imaging by multiphoton microscopy and X-ray phase-contrast tomography

WP2

WP5 – Meta Symptom Checker and related apps

WP5-Transfer of Technologies, Outreach and Public Discourse UCD, PFIZER

WP1 – Framework readiness

WP2 – Federated Machine Learning/Ensuring interoperability

1 Algorithm development

- CodeZebra development further expanding the deliverables of WP4
- Algorithm testing with regard to Symptom checkers
- Refinement of Needs for Meta Symptom checker

2 Meta Symptom Checker

- Patient and Physician facing Meta-Symptom Checker for prioritized RDs (incl optimization based on WP4 outputs)
- Building on results of Horizon scan of existing symptom checkers
- Open source Meta checker development linking to Efpia partner checkers in use

3 Patient-facing virtual clinics and apps

- Flexible open source tools development to address the needs of patients, families and clinicians
- Deep expertise from Eurordis informing the patient journeys
- Prototype of patient-facing and physician-facing S4C Platform co-designed with EURORDIS and physicians in the consortium

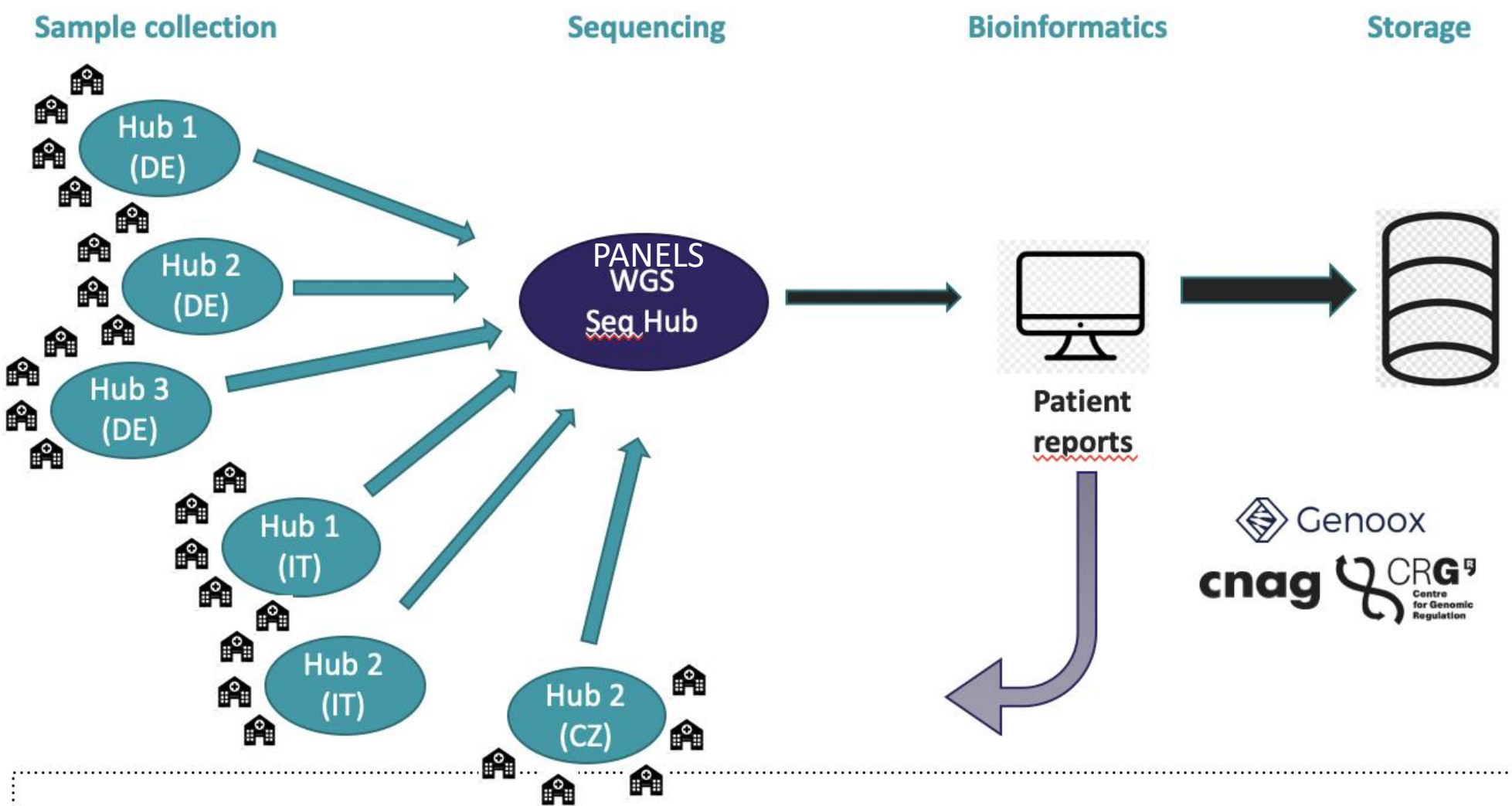
WP6 Dissemination

WP5 – Meta Symptom Checker and related apps

WP 3 S4C SCHEDULED CLINICAL STUDIES

1. Preference studies on NBS
2. ACT panel survey
3. Newborn screening pilot study for TREATable Rare Diseases
4. Newborn screening pilot study for ACTionable Rare Diseases
5. Early symptomatic whole genome sequence screening

S4C GENETIC NBS and WGS FLOWCHART



The voice of the Patient is embedded at the heart of S4C

TRANSVERSAL

PATIENT ADVISORY BOARD:
Provide strategic recommendations, guide and advise across Screen4Care activities

1 Analysis and co-creating environment (Pillar 1)

- Landscape analysis & access to resources/databases
- Contribute to development of Code of Ethics for data sharing & access
- Contribute to analysis of HTA env. for ML-based technologies

2 Genetic NBS (Pillar 3)

- Contribute to stakeholder preference assessment
- Definition & selection of Actionable RDs
- Contribute to recommendations
- Input into other needs/consultations

3 Meta Symptom Checker and Patient-facing S4C platform/app (Pillar 5)

- Patient preferences, patient journeys
- Co-design the patient facing Meta-Symptom Checker for prioritized RDs
- Co-design the S4C platform/app
- Pilot testing
- Targeted campaign/outreach

European Patient Advocacy Groups (ERNs)
National Alliances
European RD Federations Disease-specific RD PAO

Multi-stakeholder NBS Working group driven by patients
Rare Barometer survey program bringing lay patients' perspectives

Digital & Data Advisory Group
Rare Barometer survey program

SPECIFIC & INTEGRATED

S4C IMPACT ON Rare Diseases Diagnosis

Birth

- Sustainable strategy for newborn genetic screening

Early Onset

- AI algorithm to "flag" Patients with better known Rare Disease in EHR

HCP Cycling

- AI "digital clinical symptom checker"

Strategic landscape analysis of converging initiatives / platforms & RD data sources

- new diagnostic tools
- Genetic NBS strategies
- Ethical issues addressed

- RD phenotype recognition
- HER harmonization

- Novel digital tools to better address all RD stakeholders toward an appropriate diagnostic path

- **S4C can prime up further collaboration about RD based on genomic medicine and bioinformatics approaches**

ICoNS international consortium

Ongoing gNBS initiatives worldwide:

BabySeq (Robert Green) USA
Baby Beyond (Lilian Downie) Australia
Early Check (Don Bailey) USA, North Carolina
Screen4Care (Alessandra Ferlini & Nicolas Garnier) EU
Genomics England (David Bick) UK
ScreenPlus (Melissa Wasserstein) USA Einstein College
BeginNGS (Stephen Kingsmore) USA, SanDiego
GUARDIAN (Wendy Chung) USA NY

And others…

Follow #screen4care

- https://www.screen4care.eu/
- https://twitter.com/screen4care
- https://www.linkedin.com/company/screen4care/

For questions:

- Nicolas.Garnier@pfizer.com
- screen4care@unife.it

Discussion time

5.

Topic 3 - The Eurordis position statement harmonized newborn screening

- Gulcin Gumus, Research & Policy Project Manager, EURORDIS, Barcelone (France)

Newborn Screening: Harmonising approaches to NBS in EU

Gulcin Gumus, PhD
Research and Policy Senior Manager
EURORDIS

21 March 2023

Our mission

EURORDIS works across borders and diseases to improve the lives of people living with a rare disease

1028
Member patient organisations

74 countries (28 EU countries)

44 National Alliances of rare disease patient organisations

Founded in
1997

Outreach to over
2,500
patient groups

72 European Federations for specific rare diseases

40+
Staff members with offices in Paris, Brussels and Barcelona

Over
440
volunteers

Why is Newborn Screening a priority for EURORDIS?

- Most of the screened diseases are rare diseases.
- Early intervention can prevent the onset of disease symptoms or delay disease progression, improving the quality of life of the newborn, deriving a benefit for the patients, their families and the society.
- Currently there is no consensus on equal access and availability of screening programmes in Europe

*"If you have a rare disease, **your chances of being diagnosed often depend on where you are born**. This is why I am part of the EURORDIS Newborn Screening Working Group. I want to contribute to improving newborn screening programmes and earlier, accurate diagnosis of rare diseases. "*

Eduardo Lopez - President of Lysosomal Acid Lipase Deficiency Patient Organization (AELALD)

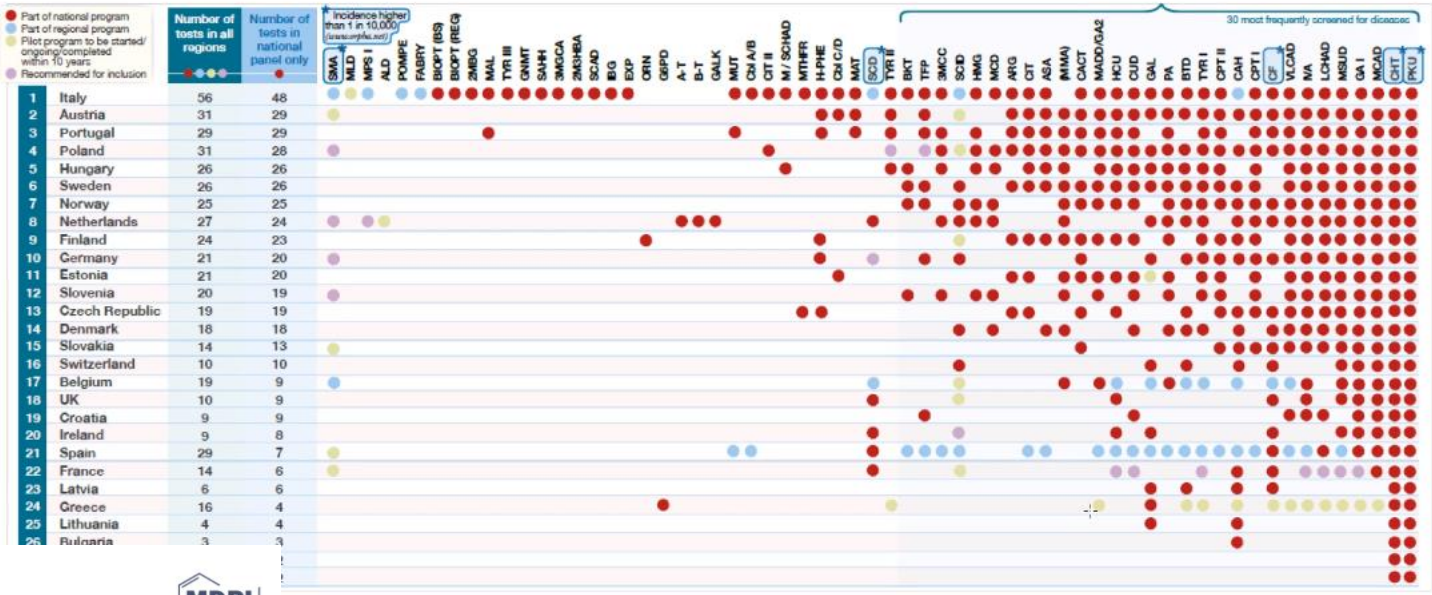
The NBS Landscape

Which specific diseases are being screened

Country data

Developments in the programmes

A matrix comparing the current state of NBS panels across Europe has been developed to highlight important disparities in screening



International Journal of *Neonatal Screening*

MDPI

Article

Neonatal Screening in Europe Revisited: An ISNS Perspective on the Current State and Developments Since 2010

J. Gerard Loeber [1,*], Dimitris Platis [2], Rolf H. Zetterström [3], Shlomo Almashanu [4], François Boemer [5], James R. Bonham [6], Patricia Borde [7], Ian Brincat [8], David Cheillan [9], Eugenie Dekkers [10], Dobry Dimitrov [11], Ralph Fingerhut [12], Leifur Franzson [13], Urh Groselj [14], David Hougaard [15], Maria Knapkova [16], Mirjana Kocova [17], Vjosa Kotori [18], Viktor Kozich [19], Anastasiia Kremezna [20], Riikka Kurkijärvi [21], Giancarlo La Marca [22], Ruth Mikelsaar [23], Tatjana Milenkovic [24], Vyacheslav Mitkin [25], Florentina Moldovanu [26], Uta Ceglarek [27], Loretta O'Grady [28], Mariusz Oltarzewski [29], Rolf D. Pettersen [30], Danijela Ramadza [31], Damilya Salimbayeva [32], Mira Samardzic [33], Markhabo Shamsiddinova [34], Jurgita Songailiené [35], Ildiko Szatmari [36], Nazi Tabatadze [37], Basak Tezel [38], Alma Toromanovic [39], Irina Tovmasyan [40], Natalia Usurelu [41], Parsla Vevere [42], Laura Vilarinho [43], Marios Vogazianos [44], Raquel Yahyaoui [45], Maximilian Zeyda [46] and Peter C. J. I. Schielen [1]

Current Status of Newborn Screening in Southeastern Europe

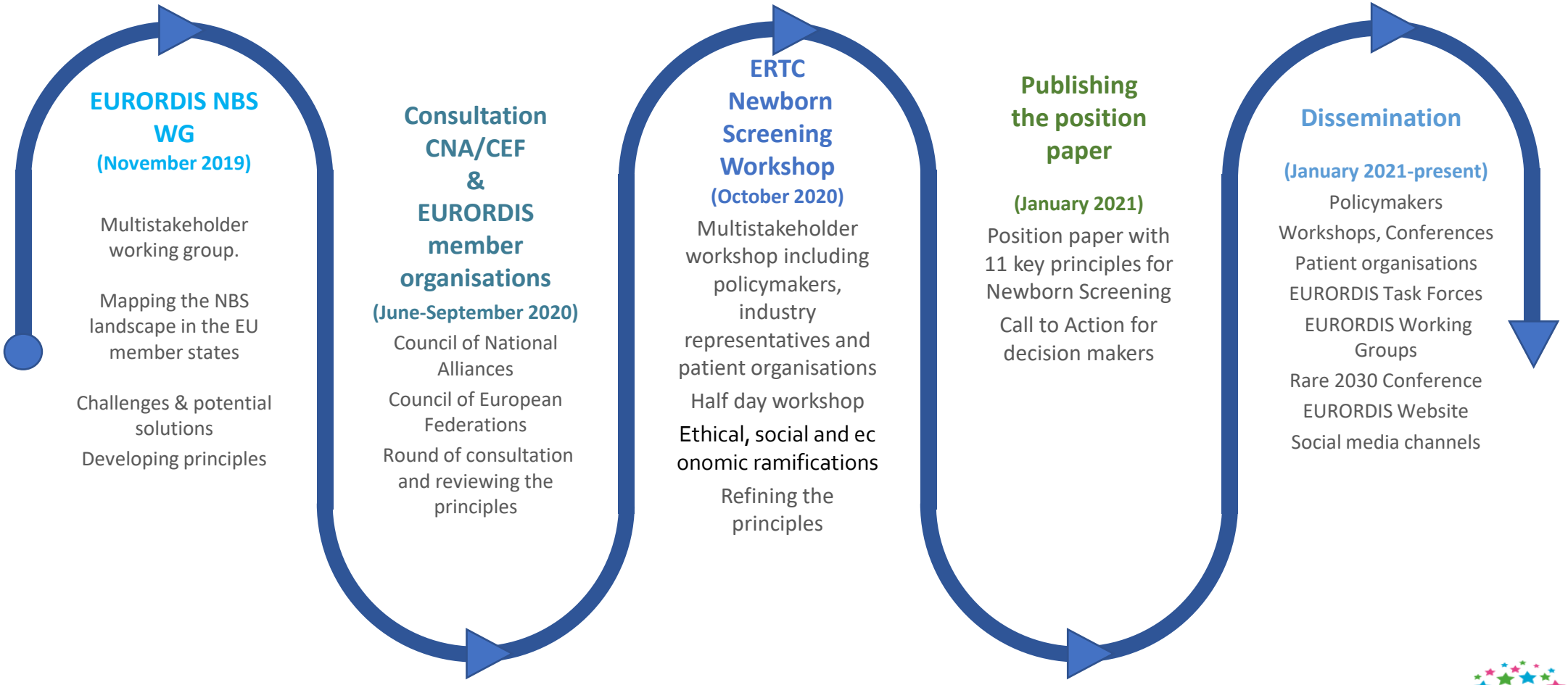
Vanesa Koracin[1], Matej Mlinaric[2], Ivo Baric[3], Ian Brincat[4], Maja Djordjevic[5], Ana Drole Torkar[2,6], Ksenija Fumic[7], Mirjana Kocova[8], Tatjana Milenkovic[9], Florentina Moldovanu[10], Vjosa Mulliqi Kotori[11], Michaela Iuliana Nanu[10], Ziga Iztok Remec[12], Barbka Repic Lampret[6,12], Dimitrios Platis[13], Alexey Savov[14], Mira Samardzic[15], Biljana Suzic[16], Ildiko Szatmari[17], Alma Toromanovic[18], Mojca Zerjav Tansek[2,6], Tadej Battelino[2,6] and Urh Groselj[2,6*]

EURORDIS Newborn Screening Working Group

The Newborn Screening Working Group **reviews current policy and practice in the field of NBS,** in order to **develop principles** for harmonious uptake of the NBS programs **across the MS** with a view to delivering maximum benefit and improving outcomes for babies born with rare diseases

- 24 Members
- 15 countries
- A multistakeholder working group

Development & Consultation Process




EURORDIS
RARE DISEASES EUROPE
KEY PRINCIPLES FOR NEWBORN SCREENING
A EURORDIS Position paper
January 2021
eurordis.org/newbornscreening
EURORDIS.ORG

Your Questions

NBS seems so far dedicated to certain type of diseases. ***Early diagnostic for*** *22q11 patients (1/2500 births)* ***is key to help the parents to take early measures*** *that will allow for adapted* ***medical, cognitive and para-medical care****. So,* ***although, the syndrome can't be healed, early diagnostic brings costs savings for the society.*** *How can we move forward on this?*

Why should testing babies for rare diseases be conditional on the ***availability of effective intervention*** *and how is the latter judged? These are two separate activities and the exclusive nature of the link prevents access to other* ***benefits of early identification*** *such as avoiding multiple affected children in the family.*

How can ***patient organisations*** *in different European countries* ***help promote the need for NBS at a European level?***

KEY PRINCIPLES FOR NEWBORN SCREENING

1. Screening should identify opportunities to help the newborn and the family as broadly as possible. That is, **screening should identify actionable diseases including treatable diseases.**
    - **Avoid the diagnostic odyssey**
    - **Plan for the newborn's care and therapy**
    - **Make informed decisions on future pregnancies**
    - **Support research**
2. **NBS should be organised as a system** with clearly defined roles, responsibilities, accountability and communication pathways that are embedded into the national health care system and recognised as a mechanism for earlier diagnosis of actionable conditions as part of the broader care pathway.
3. The family of the newborn who has been diagnosed through NBS should be provided with **psychological, social and economic support** by the competent national health authorities.

KEY PRINCIPLES FOR NEWBORN SCREENING

4. **All stakeholders should be included** in the different stages of the NBS process.
5. Transparent and robust governance for expanding NBS programmes is needed. Every country/region should have a **clearly defined transparent, independent, impartial and evidence-based process** for deciding which conditions are covered by the NBS programme that includes all stakeholders.
6. Governance of NBS programmes should be explicit, comprehensive, transparent and accountable to national authorities.
7. The evaluation process on the **inclusion/exclusion of diseases in** NBS programmes needs to be **based on the best available evidence,** reflecting health economic evidence but not determined only by health economics.

KEY PRINCIPLES FOR NEWBORN SCREENING

8. **Information and education** of all stakeholders on rare diseases and the whole NBS process is essential for a broad and fair implementation of NBS programmes.
9. European-wide standards addressing **the timing, sample collection methods, follow-up,** and information shared with parents are needed to guarantee uniformity and quality throughout the process.
10. Blood spot samples should be stored in national biobanks for research purposes while ensuring **appropriate safeguards for data protection and data access** are in place.
11. ERN affiliated centres **should be integrated in the care pathways of the different healthcare systems** and should be considered as preferential partners in providing recommendations on NBS policies.

Call to Action – a role for everyone

Expert Forum

Experts + Stakeholders
MS representatives

Actions with clear EU added value
(respecting subsidiarity)

The Steering Group on Promotion and Prevention (SGPP) → **European Commission** → **Member States**

Endorse Key Principles as best practice

Endorse best practices for funding and scaling up Recommend them to MS

Consider uptake at national or regional level

European Parliament

Support initiatives for harmonious practices in NBS
Put pressure on the other EU Institutions

From PRINCIPLES to ACTION

NBS Technical Meetings

Technical Meetings on NBS

- Achieving Equity and Innovation in Newborn Screening (11 Octber 2021, **Slovenia**)
- NBS Expert Meeting (23 July 2022, **Czech Republic**)
- Expert conference on rare diseases(25-26 October, 2022 Czech Republic)

EURORDIS' role

- One of the main stakeholders&organisers
- The views of people living with rare diseases and their families: 11 key principles & Panel discussion

Promotion of best practices

Promoting Italian model as best practice

- The most extensive newborn screening programme in Europe
- Organised as a "system"
- Embedded into the national health care system
- Aligned with 11 Key Principles !

EURORDIS' role

- Supporting and promoting the campaign to sign the petition

Screen4Care Project

Shortening the path to rare disease diagnosis by using newborn genetic screening and digital technologies

- 5-year project funded by IMI (public private partnership)

EURORDIS' role

- To facilitate networking through its stakeholder Newborn Screening Working Group.
- Stakeholder workshops on NBS
- Patient advisory board
- RBV Survey on NBS

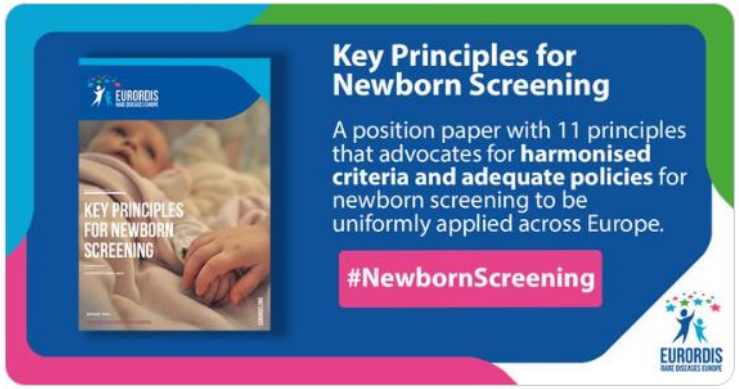
Publication & Dissemination & Social Media Outreach

Rare Diseases Europe
@eurordis

For the first time EURORDIS, alongside its members, have set out 11 Key Principles for #NewbornScreening 👣

These principles will support an harmonised European approach to NBS that will help to reduce vast inequalities across Europe.

👉 eurordis.org/newbornscreeni...

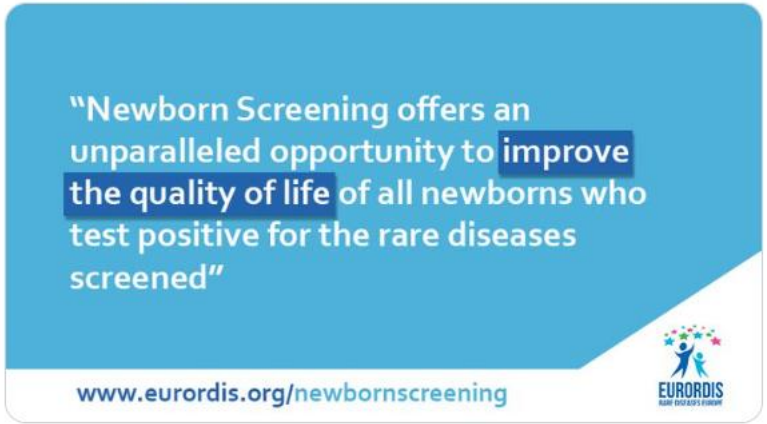


Rare Diseases Europe
@eurordis

#NewbornScreening 👣 holds one of the keys to a better future for people born with a #raredisease in the years to come

It is up to the European Union, and its Member States, to ensure this opportunity is not missed 🇪🇺

🔷 Share our 11 Key principles!
eurordis.org/newbornscreeni...



Reactions

ACURARE @ACURARE1 · 4 Şub
Yeni doğan tarama için 11 temel ilke @eurordis tarafından yayımlandı. 👇👇
🧬 #yenidoğantarama #newbornscreening

Shirlene Badger @shirlenebadger · 20 Oca
Thrilled to see the publication of this paper - the result of wonderfully inclusive and in-depth collaboration across @eurordis membership, calling for a harmonised Newborn Screening approach that leaves no families, regardless of country, in uncertainty.

Dr Suja Somanadhan @sujas15 · 20 Oca
Thank you for sharing harmonising approaches to #Newbornscreening @eurordis I note your call for action
"Responsibility for Newborn Screening programmes falls on individual countries in Europe". @DonnellyStephen @Lesmart11659095

MarenT @M_arenT_P · 20 Şub 2020
#Neugeborenenscreening rettet Leben!
Ein kleiner Fersenpiks in den ersten Lebenstagen des Babys und das Blut kann auf viele verschiedene #SelteneErkrankungen #raredisease, die behandelbar sind, untersucht werden.
Leider noch nicht in allen (europäischen) Ländern flächendeckend...

Dravet Syndrome Foundation Spain @DSFeu · 22 Oca
Does it make sense that different regions of Spain screen babies for different diseases?

Read EURORDIS' 11 Key Principles for Newborn Screening and let's make health equity and harmonized newborn screening policy a priority for 2021!

aismme
January 21 at 5:41 PM ·
LO "SCREENING NEONATALE ESTESO" ANCHE IN TUTTI GLI STATI EUROPEI: LE INDICAZIONI DELLE ASSOCIAZIONI DEI PAZIENTI
11 Principi chiave sullo Screening neonatale per una attuazione comune in tutti i paesi EU. Documento elaborato dal gruppo di lavoro #EURORDIS in cui Aismme ha partecipato con Manuela Vaccarotto e Simona Bellagambi in rappresentanza di #uniamofimr e con Domenica Taruscio dell'ISS . Call to action alle istituzioni europee e agli Stati Membri

Neuroblues @neuroblues7 · 20 Oca
El desarrollo no se mide solamente en ingresos por habitante o en índices de pobreza, NBI o desnutrición.

Ay, que lejos estamos. Cada vez más.

Dmitriy Zavgorodniy
January 20 at 8:00 PM ·
"масштабное неравенство во всей Европе"
А вытекают из этого масштабного неравенства человеческие трагедии больных людей, которые даже при явно выраженной клинике игнорируют практиктически все медицинские специалисты на Украине!
#HCU

Latvijas Reto slimību alianse
January 20 at 2:26 PM ·
11 basic principles for newborn screening in Europe 👉

Vesna Aleksovska
We have already translated it in Macedonian. It is very important document. Already advocating 😁
http://challenges.mk/.../%D0%9D%D0%B0%D1%87%D0%B5%D0%BB...
Like · Reply · 1w
1

ALAN - Maladies Rares Luxembourg
January 20 at 3:57 PM ·
Eng fréi Diagnos ka bei enger rarer Krankheet ee groussen Impakt op d'Liewensqualitéit hunn.

Den Dépistage néonatal, also d'Teste vu neigebuerene Puppelcher👶 fir verschidde vun dëse Krankheeten ze diagnostizéieren, ass dobäi immens wichteg.

An Europa ginn et beim Dépistage néonatal grouss Ënnerscheeder tëscht de Länner.

EURORDIS - European Rare Diseases Organisation plädéiert fir eng gemeinsam europäesch Approche fir dass all Puppelchen & Famill dee selwechten Accès op fréi Diagnosetester huet.

Dofir hunn EURORDIS an déi national Allianzen elo een Dokument veröffentlecht mat 11 Prinzippien a konkreten Fuerderunge fir den Dépistage néonatal ze verbesseren & harmoniséieren.

FH Europe @fhpatienteurope · 21 Oca
11 Key Principles for #NewbornScreening

EURORDIS RARE DISEASES EUROPE

Looking ahead

Position Paper available in 12 languages

Czech English
German
Georgian Greek
Italian
Macedonian Portuguese
Serbian
Slovenian Spanish
Turkish

EURORDIS.ORG

EURORDIS
RARE DISEASES EUROPE

Key messages

- Application of adequate policies for newborn screening requires **a collective effort** from all stakeholders
- **Dialogue** between patients, parents, policymakers and treatment developers, together with clinicians with academic experts on newborn screening on the technology on ethical and economic aspects
- **Collaboration** amongst the national authorities and the other stakeholders to exchange best practices is of great importance, including horizon scanning for timely decision making

- **The impact of early diagnosis can be life changing for patients**, this is what we should focus on when we are advocating for newborn screening.

Thank you for your attention

gulcin.gumus@eurordis.org

6.

- Topic 4 -The SeDeN project: a study of the acceptability of professionals and the population in France before setting up a pilot project
  - Dr. Camille Level, Study engineer in health economics at Dijon Bourgogne University Hospital, Dijon (France)

From the Social Acceptability of Expanding Newborn Screening to a Genomic Newborn Screening Pilot Project

From SeDeN to PERIGENOMED

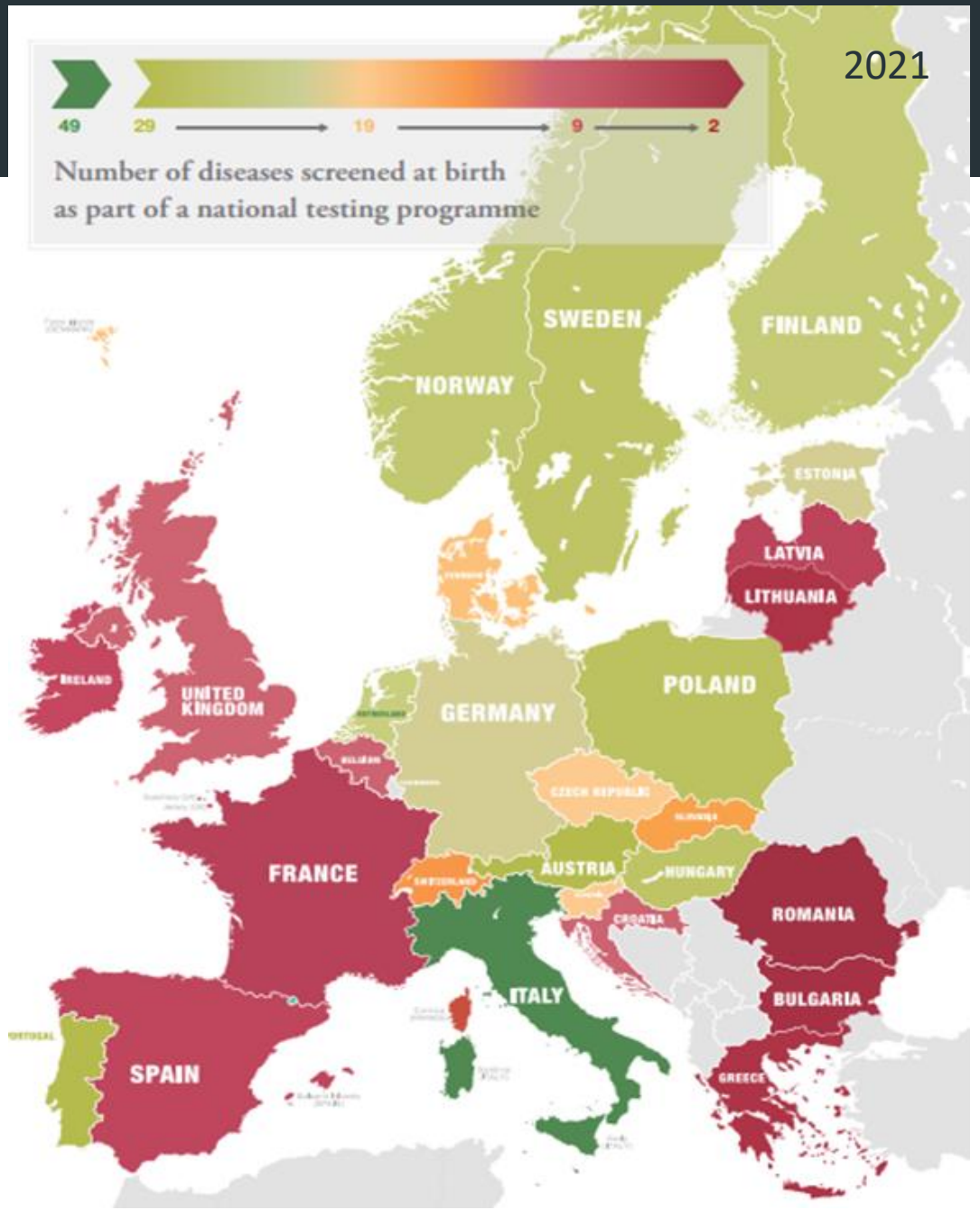
March 21, 2023

Webinar ITHACA

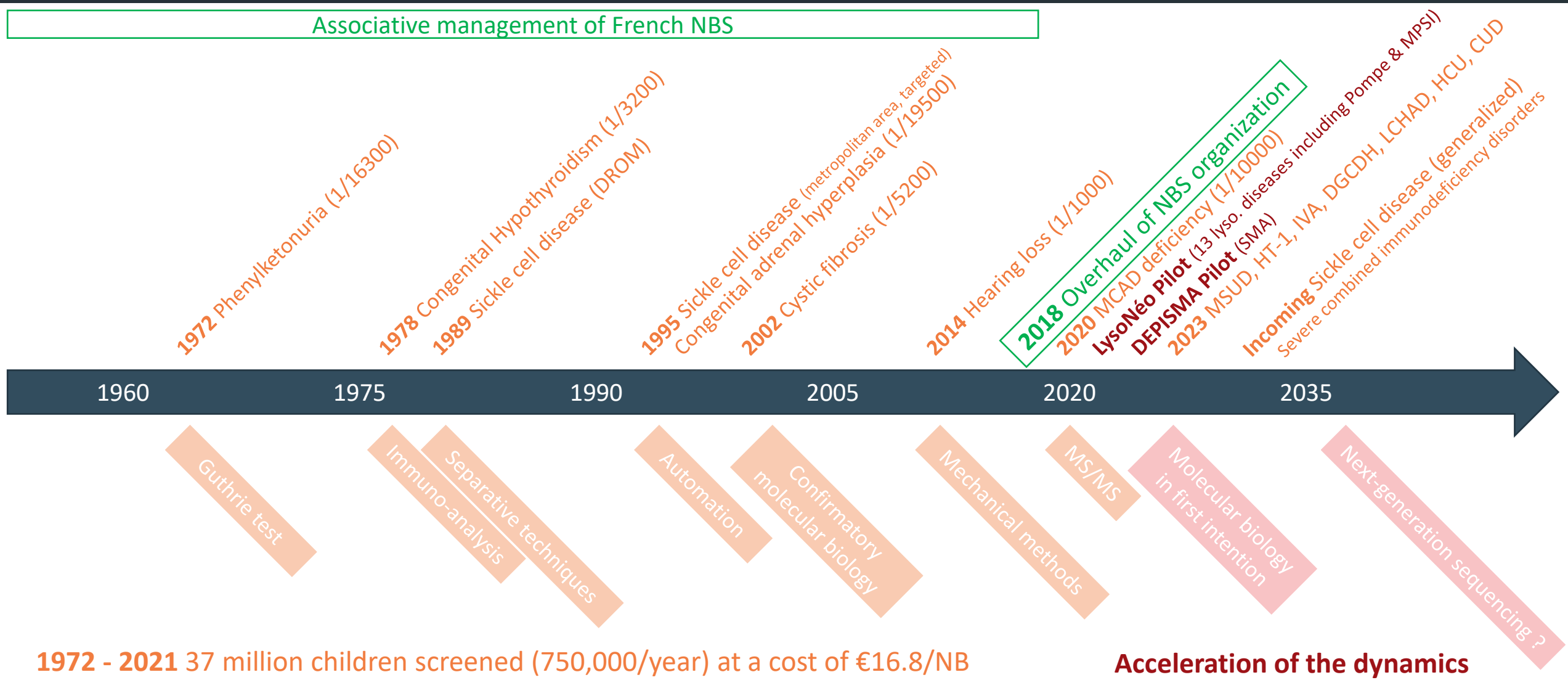
Camille LEVEL, health economist, CHU Dijon Bourgogne
camille.level@chu-dijon.fr

France

a pioneer and then a laggard?



Evolution of French Newborn Screening



1972 - 2021 37 million children screened (750,000/year) at a cost of €16.8/NB
Nearly 30,000 screened, diagnosed and treated

Acceleration of the dynamics
Millefeuille of pathologies/techniques ?

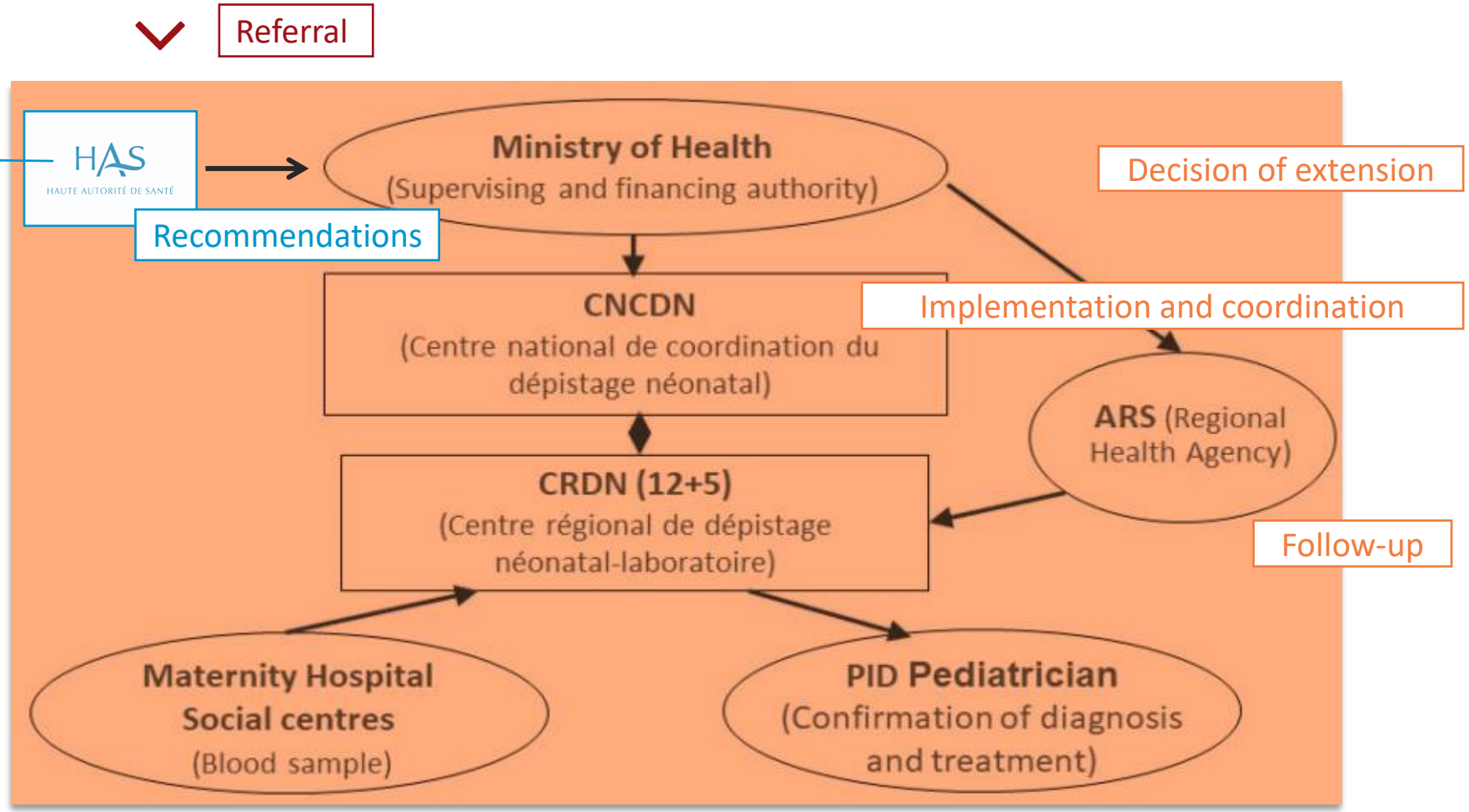
French organization of NBS

Objective
To identify asymptomatic children with a identified disease in a cohort of newborns

Learned Societies | National Health Networks for Rare Diseases | Patient's association | Literature monitoring

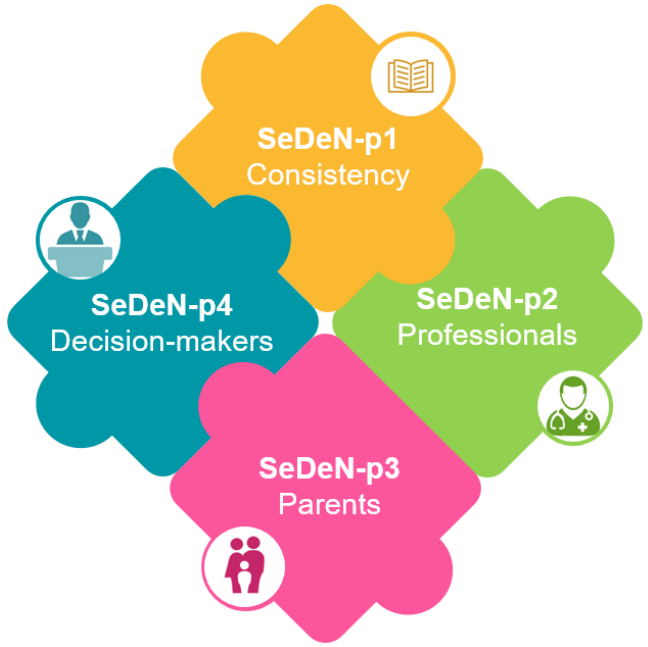
- ✓ Medico-economic studies
- ✓ Multidisciplinary group of experts
  - *Reliable technique*
  - *Quality criteria for methodology*
- ✓ Wilson and Jungner criteria
  - *Known disease with predictable evolution, pre-symptomatic period, public health problem*
  - *Treatment available and effective*
  - *Sensitive, specific and acceptable screening test*
  - *Physical and psychological inconvenience of screening less than its expected benefits*
  - *Economic cost of the test offset by the expected benefits*
- ✓ Biomedical ethics principles
  - *Autonomy*
  - *Beneficence*
  - *Non-maleficence*
  - *Justice*

→ **Completeness, equality of access, quality of tests performed, quality of care and follow-up**



Social Acceptability: SeDeN Project, 2020

Expansion of Newborn Screening with or without first-line genetic testing: views, debates and perspectives in France



Pr Laurence FAIVRE

Genetics

Pr Frédéric HUET

Paediatrics

Dr Christine PEYRON

Health economist

Camille LEVEL

Coordinator

4 complementary parts to fully assess the social acceptability of NBS expansion

Specificities due to genetics ?

SeDeN-p2

Questionnaire distributed by networks & learned societies

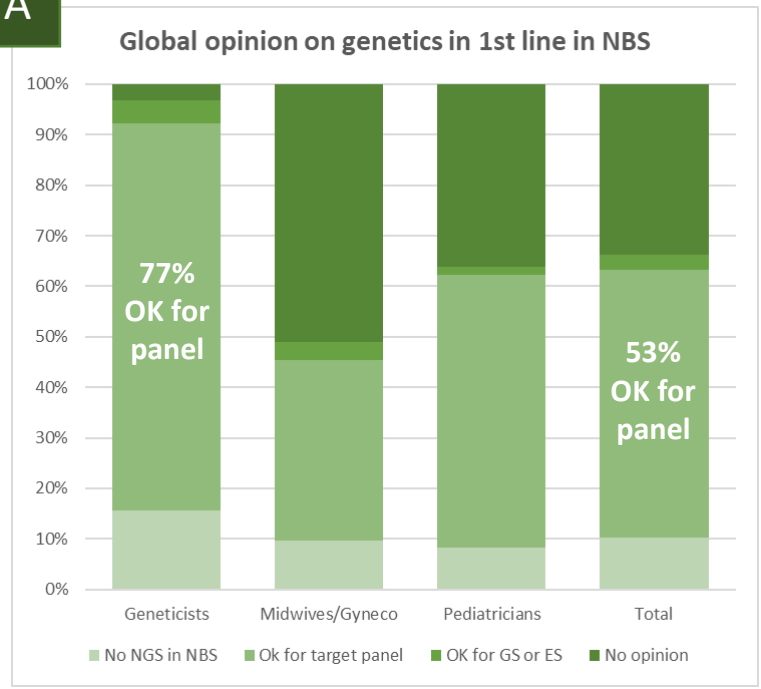
→ **1199 French health professionals**

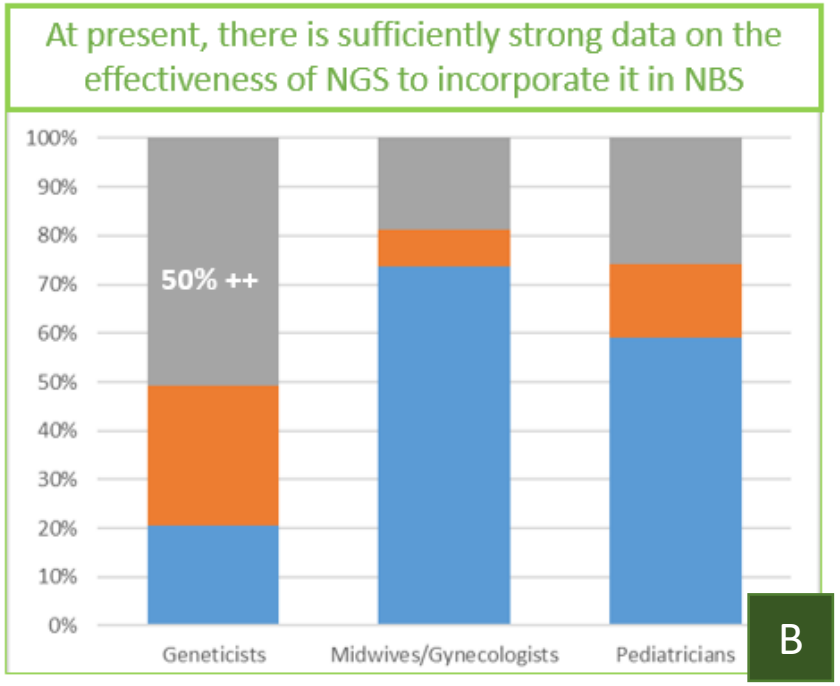
17.8% geneticists and genetic counselors
44.3% pediatricians
37.9% midwives and gynecologists

	Actionable	Non-actionable
Childhood onset	81% +++	39% - ***
Adult onset	80% ++ *	51% --- ***

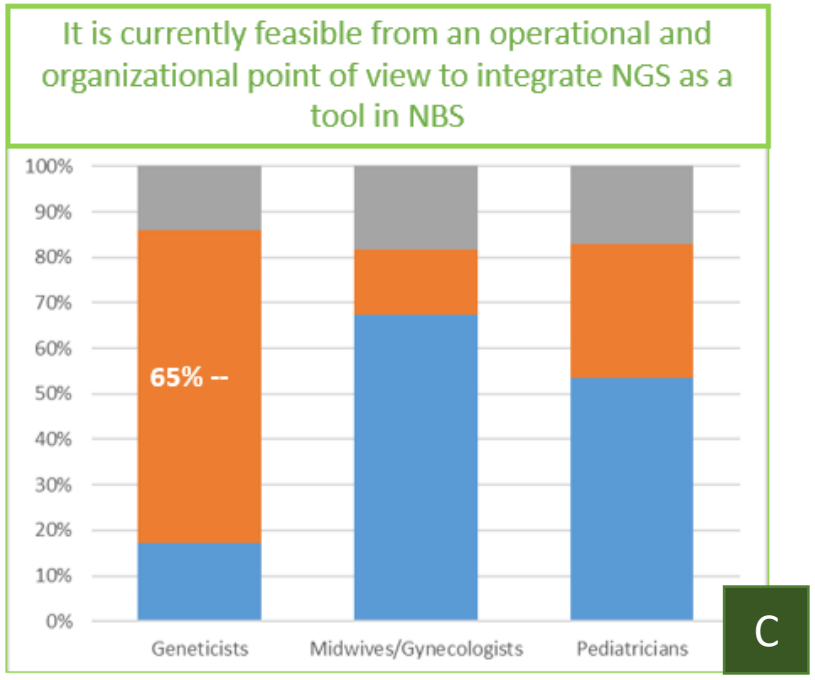
Pharmacogenetic variations	42% + *
Related to costly disease	38% + *
Heterozygous	67% -- *
Information for relatives	65% -- *
VUS	56% --- ***

A





B



C

*moderate heterogeneity based on the specialty
*** important heterogeneity based on the specialty

Rather agree / Agree
Disagree / Rather disagree
No opinion / Not my field of expertise

"PARENT IN GENERAL POPULATION" ARM

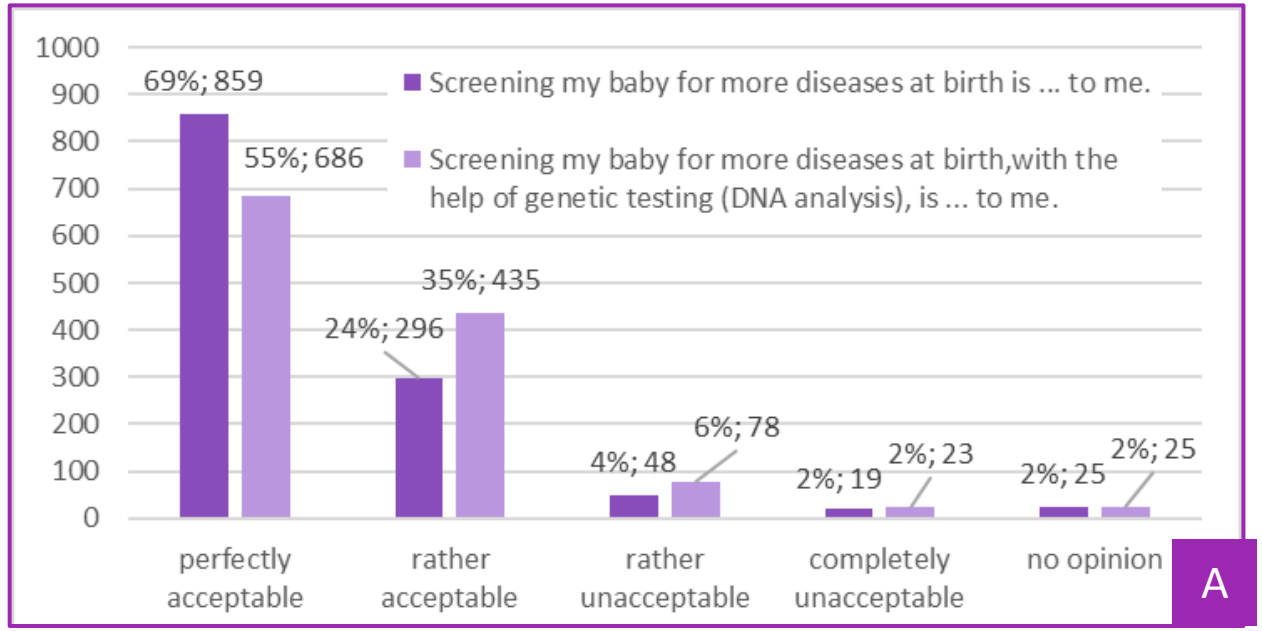
	Population 1	Population 2
Population description	Parent whose youngest child is 0-1 week old	Parent whose youngest child is between 1 week and 3 years old
Population size / Type of survey	Population 1Q: 408 (questionnaire) Population 1E: 13 (interview)	1 247 (questionnaire)
Recruitment	4 Maternity Hospitals	Polling Institute (quota method)

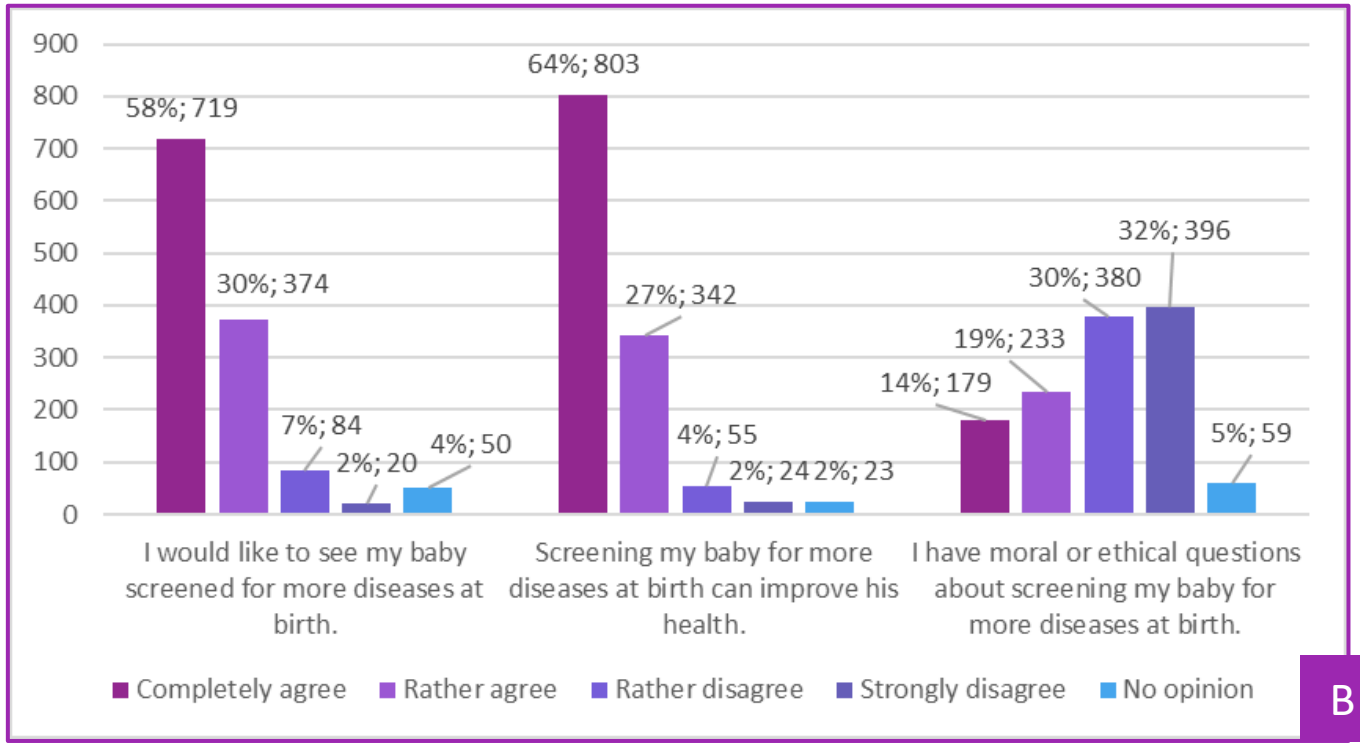
Profile 1 (minority): quest for omniscience
Know everything, even lat-onset, even without treatment
→ Anticipation and preparation

Profile 2 (majority): knowledge but restricted
Diseases with onset in childhood or adolescence and with treatment or management that improves QoL and/or life expectancy

Use of a genetic test as 1st line
Does not change what they want to know, if not more invasive for the child

SeDeN-p3 Parents





SeDeN-p3
Parents

"PARENT IN GENERAL POPULATION" ARM

"PARENT OF A SICK CHILD" ARM

	Population 1	Population 2	Population 3	Population 4
Population description	Parent whose youngest child is 0-1 week old	Parent whose youngest child is between 1 week and 3 years old	Parent whose child has been diagnosed with a disease following NBS in France	Parent whose child has been diagnosed with a disease, detected in NBS abroad but not in France
Population size / Type of survey	Population 1Q: 408 Population 1E: 13	1 247	15	15
Recruitment	4 Maternity Hospitals	Polling Institute (quota method)	Patient associations, study investigators, network, etc.	

PERIGENOMED Project (2025)

General objective of the project: To identify the barriers (technological, organizational, etc.), to develop adequate tools, in particular bioinformatics, information for parents and training for professionals, as well as circuits adapted to the routine deployment of ultrafast genome sequencing in Newborn Screening (in parallel with traditional NBS), and to study the real acceptability, the feasibility, the interest and the organizational and economic sustainability of the proposed solutions

Genome sequencing

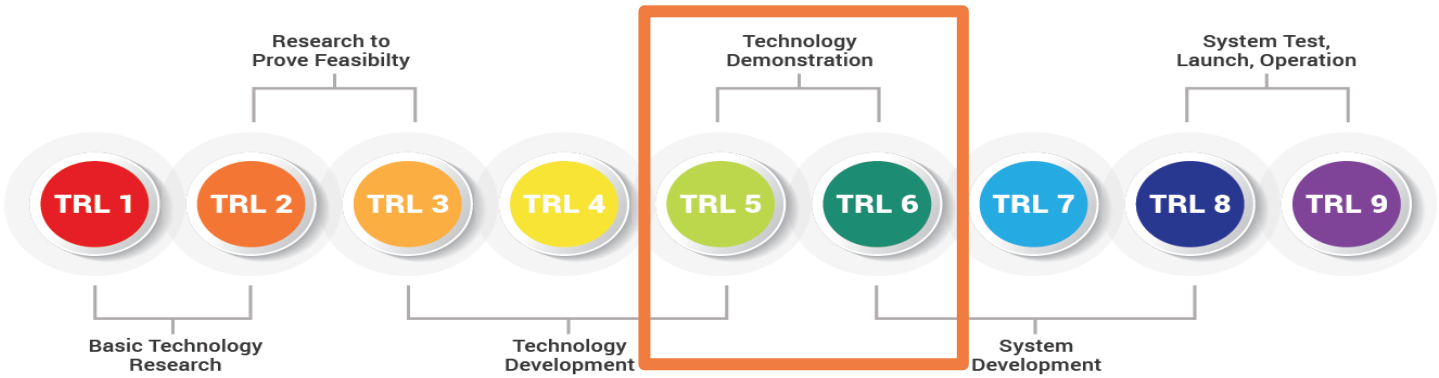
with targeted analysis of a list of variations (150-250 genes)

responsible for treatable rare diseases

of early onset (before the age of 5)

in 6 to 12 health centers

(15 to 18000 newborns)



TRL 5/6: validation and demonstration of the technology in real environment (different from operational environment = prefigurator)

Discussion time and Wrap up

Conclusion with speakers and moderator

Pr. Laurence Faivre, Centre de Génétique et Centre de Référence Anomalies du Développement et Syndromes Malformatifs, Dijon (France)

- Thank you !