**Supplementary Material**

**Table S1.** **Claus tables used to calculate lifetime breast cancer risk for each degree of relatedness combination.** The published tables did not include all combinations of relatives. This table presents the combination of relatives used for the simulation. . A). Tables for family members affected with breast cancer, from Claus et al.7 B). Tables for family members affected with ovarian cancer from Claus et al.26

A.

|  |  |
| --- | --- |
| **Original Claus Table** | **Combinations of affected relatives used for simulation** |
| Table 2: One first-degree relative affected with breast cancer | Mother  Sister |
| Table 3: One second-degree relative affected with breast cancer | Aunt (maternal or paternal)  Grandmother (maternal or paternal)  Niece |
| Table 4: Two first-degree relatives affected with breast cancer | Mother and sister  Multiple sisters |
| Table 5: Mother and maternal aunt affected with breast cancer | Mother and maternal aunt  Mother and maternal grandmother  Mother and niece  Sister and maternal aunt  Sister and maternal grandmother  Sister and niece |
| Table 6: Mother and paternal aunt affected with breast cancer | Mother and paternal aunt  Mother and paternal grandmother  Sister and paternal aunt  Sister and paternal grandmother |
| Table 7-One maternal and one paternal second-degree relative affected with breast cancer | Maternal aunt and paternal aunt  Maternal aunt and paternal grandmother  Paternal aunt and maternal aunt  Paternal aunt and maternal grandmother |
| Table 8- Two second-degree relatives affected with breast cancer | Multiple maternal aunts  Multiple paternal aunts  Multiple nieces  Maternal aunt and maternal grandmother  Paternal aunt and paternal grandmother  Niece and paternal aunt  Niece and maternal aunt  Niece and paternal grandmother  Niece and maternal grandmother  Paternal grandmother and maternal grandmother |

B.

|  |  |
| --- | --- |
| **Original Claus Table** | **Combinations of affected relatives used for simulation** |
| Table 1(column one)- One first-degree relative with ovarian cancer | Mother  Sister |
| Table 1(column two)- Two first-degree relatives with ovarian cancer | Mother and Sister |
| Table 2- One first-degree relative with ovarian cancer and one first-degree relative with breast cancer | Mother (breast) and sister (ovarian)  Sister (breast) and mother (ovarian) |

**Table S2.** **Initial vs final risk classification for average-, best- and worst-case uncertainty scenarios for each model.** Rows represent original classification strata and columns represent the final classification strata. Cell entries contain the percentage of pedigree simulations that were classified into each category with each row adding to a total of 100% classification for all simulations. The 95% confidence interval for each classification proportion is also given. Across the diagonal for each uncertainty case scenario (in bold) shows the percentage of pedigree classifications that remained unchanged. In the absence of uncertainty due to self-reported family history, the bold values would be 100% and all non-bold would be zero.

A). Uncertainty classifications for the Claus model.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Low Risk** | **Moderate Risk** | **High Risk** |
| **Average-Case** | | | |
| **Low Risk** | **61.4% ± 4.78%** | 17.6% ± 3.51% | 21.0% ± 2.88% |
| **Moderate Risk** | 15.5% ± 2.39% | **45.5% ± 2.40%** | 39.0% ± 3.58% |
| **High Risk** | 5.30% ± 1.10% | 7.68% ± 2.39% | **87.0% ± 2.88%** |
| **Best-Case** | | | |
| **Low Risk** | **69.2% ± 4.99%** | 16.0% ± 4.18% | 14.8% ± 2.16% |
| **Moderate Risk** | 15.7% ± 2.80% | **53.2% ± 2.94%** | 31.1% ± 3.65% |
| **High Risk** | 3.38% ± 0.68% | 8.29% ± 2.83% | **88.3% ± 3.06%** |
| **Worst-Case** | | | |
|  | **Low Risk** | **Moderate Risk** | **High Risk** |
| **Low Risk** | **53.3% ± 4.71%** | 18.6% ± 2.86% | 28.1% ± 3.59% |
| **Moderate Risk** | 16.8% ± 2.33% | **36.5% ± 2.48%** | 46.7% ± 3.86% |
| **High Risk** | 7.75% ± 1.64% | 7.43% ± 1.88% | **84.8% ± 2.79%** |

B) Uncertainty classifications for the BRCAPRO model.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Low Risk** | **Moderate Risk** | **High Risk** |
| **Average-Case** | | | |
| **Low Risk** | **76.9% ± 1.01%** | 10.9% ± 0.52% | 12.2% ± 0.58% |
| **Moderate Risk** | 35.4% ± 0.53% | **19.2% ± 0.36%** | 45.4% ± 0.69% |
| **High Risk** | 25.9% ± 1.02% | 12.8% ± 0.26% | **61.3% ± 1.15%** |
| **Best-Case** | | | |
| **Low Risk** | **78.6% ± 0.94%** | 11.8% ± 0.59% | 9.58% ± 0.44% |
| **Moderate Risk** | 25.0% ± 0.32% | **27.2% ± 0.60%** | 47.9% ± 0.77% |
| **High Risk** | 13.3% ± 0.55% | 11.3% ± 0.35% | **75.5% ± 0.88%** |
| **Worst-Case** | | | |
| **Low Risk** | **75.0% ± 0.83%** | 9.90% ± 0.30% | 15.1% ± 0.57% |
| **Moderate Risk** | 44.1% ± 0.63% | **14.4% ± 0.20%** | 41.5% ± 0.68% |
| **High Risk** | 37.2% ± 1.03% | 12.7% ± 0.15% | **50.1% ± 1.17%** |

C). Uncertainty classifications for the IBIS model

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Low Risk** | **Moderate Risk** | **High Risk** |
| **Average-Case** | | | |
| **Low Risk** | **39.6% ± 5.69%** | 28.0% ± 2.47% | 32.5% ± 4.04% |
| **Moderate Risk** | 4.07% ± 1.20% | **36.1% ± 5.03%** | 59.9% ± 5.34% |
| **High Risk** | 2.11% ± 0.86% | 4.73% ± 1.82% | **93.2% ± 2.33%** |
| **Best-Case** | | | |
| **Low Risk** | **51.6% ± 5.96%** | 26.3% ± 3.35% | 22.1% ± 3.14% |
| **Moderate Risk** | 3.75% ± 1.52% | **46.7% ± 5.27%** | 49.6% ± 5.38% |
| **High Risk** | 1.74% ± 0.70% | 4.40% ± 1.87% | **93.9% ± 2.25%** |
| **Worst-Case** | | | |
| **Low Risk** | **28.3% ± 5.10%** | 27.5% ± 1.83% | 44.2% ± 4.68% |
| **Moderate Risk** | 4.47% ± 1.01% | **26.9% ± 4.22%** | 68.7% ± 4.73% |
| **High Risk** | 2.29% ± 0.85% | 5.06% ± 1.69% | **92.7% ± 2.29%** |

D). Uncertainty classifications for the BOADICEA model

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Low Risk** | **Moderate Risk** | **High Risk** |
| **Average-Case** | | | |
| **Low Risk** | **62.7% ± 5.34%** | 27.5% ± 3.60% | 9.82% ± 2.37% |
| **Moderate Risk** | 5.61% ± 1.88% | **45.2% ± 4.26%** | 49.2% ± 4.86% |
| **High Risk** | 3.34% ± 1.42% | 12.7% ± 3.15% | **83.9% ± 3.95%** |
| **Best-Case** | | | |
| **Low Risk** | **72.14% ± 5.04%** | 21.9% ± 3.63% | 5.99% ± 1.86% |
| **Moderate Risk** | 5.24% ± 1.93% | **54.6% ± 4.50%** | 40.2% ± 4.91% |
| **High Risk** | 2.31% ± 0.88% | 10.6% ± 3.09% | **87.1% ± 3.57%** |
| **Worst-Case** | | | |
| **Low Risk** | **52.6% ± 5.23%** | 32.2% ± 3.13% | 15.2% ± 2.97% |
| **Moderate Risk** | 6.14% ± 1.68% | **36.5% ± 4.03%** | 57.3% ± 4.97% |
| **High Risk** | 4.43% ± 1.66% | 14.5% ± 3.26% | **81.1% ± 4.36%** |

**Figure S1.** Distribution of initial risk (with no uncertainty) by final categorization (with uncertainty present) of proband calculated by the BOADICEA risk prediction model. Lifetime risk percentages without uncertainty on the left of the diagram (Initial lifetime risk) are shown for each final risk bin category which contains uncertainty. The sizes of the initial risk bins, flows and final risk bins are relative to the number of pedigrees falling into each. The percent of total pedigrees in the initial contrived bin categories was 33% for each and the percent in each final classification is noted in the final risk bins.

