Alzheimer Quiz

To answer the questions, let's define several variables:

G+  individual has one or more ε4 alleles
G-  individual has no ε4 alleles
C+  individual meets clinical criteria for Alzheimer's disease
C-  individual does not meet clinical criteria for Alzheimer's disease
D+  individual has Alzheimer's disease (confirmed by pathological criteria at autopsy)
D-  individual does not have Alzheimer's disease (confirmed by autopsy)

Each cell in the table represents an event described by C+ G+ etc. While the format may not be what you are used to from previous exercises, all the information is there in terms of events that can be used to calculate what we need. Each individual falls into one of eight mutually exclusive categories below.

<table>
<thead>
<tr>
<th>APOE Genotype</th>
<th>Both Clinical and pathological criteria for AD</th>
<th>Only Clinical criteria for AD</th>
<th>Only pathological criteria for AD</th>
<th>Neither clinical nor pathological criteria for AD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C+  ∩  D+</td>
<td>C+  ∩  D-</td>
<td>C-  ∩  D+</td>
<td>C-  ∩  D-</td>
</tr>
<tr>
<td>G+ One or more ε4 allele</td>
<td>G+∩C+  ∩  D+  1076</td>
<td>G+∩C+  ∩  D-  66</td>
<td>G+∩C-  ∩  D+  66</td>
<td>G+∩C-  ∩  D-  67</td>
</tr>
<tr>
<td>G- No ε4 allele</td>
<td>G-∩C+  ∩  D+  567</td>
<td>G-∩C+  ∩  D-  124</td>
<td>G-∩C-  ∩  D+  61</td>
<td>G-∩C-  ∩  D-  161</td>
</tr>
<tr>
<td>Total</td>
<td>1643</td>
<td>190</td>
<td>127</td>
<td>228</td>
</tr>
</tbody>
</table>

The proposed screening test requires both clinical criteria for AD and one or more ε4 alleles. So T+ (positive test) = G+∩C+.

Part a (2.5 pts)

Sensitivity = P(T+|D+) = P(G+∩C+∩D+)/P(D+) = (G+∩C+∩D+)/(P(D+))
= 1076/1770 (i.e. Sum up all cells with a D+)
= .6079

Out of confirmed Alzheimer's cases, we would expect 60 percent to meet both the clinical criteria for Alzheimer's and have at least one ε4 allele.
Part b (2.5 points)
A negative test is one where either the clinical criteria are not met, or there are no \( \varepsilon 4 \) alleles or both occur \( T^- = (G+\cap C^+) \)

Specificity = \( P(T^-|D^-) = P((G+\cap C^+) \cap D^-)/P(D^-) \)

\[
P((G+\cap C^+) \cap D^-) = (124 + 67 + 161)/\text{total} = 352/\text{total}
\]

\[
P(D^-) = (66 + 124 + 67 + 161)/\text{total} = 418/\text{total}
\]

\[
P(T^-|D^-) = 352/418 = .8421
\]

Of individuals who do not have Alzheimer's, we would expect 84 percent to be correctly diagnosed as not having AD using the combined screening test.

Part c (3 points)

The predictive value of a positive combined screening test is obtained using Bayes' Theorem using the disease prevalence for the specific age group. (Note: the \( P(D^+) \)

obtained from the study is not a population prevalence rate as the individuals in the study are not necessarily a random sample from the population. We need to use population based, age specific rates.)

For the 65-69 age group \( P(D^+) = .011 \).

\[
P(D^+|T^+) = P(D^+|T^+|D^+)/P(T^+)
\]

\[
P(T^+) = P(D^+|T^+|D^+) + P(D^-|T^+|D^-) = .011 * .6079 + (1 - .011) * (1 - .8421) = .1628
\]

\[
P(D^+|T^+) = .011 * .6079/.1628 = .04
\]

For 66 year old individuals with clinical criteria for Alzheimer's disease and one or more \( \varepsilon 4 \) alleles, only 4 percent actually have Alzheimer's, so such test results are no cause for alarm.

2nd version of quiz:

For the 85-89 year old group with prevalence of Alzheimer's disease of 0.178,

\[
P(T^+) = .178 * .6079 + (1 - .178) * (1 - .8421) = 0.2380
\]

\[
P(D^+|T^+) = .178 * .6079/.2380 = .45
\]

For 86 year old individuals that have clinical criteria for Alzheimer's disease and one or more \( \varepsilon 4 \) alleles, 45 percent actually have Alzheimer's disease.

Part d) The sensitivity of a screening test using only clinical criteria is 1643/1770 = .928, which is much higher that the combined test. Use of the clinical criteria alone would greatly reduce the number of false negatives. The specificity is 228/418 = .545 which is lower than the combined test. The combined test will have fewer false positives. If your grandparents were being tested, which mistake do you think is worse?