Benefits and risks of Newborn Screening from medical, societal and ethical points of view

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Newborn screening

- The aim of newborn screening is easily accepted, also among lay people.
  - to detect affected newborns early in order to start treatment and thus prevent or alleviate the clinical consequences of the disease
  - as a by-product risk families are picked up and options for family planning and prenatal diagnostics can be offered

Side effects of newborn screening

- worry caused by the screening
- false positives
- unclear results
- detecting carriers
- delayed diagnosis in case of false negatives

Four ethical principles in health care

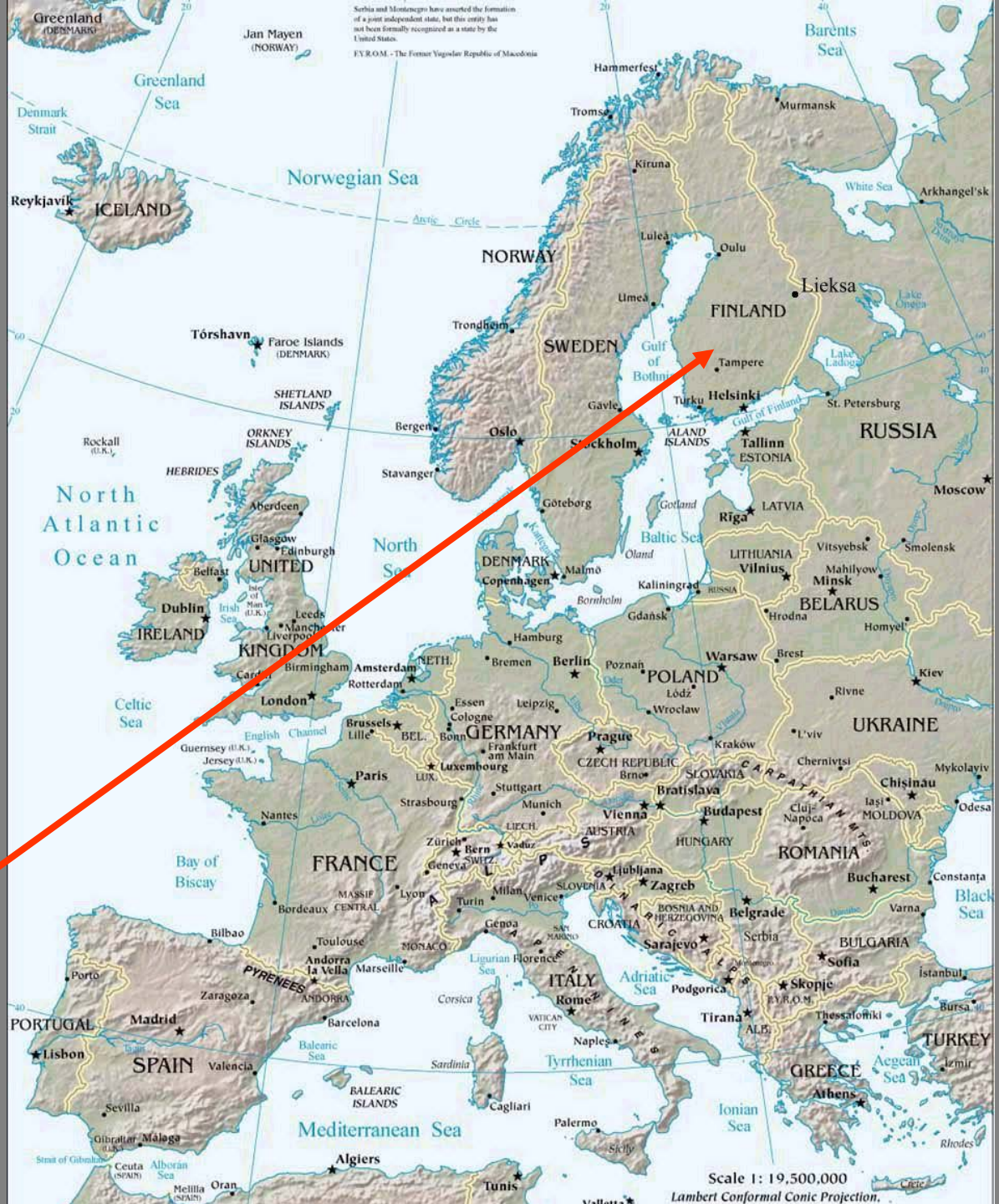
- Beneficence
- Non maleficence
- Respect for autonomy
- Justice

- What is the hierarcy among these principles?

In Finland

- We offer newborn screening for the whole population only for hypothyreosis.
- In addition, we offer PKU screening for newborns with non-Finnish ancestry.

- The reason for this is our exceptional genetic heritage, not that Finland would oppose newborn screening.


Finland
Greenland (DENMARK)
Jan Mayen (NORWAY)
Serbia and Montenegro have asserted the formation of a joint independent state, but this entity has not been formally recognized as a state by the United States.
F.Y.R.O.M. - The Former Yugoslav Republic of Macedonia
Greenland Sea
Denmark Strait
Norwegian Sea
Barents Sea
Hammerfest
Tromsø
Murmansk
Kiruna
White Sea
Arkhangel'sk
Reykjavík
ICELAND
Arctic Circle
Luleå
Oulu
NORWAY
Umeå
Lieksa
FINLAND
Lake Onega
Trondheim
Tórshavn
Faroe Islands (DENMARK)
SWEDEN
Gulf of Bothnia
Tampere
Lake Ladoga
SHETLAND ISLANDS
Gävle
Turku
Helsinki
St. Petersburg
Gulf of Finland
Bergen
Oslo
Stockholm
ÅLAND ISLANDS
Tallinn
ESTONIA
RUSSIA
Rockall (U.K.)
ORKNEY ISLANDS
HEBRIDES
Stavanger
Moscow
North Atlantic Ocean
Aberdeen
Göteborg
Gotland
Rīga
LATVIA
Glasgow
Edinburgh
North Sea
Baltic Sea
Oland
LITHUANIA
Vitsyebsk
Smolensk
Belfast
UNITED
DENMARK
Copenhagen
Malmö
Vilnius
Mahilyow
Minsk
Kaliningrad
RUSSIA
Bornholm
BELARUS
Dublin
Irish Sea
Isle of Man (U.K.)
Leeds
Manchester
Liverpool
IRELAND
KINGDOM
Gdańsk
Hrodna
Homyel'
Hamburg
Birmingham
NETH.
Amsterdam
Bremen
Berlin
Poznań
Warsaw
Brest
POLAND
Kiev
Rotterdam
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Rivne
Celtic Sea
London
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Wrocław
Brussels
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Prague
UKRAINE
English Channel
Guernsey (U.K.)
Jersey (U.K.)
Frankfurt am Main
Kraków
L'viv
Luxembourg
LUX.
CZECH REPUBLIC
Brno
SLOVAKIA
Chernivtsi
Mykolayiv
Paris
Stuttgart
Bratislava
Chişinău
Strasbourg
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Zagreb
Bucharest
Constanța
MASSIF CENTRAL
Lyon
Milan
Venice
SLOVENIA
Turin
Bordeaux
BOSNIA AND HERZEGOVINA
Belgrade
Varna
Black Sea
CROATIA
Genoa
SAN MARINO
Bilbao
Toulouse
MONACO
Serbia
Sarajevo
BULGARIA
Andorra la Vella
Marseille
Liguran Sea
Florence
Sofia
Porto
PYRENEES
ANDORRA
ITALY
Adriatic Sea
Skopje
İstanbul
Zaragoza
Corsica
Rome
Podgorica
F.Y.R.O.M.
Barcelona
VATICAN CITY
Tirana
ALB.
Thessaloniki
Bursa
PORTUGAL
Madrid
Naples
TURKEY
Lisbon
Balearic Sea
Sardinia
Tyrrhenian Sea
Aegean Sea
SPAIN
Valencia
GREECE
Izmir
Sevilla
BALEARIC ISLANDS
Cagliari
Athens
Ionian Sea
Mediterranean Sea
Palermo
Gibraltar (U.K.)
Málaga
Sicily
Rhodes
Strait of Gibraltar
Ceuta (SPAIN)
Alborán Sea
Algiers
Melilla (SPAIN)
Oran
Tunis
Crete
Scale 1: 19,500,000
Lambert Conformal Conic Projection.

Newborn screening in Finland

- As newborn screening program in Finland does not allow easy addition of new diseases, a very comprehensive Health Care Technology Assessment project was undertaken to evaluate newborn sreening.
  - Autti-Rämö I et al.: Acta Paed 2005:94:1126-1136.

Diseases evaluated

- congenital adrenal hyperplasia
- MCAD
- LCHAD
- phenylketonuria
- glutaricaciduria

What we learned during a comprehensive HTA assessment in Finland?

- HTA-assessment is extremely difficult because
  - The true incidence of the diseases (possibly) included in newborn screening programs is seldom known
  - The long term medical consequences of early diagnosis are poorly known
  - The ethical and societal costs of newborn screening are not well understood, difficult to measure and extremy difficult to handle together with ”hard” medical figures

In addition we learned

- PKU is the key to saving health care costs/human suffering in newborn screening
- If there is no PKU in a population (like in Finland), the cost-benefit ratio of newborn screening becomes very poor
- This is because PKU (and hypothyreosis) are the only diseases where treatment makes a total difference from severely affected to practically healthy

	Ethical aspects when no screening	Benefits of screening	Ethical aspects and possible harms when screening
A newborn, affected with the disease	Risk of death or severe handicap. The risk remains over lifetime	Early diagnosis and treatment gives possibility to remain symptom free.	Commitment to lifelong treatment may cause psychological stress. Identification of a disease form that might not have caused symptoms during lifetime
Newborn with one gene mutation, a carrier	Carrier status unknown which may have either positive or negative consequences for the individual	Knowledge of being a carrier and possibility for genetic counselling	Carrier status identified before being able to give consent for testing
Healthy newborn	No unnecessary examinations	Exclusion of disease	Pain caused by taking the blood sample. Unnecessary examinations when testing falsely positive
Parents of an affected child	Bitterness of parents when the child dies or is severely handicapped from a disease that could have been screened for. Feeling of unfairness when comparing the cost-effectiveness of screening to other implemented treatments.	Possibility to keep the child symptom free with proper treatment. Possibility for genetic counselling.	Identification of a severe disease in a symptom-free newborn. Commitment to lifelong treatment. Stress and fear for life-threatening situations (infections).
Parents of a healthy child	No information on the existence of rare disorders	Exlusion of the disease.	Parents of healthy children unnecessarily disturbed by the offer of screening or worried at false positive screening result
Siblings of an affected child	Knowledge of possibility of being a carrier comes through death or handicap of sibling which may be frightening. Hidden or mild forms not identified.	A possibility to test for being a carrier and get genetic counselling when needed. Identification of a disease that has been symptom-free.	Fear for being a carrier. Identification of disease that might not have caused any symptoms during lifetime.
Close relatives of an affected child	Knowledge of possibility of being a carrier comes through death or handicap of relative, which may be more frightening. Hidden and mild forms not identified and thus the risk of being a carrier is not known	Identification of genetic risk and possibility for genetic counselling.	Fear for being a carrier.
Health care system	Need to evaluate whether diagnostic and treatment possibilities are properly organized. Acceptance of the possibility that some infants may die or be severely handicapped due to delayed diagnosis.	The possibility to prevent permanent damage. Clarification of treatment and follow-up responsibilities from newborn through adulthood	The personnel at outpatient maternity units need to inform parents about disorders they have never encountered. Acceptance of b false positive and false negative results.
Society	Need to evaluate equity in relation to other rare conditions, expensive treatments in use and active screening programmes.	Lower treatment cost for cases. General knowledge about rare conditions increases.	High yearly running costs. Death or handicap of a few at the cost of causing mild side-effects in many. The high cost of treating a handicapped person are unintentionally emphasized.

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Ethical aspects and possible harms when screening	The personnel at outpatient maternity units need to inform parents about disorders they have never encountered. Acceptance of false positive and false negative results.

Society

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Screening methods may also detect carriers

- If NBS is performed by methods that detect gene mutations, also “carrier babies” will be identified
- For a while there is uncertainty on whether the baby is carrier or affected
- The waiting time for additional investigations to be completed may be extremely stressing to the family.

Potential benefits of detecting a carrier: mostly for the family!

- the possible detection of carrier couples
- presymptomatic testing of these couples' previous children who may have undetected disease
- a carrier parent informing his/her extended family members of the chance of also being a carrier.
- the child will know about the carriership in good time

Potential harms of detecting a carrier: mostly for the newborn!

- all problems associated with testing chidren
  - loss of privacy
  - loss of autonomy
  - stigmatizing the child
  - the difficulty of informing the result to the child correctly and at an optimal time
  - getting knowledge which theoretically may create problems in a future health care system
- worry and anxiety, especially immediately after the preliminary result

- ”The complexity and cost of healthcare delivery systems may set up tension between what is good for the society as a whole and what is best for the individual patient.”

  – Tavistock group: Shared ethical principles for everybody in healthcare. BMJ 1999:318:248-251.

Epposi and NBS

- Epposi is an independent, not-for-profit, partnership-led and multi-stakeholder think tank based in Brussels, Belgium.
- The goal is to work at the "cutting edge" of European health policy-making with the aim of bridging the gap between innovation and improved public health outcomes.
- Epposi has recently agreed to start Advanced Innovation Program in RD; part of this is a project: “Stakeholder perspectives on the value of systematic newborn screening programmes in Europe: ethical and costs factors”

Literature review revealed

- Limited data on information provision, including timing of the information, related to NSPs, in particular its consequences
- Limited data on informed consent / the consequences of different informed consent processes
- Limited data on how ethical factors related to benefits and harms are taken into consideration in health care decision making

Epposi is also searching for new views to HTA

- To build a framework for a societal benefits approach to HTA;
  - Focusing on how to effect attitudinal as well as systematic change in HTA structures and processes
  - Investigating how HTA methods fit to smaller, specific patient group across Europe, as well as the needs of wider populations.

A clinical geneticist's view on NBS

- There are some diseases for which NBS is really important (like PKU)
- When other diseases are added to the programme, the positive ratio between benefits and harms becomes less clear

A clinical geneticist's view on NBS

- The planning, performing and evaluating of (newborn) screening programs should give special emphasis to the availability of comprehensive pre-test information to those who want it and ample resources for immediate support and genetic counselling in case of results suggesting the baby being affected or a carrier.