

GHEP kinship exercise 2023: advanced level

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General instructions

This is a multiple-choice test consisting of 20 questions. For each question exactly one alternative is correct. There may be issues related to for instance rounding, so if your answer does not agree precisely with any alternative, you should choose the closest option.

Throughout we make the following assumptions:

- No deviations from Hardy Weinberg Equilibrium.
- No drop-out, drop-in, silent alleles or mutations.
- Pedigree founders are non-inbred and unrelated to each other.

A majority of the problems can be solved using paper, pencil, and a calculator. However, you are free to use software whenever you like. The online tool [QuickPed](#) may be useful for drawing pedigrees and calculating pedigree coefficients. The solutions to these exercises will use R.

The best of luck!

Questions

Hera, goddess of marriage and family, is married to Zeus - the king of the gods - who is also her brother. He is notoriously promiscuous, and Hera accuses him of having fathered a child, Persephone, by their sister, Demeter. Hera's accusation is shown as hypothesis H_p in Figure 1. Zeus, on the other hand, denies everything and claims that hypothesis H_d is the truth.

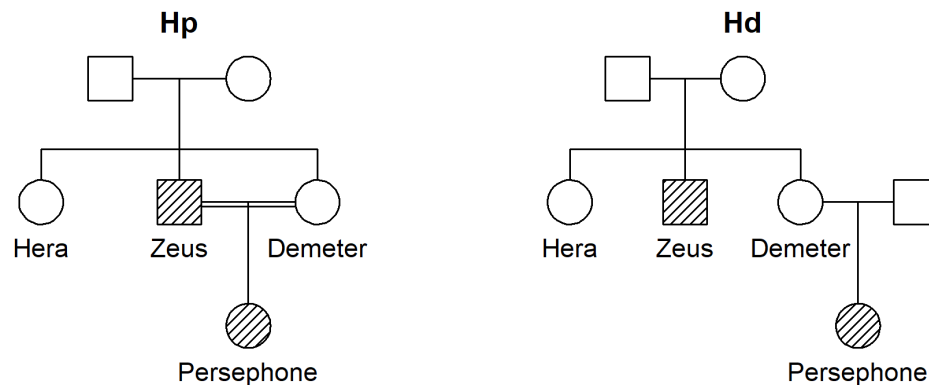


Figure 1: Hypotheses for the pedigree of Persephone.

Wanting to expose her husband, Hera applies forensic kinship testing. She types Zeus and Persephone with a SNP marker with alleles 1 and 2, and allele frequencies $p = P(1)$ and $q = P(2) = 1 - p$. It is known that the allele 2 is very rare among Greek gods, i.e., $q \approx 0$.

The first result to come through is that Zeus has genotype 2/2, while Persephone is still unknown.

1. The probability that Zeus's sister Demeter is also 2/2, is approximately
 - a) 0
 - b) 1/16
 - c) 1/8
 - d) 1/4
 - e) 1/2
 2. If Hd is true, the probability that Persephone has genotype 1/1 (excluding Zeus as her father) is approximately
 - a) 1/2
 - b) 1/4
 - c) 0
 - d) 4q
 - e) p^2
 3. It turns out that Persephone has genotype 2/2. The likelihood ratio $LR = \frac{P(\text{data} | H_p)}{P(\text{data} | H_d)}$ is
 - a) $1/q$
 - b) $1/q^2$
 - c) $1/(2q)$
 - d) $2/q$
 - e) $1/(p - q)$
-

Hera types Zeus and Persephone with another SNP, again with alleles 1 and 2, and allele frequencies $p = P(1)$ and $q = P(2) = 1 - p$. Both Zeus and Persephone are heterozygous with genotype 1/2.

Let b denote the maternal allele of Persephone (i.e., the allele she received from Demeter), and define the following conditional probabilities:

$$d_1 = P(b = 1 | Zeus = 1/2)$$

$$d_2 = P(b = 2 | Zeus = 1/2)$$

4. The likelihood ratio LR for this SNP can be expressed by the formula
 - a) $pd_2 + qd_1$
 - b) $d_1/q + d_2/p$
 - c) $d_1/p + d_2/q$
 - d) $1/(pd_1 + qd_2)$
 - e) $1/(2pd_2 + 2qd_1)$
5. If $q \approx 0$, the value of d_1 is approximately
 - a) 1/4
 - b) 1/2
 - c) 2/3
 - d) 3/4
 - e) 5/8
6. Thus, if $q \approx 0$, the LR is approximately
 - a) 1/2
 - b) 1
 - c) 8/5
 - d) 3/2
 - e) 2

7. Suppose Hera genotypes herself and finds that she is $2/2$. Assuming $q \approx 0$, this would
- increase the LR to ∞
 - increase the LR (but not to ∞)
 - decrease the LR to 0
 - decrease the LR (but not to 0)
 - not change the LR

We now extend the pedigree by including Persephone's son Zagreus. Hera believes that the father of Zagreus is in fact Zeus. He again denies any involvement, and claims that it was Persephone's husband, Hades. Hera considers three possible scenarios, as shown in Figure 2.

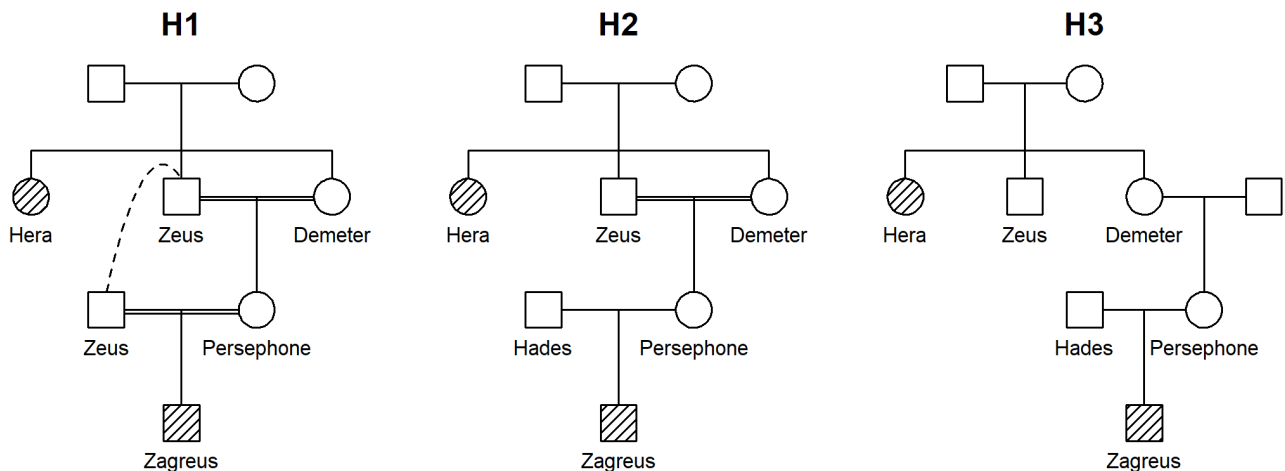


Figure 2: Three hypotheses for the pedigree of Zagreus. Hera and Zagreus are typed. Symbols connected with a dashed line represent the same person.

8. The inbreeding coefficient of Zagreus in pedigree H1 is
- $1/4$
 - $1/3$
 - $2/5$
 - $3/8$
 - $1/2$
9. According to H1, Zeus is, simultaneously, Zagreus's
- father, grandfather and uncle
 - father, grandfather and grand-uncle
 - father, grandfather and great-grandfather
 - father, uncle and first cousin once removed
 - father, uncle and grand-uncle

To test the paternity of Zagreus, Hera types him with a set of 15 forensic STR markers. Zeus refuses to participate this time, so Hera types herself instead, hoping that this gives enough information to resolve the case. The genotypes for all 15 markers are shown in the table below, and also available in the files [olympianGeno.txt](#) (compact format) and [olympianGeno2.txt](#) (GeneMapper format). Allele frequencies for the population of Greek gods can be found in [olympianFreqs.txt](#).

ID	D3S1358	TH01	D21S11	D18S51	PENTA_E	D5S818	D13S317	D7S820	D16S539	CSF1PO	PENTA_D	VWA	D8S1179	TPOX	FGA
Hera	16/17	6/9	31/33.2	12/12	7/7	11/13	8/13	8/9	11/12	10/11	12/13	17/17	13/15	8/11	23/23.2
Zagreus	17/17	6/9	30/31	12/12	13/13	11/12	12/12	8/9	11/12	10/11	12/13	17/17	13/15	8/8	25/25

Hera performs an LR computation based on the three hypotheses, using H3 as reference. Below is a partial output showing the total LRs and individual results for the first three markers:

```
##           H1:H3           H2:H3
## 12220.943938      4.032211

##           H1:H3           H2:H3
## D3S1358 3.092968 1.266109
## TH01    2.283430 1.337632
## D21S11  0.849031 1.349031
```

10. Based on the LR values for the marker D21S11 alone, the hypotheses ordered from most likely to least likely, is
 - a) H1, H2, H3
 - b) H1, H3, H2
 - c) H2, H1, H3
 - d) H2, H3, H1
 - e) H3, H2, H1
11. The total LR comparing H1 and H2, i.e. $LR_{1:2} = P(\text{data} | H1)/P(\text{data} | H2)$ is approximately
 - a) 0.0003
 - b) 3031
 - c) 12221
 - d) 12225
 - e) 49277
12. Use a software of your choice to compute $LR_{1:2}$ for all 15 markers. The marker with the highest LR is
 - a) D18S51
 - b) PENTA_E
 - c) D5S818
 - d) VWA
 - e) FGA
13. The number of markers in favour of H1 compared with H2 is
 - a) 2
 - b) 8
 - c) 9
 - d) 12
 - e) 13

Hera realises that there is a fourth alternative, H4, she hasn't considered, namely where Zeus is the father of Zagreus, but not of Persephone.

14. Use a software of your choice to compute the LR comparing H4 with H3. The overall $LR_{4:3}$ is
- 0.87
 - 4.03
 - 15
 - 465
 - 14090
15. Based on the LRs, hypothesis H4 is
- more likely than H1, H2, and H3
 - more likely than H3, but less likely than H1 and H2
 - more likely than H2 and H3, but less likely than H1
 - less likely than H1, H2, and H3
 - equally likely to H2

Zeus is confronted with the results of the analyses, but responds to Hera: *These analyses are worthless! You have forgotten that Hades, Persephone's husband, is our brother.* Admitting that he has a point, Hera formulates a new hypothesis, H5, which is identical to H2 except that Hades is properly positioned (Figure 3).

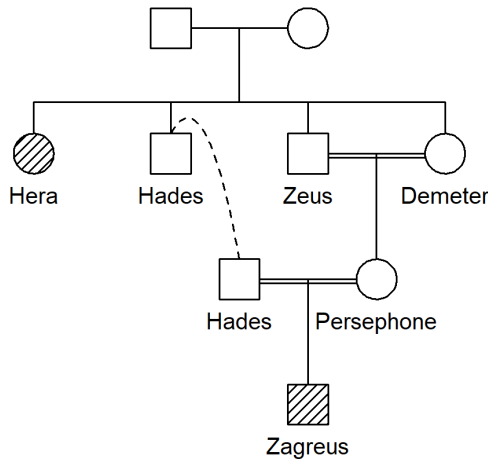


Figure 3: The hypothesis H5.

16. The inbreeding coefficient of Zagreus in H5 is
- 1/4
 - 1/3
 - 2/5
 - 3/8
 - 1/2
17. Calculate the LR comparing H1 with H5, using all 15 markers. The overall $LR_{1:5}$ is
- 1
 - 1.58
 - 15.8
 - 1922.1
 - 7750.4

Finally, Hera turns to X-chromosomal markers to gather evidence against her brother-husband. Secretly plucking hairs from her relatives, she establishes that, for a particular X-chromosomal SNP, Hades carries allele 1, Zagreus and Zeus both have allele 2, while she herself is homozygous 1/1.

Hera wants to compare H1 and H5 given the new data. But since Hades is now genotyped, he needs to be included in H1. To avoid confusion, Hera draws new pedigrees, H1x and H5x, shown in Figure 4, including the known genotypes.

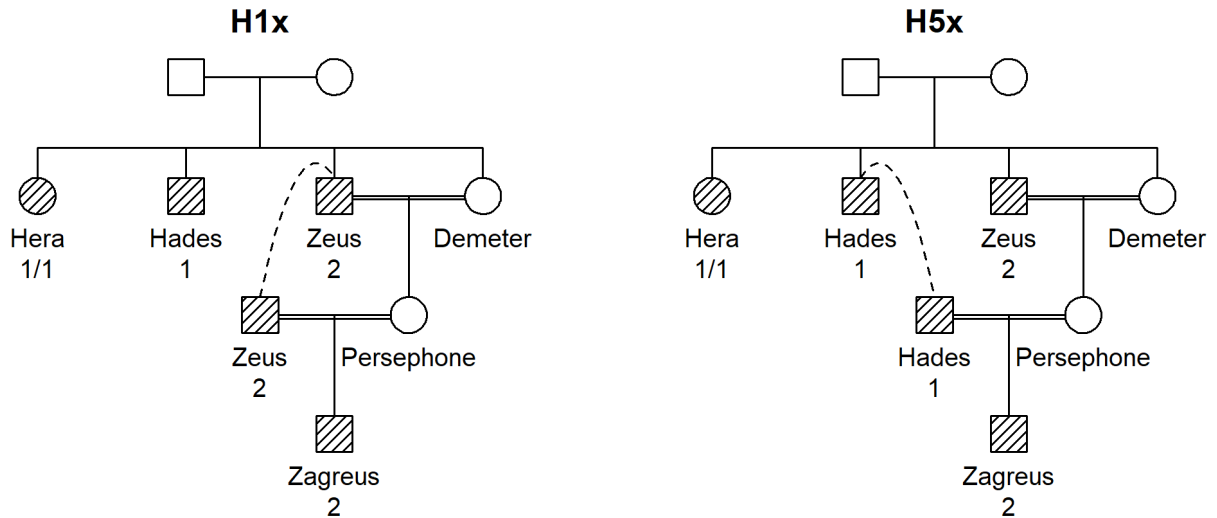


Figure 4: Pedigrees used in the X-chromosomal calculations.

18. Demeter's genotype for this marker is
 - a) 1/2
 - b) 2/2
 - c) either 1/1 or 1/2
 - d) either 1/2 or 2/2
 - e) either 1/1, 1/2 or 2/2
19. The $LR_{1:5}$ comparing H1x and H5x, for this marker alone, is
 - a) 1
 - b) 2
 - c) 3
 - d) 4
 - e) dependent on the allele frequencies
20. Finally, suppose Zagreus were female, and had genotype 1/2. The allele frequencies are $p = 0.9, q = 0.1$. In that case, $LR_{1:5}$ would be
 - a) 0.1
 - b) 0.6
 - c) 1
 - d) 1.11
 - e) 10

END