Supplemental Material: Calculations of probability of *APOL1* risk genotype in relatives (Table 1)

We make the following assumptions based the observed population frequency of *APOL1* risk genotype and Hardy Weinberg equilibrium:

Population frequency of aa (*APOL1* risk) genotype: $p^2 = 0.150$ (average in African Americans)
Allele frequency of a (*APOL1* risk allele): p = 0.387; Allele frequency of A (non-risk allele): q = 1–p = 1–0.387 = 0.613;
Population frequency of Aa genotype: 2pq = 0.474; Population frequency of AA genotype: $q^2 = 0.376$.

Q1. Given patient with genotype aa, what is the probability of sibling with genotype aa?

Step 1: Given patient with genotype aa, what are probabilities of possible parental genotypes?

First, we note that based on Mendelian transmission laws and Hardy Weinberg equilibrium the following relationships hold:
P(pt aa| parents Aa/Aa) = 0.25
P(parents Aa/Aa) = 0.474*0.474 = 0.225
P(pt aa|parents Aa/aa or aa/Aa) = 0.5
P(parents Aa/aa or aa/Aa) = 2*0.474*0.15 = 2*0.0711
P(pt aa|parents aa/aa) = 1
P(parents aa/aa) = 0.15*0.15 = 0.0225

Then, the probabilities of possible parental genotypes, given the patient has genotype aa can be computed as follows:
P(parents Aa/Aa|pt aa) = (0.25*0.225) / (0.25*0.225+0.5*2*0.0711+1*0.0225) = 0.3753754
P(parents aa/Aa or Aa/aa|pt aa) = (2*0.5*0.0711) / (0.25*0.225+ 0.5*2*0.0711+1*0.0225) = 0.4744745
P(parents aa/aa|pt aa) = 0.0225/ (0.25*0.225+ 0.5*2*0.0711+1*0.0225) = 0.1501502

Step 2: Given probabilities of each parental genotype combination for patient aa, what is probability of sibling genotype aa?

P(sibling aa & parents Aa/Aa|pt aa) = P(sibling aa|parents Aa/Aa)*P(parents Aa/Aa|pt aa) = 0.25*0.3753754 = 0.09384385
P(sibling aa & parents aa/Aa or Aa/aa|pt aa) = P(sibling aa|parents aa/Aa or Aa/aa)*P(parents aa/Aa or Aa/aa|pt aa) = 0.5*0.4744745 = 0.2372373
P(sibling aa & parents aa/aa|pt aa) = P(sibling aa|parents aa/aa)*P(parents aa/aa|pt aa) = 1*0.1501502 = 0.1501502

Overall probability of a sibling with genotype aa given patient with genotype aa represents the sum of above probabilities across all possible parental genotypes: 0.09384385+0.2372373+0.1501502 = 0.4812314 = **48%**

Q2. Given patient with genotype Aa, what is the probability of sibling with genotype aa?

Step 1. Given patient with genotype Aa, what are probabilities of possible parental genotypes?

First we note that based on Mendelian transmission laws and Hardy Weinberg equilibrium the following relationships hold:
P(pt Aa|parents AA/Aa or Aa/AA) = 0.5
P(parents AA/Aa or Aa/AA) = 2*0.474*0.376 = 0.356448
P(pt Aa|parents AA/aa or aa/AA) = 1
P(parents AA/aa or aa/AA) = 2*0.15*0.376 = 0.1128
P(pt Aa|parents Aa/aa or aa/Aa) = 0.5
P(parents Aa/aa or aa/Aa) = 2*0.474*0.150 = 0.1422
P(pt Aa|parents Aa/Aa) = 0.5
P(parents Aa/Aa) = 0.474*0.474 = 0.224676

Then the probabilities of possible parental genotypes, given the patient has genotype Aa can be computed as follows:
P(parents AA/Aa or Aa/AA|pt Aa) = (0.5*0.356448)/(0.5*0.356448 + 0.1128 + 0.5*0.1422 + 0.5*0.224676) = 0.3756339
P(parents AA/aa or aa/AA|pt Aa) = 0.1128/(0.5*0.356448 + 0.1128 + 0.5*0.1422 + 0.5*0.224676) = 0.237743
P(parents Aa/aa or aa/Aa|pt Aa) = (0.5*0.1422)/(0.5*0.356448 + 0.1128 + 0.5*0.1422 + 0.5*0.224676) = 0.1498539
P(parents Aa/Aa | pt Aa) = (0.5*0.224676)/(0.5*0.356448 + 0.1128 + 0.5*0.1422 + 0.5*0.224676) = 0.2367692

Step 2: Given probabilities of each parental genotype combination for patient Aa, what is probability of sibling genotype aa?

P(sibling aa & parents AA/Aa or Aa/AA|pt Aa) = P(sibling aa|parents AA/Aa or Aa/AA)*P(parents AA/Aa or Aa/AA |pt Aa) = 0*0.3756339 = 0
P(sibling aa & parents AA/aa or aa/AA|pt Aa) = P(sibling aa|parents AA/aa or aa/AA)*P(parents AA/aa or aa/AA |pt Aa) = 0*0.237743 = 0
P(sibling aa & parents Aa/aa or aa/Aa|pt Aa) = P(sibling aa|parents Aa/aa or aa/Aa)*P(parents Aa/aa or aa/Aa |pt Aa) = 0.5*0.1498539 = 0.07492695
P(sibling aa & parents Aa/Aa|pt Aa) = P(sibling aa|parents Aa/Aa)*P(parents Aa/Aa |pt Aa) = 0.25*0.2367692 = 0.0591923

Overall probability of a sibling with genotype aa given patient with genotype Aa represents the sum of above probabilities across all possible parental genotypes: 0 + 0 + 0.07492695 + 0.0591923 = 0.1341193 = **13%**

Q3. Given patient with genotype AA, what is the probability of sibling with genotype aa?

Step 1. Given patient with genotype AA, what are probabilities of possible parental genotypes?

First, we note that based on Mendelian transmission laws and Hardy Weinberg equilibrium the following relationships hold:
P(pt AA| parents Aa/Aa) = 0.25
P(parents Aa/Aa) = 0.474*0.474 = 0.225
P(pt AA|parents AA/Aa or Aa/AA) = 0.5
P(parents AA/Aa or Aa/AA) = 2*0.474*0.376 = 0.3564
P(pt AA|parents AA/AA) = 1
P(parents AA/AA) = 0.376*0.376=0.141376

Then, the probabilities of possible parental genotypes, given the patient has genotype AA can be computed as follows:
P(parents Aa/Aa|pt AA) = (0.25*0.225) / (0.25*0.225+0.5*0.3564+1*0.141376) = 0.1496703
P(parents AA/AA|pt AA) = 0.141376/ (0.25*0.225+0.5*0.3564+1*0.141376) = 0.3761741
P(parents AA/Aa or Aa/AA|pt AA) = (0.5*0.3564) / (0.25*0.225+0.5*0.3564+1*0.141376) = 0.4741556

Step 2: Given probabilities of each parental genotype combination for patient AA, what is probability of sibling genotype aa?

P(sibling aa & parents Aa/Aa|pt AA) = P(sibling aa|parents Aa/Aa)*P(parents Aa/Aa |pt AA) = 0.25*0.1496703 = 0.03741758
P(sibling aa & parents AA/AA|pt AA) = P(sibling aa|parents AA/AA)*P(parents AA/AA |pt AA) = 0*0.3761741= 0
P(sibling aa & parents Aa/AA or AA/Aa|pt AA) = P(sibling aa|parents Aa/AA or AA/Aa)*P(parents Aa/AA or AA/Aa |pt AA) = 0*0.4741556 = 0

Overall probability of a sibling with genotype aa given patient with genotype AA represents the sum of above probabilities across all possible parental genotypes: 0.03741758 + 0 + 0 = 0.03741758 = **4%**

Q4. Given patient with genotype aa, what is the probability of parent with genotype aa?

Probability of possible parental genotypes from Q1 above:
P(parents Aa/Aa|pt aa) = 0.3753754
P(parents aa/Aa or Aa/aa|pt aa) = 0.4744745
P(parents aa/aa|pt aa) = 0.1501502

P(parent aa|pt aa) = 0 + 0.5*0.4744745 + 0.1501502 = 0.3873875 = **39%**

Q5. Given patient with genotype Aa, what is the probability of parent with genotype aa?

Probability of possible parental genotypes from Q2 above:
P(parents AA/Aa or Aa/AA | pt Aa) = 0.3756339
P(parents AA/aa or aa/AA | pt Aa) = 0.237743
P(parents Aa/aa or aa/Aa | pt Aa) = 0.1498539
P(parents Aa/Aa | pt Aa) = 0.2367692

P(parent aa|pt Aa) = 0 + 0.5*0.237743 + 0.5*0.1498539 + 0 = 0.1937985 = **19%**

Q6. Given patient with genotype aa, what is the probability of child with genotype aa?

Probabilities of possible spouse genotypes (correspond to population genotype frequencies):
P(spouse aa) = 0.150; P(spouse Aa) = 0.474; P(spouse AA) = 0.376
P(child aa| pt aa) = 0.150 + 0.5*0.474 + 0 = 0.387 = **39%**

Q7. Given patient with genotype Aa, what is the probability of child with genotype aa?

P(child aa| pt Aa) = 0.5*0.150 + 0.25*0.474 + 0 = 0.1935 = **19%**

Q8. Given patient with genotype AA, what is the probability of child with genotype aa?

P(child aa| pt AA) = 0*0.150 + 0*0.474 + 0*0.376 = **0%**