IN THE NAME OF ALLAH,
THE MOST MERCIFUL,
THE MOST BENEFICIENT

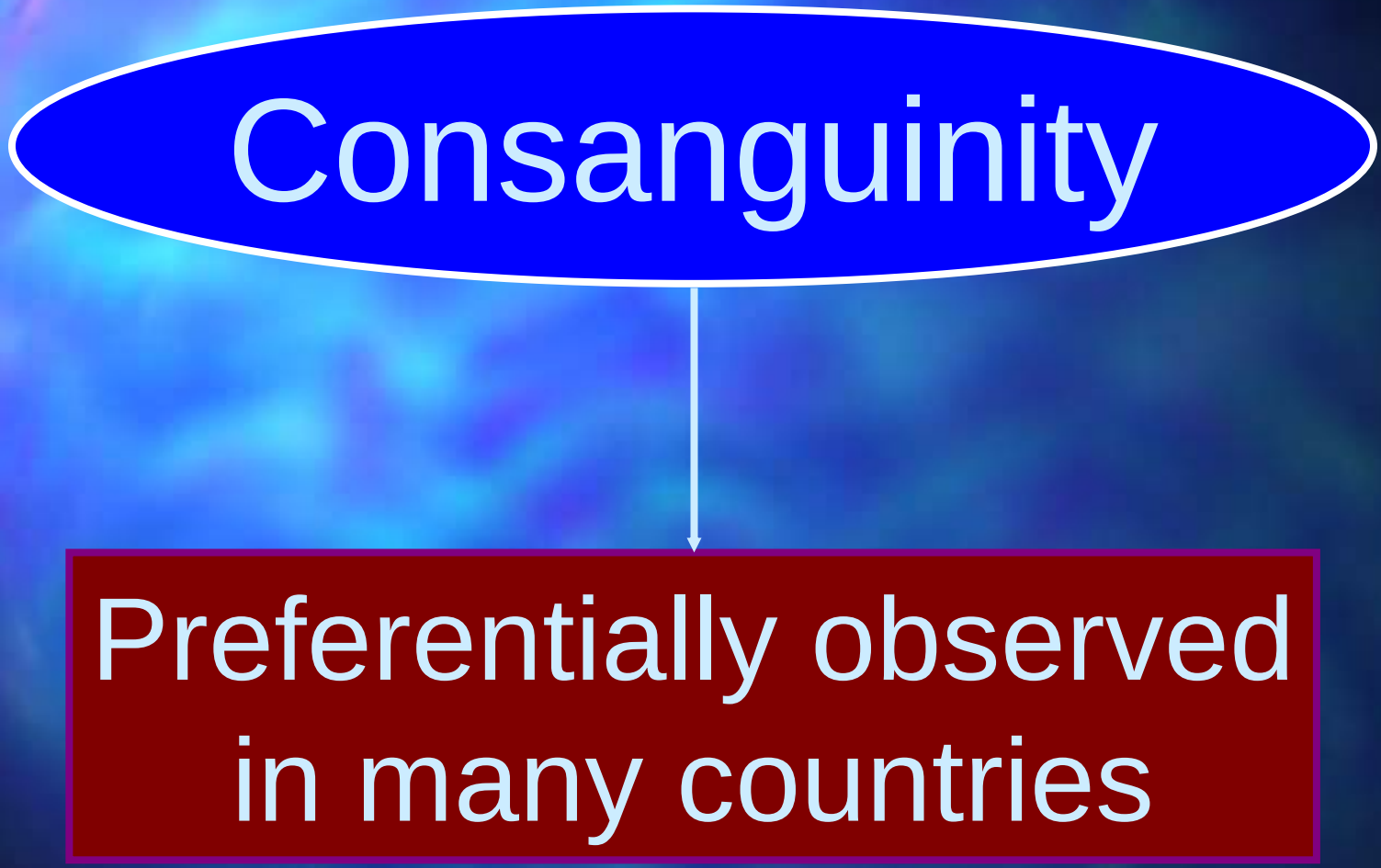
Consanguinity and Genetic Disorders -

Is there an influence?

Presentation Outline

- Consanguinity:
  - Pros
  - Cons
- Effect of consanguinity on frequency of genetic disorders:
  - Single genes
  - Multifactorial
- Consanguinity in Saudi Arabia:
  - National studies
  - Counselling
- Conclusions.

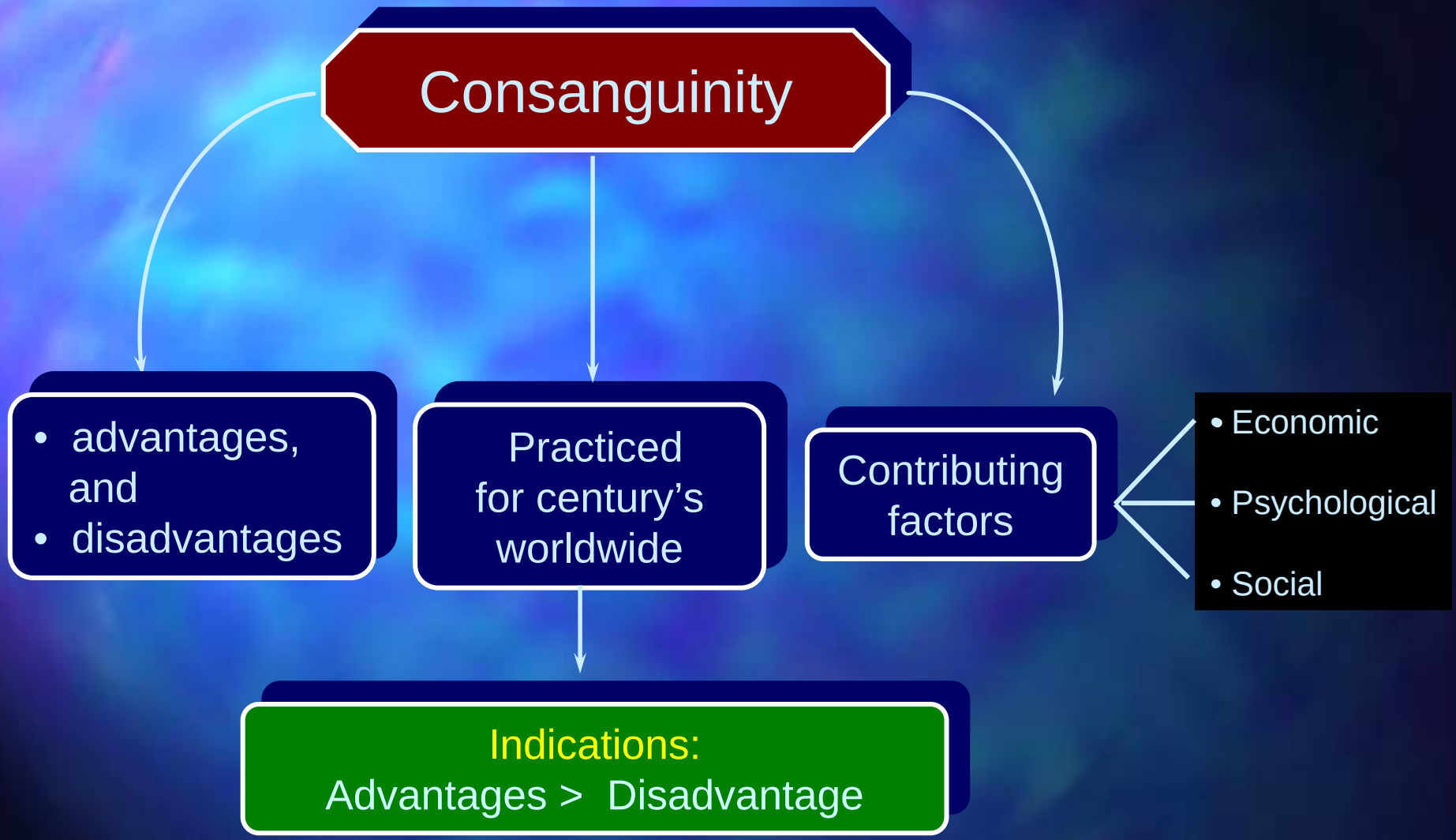
- Consanguinity:
  - related by blood.
- Consanguineous marriages:
  - marriages between blood relatives.
- Genetics classification:
  - second cousins marriages or closer.

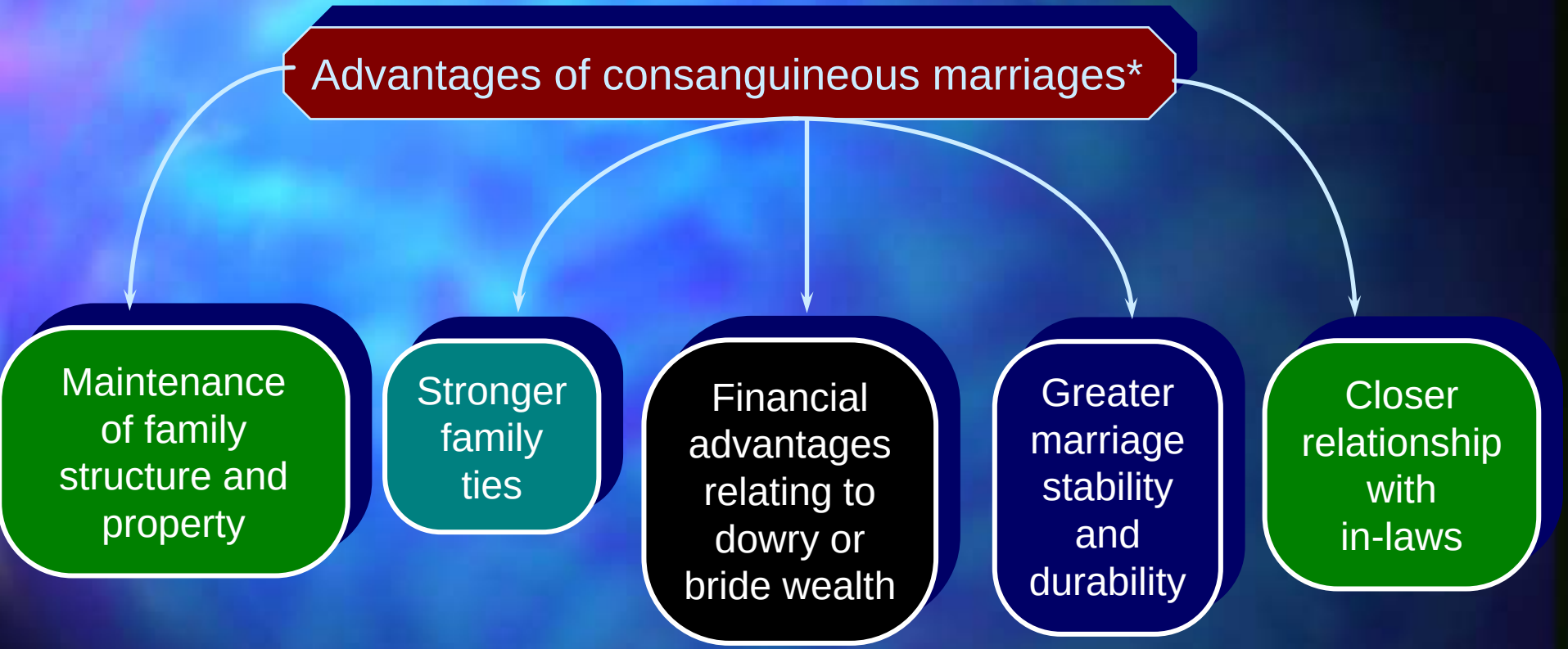

Consanguinity
Preferentially observed in many countries

PREVALENCE OF CONSANGUINITY IN SOME COUNTRIES

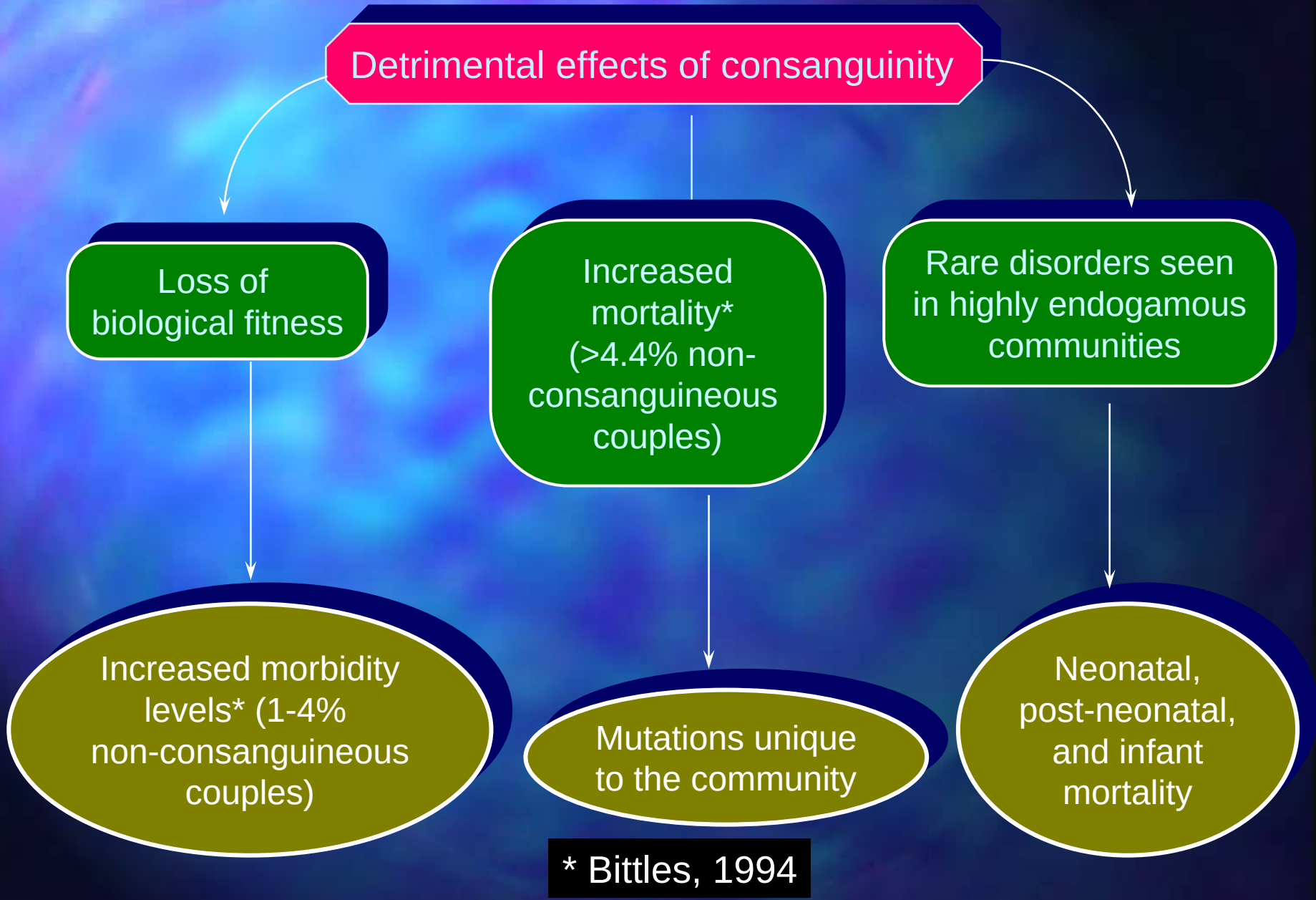
	Prevalence (%) of consanguinity*
Arabs	
Kuwait	54
Syria	33
Egypt	28
Lebanon	25
Algeria	23
Jordan	50
Asians	
Pakistan	38 - 49
India	5 - 61
Japan	1.6 - 3.9
Americas	
Brazil	0.62 - 9.0

*El-Hazmi et al, 1996


Consanguinity
• advantages, and
• disadvantages
Practiced for century's worldwide
Contributing factors
• Economic
• Psychological
• Social
Indications:
Advantages > Disadvantage



* Bittles, 1994


Detrimental effects of consanguinity
Loss of biological fitness
Increased mortality* (>4.4% non-consanguineous couples)
Rare disorders seen in highly endogamous communities
Increased morbidity levels* (1-4% non-consanguineous couples)
Mutations unique to the community
Neonatal, post-neonatal, and infant mortality
* Bittles, 1994

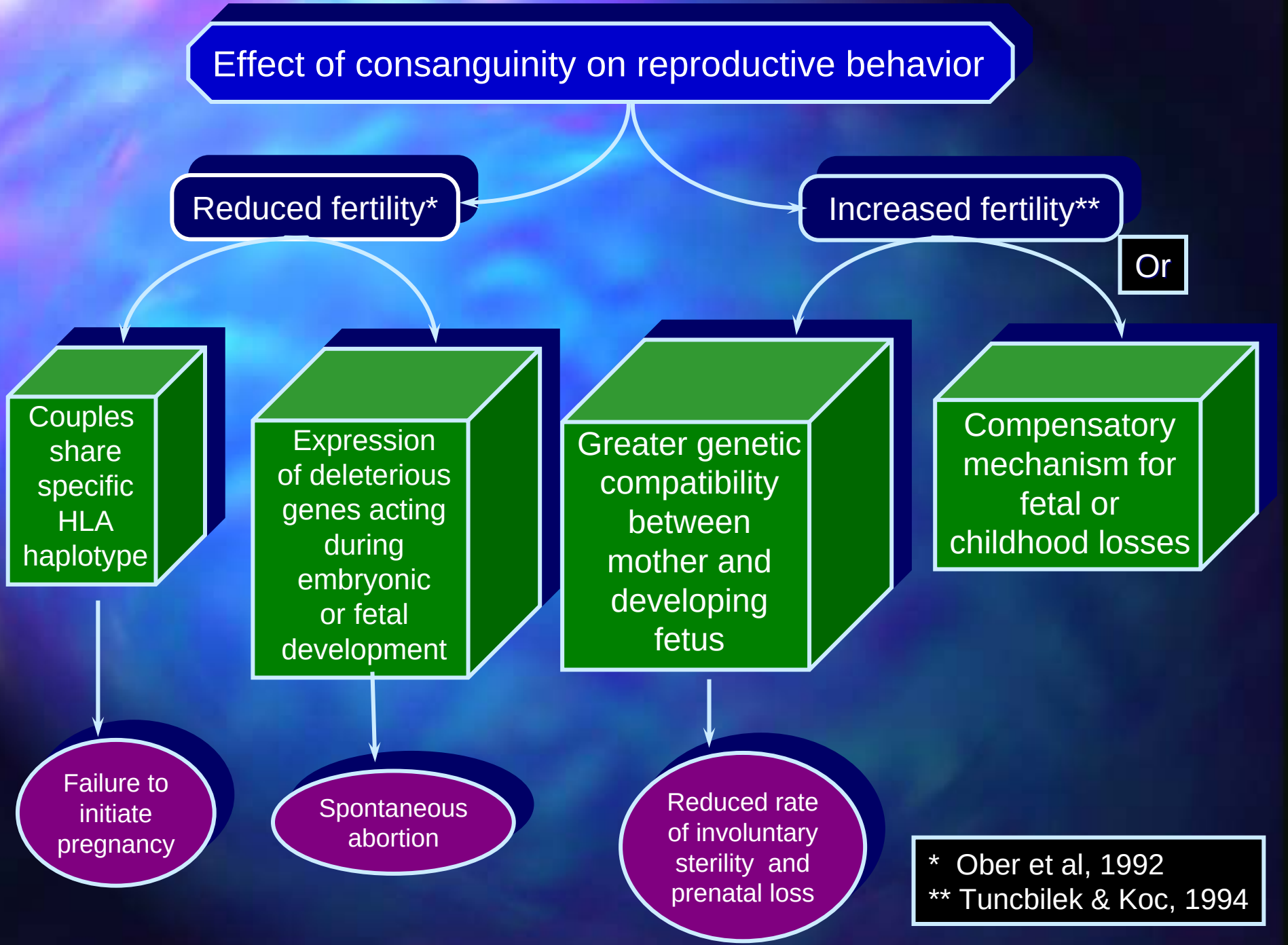
Effect of consanguinity on Reproductivity

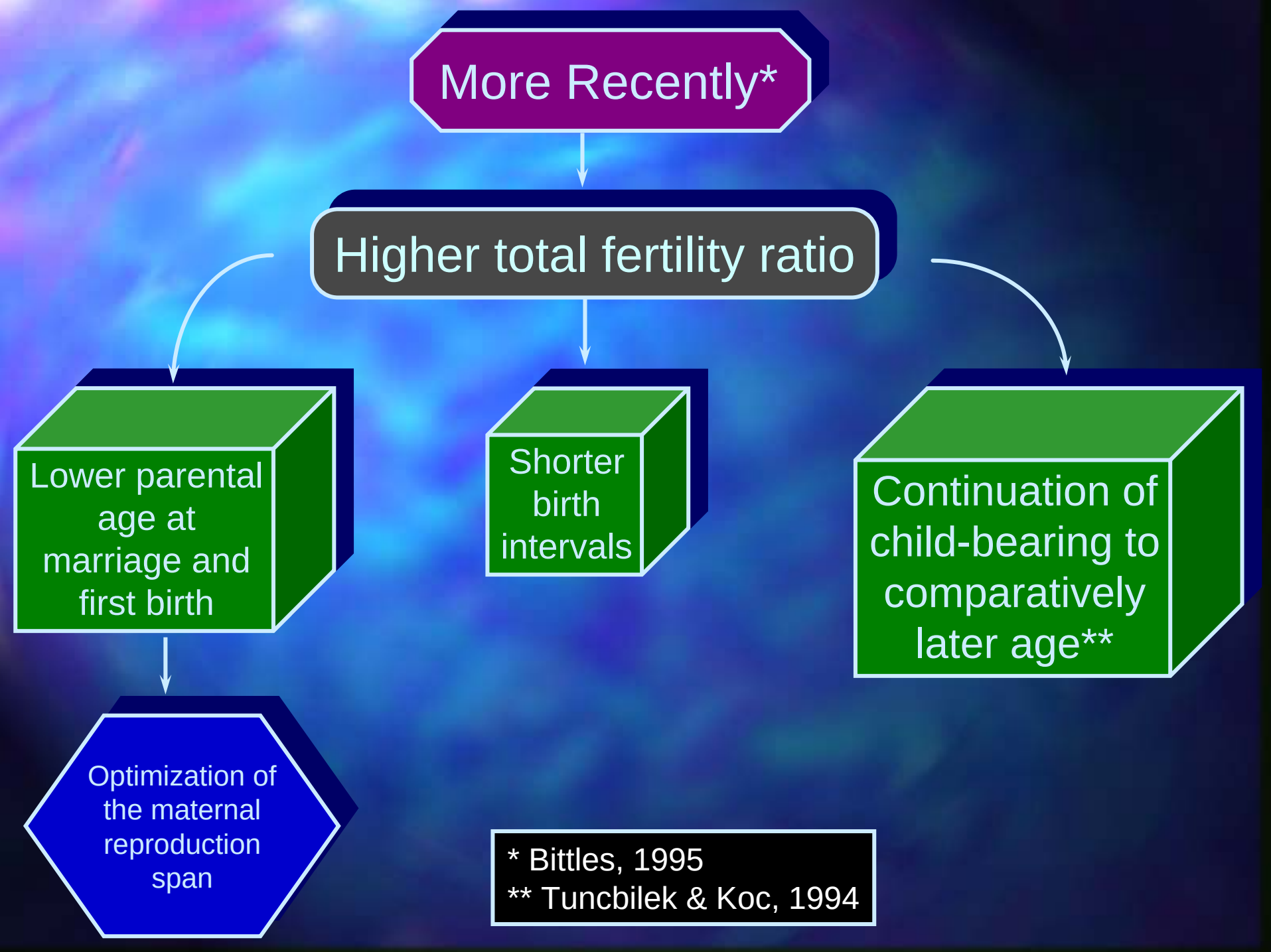
Conflicting Reports

- Increased sterility
- Increased rate of abortions
- Still births
- Perinatal losses
- Neonatal deaths
- Decreased birth weight

Vs

- Increased fertility in women
- No or very little effect on:
  - abortion rate,
  - still births,
  - perinatal loss,
  - neonatal death.

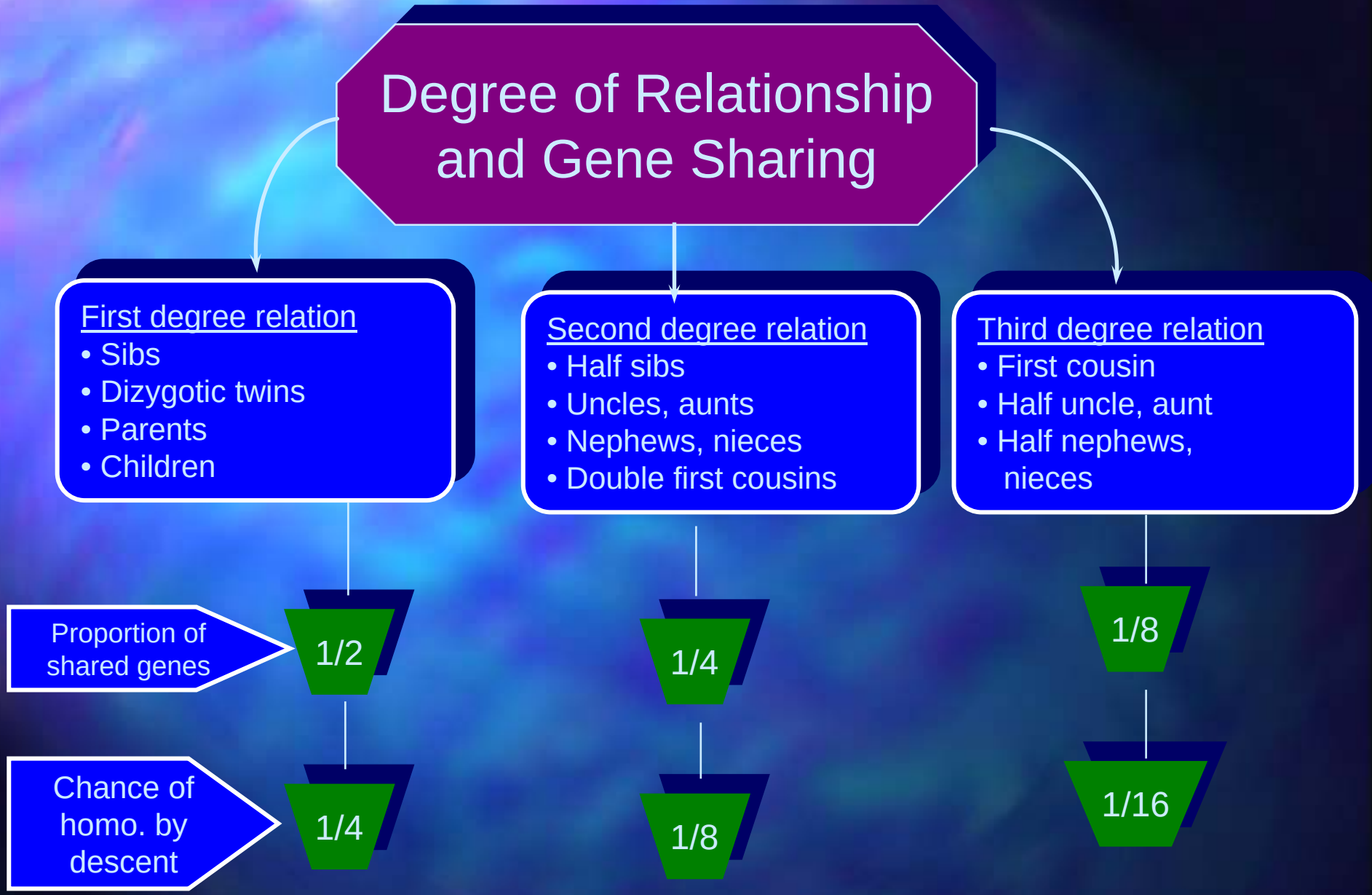

Effect of consanguinity on reproductive behavior
Reduced fertility*
Increased fertility**
Or
Couples share specific HLA haplotype
Expression of deleterious genes acting during embryonic or fetal development
Greater genetic compatibility between mother and developing fetus
Compensatory mechanism for fetal or childhood losses
Failure to initiate pregnancy
Spontaneous abortion
Reduced rate of involuntary sterility and prenatal loss
* Ober et al, 1992
** Tuncbilek & Koc, 1994


More Recently*
Higher total fertility ratio
Lower parental age at marriage and first birth
Shorter birth intervals
Continuation of child-bearing to comparatively later age**
Optimization of the maternal reproduction span
* Bittles, 1995
** Tuncbilek & Koc, 1994

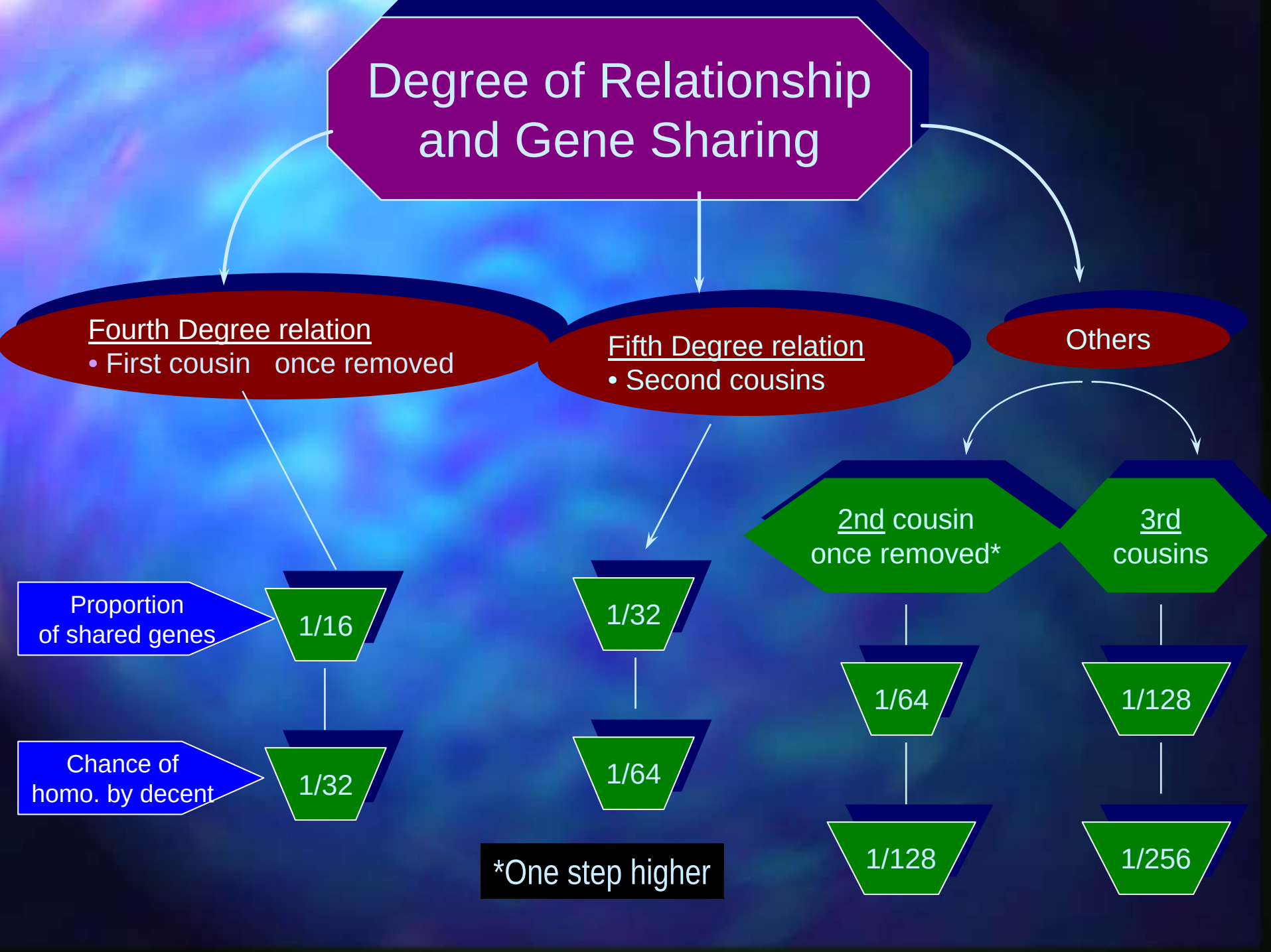
Detrimental Health effects of consanguineous marriages due to:

Expression of rare, recessive genes inherited from a common ancestor

Degree of Relationship and Gene Sharing



Degree of Relationship and Gene Sharing



- Consanguinity:
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  - Cons
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- Consanguinity in Saudi Arabia.
- Conclusion.

Effect of consanguinity on congenital malformation

Increased by 2-5 times (of unrelated parents)

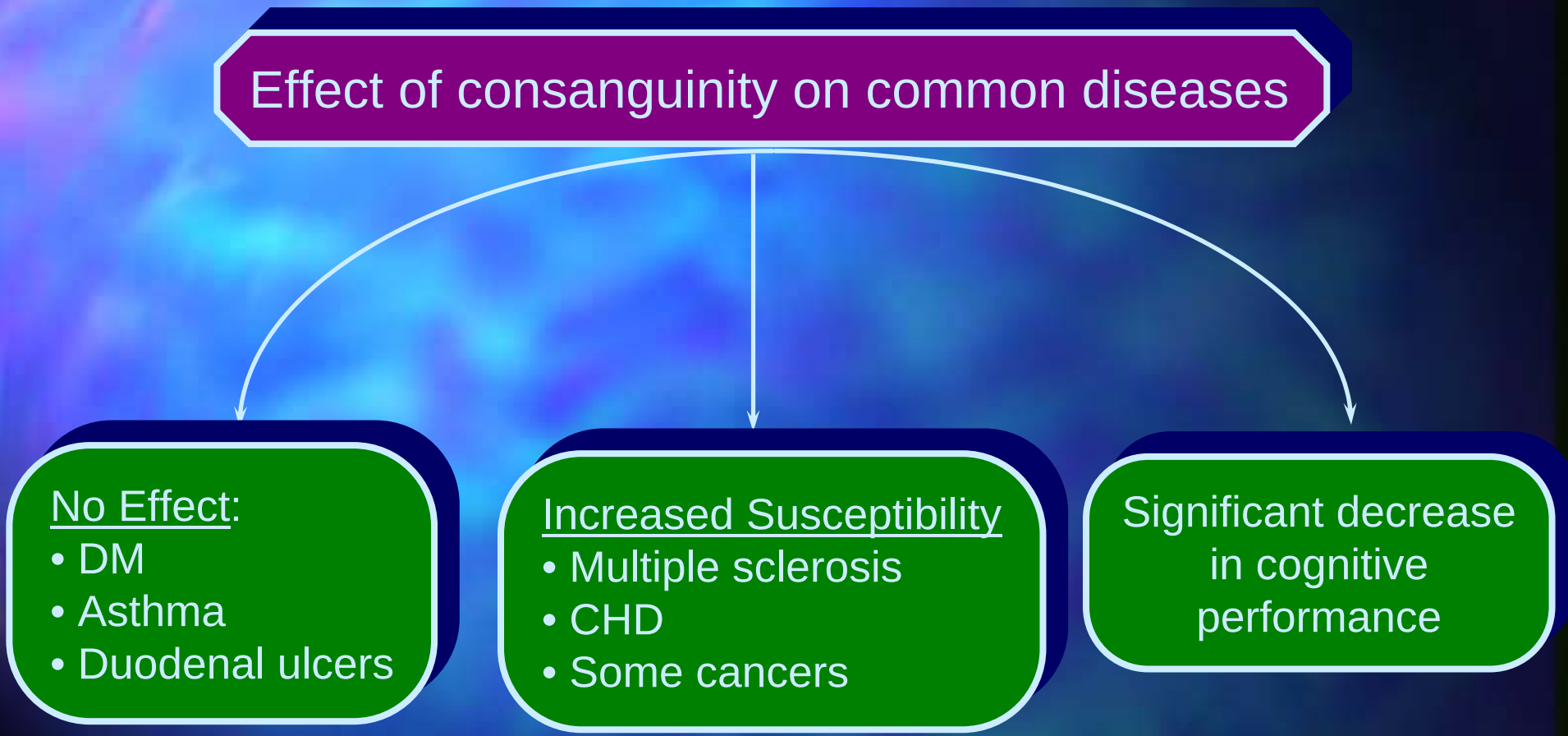
<u>Examples:</u>
- Cardiovascular
- CNS
- Urogenital
- Ophthalmic
- Gastro-intestinal
- Skeletal
- Cutaneous
- Multiple malformations

<u>Mechanism?</u>
- AR disorders (↑ Homozygosity at several loci)

AR disorders

Chromosomal structural disorder

Effect of consanguinity on common diseases



Consanguinity and Dominant Disorders

- No significant effect.
  (as these disorders are transmitted independently of the genetic make-up of the partner)

CONSANGUINITY AND RECESSIVE DISORDERS

- Consanguineous marriages:

  Favor the manifestation of rare recessively inherited disorder (carrier, frequency <1%). including:

  - Most inborn errors of metabolism
  - Some congenital malformations
  - Genetic forms of deafness
  - Mild to moderate mental retardation

- The rate of homozygous births approx. double the common recessive genes in first cousin marriages, including:

  - Hb S
  - α–Thalassaemia
  - β-Thalassaemia

CONSANGUINITY AND VERY RARE RECESSIVE DISORDERS

- A large number of disorders are very rare in human populations (carrier frequency <1%).
- Even if consanguineous marriages are very common in a population, these disorders remain rare (birth rate < 0.3 per 1000), but is several times more than in random mating.
- In customary consanguineous marriages, increase in incidence of rare disorders (e.g. deafness, mental retardation, congenital malformation) is anticipated.

Saudi Arabia

- Consanguinity:
  - Pros
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Studies Conducted in Saudi Arabia

Population screened

Two National Studies

Study of Diabetes Mellitus, HT, Obesity in Saudi Arabia

No. screened:25,337

Study of Disability in Saudi Arabia

No. Screened: 60,630

PREVALENCE OF CONSANGUINITY IN SAUDI ARABIA

Province	Prevalence (%) of consanguinity			
	1st Cousin	2nd Cousin	Others	Total
CP	29.8	13.4	17.6	60.8
NP	17.9	17.4	17.4	52.1
NWP	27.3	20.8	19.6	67.7
SWP	26.0	12.4	12.4	54.2
EP	40.9	9.1	9.1	59.1

Prevalence of consanguinity in Saudi SCD and β-thalassaemia major patients

Between 70-80% of SCD and β-thalassaemia major patients are the outcome of consanguineous matings

CARRIER FREQUENCY OF HbS IN DIFFERENT REGIONS OF SAUDI ARABIA AND EXPECTED HOMOZYGOUS BIRTH RATE IN RANDOM MATING AND IN 30% FIRST COUSIN MARRIAGES

Province	Hb S Carrier Frequency	Homozygous births/1000		Multiplication factor 30% IC/ random	P-Value
		Random	30% First cousin		
EP	21.3	12.0	14.3	1.2	NS*
CP	0.83	0.009	0.08	8.9	S
SWP	12.0	3.25	5.5	1.7	NS*
NWP	7.54	0.8	1.6	2.0	NS*
NP	1.3	0.030	0.21	7.0	S

*In AR high frequency province, the cousin marriages does not significantly increase the homozygous affected bitrh.

CARRIER FREQUENCY OF b-THAL. IN DIFFERENT AREAS OF SAUDI ARABIA AND EXPECTED HOMOZYGOUS BIRTH RATE IN RANDOM MATING AND IN 30% FIRST COUSIN MARRIAGES

Area	β-Thal. Carrier Frequency	Homo. Births/1000 Random Mating	30% IC	Multiplication factor 30% IC/rando	P-value
Al-Hafouf	13.0	3.7	5.9	1.6	NS*
Riyadh	3.6	0.5	1.0	2.0	NS*
Najran	15.3	5.0	6.5	1.3	NS*
Jaizan	5.9	0.72	1.2	1.7	NS*
Khaiber	4.0	0.6	1.1	1.83	NS*
Al-Ula	12.0	3.4	4.7	1.4	NS*

*In AR high frequency province, the cousin marriages does not significantly increase the homozygous affected bitrh.

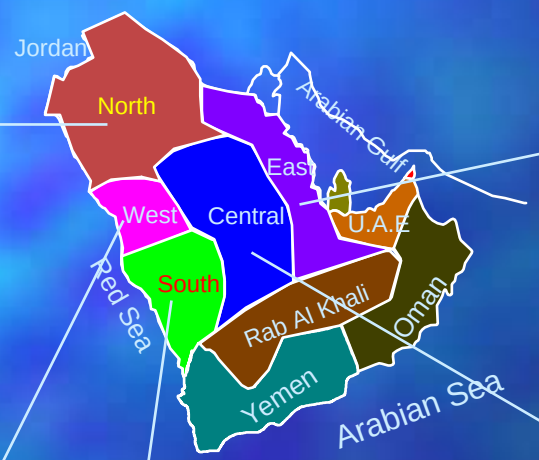

Jorda
North
East
Arabian Gulf
West
Central
U.A.E
South
Rab Al Khali
Oman
Red Sea
Yemen
Arabian Sea

Prevalence of consanguinity in different types of disabilities

Type of Disability	Prevalence (%) of Consanguinity		
	1st Cousin	2nd Cousin	Total Cousin
Mental	39.0	28.8	67.8
Physical	8.8	28.8	37.6
Speech	37.0	27.3	64.3
Hearing	35.0	30.2	65.2
Visual	35.0	25.0	60.0
Behavioral disorders	37.0	28.4	65.4
Learning difficulties	38.0	28.2	66.2
Epilepsy	35.0	28.7	63/7
Chronic diseases	33.0	27.2	60.2
Other disabilities	27.0	42.0	69.0
Normal	25.8	14.8	56.8

Prevalence of Consanguinity in Diabetic and Normal Saudis*

Consanguinity (%)	
DM	Normal
41.2	52.1



Consanguinity (%)	
DM	Normal
60.0	59.1

Consanguinity (%)	
DM	Normal
40.2	67.6

Consanguinity (%)	
DM	Normal
42.4	54.2

Consanguinity (%)	
DM	Normal
49.2	60.8

*p-value: NS

Prevalence of Consanguinity in Obesity and Normal Saudis*

Consanguinity (%) (NP)	
Obese	Normal
43.1	52.1

Consanguinity (%) (EP)	
Obese	Normal
37.5	59.1

Consanguinity (%) (WP)	
Obese	Normal
46.0	67.7

Consanguinity (%) (SP)	
Obese	Normal
39.9	54.2

Consanguinity (%) (CP)	
Obese	Normal
50.6	60.8

*p-value: NS

Prevalence of Consanguinity in Hypertensive and Normal Saudis*

Consanguinity (%) (NP)	
HT	Normal
51.5	52.1

Consanguinity (%) (EP)	
HT	Normal
39.4	59.1

Consanguinity (%) (WP)	
HT	Normal
50.8	67.7

Consanguinity (%) (SP)	
HT	Normal
38.9	54.2

Consanguinity (%) (CP)	
HT	Normal
42.1	60.8

*p-value: NS

CONSANGUINITY AND GENETIC COUNSELLING

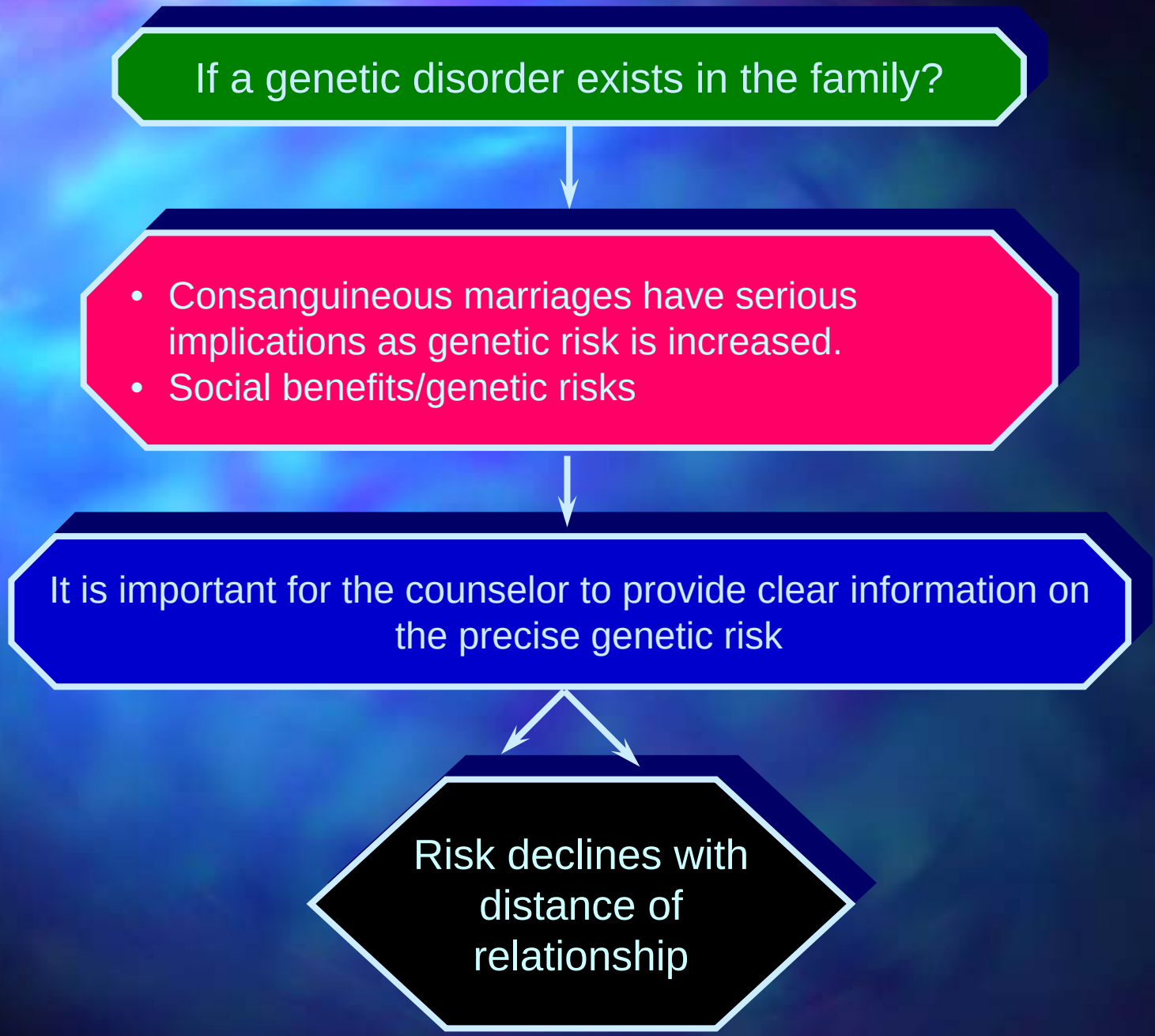
The following aspects deserve special considerations:

- Relationship of two individuals?
- Risk of genetic disorders influenced by consanguinity?
- Likelihood of a harmful gene being transmitted by both parents to the child?

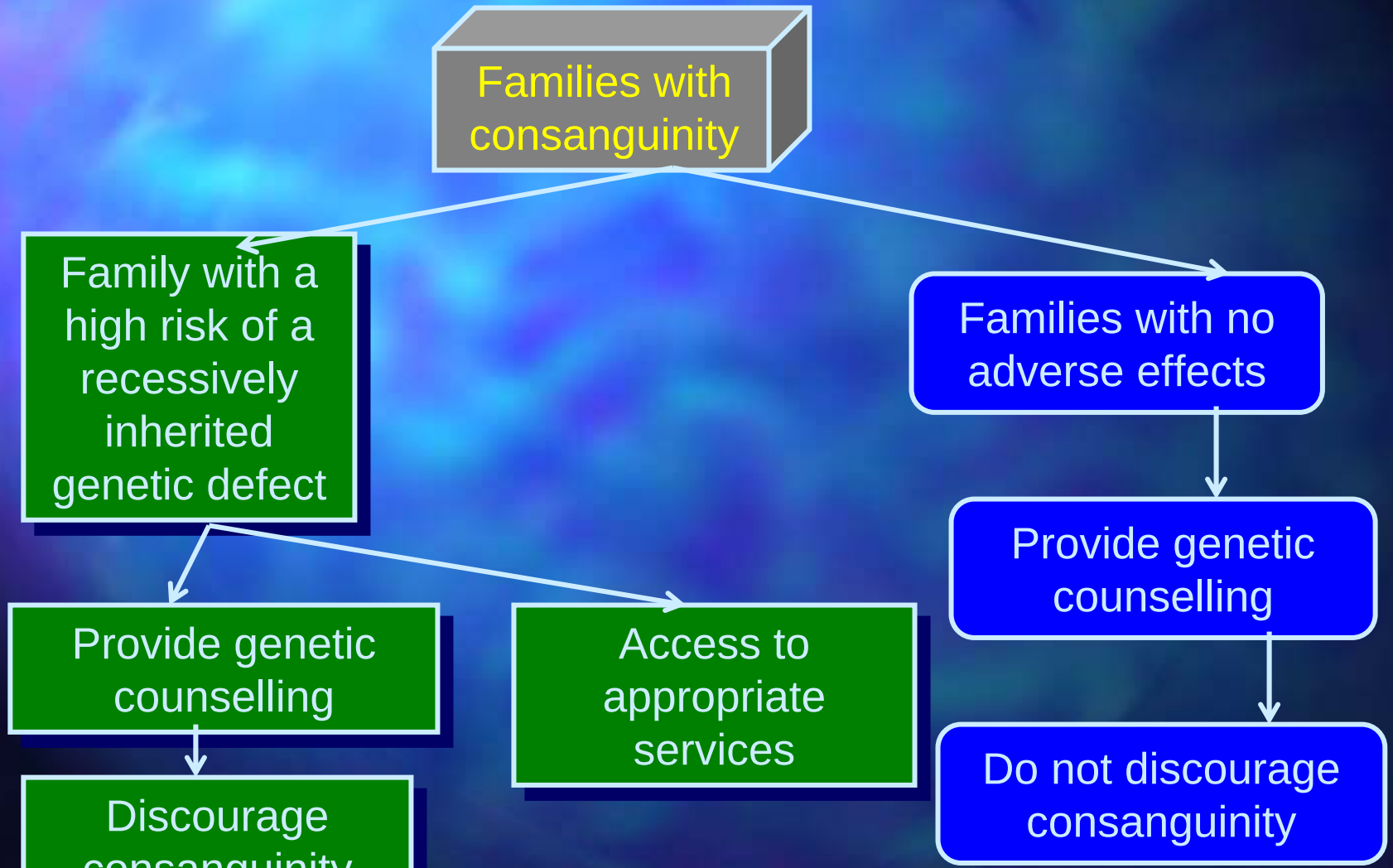
How to provide genetic counselling in Arab/Islamic societies that favor consanguineous marriages

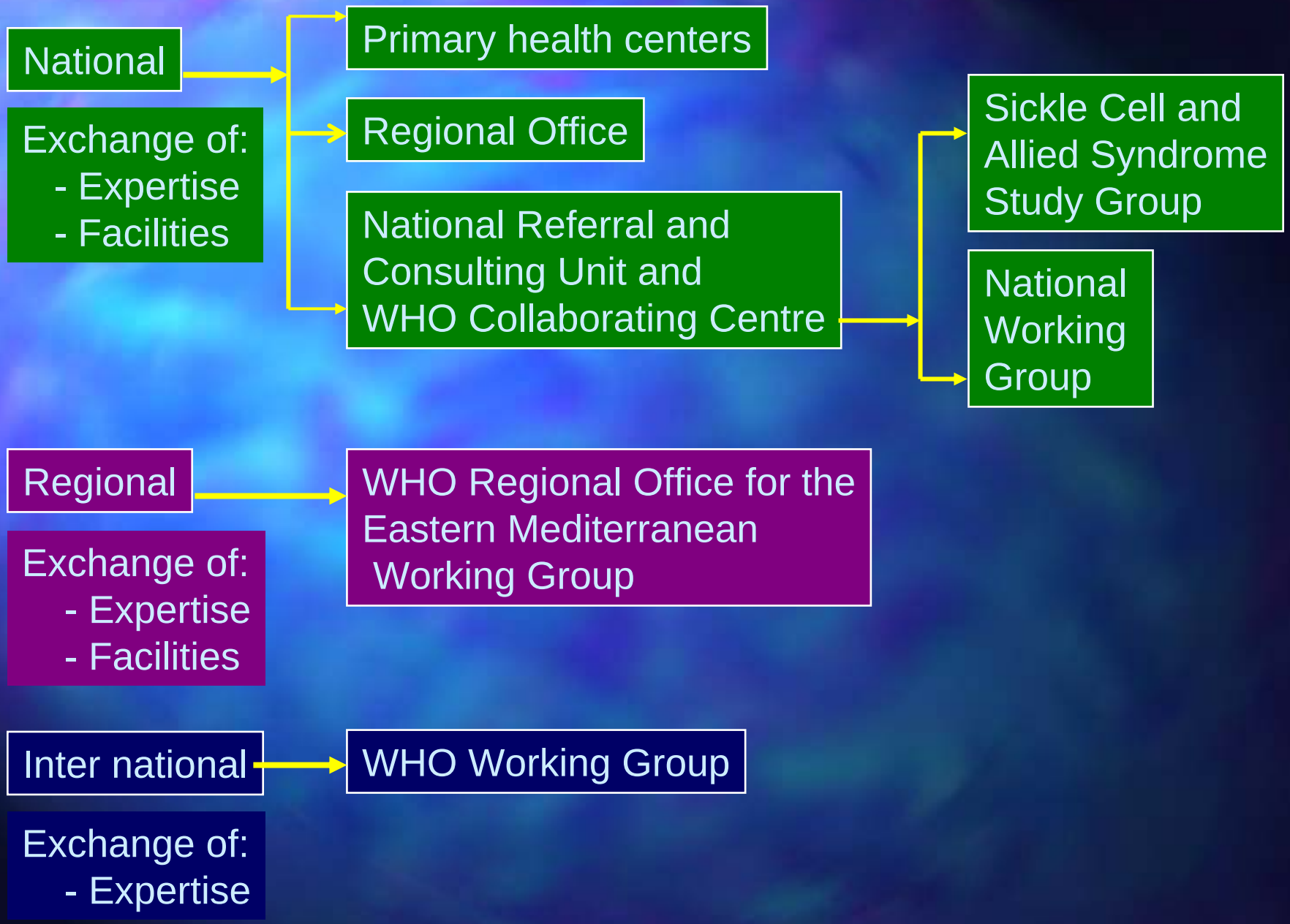
Dilemma for families and health workers

- Research information on role of consanguinity and adverse effects of consanguinity on fertility, infant and childhood mortality and morbidity:
- Stability of the family
- Stability of the society


If a genetic disorder exists in the family?
• Consanguineous marriages have serious implications as genetic risk is increased.
• Social benefits/genetic risks
It is important for the counselor to provide clear information on the precise genetic risk
Risk declines with distance of relationship

A proposed genetic counselling plan in societies favoring consanguineous marriages




National
Exchange of:
- Expertise
- Facilities
Primary health centers
Regional Office
National Referral and Consulting Unit and WHO Collaborating Centre
Sickle Cell and Allied Syndrome Study Group
National Working Group
Regional
Exchange of:
- Expertise
- Facilities
WHO Regional Office for the Eastern Mediterranean Working Group
Inter national
Exchange of:
- Expertise
WHO Working Group

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Conclusion

- Consanguinity is of frequent occurrence in Saudi Arabia.
  - First cousin marriages are most frequent.
- Prevalence of consanguinity is higher in patients with AR (SCD, β-thal.) disorders.
- Rare AR disorders occur at a significantly higher frequency in consanguineous marriages.
- Multifactorial disorders are not significantly higher in consanguineous marriages.


Thank you
for
Listening