In the 10 years since the identification of the BRCA1 gene, many cancer families have been tested throughout the world, and there is ongoing interest in estimating the cancer risks for women with mutations in this gene. There is some evidence that families with mutations in the central part of BRCA1 (nucleotides 2401 to 4190) have a higher than expected ratio of ovarian to breast cancers, due to a lower than average risk of breast cancer. The absolute and relative risks of breast and ovarian cancers associated with different mutations have been difficult to quantify, in part because of the large number of different mutations in the gene, the rarity of mutations in the general population, and the expense of testing. The majority of established BRCA1 mutations are protein truncating, although a number of deleterious missense mutations have also been identified.

Poland is ideally suited to the study of the genetic epidemiology of BRCA1 mutations because the country is ethnically homogeneous, and because three common BRCA1 mutations comprise 91% of all BRCA1 mutations found in the population. Since 1999, we have tested large numbers of unselected cancer patients and cancer families throughout Poland. To estimate the prevalences and relative risks associated with each of the three founder mutations, we genotyped 2012 unselected cases of breast cancer, 364 unselected cases of ovarian cancer, and 2000 population controls. The breast cancer patients were consecutively diagnosed from eight hospitals throughout Poland. Patients were unselected for age (range 21 to 80 years) or for family history, and had been diagnosed between 1999 and 2002. The ovarian cancer patients were from two hospitals in Szczecin, Poland, and have been described previously. The control population consisted of 1000 newborn children from throughout Poland and 1000 adults unaffected with cancer from the practices of family physicians in Szczecin.

The distribution of mutations is shown in table 1. The 4153delA allele is under-represented among breast cancer patients in this distribution and the ratio of breast to ovarian cancers with this mutation is atypical. Among carriers of the 5382insC mutation, the odds ratio for breast cancer is 10.9 (95% confidence interval (CI) 3.9 to 30.4).

Among carriers of the 4153delA mutation, the odds ratio for breast cancer is 1.0 (95% CI 0.06 to 16.2). The equivalent odds ratios for ovarian cancer for the 5382insC mutation and the 4153delA mutation are 43.6 (15.2 to 125.3) and 50.0 (6.2 to 400) respectively.

To confirm the hypothesis that the 4153delA BRCA1 mutation confers a comparatively low risk of breast cancer, we compared the ratio of breast to ovarian cancers in an independent set of families who had been referred to the hereditary cancer clinic of the Szczecin because of two or more cases of breast or ovarian cancer. These families had been referred for genetic counselling to cancer genetics clinics throughout Poland. At the time the pedigrees were created, no patient in these families had undergone prophylactic mastectomy or had taken tamoxifen as a preventive measure.

### Table 1 Distribution of BRCA1 founder mutations in cancer cases and controls (number (%))

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Cancer Cases</th>
<th>Controls</th>
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</thead>
<tbody>
<tr>
<td>C61G</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4153delA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5382insC</td>
<td></td>
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</tr>
</tbody>
</table>

- **Breast**
  - C61G: 15 (0.7%)
  - 4153delA: 1 (0.05%)
  - 5382insC: 43 (2.1%)
  - Total: 59 (2.9%)

- **Ovarian**
  - C61G: 13 (3.6%)
  - 4153delA: 8 (2.2%)
  - 5382insC: 28 (7.7%)
  - Total: 49 (13.5%)

- **Controls**
  - C61G: 1 (0.05%)
  - 4153delA: 1 (0.05%)
  - 5382insC: 4 (0.2%)
  - Total: 6 (0.3%)
for the different risks is unknown. Interestingly, the situation is different for Ashkenazi Jews; women in this population group with the two common founder mutations in BRCAL face similar risks of breast and ovarian cancer.16 Our sample is relatively small, and it is likely that the risk of breast cancer in carriers of the 4153delA mutation is elevated and that further studies will be required to estimate with accuracy the extent of this risk. It will be helpful to have mutation specific risks for counselling women in Poland so that they can make informed choices regarding preventive surgery.

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