REVIEW ARTICLE

# PSYCHOSOCIAL IMPLICATIONS OF CANCER SCREENING IN GENETIC CANCER SYNDROMES

**Tariq Parvez, *Babar Parvez, Abdullah Ali Al-Taifi**

Al-Madina Kingdom of Saudia Arabia, *Babar Clinic Ichra Lahore

## INTRODUCTION

Genetic mutations linked with cancer are increasingly found. Improvements in gene mutation screening will increase the sensitivity, accuracy and therefore the applicability of genetic testing in these conditions [1]. Similarly their use for screening is becoming widespread. Genetic analysis is now becoming available to diagnose such mutations which predispose to inherited cancer diseases. Among them some more important are hereditary breast and ovarian cancer (HBOC), hereditary non-polyposis colon cancer (HNPCC) and familial adenomatous polyposis (FAP). Familial colorectal cancer (CRC) is noted in about 15% of CRC cases, and this type occur at age less than 50 years. Familial adenomatous polyposis (FAP) and hereditary non-polyposis colon cancer (HNPCC) account for about 40% of familial cases [2].

As with other genetic testing a detailed family and personal history is under taken, the health professional then provides the individual with a genetic risk assessment, based on the information which he has collected in the interview, and reviews with the patient the benefits, limitations and risks of genetic testing [3,4]. The individual is then given a chance to decide, after which the samples are collected and then analyzed. Once the results are obtained, the health professional takes the individual a written informed consent from the individual for his participation in counseling. The individual is then informed about the result and then options for medical management are offered. In case of HBOC, a positive test result for an individual has an increased risk of developing cancer; but, it doesn't mean that this individual will certainly develop cancer. Similarly, a negative test result in a patient with family history of genetic disease means that the individual has only an average risk equal to that of general population for developing HBOC. Cancer could still develop in such a person because of other genetic and/or environmental factors. Whereas, families in which no mutations have been identified a positive or negative result will not be in any way informative. Every genetic disease has its own counseling process, implications and outcomes for its testing process. Despite this potential, the whole issue poses complex psychological, social and ethical concerns.

American Society of Clinical Oncology (ASCO) recommends that genetic testing be offered when the individual has personal or family history suggestive of genetic cancer susceptibility, the test can be adequately interpreted, and the results will aid in diagnosis or influence the medical or surgical management of the patient or family members at hereditary risk of cancer. Genetic testing should only be done in the setting of pre- and post-test counseling, which should include discussion of possible risks and benefits of early cancer detection and prevention modalities. It should also include discussion of possible risks and benefits of cancer early-detection and prevention modalities, some of which have presumed but unproven efficacy for individuals at increased hereditary risk of cancer. The decision to offer testing to potentially affected children should take into account the availability of evidence-based risk-reduction strategies and the probability of developing a malignancy

**Correspondence:** Dr Tariq Parvez, Consultant Oncologist, King Fahad Hospital, Madina Munawra, Kingdom of Saudi Arabia.

during childhood. Where risk-reduction strategies are available or cancer predominantly develops in childhood, it believes that the scope of parental authority encompasses the right to decide for or against testing. In the absence of increased risk of a childhood malignancy, it recommends delaying genetic testing until an individual is of sufficient age to make an informed decision regarding such tests. As in other areas of pediatric care, the clinical cancer genetics professional should be an advocate for the best interests of the child. Quality assurance mechanisms by laboratories should include oversight of the reagents used in genetic testing, inter-laboratory comparisons of reference samples, standardization of laboratory genetic test reports, and proficiency testing [5].

ASCO supports establishing a federal law to prohibit discrimination by health insurance providers and employers on the basis of an individual's inherited susceptibility to cancer. Protections against genetic discrimination should apply to those with group coverage, those with individual health insurance policies, and the uninsured. It also supports efforts to ensure that all individuals at significantly increased risk of hereditary cancer have access to appropriate genetic counseling, testing, screening, surveillance, and all related medical and surgical interventions, which should be covered without penalty by public and private third-party payers. All concerned should make concerted efforts to protect the confidentiality of genetic information. However, they should remind patients of the importance of communicating test results to family members, as part of pretest counseling and informed consent discussions [5].

ASCO believes that the cancer care provider's obligations (if any) to at-risk relatives are best fulfilled by communication of familial risk to the person undergoing testing, emphasizing the importance of sharing this information with family members so that they may also benefit. There should be continuing educational opportunities for physicians and other health care providers regarding the methods of cancer risk assessment, the clinical characteristics of hereditary cancer susceptibility syndromes, and the range of issues related to genetic testing, including pre- and post-test genetic counseling, and risk management, so that health professionals may responsibly integrate the care of persons at increased genetic risk of cancer into the practice of clinical and preventive oncology.

All researchers proposing to use or store human biologic specimens for genetic studies should consult either the responsible institutional review board (IRB) or a comparable body specifically constituted to assess human tissue research, to determine the requirements for protection specific to the study under consideration. This consultation should take place before the project is initiated. The determination of the need for informed consent or authorization in such studies should depend on whether the research involves tests for genetic markers of known clinical significance and whether research data will be linked to protected health information, as well as other considerations specific to the study proposed. Special attention should also be paid to whether future research findings will be disclosed to the research participants, whether future contact of participants is planned, and whether and how protected health information about the tissue donors will be stored, and what will happen to study specimens after the trial ends. In addition, the right of people contributing tissue to a databank to rescind their permission, in accordance with federal privacy regulations is met [5].

This review article primarily deals with the implications arising from testing for genetic cancers.

## GENETIC TESTING

Initially, linkage analysis was used to identify genetic markers that were associated

with disease susceptibility in families with a preponderance of breast, ovarian and/or colon cancer. First specific genetic marker was found in proximity to BRCA1 gene among the members of families suffering with HBOC [6]. This work was soon extended to hereditary colon cancer syndromes, such as HNPCC and FAP [2]. A list of more prevalent cancer syndromes, genes involved and cancer produced (table). Before these tests become available studies were done to examine whether individuals would be interested in genetic testing and to identify the possible factors that influence such decisions. The results of these studies showed that over 70% of individuals in the general population and at least 80% of respondents with family histories of cancer were highly interested in undergoing these tests [7,8]. Genetic testing for inherited breast cancer risk may increase screening behaviors among mutation carriers. However, utilization of some screening tests remains low among mutation carriers [9]. But in one study where the majority of families counseled were eligible for BRCA1/BRCA2 testing, only 18% elected to proceed with the test [10]. Persons at increased cancer risk because of family history warrant a surveillance strategy for early detection [11]. There are many factors which can influence these decisions. These can be personal and family based [12]. Affected and unaffected person's attitude can be different. Similarly the family responses can vary [6].

A study was done to find out difference in attitudes between affected and unaffected women. The majority of both previously affected and unaffected women felt that preventive decisions, screening, assessment of children's risks, and cancer anxiety were important issues for their thoughts about genetic testing. Similarly more affected women took family member's opinion more oftenly [13]. There are many reasons why potential candidates might refuse genetic testing for cancer susceptibility. This is because of the uncertainty associated with positive results, psychological distress, family stress, lack of health insurance and concerns regarding potential discrimination [9]. Surprisingly, relatively few individuals who received genetic testing for breast cancer susceptibility accepted that they sought testing as a result of a physician's recommendation [14]. This might be due to the fact that many physicians are not adequately prepared to recognize familial cancer syndromes or to make appropriate referrals [15].

In one study to analyze health care provider's opinions about whether or not they should undergo testing, it was reported that over three-quarters of women who considered clinical testing for BRCA1/2 mutations wanted to know the opinions of their genetics doctors and almost half wanted to know their general physician's opinion about whether or not they should undergo testing. The most frequently reported reason for not getting a mammogram was because the participant's doctor had not suggested it [16]. Besides, doctors having proper knowledge a detailed operational model are a very useful tool in helping to make decisions about screening at national and local levels [17].

Physician can get help in communicating his opinion from genetic counseling models already established for this purpose. These results support the use of models of genetic counseling that allow for sharing the health care provider's opinions when desired by the patient [18]. The model suggested that affective barriers could be reduced by increasing knowledge, which could be enhanced by acculturation, social support, and physician recommendation. Interventions that focus on increasing such knowledge could reduce affective barriers to cancer screening for this population when taking the enhancement of communication skills and interpersonal interactions into account [19].

Although tailored print materials (TPMs) have been assessed for a variety of behavioral change, their effectiveness as decision aids for genetic testing had not been evaluated widely. But one study compared TPMs and

non-tailored print material (NPMs) that included similar content about genetic testing for breast and ovarian cancer susceptibility. TPMs showed an advantage in increasing knowledge and enhancing accuracy of perceived risk. In one study it was seen that there was a high effectiveness of the culturally tailored genetic education and counseling materials [20].

Although there are many important components of informed decision making but at least knowledge makes many things more clear [21]. For cancer screening concerted efforts by insurance and health-care providers are needed to improve adherence to the recommended cancer screening guidelines, both by consumers and service providers [22]. Inadequate public health education, lack of patient-friendly health services, socio-cultural health beliefs, gender roles, and personal difficulties were the most salient barriers to screening [23]. Contrary to a commonly held view, high participation in screening programs is not necessary to achieve cost-effectiveness. Setting high target participation rates in screening programs does not guarantee cost-effectiveness and may in certain circumstances reduce the cost-effectiveness [24]. Genetic counseling may turn risk information into cancer prevention behavior by modifying health beliefs, cancer-related distress and increase the likelihood of screening [25]. Genetic counseling had a positive impact on management of breast cancer risk [26].

Inconsistent messages about the value of genetic screening for breast cancer in both ethnic and non-ethnic newspapers can produce negative effect. The publication of discrepant research findings and the perplexing statistical information consequently brought into question the credibility of the scientific process and the recommendations of health care professionals [27]. But women's movements at different level of society can be helpful in providing useful suggestions to improve breast cancer prevention modalities [28]. It was seen that a program of genetic testing and screening for breast cancer in a high-risk population could be cost-effective [29].

## PSYCHOSOCIAL ASPECTS

Although psychological and social concerns might stop some high risk individuals from genetic testing, the data have not provided adverse psychological impact of testing [30]. In fact, research data from families with hereditary cancer and from individuals who were tested in clinical settings indicate that there are positive psychological benefits for members of high risk families who test negative, such as a decrease in psychological distress [31]. Surprisingly, there is little evidence of negative psychological effects in identified mutation carriers, possibly because many high risk individuals already assume that they are mutation carriers, and consequently learning their mutation status is no more distressing than fearing the outcome [31]. By contrast, in one study of BRCA1/BRCA2 linked families, individuals who experienced high levels of cancer related distress during pre-counseling and then refused to be tested were at the greatest risk of depression [32]. So, the decision to refuse testing could actually promote, rather than remove the distress for some individuals. Facing the test may temporarily produce stress in such cases but ultimately they benefit.

Although the available data indicate that we should be optimistic about the psychological consequences of receiving the test results of cancer probability testing, but there are pitfalls also. First, genetic testing cause anxiety, cancer related worries, family stresses and difficulty with medical decision making in individuals who tested positive [30]. Second, although psychological reactions to genetic testing might be favorable, but there are clearly a small subset of individuals who could be at risk of adverse psychological consequences [33]. The development and execution of more intensive counseling programmes for such individuals presents another important challenge in this field. In

one study it was found that acceptance of genetic services were related to the magnitude of the threat i.e. how many cancers in the family, perceived ability to deal with the threat e.g. good health and a supportive network, and a desire to inform relatives and siblings. The two approaches to educating patients, viz. direct patient education vs. education via their physician, did not significantly differ in terms of percentages of patients receiving counseling or the percentage choosing DNA testing [34].

## BEHAVIOUR CHANGE

Positive result may motivate high risk individuals to alter their behavior to reduce cancer risk. This may include increasing the frequency of cancer screening and making healthy lifestyle changes, such as nutritional or dietary changes, stopping smoking, or increasing physical activity. Indeed, being informed about the need to increase cancer screening and prevention practices is taken frequently as a motivation for seeking genetic testing [13]. Most studies for cancer detection and management following genetic testing have focused on BRCA1/BRCA2 mutations, because these were the first to be widely available. Irrespective of the testing, about 30-40% of mutation carriers do not receive the recommended mammography within the 12 months of the testing [35]. In addition, although prophylactic oophorectomy, can reduce the risk of breast and other BRCA1/BRCA2 related cancers, only a small proportion of women choose this option, and the rates are variable among different studies [36]. Although only a few unaffected carriers opt for prophylactic mastectomy, a positive BRCA1/BRCA2 test after a new diagnosis of breast cancer increases the likelihood of woman choosing for prophylactic bilateral mastectomy instead of breast conserving surgery. Among women with an increased risk of developing breast cancer, anxiety and cancer worries can also facilitate decision making [37].

Information about breast/ovarian cancer risk and test availability was generally well transmitted, predominantly to first-degree relatives. Whereas, testing participation was low and principally occurred among sisters and daughters. Generally there was low knowledge despite a high level of satisfaction regarding the information transmitted by the geneticist. Family support and the knowledge of principal cases about the transmission of BRCA1/2 mutations in the family were playing a positive role and affected the testing decision by first-degree relatives. Difficulties in informing relatives were due to poor understanding of the information by principal cases including fear, and avoidance among close relatives. A major concern in genetic counseling should be to ensure complete information, patient understand this information, and ready to accept the test result before deciding to undergo the test [38].

Less research has been done to evaluate screening procedure after the genetic testing for colon cancer, although colonoscopy is important in colon cancer prevention. Colonoscopy can find pre-malignant polyps and then remove before the cancer becomes life threatening. Available data indicate that at least three quarters of the unaffected carriers undergo recommended bowel screening [39]. Although a negative test indicates an average risk, some do not feel confident in the test results to change their screening practices. On the other hand, some individuals with a negative test may even refrain from normal screening recommendations for the general population. In one study differences in the health professionals communication with patients was found. This may explain the difference in results from one place to another. Physician's training in communication may change patient's perceptions and, in return, their behavior and actions after test result [40]. In another study it was found that genetic counseling and testing increases overall patient adherence with recommended colon screening, especially for those with positive genetic test results. However, patients with negative results may receive false reassurance

about cancer risks and fail to follow recommended screening.

A study was done to explore distress and health beliefs before and after comprehensive counseling in families at risk for hereditary non-polyposis colorectal cancer (HNPCC). It was seen that distress and worries declined after counseling. Author also noted a greater ability to cope with a positive gene test after counseling. Changes after counseling were more found in persons at risk, as compared to patients with cancer. The decrease in distress was due to an increase in self-confidence. One-third reported better communication within the family after counseling. A small percentage experienced increased worry and physical symptoms after counseling. Overall, the subjects demonstrated less stress and less perceived cancer threat as well as enhanced beliefs regarding personal control over cancer, suggesting an overall benefit from comprehensive counseling [41].

In one study individuals were assessed for sharing their test results for a BRCA1 gene mutation. They most likely communicated results to family members, followed by co-workers, and insurers. High rates of disclosure to family members should promote awareness of hereditary cancer risk [42]. One study was done to investigate the impact of BRCA1 and BRCA2 testing on women previously diagnosed with breast or ovarian cancer. The testing was not anxiety provoking. The benefit of positive test result was seen as an end to uncertainty, whereas the negative impact was difficulties in disclosing information to dear ones and increased anxiety about cancer risks. Women receiving an inconclusive test result reported a range of emotional reactions. There was evidence that some women misunderstood the meaning of this result, interpreting it as definitive confirmation that a cancer predisposing mutation was not present within the family. It was further concluded by this study that women with cancer who participate in BRCA1 and BRCA2 testing need to receive clear information about the meaning and implications of the different types of test results [43].

## ETHICAL AND SOCIAL CONSIDERATIONS

Any ethical analysis must always balance the potential benefits with the possible harms of undergoing testing. Genetic testing for cancer susceptibility may become widely available in the future, and has important ethical and management implications [44]. Despite the benefits, there are several sources of harms, beyond the psychological stress at the individual and family levels. These ethical and social considerations include breaches of privacy and genetic as well as racial discrimination based on differences in the frequency of risk. One of the primary sources of harm to patients is inadequate protection of privacy and potential discrimination after disclosure of genetic information to third parties such as insurance companies and employers [45]. Nearly two thirds of Americans would refuse a genetic test if employers or health insurers could access the results. This is because they did not want to harm their job [46].

Approximately 15% of Americans who are at risk of inheriting a condition reported that they had been asked questions about genetic diseases on job applications; 13% reported that they or a family member had been fired or denied a job because of a genetic condition in the family. Also, 22% of those with a known genetic condition reported that they had been refused insurance coverage; even if asymptomatic [47]. Privacy laws must provide assurance that genetic testing will not be used to discriminate against them. Once privacy has been breached, patients must depend on anti-discrimination legislation to protect them from possible abuses. Failure to address privacy concerns will seriously undermine ability to integrate genetic testing into cancer prevention and treatment programs. Certain racial/ethnic groups are more predisposed than others. Once a

particular group is identified as having a higher prevalence of risk, there are increased concerns about discrimination and stigmatization against these individuals and communities [48]. Recruitment of family members for genetic testing raises ethical concerns due to the tension between protecting participant's privacy and promoting research quality, and guidelines for these activities are not well established. Recruitment of family members should be viewed as part of the research protocol and should require appropriate informed consent of the already-enrolled participant. Investigators should inform prospective participants why they are being contacted, how information about them was obtained, and what will happen to that information if they decide not to participate. The recruitment process should also be sensitive to the fact that some individuals from families at increased genetic risk will have no prior knowledge of their risk status [49]. Freeze preservation and prolonged storage of living cells and tissue fragments have been met with increasing interest in medicine during the recent years, for diagnostic, therapeutic as well as research purposes. At present such techniques are used in reproductive medicine, with storage of human embryos after in vitro fertilization. In addition, cells are increasingly used for other therapeutic purposes, from haemopoietic stem cells to tissue fragments from skin and joint cartilage. Large biobanks of living, frozen cells are now being established in several countries. Issues arising from the collection, storage, and use of Human biological materials (HBMs) in research are comprehensive covered by Meslin and Quaid in their review article [50]. Biobanks raise many ethical concerns, to which authorities are responding by introducing specific regulations. Genomics research, which thrives on the sharing of samples and information, is affected by two prominent ethical questions: do ethical principles prevent or promote the sharing of stored biological resources? How does the advent of large-scale biobanking alter the way in which ethical issues are addressed? [51]. However in one study it was found that research participants authorize to use of their samples for important research to proceed [52].

## LIMITATIONS

As our understanding of cancer genetics increases, demand for trained medical geneticists will increase. As genetic testing becomes more useful in directing clinical treatment for complex conditions such as cancer, the appropriate content of genetic counseling is likely to change. However, it will remain essential that genetic counselors, or physicians, are able to communicate complex information to patients related to the meaning of test results, the implications for treatment choices and the social risks that are associated with testing. Despite the growing need for genetics services, there are insufficient numbers of trained medical geneticists [50]. Therefore, primary care physicians, oncologists and other non-geneticists must have a greater role in providing genetic services. Unfortunately, however, most physicians have little formal training and limited knowledge of clinical genetics. In a recent survey, fewer than 30% of physicians and only 50% of oncologists felt qualified to provide genetic counseling. In another study of general practitioner's attitudes towards genetic testing including breast cancer, 50% reported counseling patients about genetic testing in the last year, whereas only 21% felt sufficiently prepared to perform this task [51].

Time constraints, management problems and inadequate education of those providing the care are a few of the many problems. Although recent guidelines emphasize that genetic testing should only take place in the presence of pre- and post-test counseling, but in many situations this was not possible due to resource constraints [3]. Despite these inhibitory issues, rates of referral to genetic specialists are low. In a national review of cases in the United Kingdom, fewer than half

**Table: Genetic cancer syndrome, genes detected and possible cancers involved.**

| Genetic cancer syndrome | Genes present | Cancer types involved |
|---|---|---|
| Hereditary breast and ovarian cancer | BRCA1, BRCA2 | Breast cancer, ovarian cancer |
| Cowden syndrome | PTEN | Breast cancer, thyroid cancer, endometrial cancer |
| Familial adenomatous polyposis | APC | Gastrointestinal cancer, Papillary thyroid cancer |
| Hereditary non-polyposis colorectal cancer | MSH2, MSH6, MLH1, PMS1, PMS2 | Colorectal and endometrial cancer |
| Hereditary papillary renal carcinoma | MET | Papillary renal cell carcinoma |
| Hereditary diffuse gastric cancer | CDH1 | Diffuse adenocarcinoma of gastric wall |
| Juvenile polyposis coli | MADH4 | Gastrointestinal malignancies |
| Li-Fraumeni brain | TP53 | Breast cancer, soft tissue sarcoma, adrenocortical tumor, leukemia |
| Multiple endocrine neoplasia type 1 | MEN1 | Pancreatic islet cell tumor, anterior pituitary tumors |
| Multiple endocrine neoplasia type 2 | MEN2 | Medullary thyroid carcinoma, pheochromocytoma, mucosal neuroma |
| Nevoid basal cell carcinoma | PTCH | Basal cell carcinoma |
| Neurofibromatosis type 1 | NF1 | Neurofibroma, astrocytoma, melanoma, rhabdomyosarcoma, chronic myeloid leukemia |
| Neurofibromatosis type 2 | NF2 | Bilateral vestibular schwannoma, meningioma, spinal tumor, skin tumor |
| Peutz-jeghers | STK11 | Gastrointestinal carcinoma, breast cancer, testicular cancer, gynaecological cancers |
| Pheochromocytoma | SDHB, SDHC, SDHD | Pheochromocytomas, glomus tumor |
| Retinoblastoma | RB | Pediatric retinal tumors |
| Tuberous sclerosis complex | TSC1, TSC2 | Multiple hamartomas, renal cell carcinoma, astrocytoma |
| Von Hipple Lindau | VHL | Renal cell carcinoma, retinal and central nervous system, hemangioblastoma, pheochromocytoma |

of patients with known high risks of genetic disorders were referred to medical geneticists [50]. In a similar study in the United States, only 7% of patients at a heightened risk of developing cancer based on family history were referred by oncologists for genetic consultation. There is some evidence, however, that rates of referral to cancer genetics services are increasing in some countries [52]. Clearly, further efforts to educate and support health care providers will be essential to realize potential future benefits of genetic research in reducing morbidity and mortality.

## FUTURE CONSIDERATIONS

With improvement in technology common genetic variants that predispose to cancer by promoting the carcinogenic affects of the causes of cancer or by increasing risk behaviors will be highlighted. For example, genetic variants that alter estrogen metabolism might influence harm from the use of hormone replacement therapy and, therefore influence cancer risk [53]. Furthermore, there is emerging evidence that genetic variation in neurotransmitter receptors, reuptake proteins, and metabolizing enzymes might contribute to the tendency to cigarette smoking and obesity, two of the main causes of cancer mortality which can be prevented [54,55]. As we progress in genetics and cancer risk behaviors we could form more effective and individualized cancer prevention strategies; like diet, exercise, pharmacological interventions and frequency of screening can be tailored to each individual based on their genotype.

Despite the potential medical and psychosocial benefits of genetic testing for cancer susceptibility, the widespread application of this technology in practice faces several barriers. Concerns about privacy and genetic discrimination, particularly with

respect to affordable health insurance, remain a deterrent for both patients and providers. The communication of cancer genetics research that identifies certain sub-populations must also be addressed with care, lest this information lead to sub-optimal care or increase the risk of discrimination for members of identified communities. Further guidelines for cancer susceptibility testing, as well as better education, are needed [56]. Finally, as the use of genetic testing for cancer and related behaviors increases, the plan for population based genetic screening will have to be evaluated [57]. At present, genetic testing for cancer have not been proposed for population screening. We have to ensure its cost effectiveness and availability of screening and preventive interventions, and adequate safeguards to ensure privacy [57].

## REFERENCES


1. Tischkowitz M, Rosser E. Inherited cancer in children: practical/ethical problems and challenges. *Eur J Cancer* 2004; 40(16): 2459-70.
2. Figer A, Kaplan A, Geva R, Flex D, Yaron M, Levy T, et al. Mutational analysis of the hMSH6 gene in familial and early-onset colorectal and endometrial cancer in Israeli patients. *Genet Test* 2002; 6(4): 323-6.
3. Rosenthal MS, Pierce HH. Inherited medullary thyroid cancer and the duty to warn: revisiting Pate v. Threlkel in light of HIPAA. *Thyroid* 2005; 15(2): 140-5.
4. Isaacs CJD, Peshkin BN, Lerman C. Evaluation and management of womenwith a strong family history of breast cancer. In: Harris JR, Lippman ME, Morrow M, Osborne CK. *Diseases of the Breast*. Philadelphia: Lippincott-Williams & Wilkins; 2000. p. 237-354.
5. American Society of Clinical Oncology. American Society of Clinical Oncology policy statement update: genetic testing for cancer susceptibility. *J Clin Oncol* 2003; 21(12): 2397-406.
6. Bluman LG, Rimer BK, Regan Sterba K, Lancaster J, Clark S, Borstelmann N, et al. Attitudes, knowledge, risk perceptions and decision-making among women with breast and/or ovarian cancer considering testing for BRCA1 and BRCA2 and their spouses. *Psychooncology* 2003; 12(5): 410-27.
7. Tambor ES, Rimer BK, Strigo TS. Genetic testing for breast cancer susceptibility: awareness and interest among women in the general population. *Am J Med Genet* 1997; 68: 43-9.
8. Berth H, Balck F, Dinkel A. Attitudes toward genetic testing in patients at risk for HNPCC/FAP and the German population. *Genet Test* 2002; 6: 273-80.
9. Halbert CH. Decisions and outcomes of genetic testing for inherited breast cancer risk. *Ann Oncol*. 2004; 15(1): I35-9.
10. Hartenbach EM, Becker JM, Grosen EA, Bailey HH, Petereit DG, Laxova R, et al. Progress of a Comprehensive Familial Cancer Genetic Counseling Program in the Era of BRCA1 and BRCA2. *Genet Test* 2002; 6(2): 75-8.
11. Eberl MM, Sunga AY, Farrell CD, Mahoney MC. Patients with a family history of cancer: identification and management. *J Am Board Fam Pract* 2005; 18(3): 211-7.
12. Kudadjie-Gyamfi E, Consedine N, Magai C, Gillespie M, Pierre-Louis J. Breast self-examination practices among women from six ethnic groups and the influence of cancer worry. *Breast Cancer Res Treat* 2005; 92(1): 35-45.
13. Brandt R, Hartmann E, Ali Z, Tucci R, Gilman P. Motivations and concerns of women considering genetic testing for breast cancer: a comparison between affected and at-risk probands. *Genet Test* 2002; 6(3): 203-5.
14. Tinley ST, Houfek J, Watson P, Wenzel L, Clark MB, Coughlin S, Lynch HT. Screening adherence in BRCA1/2 families

is associated with primary physicians' behavior. *Am J Med Genet A* 2004; 125(1): 5-11.

15. Sweet KM, Bradley TL, Westman JA. Identification and referral of families at high risk for cancer susceptibility. *J Clin Oncol* 2002; 20: 528-37.
16. Davis C, Emerson JS, Husaini BA. Breast cancer screening among african american women: adherence to current recommendations. *J Health Care Poor Underserved* 2005; 16(2): 308-14.
17. Harper PR, Jones SK. Mathematical models for the early detection and treatment of colorectal cancer. *Health Care Manag Sci* 2005; 8(2): 101-9.
18. Armstrong K, Stopfer J, Calzone K, Fitzgerald G, Coyne J, Weber B. What does my doctor think? Preferences for knowing the doctor's opinion among women considering clinical testing for BRCA1/2 mutations. *Genet Test* 2002; 6(2): 115-8.
19. Honda K, Gorin SS. Modeling pathways to affective barriers on colorectal cancer screening among Japanese Americans. *J Behav Med* 2005; 28(2): 115-24.
20. Baty BJ, Kinney AY, Ellis SM. Developing culturally sensitive cancer genetics communication aids for African Americans. *Am J Med Genet A* 2003; 118(2): 146-55.
21. Skinner CS, Schildkraut JM, Berry D, Calingaert B, Marcom PK, Sugarman J, et al. Pre-counseling education materials for BRCA testing: does tailoring make a difference? *Genet Test* 2002; 6(2): 93-105.
22. Chattopadhyay SK, Ebrahim SH, Tao G, McKenna MT. Use of cervical cancer screening among insured women: the extent of missed opportunities. *Health Policy* 2005; 73(2): 194-201.
23. Markovic M, Kesic V, Topic L, Matejic B. Barriers to cervical cancer screening: A qualitative study with women in Serbia. *Soc Sci Med* 2005; (In press).
24. Howard K, Salkeld G, Irwig L, Adelstein BA. High participation rates are not necessary for cost-effective colorectal cancer screening. *J Med Screen* 2005; 12(2): 96-102.
25. Codori AM, Waldeck T, Petersen GM, Miglioretti D, Trimbath JD, Tillery MA. Genetic counseling outcomes: perceived risk and distress after counseling for hereditary colorectal cancer. *J Genet Couns* 2005; 14(2): 119-32.
26. Watson M, Kash KM, Homewood J, Ebbs S, Murday V, Eeles R. Does genetic counseling have any impact on management of breast cancer risk? *Genet Test* 2005; 9(2): 167-74.
27. Donelle L, Hoffman-Goetz L, Clarke JN. Portrayal of genetic risk for breast cancer in ethnic and non-ethnic newspapers. *Women Health* 2004; 40(4): 93-111.
28. Mosconi P, Leccese A. Genetic testing and breast cancer: the women's point of view. *Ann Oncol* 2004; (1): I40-42.
29. Balmana J, Sanz J, Bonfill X, Casado A, Rue M, Gich I, et al. Genetic counseling program in familial breast cancer: analysis of its effectiveness, cost and cost-effectiveness ratio. *Int J Cancer* 2004; 112(4): 647-52.
30. Meiser B, Butow P, Friedlander M, Barratt A, Schnieden V, Watson M, et al. Psychological impact of genetic testing in women from high-risk breast cancer families. *Eur J Cancer* 2002; 38: 2025-31.
31. Schwartz MD, Peshkin BN, Hughes C, Main D, Isaacs C, Lerman C. Impact of BRCA1/BRCA2 mutation testing on psychologic distress in a clinic-based sample. *J Clin Oncol* 2002; 20: 514-20.
32. Lerman C, Hughes C, Lemon SJ, Main D, Snyder C, Durham C, et al. What you don't know can hurt you: adverse psychologic effects in members of BRCA1-linked and BRCA2-linked families who decline genetic testing. *J Clin Oncol* 1998; 16: 1650-4.

33. Dorval M, Patenaude AF, Schneider KA, Kieffer SA, DiGianni L, Kalkbrenner KJ, et al. Anticipated versus actual emotional reactions to disclosure of results of genetic tests for cancer susceptibility: findings from p53 and BRCA1 testing programs. *J Clin Oncol* 2000; 18: 2135-42.

34. Loader S, Shields C, Levenkron JC, Fishel R, Rowley PT. Patient vs. physician as the target of educational outreach about screening for an inherited susceptibility to colorectal cancer. *Genet Test* 2002; 6(4): 281-90.

35. Peshkin BN, Schwartz MD, Isaacs C, Hughes C, Main D, Lerman C. Utilization of breast cancer screening in a clinically based sample of women after BRCA1/2 testing. *Cancer Epidemiol Biomarkers Prev* 2002; 11: 1115-8.

36. Rebbeck TR, Lynch HT, Neuhausen SL, Narod SA, Van't Veer L, Garber JE, et al. Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. *N Engl J Med* 2002; 346: 1616-22.

37. van Dijk S, Otten W, Zoeteweij MW, Timmermans DR, van Asperen CJ, Breuning MH, et al. Genetic counseling and the intention to undergo prophylactic mastectomy: effects of a breast cancer risk assessment. *Br J Cancer* 2003; 88: 1675-81.

38. Blandy C, Chabal F, Stoppa-Lyonnet D, Julian-Reynier C. Testing participation in BRCA1/2-positive families: initiator role of index cases. *Genet Test* 2003; 7(3): 225-33.

39. Johnson KA, Trimbath JD, Petersen GM, Griffin CA, Giardiello FM. Impact of genetic counseling and testing on colorectal cancer screening behavior. *Genet Test* 2002; 6: 303-6.

40. Michie S, Collins V, Halliday J, Marteau TM. Likelihood of attending bowel screening after a negative genetic test result: the possible influence of health professionals. *Genet Test* 2002; 6(4): 307-11.

41. Keller M, Jost R, Haunstetter CM, Kienle P, Knaebel HP, Gebert J, et al. Comprehensive genetic counseling for families at risk for HNPCC: impact on distress and perceptions. *Genet Test* 2002; 6(4): 291-302.

42. Smith KR, Zick CD, Mayer RN, Botkin JR. Voluntary disclosure of BRCA1 mutation test results. *Genet Test* 2002; 6(2): 89-92.

43. Hallowell N, Foster C, Ardern-Jones A, Eeles R, Murday V, Watson M. Genetic testing for women previously diagnosed with breast/ovarian cancer: examining the impact of BRCA1 and BRCA2 mutation searching. *Genet Test* 2002; 6(2): 79-87.

44. Hodgson SV, Morrison PJ, Irving M. Breast cancer genetics: unsolved questions and open perspectives in an expanding clinical practice. *Am J Med Genet C Semin Med Genet* 2004; 129(1): 56-64.

45. Lowrey KM. Legal and ethical issues in cancer genetics nursing. Semin Oncol Nurs 2004; 20(3): 203-8.

46. Goldman J. Protecting privacy to improve health care. *Health Aff* 1998; 17: 47-60.

47. Hudson KL, Rothenberg KH, Andrews LB, Khan MJE, Collins FS. Genetic discrimination and health insurance: an urgent need for reform. *Science* 1995; 270: 391-3.

48. Beskow LM, Botkin JR, Daly M, Juengst ET, Lehmann LS, Merz JF, Pentz R, Press NA, Ross LF, Sugarman J, Susswein LR, Terry SF, Austin MA, Burke W. Ethical issues in identifying and recruiting participants for familial genetic research. *Am J Med Genet A* 2004; 130(4): 424-31.

49. Lehmann LS, Weeks JC, Klar N, Garber JE. A population-based study of Ashkenazi Jewish women's attitudes toward genetic discrimination and BRCA1/2 testing. *Genet Med* 2002;4:346-52

50. Meslin EM, Quaid KA. Ethical issues in the collection, storage, and research use of

human biological materials. *J Lab Clin Med* 2004; 144(5): 229-34.

51. Cambon-Thomsen A. The social and ethical issues of post-genomic human biobanks. *Nat Rev Genet* 2004; 5(11): 866-73
52. Chen DT, Rosenstein DL, Muthappan P, Hilsenbeck SG, Miller FG, Emanuel EJ, et al. Research with stored biological samples: what do research participants want? *Arch Intern Med* 2005; 165(6): 652-5.
53. Harris R, Lane B, Harris H, Williamson P, Dodge J, Modell B, et al. National Confidential Enquiry into counseling for genetic disorders by non-geneticists: general recommendations and specific standards for improving care. *Br J Obst & Gynae* 1999; 106: 658-63.
54. Suchard MA, Yudkin P, Sinsheimer JS. Are general practitioners willing and able to provide genetic services for common diseases? *J Genet Couns* 1999; 8: 301-11.
55. Campbell H, Holloway S, Cetnarskyj R, Anderson E, Rush R, Fry A, et al. Referrals of women with a family history of breast cancer from primary care to cancer genetics services in South East Scotland. *Br J Cancer* 2003; 89: 1650-6.
56. Halman CA, Hankinson SE, Colditz GA, Hunter DJ, De Vivo I. A polymorphism in CYP17 and endometrial cancer risk. *Cancer Res* 2001; 61: 3955-60.
57. Lerman C, Berrettini W. Elucidating the role of genetic factors in smoking behavior and nicotine dependence. *Am J Med Genet* 2003; 118B: 48-54.
58. Rosmond R, Bouchard C, Bjorntorp P. 5-HT2A receptor gene promoter polymorphism in relation to abdominal obesity and cortisol. *Obestet Res* 2002; 10: 585-9.
59. Freedman AN, Wideroff L, Olson L, Davis W, Klabunde C, Srinath KP, et al. US physicians' attitudes toward genetic testing for cancer susceptibility. *Am J Med Genet* 2003; 120A: 63-71.
60. Khoury MJ, McCabe LL, McCabe ER. Population screening in the age of genomic medicine. *N Engl J Med* 2003; 348: 50-8.