



Background information on Newborn Screening

This document gives a brief overview of Newborn Screening (NBS). It focuses mainly on information and activities that are relevant to reducing the burden of congenital disorders.

What is Newborn Screening?

Newborn or neonatal screening aims to identify newborns with serious, treatable disorders, so as to facilitate appropriate interventions to prevent or ameliorate adverse outcomes such as developmental delay, serious disability or death.

Newborn screening is more than laboratory testing. It is a coordinated and comprehensive system that includes parent and provider education, administration of the screening test, sample collection and processing, follow-up, diagnosis, treatment, management and programme evaluation.

Newborn screening tests include not only blood tests but also other types of investigation including hearing tests and physical examination.

Factors to consider in determining whether to screen for a disorder

The recommendations for screening policy vary from country to country and region to region, depending on the local burden of specific conditions, local economic factors, and how public health is organised.

The International Society for Neonatal Screening (<http://www.isns-neoscreening.org/htm/generalguidelines.htm>) recommends newborn screening for disorders where:

- there is demonstrated benefit from early diagnosis
- the benefit is reasonably balanced against financial and other costs
- there is a reliable test suitable for newborn screening
- there are satisfactory systems in operation to deal with diagnostic testing, counselling, treatment and follow-up of newborns identified by the test.

Introduction of a screening programme may not be recommended where there is poor communication between central services (such as laboratory services) and the primary care

level, where resources are limited, or where appropriate referral and follow-up are not in place or cannot be assured to all.

The WHO criteria developed for countries where resources are limited have been used as the illustrative example within the Toolkit (Appendix 1). Other criteria are available and countries are free to use the criteria that best suit their needs.

Examples of conditions included in newborn screening

Newborn screening can be divided into three main areas: newborn physical examination, newborn hearing screening, and screening for biochemical defects such as inborn errors of metabolism, haemoglobinopathies, glucose-6-phosphate dehydrogenase deficiency and cystic fibrosis.

Conditions detected by physical examination

Physical examination, by 72 hours and again at 6-8 weeks after birth, aims to detect conditions and abnormalities such as congenital heart disease; other congenital malformations including congenital dislocation of the hip; cryptorchidism and undescended testes; congenital cataracts and other media opacities; anatomical abnormalities and other dysmorphologies. Some of these abnormalities may not be obvious by simple observation.

Hearing defects

Newborn hearing screening, by 4-5 weeks after birth, aims to identify newborns with moderate to profound bilateral deafness or hearing impairment. This supports earlier intervention (communication support, hearing aids, cochlear implants) which can enable the child to develop better language and communication skills, and consequently lead to improved educational and social development.

Hearing loss is one of the most common congenital disorders worldwide, with an incidence of around 1-3/1,000 births. It has been estimated that 718,000 infants are born each year with congenital or early onset permanent bilateral hearing loss, and more than 90% of these births occur in developing countries. Consanguineous marriage, high prevalence of infectious diseases and inadequate management of birth asphyxia contribute to higher rates of congenital hearing loss in developing countries. A large proportion of cases (around two thirds of total cases) with moderate to profound hearing loss will not be identified if only neonates with risk factors are screened for hearing loss. Though the optimum period for intervention to increase communication development is ill-defined, it is clear that cases detected earlier tend to have better language development. For these reasons, a universal newborn screening programme has been adopted by many countries.

Biochemical defects

Screening for biochemical defects is usually offered between 24 hours and 7 days after birth. Earlier screening is usually carried out before discharge from hospital, if no follow-up or home visits are carried out or if screening involves testing of cord blood (for example, for glucose-6-phosphate dehydrogenase deficiency). Worldwide, phenylketonuria (PKU) and congenital hypothyroidism (CHT) are the two most frequently screened conditions. Screening for PKU allows prevention of severe disability as the initiation of a low-phenylalanine diet immediately after birth can prevent neurological damage and learning disability. Similarly, in CHT, early treatment of the newborn with oral thyroxin can prevent learning disability and lead to resumption of growth. In addition to PKU, a large number of

other inborn errors of metabolism have been identified. The common feature of these conditions is lack or insufficient activity of an enzyme in a metabolic pathway, leading to accumulation of metabolic intermediates that are toxic in high concentrations. Examples include galactosaemia, maple syrup urine disease, and medium chain acyl CoA dehydrogenase deficiency. Dietary modification or enzyme replacement therapy, initiated as soon as possible after birth, can prevent symptoms including developmental delay, convulsions, jaundice and liver damage.

In some countries and among some ethnic groups, the genetic mutations causing certain other types of biochemical defects occur with elevated frequency. For example, sickle cell disease, a disorder of haemoglobin production, is relatively more common in populations of sub-Saharan African origin. Signs and symptoms of sickle cell disease include anaemia, repeated infections, and periodic episodes of pain. Diagnosis in the newborn period and prompt initiation of treatment, particularly antibiotic prophylaxis to prevent infections, reduces mortality and morbidity.

Glucose-6-phosphate dehydrogenase deficiency occurs with increased frequency in Africa, as well as in the Middle East, the Mediterranean and Asia. Newborn screening to identify severe forms of the disease enables preventive treatment to avoid neonatal hyperbilirubinaemia and acute haemolysis resulting from oxidative stress caused by infection, oxidative drugs or ingestion of fava beans.

Cystic fibrosis (CF), caused by mutations in a protein that regulates the transfer of salt and water across cell membranes, causes severe pathology of the lungs and digestive system as a result of the accumulation of thick mucus. Early recognition enables alleviation of symptoms by, for example pancreatic enzyme supplementation, antibiotic treatment to prevent recurrent lung infections, and bronchodilator drugs and physiotherapy to help clear airways.

The number of conditions currently tested for in newborn screening programmes varies considerably by country or region. Further information on conditions tested for and examinations made in the newborn period across some low and middle income countries (LMIC) are given in Append 2: Tables 1a, 1b and 1c. The tables are not intended to be exhaustive and should only be used as a guide to activity in these countries. It will be possible to update this resource as fresh information becomes available. Estimates for haemoglobin disorders by country can be found by through following the link at the UCL Centre for Health Informatics & Multiprofessional Education (CHIME). CHIME link (<http://www.chime.ucl.ac.uk/work-areas/cab/hb/world.sear.pdf>).

Newborn screening tests

The performance of a screening test is measured by its sensitivity and specificity. Sensitivity indicates the proportion of all newborns with the condition that are identified by screening. Specificity indicates the proportion of newborns with a negative test among all screened who are condition-free. A screening test, in addition to abnormal or borderline diagnoses, will give false-positive results (a newborn without the disease having positive test result) and false negative results (a newborn with the disorder having a negative test result). False negative results may lead to delayed diagnosis and treatment for affected children.

Physical examination

Basic physical examination of the newborn can be performed immediately after birth by a birth attendant or a trained health care worker. It is based on observation of the baby's general condition including colour, breathing, pulse, behaviour, activity and posture and detection of some obvious gross abnormalities.

Examination for gross abnormalities may include, in addition to the basic physical examination, observation for general symmetry of the head and facial features; examination of the fontanelles; examination of the eyes for discharge and obvious opacities; observation of the limbs, hands, feet and digits for symmetry; inspection of the bony structures and skin of the newborn's spine; observation of the genitalia and anus to check for completeness and patency; noting of birth weight; sound of newborn's cry; and maternal/household psychosocial and socioeconomic risks.

Detailed physical examination, by 72 hours and again at 6-8 weeks after birth, is ideally performed by a trained health care professional and requires instruments such as an ophthalmoscope, stethoscope, tape measure, a flat surface and a well-lit and warm environment. It includes measurement of head circumference and birth weight; inspection for cleft palate visually using light and tongue depressor or digitally if submucous cleft palate is suspected; examination of the eyes using ophthalmoscope for opacities including cataract and retinoblastoma (red reflex); examination of the heart (cyanosis, tachypnoea, murmur, femoral pulses); examination of the genitalia for cryptorchidism/undescended testes; and examination for congenital hip dysplasia using the Barlow and Ortolani manoeuvre.

The ability to detect some of these conditions depends on the level of expertise of the examiner and the severity of the condition. Detailed physical examination also includes a review of family, maternal and perinatal history.

The routine use of imaging methods, such as ultrasound, may yield higher detection rates for congenital anomalies, but has important cost implications.

Hearing screening

Simple measures for checking hearing include parents/carers following the developmental milestones of the infant; for example, noting if the infant has delayed babbling and is not responding to non-visual stimuli. However, this approach may lead to late diagnosis and missing the benefits of early intervention.

The Infant Distraction Test (IDT) may be offered to infants 8 months or older. A stimulus, usually live voice, a 'warble' electronic tone or a rattle, is presented to the side and slightly behind the infant by a health worker whilst the infant is sitting on the parent's knees.

Localising the sound on each side represents a pass. If the stimuli are not localised the test is repeated at a later date. Following a second failure to localise the infant is referred for further assessment. The sensitivity of this test is highly dependent on the severity of the hearing impairment. Its major benefit is that it is not dependent on specialist equipment or highly skilled personnel and may be undertaken in the infant's home. However it has low sensitivity and specificity; that is, it can miss infants with hearing loss or falsely identify an infant as having hearing impairment.

Equipment-based screening can be based on using Otoacoustic Emission (OAE) testing and/or Auditory Brainstem Response (ABR) testing. In OAE, a probe is placed into the infant's ears. The probe emits a series of clicks and records the response generated. The equipment specifies 'pass' or 'refer' depending on presence of response. This approach gives an early (even from the first day of birth) and objective assessment. Non-specialist staff may be trained to perform OAE with high levels of specificity and sensitivity. However, it requires specialist equipment and it is not sensitive to defects beyond the inner ear (e.g. cortical deafness). Middle ear pathology (such as middle ear effusion) and high ambient noise levels can give false positive responses.

In ABR, a probe is placed into the infant's ears, clicks are generated by the probe and the corresponding electrical activity in the brain is recorded through sensor electrodes placed on the scalp. ABR is best performed when the infant is asleep. ABR detects function in the outer, middle and inner ears and the auditory pathways to the brainstem; however, it is only able to detect pathology, not to locate it. ABR testing is usually performed as a second stage screening for those who have a positive or borderline finding on OAE.

The combined programme sensitivity of OAE and ABR is around 85%, i.e. such a screening programme can detect 85% of the infants with hearing loss. Equipment-based screening can be done in hospital after birth and before discharge, or in the community setting. Testing before discharge from hospital is convenient and ensures high uptake, but delaying OAE to around 4 - 5 weeks can reduce the false positive findings caused by middle ear effusion, thus reducing the need for subsequent testing with ABR. With this in mind, delaying screening until the time of immunisations (4 to 8 weeks) may be recommended, allowing screening tests to be coordinated with clinics. Immunisation clinics provide a good opportunity to offer integrated services for newborn care including screening for hearing loss.

Newborn bloodspot test

The most common approach is the analysis of bloodspots collected on 'Guthrie cards'. In the Guthrie method, a blood sample from a heel-prick is allowed to drop on to a filter paper card to form a series of discrete spots. The card is then dried and transported to the screening laboratory, where small discs are punched from the dried bloodspots and used in a bacterial inhibition assay or other enzyme assays. An alternative approach is to collect the blood sample in a small heparinised capillary tube; this is more laborious but gives better results for several tests.

A range of biochemical disorders can be diagnosed through analysis of Guthrie spots, including fatty acid oxidation defects, organic acidaemia, urea cycle defects, amino acidopathies, haemoglobin disorders and glucose-6-phosphate deficiency. The Guthrie method is robust, cheap and has good performance, but is semi-quantitative. Recent technological developments such as tandem mass spectrometry (tandem-MS) could allow a

large number of conditions to be detected from a single dried bloodspot. However, it cannot be used for screening of all disorders and conditions such as CHT, CF and haemoglobinopathies will require other assays for screening.

For the two most commonly screened conditions, CHT and PKU, the overall sensitivity of screening is more than 95% and 98% respectively. The false-positive rate is less than 1% for both conditions. However, the variability in some disorders can affect the test performance. A screening test designed to detect the 'classical' clinical form, for example of an inborn error of metabolism, may miss milder variants. This can result in some minor biochemical variants of no clinical significance being considered as false positives. Factors that can contribute to false negative results include contaminated specimen, mislabelled or denatured specimen (heat, alcohol etc.), a test undertaken at too early an age when there has been inadequate substrate intake to produce metabolite accumulation, genetic heterogeneity, poor discrimination between normal and affected ranges, poor performance of the laboratory assay, and laboratory error.

Steps that follow abnormal screening results include retesting within the laboratory on the same sample, either for the same analyte and/or a different one, requesting a repeat blood specimen, follow up testing (for many disorders, a presumptive positive diagnosis can be made without requiring follow-up testing), and clinical referral.

It is important to have screening protocols in place to clearly define what is to be screened for and at what age; how the samples will be collected and analysed; what analyte will be used as an initial screen and whether the first screen will be followed by a secondary test to optimise sensitivity and specificity; the cut-off point to define positive and negative results; and follow-up of screening test results.

Care pathway and Newborn Screening

Newborn screening is part of an overall care pathway that includes family planning and reproductive health care services; preconception care, focusing on preparing for a healthy pregnancy and incorporating preconception carrier testing where appropriate; prenatal care and screening services with clearly defined links to the newborn screening programme; newborn screening; and care planning and service delivery for any disorders identified.

The components of the pathway should be integrated, so that risk factors identified before conception in the mother are carefully monitored during the prenatal period and any effects on the child are identified in the newborn period. At each stage, an appropriate plan for treatment and care of affected individuals needs to be considered and put into place.

Newborn bloodspot testing and physical examination (including a hearing test) of the newborn allows early diagnosis and planning of care. This may involve surgical procedures to treat a structural defect, dietary intervention or enzyme replacement for inborn errors of metabolism, early recognition and treatment of complications (for example, antibiotic treatment to prevent infections in sickle cell disease and glucose-6-phosphate dehydrogenase deficiency). Consideration must also be given to the social and psychological needs of people with disabilities and their families.

The components of a newborn screening programme

There are various components of a newborn screening programme that go beyond the actual tests and examinations that are undertaken. The following components have been identified.

- **Protocols/policy statement:** There should be policies/protocols/guidelines for all components of the programme including follow up, treatment and monitoring. Ideally they should be evidence-based.
- **Education of parents and providers:** Educational materials and other interventions should be linguistically and culturally appropriate. Processes should be in place for review and update.
- **Data collection/evaluation:** Clarity is needed on what data are to be collected, by whom and when. Decisions must be made on whether data systems will be local, regional or centralised, and whether records will be held on computer, on paper or a mix. Ethical practice should be ensured, including recording consent of parents/carers, and maintaining confidentiality of information. Procedures should be in place for back-up of information and storage of biological samples. Quality control procedures include protocols on whom/what is to be checked, how checking will be done, and how the information will be analysed.
- **Equipment/technology:** Consideration needs to be given to the availability and maintenance of appropriate equipment and technology, and training in its use. Measures for ensuring quality control, validation of results and back up should be in place.
- **Coverage:** Newborn screening for certain conditions is mandatory in some countries; for other conditions, there may be a predetermined target for coverage. Consideration needs to be given to health inequalities if screening is not, or is not intended to be, universal. Coverage should be monitored and records should include details on refusals.
- **Resources:** Resources include equipment, medical and paramedical staff (including training), buildings, maintenance, transport, and administrative support. The programme needs to be adequately financed, with decisions made on whether financing will come from private payments, insurance, public funds or outside agencies (such as charities or NGOs). There should be integration into business plans to ensure stability of the programme over the medium/long term.
- **Responsibility:** There should be clarity on how the service is run and by whom, how the programme is coordinated and what the structure looks like, e.g. local, regional or central. When a genetic condition is identified, it should be clear who is responsible for communicating the implications to family members.

Cost-effectiveness of screening

Studies looking at cost-effectiveness of newborn screening in developed countries usually agree that screening is cost-effective and/or cost saving for certain conditions but not necessarily all. Results depend on the costs involved, test characteristics and the birth prevalence of the condition(s). Key to realising the benefit of screening is the ability to detect a condition at an early stage where treatment can potentially avoid or reduce sequelae of the disease. In the developed world, costs include health care and social care costs that may not be transferable to a low or middle income country.

Countries are advised to undertake their own analysis that is relevant to their particular needs. For cost-effectiveness cut-off points for different regions of the world, go to http://www.who.int/choice/costs/CER_levels/en/index.html, and for costs for specific items by region and county, go to <http://www.who.int/choice/costs/en/>.

What are the main ethical legal and social issues (ELSI) to consider?

Some countries and professional organisations have guidelines for newborn screening that include consideration of ethical, legal and social issues. Examples include the International Society for Neonatal Screening (see key references).

The balance of harms and benefits

Newborn screening is only justified ethically where there are demonstrable clinical benefits to the child. If early diagnosis does not improve clinical outcomes, if treatment is not available or is restricted to those with sufficient resources to pay for it, or if follow-up treatment and care are of poor quality, the harms of screening may outweigh the benefits. These considerations are particularly important if screening is mandatory. In the case of genetic conditions, it may be justifiable to consider the benefits of early diagnosis in making parents aware of any risk to subsequent pregnancies.

Consent

Unless screening is mandated by the state, the informed consent of the parent(s) is required. Important issues in seeking consent include the information provided before and after testing (both about the screening process itself and the consequences that flow from acceptance or refusal); the process for obtaining informed consent and how it is documented; and the balance between the rights of the parents to refuse screening on moral or religious grounds, and the rights of the child to benefit from screening. As screening is carried out before the individual concerned is able to give their own consent, any subsequent desire not to know this information cannot be respected.

Equity

Equity relates to the ability of all of the population at risk being able to benefit from screening and whether the programme will be universally accessible.

Potential discrimination and stigmatisation

Screening for diseases risks labelling and stigmatising individuals found to have a condition, even if the condition does not cause symptoms (for example, if the individual is identified as a carrier) or treatment is available which renders the individual asymptomatic. Stigmatisation may lead to discrimination in job, insurance and marriage prospects.

Psychosocial issues

False positive or false negative results from screening tests may cause parents unnecessary stress or false reassurance, respectively. Distress may also be caused by disclosure of incidental findings such as carrier status for recessive genetic conditions.

Confidentiality of information

Measures should be in place to ensure the confidentiality of the test itself and any information arising from it. Issues that must be considered include communication with other family members who may be affected, in the case of genetic conditions; and criteria

governing wider dissemination or restriction of information to other interested parties (such as insurers, employers or the state).

Storage of samples

Samples such as Guthrie cards may be stored for many years. Procedures must be in place for secure storage, with clear criteria for who may have access to samples and for what purposes (e.g. research, forensic use etc.).

KEY REFERENCES

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Driscoll CJ, McPherson B. *Newborn Screening Systems: The Complete Perspective*. San Diego, USA: Plural Publishing Inc; 2010.

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RELATED TOPICS

Congenital hypothyroidism
G6PD deficiency
Sickle cell disease
Thalassaemias
Preconception screening and care
Health services
Teratogens

APPENDIX 1: World Health Organisation criteria for deciding whether or not to use health screening in the context of resource limited countries

1. Is the condition to be detected of public health importance?
2. Are there effective preventive or curative measures to deal with the condition when it is detected at an early stage?
3. Is there a safe, ethical and efficacious procedure for detecting the condition at a sufficiently early stage to permit effective intervention?
4. Are the screening procedures, definitive diagnosis and the appropriate interventions acceptable to the population?
5. Is it feasible to carry out the relevant screening, diagnostic and timely intervention practices in a population based fashion with existing resources or with resources that could be obtained during the planning period, given sufficient political will?
6. Will the adoption and implementation of the screening, diagnostic and timely intervention practices strengthen development of the health system and overall societal development, in a manner consistent with primary health care principles?
7. Is the cost of the screening and timely intervention efforts warranted, given all the considerations in items 1-6 above and in comparison with alternative uses of the resources?

APPENDIX 2: Newborn Screening in LMIC countries

Table 1a: Newborn screening in low income countries

Country	Blood screening	Newborn incidence/prevalence
Bangladesh	CHT pilot in 2003 (2003), now offered to whole population (2007)	CHT incidence 1 in 1,300 (2003)
Benin	SCD in two maternity services in Cotonou (2009)	
Burkina Faso	Pilot for SCD (2009)	SCD incidence 1 in 57 in Ouagadougou (2009)
Burundi	Pilot for SCD in Central Africa 2004 - 06 (2007)	As part of study in central Africa SCD incidence 5.32% (2007)
Central African Republic	Pilot for SCD in Central Africa 2004 - 06 (2007)	As part of study in central Africa SCD incidence 5.32% (2007)
Congo, Dem. Rep	SCD programme introduced (2009)	16.9% sickle cell trait, 1.4% homozygous for HbS (2009)
Ethiopia	Pilot CHT testing 1996/97 (2000)	
Myanmar	Pilot testing/select population screening for CHT (2007)	
Senegal	Pilot for SCD reported in 2003 (2003)	Incidence SCD 11.1% (2003)
Vietnam	Pilot testing/select population screening for CHT and G6PD deficiency (2007)	
Yemen, Rep.	Pilot was expected August 2008 for CHT and PKU (2009)	

Years in brackets refer to the year the document was published from where the information was obtained.

CHT: Congenital hypothyroidism

G6PD def: Glucose-6-phosphate dehydrogenase deficiency

HbS: Haemoglobin S

PKU: Phenylketonuria

SCD: Sickle cell disease

Table 1b: Newborn screening in lower middle income countries

Country	Blood screening	Other screening	Newborn incidence/prevalence
Armenia	CHT nationwide (2007)		
Bolivia	Tests made on request: CHT, PKU, CF, galactosaemia, CAH, biotindias & MSUD (2007)		Incidence of CHT 1 in 3,171 (2007)
China	Varies across country. Most of testing is not free (2009). CHT, PKU and G6PD deficiency are some of the diseases tested for (2003, 2009). Pilot reported for Fabry disease (2009). CHT and PKU offered to full population being screened, other amino acid disorders, fatty acid oxidation disorders, organic acid disorders pilot testing or select population screening (2007)	Possible checks for hip dysplasia (various papers consider different techniques for hip dysplasia) Hearing: OAE in Hong Kong from 2003. 95% coverage 1st year.	
Ecuador	Tests made on request for: CHT, PKU, CF, galactosaemia, CAH, MSUD and aminoacidopathies (2007)		
Egypt, Arab Rep.	CHT, consideration of PKU, galactosaemia, β thalassaemia. Some samples sent to Saudi Arabia for MS/MS for MSUD, MMA, PPA, MCADD, PKU, GA1 and urea cycle defects (2007)		
Guatemala	CHT, PKU, galactosaemia and CAH as non-mandatory programmes (2007)		CHT incidence 1 in 1,715 (2007)
Honduras	Pilot for metabolic disorders (2009). No newborn screening activities (2007)		
India	National pilot for CHT and CAH covering 100,000 infants due to start (2009). Pilot or select population screening for: CHT, PKU, galactosaemia, MSUD, CAH, homocystinuria, CF, G6PD def, other amino acid disorders, fatty acid oxidation disorders (2007)	Hearing programme in Pune using OAE (2009)	
Indonesia	Pilot or select population screening for CHT (2007)		
Iran, Islamic Rep.	Screening project for CHT done in Isfahan 2002 - 05 (2005)		CHT 1 in 350 in Isfahan (2005)
Jordan	Plans for CHT to be in place by end 2008 then for PKU to be added (2009)	Hearing: Done on pilot basis, to be initiated on a national basis (2009)	
Maldives	Possibly CAH (1989)		
Moldova	PKU nationwide but temporarily suspended (2007)		

Table 1b: continued

Mongolia	Pilot for CHT done in Ulaanbaatar (2003). CHT offered on pilot/select population screening (2007)		
Morocco	Pilot plan for CHT from 2009 for 1 yr (2009)		
Nigeria	SCD screening has been considered (2008)	Pilot for universal screening in Lagos 2005 - 08 used transient evoked OAE and automated ABR test (2009)	SCD in newborns at hospital in Benin city 3% (2008)
Pakistan	All babies born at Aga Khan University are screened for CHT (2009). Pilot testing or select population screening for CHT (2007)		
Paraguay	Pilot in 1999 for CHT and PKU (2004)		

Years in brackets refer to the year the document was published from where the information was obtained. Full references are given in the reference paper.

ABR: Auditory brainstem response
 CAH: Congenital adrenal hyperplasia
 CF: Cystic fibrosis
 CHT: Congenital hypothyroidism
 G6PD def: Glucose-6-phosphate dehydrogenase deficiency
 GA1: Glutaric acidaemia type 1
 MCADD: Medium Chain acyl CoA dehydrogenase deficiency
 MMA: Methylmalonic acidaemia
 MS/MS: Tandem mass spectrometry
 MSUD: Maple syrup urine disease
 OAE: Otoacoustic emission
 PKU: Phenylketonuria
 PPA: Propionic acidaemia
 SCD: Sickle cell disease

Table 1c: Newborn screening in upper middle income countries

Country	Blood screening	Other screening	Newborn incidence/prevalence
Algeria		Possibly hip checks but needs improving (1990)	
Argentina	Mandatory testing for CHT and PKU. Tests for CF, galactosaemia, CAH, biotinidase deficiency, MSUD, aminoacidopathies, organic aciduria are made on request. Newborns tested for Chagas disease and syphilis where mother is positive (2007)		Incidences: CHT 1 in 2,225 PKU 1 in 27,275 (2007)
Belarus	PKU and CHT nationwide (2007)		PKU prevalence 1 in 7,309 (2007)
Bosnia and Herzegovina	CHT may not be country wide (2009). CHT and PKU nationwide (2007).		CHT prevalence 1 in 3,957 (2009)
Brazil	National programme started 2001 for PKU, CHT, SCD and CF (mandatory) (2008). Studies done for congenital toxoplasmosis and galactosaemia (2009). Galactosaemia, CAH, biotinidase deficiency, MSUD, G6PD deficiency, aminoacidopathies, MCADD, congenital toxoplasmosis, Chagas disease, rubella, HIV and CMV tests made on request (2007)		Incidences: CHT 1 in 2,453 PKU 1 in 25,294 (2009) 1 in 770 live births in Minas Gerais state positive for congenital toxoplasmosis (screened for IgM on dried bloodspot) in study (2009).
Bulgaria	Probably CHT (1997)	Dislocation of hip, Stara Zagora (1996) Hearing: national programme, organised differently across the country (2004)	
Chile	Mandatory programme covers CHT & PKU. Tests on request cover: MSUD, Tyr1, PPA, MMA, IVA, MCADD, SCADD and GA1 (2007).		Incidences: CHT 1 in 3,069 PKU 1 in 19,510 (2007)
Colombia	Mandatory programme covers CHT only. Tests on request cover: galactosaemia, CAH, biotinidase def, MCADD & LCHADD. Pilot programme/on request: PKU & haemoglobinopathies (2007)		CHT incidence 1 in 2,186 (2007)

Table 1c: continued

Costa Rica	Mandatory programme covers: CHT, PKU, galactosaemia, MSUD, CAH, haemoglobinopathies, PA, MMA, IVA, GA1, 3 methylcrotonyl-CoA dehydrogenase def, β -ketothiolase def and 3 hydroxy 3 methyl glutaric aciduria, MCADD, VLCADD, LCHADD, SCADD, CPTIID & glutaric acidaemia type II. Pilot programmes for CF and biotinidase def (2007)		Incidences: CHT 1 in 3,195 PKU 1 in 49,179 (2007)
Cuba	CHT and PKU (2004). Consideration of testing for biotinidase def (2006). Non-mandatory programme but of systematic and universal scope: CHT, PKU, galactosaemia, CAH, biotinidase def (2007).	Physical exam: possibly some sort of programme (2005)	
Dominican Republic	Tests on request: PKU, haemoglobinopathies. Pilot: CHT (2007)		CHT incidence 1 in 3,600 (2007)
Jamaica	SCD (2007)		
Latvia	CHT mass screening started 1996 and PKU mass screening started 1987.		Prevalences: PKU 1 in 6,780 CHT 1 in 3,390 (2007) Incidences: PKU 1 in 8,700 CHT 1 in 6,450 (1999)
Lebanon	40 diseases privately. Approx 50% coverage. MS/MS with international support (2008). Consideration of G6PD deficiency screening in males (2007).		
Libya	National programme for CHT and PKU to start 2009.		
Lithuania	CHT and PKU (2007)		Prevalences: PKU 1 in 9,718 CHT 1 in 9,718 (2007)
Macedonia, FYR	CHT (2008) and PKU (2007)		
Malaysia	G6PD deficiency and CHT offered to full population being screened. Other amino acid disorders, fatty oxidation disorders and organic acid disorders available as pilot testing or select population screening (2007).	Hearing (2008)	CHT incidence varies from 1 in 2,400 to 1 in 3,666 (2007)

Table 1c: continued

Mexico	Mandatory programme for CHT. Tests on request/ non-mandatory programme: aminoacidopathies, organic aciduria, fatty acid oxidation. Pilot: CAH, biotinidase def, MSUD, PKU (2007).		Incidences: CHT 1 in 2,497 (2007) CHT 1 in 2,326 (2008) In Nuevo Leon estimated incidence IEM 1 in 5,000 (2008)
Montenegro	CHT and PKU (2007)		
Palau	Contracted with Philippines to offer CHT, PKU, galactosaemia and MSUD (2007).		
Panama	Tests made on request: CHT, PKU, galactosaemia, G6PD deficiency (2007).		
Peru	CHT mandatory since 2006, non-mandatory programme CAH (2007).		CHT incidence 1 in 2,439 (2007)
Poland	Population based for CHT and PKU (2007). MS/MS for PKU, MSUD, Tyr1, MCADD, LCHADD, VLCADD, CPTID, CPTIID/CACT, CTD, IVA, GA1 (2007)	Possibly check for dysplasia of hip. Hearing: universal OAE testing started 2002	
Romania	PKU and CHT (2008)		
Russian Federatio	Pilot CAH and CF, universal CHT and PKU (2007). Universal CF from Jan 2007 (2007).		Prevalences: PKU 1 in 7,714 CHT 1 in 3,102 CAH 1 in 8,000 CF 1 in 3,714 (2007)
Serbia	CHT and PKU nationwide (2007)		Prevalences: PKU 1 in 11,420 CHT 1 in 3,001 (2007)
St. Lucia	CHT and possibly galactosaemia (1988, 1991)		
Uruguay	Mandatory programme CHT. Tests made on request/pilot PKU, pilot programme CAH (2007).		CHT incidence 1 in 2,064 (2007)
Venezuela, RB	Tests made on request: CF, galactosaemia, G6PD deficiency. Tests made on request/ non-mandatory programme: CHT and PKU (2007)		CHT incidence 1 in 3,333 (2007)

Years in brackets refer to the year the document was published from where the information was obtained. Full references are given in the reference paper.

CACT: Carnitine acylcarnitine translocase deficiency
CAH: Congenital adrenal hyperplasia
CF: Cystic Fibrosis
CHT: Congenital hypothyroidism
CMV: Cytomegalovirus
CPTID: Carnitine palmitoyltransferase I deficiency
CPTIID: Carnitine palmitoyltransferase II deficiency
CTD: Systemic carnitine transporter deficiency

GA1: Glutaric acidaemia type 1
G6PD: Glucose-6-phosphate dehydrogenase
IgM: Immunoglobulin M
IVA: isovaleric acidaemia
LCHADD: Long Chain L 3 hydroxyacyl CoA dehydrogenase deficiency
MCADD: Medium Chain acyl CoA dehydrogenase deficiency
MMA: Methylmalonic acidaemia
MS/MS: Tandem mass spectrometry
MSUD: Maple syrup urine disease
OAE: Otoacoustic emission
PKU: Phenylketonuria
PPA: Propionic acidaemia
SCADD: Short Chain acyl CoA dehydrogenase deficiency
SCD: Sickle cell disease
Tyr1: Tyrosinaemia type I
VLCADD: Very long chain acyl CoA dehydrogenase deficiency