Community Genetic services in LMIC: Impediments, needs and proposed strategies

Hanan Hamamy
Geneva University
hananhamamy@yahoo.com

Training Course in Sexual and Reproductive Health Research
Geneva 2016

- Community genetics and Congenital disorders
- Needs and Impediments for community genetic services in the LMIC
- Community genetic services and proposed strategies for the care and prevention of congenital disorders in LMIC

What is meant by Community Genetics

- ✓ It means the care and prevention of congenital disorders through community based services
- ✓ Provide services with **equity** and **efficiency** to all those in need
- ✓ Reducing the birth prevalence and the health impact of congenital disorders
- ✓ while respecting voluntary reproductive decisions

Community genetic services

Preconception care

Carrier screening, new born screening and prenatal screening

Genetic counseling and prenatal diagnosis

Epidemiology, surveillance and registries of congenital disorders

Improving Genetic literacy/education among the public and health care providers

Management and rehabilitation of affected

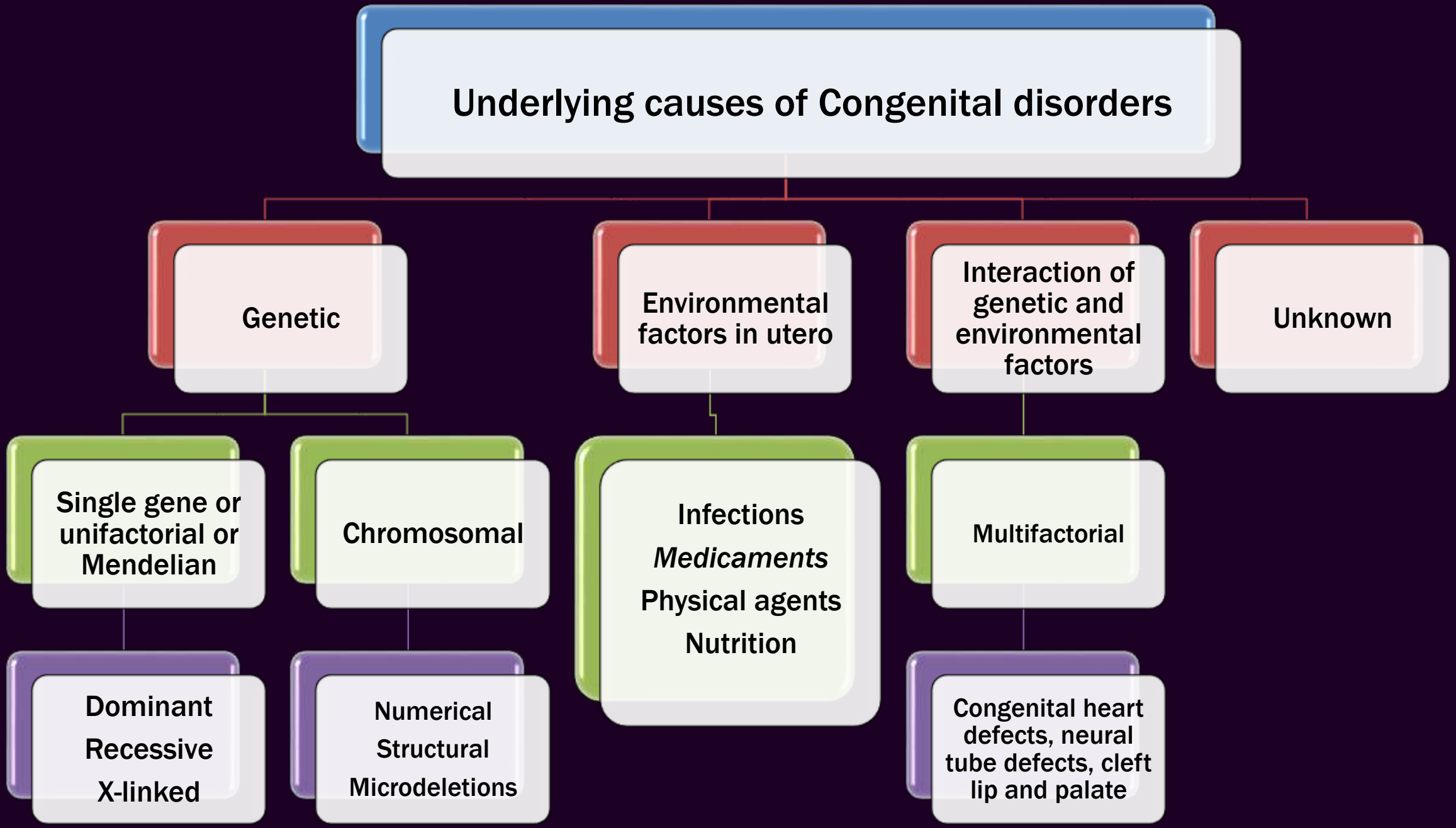
What are Congenital disorders?

- 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

Birth defects (Congenital Disorders)

Categories:

1. Genetic disease (Chromosome or single gene abnormality)
2. Congenital malformations (structural defects)
3. Intrauterine infections as toxoplasmosis and exposure to teratogenic drugs
4. Intellectual disability


Underlying causes of Congenital disorders
Genetic
Environmental factors in utero
Interaction of genetic and environmental factors
Unknown
Single gene or unifactorial or Mendelian
Chromosomal
Infections
Medicaments
Physical agents
Nutrition
Multifactorial
Dominant
Recessive
X-linked
Numerical
Structural
Microdeletions
Congenital heart defects, neural tube defects, cleft lip and palate

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

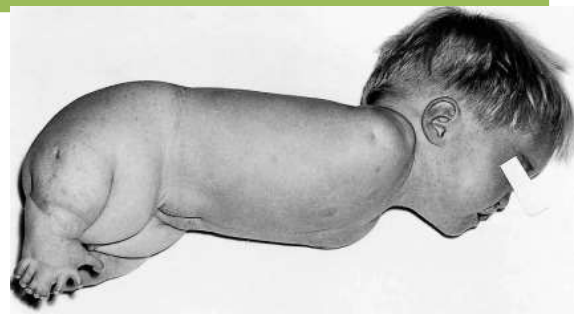
MARCH OF DIMES
GLOBAL REPORT ON BIRTH DEFECTS
THE HIDDEN TOLL OF DYING AND DISABLED CHILDREN

Teratogens

A teratogen is an environmental agent affecting the fetus in utero and may cause a birth defect by interfering with normal embryonic or fetal development

Medicaments such as

Thalidomide



Infections such as

Rubella, Toxoplasmosis, Syphilis, Zika

alcohol

Physical agents such as

Radiation,

smoking

Why do community genetic services have a low priority as health programs in LMIC

- Paucity of resources, genetic services thought to be expensive
- Inadequacy of data on magnitude and burden of genetic disorders
- Insufficient numbers of trained health professionals in the area of medical genetics
- Presence of other competing priorities (communicable diseases, diabetes, cancer)
- Cultural, social and religious limitations

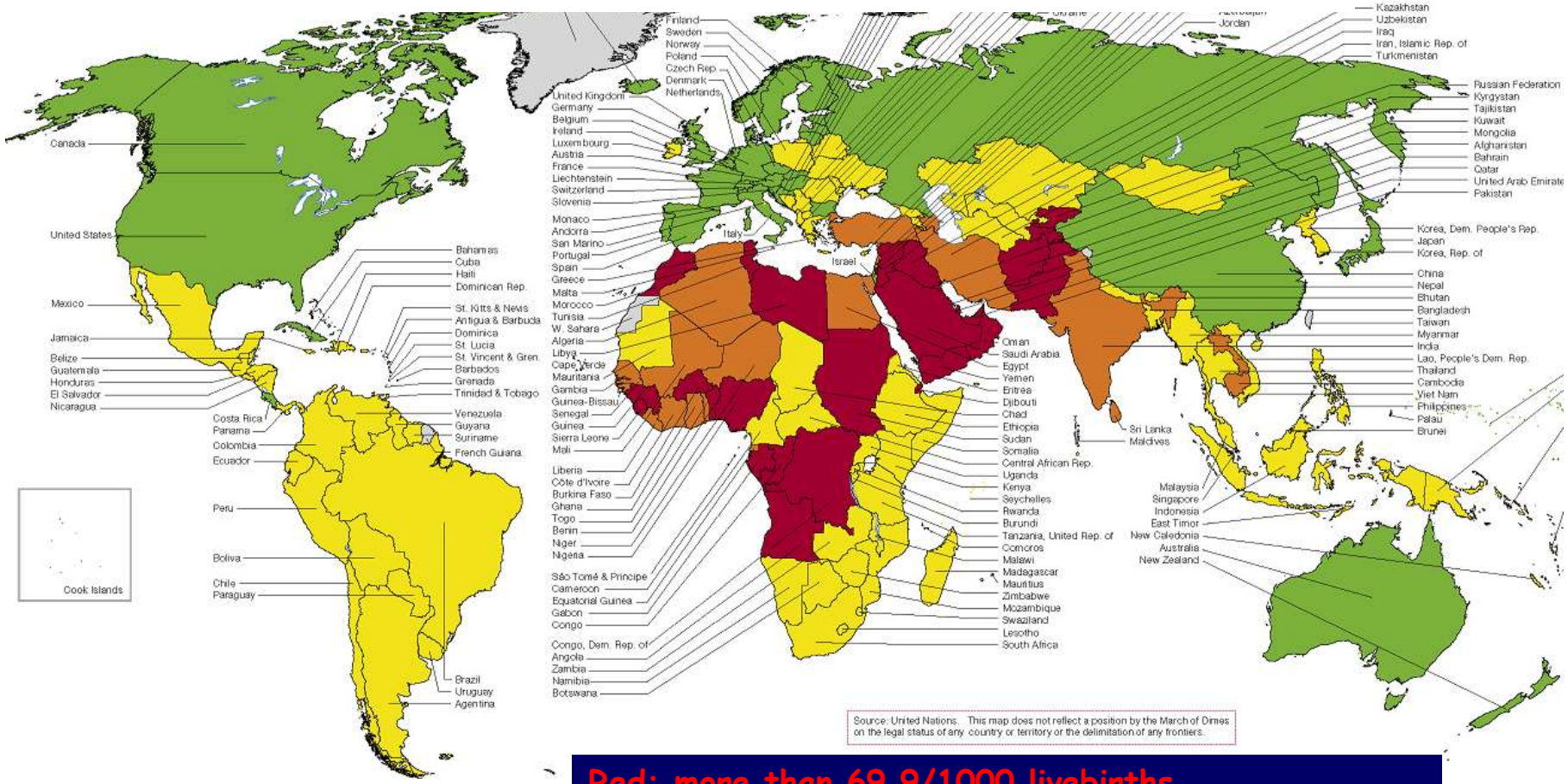
The need to introduce community genetic services in LMIC

- Declining infant mortality
- Good coverage of primary health care
- Rates of congenital disorders estimated to be among the highest in the World
-
-
-

MARCH OF DIMES

GLOBAL REPORT ON BIRTH DEFECTS

THE HIDDEN TOLL OF DYING AND DISABLED CHILDREN



Christianson A, Howson C, Modell B, 2006

Red: more than 69.9/1000 livebirths

Orange 61-69.9

Yellow 52.1-60.9

Green less than 52.1

Grey no data

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

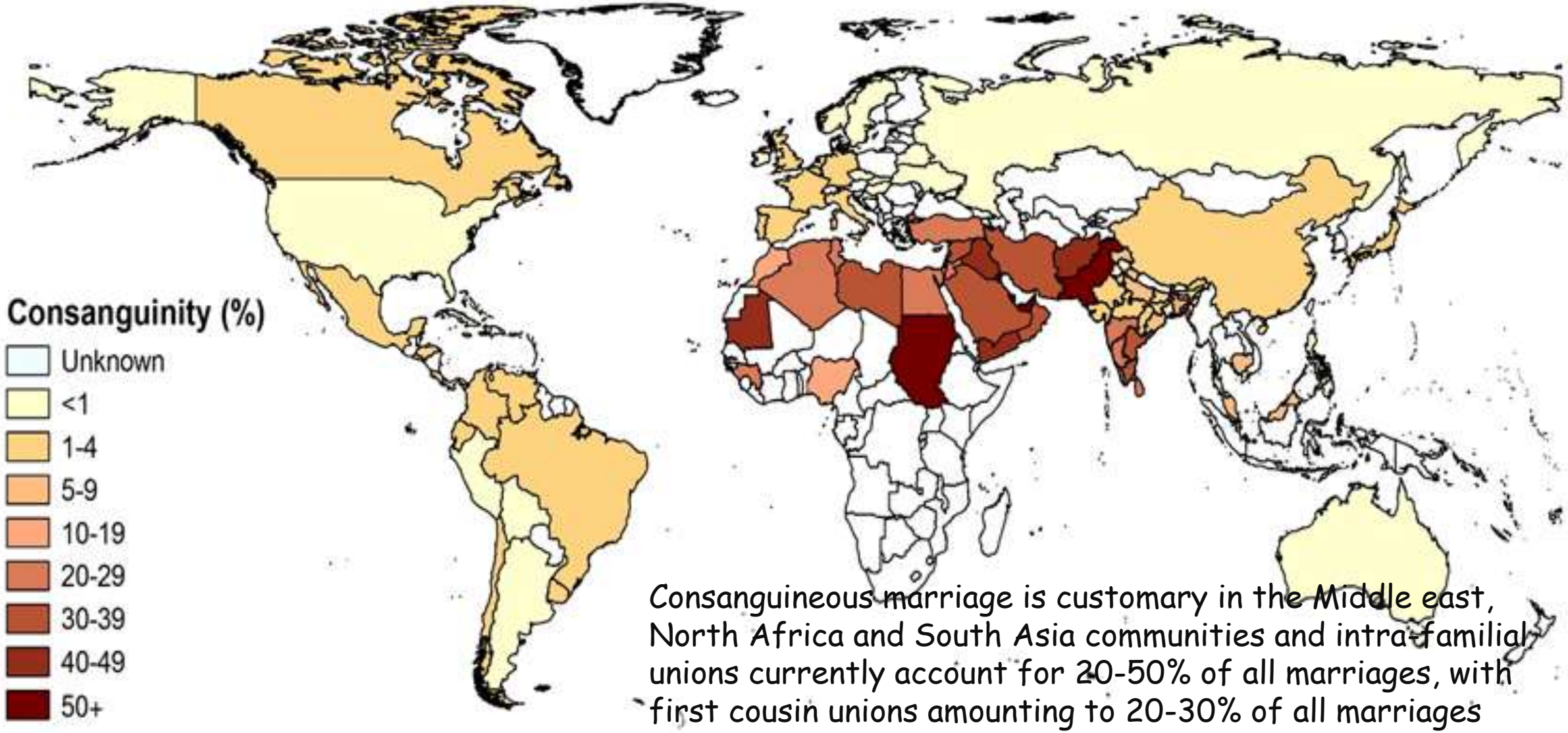
- The general low availability of genetic services and inadequate health care prior to and during pregnancy including poor maternal nutrition, maternal infections, lack of environmental protection; prenatal genetic screening is not widespread, and the limitations on selective termination of affected fetus
- The high frequency of haemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency in many countries
- The high consanguinity rates in Middle East, North Africa and South Asia could contribute to the increase in the expression of recessively inherited diseases
- In many countries, women continue to conceive to an advanced age, which increases the predisposition to chromosomal trisomies such as Down syndrome (related to advanced maternal age)

The need to introduce community genetic services in LMIC

- Declining infant mortality
- Good coverage of primary health care
- Rates of congenital disorders estimated to be among the highest in the World
- **High consanguinity rates**

Global Consanguinity rates

http://consang.net/images/c/c4/Globalcolourlarge.jpg



Consanguineous marriage is customary in the Middle east, North Africa and South Asia communities and intra-familial unions currently account for 20-50% of all marriages, with first cousin unions amounting to 20-30% of all marriages

Consanguinity and congenital disorders

First cousin couples have:

- Slightly higher risk of stillbirths and infant mortality rates among offspring
- 4-6% risk to have an offspring with birth defect
- **Higher risk of having offspring with autosomal recessive disorder if present in the family**

The need to introduce community genetic services in LMIC

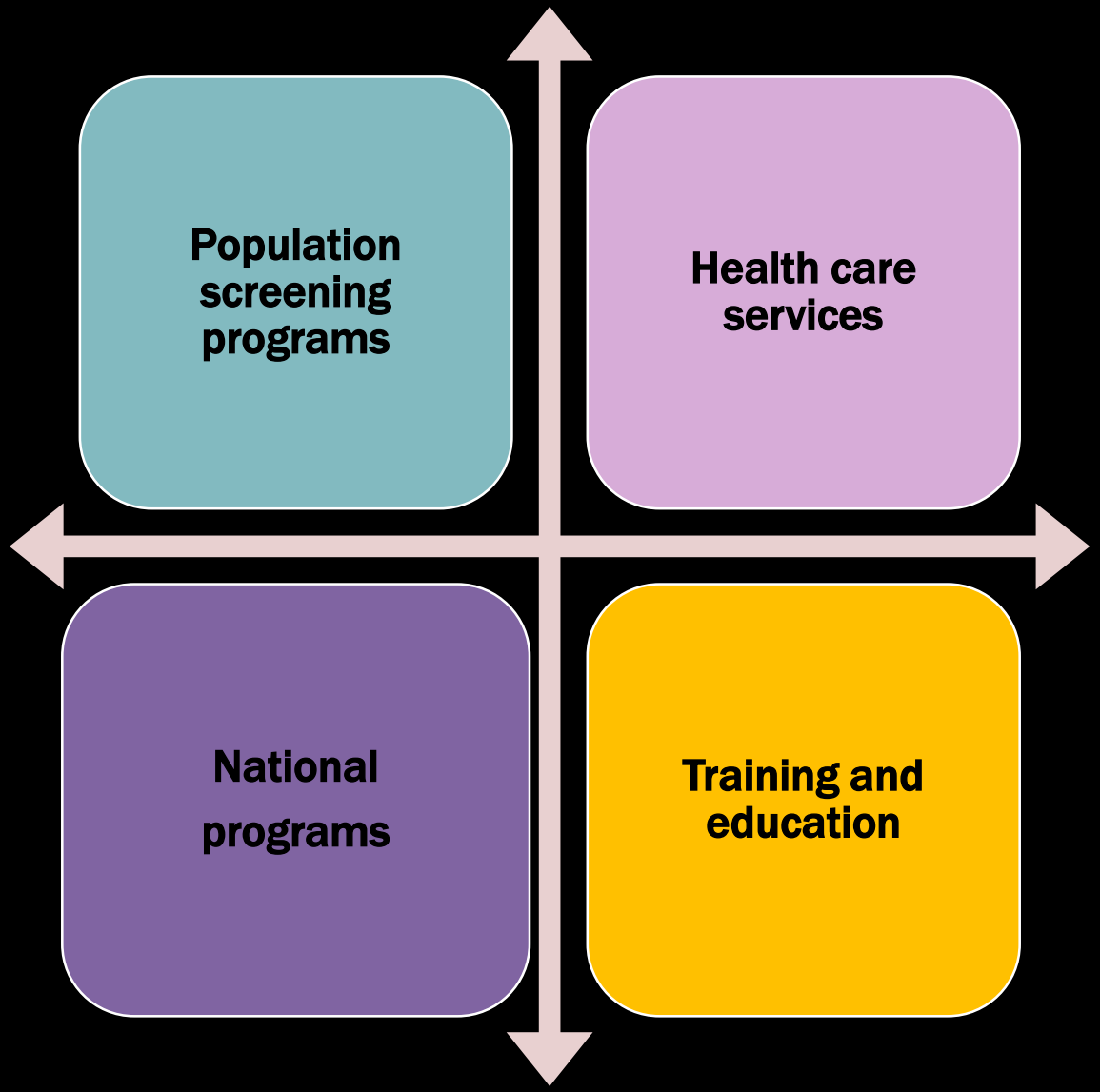
- Declining infant mortality
- Good coverage of primary health care
- Rates of congenital disorders estimated to be among the highest in the World
- **High consanguinity rates**
- Prevention feasible and cost-effective
- **Public and health professionals demand more genetic services**

Proposed interventions and strategies for the care and prevention of congenital disorders in LMIC

Community Genetic programs should be integrated into the already existing national health care and reproductive programs

Community based interventions to reduce burden of congenital disorders

- Premarital and preconception carrier screening
- Prenatal screening
- Newborn screening

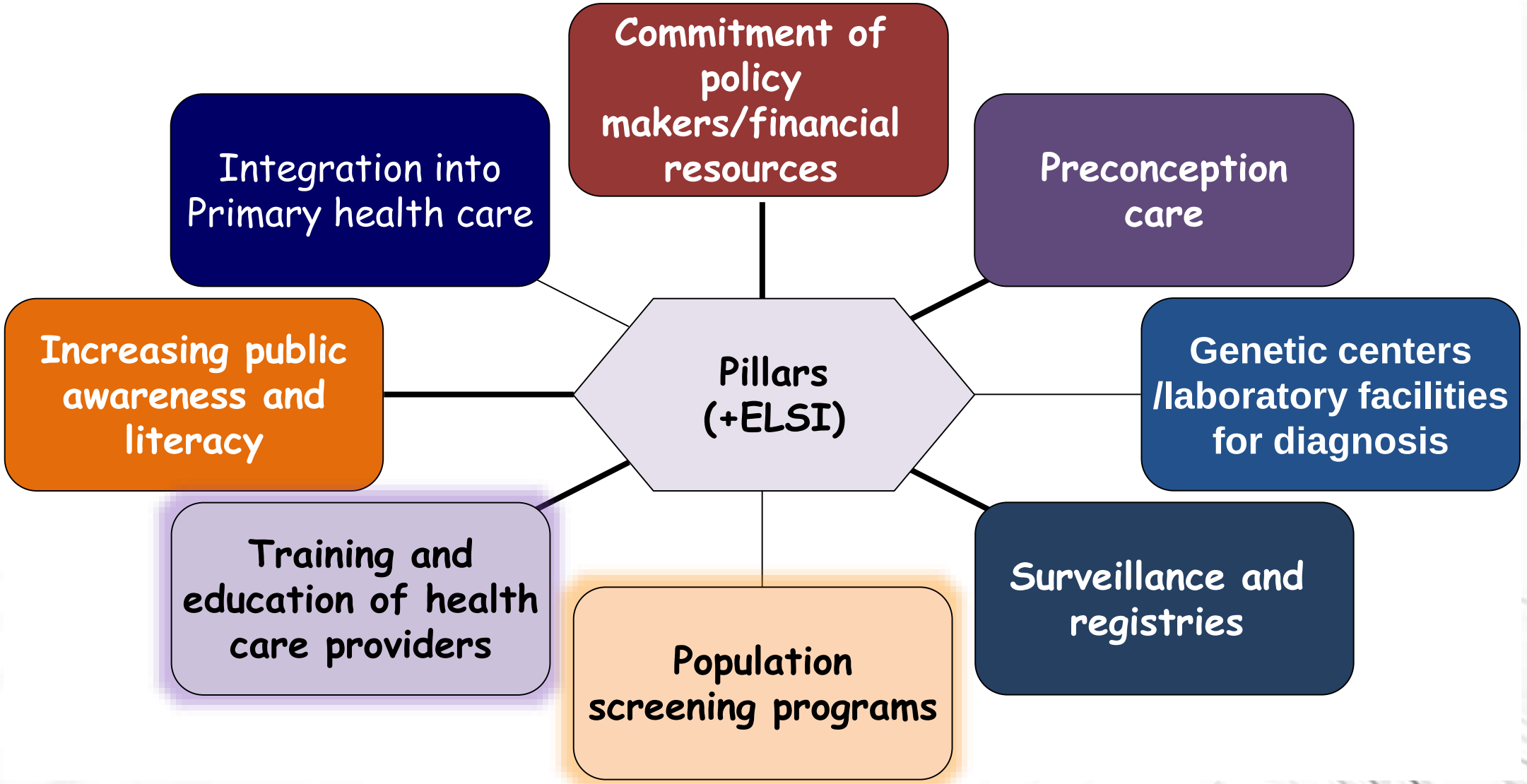


- Preconception care
- Genetic counselling
- Prenatal care
- Prenatal genetic diagnosis
- Management and rehabilitation

- Immunization
- Food fortification
- Registries for congenital disorders
- Promoting healthy lifestyles

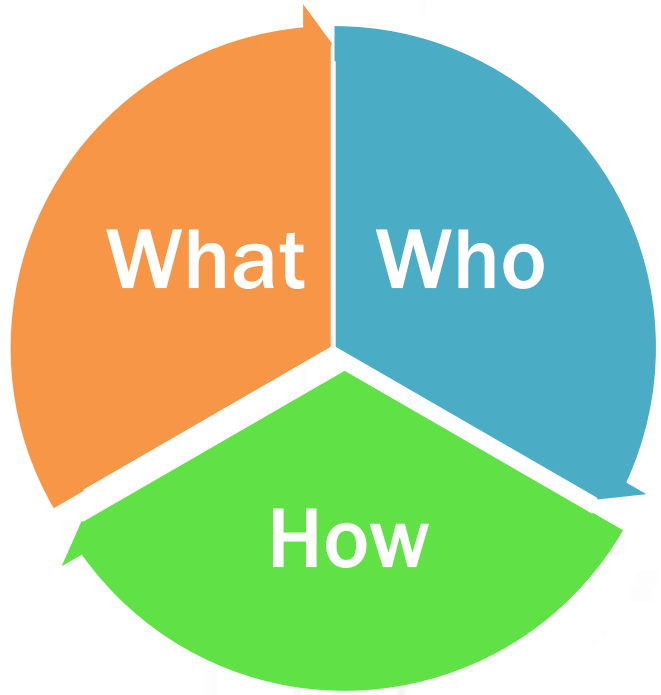
- Health care providers
- Population education
- Medical and nursing students

Pillars for introduction of community genetic services



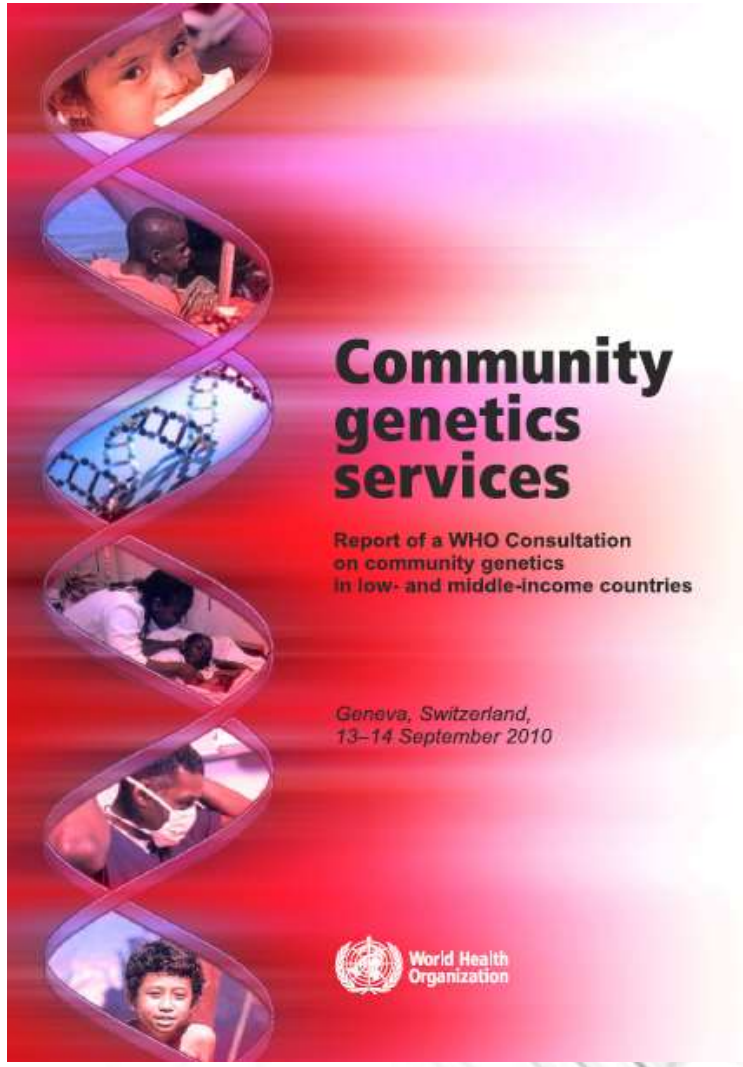
Improving genetic literacy

- Who should be targeted?
- How can they be reached?
- What knowledge should they obtain?



WHO recommendations

- Experience and examples from different countries indicate that the most common genetic services at the community level ("minimum package of interventions") are:
- *Training health professionals in basic concepts of genetics and their application to community genetics services;*
- *Use of family history as an instrument to detect genetic risks;*

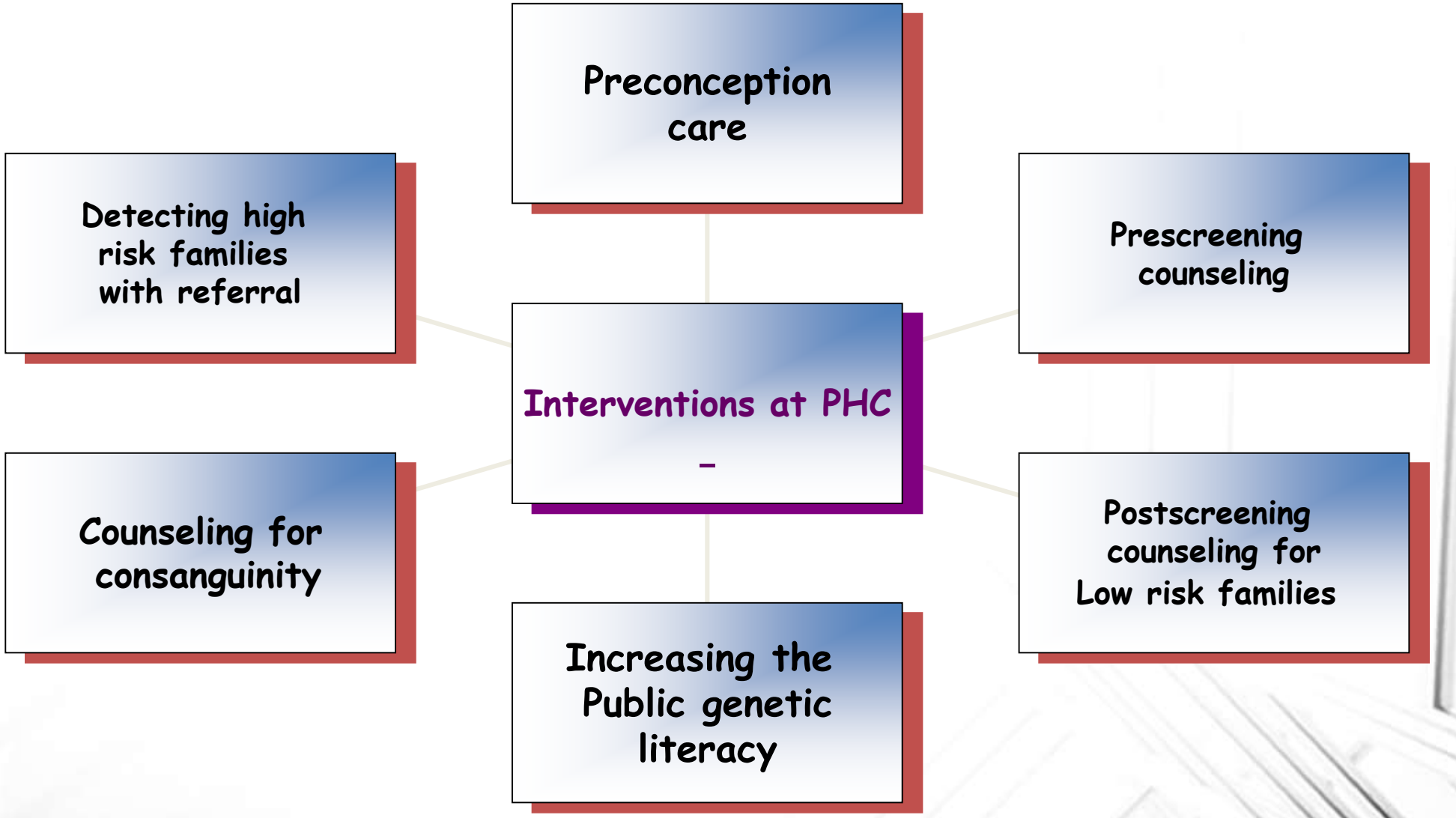


http://whqlibdoc.who.int/publications/2011/9789241501149_eng.pdf

Education and training

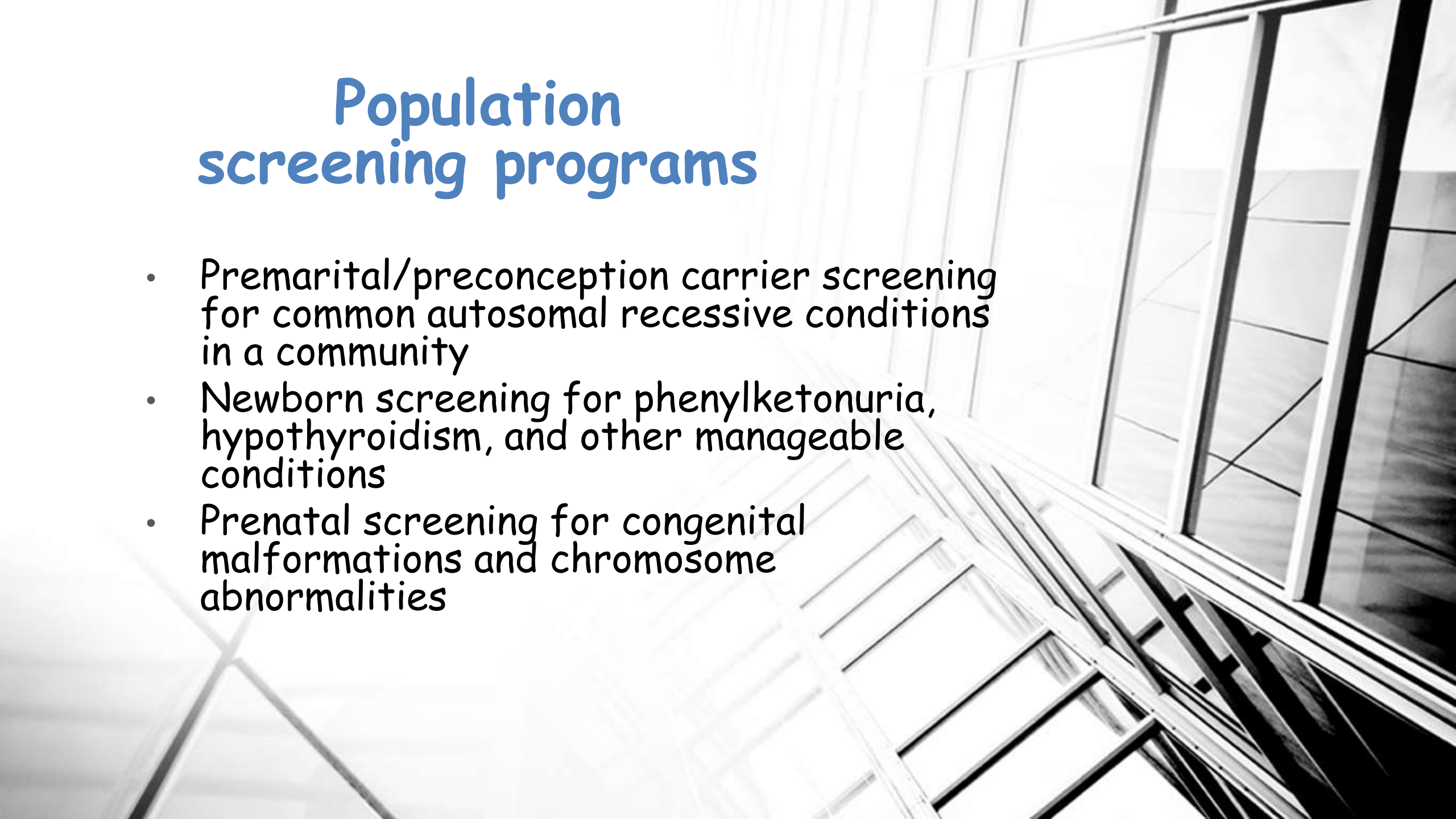
Who?	How?	What?
Medical and Nursing students	Strengthening and updating medical and nursing curricula	Introduce and upgrade community genetics modules
Health care providers Doctors, nurses, paramedics	Training courses Web based courses	Public health approaches for the care and prevention of congenital disorders.
School students	Courses to biology and other teachers	common congenital disorders and importance of screening programs
General population Couples	Pamphlets, clinics Web based information social media	population screening programs Preconception care

The role of primary health care provider in offering community genetic services



Population screening programs

- Premarital/preconception carrier screening for common autosomal recessive conditions in a community
- Newborn screening for phenylketonuria, hypothyroidism, and other manageable conditions
- Prenatal screening for congenital malformations and chromosome abnormalities



Programs for preconception and premarital screening for autosomal recessive disorders: are they successful?

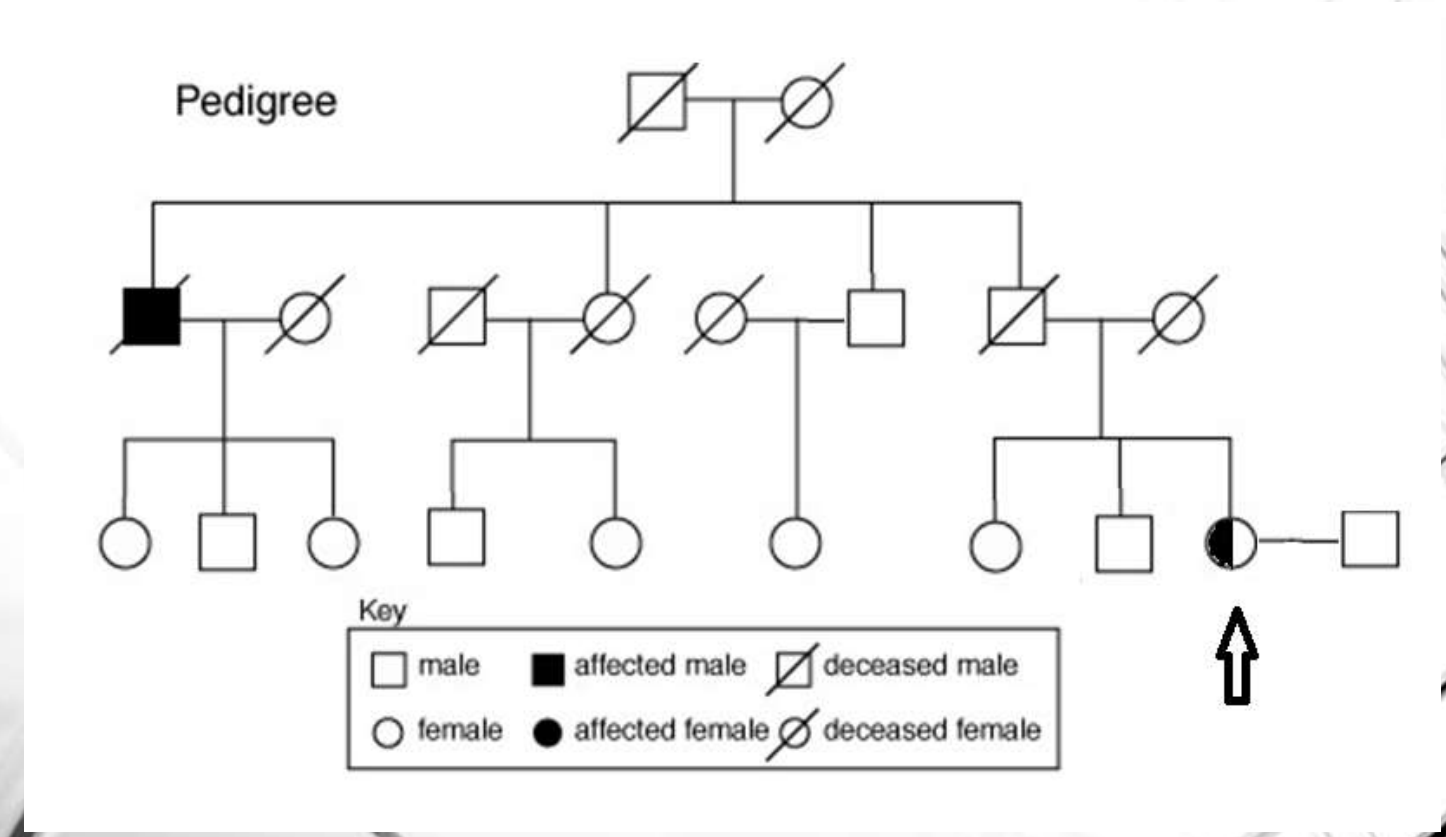
Tay-Sachs disease

After 40 years of preconception screening for Tay-Sachs disease among Ashkenazi in North America the incidence of TSD has been reduced by more than 90%

Beta thalassemia

- In Sardinia, the program showed an effective prevention of 85%
- In North Cyprus, number of affected births went down from 18-20 cases per year to one in every 2-3 years (*Bozkurt, 2007*).
- In Iran, the average fall in affected thalassemia births was 80.82% (Dehshal, 2014)
- In Northern Iraq, affected birth rate of major hemoglobinopathies was reduced by 21.1-65% in different regions (Al-Allawi, 2013 and 2015)

An outcome of carrier screening, other than providing reproductive choices, is that it can provide information for other family members who may also be at risk of being a carrier for an inherited condition.



Future prospects

Can premarital and preconception carrier screening target other AR conditions???

Expanded Carrier screening?

Exome sequencing to define carrier status of known autosomal recessive pathogenic variants

Recent developments in genetic testing technologies enable a move from screening for one genetic condition to screening for multiple conditions at one time point providing the opportunity for cost effective and time efficient carrier screening.

Kingsmore *et al. Genome Medicine* 2012, **4**:25
http://genomemedicine.com/content/4/3/25

Genome Medicine

OPINION

Next-generation community genetics for low- and middle-income countries

Stephen F Kingsmore*, John D Lantos, Darrell L Dinwiddie, Neil A Miller, Sarah E Soden, Emily G Farrow and Carol J Saunders

European Journal of Medical Genetics 57 (2014) 613–616

Contents lists available at ScienceDirect

European Journal of Medical Genetics

journal homepage: http://www.elsevier.com/locate/ejmg

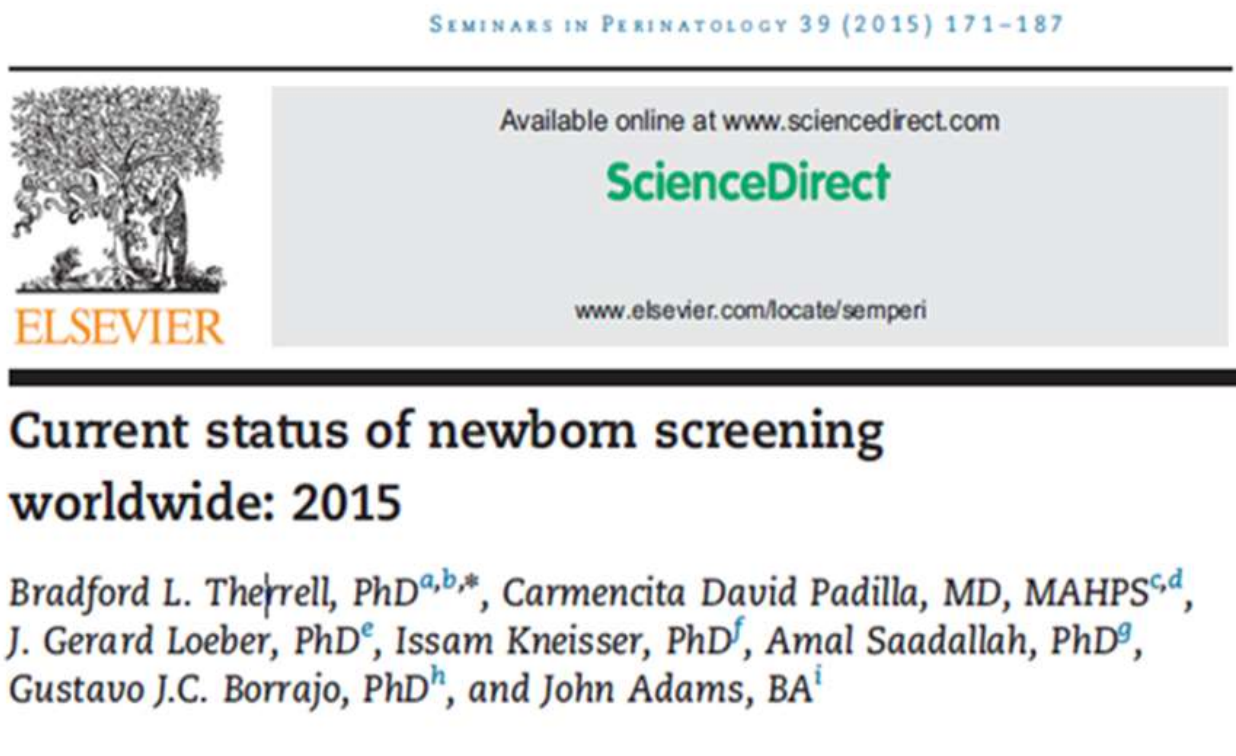
Clinical research

First steps in exploring prospective exome sequencing of consanguineous couples

Marieke Teeuw[a,b], Quinten Waisfisz[a,*], Petra J.G. Zwijnenburg[a], Erik A. Sistermans[a], Marjan M. Weiss[a], Lidewij Henneman[a,b], Leo P. ten Kate[a,b], Martina C. Cornel[a,b], Hanne Meijers-Heijboer[a]

Newborn screening

- Newborn screening describes various tests that can occur during the first few hours or days of a newborn's life and have the potential for preventing severe health problems, including death.
- Newborn screening has evolved from a simple blood or urine screening test to a more comprehensive and complex screening system capable of detecting over 50 different conditions.


SEMINARS IN PERINATOLOGY 39 (2015) 171–187

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/semperi

Current status of newborn screening worldwide: 2015

Bradford L. Therrell, PhD[a,b,], Carmencita David Padilla, MD, MAHPS[c,d], J. Gerard Loeber, PhD[e], Issam Kneisser, PhD[f], Amal Saadallah, PhD[g], Gustavo J.C. Borrajo, PhD[h], and John Adams, BA[i]*

Newborn screening with proper management of conditions like Congenital hypothyroidism, phenylketonuria, sickle cell anemia, cystic fibrosis and other conditions where early diagnosis and management ameliorate the adverse outcomes is a feasible and cost effective preventive intervention

Future prospects:

Rapid analysis of infant genomes is aiding diagnosis and treatment of inexplicably ill babies

NEWS IN FOCUS

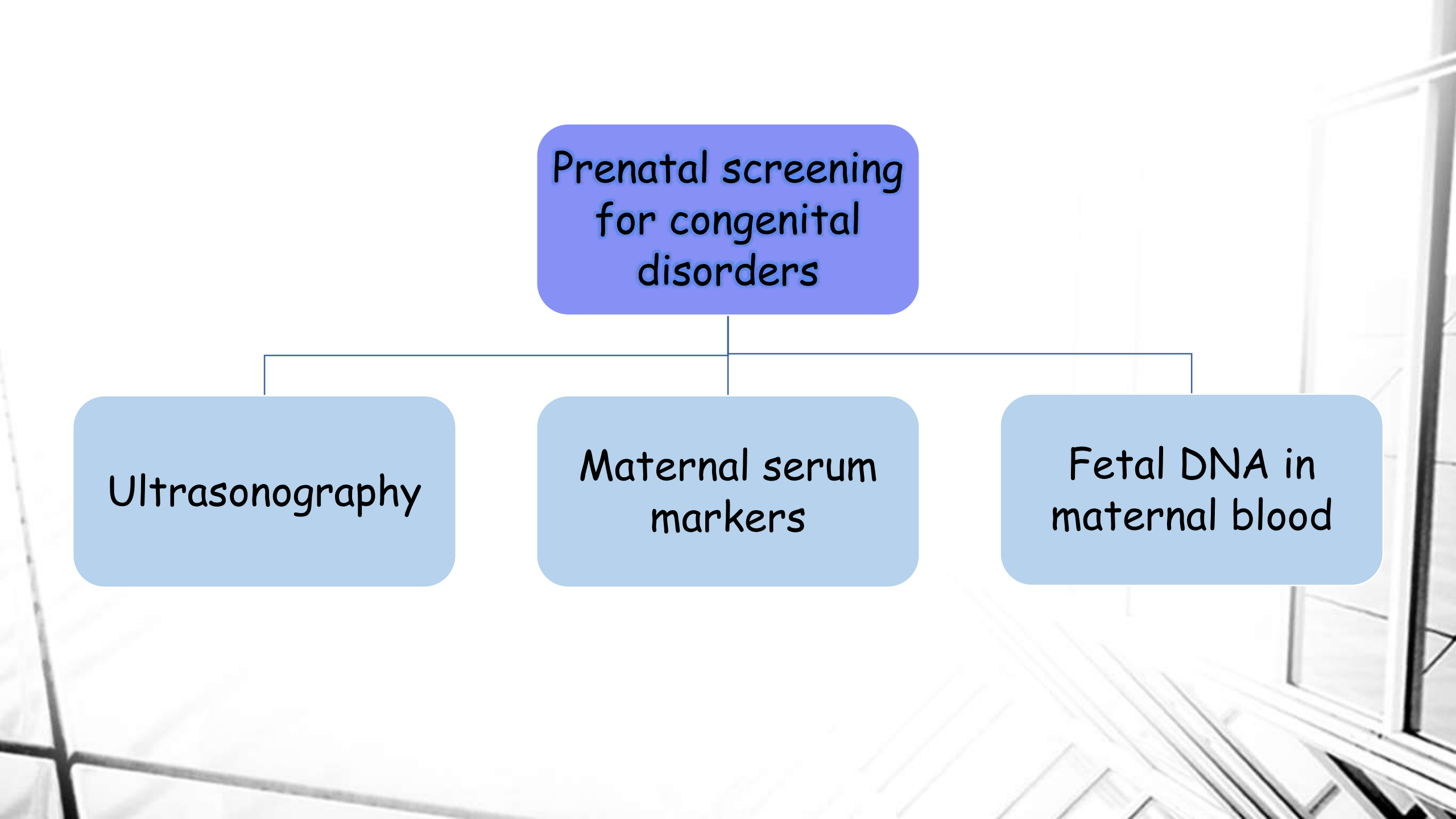
Fast sequencing saves newborns

Rapid analysis of infant genomes is aiding diagnosis and treatment of inexplicably ill babies.

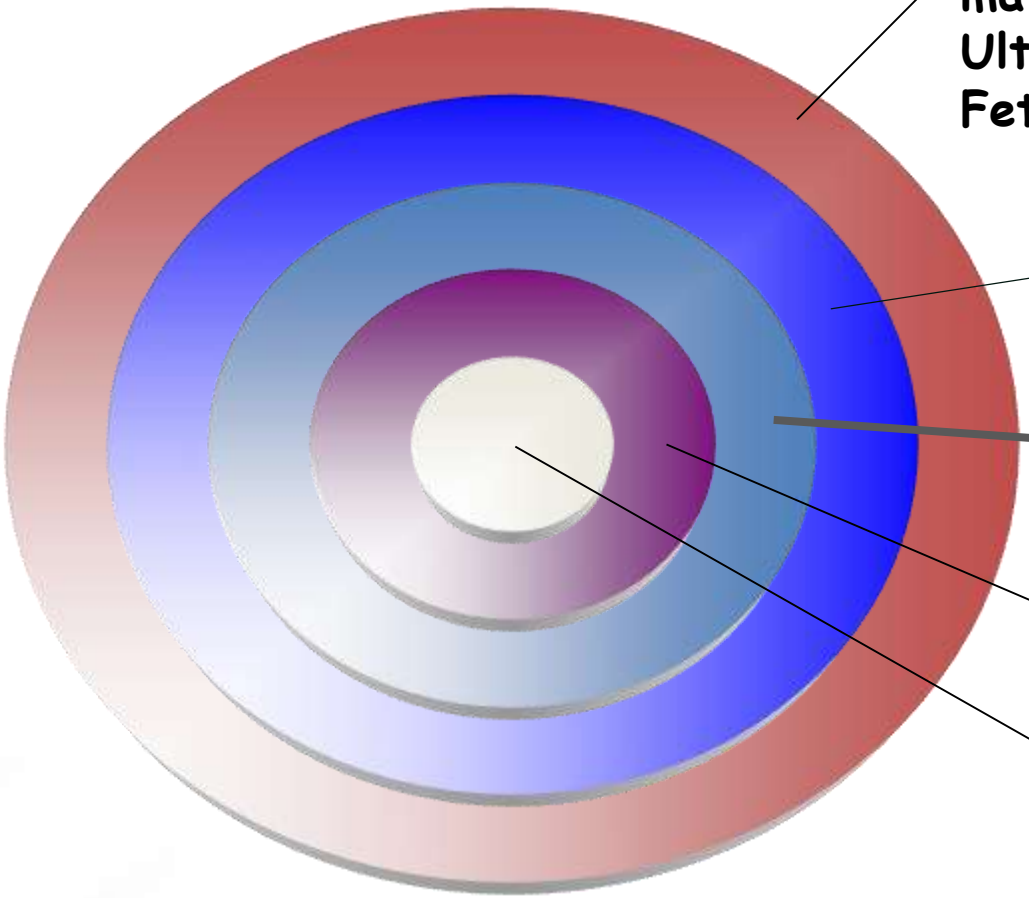
BY SARA REARDON

- The boy is one of 44 sick infants whose genomes Kingsmore's group has sequenced using a process that can provide a diagnosis in as little as 24 hours. In 28 of these cases, the researchers have been able to diagnose the baby's condition. And in about half of these, they have been able to recommend changes in treatment

Reardon S. Fast genetic sequencing saves newborn lives. Nature. 2014 Oct 2; 514(7520):13-4.


Prenatal screening for congenital disorders
Ultrasonography
Maternal serum markers
Fetal DNA in maternal blood

Progression of Prenatal screening



maternal serum markers
Ultrasound
Fetal DNA sampling in maternal blood

Abnormal Results:
Problem:interpretation and risk assessment

prenatal diagnosis by CVS,
Amniocentesis and ultrasound

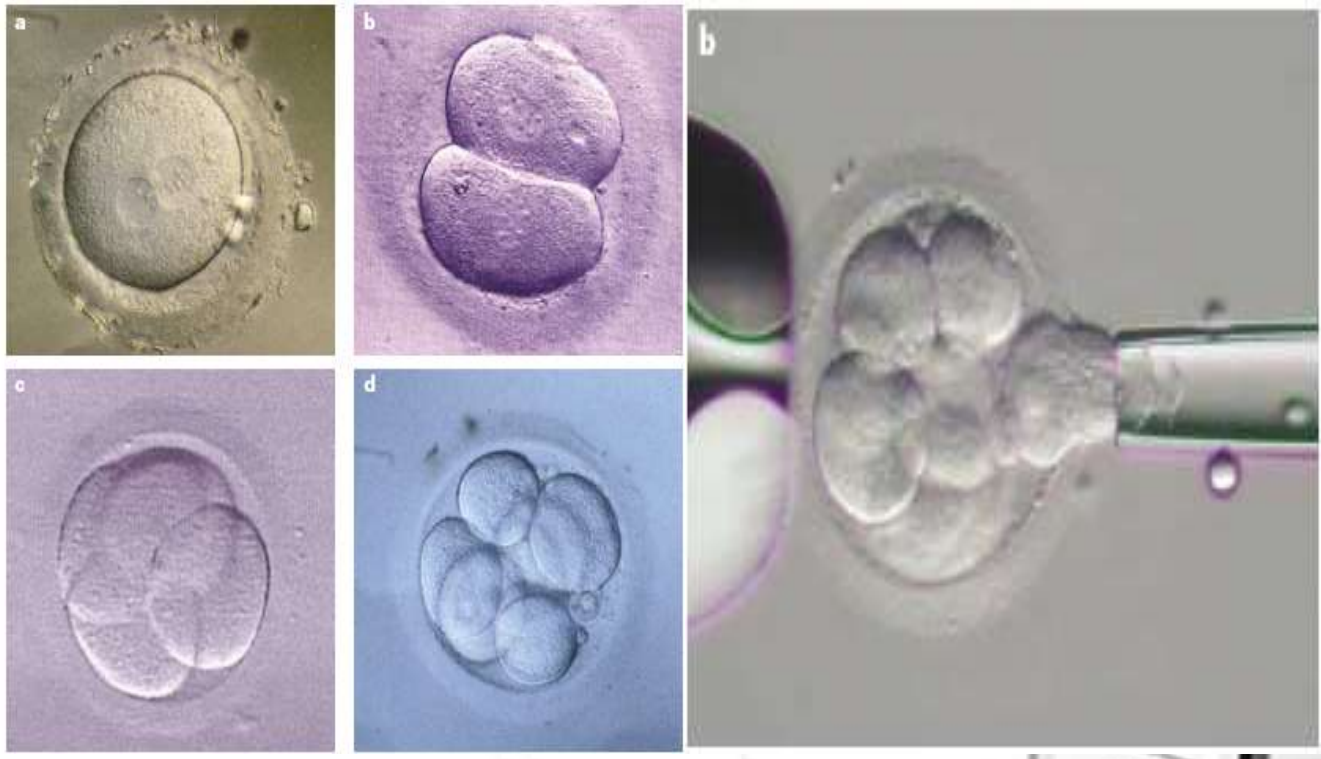
Abnormal results

Termination
or continuation of pregnancy

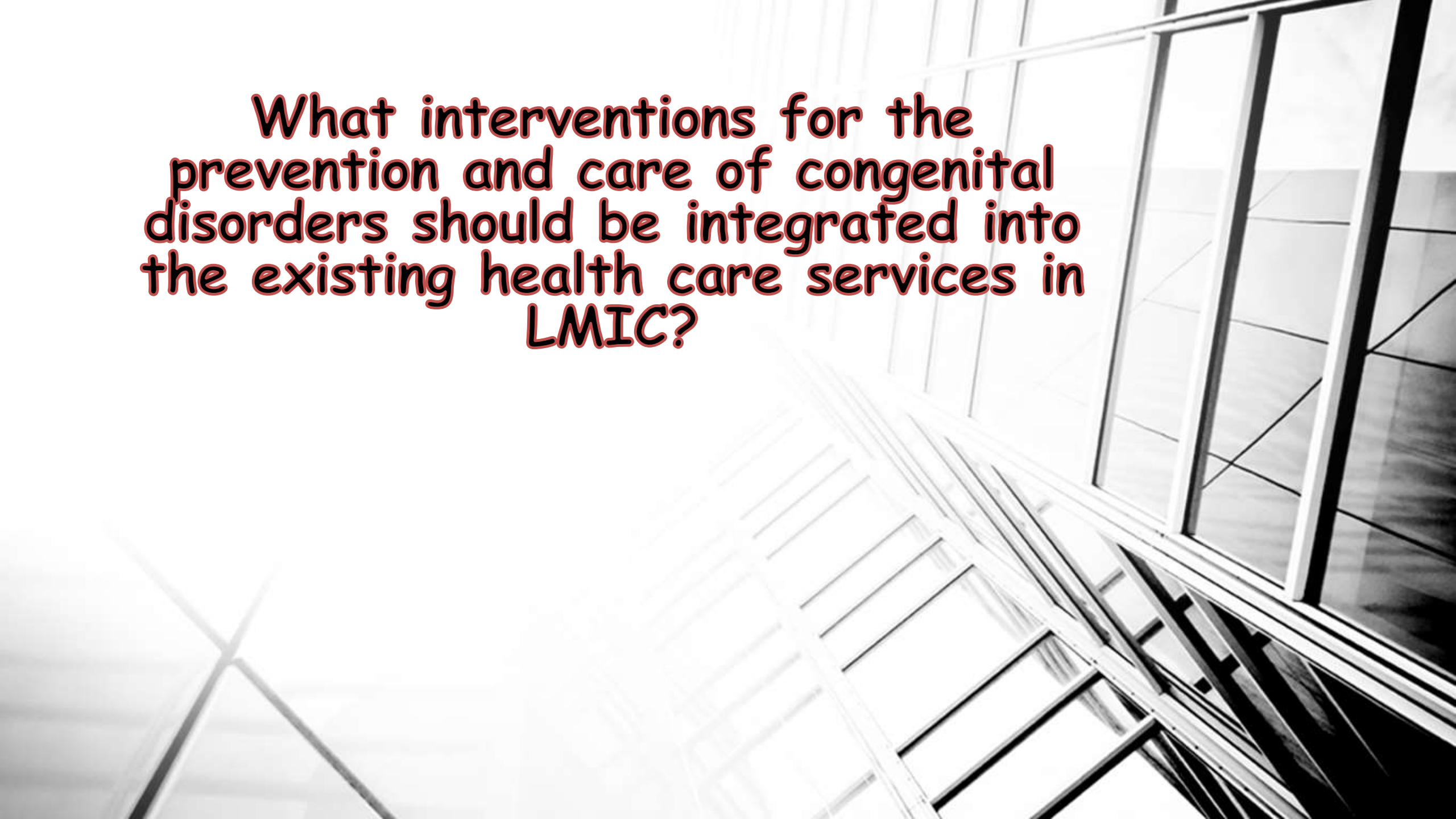
Problem: If no guidelines on termination of affected fetus

Preimplantation genetic diagnosis (PGD)

- Preimplantation Genetic Diagnosis (PGD) uses in vitro fertilisation (IVF)
- Tests one or two cells from each embryo for a specific genetic abnormality
- Identifies unaffected embryos for transfer to the uterus
- The approach through PGD assists couples at risk of an inherited disorder to avoid the birth of an affected child without going through selective pregnancy termination



What interventions for the prevention and care of congenital disorders should be integrated into the existing health care services in LMIC?



Interventions at the preconception period (includes premarital)

Supplementation and fortification with folate, iron

Immunization Rubella, hepatitis B

Screening for carriers of common autosomal recessive disorders

Screening and treatment of infections such as syphilis, toxoplasmosis and HIV/AIDS

Screening , diagnosis and optimal management of diabetes and other maternal chronic conditions

Blood grouping including Rh typing

Genetic family history to identify and refer high risk families

Healthy life style: advice on cessation of smoking, weight management and healthy lifestyle

Interventions during pregnancy

Supplementation with iron , folate	Management of maternal conditions like diabetes	Avoidance of tobacco use, alcohol and exposure to pollution
Avoidance of teratogens (drugs, infections)	Treatment of infections	Prenatal screening and diagnosis +/- TOP

Interventions after birth

Newborn screening

Diagnosis and Management of affected

Care and rehabilitation of affected

Counseling parents of affected

Extended family screening, testing and counseling

Conclusion

- The considerable challenge posed by congenital disorders calls for the development of care and prevention programmes through the establishment of community genetics services.
- The strategies do not necessarily require sophisticated technical facilities but are primarily based on strengthening the training of health professionals and public education.
- The World Health Organization (WHO) has a crucial role to help LMIC plan and implement community genetic services to reach all those in need with equity and quality.