

**Consanguineous marriages in the
Middle East:
Trends, impact on reproductive
health and research priorities**

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http://www.gfmer.ch/Medical_genetics_education_research/Hanan_Hamamy.htm

Consanguineous marriages

- Consanguineous means related by blood
- As a working definition, unions contracted between persons biologically related as second cousins or closer are categorized as consanguineous. (1,2)

1) Alwan A, Modell B. (1997). Community control of genetic and congenital disorders, EMRO Technical Publications 24,

2) www.consang.net

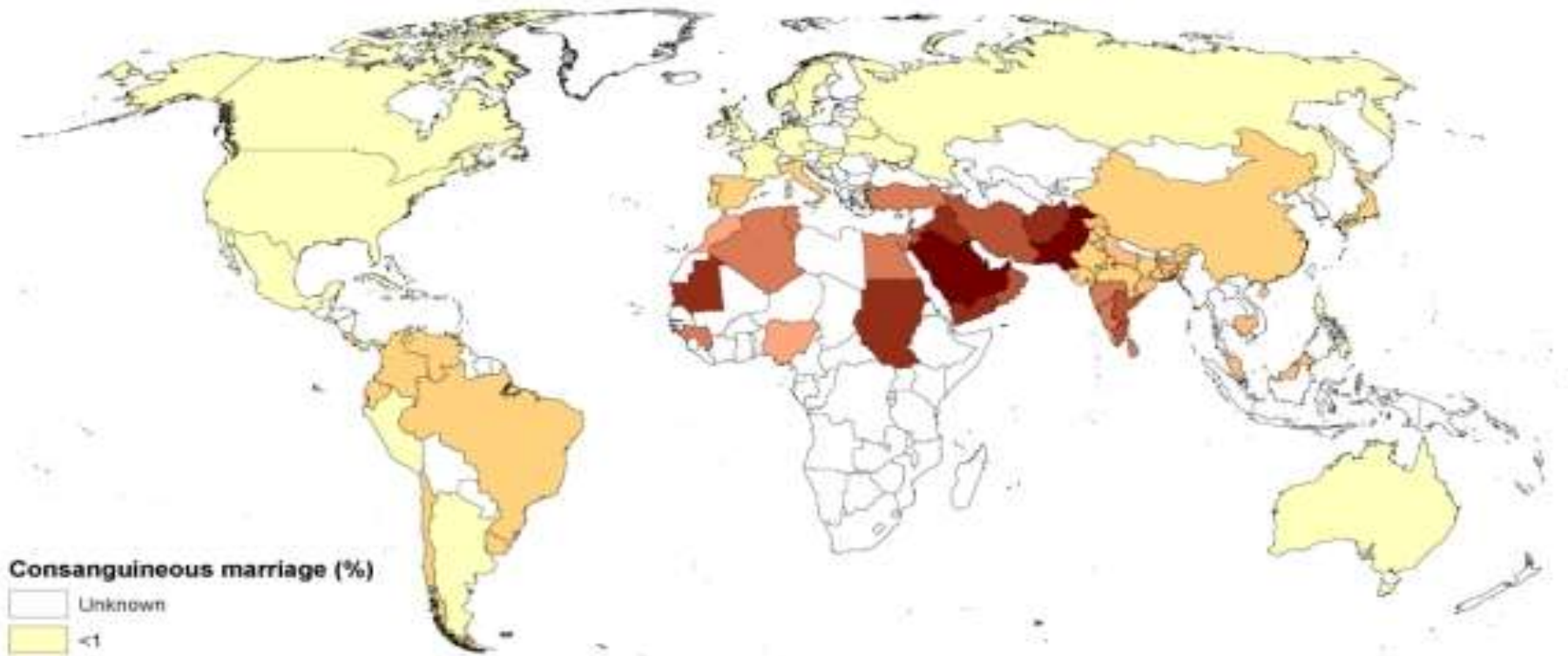
Types of consanguineous marriages

1. Double first cousins, $F=0.125$
2. First cousins, $F= 0.0625$
3. First cousins once removed $F=0.0313$
4. Second cousins, $F= 0.0156$

Beyond second cousins, from the tribe and distant relations are endogamous marriages that are sometimes included as consanguineous in some studies

F: Mean coefficient of inbreeding

Global prevalence of consanguinity



- Less than 1%: North America, Europe, Russia, Australia
- 1-10%: South America, North India, Japan
- 20-50+%: Arab countries, Turkey, Iran, Pakistan, South India.

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(www.consang.net)

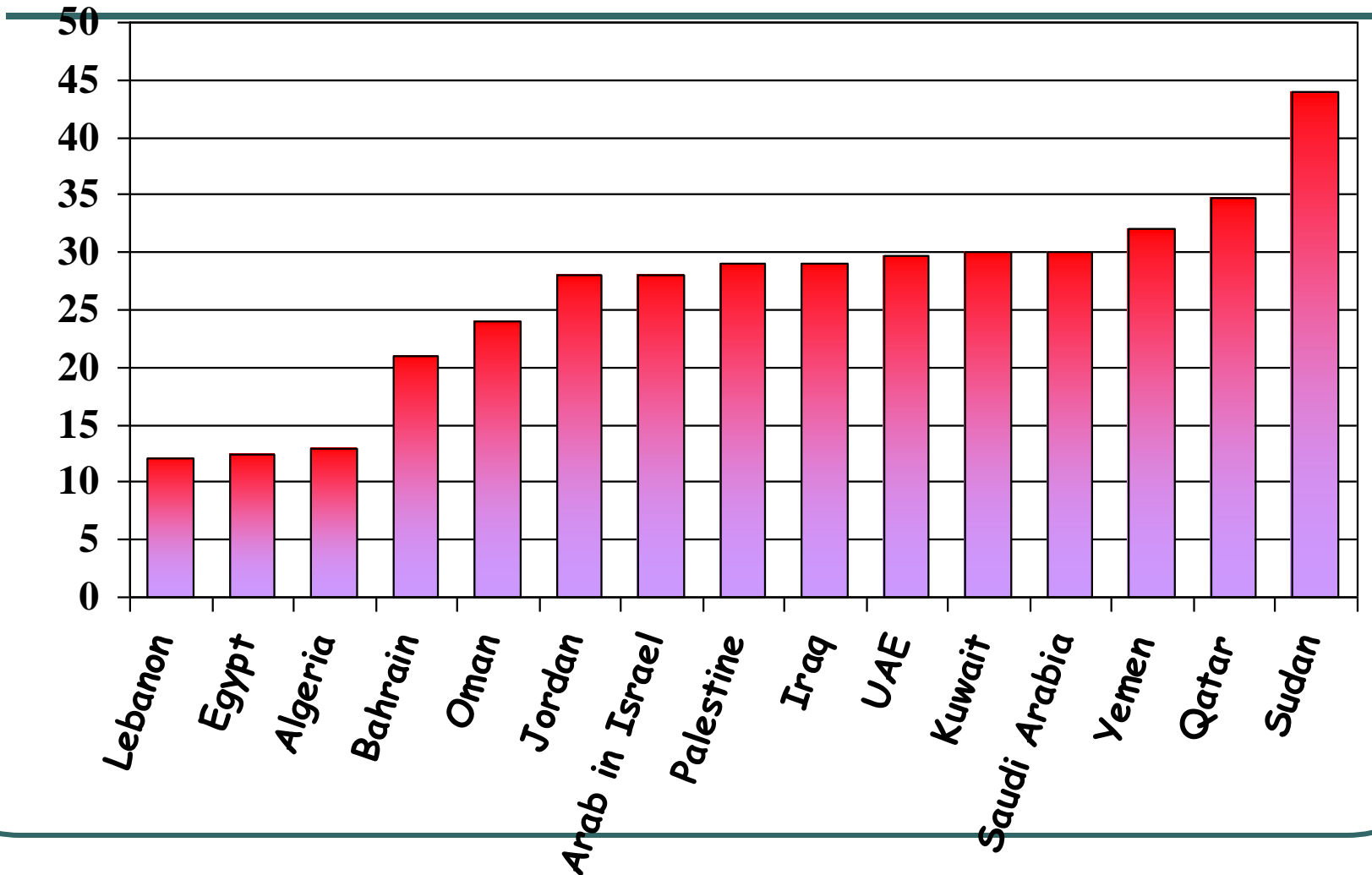
Why should consanguinity in the Eastern Mediterranean Region be studied?

- Highest rates in the world (20-50% of all marriages).
- Adverse effects of consanguinity on health?
- Advantages versus disadvantages?
 - In families with a genetic disease
 - In families with no genetic disease
- What are the evidence-based steps that could minimize the adverse effects of consanguinity?
- What are the evidence-based guidelines regarding genetic counseling for consanguinity?

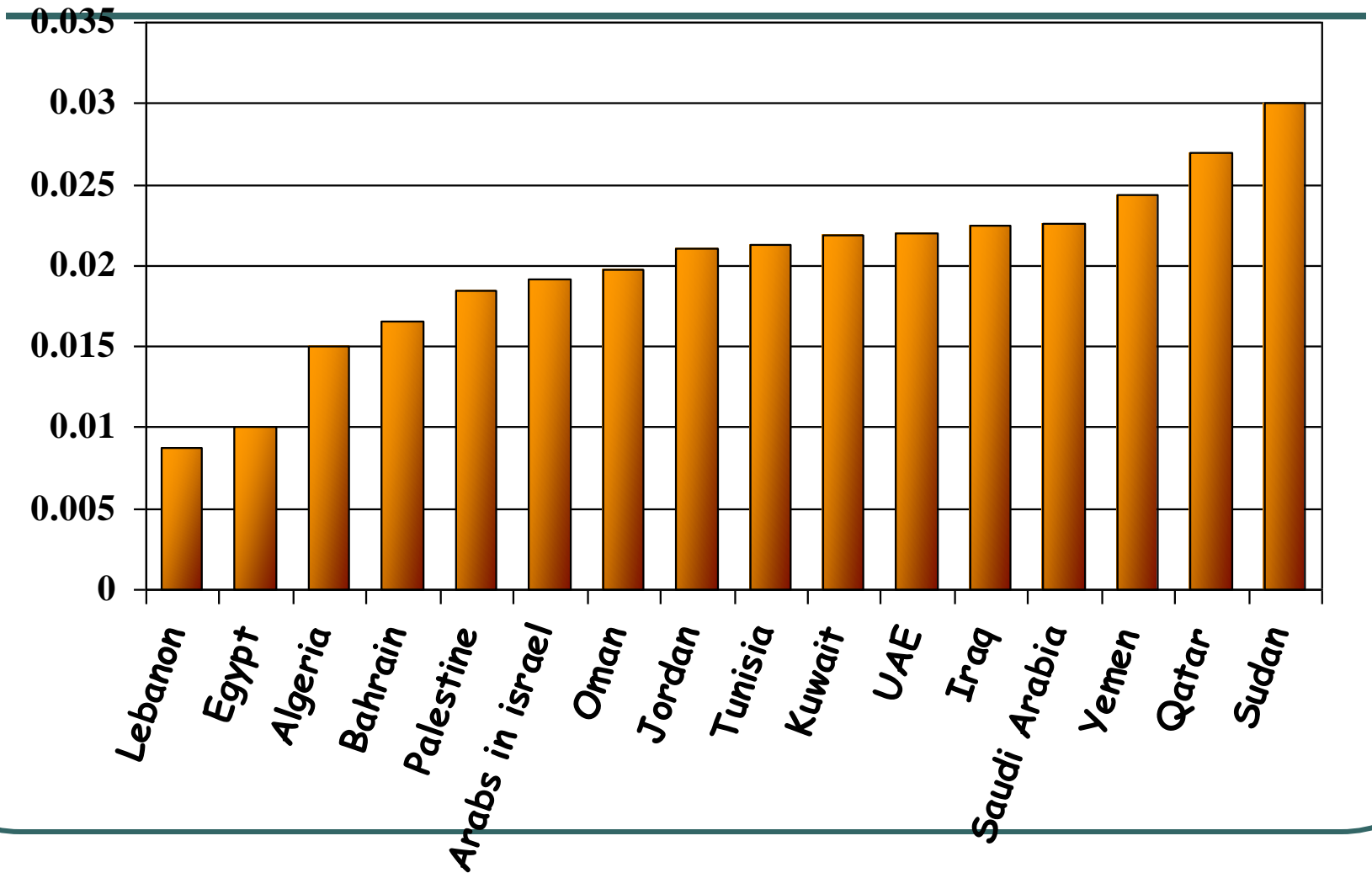
Trends in consanguineous marriages in Arab countries



Percentages of first cousin marriages in some Arab countries



Coefficients of inbreeding (F) in some Arab countries

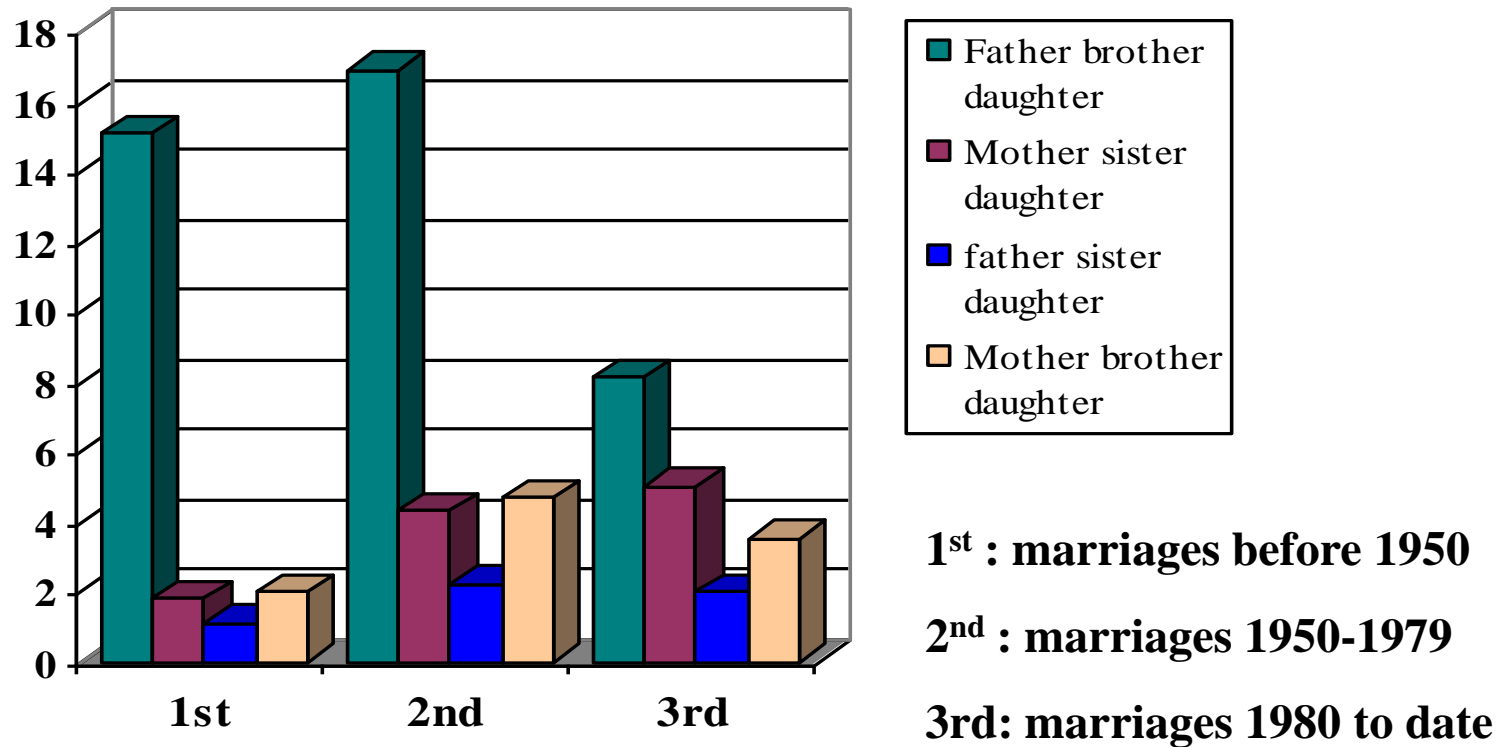


Secular changes in consanguinity rates

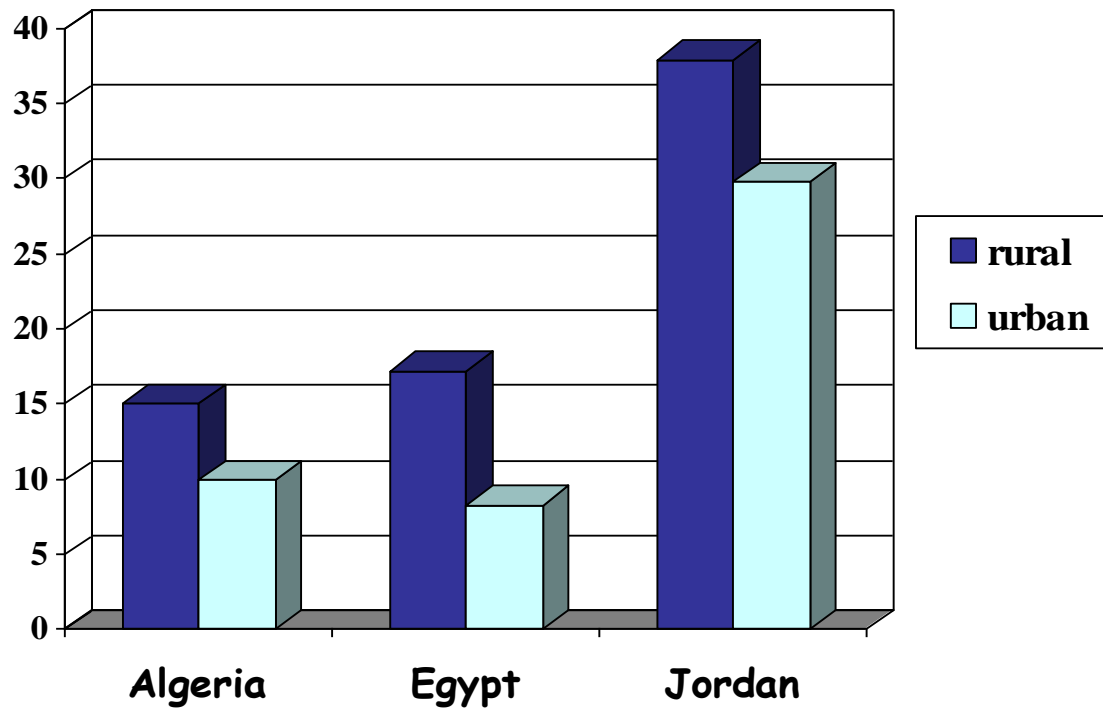
Some studies reported a decline of consanguineous marriages in: Jordan, Lebanon, Morocco, Mauritania and Arabs in Israel.

Some studies reported increase in rates of consanguineous marriages in Qatar, UAE and Yemen

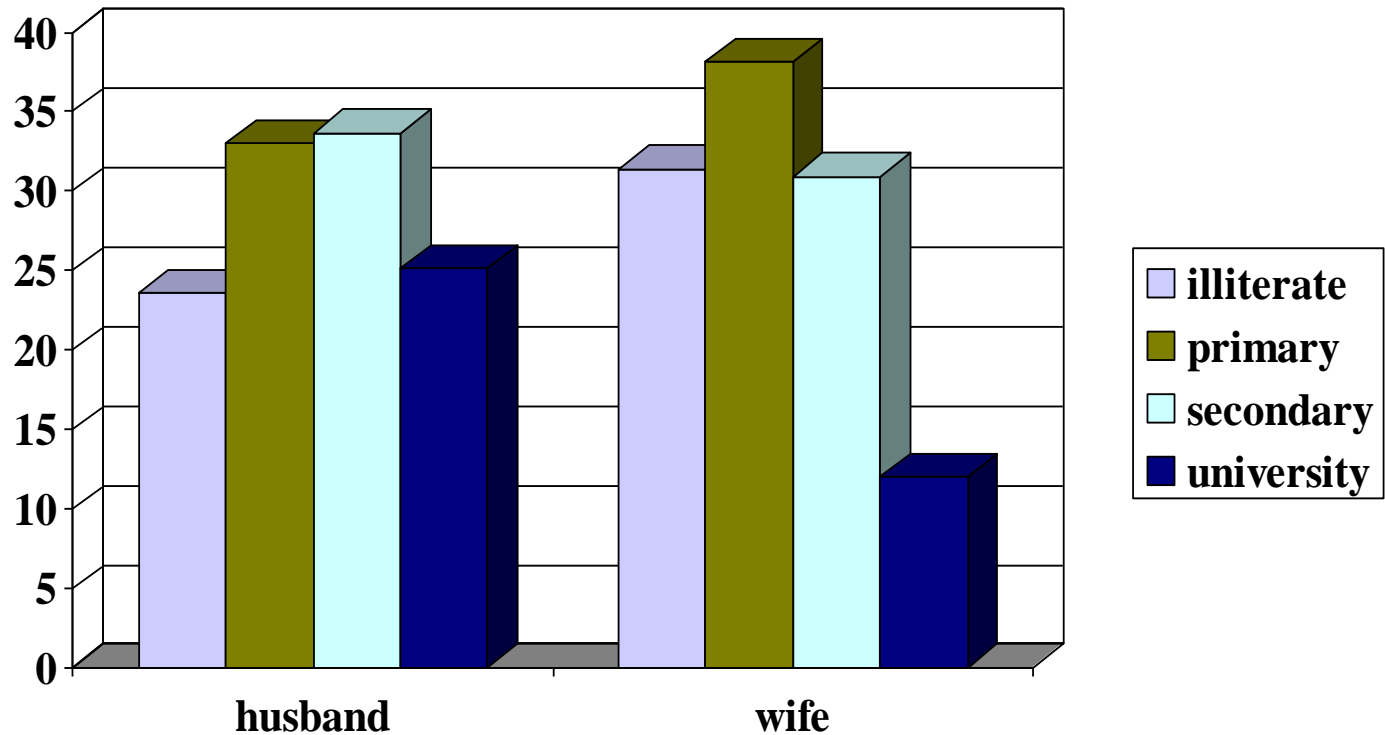
Time trend in percentages of subtypes of first cousin marriages among all marriages in Amman



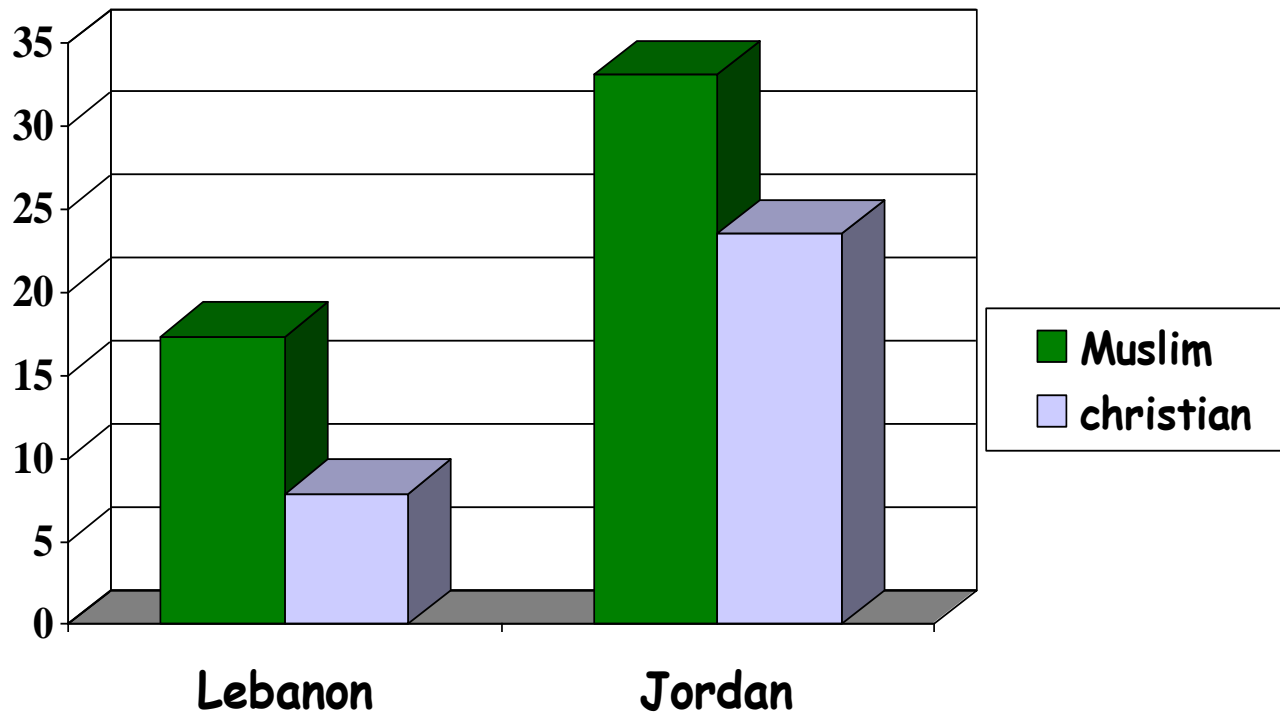
Urban/rural percentages of first cousin marriages among all marriages



Relation of education level to first cousin marriage percentages in Jordan



Percentages of first cousin marriages in relation to religion



Quoted from references in Hamamy et al, *Clin Genet*. 2005 Jun;67(6):511-6

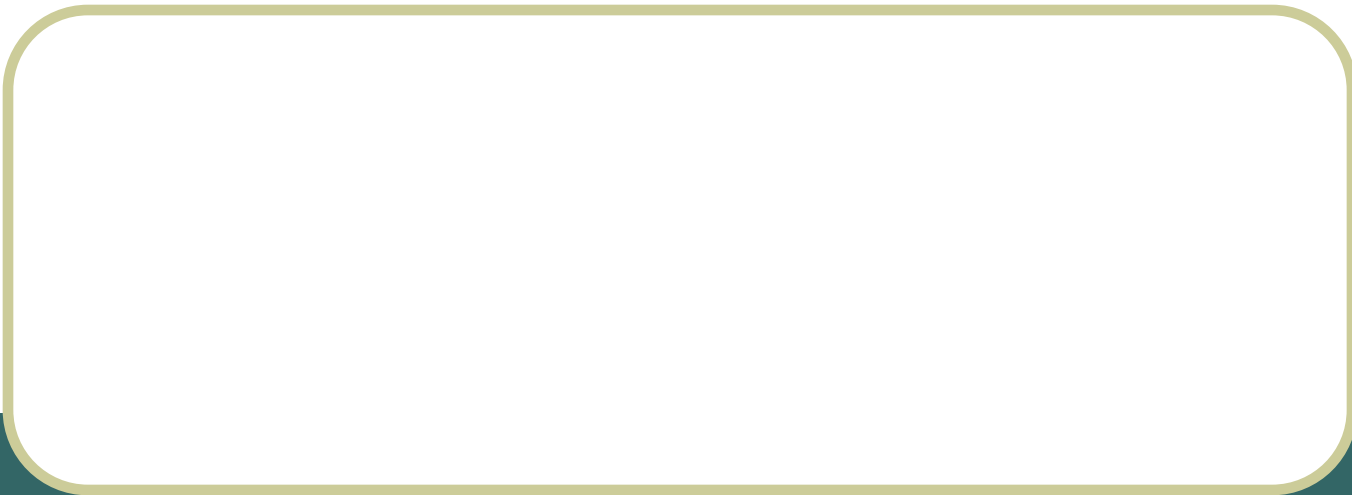
Reasons for choosing to marry a cousin

- Consanguinity is a deeply rooted cultural trend
- 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.

What factors may decrease consanguinity rate?

- ❖ 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

- ❖ 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

- 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

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 birth defects

- Many studies have shown a positive association between parental consanguinity and birth defects in the offspring. Some but not all studies done on specific birth defects such as neural tube defects, heart defects, cleft lip and palate showed a positive association with consanguinity
- *Some reports give the frequency of congenital malformations among newborns of first cousin unions as twice the frequency among non-related parents.*
Further studies would verify this risk figure.

Some studies on the association of consanguinity with birth defects

Reference	Population studied	Risk in general population	Risk to offspring of first cousins
Jaber et al (1998)	Compiled data from 9 populations	2.1% major malformations	4.5% major malformations
Demirel et al (1997)	1120 mothers Turkey	0.8% congenital anomalies	2.5% congenital anomalies
Stoltenberg et al (1999)	1.56 million births Norway	1.5% birth defects neonatal	3.6% birth defects neonatal
Khoury and Massad (2000)	1867 mothers Jordan	1% birth defects	1.8% birth defects (all consanguineous couples)

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

- 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

Inbreeding increases the risk of expression of rare autosomal recessive conditions in the offspring.

Population carrier rate of a certain recessive disorder	Affecteds birth rate/1000 (random mating)	Affecteds birth rate/1000 (30% of all marriages are first cousins)	Multiplication factor
0.1	0.000025	0.0093	37
0.5	0.00625	0.053	8.5
1	0.025	0.119	4.8
5	0.63	1.1	1.7
10	2.5	3.44	1.4
16	6.4	7.91	1.23

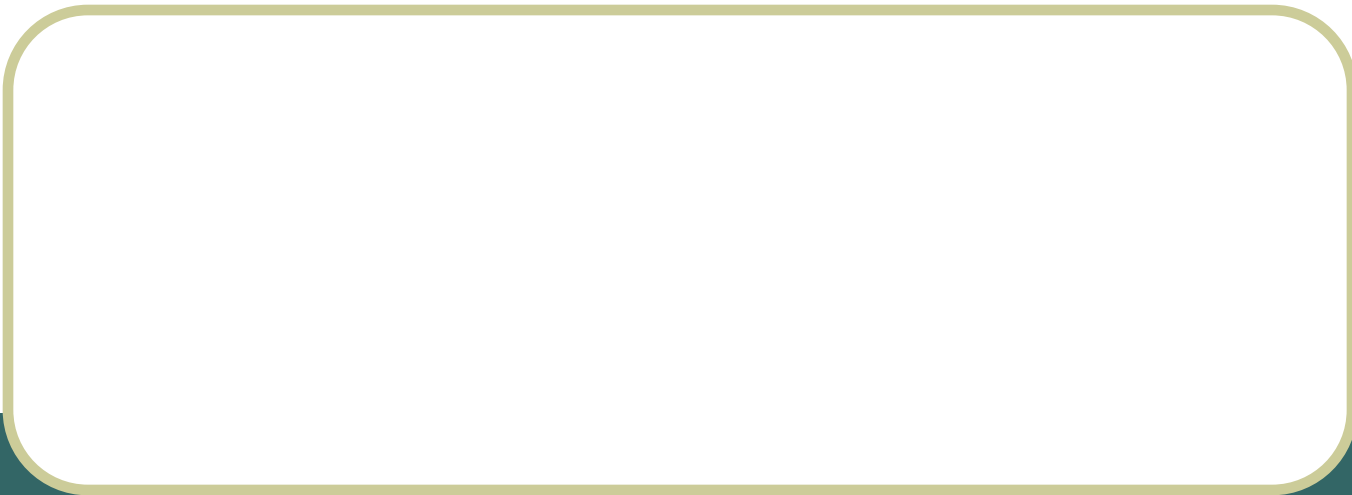
Consanguinity and Down Syndrome

- The association of DS with parental consanguinity is disputable.

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

The association of NCD's with parental consanguinity is still not clear. Controlled studies in populations with high consanguinity rates are needed.

Consanguinity and Genetic Counseling



Premarital counseling for consanguinity

Premarital counseling for consanguinity is sought when:

- 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 counseling for a consanguineous couple

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 counseling for a consanguineous couple with no known genetic disease in the family

- 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

- Establish Clinical and Molecular diagnosis whenever possible
- Premarital 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

Research priorities on consanguinity in populations with high consanguinity rates

Questions that need evidence-
based answers include:

Research Questions

- Will diminishing the consanguinity rates diminish the prevalence of genetic and 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

- 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

- 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

- What can we tell consanguineous couples requesting premarital counseling?
- What steps can be advised to minimize the adverse effects of consanguinity on offspring in already 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

- 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

- 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

- 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

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