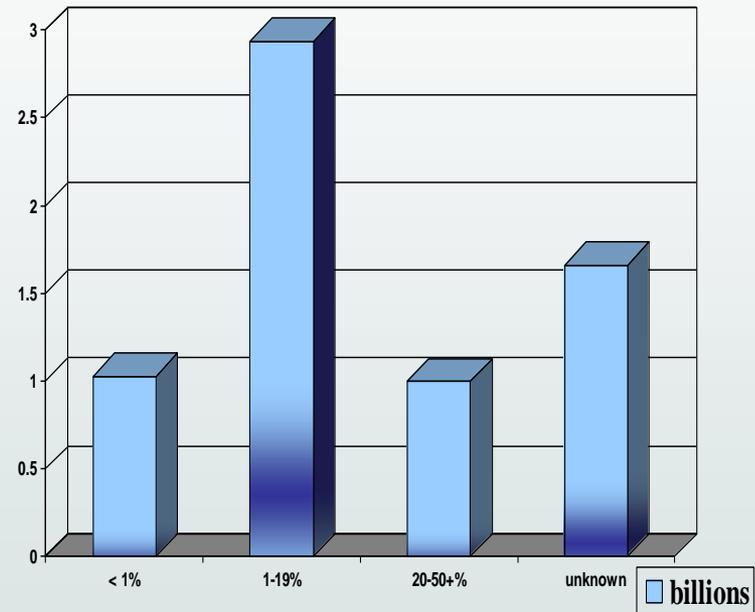


# Consanguineous marriages Trends, impact on reproductive health and research priorities

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# Why are we interested in studying consanguinity?

- High consanguinity rates of 20-50% in about one billion of the world population



Global Consanguinity Rates  
(Bittles ,2008)

## Why are we interested in studying consanguinity?

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- Do we really know the adverse effects of consanguinity on health?
- Do we really know if there are advantages versus disadvantages?
- Do we know the evidence-based steps that could minimize any adverse effects of consanguinity in communities?

## Why are we interested in studying consanguinity?

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- What are the evidence-based guidelines regarding genetic counseling for consanguinity?
- New genetic technologies provide opportunities for research in highly consanguineous populations.

*Global Consanguinity  
rates*

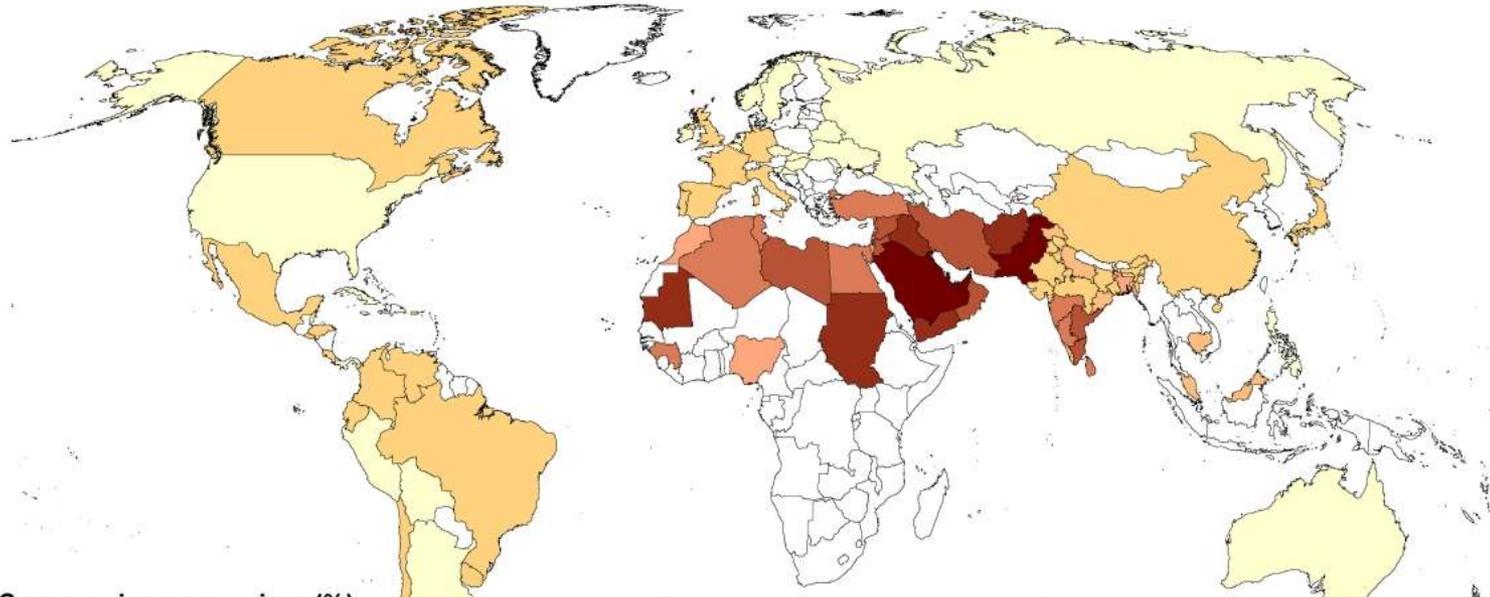
# Consanguineous marriages

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- Consanguineous means related by blood
- As a working definition, unions contracted between persons biologically related as second cousins or closer are categorized as consanguineous, having one or more ancestors in common no more remote than a great-grandparent (consag.net; WHO document 1997, EUROCAT)

# Global Prevalence of consanguinity

[http://www.consang.net/index.php/Global\\_prevalence](http://www.consang.net/index.php/Global_prevalence)



Consanguineous marriage (%)



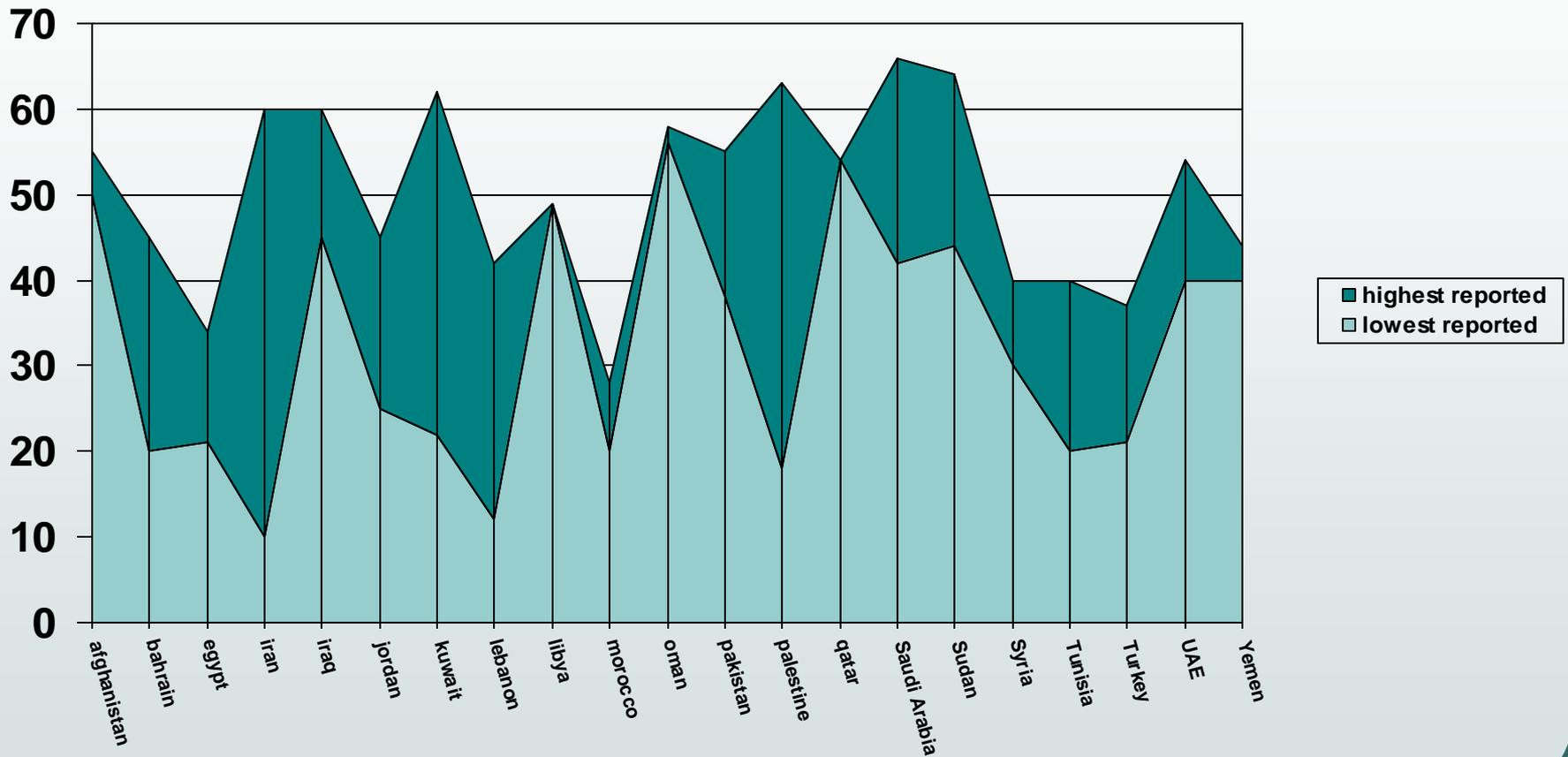
- Less than 1%: United States, Russia, Australia, parts of Latin America and Europe
- 1-10%: China, Latin America, North India, Japan, South Europe and Canada
- 10-50%: Arab countries, Turkey, Iran, Pakistan, Afghanistan, South India.
- Unknown: Parts of South-East Asia, most Africa

## *Population types favouring consanguineous marriages*

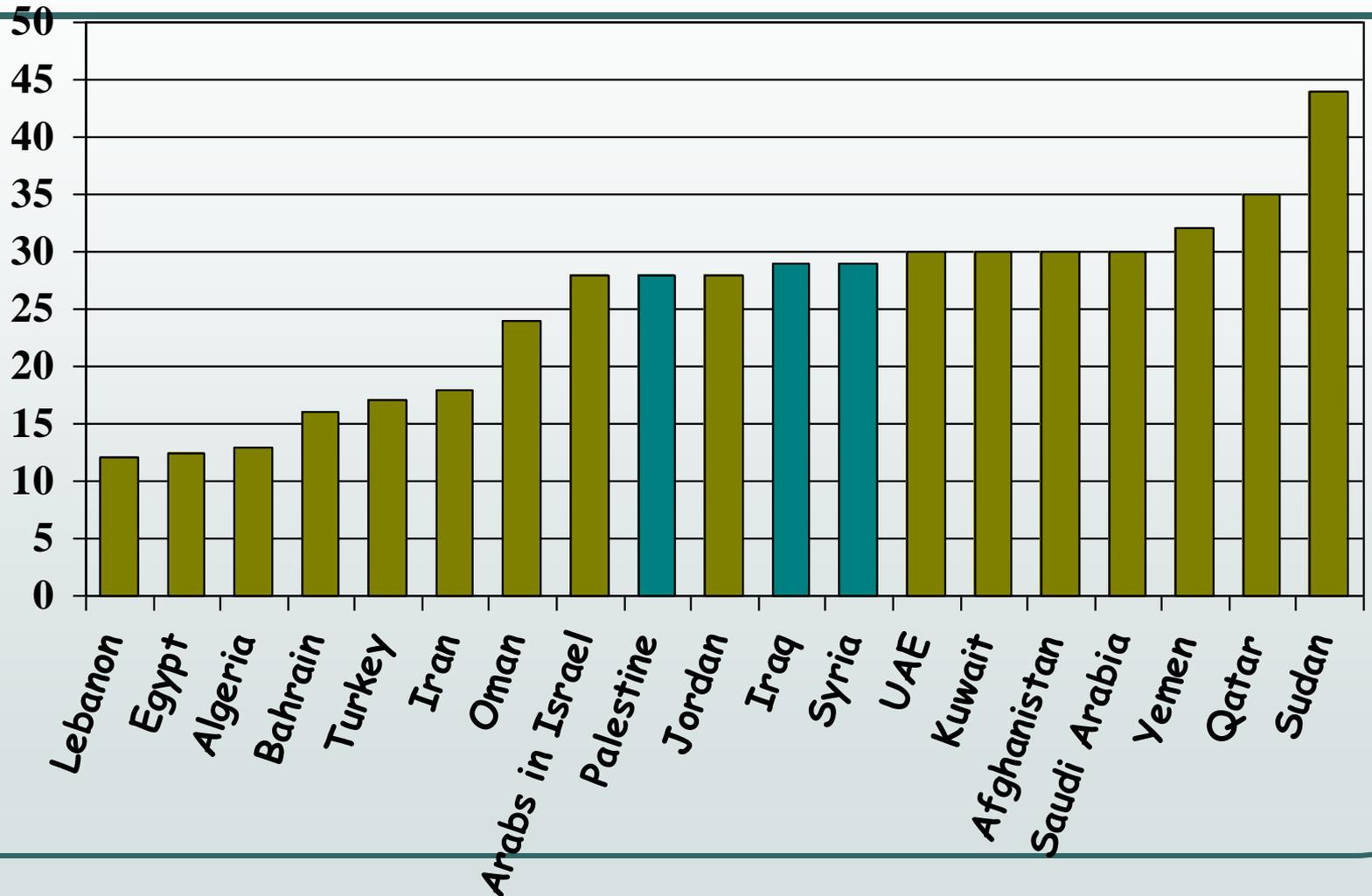
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- Major populations in Middle East, North Africa, South Asia (20-50+% of all marriages are consanguineous)
- Major populations in Latin America, Japan, China ( 1-10% of all marriages are consanguineous)
- Recent migrants from Pakistan, India, the Middle East, North Africa and South Asia, becoming permanent residents in Europe , USA and Canada. ( e.g. 2 millions Maghrebians in France, 1.5 million Turks in Germany, 0.5 million Pakistanis in the U.K.)
- Small population isolates where inbreeding is common account for a very small percentage of the world population( e.g. Amish).

# Range of consanguinity rates in highly consanguineous populations

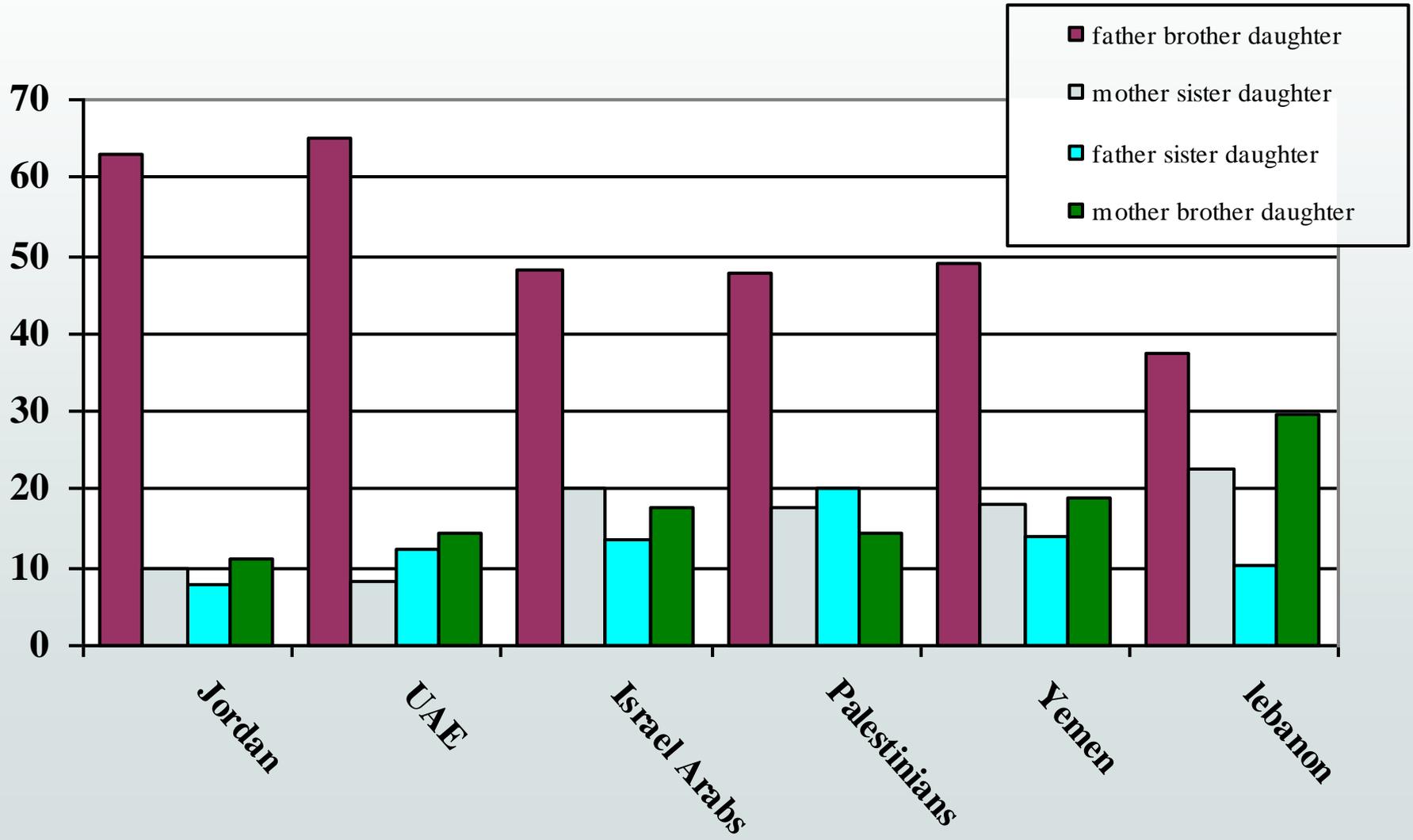


# Rates of first cousin marriages in highly consanguineous populations (+/- double first cousins)



*Types of first cousin  
marriages*

# Patterns of first cousin marriage



## Reasons for choosing to marry a cousin

- Consanguinity is a deeply rooted cultural trend in certain communities.
- More favourable for the women`s status. The wife would have better relationship with her in-laws and could be protected by them in time of need.
- There is a general belief that marrying within the family reduces the possibilities of hidden health and financial uncertainties.
- Premarital negotiations regarding financial matters of marriage are more easily conducted, keeping the money and property within the family.
- Strengthens family ties, and enforces family solidarity.

# Factors affecting consanguinity rates

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- Consanguinity rates are higher in rural than urban settings of a certain community.
- Higher female education reduces the rate of first cousin marriages.
- First cousin marriages are more common when the parents of the couple are consanguineous.
- In the same community, consanguinity rates are higher among Muslims than among Christians, for example in Lebanon, Jordan, South India.

*Secular trends in  
consanguinity rates*

## Are consanguinity rates changing with time?

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- They have declined in North America and Western Europe. First cousin marriages rate now is around 0.6%
- They have also declined in Japan: cousin marriages accounted for 5.9-14.7% until 1960's, 5.7% in 1972, and 3.9% in 1983.

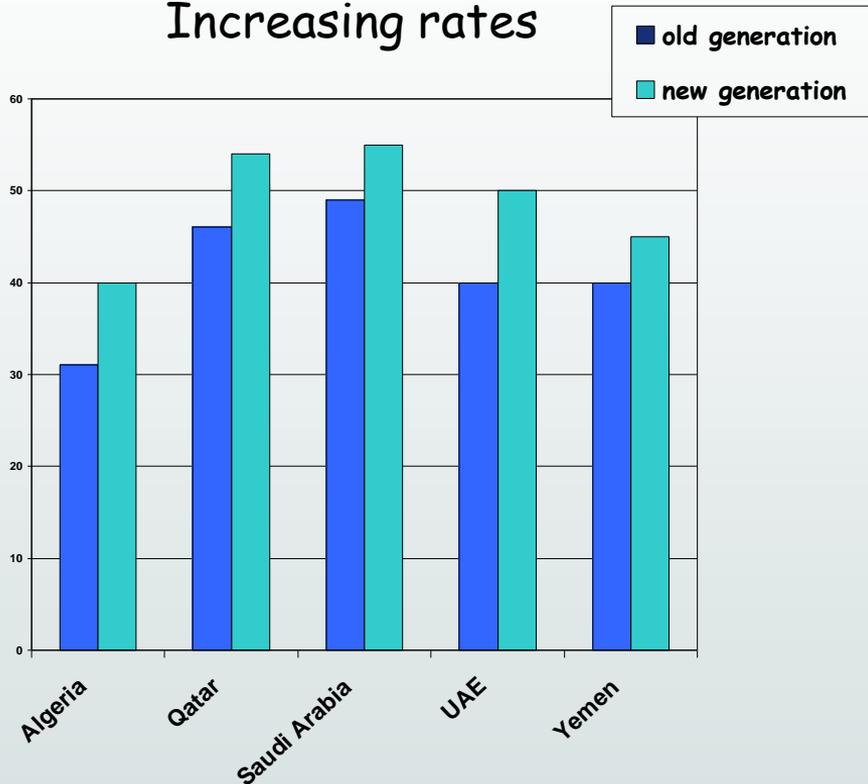
# Are consanguinity rates changing with time?

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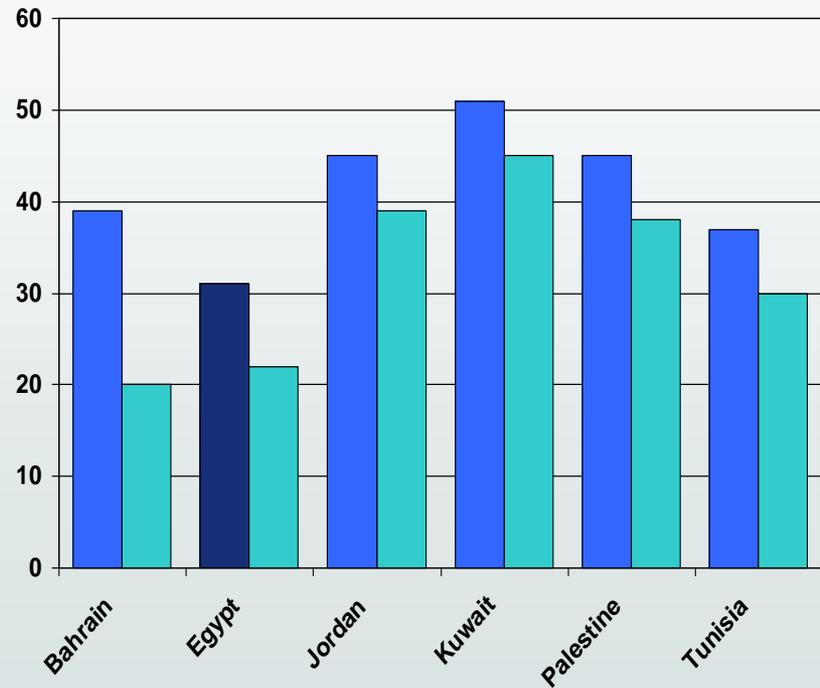
- **Variable secular changes were reported in most countries of North Africa, the Middle East, and South Asia. However, the rate in the present generation in most countries remains at 20-55+%.**

# Secular trends in consanguinity rates in highly consanguineous populations

## Increasing rates



## Decreasing rates



■ Among British Pakistanis the coefficient of inbreeding seems to have increased in a single generation from about 0.024 to 0.0375 ([Darr A](#), [Modell B](#), 1988)

## Why are consanguinity rates not declining in North Africa, West and South Asia?

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- Consanguinity is a deeply rooted cultural trend.
- It might offer social, psychological and economic advantages.
- With improvement in health, there will be more relatives to intermarry.
- The adverse genetic effects on health do not affect 90% of all related marriages.

## What factors may decrease consanguinity rate?

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- ❖ Higher female education
- ❖ Higher age at marriage
- ❖ Lower fertility
- ❖ More mobility from rural to urban
- ❖ better economic status of families

# Consanguinity and Reproductive Health



# Consanguinity and prenatal losses

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- ❖ Generally speaking, abortion rates among consanguineous and non-consanguineous couples are comparable.
- ❖ Available data suggest that stillborn rates are either similar or slightly higher among consanguineous couples than the non-related couples.

# Consanguinity and postnatal mortality

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- There is a positive association between parental consanguinity and increased infant and childhood mortality.
- Compiled data from 38 populations (600000 pregnancies) gave a 4.4% increased pre-reproductive mortality above background risk for offspring of first cousin unions. (*Bittles and Neel, 1994*)

# Consanguinity and fertility

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Most studies have shown similar or higher fertility rates among consanguineous versus non-consanguineous couples.

This may be attributed to:

- Younger female age at marriage leading to increased maternal reproductive span.
- Compensation for the higher infant mortality among consanguineous couples.
- Lower prenatal losses among consanguineous couples.

# Consanguinity and congenital malformations

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- Generally speaking, frequency of congenital malformations among newborns of first cousin unions is about 2 times the frequency among the general population, i.e. about 4-6%.
- Another estimate puts the offspring of first cousin unions at a 1.7-2.8% increased risk above the population background risk ( Bennett et al, 2002).

# Consanguinity and specific congenital malformations

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- Many studies have shown a positive association between parental consanguinity and congenital heart defects.
- The association of consanguinity with cleft lip and palate, and neural tube defects is not clear.

# Summary of Reproductive Health Parameters among consanguineous versus non- consanguineous couples

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- Earlier parental age at marriage
- Younger maternal age at first live-birth
- Higher number of infants born to consanguineous parents
- Lower rates of primary sterility
- Same or lower rates of abortion
- Higher rates of postnatal mortality in offspring
- Higher rates of congenital malformations in offspring
- Higher risk of having offspring with autosomal recessive disorder if present in the family

# Consanguinity and genetic disorders

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- No association of consanguinity with autosomal dominant, X-linked and chromosomal disorders (such as Down syndrome)

# Consanguinity and genetic disorders

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- Among genetic disorders, only autosomal recessive disorders are strongly associated with consanguinity, approximately 30% of sporadic undiagnosed cases of mental retardation, congenital anomalies and dysmorphism may have an autosomal recessive etiology with risks of recurrence in future pregnancies.
- *Hamamy et al 2007 SMJ*

# Consanguinity and genetic disorders

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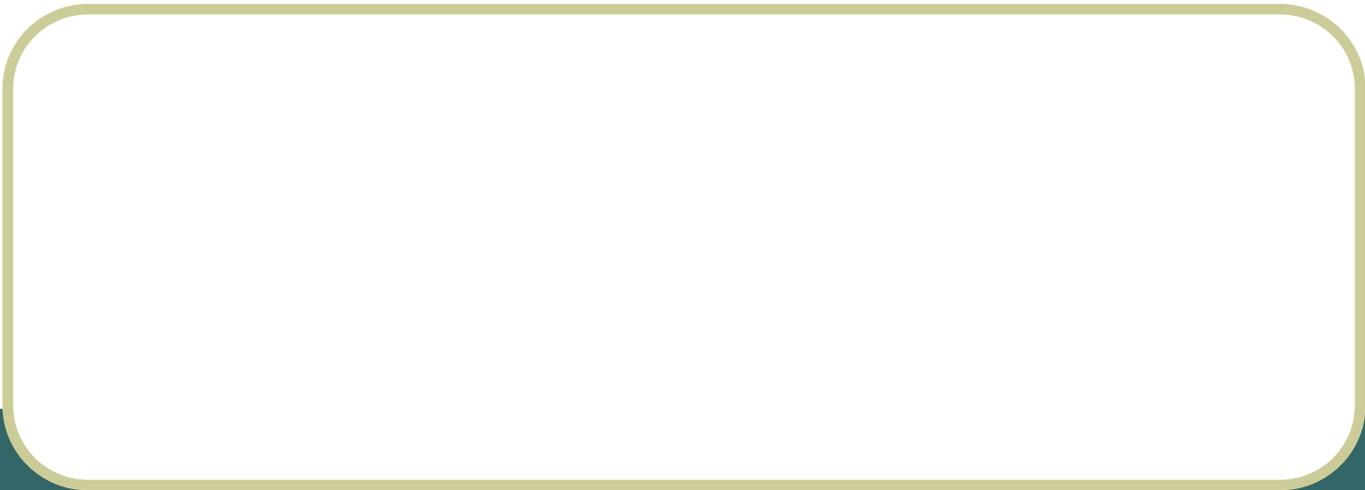
- consanguinity increases the risk of expression of autosomal recessive conditions in the offspring. This effect is more pronounced for rare disorders.

# Consanguinity and chronic adult non-communicable diseases (NCD's)

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The association of NCD's ( such as diabetes, hypertension) with parental consanguinity is still not clear. Controlled studies in populations with high consanguinity rates are needed.

# Consanguinity and Genetic Counseling



# Premarital and preconception counseling for consanguinity

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- There is a genetic disease in the family and the couple are consanguineous
- There is no known genetic disease in the family and the couple are consanguineous

# Premarital and preconception counseling for a consanguineous couple

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Distinguish between families with a known genetic or inherited disorder and those with no known such disorder by taking a detailed family history with specific questions on the presence of

- Any known genetic disease
- Congenital malformations or birth defects
- Childhood hearing and/or vision impairment
- Mental retardation
- Unexplained neonatal or infant deaths
- Failure to thrive
- Inherited blood disorders

## Premarital and preconception counseling for a consanguineous couple with no known genetic disease in the family

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- If there is no known inherited disorder in the family, then first cousin marriages are sometimes given a risk for birth defects of about twice the risk in the general population, for example 4% instead of 2%, however studies are still needed to verify this risk figure
- Risks for other conditions are not established.

# Counseling families with a known autosomal recessive disorder

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- Establish Clinical and Molecular diagnosis whenever possible
- Premarital and preconception carrier testing for the consanguineous couple
- If carriers cannot be diagnosed, give risk estimate
- Counseling to minimize further consanguinity unless carriers can be diagnosed
- Counseling couples with affected children by giving reproductive options such as prenatal diagnosis if feasible

## Recommendations of the National Society of Genetic Counselors (Bennett et al, 2002)

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- Offspring of first cousin union have 1.7-2.8% increased risk for congenital defect above the population background risk
- Offspring of first cousin union have 4.4% increased risk for prereproductive mortality above the population background risk
- The most useful tool for screening for any adverse effects is through a detailed family history
- For newborns of consanguineous couples, newborn screening by tandem mass spectrometry is offered at one week postnatal
- Offer hearing screening by 3 months of age

# Research priorities on consanguinity in populations with high consanguinity rates

Questions that need evidence-based answers include:

# Research Questions

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- ➔ Will diminishing the consanguinity rates diminish the prevalence of congenital disorders in the community?
- ➔ Will diminishing the consanguinity rates diminish the prevalence of adult non-communicable diseases in the community?
- ➔ Will diminishing the consanguinity rates diminish the infant mortality rate in the community?

# Research Questions

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- ➔ Will diminishing the consanguinity rates increase the deleterious recessive genes in the gene pool in the future?
- ➔ Will diminishing the consanguinity rates diminish stability and solidarity of the family structure in the community?

# Research Questions

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- Are consanguinity rates increasing or decreasing? What are the implicated factors?
- What are the advantages and disadvantages of consanguinity that should be known to health care providers and to the population?
- What are the views of society and health care personnel related to consanguineous marriages?
- Are the consanguinity health risks in populations with high rates similar to the calculated risks in western countries with low consanguinity rates?

# Research Questions

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- What can we tell consanguineous couples requesting premarital and preconception counseling?
- What steps can be advised to minimize the adverse effects of consanguinity on offspring in married consanguineous couples?
- What are the safe, scientific and evidence-based messages that can be delivered through the media regarding consanguinity?

# Standardized methodology should be used for all research on consanguinity

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- All studies on consanguinity should be standardized
- Accurate definition of the condition for which consanguinity studies are done
- Consanguinity among patients population should be compared to consanguinity in the general population in the same area
- Specify the relationship of consanguinity exactly. Saying consanguineous marriages is not enough

# Standardized methodology should be used for all research on consanguinity

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- When quoting consanguinity figures, it is important to clarify the number of individuals and how and what were the questions posed to the population studied.
- Were confounding factors taken into consideration?
- Inbreeding coefficient is the most accurate determinant of consanguinity in the population studied.

# Conclusions

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- Consanguineous marriages remain culturally and socially favored and respected in many countries, mostly in Arab countries, Iran, Pakistan, Turkey and parts of India.
- The risks of consanguinity are highest among families with severe segregating autosomal recessive conditions.

# Conclusions

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## Research on consanguinity could focus on:

- ✓ Formulating evidence-based practical guidelines for counseling
- ✓ Formulating scientific and feasible Community-based recommendations
- ✓ Deciding research priorities
- ✓ Establishing joint research projects