Community genetics services

Report of a WHO Consultation on community genetics in low- and middle-income countries

Geneva, Switzerland,
13–14 September 2010

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Executive summary

Community genetics has been defined as "the art and science of the responsible and realistic application of health and disease-related genetics and genomics knowledge and technologies in human populations (communities) to the benefit of individual persons." The objective of this Consultation was to develop an evidence-based report on community genetics services to provide guidance to low- and middle-income countries (LMIC) in accordance with the *2008–2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases* (NCDs). The goal of community genetics in LMIC is to prevent congenital disorders and genetic diseases at population level and, at the same time, to provide genetics services (diagnosis and counselling) in the community for individuals and families. The term "prevention" is used in this report to indicate actions implemented with the indivisible objectives of reducing the birth prevalence and health impact of congenital disorders and genetic diseases, while respecting voluntary reproductive decisions.

A Group of experts (listed at the end of this report), all internationally-recognized specialists in the field of community genetics in LMIC, was convened for the purposes of the Consultation. The Group agreed that availability of community genetics services in LMIC is less than adequate. This may be due to a number of reasons: paucity of resources; genetic conditions not being considered priorities; misconceptions that the control of common congenital disorders is too expensive and linked with sophisticated technology; low genetics literacy; cultural, legal and religious limitations such as the fear of stigmatization within the community and the legal or religious restrictions to selective abortion of affected fetuses; an insufficient number of trained health professionals; and inadequate data on the true magnitude and economic burden of congenital disorders.

Congenital disorders (birth defects) are defined as structural or functional abnormalities which are present from birth, whether recognized at birth or later. They constitute a major health problem worldwide especially in LMIC. Factors that may contribute to the high rates of congenital disorders in LMIC include the general low availability of public health measures directed at the care and prevention of these disorders, the high frequency of haemoglobinopathies in Africa, Middle-East and South-East Asia, the high consanguinity rates in the Eastern Mediterranean and South-East Asia regions that can increase the occurrence of recessively inherited diseases, advanced maternal age at conception in many low- and middle-income countries, which increases the predisposition to chromosomal trisomies such as Down syndrome, and large family size that may increase the number of affected children in families with autosomal recessive conditions.

It is worth noting, however, that prevention programmes have been successfully implemented in some low- and middle-income countries, thus reducing the burden of congenital disorders or genetic diseases. Examples of countries adopting such programmes are, among others, Bahrain Cyprus and Iran.

The services required for the prevention and care of congenital disorders and genetic diseases include prevention strategies at primary, secondary and tertiary health-care levels. The Group emphasized specifically the need for education in genetics to be provided to all health professionals, policy-makers, and the general public. This also includes the sensitization to ethical, legal and social issues (ELSI) which are of key concern in the context of congenital disorders and

genetic diseases. WHO regional offices, international experts, academic institutions, professional organizations, philanthropic organizations, parent–patient associations, private sectors and donors need to work together for the implementation of community genetics services in LMIC.

In conclusion, the Group recommended all appropriate stakeholders convene to carry out the following:

- conduct epidemiological studies to determine the most prevalent congenital disorders and genetic diseases and the resulting health-care needs, through the establishment of registers for these conditions;
- establish clear and measurable objectives and goals;
- determine the most efficient interventions to achieve the specific goals;
- implement the interventions identified, following the ethical, legal and social guidelines, and evaluate outcomes.

In relation to determining the most efficient interventions, experience and examples from different countries indicate that the most common genetics services at community level (i.e. "minimum package of interventions") are:

i) training health professionals in basic concepts of genetics and their application to community genetics services;

ii) use of family history as an instrument to detect genetic risks;

iii) pre-conception and prenatal care, including folic acid fortification or supplementation, addressing the genetic risks of maternal age and consanguinity, genetic counselling when needed, prenatal ultrasound screening to detect fetal abnormalities, and referring detected genetic problems to a tertiary centre for proper management;

iv) public education to avoid alcohol, tobacco and potential teratogens in gestation;

v) carrier detection for haemoglobinopathies in countries where these conditions are a significant burden to public health, followed by genetic counselling and the option of prenatal diagnosis where voluntary termination of affected pregnancies is acceptable;

vi) clinical detection of congenital disorders in newborns and appropriate referrals to higher levels of care for diagnosis and treatment;

vii) newborn screening for congenital conditions in which early intervention is effective, such as congenital hypothyroidism, followed by treatment and other services for life. Newborn screening for haemoglobinopathies should be considered in countries where hereditary anaemias constitute a significant burden of disease.

From the perspective of WHO Human Genetics, it would be desirable to start by supporting the development of community genetics services in selected countries as demonstration projects.

1. Objective of the Consultation

The objective of the WHO Consultation was to develop an evidence-based report on community genetics services to provide guidance to low- and middle-income countries in accordance with the 2008–2013 NCD Action Plan. The Group of experts noted that the World Health Organization (WHO) has dealt with issues related to prevention and control of genetic diseases and congenital disorders and the organization of genetics services at community level on several occasions in past years (Alwan & Modell, 1997; WHO 1999; WHO 2006a; WHO 2006b).

2. Definitions

2.1. Community genetics

The Group endorsed the definition of community genetics as being "the art and science of the responsible and realistic application of health and disease-related genetics and genomics knowledge and technologies in human populations (communities) to the benefit of individual persons." (ten Kate et al., 2010). They noted, however, that in low- and medium-income countries, genetics services at community level are usually planned and implemented by the public health sector of the state. The dual and indivisible goal is to prevent congenital disorders and genetic diseases at population level and, at the same time, provide genetics services (diagnosis and counselling) in the community for individuals and families. The public health component of this indivisible goal of population health promotion and reduction of the prevalence of congenital disorders and genetic diseases, is not in contradiction with the genetics services component for individuals and families. Both should respect the right of individuals to make autonomous decisions in health and reproductive matters without coercion of any kind and from any source.

2.2. Meaning and use of the term "prevention"

The Group discussed in depth the meaning and use of the term "prevention," applied, typically, to the role of the health sector regarding genetic diseases. The Group decided to use the term "prevention" to indicate actions of primary, secondary and tertiary prevention, including those with the objective of reducing the birth prevalence and the health impact of congenital disorders and genetic diseases, while respecting voluntary reproductive decisions. The Group also agreed that in genetics the notion of "autonomy" should always take precedence over the objective of "prevention," whether in public health genetics programmes or in community genetics services for individual or family services. In practice, in LMIC, community genetics services and population prevention of congenital disorders and genetic diseases are facets, sharing the same goal, i.e. that

the prevention of congenital disorders and genetic diseases can be accomplished only by encouraging and respecting the educated and autonomous decisions of individuals and families. This is the meaning of the word "prevention," as endorsed by the Group in its use throughout this document, while acknowledging that some authors prefer not to use the term "prevention" when it involves the voluntary termination of affected pregnancies (Ten Kate, 2002; Dolk et al., 2009).

3. Role and availability of community genetics services

3.1. Role of community genetics services

Community genetics services include a number of activities for the diagnosis, care and prevention of genetic diseases at community level (Alwan & Modell, 1997; Penchaszadeh 2002; Christianson & Modell, 2004):

- diagnosis of congenital disorders and genetic diseases: clinical and laboratory (cytogenetics, biochemical assays, DNA testing, etc.);
- genetics counselling;
- pre-conception care;
- prenatal screening;
- prenatal and pre-implantation genetic diagnoses;
- newborn screening;
- carrier screening;
- population genetic screening according to other established policies.

These activities are implemented with different emphases and complexities in the primary, secondary and tertiary levels of care. In addition, community genetics is concerned with:

- improving genetics literacy and education among the public and health-care providers;
- the epidemiology of congenital disorders and genetic diseases;
- regionalization of genetics services with emphasis on primary care;
- registries of congenital and genetic disorders;
- special education and rehabilitation;
- public consultation regarding genetics issues;
- population medical genetics;

- economic issues;
- psychosocial issues;
- ethical and legal issues;
- policy issues.

3.2. Availability of community genetics services

Availability of community genetics services in LMIC is less than adequate due to a number of issues, including the following (Penchaszadeh, 2004; Hamamy et al., 2007):

- paucity of resources – genetic conditions not being considered priorities by the medical profession and public health officials;
- numerous unaddressed needs in other areas of health care, such as infectious diseases, malnutrition, antenatal care, labour and delivery care, and newborn care;
- the presence of other competing priorities, such as the needs for the control of communicable diseases and noncommunicable chronic disorders such as cardiovascular diseases, cancer and diabetes;
- misconceptions that the control of common congenital disorders is too costly and linked to sophisticated technology, thus limiting its introduction to the general public; genetics services being misperceived as costly and dealing only with rare diseases;
- low genetics literacy among the health sector and general public with lack of awareness of genetic risks and possibilities for prevention of congenital disorders;
- community services possibly being restricted by certain cultural, legal and religious limitations such as the cultural fear of families with genetic diseases to be stigmatized within their community and the legal and religious restrictions to selective abortion of an affected fetus;
- the public being largely unaware of genetic risks and the possibilities of prevention;
- an insufficient number of trained health professionals;
- inadequate data on the magnitude of the health and economic burden of congenital disorders.

4. Needs and prerequisites for developing community genetics in low- and middle-income countries

4.1. Place of community genetics in the health system of LMIC

As with all actions promoting and maintaining health and preventing disease, genetics services in a particular community must define their objectives and methods according to the local epidemiology, need assessments, demands of the population, health system infrastructure and budget.

The occurrence of congenital disorders and genetic diseases in a population, with its share of ill health, suffering and premature death, prompts the need for actions and services to treat the affected and prevent the occurrence of these conditions in the community.

In the past three decades, a number of interventions aimed at the early detection, prevention and care of health problems caused by genetic factors have been implemented in high-income countries. These developments have been facilitated by new or improved diagnostic technologies. In contrast, low- and middle-income countries have been behind in their implementation of public policies for the care and prevention of congenital disorders (WHO 2006).

The need and relevance for genetics services, therefore, has to be weighed in its priority and scope with the many other needs for curative and preventive health services in a particular population. In addition, the need may not be perceived until new knowledge and technologies appear to address the issues that congenital disorders and genetic diseases pose to individuals and society. Policy-makers and society at large then face decisions to invest resources in addressing that need. This, as with many state policies, has been the history of development of genetics services at community level. Key examples are the care and prevention of thalassaemia in the Mediterranean region (Angastiniotis & Hadjiminas, 1981), the development of a prevention programme for haemoglobinopathies in Bahrain (Al Arrayed, 2005), the development of prenatal diagnosis in Iran, and the establishment of treatment centres for Gaucher disease in Brazil.

4.2. Need for community genetics services in LMIC

The need for genetics services in a community is established when:

- epidemiology demonstrates that a congenital disorder or a genetic disease imposes a significant burden to the community, either because of its prevalence or severity or both;
- the community perceives that the congenital disorder or genetic disease is a burden and requests care and preventive services;
- the development of medical technology allows cost-efficient preventive and therapeutic curative interventions.

Congenital disorders (birth defects) are structural or functional abnormalities, which are present from birth, whether recognized at birth or later and constitute a major health problem worldwide

(Christianson et al., 2006; WHO 2006; World Health Assembly Resolution WHA63.17, 2010). Studies of the birth prevalence of "severe" congenital disorders that are either lethal or cause lifelong impairment if untreated, indicate that, of the six WHO regions, the highest rate was reported in the Eastern Mediterranean region with >65 affected children/1 000 live births. (Alwan & Modell, 2003). These figures are supported by the recent global report of the March of Dimes which estimated the prevalence of birth defects to be >69.9/1 000 live births in most WHO Eastern Mediterranean countries, in contrast to <52.1/1 000 live births in Europe, North America and Australia (Christianson, Howson & Modell, 2006).

4.3. Factors that could contribute to the high rates of congenital disorders in LMIC

Contributing factors could include (Hamamy & Alwan, 1994; Modell & Kuliev, 1998; Khneisser et al., 2007; Lindner et al., 2007)**:**

- general low availability of public health measures directed at the care and prevention of congenital disorders and the dearth of genetics services and inadequate health care prior to and during pregnancy;
- high frequency of haemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency in many countries in Africa and Middle-East and South-East Asia;
- high consanguinity rates in many countries in the Eastern Mediterranean and South-East Asia regions which possibly contribute to the increase in the expression of recessively inherited diseases;
- the advanced age to which women in many LMIC continue to conceive, which increases the predisposition to chromosomal trisomies such as Down syndrome (related to advanced maternal age). On the other hand, advanced paternal age increases the risk of occurrence of new mutations causing certain autosomal dominant disorders;
- large family size in many LMIC, which may contribute to the increase in the number of affected children in families with autosomal recessive conditions.

4.4. Comprehensive national initiatives on the development and strengthening of basic genetics services

Comprehensive national initiatives are currently demanded because of the following.

- In many LMIC, infant mortality rates have declined markedly. When this occurs, the proportion of deaths due to congenital disorders becomes higher, indicating the importance of introducing effective care and prevention measures for such disorders.
- Many LMIC have good coverage of reproductive and other primary health-care programmes where community genetics services can be feasibly integrated.
- In some countries, consanguinity rates are in the range of, approximately 20–50%, indicating the need to understand the relationship of consanguinity to morbidity and

mortality, as well as to understand the advantages and disadvantages related to consanguineous marriages.

- The high rate of haemoglobinopathies and other single gene disorders in some countries indicate the great potential of establishing cost-effective care and prevention programmes. Examples of countries successful in the use of programmes reducing the burden of these disorders are Bahrain, Cyprus and Iran.
- The public is becoming more aware of the availability of certain effective services, such as genetic risk assessment, genetic counselling, genetic testing and prenatal diagnosis. This has resulted in a demand for the introduction of such genetics services to the health system.
- Genetics is becoming an essential part of most medical specialties worldwide.

4.5. Prerequisites for developing community genetics services in LMIC

Reliable epidemiologic and burden-of-disease data collection and needs-assessment analysis are needed to focus on priorities in planning care and prevention programmes for congenital disorders and genetic diseases. Data on the extent and availability of community genetics services, manpower, and laboratory facilities in countries should be obtained. Political will and commitment and financial resources are needed for funding, and planning programmes for the care and prevention of congenital disorders. The creation of national committees in genetics and health care with a focal person responsible, in collaboration with the WHO country office, is essential for planning a community-based care and prevention programme for congenital disorders and genetic diseases.

The prerequisites for the development of genetics services at community level are:

- the existence of an organized, functional, regionalized public sector health system with universal access;
- knowledge and technology being available for treatment and prevention of specific genetic conditions;
- studies demonstrating that community genetics services are both effective and a health priority;
- health professionals being capable and interested in leading the actions;
- patient organizations being involved;
- policy-makers allocating appropriate funding;
- agencies being organized to monitor quality of services and adherence to established objectives.

5. Types of services required for the prevention and care of congenital disorders and genetic diseases at different health-care levels

Before addressing the services according to level of care, it is appropriate to discuss the nature of services according to prevention strategies, i.e. primary, secondary and tertiary prevention.

5.1. Services according to prevention strategies

5.1.1. ***Primary prevention***

The goal of primary prevention is to reduce the incidence of congenital disorders and genetic diseases through the removal of causative factors. The majority of identified causes of congenital disorders are non-hereditary and the main primary prevention measures include the following:

1. *Expansion of rubella immunization:* The implementation of immunization programmes are a function of political will expressed as appropriate funding and a minimum of infrastructure, cold chains and adequate organization at community levels. In Latin America and the Caribbean, the WHO Pan American Sanitary Bureau has been promoting rubella vaccination as part of childhood immunization since the late 1990's. Eradication of congenital rubella syndrome is within reach in Latin America and the Caribbean by the end of this decade.
2. *Folic acid fortification:* Pre-conception multivitamin intake reduces the risk of neural tube defects in the offspring, and the key protective factor is folic acid. Many LMIC have instituted folic acid fortification of main staples, and abundant data confirm the beneficial effect in reducing neural tube defects by at least 50%. Beneficial effects in the prevention of other congenital and adult conditions are being studied.
3. *Pre-conception care and family planning:* Pre-conception care is known to improve pregnancy outcome. Family planning is a basic human right of women and has a positive role in reproductive health and the improvement of pregnancy, including a decline in birth prevalence of congenital disorders. Genetic components of pre-conception care include: detection of genetic risks through family history; addressing the issue of consanguinity if relevant; explaining programmes of prevention of congenital disorders and genetic diseases that exist in the community; and genetics counselling as appropriate.
4. *Adequate prenatal care:* Prenatal care includes nutrition and control of maternal infections and other illnesses.
5. *Avoidance of potential teratogens in pregnancy:* Traditions, socioeconomic factors and medical culture make it difficult to avoid exposure to teratogens. Certain cultures in developing countries resort to home remedies of unknown composition and teratogenic potential. Moreover, in some developing countries pharmaceutical companies market their products directly to consumers, who can purchase and consume most medications without medical prescription, even during pregnancy. Compounding these factors, environmental quality regulations tend to be lax and pregnant women are commonly

exposed to environmental pollutants. Avoidance of teratogens, including smoking, alcohol intake and unwarranted medications, should be recommended. Teratogen information services are a valid strategy to prevent exposure to known teratogens.

5.1.2. ***Prevention based on reproductive options***

The limitations and difficulties of primary prevention programmes for congenital disorders have led to the implementation of prevention by reproduction options, in which couples at risk are detected and offered voluntary options to avoid having an affected child. This approach includes:

1. *Detection of heterozygotes (carriers) for autosomal recessive conditions:* These may be particularly prevalent and severe in a community. The purpose of carrier-testing in this context is to help couples at risk plan their reproduction to avoid having an affected child. Carrier-testing for reproductive purposes may be voluntary or mandated by law (for example premarital testing for thalassaemia in Cyprus and Iran), depending on the country. When both spouses are carriers, community genetics services should offer voluntary genetic counselling on the reproductive options available to avoid affected offspring. These options should be voluntary and devoid of coercion of any kind, and generally include (a) not marrying (if detection is premarital), (b) abstaining from reproduction, (c) running the genetic risk, or (d) availing to prenatal diagnosis, followed by the option of continuing or interrupting an affected pregnancy, depending on the legislation on abortion. The reproductive options approach has a number of ethical nuances – it must be voluntary, and it requires social consensus, organization and resources. Prime examples include the thalassaemia prevention programmes in Cyprus, Greece, Italy, Iran and other countries (Angastiniotis & Hadjiminas, 1981; Samavat & Modell, 2004; Ayesh et al., 2005; Elgawhary et al., 2008), and the prevention of recessive diseases common in Ashkenazi Jews worldwide (Kaback, 2000).
2. *Non-invasive prenatal screening for Down syndrome:* This can be followed by prenatal diagnosis in positive screens if desired by the couple.
3. *Genetics reproductive services (genetic counselling, prenatal diagnosis):* These can be adopted for other genetic diseases according to their burden in the community.
4. *Presymptomatic diagnosis of autosomal dominant conditions of late onset*: Diagnosis can be followed by the same reproductive options mentioned above. This approach also must be voluntary due to a number of ethical and psychosocial issues. There are many examples of such prevention programmes when the condition is severe, has no treatment, and is highly prevalent in a community, for example, spinocerebellar atrophy in Holguín, Cuba, and Huntington disease in Lake Maracaibo, Venezuela.

5.1.3. ***Secondary prevention (early diagnosis and treatment to avoid complications)***

1. *Newborn screening:* This is the prime example of secondary prevention of congenital disorders. There are a number of requisites and conditions for its effective implementation, including the selection of conditions to screen for, the organizational aspects, cost/benefit considerations, follow-up of initial positives, treatment of confirmed positives, etc.

2. *Predictive genetic testing:* For conditions in which there are proven and cost-effective preventive or therapeutic interventions on those who test positive.
3. *Follow-up of children:* For children with congenital disorders and genetic diseases with the strategy of anticipatory guidance and interventions to prevent complications and improve quality of life (e.g. haemoglobinopathies, deafness).

5.1.4. ***Tertiary prevention (surgical repair and rehabilitation)***

1. *Surgical treatment of congenital defects:* For defects such as congenital heart defects, cleft lip and palate, neural tube defects.
2. *Rehabilitation programmes:* For learning disabilities, cognitive impairment, musculoskeletal and other conditions.

5.2. Basic pillars in planning and implementing community genetics services

5.2.1. ***Commitment of policy-makers***

Political will and commitment is needed for funding, planning and managing the care and prevention initiatives. It is important to form a national committee addressing the care and prevention of congenital disorders that collaborates closely with WHO country and regional offices. Policy-makers become more aware of the health burden of congenital disorders when reliable data on prevalence and burden of congenital disorders become available.

Epidemiological studies on frequency of the disorders and their impact on public health and social life should therefore be conducted without delay. Morbidity and mortality burden data are needed. Decisions need to be made on whether genetics services should be comprehensive or start with specific priorities dictated by local needs and available resources. Priorities are defined by carrying out standardized epidemiological surveys and collecting demographic data, to identify the principal national problems related to congenital disorders, and to clarify the situation on the availability, extent and quality of genetics services.

Planned prevention programmes, besides being cost-effective, should take into consideration local beliefs and social attitudes. For example, premarital screening and pre-conception counselling as preventive measures are more acceptable than terminations of affected pregnancies in many countries where the latter is not acceptable.

Epidemiological studies should address the following:

- data on the prevalence and burden of congenital disorders in the country;
- data on available genetics services, both clinical and diagnostic laboratory services;
- data on available human resources in clinical genetics and genetics laboratory personnel;
- data on number and capacities of special schools for the care and rehabilitation of affected;

- data on college curricula related to genetics and genetics services.

5.2.2. ***Integration of community genetics services into the primary health-care system***

Integration of community genetics services into existing health-care systems can be feasibly implemented in most low- and middle-income countries (Penchaszadeh, 2000; Alwan & Modell, 2003; Christianson & Modell, 2004; Qureshi et al., 2004). The establishment of vertical programmes is hard to implement with a high demand for sustainable funds and human resources. Integration of public health approaches into the existing primary care and reproductive health clinics is probably the most appropriate, sustainable and cost-effective approach. Although some additional training and resources will be required, the potential benefits are considerable (Hamamy & Bittles, 2009).

An example of the integration of community genetics services into primary health-care programmes is the inclusion of pre-conception and post-conception counselling and screening in reproductive health clinics. The approach includes pre-conception information and risk detection (nutrition, maternal infections, Rh status, parental age, maternal disease, teratogenic drugs and chemicals, counselling for consanguinity), referral of couples at high genetic risk to specialized centres, carrier screening and newborn screening programmes, and care for the affected individuals and their families. Community genetics services in secondary and tertiary care would include the provision of specialist genetics counselling for high-risk families and care for the affected.

5.2.3. ***Registries of congenital disorders and genetic diseases***

The expected benefits of registries are to determine the baseline birth prevalence of each type of congenital disorder, to increase awareness within the medical community of these conditions, and to improve the quality of diagnosis and recording (Rajab, Patton & Modell, 2000; Al Hosani et al., 2005). The aim is to establish a priority list of preventive measures and help organize better care for patients with special needs, for example those with Down syndrome. In addition, the register can have a surveillance function for the identification of significant changes in the baseline rate for specific congenital disorders, which may indicate the existence of particular personal or demographic factors.

Certain requirements need to be addressed in initiating genetics registries. These include:

- selecting the conditions that should be initially registered;
- performing personnel training;
- defining responsibilities;
- recruiting experts for planning and implementing the registry;

- providing training for physicians and nurses on examination of newborns to detect congenital disorders.

A problem that can face the implementation of a national registry is the reluctance of health-care personnel to complete the registry forms, which requires their time and effort. Incentives to encourage this are important to consider in low- and middle-income countries.

5.2.4. ***Population screening programmes***

Population screening involves the following programmes:

1. *Newborn screening:* Newborn screening, the "dean" of genetic screening programmes, has been applied on very large and systematic scale for the past 40 years, both in high-income countries and in some low- and middle-income countries (Al Hosani et al., 2005; Khandekar et al., 2006; Al Arrayed et al., 2007; Saadallah & Rashed, 2007). Newborn screening began in developed nations in the 1960s with screening for phenylketonuria, followed soon after by screening for congenital hypothyroidism. There are a number of prerequisites for the development and implementation of newborn screening (WHO 2006a). Newborn screening programmes vary in different countries according to the prevalence of specific conditions:

   i) All countries that conduct newborn screening, screen for congenital hypothyroidism, which is one of the most common preventable causes of mental retardation worldwide (Rose et al., 2006; Jain et al., 2008).

   ii) Some countries with a large proportion of the population being of European descent, test also for phenylketonuria and cystic fibrosis.

   iii) Some countries with a large proportion of the population being of African, Mediterranean or Asian descent conduct newborn screening for genetic blood disorders which benefit from early detection and management, such as sickle cell anaemia and G6PD deficiency (Al Arrayed et al., 2007).

   Newborn screening for congenital hypothyroidism should be introduced in all low- and middle-income countries, irrespective of the economic status, as a robust preventive measure of mental retardation.

2. *Carrier screening:* Carrier screening, used among healthy people, detects those who are heterozygote for recessive genes particularly prevalent in the community. The goal of these programmes is to expand the reproductive options of carrier individuals. These options should always be voluntary and could include: (a) avoid marrying someone who is also a carrier; (b) opt for prenatal diagnosis of the disorder in question (e.g. thalassaemia), followed by voluntary termination of affected pregnancies. The combination of these interventions has reduced the prevalence of thalassaemia by more than 90% in Cyprus, with significant reduction also in Greece, Italy, Bahrain and Iran, among others (Al Arrayed, 1997; Angastiniotis & Hadjiminas, 1981; Al-Arrayed et al., 2003; Samavat & Modell, 2004).

3. *Prenatal screening:* Prenatal screening detects chromosome abnormalities such as Down syndrome, neural tube defects and major fetal malformations, as well as haemoglobinopathies. This is conducted by ultrasound and biochemical assays in maternal blood. Few countries have explicit prenatal screening policies, although such interventions are standards of obstetrical practice in most developed countries and in limited scale (usually restricted to the high-income groups) in all countries. The obvious aim of these interventions is to allow couples to decide whether or not they wish to pursue an affected pregnancy. Thus, these services are recommended particularly when the voluntary option to terminate an affected pregnancy is available and accessible (Chaabouni et al., 2001).

5.2.5. ***Genetics centres and introduction of new technology***

The molecular revolution that characterized the last three decades has introduced into medical practice many procedures that aid the diagnosis and prevention of congenital disorders. Such technologies can be introduced gradually into a country's care and prevention programmes of congenital disorders, according to their proven validity and utility as well as their cost and effectiveness. Intercountry collaboration programmes should be stimulated.

5.2.6. ***Improving care and rehabilitation for those affected with congenital disorders***

Several efficient care and rehabilitation management procedures exist for those affected with congenital disorders, including surgery for congenital malformations, dietary therapy for some metabolic disorders and rehabilitation for those with mental and physical disabilities. Haemoglobinopathies are amenable to efficient management and good prognosis despite the difficulties. For example, thalassaemia is a significant issue for medical centres throughout the world because of the constant demand for blood transfusions and for self-administered iron chelation therapy. When thalassaemia was first described, the prognosis for patients was poor because the condition was incompatible with life. However, continuous blood transfusions and iron chelation therapy led patients with thalassaemia to have a normal lifespan, provided they comply with their therapy. Because patients face the burden of a chronic illness, psychosocial problems are common (Gharaibeh, Amarneh & Zamzam, 2009), as are the psychological issues that interfere with compliance to ongoing therapy (Musallam, Cappellini & Taher, 2008). The proportion of patients administering desferrioxamine at least four days per week in Egypt and Iran was just below 60% and in Jordan, around 75%. The most frequently reported category of reasons for patients missing a dose related to their beliefs and feelings about the treatment (Ward et al., 2002). Furthermore, severe complications related to the repeated blood transfusions in thalassaemic patients still exist, such as life-threatening heart disease as a consequence of iron overload (Caro et al., 2002; Al-Hawsawi et al., 2003; Inati et al., 2006; Charafeddine et al., 2008). Other serious complications related to thalassaemia include the risk of hepatitis C in thalassaemic patients (Al-Fuzae, Aboolbacker & Al Saleh, 1998), and the occurrence of thromboembolic events (Taher et al., 2006).

5.3. Community genetics services according to level of health care

Health systems are organized by level of care. Primary care is both a comprehensive approach to health care, with components of prevention and treatment, as well as the port of entry of the population to the health system. Secondary and tertiary levels of care deal increasingly with complex health issues. At these levels therapeutic medicine and high technology are more developed. In all countries, and particularly in LMIC, the bulk of health care occurs at primary-care level. Accordingly, community genetics actions must have an emphasis in primary care.

5.3.1. ***Community genetics in primary health care***

The following are community genetics services that should be available in the primary health-care level:

- use of family history as a strategy to detect genetic risk factors;
- clinical suspicion, at all ages, of disorders that could be caused by genetic factors, followed by appropriate referrals to secondary and tertiary levels of care;
- follow-up of results of newborn screening and referrals of presumed positives to higher level centres;
- pre-conception counselling and care in reproductive health clinics , including avoidance of alcohol, smoking and teratogens, family planning and discussion of genetic and environmental risks;
- detection of heterozygotes for a particular recessive condition when that is part of a prevention programme in the community;
- presymptomatic diagnosis and genetic counselling of late-onset, single-gene disorders when that is part of a prevention programme in the community (e.g. Huntington's disease in Lake of Maracaibo, Venezuela, and spinocerebellar atrophy in the province of Holguin, Cuba);
- genetic counselling in low complexity situations or as part of a particular prevention programme (e.g. thalassaemia, sickle-cell disease, spinocerebellar atrophy);
- prenatal care including counselling on avoidance of exposures to teratogens and ultrasound in gestation for the detection of fetal malformations.

As recommended for all health services provided at primary-care level, guidelines for referrals to higher levels of care should be available also for genetic conditions and congenital anomalies.

5.3.2. ***Community genetics in secondary and tertiary health-care levels***

Community genetics in these health-care levels include the following:

- supervision of services provided in the primary-care level;
- clinical genetics diagnostic services;

- genetic counselling;
- genetic testing for diagnosis: cytogenetic, DNA testing;
- prenatal diagnosis;
- predictive testing;
- education to health professionals, policy-makers, the public.

5.3.3. ***Education in genetics***

Education in genetics should be provided to all health professionals, policy-makers, and the public and needs to include topics such as: consanguinity; prenatal and newborn screening and detection of signs of possible genetic conditions common in the area; prevention and care programmes that take place in the community; and ethical, legal and social issues. Education in genetics is required to implement efficiently community genetics services in primary health care.

6. Design of training and teaching programmes in connection with genetics services delivery

Medical genetics education assumes particular importance in LMIC with high frequency of genetic disorders and, generally, low level of genetics literacy. It is often erroneously assumed that medical training equips doctors to provide adequate genetic counselling, but current teaching methods in many LMIC rarely prepare medical graduates in a manner that enables them to discuss complex issues with their patients or help patients reach their own decisions. In most LMIC, health services are delivered by a network of primary health-care centres in which the staff consists of medical graduates who have not undertaken any higher specialization, and whose only formal exposure to medical genetics occurred during their undergraduate years (Hamamy & Bittles, 2009).

While family medicine physicians and paediatricians may be more knowledgeable in providing genetic counselling, they are aware of the possibility of potentially serious diagnostic misunderstanding and therefore may be reluctant to deal with genetics problems, which they consider as complex, sophisticated and difficult. A basic and essential strategy for the prevention of genetic disorders in LMIC would be to energetically formulate and implement ongoing short courses in genetic counselling for health-care providers.

Training and teaching on genetics services delivery include the following:

- Programmes for the teaching of medical genetics to all health professions (physicians, nurses, psychologists, public health professionals, etc.) both at undergraduate and postgraduate levels. Workshops for medical school leaders and faculty in developing countries to establish competencies and a core-curriculum in clinical genetics at community level, tailored to national and regional needs.
- Special courses and workshops for public health professionals and health policy-makers on the relationship between genetics, community health and public health. In addition to

health professionals, key targets for workshops in genetics education are: policy-makers and opinion leaders, parent–patient organizations, journalists, and the general public.

- Development of educational materials for different targets according to local needs. Such educational materials should be culturally appropriate and harness the advances in information technology (CD roms, Internet, etc.). One example is the course on community genetics offered by the Geneva Foundation of Medical Education and Research (GFMER, 2010).
- The ethical, legal and social implications of community genetics services and their supporting genomic technologies should be an integral part of the education in genetics at all levels and for all targets (WHO 2006a).

7. Relevant ethical, legal and social issues in community genetics in low- and middle-income countries

7.1. Ethical and legal issues in community genetics

Ethical, legal and social issues in community genetics are specific for communities, countries and regions, because of cultural, historic and religious factors. Principal ELSI in genetics include the following:

- inequities in access to genetics services in general, as a result of lack of trained geneticists, underfunding in the public sector and poor coverage by social and private health insurance;
- inequities in access to prenatal diagnosis. This is not usually provided by the public sector. However, in the private sector it is relatively well developed and follows market rules, in many instances with no clear indications, no quality control, no statistics and no known outcomes;
- legal restrictions for the termination of pregnancies affected with fetal defects, with inequity in its enforcement, as those with economic means can access safe pregnancy termination.
- deficiency of health professionals with adequate training in clinical genetics, genetics counselling and genetic testing.
- weakness of regulations to enforce privacy of genetics information.
- overt or covert discrimination to, and stigmatization of, people with disabilities and patients with congenital disorders and genetic diseases.
- weakness of parent–patient organizations, which need to be better supported.
- weak or non-existent governmental regulation of genetic tests, resulting in the introduction of testing according to commercial interests without demonstration of clinical validity or utility, or provision of genetic counselling.

- lack of appropriate control of international collaborative genetic research initiatives, which should ensure proper ethical safeguards and concerns for technology transfer and capacity building.

7.2. Confidentiality issues

Clinical genetics practice has some responsibility for informing relatives of the affected of their "at-risk" status when that is the case. Genetic registers incorporating long-term follow-up and a proactive approach to at-risk subjects have been recommended as a means of improving access to genetic counselling for families with inherited disorders. Carrier individuals have the right to know what genetic risks there are in having affected offspring and the ways in which that risk could be avoided (e.g. by not marrying a close blood relative or another proven carrier, or having prenatal diagnosis in gestation when the disorder is diagnosable *in utero*).

However, the right of family members to this information may conflict with the proband's right to confidentiality. Initial WHO guidelines on ethical issues in medical genetics suggest that, where appropriate, and as part of their general duty to educate, counsellors should inform clients that genetic information could be of importance to their relatives. Under these circumstances, individuals might reasonably be invited to request their relatives to seek genetic counselling (WHO 1998).

A more recent WHO report changed the balance of the advice recommended for highly consanguineous communities in which arranged marriage is commonly practiced. Since a genetic disease could potentially influence all members of the extended family, in such communities, it was proposed that respect for patient confidentiality may need to be considered alongside the rights of other family members, for whom information about genetic risk could influence decision-making on their own health or reproductive choices (WHO 2006a).

7.3. Ethical standards for community genetics services

The principal ethical standards for community genetics services are based on maximizing benefit, minimizing harm, respecting privacy and autonomy and ensuring equity (WHO 1998; WHO 2006a; WHO 2006b; Ten Kate et al., 2010) and can be summarized as follows:

- fair allocation of public resources so that genetics services reach all those in need (justice);
- freedom of choice in all matters relevant to community genetics services; the necessity of voluntary approaches in services, including approaches to testing and treatment; the avoidance of coercion by government, society, or health professionals (autonomy);
- respect for human diversity, religious, cultural and social beliefs and psychosocial well-being (autonomy, non-maleficence);

- education in genetics for the public, medical and other health professionals, teachers, clergy and others (beneficence);
- provision of ongoing quality control of services, including laboratory procedures (non-maleficence).

8. The role of WHO regional offices and other interested parties

The World Health Organization is currently promoting a plan of action for the prevention and care of congenital disorders through Resolution WHA63.17 adopted at the 63rd World Health Assembly in May 2010.

Globally, WHO promotes the collection of data on the frequency rates, morbidity and mortality burden of congenital disorders through strengthening epidemiological research.

At regional level, WHO can organize consultations attended by representatives from Member States (e.g. geneticists, Ministry of Health and other policy-makers) and international experts to discuss the programming and implementation of the action plan and any foreseen problems or limitations.

At national level, WHO can support Member States in forming a national committee with a designated focal person to formulate plans and strategies for the care and prevention of congenital disorders at primary health-care level.

WHO can also support Member States in developing ethical and legal guidelines in relation to congenital disorders in line with local culture, social and religious norms and can help organize training and education courses for primary health-care providers to increase genetics literacy.

WHO can play a crucial role in helping low- and middle-income countries plan and implement, with equity and quality, community genetics services to all those in need. Moreover, WHO can lead the initiative in encouraging collaborations among these countries in the fields of clinical and diagnostic laboratory genetics services. WHO can also play an important role in disseminating information to promote synergistic actions and collaborations in different countries.

Several steps are required for the further expansion of current genetics services to include community-based operations in primary care. Firstly, epidemiological research must be stimulated to provide better data on the prevalence and types of congenital disorders, genetic diseases and genetic predisposition to common diseases. Genetics professionals must be educated in community health and public health genetics, and public health professionals in the goals and methods of community genetics. Interactions between clinical geneticists, public health personnel, primary health-care workers and community organizations must be stimulated. Duplication of services can be avoided by appropriate regionalization.

Public health officials must become familiar with the applications of medical genetics for the public's health, and define realistic goals for genetics services, centred on the health and well-being of individuals and families, not on rigid population goals. The voluntary nature of genetic testing and cultural diversity in reproductive decision-making must be respected, and discrimination by genetic characteristics rejected.

A comprehensive effort is needed in medical genetics education. Attention should be directed towards training in medical genetics, including genetic counselling, for general physicians and allied health professionals, such as nurses, psychologists, social workers, etc. Practical aspects of medical genetics, with a community-based approach, need to be taught both in medical schools and in schools of public health. Health officials need to become involved in the design and implementation of community-based programmes for care and prevention of birth defects and genetic disabilities. Finally, the public at large needs to be educated in medical genetics to address common misconceptions and fears, and to inform them of available services.

There is a necessity for transition from tertiary care-based genetics services to a more sustainable model based in primary care. A public health infrastructure is essential for the development of community genetics services. Interestingly, that structure is largely present in many LMIC, and certainly in most Latin American countries. However, it is inefficient and underfunded, and clear goals and political will are essential for the successful prevention and care of genetic disorders at community level.

The accomplishment of this goal requires the synergistic action of all stakeholders mentioned in this section. A strategy worth supporting is that of partnerships between institutions and organizations of LMIC with similar LMIC institutions and organizations (South–South collaborations) and of high-income countries (North–South collaborations).

8.1. Role of WHO and its regional offices

WHO is the world leader in establishing health priorities and in identifying the principal determinants of health and disease, particularly in developing countries.

WHO has also been the world leader in introducing the need to address congenital disorders and genetic diseases as targets for prevention and care in developing countries. It is essential that WHO now uses its leadership and reputation to ensure that the scientific and technological developments in genomics and allied disciplines are used equitably. This will serve to guarantee improvement in the means for early detection, treatment and prevention of diseases and conditions influenced by genetic factors, to benefit all populations irrespective of their economic means. To this end, WHO needs to bring together all other stakeholders for high-level discussions on the most efficient ways to proceed in the care and prevention of congenital disorders and genetic diseases at community level. Given the cultural, historical, economic and health status heterogeneity in the different regions of the world, it would be more appropriate and effective for this activity to be conducted by WHO regional offices in the countries of their regions. Initial steps could involve workshops, organized by each regional office, with the participation of the

ministries of health of the countries of each WHO region, to which the other stakeholders would be invited.

During the years 2007 to 2009, WHO Regional Office for the Americas conducted a series of sub-regional workshops in community genetics and public health in Latin America and the Caribbean. These delivered excellent results in terms of commitment by ministries of health to the support of community genetics programmes (Penchaszadeh 2009, unpublished).

In 2010, WHO Eastern Mediterranean Regional Office (NCDs) prepared a report on the situation analysis of congenital disorders in their region. The principal objective of the report was the collection of available data from countries of the Eastern Mediterranean region on the epidemiological profile and available genetics services for congenital disorders. The aim also was to direct planning of appropriate future strategies for the care and prevention of congenital disorders in Eastern Mediterranean region countries (Hamamy 2010, unpublished).

The involvement of WHO Collaborating Centres should be pursued. At present, there are 12 collaborating centres in Human Genetics.

8.2. Role of international experts

International experts have a significant role to play, particularly in discussing with local authorities and health professionals in the host countries the experiences of other countries in the development of community genetics services. Care should be taken, however, to ensure that the experts in those countries are recognized and take the lead.

8.3. Role of academic institutions

Academic institutions need to engage in the teaching of community genetics at all levels of their educational programmes for health professionals. They will, thus, become excellent resources when it comes to designing and implementing education programmes in community genetics to policy-makers, other stakeholders and the general public. They can also lead research projects related to community genetics in their countries.

8.4. Role of professional organizations

It is important that professional organizations, dealing with medical genetics and public health in different countries, support the notion of genetics services at community level (as defined above in this document), as being the best strategy to convey the benefits of genetics to the population. Public health professional organizations are essential in achieving consensus on the importance of autonomy and freedom of choice for individuals and couples, and in establishing priorities, cost–benefit considerations, resource allocation, and predicted outcomes of interventions. Partnerships

with similar institutions and organizations in high-income countries have been considered valuable for both professional and parent–patient associations.

8.5. Role of philanthropic organizations, the private sector and donors

Public–private partnerships need to be developed to allow the private sector to return a proportion of their earnings to the public. However, a democratic decision needs to be made by the populations of the relevant countries, in line with evidence-based criteria, as to the policies, priorities and methodologies of the use of these funds, so that they benefit local communities.

8.6. Role of parent–patient associations

Parent–patient associations strive to make government officials and political leaders aware of the needs of patients and families afflicted by congenital disorders and genetic diseases. These organizations tend to work closely with academic clinical genetics centres and, with their support, are able to produce comprehensive educational materials for the general public. The materials include audio-visual presentations, audiotapes and lesson packages of teaching materials for schools. Parent–patient associations establish public awareness campaigns that distribute information on the availability of genetics services. Recent campaigns addressed the importance of folic acid in primary prevention in the pre-conception period and described the available services making use of free publicity, advertisements etc. Parent–patient associations also take a stand on topics such as patenting of genetics material, the various international declarations pertaining to the human genome in the context of human rights, and the need for genetics services at community level.

The media and the political leaders have shown an increasing interest in the opinions of parents and adult patients, who, due to their own personal experiences, have become experts themselves. Parent–patient associations also contribute to research efforts by encouraging their members to participate in biomedical research. In most countries the alliances are recognized by governmental bodies. They have increasing political influence because of the large numbers of individuals whom they represent.

Some parent–patient associations, such as the World Federation of Hemophilia, have successfully developed twinning programmes worldwide [1].

Parent–patient associations in developed and developing countries play an important role in a number of ways in the well-being of individuals affected with congenital disorders and genetic diseases. They should be partners in any programme to develop community genetics services.

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[1] Information on the World Federation of Hemophilia twinning programmes can be found at: http://www.wfh.org/index.asp?lang=EN >programs > twinning.

9. Recommendations and conclusions

9.1. Recommendations

Recommendations for the development of genetics services at community level should adopt the following procedures:

1. *Convene all appropriate stakeholders:* Stakeholders include ministries of health, public health professionals, physicians and other health professionals, parent–patient organizations, medical geneticists, community leaders, and others according to the specifics of the country.

2. *Identify problems and needs:* This involves conducting epidemiological studies and needs assessment analyses to determine the most prevalent congenital disorders and genetic diseases, the burden they impose on health and the existence of preventive and therapeutic interventions of proven validity and utility. Registers of congenital disorders and genetic diseases are the best instrument in the collection and analysis of such data.

3. *Establish clear and measurable objectives and goals:* This involves training health professionals in basic concepts of genetics and their application to community genetics services, implementing specific interventions, such as preconception and prenatal care, genetics counselling, carrier detection and newborn screening.

4. *Determine the most efficient interventions to achieve the goals:* Experience and examples from different countries indicate that the most common genetics services at community level (i.e. "minimum package of interventions") (WHO 2010) are:
   i) Training health professionals in basic concepts of genetics and their application to community genetics services;
   ii) Use of family history as an instrument to detect genetic risks;
   iii) Pre-conception and prenatal care, including folic acid fortification or supplementation, addressing the genetic risks of maternal age and consanguinity, genetic counselling when needed, prenatal ultrasound screening to detect fetal abnormalities, and referring detected genetic problems to a tertiary centre for proper management;
   iv) Public education to avoid alcohol, tobacco and potential teratogens in gestation;
   v) Carrier detection for haemoglobinopathies in countries where these conditions are a significant burden to public health, followed by genetic counselling and the option of prenatal diagnosis where voluntary termination of affected pregnancies is acceptable;
   vi) Clinical detection of congenital disorders in newborns and appropriate referrals to higher levels of care for diagnosis and treatment; and
   vii) Newborn screening for congenital conditions in which early intervention is effective, such as congenital hypothyroidism, followed by treatment and other

services for life. Newborn screening with proper management for genetic conditions common in each country could also be considered.

5. *Implement the interventions identified, following the ethical, legal and social guidelines, and evaluate outcomes.*

9.2. Conclusions

From a WHO Human Genetics perspective it would be desirable to start by supporting the development of community genetics services in selected countries as demonstration projects (perhaps one country per WHO region), on the basis of demographics, politics, epidemiology, state of health services, cultural and religious factors, etc. Among the political aspects that must be considered are the motivation and political will of health policy-makers in implementing model community genetics programmes in their countries.

Health authorities need to create within the ministry of health of each country a particular interdisciplinary committee in community genetics, composed of specialists in clinical genetics, clinical medicine, epidemiology, public health, community health, bioethics, and other relevant disciplines, with the significant participation of parent–patient support groups. This task force would be in responsible for being in contact with the relevant country and WHO regional office, and thus have access to international expertise, preferably from the same region, or South–South collaborations.

On the basis of the objectives set out in the 2008–2013 NCDs Action Plan, the following could be applied similarly to the action plan for the care and prevention of congenital disorders:

- to raise the priority accorded to congenital disorders at global and national levels, and to integrate care and prevention of such diseases into policies across all government departments;
- to establish and strengthen national policies and plans for the care and prevention of congenital disorders;
- to promote interventions to reduce the modifiable risk factors for congenital disorders e.g. tobacco and alcohol use during pregnancy, micronutrient deficiencies, prevention and timely management of teratogenic infectious diseases, proper management of maternal illness such as diabetes and epilepsy, and control of occupational hazards to pregnant women;
- to promote research for the care and prevention of congenital disorders;
- to promote partnerships for the care and prevention of congenital disorders;
- to monitor the progress of the programme for the care and prevention of congenital disorders at national, regional and global levels.

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Appendix

WHO resolutions regarding human genetics

- Resolution WHA63.17. Birth defects. In: *Sixty-third World Health Assembly, Geneva, 17–21 May 2010*. Geneva, World Health Organization, 2010 (WHA63/2010/REC/1).

- Resolution EB117/R3. Sickle-cell anaemia. In: *Executive Board, 117th session, Geneva, 23–27 January 2006*. Geneva, World Health Organization, 2006 (EB117/2006/REC/1).

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