Newborn screening for PID

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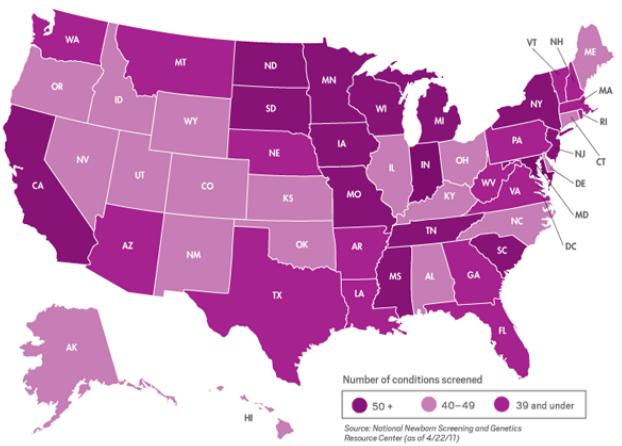
Methods for newborn screening

- MS-MS
- DNA based
  - TREC/KREC
  - Cystic fibrosis, Glutaric acidemia type I, PID
- Protein based

Newborn screening in the USA



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TREC screening in the USA

- 3 030 083 children screened
- 52 children with SCID (1/58 000)
- 92 % survival after therapy
- No SCID patient missed

Kwan et al, JAMA 2014

TREC screening in Taiwan

- 106 391 children screened
- 19 (0.017 %) abnormal TREC results
- 5 children with SCID
- No SCID patient missed
- 5 DiGeorge patients

Chien et al, J Formosan Med Ass 2015

TREC screening in Israel*

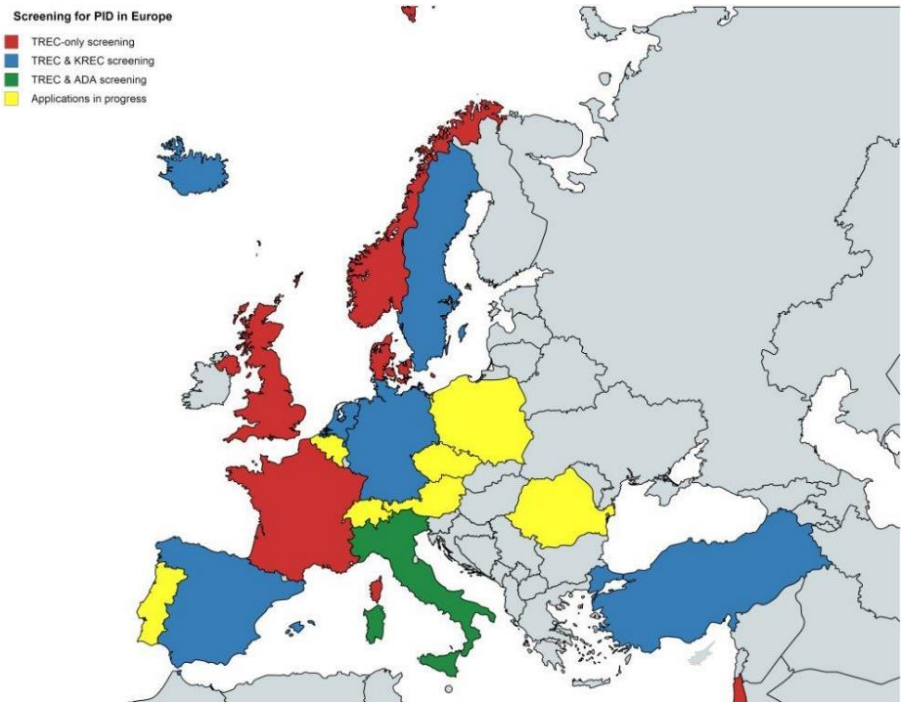
- 186 794 children screened
- 43 (0.02 %) abnormal TREC results
- 8 children with SCID
- No SCID patient missed
- 2 DiGeorge patients

*Courtesy of Dr. Somech Raz, 2016

TREC/KREC screening in Sweden

- 89 462 children screened
- 2 children with SCID (1/45 000)
- 3 additional children with A-T/CID
- No SCID patient missed

Zetterström et al, Int J Newborn Screening, 2017



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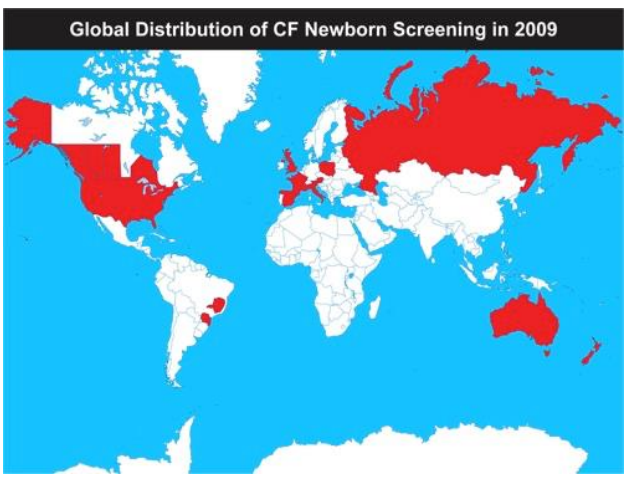
Cystic fibrosis



Glutaric acidemia type I

- Manitoba - Ontario
- 1176 infants screened
- 69 carriers detected
- 4 children affected

Greenberg et al, Mol Genet Metabol 2002

WGS based screening strategies

- Targeted sequencing
- Unconditional sequencing

Future NBS strategies

- Prenatal screening
- Protein based assays

Complement factors, granulocyte specific proteins

- WES
- WGS

Prenatal screening

- SCID
- Downs syndrome
- Edwards syndrome
- Turners syndrome
- Cri-du-chat syndrome
- Gender

Future NBS strategies

- Prenatal screening
- Protein based assays

  Complement factors
- WES
- WGS

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- Prenatal screening
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Complement factors, granulocyte specific proteins

- WES
- WGS

WGS based screening strategies

- Targeted sequencing
- Unconditional sequencing

Targeted WGS

- Metabolic diseases
  - CMMS, SciLife
- Immunodeficiency
- Other diseases

Targeted WGS

- Metabolic diseases
- Immunodeficiency
  - Clinical Immunology, SciLife
- Other diseases

Targeted WGS

- Metabolic diseases
- Immunodeficiency
- Other diseases
- ICU

WGS based screening strategies

- Targeted sequencing
- Unconditional sequencing

Ethical concerns

- Consent (opt-in, opt-out)
- Big data (the digital you)
- Data security (big brother)
- Serendipidous findings
- Counseling (patients, relatives)

Unconditional WGS

- Metabolic diseases
  - Cystic fibrosis, Glutaric acidemia type I
- Immunodeficiency
- Other diseases

Unconditional WGS

- Metabolic diseases
- Immunodeficiency
  - PID, SCID (NSIGHT project)
- Other diseases

WGS for PID

- 1349 newborn-parent trios
- Evaluation of 329 PID genes
- One child with PID (C9 deficiency)
- 3 ”other” diseases
  - (NAA10, GLRA1, HADHB gene mutations)

Pavey et al, Genet Med, 2017

NSIGHT (NIH)

Principal Investigator	Institution	Title
Robert Green and Alan Beggs	Brigham and Women's Hospital	Genome Sequence-Based Screening for Childhood Risk and Newborn Illness
Stephen Kingsmore	Children's Mercy Hospital	Clinical and Social Implications of 2-day Genome Results in Acutely III Newborns
Robert Nussbaum	University of California, San Francisco	Sequencing of Newborn Blood Spot DNA to Improve and Expand Newborn Screening
Cynthia Powell and Jonathan Berg	University of North Carolina at Chapel Hill	NC NEXUS, North Carolina Newborn Exome Sequencing for Universal Screening

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Francis Collins (director of the NIH)

Over the course of the next few decades, the availability of cheap, efficient DNA sequencing technology will lead to a medical landscape in which each baby´s genome is sequenced, and that information is used to shape a lifetime of personalized strategies for disease prevention, detection and treatment.

July 7th, 2014.

Ethical concerns

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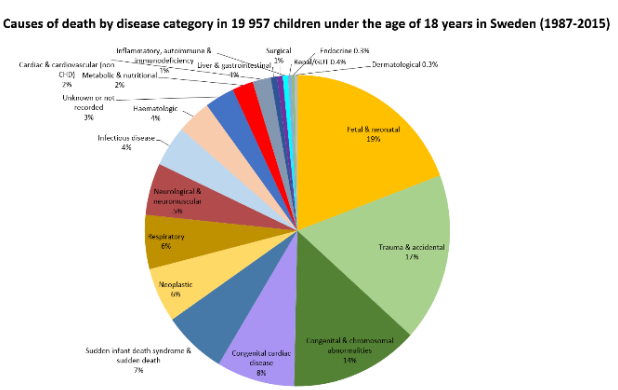
Causes of death in Swedish children



King et al, Int J Newborn Screening 2017