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Citation

Authors' objectives
This qualitative review describes the current molecular basis of breast and prostate cancer, assesses the clinical relevance of genetic susceptibility, addresses non-directive counselling, and explores the ethical, psycho-social, and policy implications associated with genetic testing.

Authors' conclusions
Breast and prostate cancer are the second leading causes of death and the most frequently diagnosed malignancies in Canadian women and men, respectively. Age, ethnicity, and family history are definite risk factors for breast and prostate cancer. Hereditary breast and prostate cancers have been associated with alterations in the expression of tumour suppressor genes and oncogenes.

The majority of hereditary breast cancers can be attributed to germ-line mutations in the breast cancer susceptibility genes BRCA1 and BRCA2, with the remaining cases attributed to over-expression of oncogenes and other genetic aberrations. BRCA1 mutations have been shown to have greater prevalence in families in which there is presence of both breast and ovarian cancer. BRCA1-associated breast cancers are often of higher grade, over-expressing tumour suppressor protein 53, and are estrogen-receptor negative. In contrast to BRCA1, BRCA2 has been associated with fewer incident cases of ovarian cancer and several cases of male breast cancer. Two founder mutations in BRCA1 and one founder mutation in BRCA2, appear in about one-third of the breast cancer patients of Ashkenazi Jewish descent. Protein expression of the oncogene Bc1-2 (B cell leukemia/lymphoma-2) and p53 have roles as independent prognostic markers for disease-free survival after radical treatment for prostate cancer. Predisposing mutations in the hereditary prostate cancer 1 gene (HPC1) are responsible for only a minority of familial prostate cancer cases and they are likely to be most important in families of African-American origin and in families with at least four cases of the disease. Studies involving larger subsets of families should lead to the identification of further genetic susceptibility genes for prostate cancer, although by analogy with HPC1, the process is unlikely to be simple.

Key ethical implications arising from genetic testing for hereditary breast and prostate cancer include; informed consent, privacy and confidentiality, and familial implications. Significant psychological factors including stigmatization, lowered self-esteem, and anxiety are experienced by those of both carrier and non-carrier status. Predictive genetic testing for breast and prostate cancer has brought forth social issues such as the potential creation of a genetic subclass. Ethnic and gender issues compound the risk of genetic discrimination faced by carriers seeking insurance, employment, or adoption. Cost-utility data are required to assess the cost-effectiveness of genetic testing compared with conventional testing options for hereditary breast and prostate cancers.

Currently, genetic testing in Canada is only offered as part of clinical research programs that explore genetic testing as a potential component of routine medical care. As public awareness and new technology develops, the pressure for greater genetic testing services is inevitable. Given the high public profile, vested private sector interest due to potential financial gain, and ethical, psycho-social, and policy implications associated with testing, it would be of benefit to establish clinical research guidelines for predictive genetic testing for families with significant family histories. For both breast and prostate cancer susceptibility, these guidelines could include: (i) a process for ensuring up-to-date information of the medical issues such as a standing panel comprising relevant disciplines; (ii) detailed training in
cancer genetics for health care professionals who provide information and counselling in this area; (iii) the placement of genetic testing services in appropriate centres; (iv) non-directive counselling on the ethical, psycho-social, and policy issues; (v) the importance of obtaining informed consent; and (vi) encouraging individuals to participate in research.

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