Research priorities in integrating community genetic services in primary care settings

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Outline

- What are community genetic services
- Birth defects
- Needs and Impediments in LMIC
- Proposed strategies for community genetic services in LMIC
- Priorities for research in integrating community genetic services into primary health care in LMIC

What is community genetics

Reproductive Health and Community Genetics

- The World Health Organization definition of Reproductive Health encompasses the right of men and women to be informed and to have access to safe, effective, affordable and acceptable methods of fertility regulation of their choice, and the right of access to appropriate health care services that will enable women to go safely through pregnancy and childbirth and **to provide couples with the best chance of having a healthy infant**.
- **One of the main goals of community genetic services is to maximize the chances for couples to have healthy babies.**

What is meant by Community Genetic Services

- It means genetic services targeted to the population with the goal of **reducing the burden** imposed by birth defects (congenital disorders) on all individuals in the population.
- Involve programs for the **prevention and care** of congenital disorders specifically at the **primary health care** level through integrating these services into maternal and child health programs.
- Provide services with **equity** and **efficiency** to all those in need.

What is meant by specialized genetic services

- They comprise genetic services targeted to individuals and families who request them with the goal of enabling people with a genetic disadvantage to live and reproduce as normally as possible and to make informed and voluntary choices on reproductive matters.
- They are provided by specialists in secondary and tertiary centers.

Prevention means:

- reducing the birth prevalence and the health impact of congenital disorders
- while respecting voluntary reproductive decisions.

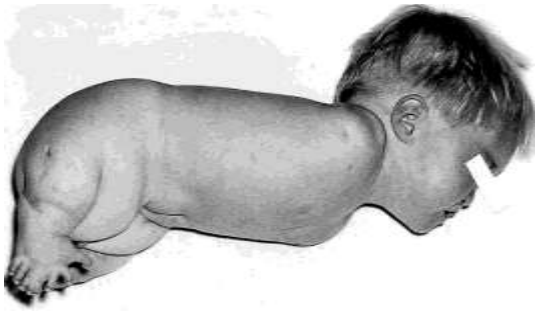
What are birth defects?

What are Congenital disorders?

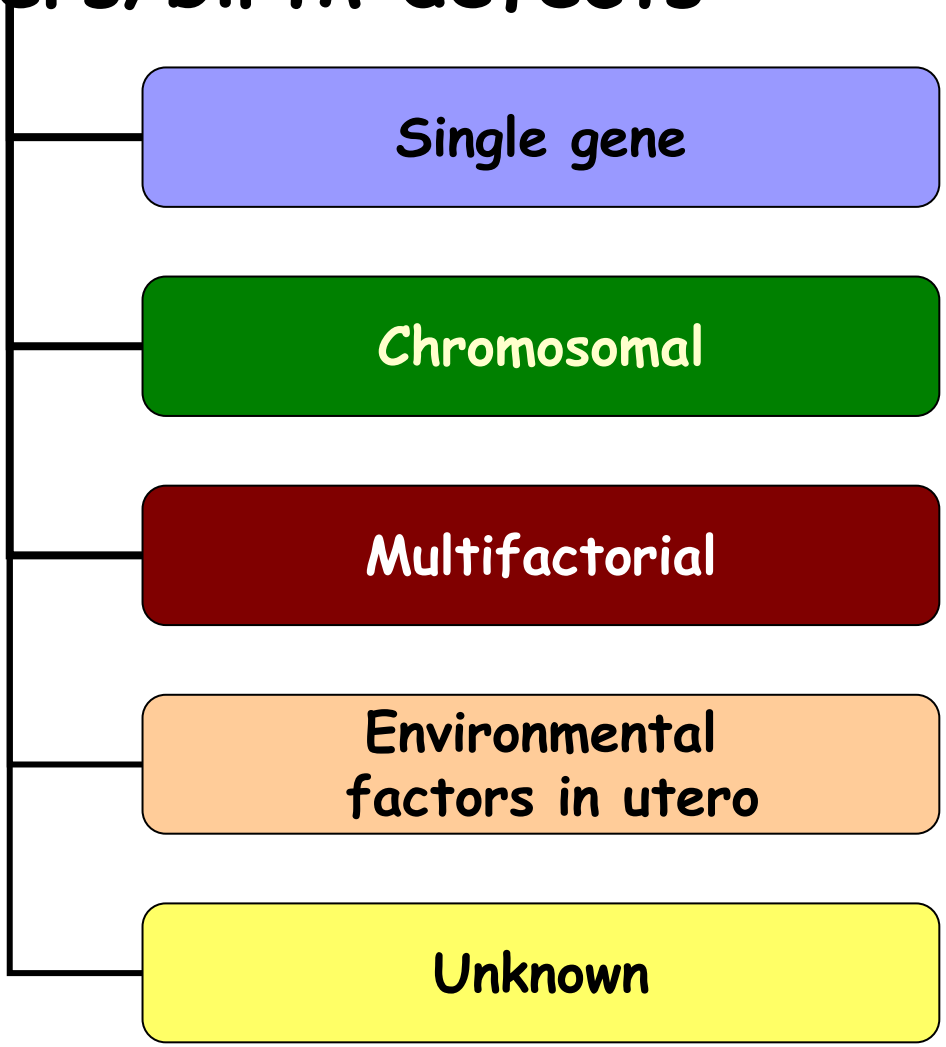
- According to the World Health Organization, the term congenital disorder includes any morphological, functional and biochemical-molecular defects that may develop in the embryo and fetus from conception until birth, present at birth, whether detected at that time or not.
- This term is synonymous with the term birth defect used in the USA.

Categories of Congenital Disorders

- Congenital malformations (structural defects)
- Genetic disease (Chromosome or single gene abnormality)
- Intrauterine infections as toxoplasmosis and exposure to teratogenic drugs (such as thalidomide)

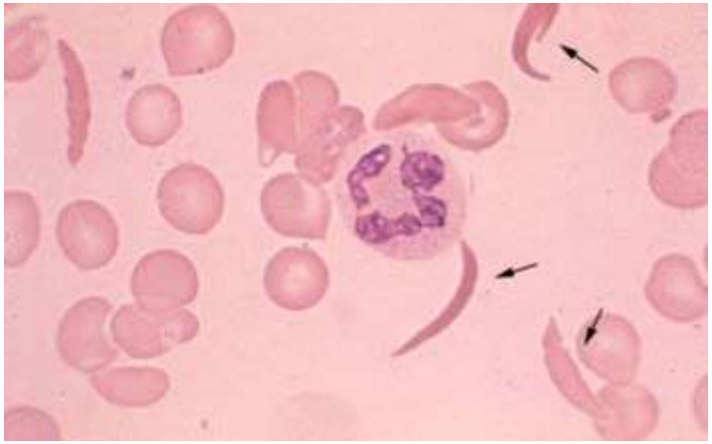


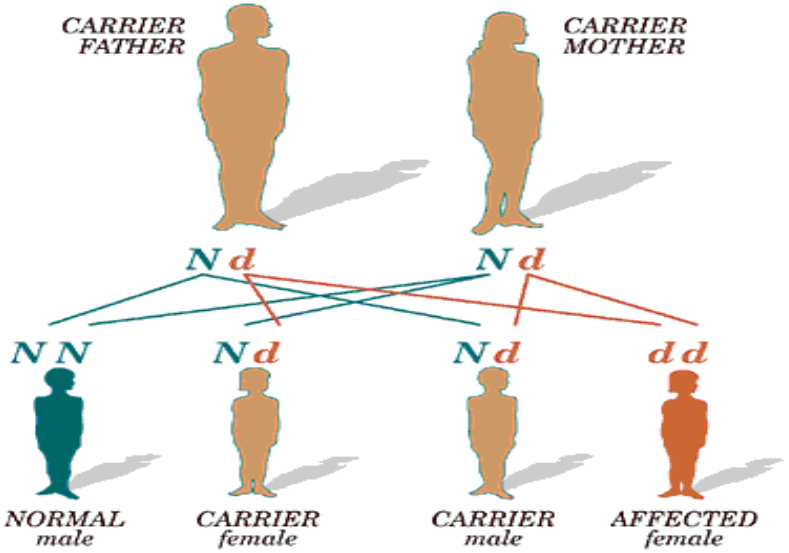
Underlying etiology of Congenital disorders/birth defects



Single gene disorders

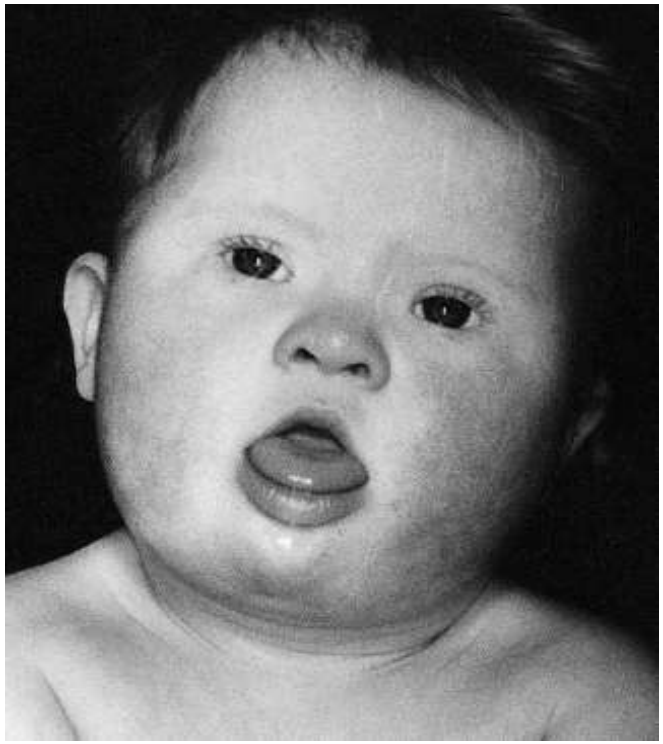
- Single-gene disorders occur in about 1% of in neonates
- There are thousands of different single gene disorders
- **sickle cell anemia is one example**
- **If a child is affected, risk of affection to his future brother or sister is 25%**





Chromosomal disorders

- Chromosome abnormalities occur in about 0.5% in neonates
- More than 20,000 different chromosomal abnormalities have been reported
- Down syndrome is the most common (about 1/600 livebirths)
- ***Risk of having a child with Down syndrome increases with advance in maternal age***



Multifactorial disorders : congenital abnormalities/malformations

- Of all neonates, 2-3% have at least one major congenital abnormality (structural defect).
- Most **congenital abnormalities** such as congenital heart defects, neural tube defects and cleft lip/palate have multifactorial etiology which is an interaction between both genetic and environmental factors to cause the condition.
- After the birth of a child with for example spina bifida, the risk of recurrence in a future pregnancy is increased to around 4% and increases with increase in number of affected in the family.
- Supplementation by folic acid pre- and postconception can markedly decrease the risk for neural tube defects.

In utero environmental factors (infections, drugs, chemicals)

Example: congenital syphilis

- Pregnant women who are infected with syphilis can transmit the infection to their fetus, causing congenital syphilis, with serious adverse outcomes for the pregnancy in up to 80% of cases.
- An estimated two million pregnancies are affected annually; approximately 25% of these pregnancies end in stillbirth or spontaneous abortion, and in a further 25% the newborn has a low birth weight or serious infection, both of which are associated with an increased risk of perinatal death.
- *A large reduction in congenital syphilis is feasible with relatively simple interventions focused on maternal and newborn care.*

The 5 most serious and prevalent birth defects that constitute about 25% of all disorders are:

- Hemoglobin disorders (thalassemia and sickle cell anemia)
- Down syndrome
- Neural tube defects
- Congenital heart defects
- G6PD deficiency

MARCH OF DIMES
GLOBAL REPORT ON BIRTH DEFECTS
THE HIDDEN TOLL OF DYING AND DISABLED CHILDREN

Global burden of birth defects

Burden of congenital disorders

- Every year around 8 million infants are born with a serious birth defect, of which several hundred thousands are caused by teratogens (alcohol, rubella, syphilis, iodine deficiency). 3.3 million die, 3.2 survive with severe disability.
- According to experience from industrialized countries, up to 70% of birth defects can be prevented or adequately managed.

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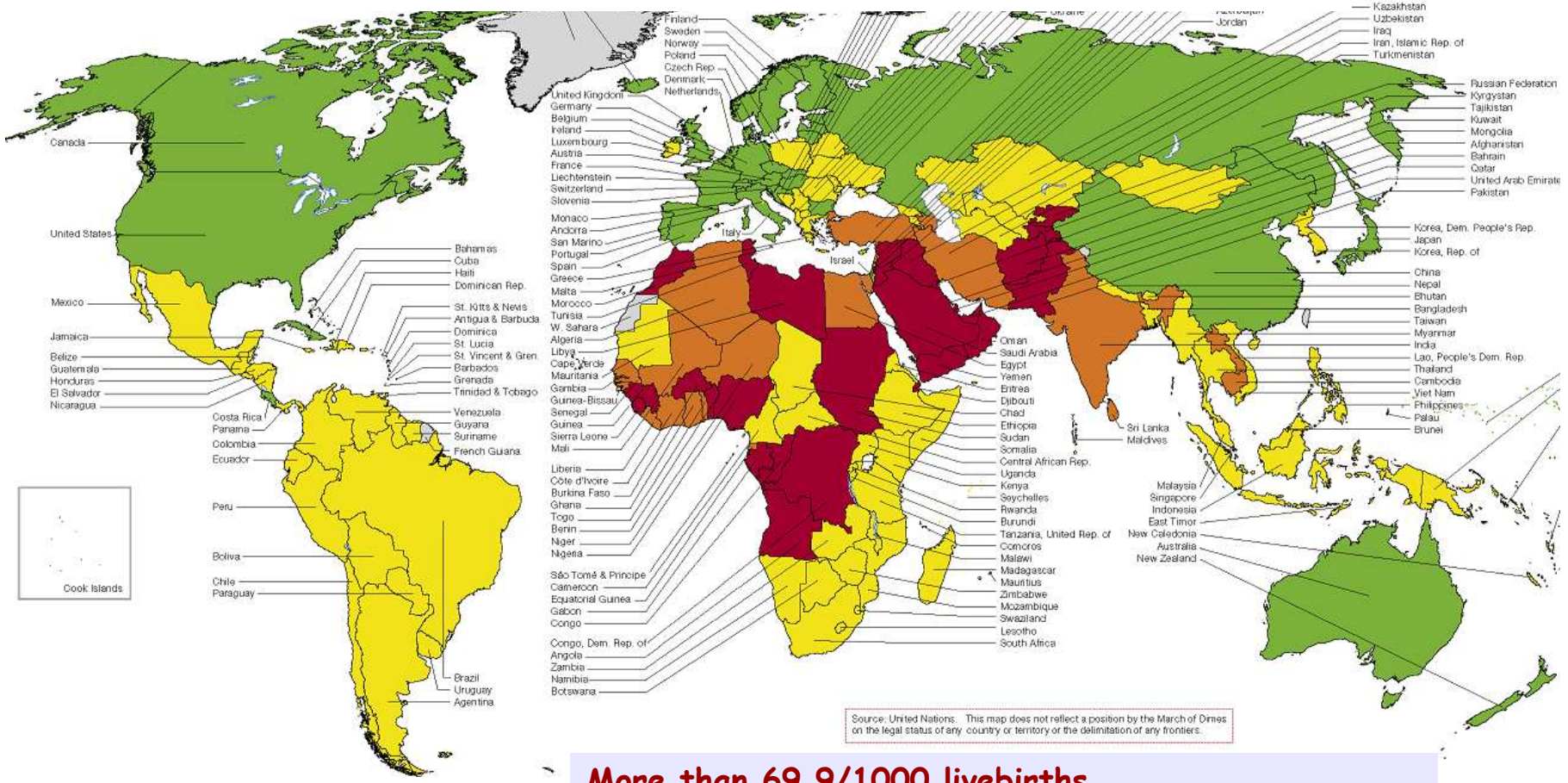


More than 69.9/1000 livebirths

61-69.9

52.1-60.9

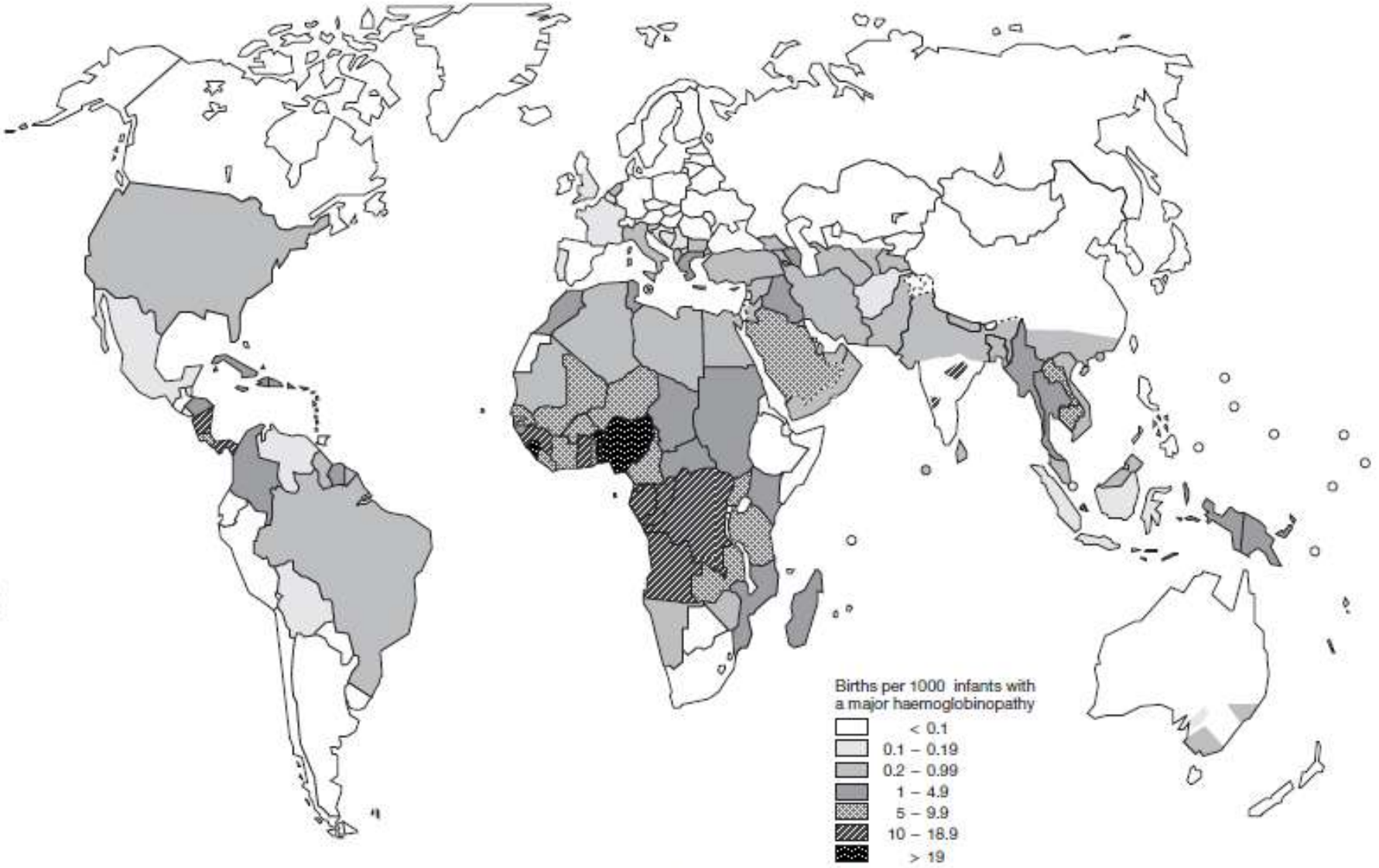
less than 52.1

Christianson A,Howson C, Modell B, 2006

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

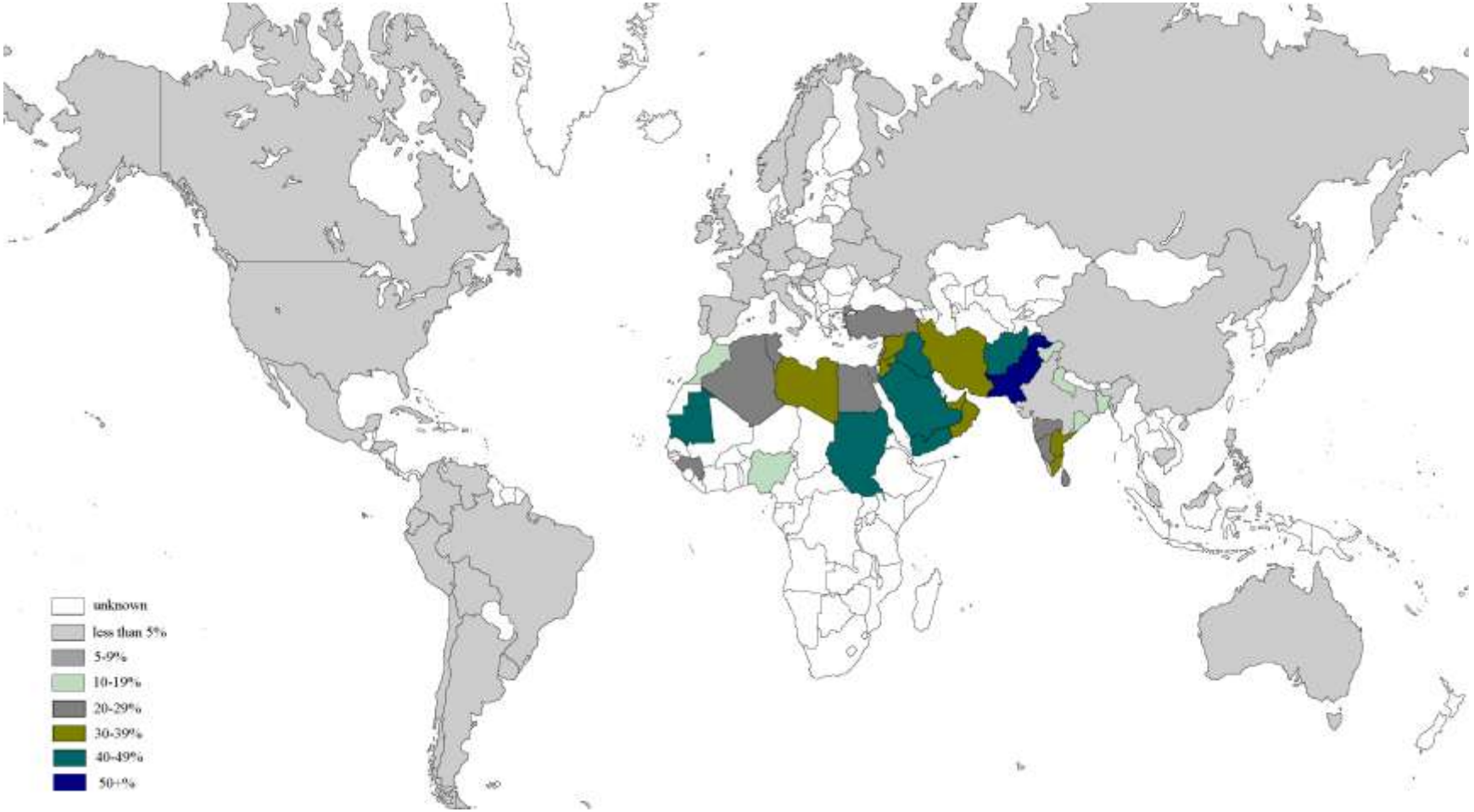
- The high frequency of haemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency;

Global distribution of haemoglobin disorders, in terms of births of affected infants per1000 births



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines represent approximate border lines for which there may not yet be full agreement.

- The high consanguinity rates could contribute to the increase in the expression of recessively inherited diseases;



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

- Women continue to conceive to an advanced age, which increases the predisposition to chromosomal trisomies such as Down syndrome.
- The large family size may contribute to the increase in the number of affected children in families with autosomal recessive conditions such as SCA.

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

- Poor maternal nutrition, more maternal infections, lack of environmental protection.
- Main teratogens are: congenital infections, maternal illness (diabetes and hyperthermia) and drugs.
- Prenatal genetic screening for detection of morphological malformations is not widespread, plus the limitations on selective termination of affected fetus.

Why are community genetics services inadequate in LMIC (1)

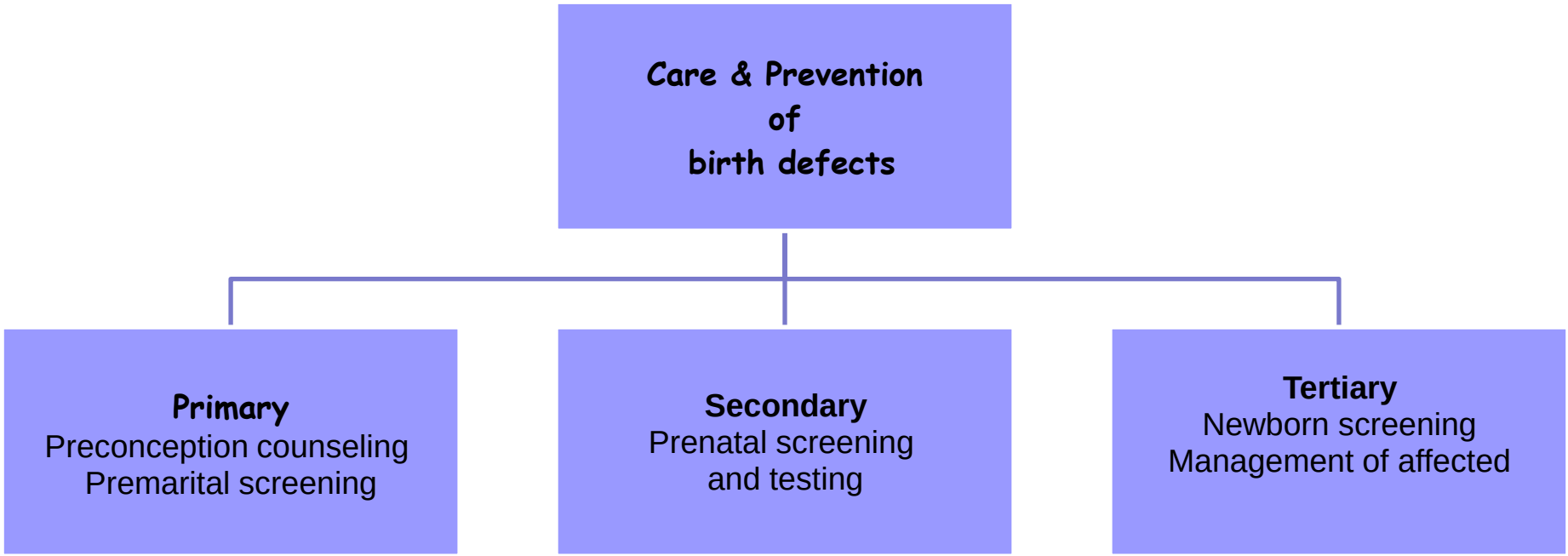
- Paucity of resources and genetic conditions not considered priorities by the medical profession and public health officials.
- Presence of other competing priorities, such as the needs for the control of communicable diseases and non-communicable chronic disorders as cardiovascular diseases, cancer, and diabetes.
- Misconceptions that the control of common congenital disorders is too expensive and always linked with sophisticated high technology, limiting its introduction to the general public; genetic services are misperceived as expensive and dealing only with rare diseases.
- Insufficient number of trained health professionals.

Why are community genetics services inadequate in LMIC (2)

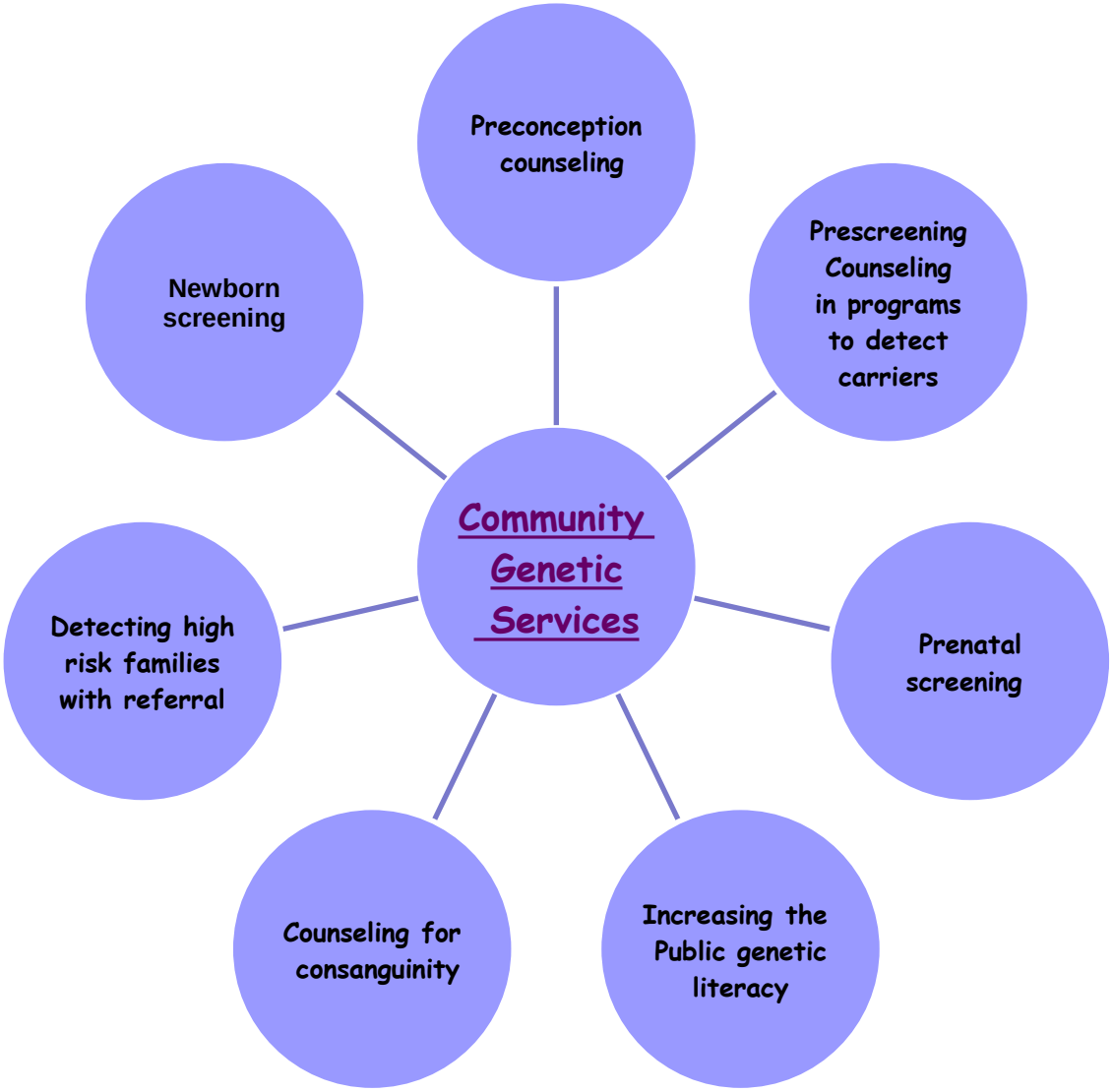
- Low genetic literacy among the health sector and the public with lack of awareness of genetic risks and possibilities for prevention of congenital disorders.
- Community services may be restricted by certain cultural, legal and religious limitations such as the cultural fear of families with genetic diseases to be stigmatized within their community and the legal and religious restrictions to selective abortion of an affected fetus.
- Inadequate data on the real magnitude, health and economic burden of congenital disorders.

Community genetic services: goals and interventions

Goals of community genetic Services



Basic Community Genetic Services that can be offered by primary health care providers



Preconception counselling to maximize the chances of a couple to have a healthy baby

1. Preconception nutritional supplementation for example proper intake of folic acid can minimize the risks for neural tube and other defects
2. Prevention and treatment of maternal infections (Rubella, TORCH, Syphilis)
3. Diagnosis of maternal Rh status
4. Information on risks of advanced maternal age at conception
5. Avoidance of teratogenic drugs and chemicals
6. Cessation of smoking and alcohol intake
7. Family planning
8. Monitoring of maternal health before and during pregnancy (diabetes, hypertension, epilepsy, hyperthermia)

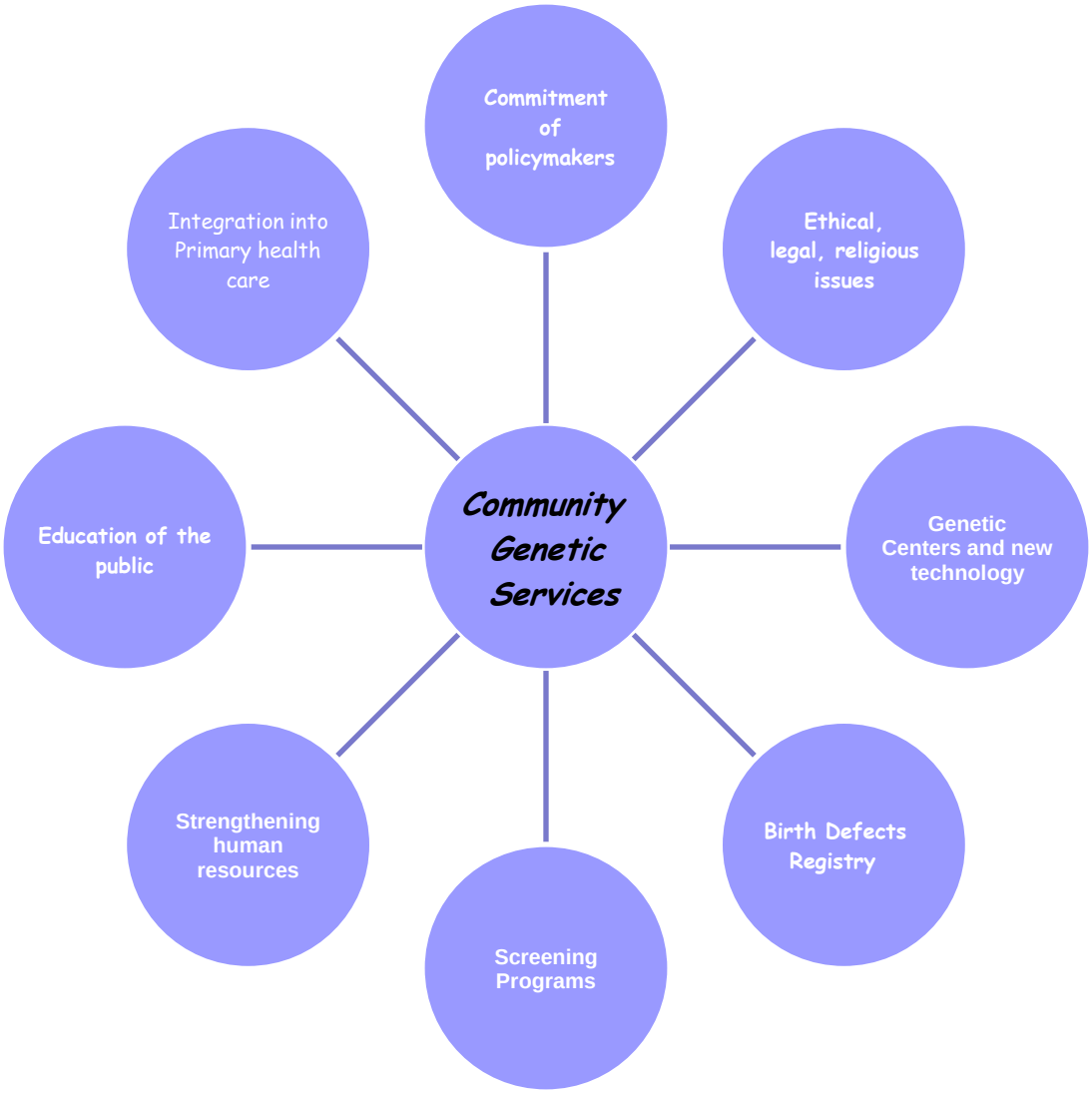
Counseling related to population screening programs

- Newborn screening for example for congenital hypothyroidism and phenylketonuria
- Screening for carriers of common autosomal recessive conditions for example beta thalassemia
- Prenatal screening
- Referral of high risk couples to specialised centers

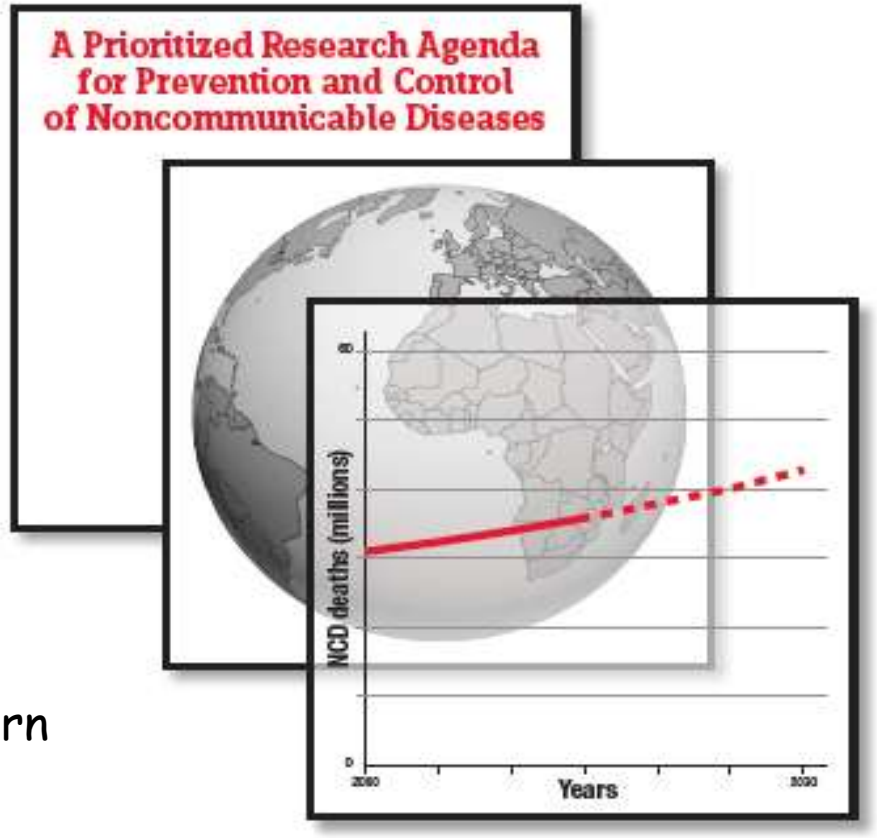
Counseling related to consanguinity in communities where consanguineous marriages are common and referral when indicated

- Detailed family history should be taken to recognize any congenital disorder
- If a genetic disorder is suspected in the family, refer the couple to a specialized genetic counseling clinic
- If there is no known inherited disorder in the family, first cousin marriages are given a risk for birth defects of double the population risk (for example instead of 2.5%, it becomes 5%)

Pillars for introduction of community genetic services



Research priorities for introducing community genetic services in LMIC



Globally at least 7.6 million children are born annually with severe genetic or congenital disorders. Nearly 90% of these infants are born in low- and middle-income countries.

World Health Organization

Develop methods and instruments for assessing the health and economic burden of congenital disorders.

- ✓ Data on the prevalence of congenital disorders in the country (carriers, affecteds).
- ✓ Data on available genetic services, both clinical and diagnostic laboratory services.
- ✓ Data on available human resources in clinical genetics and genetic laboratory personnel.
- ✓ Data on number and capacities of special schools for the care and rehabilitation of affected.
- ✓ Outcomes for affected children in terms of survival.
- ✓ Data on college curricula related to genetics and genetic services.

Develop approaches applicable in primary health care for genetic risk assessment, information and counselling

- Develop approaches to facilitate equitable access to low-cost genetic testing and treatment of genetic disorders.
- Adapt medical record systems to include genetic and family history information.
- Develop informatics approaches for delivering information for health decision-makers, and instruments for professional education and information for patients and the community.

Develop community genetics services, suitable for the country

- Develop locally appropriate approaches for carrier screening of haemoglobinopathies.
- Develop locally appropriate information about reproductive risk and availability and acceptability of options for reducing it.
- Investigate requirements for patient care and cost-effective models of care to address birth defects.

Education

Develop cost-effective tools for delivering information on congenital disorders for health decision-makers, for patients and the community and for professional education

Implement and evaluate preventive approaches for birth defects at:

- before pregnancy (e.g. folic acid food fortification, detection and counselling for carriers, such as sickle cell anaemia or thalassaemia);
- during pregnancy (e.g. fetal anomaly scanning and other forms of prenatal diagnosis);
- at the end of pregnancy (anti-D to prevent rhesus haemolytic disease in subsequent pregnancies);
- in the newborn period (neonatal screening).
- Assess changes in affected birth prevalence and patient outcome in response to interventions addressing birth defects,

Gaps

- There is no agreed primary health care genetics curriculum (good educational material is available on the internet, but most is adapted to a high-income setting, and presented at too sophisticated a level).
- There is no agreement on the requirements for the verbal and graphical content of genetic information materials for practitioners, patients and the public.
- No validated instruments for assessing local epidemiology and costs, establishing surveillance, or providing information, education and training, are available to help decision-makers with planning genetics services.

Research priorities on consanguinity in populations with high consanguinity rates

Questions that need evidence-based answers could include:

Research Questions

Will diminishing the consanguinity rates diminish the prevalence of congenital disorders in the community?

Will diminishing the consanguinity rates diminish stability and solidarity of the family structure in the community?

Will diminishing the consanguinity rates diminish the infant mortality rate in the community?

What can we tell consanguineous couples requesting premarital and preconception counseling?

What are the safe, scientific and evidence-based messages that can be delivered through the media regarding consanguinity?

Recommendations

- Conduct epidemiological studies to determine the most prevalent congenital disorders and genetic diseases and the resulting health care needs.
- Development of approaches applicable in primary health care, for genetic risk assessment, information and counselling.

Recommendations

- Increasing genetic and genomic literacy among the public, health care providers and policymakers through evidence-based WHO guidelines focusing on low and middle income countries.

- Development of internet-based systems for delivering community genetic resources for health decision makers, for professional education, and for patient information.

The overall goal of community genetic services would be to maximize the chances for having healthy babies and to achieve a progressive decline in the rates of congenital disorders for the benefit of families in the community.

Thank You