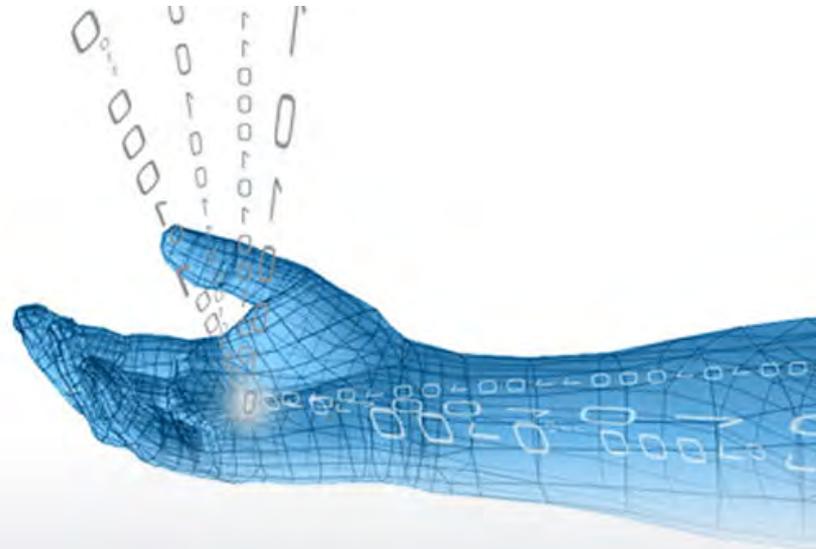


**Advanced Innovation**  
**Rare Diseases**



## EPPOSI'S RARE DISEASE INTEREST GROUP REPORT

*“Stakeholder perspectives on the organisation of systematic neonatal screening programmes in Europe: decision making and ethical implications”*

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## Abstract

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### Objective

Epposi’s Rare Disease Interest Group aims with this critical literature review to map and identify key gaps in the current decision making processes and ethical considerations on systematic neonatal screening programmes in Europe with an emphasis on the involvement of families and patients’ representatives. In detail the main questions are:

1. How does the decision-making process on the systematic neonatal screening programmes take place on the policy and family level? What are the ethical implications?
2. What are the key ethical factors of neonatal screening programmes for patients and their families?

### Methods

Studies not older than year 2005 from the databases Google, Medline, Embase and Science direct were collected, and also the EU Tender evaluation of population newborn screening practice in the European Union was used. A valuable list of 68 references was thus collected.

### Results

Newborn screening is used to improve the outcome for affected children. New technical possibilities generate discussion about potential extensions of systematic neonatal screening programmes. Decisions at a policy level tend to involve multiple stakeholders.

- i) The economical perspective and availability of screening tests are crucial for the decision making process at the policy level. Evidence shows that also topics related to ethics are considered, like the sensitive nature of the test, risk of discrimination or other complex issues at the level of each family requires proper information provision and communication methods. Due to the many ethical, legal and social areas it is important that citizens and patient representatives are involved in policy-making decisions.
- ii) The literature review detected as key ethical factors the availability of treatment for the disorders in the New Born Screening programme (NBS) and ample medical infrastructure. Also the psychological influence of screening of diseases if no sufficient treatment is available or false negative results were noticed as ethical risk factors.

In addition, the need to take the quality of life issues and risk of discrimination into consideration were noticed. The Epposi Rare Disease Interest Group (Epposi RDIG) decided not

to conduct a traditional cost-benefit analysis or mathematical analysis. The examples of PKU and hypothyroidism screening and early treatment displayed the benefit of the easy diagnostic tool and an astonishing outcome for the affected children, to live their life without marked symptoms of the disease, which affects also their productivity.

Not for all diseases screened today, the outcome is similarly positive.

### **Conclusion**

Ethical consideration of the decision making process related to newborn screening programmes is an important factor both on policy level and on the family level. On policy level, issues like cost effectiveness and preventing possible discrimination are important elements.

Several studies have suggested that a better information provision including information about possible false positive/negative results is needed for the families to enable informed decision making.

## **Background**

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Due to scientific progress and development of diagnostic techniques the possibilities for the detection of both individuals and the whole family have increased tremendously. As the genetic data affects not just the individuals concerned but also the whole family, the ethically acceptable use of this sensitive information is very important. The strictly focused newborn screening programmes (NBS) in the past were though more simple turned out to be very successful. To reach the same acceptance and success in the future, ethical consideration from a multi-stakeholder perspective is crucial.

With this background, Epossi Rare Disease Interest Group (Epossi RDIG) conducted this critical literature review which maps and identifies key gaps in the current decision making processes and ethical considerations on systematic neonatal screening programmes in Europe with an emphasis on the involvement of families and patients.

## **Method**

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Studies from the databases Google, Medline, Embase and Science direct, not older than year 2005 were collected and results of the EU Tender evaluation of population newborn screening practice for rare disorders in Member states of the European Union were also used. Abstracts were selected and the full text of the selected articles were grouped and analysed. The decision making processes was the main starting point for all ethical implications.

Due to this the report starts with the involvement of ethical implications at the policy versus family level. This includes also the methods of communication to support the parents in their

individual decision-making process. The second part focuses on other ethical implications like the availability of treatment, the influence of NBS on quality of life and the other consequences of screening.

## Results

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### *Including ethical implications in decision-making process at policy level*

The economical perspective and availability of screening tests are crucial elements when deciding which diseases are included in NBS. Our review proved also that topics related to ethics like the sensitive nature of the screening (Autti-Rämö, 2005), risk of discrimination or other complex issues have been considered.

For instance, in the Netherlands the decision making process not to implement NBS for cystic fibrosis (CF) in 2005 was based on different perspectives discussed by stakeholders at the Health Council. The group balanced the pros and cons according to the Wilson and Jungner criteria, to consider the benefit of CF screening for patients. The low specificity of the test was considered to lead to a high rate of diagnostic testing of healthy infants (sweat tests). The test that was available in 2005 had a low sensitivity for immigrants. Also the detection of less severe phenotypes and carriers were considered problematic (Cornel, 2012). The Health Council recommended to undertake a pilot screening project (CHOPIN - Cystic fibrosis heelprick screening in a newborn population in the Netherlands), which led to a 4-step protocol to improve the evidence and test sensitivity to avoid false negative results. Finally an improved CF screening in the Netherlands started in 2011.

Another example is the disease group of haemoglobinopathies (HbP)<sup>1</sup>, e.g. sickle cell disease and thalassaemia, which are serious autosomal recessive disorders and occurred in the past mainly in areas with malaria, such as Africa, the Mediterranean area, the Middle East and South-East Asia. Due to the increasing migration they are now also common in most countries worldwide (Weatherall and Clegg 2001). “As opposed to a long history of neglect of African-American health in the United States, the heritage of the Second World War influenced the decision-making process caused by reproductive issues and fear of eugenics. In 2010 a witness seminar was organised in the Netherlands to discuss the screening implications” (Jans, 2011).

Furthermore an interesting example is also Finland which as present offers screening only for congenital hypothyroidism. This is due to the fact that the incidence of PKU is very low in Finnish population (less than 1:100.000) and therefore PKU-screening is offered just for immigrants (Autti-Rämö, 2012). The multistakeholder group evaluating NBS in Finland concluded that “lacking reliable data on incidence and natural course of the possible other

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1 Haemoglobinopathies (HbP): genetic defect, abnormal structure of one of the globin chains of the hemoglobin molecule

disorders in NBS, sensitivity and specificity of the screening tests, and the effect of early diagnosis and early treatment raised many ethical questions”(Autti-Ramö, 2012). It became evident that a thorough ethical evaluation, further pilot studies and public discussions are needed before NBS can be soundly instituted into the public health care in Finland.

These examples display the complexity of the process of NBS discussions. The hypothesis that the decision making process on the policy level considers also ethical implications was proven in these countries.

### ***Involvement of patients and families in the decision making process at policy level***

The results of the EU evaluation about New Born Screening (NBS) have shown that parent and patient groups do not exist everywhere, and that they were involved in the discussions in only about half of the countries (Burgard et al., 2012, p. 145; Burgard et al., 2011; Cornel et al., 2012, p. 18). It is important to note that even if relevant patient groups existed they were still not always involved in NBS policy-making. However the contribution of patients and families could be very valuable regarding expectations in ethical, legal, social and other issues (Andermann, 2010). From the patient and family perspective the interest of the child should be central in the assessment of pros and cons of NBS, according to European experts (Cornel, 2014). Newborn screening can lead to early diagnosis of several rare diseases, in which considerable, irreparable damage can be prevented.

According to McAllister (2012) patient empowerment is in particular necessary in chronic conditions, such as genetic, endocrine or metabolic conditions in NBS programs. Several literature reviews about patient involvement or empowerment state clearly that this term is not well-defined; rather it is a multidimensional construct. (McAllister, 2012; EPF, 2010, EC, 2012, Moumjid, 2013). The hypothesis that patients and families are essential stakeholders in the decision making process was proved, however these groups are not always involved in the decision process.

### ***Communication and information provision at the level of individual decision making***

An important aspect of the decision-making process for the individual families is the informed consent. Most EU member states emphasise the benefit of screening and therefore half of the countries mandate participation at the screening programme without an informed consent process. However, following the ethical principle of autonomy some countries have an opt-out system (parents will have their child screened unless they specifically state that they do not want this to happen) and some countries have chosen the opt-in procedure (parents are specifically asked to agree to have their baby tested) (Burgard et al, 2012).

Systematic neonatal screening is typical population screening where policy-makers take a measure for the sake of improving public health, without deeming it necessary to consult

everyone and not always respecting their individual choice for consent or agreement (Baily & Murray, 2008). For some conditions as phenylketonuria (PKU)<sup>2</sup> or congenital hypothyroidism (CH)<sup>3</sup> in which early treatment has clearly beneficial outcomes and minimal side effects, it has been considered justified to override parental consent (Orzalesi & Danhaive, 2009).

With new methods and a wider selection of diseases, there is not always soundly proven health benefit for the child. This weakens the paternalistic argument based on the fact that there are strong health benefits for the child (Grill, 2011; Childress et al, 2002). Austoker (1999) stated that in this case an opportunity should be provided to the parents for an informed decision about the neonatal programme.

When there is uncertainty of the outcome of the New Born Screening (NBS) related to a certain disease, advice should be provided based on the best available evidence. Yet, even if an informed consent is considered as necessary, it is not clear what information should be given.

Most European member states inform the parents about NBS already during pregnancy and some specifically in the third trimester of the pregnancy. The parents are informed at two or even three time points in about 40% of the programmes (12 out of 29) (Burgard et al, 2012). Loeber et al. (2012) suggest that the optimal period to provide information seems to be during the last trimester of pregnancy, separated from the information about prenatal screening. However, Burgard and his team reported that 13 of the 29 member states inform the parents only after birth at the time of blood sampling (2012). Loeber argued that it is obvious that “the postpartum period should be avoided because the magnitudes of events and emotions new parents have to face” (Loeber et al, 2012).

All NBS programs provided written information, it was printed (66%), digital (7%) or both (27%) (Burgard et al 2012). An expert group for genetic testing invited by the European Commission emphasised already in 2004 that the provision of simple, printed information that can be consulted by the individual after counselling has been shown to be extremely valuable (McNally et al, 2004, p. 16). According to the American Academy of Pediatrics (AAP) - Task Force on Newborn Screening for information provision to parents (2000) the following facts should be included:

- 1) The benefits of screening;
- 2) The potential risks of the screening test;
- 3) How parents will be informed of screening results;
- 4) The possibility of a false-positive test result;

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2 autosomal recessive metabolic genetic disorder, mutation in the gene for the hepatic enzyme phenylalanine hydroxylase (PAH)

3 Congenital hypothyroidism (CH): a condition of thyroid hormone deficiency present at birth



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- 5) The importance of responding to a positive test result;
- 6) How to respond to a positive test result;
- 7) The screening programme's policy for sample storage and use of stored samples.

Most of the screened disorders are not familiar to the broad population. They are usually very rare and the treatment protocols are complicated. If parents or caretakers gain proper information, including written material at the time of the possible diagnosis, an effective transmission of information and understanding of the child's problem happens and the compliance improves tremendously.

In general several authors were concerned that the readability grade level of information is very high and difficult to understand for people with low literacy (Arnold et al 2006; Fant, 2006). Grosse et al. (2009) points out that parents and experts agreed that there is a need to improve parental education about neonatal screening.

Providers of NBS wanted a brief checklist of necessary information and resources to prepare such information to educate parents effectively (Davis, 2006). Due to the fact that further information of positive results is given usually by the child's primary care physician, there are arguments that information in advance is unnecessary.

Furthermore it is one thing to push an informational folder into the hand of every distracted new parent, but should we really ask a health professional to spend ten or fifteen minutes explaining PKU (and other rare diseases) to each parent when that discussion will prove largely irrelevant 14,999 times out of 15,000?” (Davis, p.45, 2013). Yet, providing information might decrease parental anxiety by emphasizing that an abnormal screening test does not confirm a disease and might enhance timely follow-up by underscoring the need for quick follow-up testing.

The biggest challenge for parents is facing a positive screening result. “Being told that a test result suggests that your healthy-appearing child might have a disease can be an emotionally jarring experience for parents. Within this emotional fog, it may be difficult for parents to process information effectively” (Tarini, 2012). This situation is a demanding challenge for the information provider, usually a physician. There exist mixed opinions whether a face to face communication or a first telephone information is better, also depending on the severity of disease (Salm, 2012). Another study from DeLuca has proven that the first source of additional information after the positive screening result was the internet, even if parents were warned from physicians not to rely on the information there. However, “we were furiously looking on the Internet trying to figure out what it is!” (De Luca, 2011, p. 56). The overwhelming feedback was that the information at the internet was too professional or just scary.

A very positive impression was visiting a metabolic treatment centre, “We felt like we had a

better understanding. We knew the effects, if he had (disorder). We just didn't know what the treatment was like. She was really good about answering our questions about the treatment” (De Luca, 2011, p.56).

Related to the communication behaviour of the physician, Estroff (1994) points out that “since patients will not always share their inner thoughts and feelings with physicians, it is critical that physicians elicit these unspoken emotions. Otherwise, parents and children may continue to suffer in silence and/or present to the physician later on with issues related to a prior traumatic medical experience” (Tarini, 2012). Furthermore communication skills as a part of training of physicians should include a tool to measure “precautionary empathy” (Tarini, 2012). Parents expect the information providers to be well informed, honest, and calm; to disclose the results personally, to avoid jargon, to listen carefully and encourage questions, to recognize parental distress, and to offer realistic reassurance. The pace, amount and rate of information should be appropriate and the physician should assess the parents' understanding. When needed, the family should be referred to a specialist (Salm, 2012). The compliance is better if the values of the families are honoured (Dillard, 2005).

In ethical discussions, “the most commonly expressed fear is that genetic information will be used in ways that could harm people, for example, to deny them access to health insurance, employment, education, and even loans” (Saarni SI, 2008). Europe and the Member states have bundles of antidiscrimination legislation and directives against discrimination regarding employment and insurance. At the regulatory level the situation across the EU appears to be uneven (Varga et al, 2012). Varga et al said that “it is important to note that most EU27 MS have not yet developed legislation or other legal norms relating specifically to genetic testing”. They explained this to be due to a lack of understanding of the specificities of genetic testing (particularly in healthy persons), and its familial, ethical and social implications. An additional reason could be avoiding genetic exceptionalism, deliberately leaving genetic testing to be covered under general health care regulation (Varga et al, 2012).

This view is not shared by everybody. The USA passed in 2008 the Genetic Information Non-discrimination Act (GINA) which prohibits the use of genetic information in health insurance and employment. The National Human Genome Research Institute (NHGRI) in the USA believes that such legislation is necessary so that patients are comfortable availing themselves to genetic diagnostic tests.

According to Henneman and van Hoyweghen (2012), “given recent actions of the Council of Europe's consultation round on ‘Predictivity, genetic testing and insurance’ in the context of the development of a supranational legal instrument (Council of Europe, 2012), the use of genetic information in private insurance remains a timely and hotly debated topic, certainly one to watch on the EU policy agenda”.

In Europe the main on-going discussion about the reconstruction of the Data Protection

Regulation from 1995 is about research, use and storage of health data. According to the first draft from the rapporteur Jan-Philipp Albrecht<sup>4</sup> (2012) “Processing of sensitive data for historical, statistical and scientific research purposes are not as urgent or compelling as public health or social protection. Consequently, there is no need to introduce an exception which would put them on the same level as the other listed justifications. Since then other interest groups have argued that this premise contradicts the international efforts to enhance and promote health research at global level. “The potential exists for rapid advances in (...) healthcare resulting from Whole Genomic Sequencing. Essential to achieving those advances is the need to share, compare and pool data” (EURORDIS, 2013). The discussion is still ongoing and member States are in the process of commenting the present draft.

Burgard et al (2012) argued in the context of storage of the sample/data that there is a widely shared opinion among the neonatal screening community that a length of storage of up to 5 years is usually sufficient to check retrospectively the correctness of the original screening results. The duration of the blood spot storage in the European member states ranges from 3 months like in Germany, up to “1000” years in Denmark or Sweden. The authors Burgard et al (2012) emphasised the potential interest for research and on the other hand, the possible misuse of residual newborn screening specimens. According to the paper from Loeber et al (2012) “informed consent for storage of the dried blood spot sample after the screening (...) and further (scientific) use of the blood sample is lacking in 16 countries while in another eight this information could not be obtained”.

### **Availability of treatment**

One main driver to implement certain screening programmes is specific medical infrastructure, like specific techniques or lab tests, which leads also to the need of specialised experts. NBS has epidemiological value and the results can be used in genetic counselling even in situations where there is no effective treatment. However, as NBS is promoted as a way to improve the treatment of the newborn child, the availability of treatment is a key issue.

According to the research team Loeber et al (2012) “it was to be expected that countries with a lower socio-economic status have a smaller screening panel. On the other hand, preventive medicine through screening can be considered to be cost effective and even some countries with a relatively high socio-economic status still have a relatively small screening panel.” Loeber et al concluded that also requirements for scientific evidence, ethical considerations as detecting of carriers, uncertainty about treatability, etc must be determining factors to implement certain screening programmes.

Goldenberg (2012) continued that “appropriate utilization of these technologies will require the

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4 Member of European Parliament

capacity to manage, interpret, and communicate large amounts of personal genetic information”. Yet the medical and diagnostic infrastructure is facing a recognizable shortage of experts in particular in the field of biochemical genetics across Europe. Even if a treatment is available the scattered access to health care among rare diseases and treatment could increase distress. When executing a systematic neonatal screening programme, the goal is to detect many ill newborn. However, the benefits are linked with the effectiveness of the test and the availability of treatment afterwards (Howell, 2006).

NBS program should provide appropriate clinical pathways for the affected families among national screening programmes (Nährlich & Zimmer, 2013). The authors compared the implementation of cystic fibrosis screening in Switzerland and Germany.

- 1) Both of those countries inform parents: in Switzerland all babies are screened, yet parents can opt out, in Germany parents are asked if they want to have their baby screened - opt-in option.
- 2) In Switzerland the parents receive a telephone call from the cystic fibrosis centre after a positive screening test only when an appointment for further testing can be given there within two days. “Thus, they were never called before the weekend (Rueegg et al, 2013). In Germany, the law requires that the parents must be informed of the results of screening within 72 hours; once informed, the parents must actively seek an appointment for further testing.
- 3) Switzerland has one newborn screening laboratory for all samples, in Germany there are different centres, which could lead to differences in the detection process if different techniques are used (Nährlich and Zimmer, 2013; Rueegg et al, 2013).

The authors recommend steady evaluation and adjustments of the screening strategy across Germany. Cystic fibrosis (CF) is a disease which can't be cured or prevented, nevertheless many studies from around the world show evidence that neonatal screening for CF and early treatment improve the physical development, lung function, and survival of the affected patients (Nährlich and Zimmer, 2013). Another benefit is (Grosse, 2004) that the difficulties of diagnosing CF based on early symptoms are avoided and save the family and health-care system from misdiagnoses, multiple office visits, unnecessary diagnostic tests and hospitalizations (McKaye, 2005; Dijk, 2011).

The possible benefits of NBS are more difficult to show in a disease such as Duchenne muscular dystrophy, where the symptoms manifest only after some years. Timmermans and Buchbinder (2010) suggest calling patients in this situation "patients-in-waiting", as an umbrella concept for those under medical surveillance between health and disease. “Doctors are sharply divided about whether to begin treatment in hopes of preventing the disease's onset” (Dockser, 2013). The Cystic Fibrosis Foundation in the United States, for example, recommend close initial monitoring of these patients (Ren et al, 2011), other experts believe that treatment for the

disease as a preventive measure could be a benefit for the patients (Dockser, 2013). Orzalesi & Danhaive (2009) doubt whether an expanded neonatal screening programme for later-onset diseases can be recommended on ethical grounds. Parents stated that one of main reasons to justify a neonatal screening programme is the avoidance of a long diagnostic quest; arguments relating to reproduction were hardly mentioned in this study (Plass, Pieters, & Cornel, 2010).

The availability of treatment versus non treatment is an important ethical factor. Parents require different informed consent to understand and accept the screening programme in cases like cystic fibrosis where the early diagnosis and treatment available only slightly improves the medical outcome. It may be difficult for parents to comprehend the situation, if disease with effective treatment and no treatment are screened in the same NBS programme.

### *Consequence of Screening and Quality of Life*

Epposi RDIG addressed the question of cost-benefit analysis associated with the whole process including the possible anxiety created as well as the burden of unclear/wrong results and their interpretation. The possible benefits for the wider society should be taken into consideration. The hypothesis included the question to what extent neonatal screening programmes are efficient to improve the overall quality of life of the new citizens, increases their productivity and therefore the economic benefit for the society.

From the ethical point of view Wilson and Jungner (1968) already underlined the importance of a good long-term outcome which should be the ultimate goal of a NBS programme. In the opinion of Baily and Murray (2008), public debates about cost-effectiveness of neonatal screening are often seen as non-ethical. Epposi RDIG felt, that comprehensive cost-benefit analysis, including the views expressed in the [Epposi HTA model how societal benefits can be integrated into National Health Technology Assessment](#), should be performed when deciding about starting a NBS program or adding new diseases to the panel (Epposi -AIP-HTA, 2013). The example of PKU screening and early treatment displays very well the benefit of an easy diagnostic tool and an astonishing outcome for the affected children, to live their life in a good health, which affects also their productivity (Pollit, 1997). The quality of life and cost effectiveness is the most vulnerable ethical point; the measurement of QALYs and DALYs is a possibility to compliment the human factor into the economical calculation.

Detecting carriers and prenatal diagnosis would offer a possibility to prevent the birth of affected children. However, some countries choose not to disclose carrier status of a newborn to the parents on the grounds of lack of immediate medical relevance to the newborn and the view that testing violates the rights of privacy, confidentiality and autonomous decision-making of the newborn (Grosse et al., 2009). Yet, the identification of the carrier status of a newborn might tell that the family is at risk of having an affected child. More often, it would only affect other family members with stress and fear of the knowledge of being a carrier (Autti-Rämö et al., 2012). When weighing the benefits and harms of neonatal screening for carriers it should be noted that finding out the carrier status is not the goal of neonatal screening (Kääriäinen,



2011). Zhang (2004) raised the ethical question if it is morally wrong for couples who found out that they are both carriers of an autosomal recessive disorder to have children given the risk of transmitting a hereditary disease? Zhang in her hypothesis the motivation of people who would argue against pregnancy believe that a child with a disorder would certainly be affected by unhappiness or that the burden of a sick child would lower their quality of life of the family. According to her discussion about the moral duty of the parents not to carry out the child, would be based on the assumption that they would be doing some good for the future of the child, saving it from pain and harm or low quality of life. Actually she fenced that “many people with disabilities have testified the complete opposite and while acknowledging the fact that their condition possesses serious challenges, they may consider their life of very high quality” (Zhang, 2004).

Another issue which affects the quality of life as well as could have economical consequences are false positive results. The percentage of positive test results, when a disease is present is known as sensitivity, the percentage of a negative result when a condition is absent is called specificity (Lalkhen et al, 2008; Tarini, 2007). A lower specificity leads to a higher number of false positive results (Autti-Rämö et al., 2012; Orzalesi & Danhaive, 2009). In the early years of PKU screening, medical professionals observed that mothers of newborn with false-positive PKU results manifested persistent anxiety about the general health of their child despite reassurance that the initial test result was a false positive. Some mention that parents might feel guilt and have problems with self-esteem after discovering their own genetic findings could affect their siblings (Simopoulos & Committee for the Study of Inborn Errors of Metabolism (SIEM, 2009). Thus, a distorted parent-child relationship: “vulnerable child syndrome” might also be developed. The study from Waisbren et al (2003) revealed that infants with false-positive newborn screening results had twice as many hospitalizations for unrelated illness compared with infants with normal results (21% vs 10%) (Waisbren et al, 2003).

The consequences are that children “are inappropriately restricted from normal activity, have more school absences and behavioural disorders, suffer from anxiety, and use more health care resources” (Tarini, 2007). Tarini warned that this potential harm must be recognized and understood, especially if the number of screened diseases will increase, which will lead to an increased number of also false positive results. According to the author it is important to develop interventions to mitigate these problems (Tarini, 2007).

In addition, a false-positive result requires additional diagnostic testing (Grosse et al., 2009), which also triggers fear and self-reproach to afflict their child with these examinations, in particular if multiple retesting procedures are necessary. “His levels were low, but they weren’t low enough, come back. So much that when [my baby] saw the nurses, he would just cry” (Schmidt, 2012).

Some even worry that an excessive increase in use of resources can be at the expense of more useful and less controversial interventions (Autti-Rämö et al., 2012; Orzalesi & Danhaive, 2009).

However, it is important to keep in mind that getting finally a negative test results is a most liberating feeling that all parents are waiting for (DeLuca et al, 2011).

Furthermore, reproductive decisions can also be influenced by a false positive result. Therefore effective and adequate communication, before and after the test is of paramount importance (Orzalesi & Danhaive, 2009).

The Universal Declaration on the Human Genome and Human Rights, issued by the UNESCO in 1997, says in Article 5 (c) that “The right of each individual to decide whether or not to be informed about the results of genetic examination should be respected”. Furthermore the WHO and the Council of Europe acknowledged the right to remain in ignorance: “the wish of individuals and families not to know genetic information, including test results, should be respected” (WHO, 1997; EC,1997).

Swartling et al (2007) stated that the ‘right not to know’ one’s genetic status has been increasingly more recognised in ethical and legal instruments. They carried out a longitudinal clinical cohort study in a time span of 5 years, with 7206 families in South-East Sweden in their fifth year of participation in the ABIS study (All Babies in South-East Sweden). “While the majority were positive towards disclosing information, two percent (n=142) of the study population stated that they did not want to be informed, regardless of whether a prevention or intervention was available” (Swartling et al 2007).

In the recent survey from Vermeulen et al (2013), about the perceptions of genetic testing, half of the respondents expressed an interest in genetic testing to prevent specific diseases (cancer, cardiovascular disease, diabetes or dementia). Interestingly, people with lower education show more interest than higher-educated respondents. Just 24% agreed that people should be predictively tested for all kinds of diseases, if they are curable (57%) or preventable diseases (69%). Vermeulen and his team reported that of the responder 1399 respondents 978 believed that family history assessment could be helpful to prevent disease, but only 21% thought it should be collected from everyone, as this could cause people to be worried. It was concluded that different interests in preventive genomics exist, which varies depending on sex, age and level of education (Vermeulen et al, 2013).

Henneman and van Hoyweghen (2013) argued in their paper “Moving beyond public fear of genetic discrimination” that the predictive in medicine is clearly not only based on genetics, other risk factors may be even more important such as family history, past history of diseases and lifestyle factors.

It is indeed not easy to cope with the consequences of a lifelong treatment, in particular with diseases which can’t be cured or prevented like cystic fibrosis (Cornel, 2010). However screening provides a big chance for the children, their family and at least for the society to support people with a life threatening diseases.

## Conclusion

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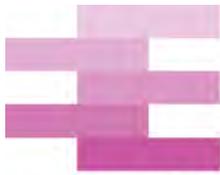
According to our literature review, the following issues seemed to be important in relation to NBS programs. The economic perspective and availability of screening tests are crucial for the decision making process at the policy level. However, studies in the Netherland and Finland have shown that also topics related to ethical and scientific issues like test properties, discrimination or other complex issues were included in the discussion. The literature review could also prove that patient and family representatives are important stakeholders among the decision making process. McAllister has shown the importance of patient empowerment in the field of genetics to support the families in their decisions.

Regarding the decision making process of the families, there is discussion on the justification of informed consent if NBS is based on paternalistic argument that refers only to benefit of the child. Proper prior information for the parents is seen useful not only as related to consent but also to prepare the parents to the different outcomes of the test. In the context of communication, studies have shown that “availability of written material can be regarded as particularly important, since it can support parents understanding of and coping with the diagnosis of the chronic disorder in their children” (Burgard et al 2012), this includes increasingly also digital information sources. Parents should be aware in advance what will happen and what this screening means for their child. However, there is no consistency about the optimal timing. Related to the communication, also information about data protection and storage of blood sample are important points which should not be neglected.

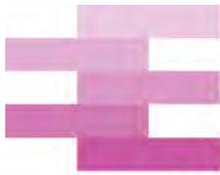
The example of PKU screening and early treatment displayed the benefit of an easy diagnostic tool and an excellent outcome for the affected children. QALYs and DALYs are good possibility to complement the human factor into the economical calculation. Even if the screening is increasingly accepted among the population, there are still elements that could be improved. As Deigh (1995) defined ethics as norms or moral implication of a group who decides about an acceptable or unacceptable behaviour, a better communication, education and public discussion is urgently needed.

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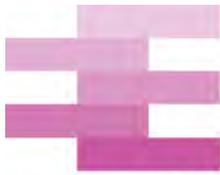


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