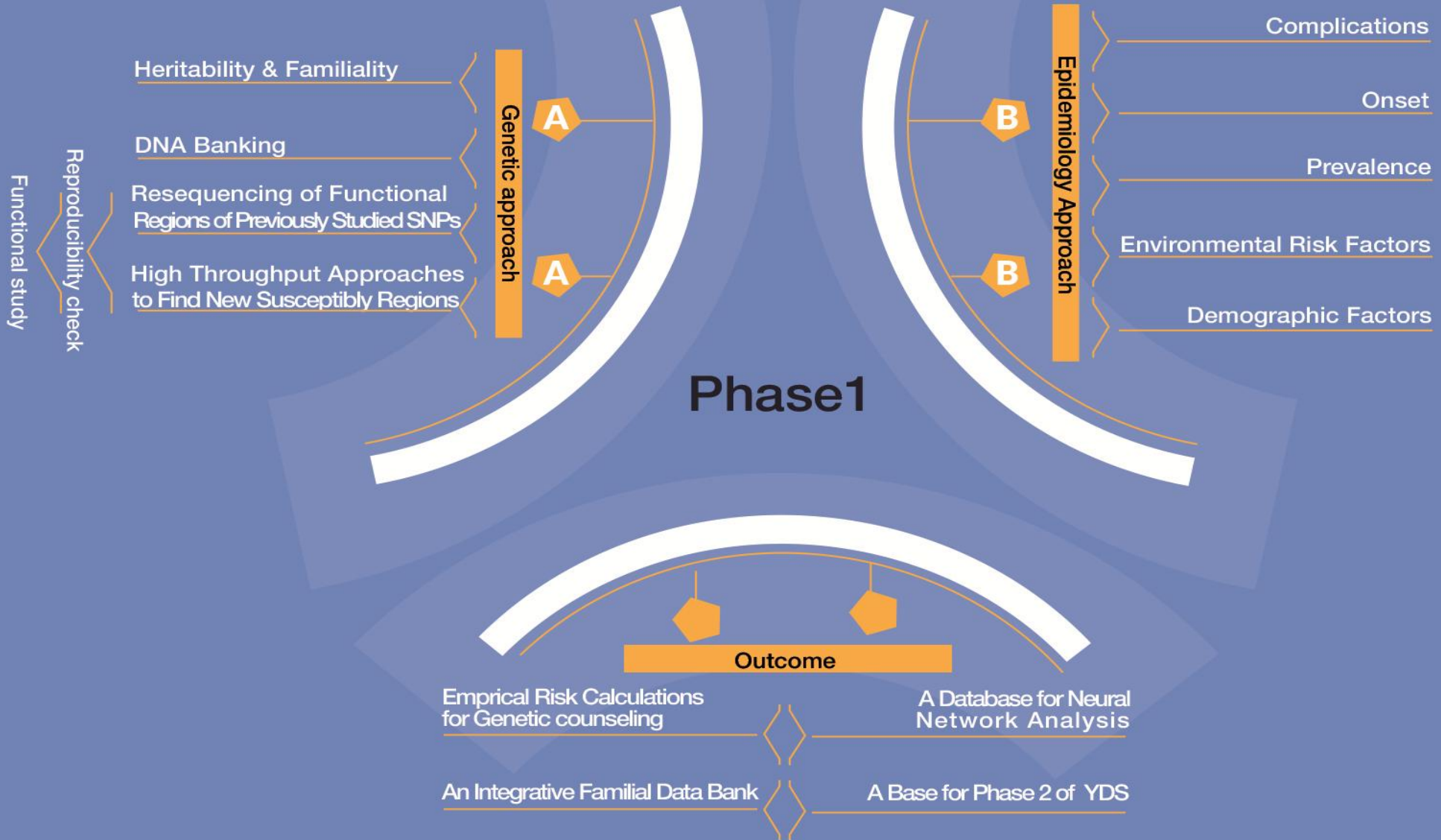


*Human beings are members of a whole
In creation of one essence and soul*

*If one member is afflicted with pain
Other members uneasy will remain*

*If you've no sympathy for human pain
The name of human you cannot retain*



Heritability And Familiality of Type 2 Diabetes in Yazd Population, Iran

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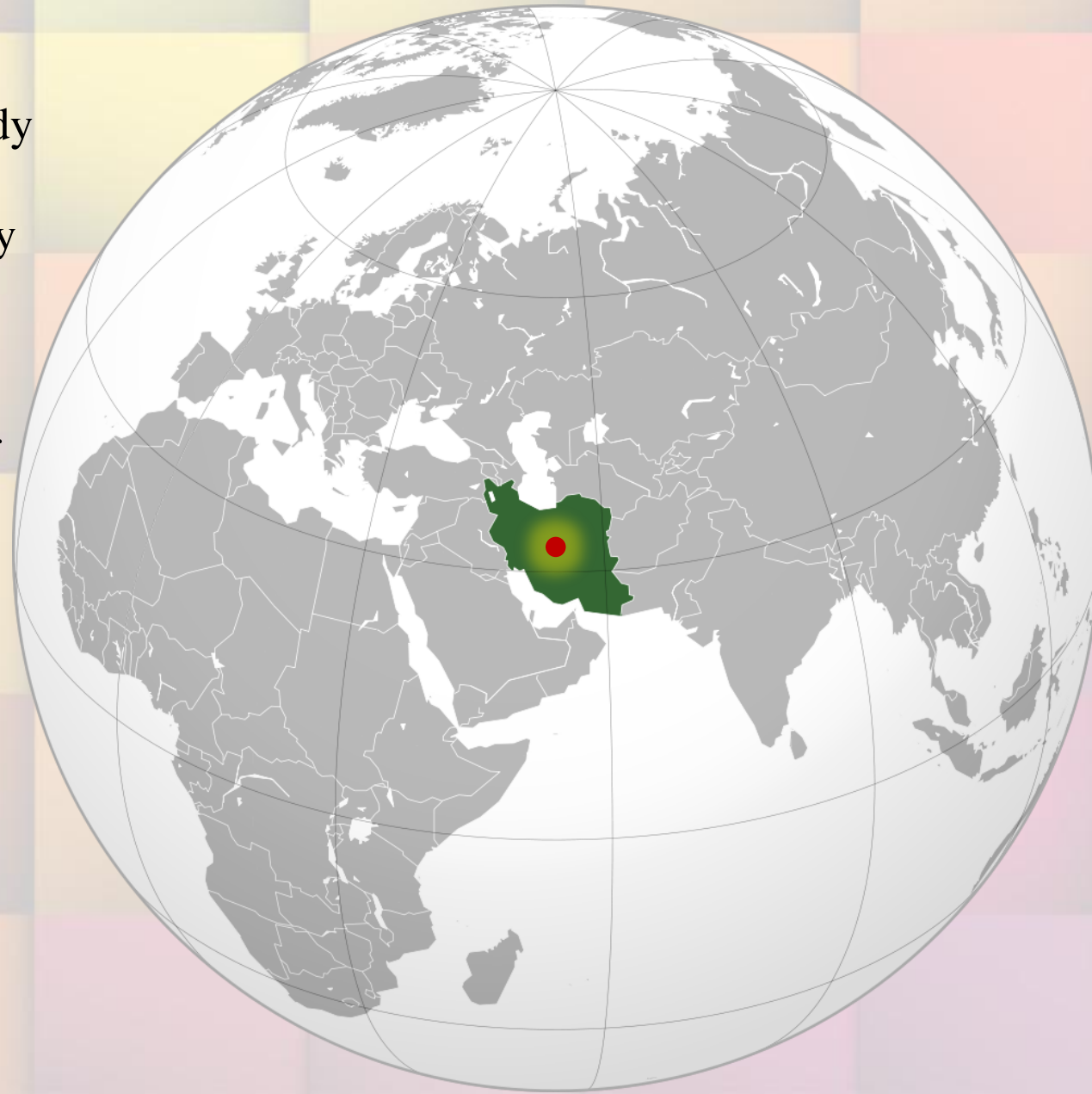
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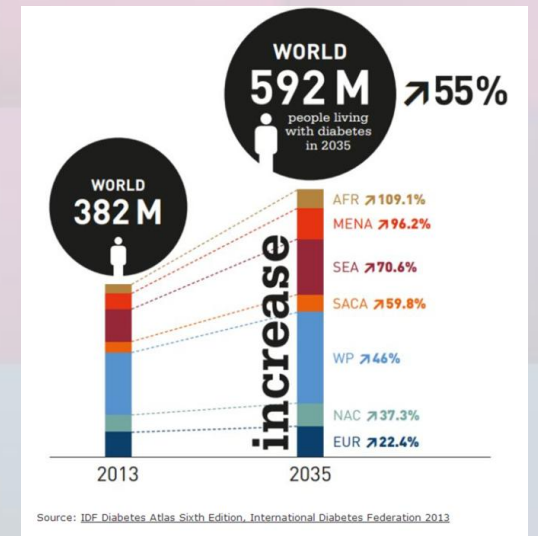
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Introduction



- ✓ First step in genetic study is to estimate heritability
- ✓ Heritability (h^2) is estimated as the ratio of the phenotypic variance explained by additive polygenic effects at the particular time, age and on specific population.



Yazd Population

- High level of consanguineous marriage
- low relocation rates
- A relatively high standard of living
- large family sizes

Materials & Methods

Subject selection

Subjects' recruitment were started since 2012. Written informed consent was obtained from all individuals before participation and the study protocols were approved by local ethics committees. The diagnosis of type 2 diabetes for all participants was based on clinical characteristics and WHO 1998 criteria. A structured valid questionnaire of 100 parameters including smoking habits, diets, physical activity and clinical assessment were collected from all participants.

Probands

Adults-onset diabetes were selected randomly from records of Yazd Diabetic Research Center.

Family member

The first-, second- and third- degree family member of probands, aged ≥ 20 were interviewed door to door. If another diabetic individual was identified in the family, the family was expanded further to include that person's family members similar as others.

Measurements

Height (to the nearest cm without shoes) and weight (to the nearest kg in light indoor clothing) were recorded. BMI was calculated as the weight (kg) divided by the height (m) squared. Although, expanded pedigree for each family was recorded.

Data Analysis & Heritability Calculation

- Heritability was calculated for Type2diabetes in SOLAR software package and was adjusted for common covariates (age, sex, age \times sex, age² and BMI).
- It was estimated using a liability threshold model implemented in SOLAR.
- Sibling, nuclear family and expanded family relative risk was calculated as risk of diabetes in respectively, siblings, nuclear family and expanded family of patients with type2 diabetes compared with background population.
- The parent-offspring correlation for diabetes was calculated to assess the difference of transmission of disease from mother or father.

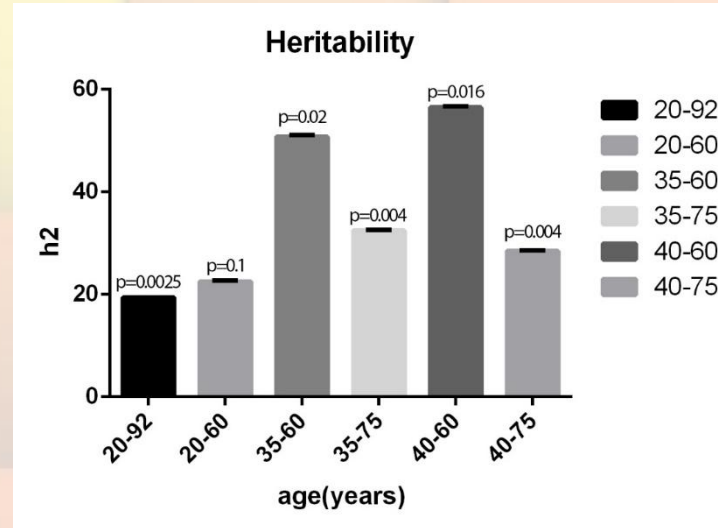
Results

Parent- offspring correlations for type2 diabetes

Father	Mother	Male Diabetic offspring/total male	Female Diabetic offspring/total male	OR(95%CI)	P-value
Non-Diabetic	Diabetic	0.4	0.27	1.73(1.06-2.81)	0.027
Diabetic	Non-Diabetic	0.38	0.43	0.8(0.43-1.42)	0.43
Diabetic	Diabetic	0.25	0.34	0.64(0.33-1.23)	0.18

λ_s	λ_R (Nuclear Family)	λ_R
3.14	3.42	2.4

Heritability of type 2 diabetes



Age Range	H ² ±SE	Pvalue	Loglike	Kullback-leibler R-squared
20-92	0.1935580±0.07	0.0025124	-867.9068	0.1551934
20-60	0.2245±0.200	0.1146199	-671.183130	0.2118744
35-60	0.5080729±0.27	0.0209104	-535.531924	0.2692349
40-60	0.564569±0.28	0.0165230	-474.447756	0.0362839
35-75	0.3249571±0.11	0.0004070	-738.814603	0.0506107
40-75	0.2847715±0.11	0.0039717	-732.045135	0.0307852

Discussion

- ✓ h^2 is the resemblance between children and their parents and ranges from 0.0 to 1.0
- ✓ h^2 : environmental factors x genetic factors.
- ✓ High heritability : represented that phenotype is related to genotype



By knowledge of genotype we could not predict phenotype due to environmental factors influence

- ✓ In population with high h^2 , it is possible to find gene with large influence on phenotype of disease



When h^2 is low, we could not understand that additive genetic have a small role on the phenotype

- ✓ h^2 is used either for comparison of traits across the population or in different age groups of a population, also comparison of different traits, which could be different phenotypes of a disease, in one population
- ✓ The heritability of type2 diabetes is ranging from 0.19 to 0.56 in different age groups (20-85 years) at the under study population. However, the h^2 in botany study in 16-75 years is in range of 0.25 to 0.69

Conclusion

- ✓ Our study indicated that h^2 estimates of 40-60 years age range shows a higher value, compared to other age groups (56 ± 0.28)
- ✓ These results may be due to higher influence of environmental factors in 60-75 age groups
- ✓ On the other hand lower h^2 in individuals younger than 40 years, may be due to incomplete penetrance of T2D
- ✓ These results also lead us to the best age group for genetic studies , which is 40- 60 age range

- ✓ After a deep understanding on high risk genetic factors, discovery of low risk genetic factors can more easily be accomplished in individuals older than 60 years old
- ❖ Finally, heritability estimates in Yazd population showed us that environmental factors play a pivotal role in etiology of T2D as well as genetic factors and it is probable to observed genetic risk factors with $OR \geq 2$

Thank

you

for

Your

Attention

D I A B E T E S

