To date, little is known about the heritability of primary biliary cirrhosis (PBC). Although one previous study has demonstrated that concordance rates for the disease are substantially higher among monozygotic twins than dizygotic twins [3], the sample size for this study was too small to draw meaningful conclusions regarding the heritability of PBC.

We obtained approximate estimates for the heritability of PBC using the following formulas adapted from [4]:

\[
T = \Phi^{-1}(1 - K)
\]

(1)

\[
T_1 = \Phi^{-1}(1 - \lambda_S K)
\]

(2)

\[
z = \frac{1}{\sqrt{2\pi}} e^{-T^2/2}
\]

(3)

\[
i = z/K
\]

(4)

\[
h^2_L = \frac{2}{i} \left[ T - T_1 \sqrt{1 - (T_1^2 - T^2)(1 - T/i)} \right]
\]

(5)

where \(K\) is the prevalence of the disease, \(\lambda_S\) is the sibling relative risk, and \(\Phi\) is the standard normal cdf. The above formulas work by using a polygenic liability-threshold model for the disease, and assuming the absence of shared environmental contributions to disease liability between siblings.

Some calculations are shown below:

<table>
<thead>
<tr>
<th>(K)</th>
<th>(\lambda_S)</th>
<th>(h^2_L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.000392</td>
<td>10.459184</td>
<td>0.426632</td>
</tr>
<tr>
<td>0.000392</td>
<td>1.000000</td>
<td>0.000000</td>
</tr>
<tr>
<td>0.000392</td>
<td>25.510204</td>
<td>0.632376</td>
</tr>
</tbody>
</table>

In the above, 0.000392 corresponds to the prevalence of probable or definite PBC within the population of Newcastle-upon-Tyne in 1994, according to [1]. The same study reported sibling prevalence estimates of 0.0041 (95% CI: 0.002-0.010). Using the overall population prevalence as a more sensible lower bound on the sibling prevalence, the sibling relative risk (\(\lambda_S\)) can be estimated as \(0.041/0.000392 = 10.459184\), with a confidence interval ranging from 1 to 0.010/0.000392 = 25.510204. Using the formulas, a reasonable range of estimates for heritability would be 0 to 0.63, with a point estimate of 0.43.

References


1\textsuperscript{1}We note that a somewhat lower prevalence of 0.000227 was reported for the Calgary Health Region in 2002, according to [2]. For the purpose of heritability estimation, however, we opted to use the prevalence estimate from [1] for consistency, since sibling prevalence estimates (used to estimate \(\lambda_S\)) were available for the latter population but not the former.
