



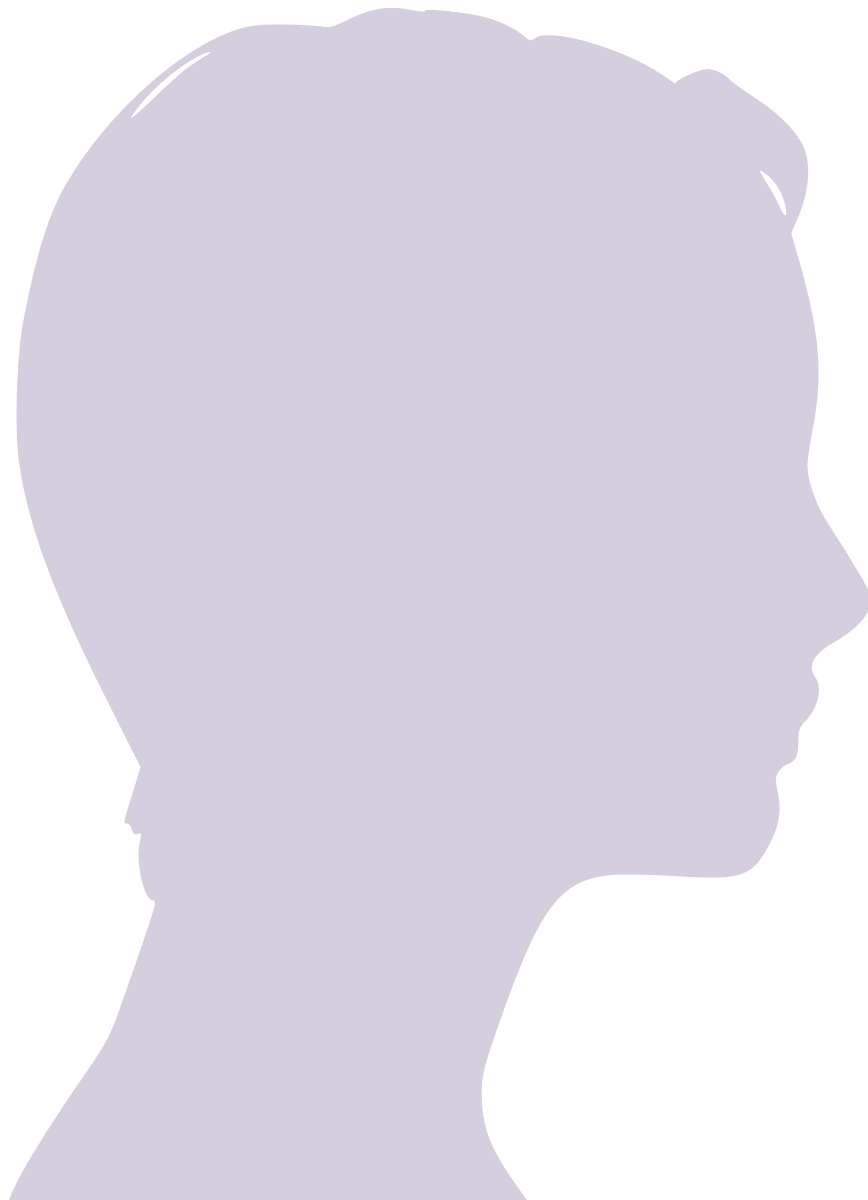
Genetic testing for *BRCA* mutations: country profile for Italy

2019

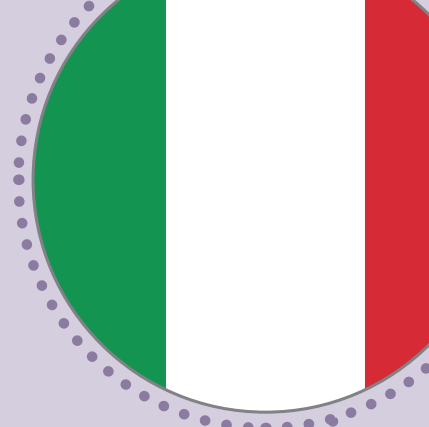
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Genetic testing for *BRCA* mutations: country profile for Italy



Key facts and figures on breast cancer and *BRCA* mutations in Italy

- Italy has the 7th highest incidence rate and the 22nd highest mortality rate of female breast cancer in Europe.¹
- In Italy, nearly 40% of women with a *BRCA* gene mutation will develop breast cancer during their lifetime.²



Introduction

Mutations in the *BRCA1* and *BRCA2* genes put women at significant risk of developing breast cancer. Based on international data, it is thought that most women have a 12.5% risk of developing breast cancer in their lifetime. This risk increases to 60–90% among women with a *BRCA1* mutation and 45–85% among women with a *BRCA2* mutation.³⁻⁵ Breast cancers related to *BRCA1* mutations are more likely to be triple-negative breast cancer, which is difficult to treat.⁶

It is important for women to know whether they carry a *BRCA* mutation. *BRCA*-mutation carriers who are asymptomatic can be supported to make an informed choice to reduce their risk of developing breast cancer through, for example, preventive surgery and, in some countries, chemoprevention. They can also reduce their chance of breast cancer mortality through regular monitoring which can pick up earlier cases of the disease. Knowing whether a woman with breast cancer carries a *BRCA* mutation can also help to inform decisions around treatment and surgery. In addition, identifying *BRCA*-mutation carriers allows for family members to be tested.⁷

Men can also benefit from knowing they carry a *BRCA* mutation. *BRCA* mutations can increase the risk of prostate and other cancers, so men with identified mutations can be closely monitored for early signs of the disease.⁸ In addition, men who carry a *BRCA* mutation can pass it on to their daughters.

However, many people at high risk of *BRCA*-related breast cancer cannot access a genetic test, while many who have been found to carry a *BRCA* mutation face gaps in accessing ongoing care and support.

This country profile presents an overview of the *BRCA* policy landscape in Italy with a view to guiding policy development. It considers gaps, challenges and advances in four areas policymakers should prioritise when looking to improve access to genetic testing and care for people with *BRCA* mutations:

1. Comprehensive, evidence-based policies for *BRCA* testing and the management of *BRCA*-related breast cancer
2. Greater public and patient understanding
3. Comprehensive care pathways
4. Improved awareness and knowledge among healthcare professionals.

Comprehensive, evidence-based policies for *BRCA* testing and the management of *BRCA*-related breast cancer

National plans to improve the prevention of hereditary breast cancer have been developed, but the extent to which they are being implemented at the regional level is unclear.

Inclusion of *BRCA* genetic testing in national plans for cancer and genetics

Italy's national prevention plan includes clear objectives to improve the prevention of hereditary breast cancer. The *Piano nazionale prevenzione 2014–2018* (National Prevention Plan 2014–2018) called on the Italian regions to implement standard pathways for the prevention of hereditary breast cancer by 2018 – including genetic testing for *BRCA* mutations.^{9,10} However, it is not clear whether all regions have achieved this.¹¹

Italy also has guidelines on medical genetics and a national plan to support people with rare diseases. Italy was the first country in Europe to develop a plan and framework for Public Health Genomics.⁹ Medical genetics are included in the *Piano nazionale della prevenzione 2010–2012* (National Prevention Plan 2010–2012) and in the 2013 *Linee di indirizzo sulla genomica in sanità pubblica* (Guidelines on genomics in healthcare) which described 18 priority actions in genomics.⁹

National registries to collect data on *BRCA* genetic testing

The Italian healthcare system does not have a national registry for *BRCA*-mutation carriers. This means there is a lack of comprehensive data on people taking *BRCA* genetic tests, although data are (or will soon be) available for some regions, such as Lombardia where a regional registry for genetic mutations is being established.^{12–14} There is also a lack of information on the centres that provide the test.¹³ A national registry could improve public scrutiny and support evidence-based policymaking and programming.

Policies to support cost-free access to BRCA genetic testing and personalised follow-up care

Most regions in Italy do not provide cost-free access to genetic testing through the public health system. BRCA testing is not included in the new LEA (Essential Levels of Assistance that the Italian healthcare system must provide) published by the Italian government in 2017.¹⁵ In addition, despite a national aspiration for free BRCA testing, access and eligibility criteria – including whether a co-payment is required – vary across regions.^{16 17} Women who have had breast cancer, however, are exempt from paying a fee.¹⁸

Legal protection of BRCA-mutation carriers

Italian legislation protects the rights of people who undergo genetic testing. The Garante per la protezione dei dati personali (Personal Data Protection Authority) specified in *Autorizzazione 2/2000* states that genetic testing data should be considered as very sensitive personal data. Additional pieces of legislation specify that, firstly, sensitive health data cannot be sent to health insurance companies, banks or relatives of the person undergoing the test, and secondly, only the Personal Data Protection Authority can authorise the possible uses of genetic data.¹⁹

Greater public and patient understanding of BRCA mutations and their association with breast cancer

Patient organisations are active in raising awareness of BRCA in Italy, but overall understanding among the population appears to be low.

Several patient organisations have contributed to help raise awareness of BRCA in Italy, and public understanding of BRCA testing seems to be increasing.¹¹ One of the most active organisations representing people who carry BRCA mutations is Salute Donna Onlus. The association is engaged in various awareness-raising and advocacy initiatives including organising a conference in Milan in 2001 and advocating in the Italian Senate to reduce inequalities in access to testing for those with BRCA mutations.^{17 20} It also leads a coalition of 24 organisations known as La Salute Bene da Difendere, Diritto da Promuovere (Health: a Good to Defend, a Right to be Promoted) through which stakeholders including patient organisations and policymakers collaborate with the

aim of promoting the rights of cancer patients. The coalition has an agreement in place with all political parties which comprises 15 key demands, including the exemption of payment for testing and surveillance of BRCA mutations.²¹

Overall, despite these efforts, the quality and comprehensiveness of public information is insufficient.¹¹ A 2015 survey found that awareness of BRCA is low and that most women with some BRCA knowledge learn about it from their gynaecologist.²² Evidence suggests that information on BRCA, even from healthcare providers, does not seem to be sufficient to support people in understanding whether or not they should undertake a BRCA test.¹¹

Comprehensive care pathways

A range of barriers limit access to comprehensive care for people with *BRCA* mutations – including a lack of national guidelines for many healthcare professionals, the uneven geographic spread of genetics centres and poor access to genetic counselling.

Evidence-based national eligibility criteria for *BRCA* testing

Italian guidelines on breast neoplasia include guidance for oncologists on the management of *BRCA* mutations.²³ The *Linee guida neoplasia della mammella* (Breast cancer guidelines), published by the Associazione Italiana di Oncologia Medica (AIOM; Italian Association of Medical Oncology) include testing criteria and recommendations for follow-up monitoring. It has been noted, however, that the AIOM guidelines focus only on recommendations for oncologists and fail to engage other healthcare professionals who support people with *BRCA* mutations.¹²

Despite this, some regions have made excellent progress in developing and implementing the pathways for the prevention of hereditary breast cancer described in the *Piano nazionale prevenzione 2014–2018*. In Emilia-Romagna, for example, a clear referral pathway is in place which describes the steps required to access a genetic test, the centres involved and the role of the healthcare professional at each stage.²⁴ Furthermore, La Salute Bene da Difendere, Diritto da Promuovere is working with policymakers in Lombardia and Sicily to develop *Percorsi Diagnostico e Terapeutici Assistenziali* (Assisted Diagnostic and Therapeutic Pathways) for those carrying *BRCA* mutations.^{14 25}



Equitable and timely access to genetic testing

The number of centres providing BRCA testing in Italy is growing. This is due to increasing demand for genetic tests and a reduction in the cost of providing them.¹¹ Testing is also available in private medical centres for people who do not want to wait for a test from a public facility.²⁶ However, the cost of a private test could be a barrier for some.

Despite this, there are significant geographic inequalities in access to genetic testing. Specialist centres are often too far from where people live, which has led to wide variation in access to BRCA testing.¹¹ For example, a 2015 study found that there were no hospital centres offering a complete pathway for BRCA testing in Molise, Valle d'Aosta and Basilicata.²⁷ Lombardia, however, had nine centres and Emilia-Romagna had four.²⁷

Furthermore, designation of specialist centres able to interpret BRCA test results is not always clear. Standardised criteria at the national level could help identify specialist centres that can offer the test.¹¹

Access to genetic counselling

The importance of genetic counselling is emphasised in national guidelines. The *Linee guida per le attività di genetica medica* (Guidelines on medical genetics) recommend genetic counselling before taking a BRCA genetic test.²⁸ Guidelines also recommend involving a multidisciplinary care team – including oncologists, psychologists and geneticists – in the counselling process.^{28 29} It has been noted by the women's health organisation Osservatorio Nazionale Sulla Salute Della donna, however, that these services are not always available.¹¹

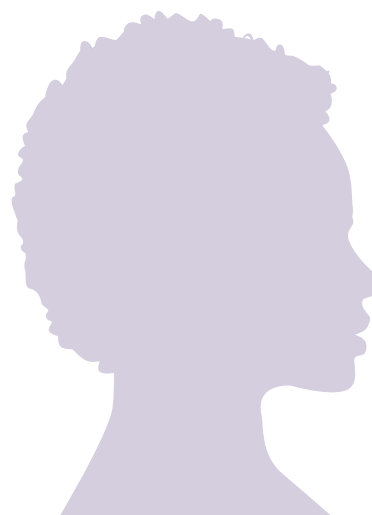
In addition, there can be significant variability in genetic counselling services provided across the country.^{9 29} In many cases, it seems that women do not undergo genetic counselling before a test, and that they often take the test without a clinically defined risk.^{9 29}

Genetic counselling centres are mainly available in research institutions such as university hospitals and research institutes.²⁹ There are, however, no clear guidelines on the skills and competences required by genetic counsellors.²⁶ This has limited the availability of training programmes to increase the number of professionals who can provide this service.²⁶

Follow-up care and support for BRCA-mutation carriers

Strategies to reduce the risk of developing breast cancer among BRCA-mutation carriers are outlined in national guidelines, but their implementation seems suboptimal. Recommended preventive strategies in the *Linee guida neoplasia della mammilla* include prophylactic surgery and chemoprevention.²³ Around 10% of women seem to opt for prophylactic surgery, a proportion lower than in France but higher than in Spain.³⁰

Intensive surveillance is also recommended in the guidelines, but cost may be a barrier to access. Financial barriers associated with the cost of intensive surveillance, for example through the use of magnetic resonance imaging (MRI) scans, could be an obstacle for the monitoring of some people with BRCA mutations.¹²



Improved awareness and knowledge among healthcare professionals

Low availability of appropriately trained healthcare professionals is limiting access to genetic testing.

Clinicians generally do not receive enough training on genetics¹¹ and do not seem to have the necessary knowledge to support those who need genetic testing.³¹ A survey among Italian clinicians found that 26.7% of those surveyed did not know that *BRCA* testing could predict higher risk of breast cancer, and only around 20% had received training on genetic testing during their graduate or postgraduate studies.³² In some cases, personal requests, rather than clinical need, seem to drive referrals for *BRCA* testing.³¹ This could contribute to unnecessary tests which place additional costs on the healthcare system.³¹ The number of trained geneticists also appears to be low,¹¹ which could contribute to delays for people referred for testing.

Conclusions and recommendations

The prevention of hereditary breast cancer is a stated priority of the Italian government. Despite this, implementation of comprehensive care pathways at the regional level seems patchy. Awareness among the public and healthcare professionals is low^{22 31} but seems to be increasing and is supported through the efforts of active national patient support organisations. Comprehensive clinical guidelines are not available so there is wide variation in how services are provided to people with *BRCA* mutations across their whole patient journey. Given these challenges, there are several priorities for consideration by policymakers who wish to improve the prevention of *BRCA*-related breast cancer.

Equitable and timely access to genetic counselling and *BRCA* testing for women at high risk of *BRCA*-related breast cancer must urgently improve. There is a geographic imbalance in the location of facilities able to test for *BRCA* mutations.¹¹ In addition, there is a lack of information about these facilities, leaving some people with significant barriers to access.¹³ Furthermore, genetic counselling which should accompany testing may not be available or delivered in a consistent way that supports the needs of *BRCA*-mutation carriers.^{9 11 29}

A national registry for *BRCA*-mutation carriers is needed, to support evidence-based policymaking and programming. Available information on those who receive a test and their results is fragmented.^{12 13} In addition, data are often unavailable on the centres that provide *BRCA* testing.^{11 13}

Greater efforts are needed to improve the *BRCA*-related knowledge of many healthcare professionals. The level of *BRCA* knowledge among healthcare professionals is inadequate to support people to access testing. For example, GPs often do not refer high-risk individuals to *BRCA* testing,^{12 13} and personal requests may sometimes override clinical need in driving referrals.³¹

The cost of testing and ongoing management of asymptomatic *BRCA*-mutation carriers presents real and significant financial barriers for some people with *BRCA* mutations in Italy. It is not just the cost of the test that is problematic in some regions, but also the cost of ongoing care for women who have been identified as mutation carriers. The cost of regular MRI scans, for example, can be high and may therefore prevent women from accessing these services.^{12 13 16}

References

1. European Cancer Information System. 2018. Estimated of cancer incidence and mortality in 2018, for all countries. Available from: [https://ecis.jrc.ec.europa.eu/explorer.php?%0-0%1-All%4-2%3-29%6-0,14%5-2008,2008%7-8%2-All%CEstByCountry%\\$X0_8-3%\\$X0_19-AE28E%\\$X0_20-No%CEstRelative%\\$X1_8-3%\\$X1_9-AE28E%\\$X1_19-AE28E%CEstByCountryTable%\\$X2_19-AE28E](https://ecis.jrc.ec.europa.eu/explorer.php?%0-0%1-All%4-2%3-29%6-0,14%5-2008,2008%7-8%2-All%CEstByCountry%$X0_8-3%$X0_19-AE28E%$X0_20-No%CEstRelative%$X1_8-3%$X1_9-AE28E%$X1_19-AE28E%CEstByCountryTable%$X2_19-AE28E) [Accessed 26/11/18]
2. Toss A, Grandi G, Cagnacci A, et al. 2017. The impact of reproductive life on breast cancer risk in women with family history or BRCA mutation. *Oncotarget* 8(6): 9144-54
3. National Cancer Institute. 2017. BRCA1 and BRCA2: Cancer Risk and Genetic Testing. Available from: <https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet> [Accessed 08/04/19]
4. Ovarian Cancer Action. 2017. *Acting on BRCA: Breaking down barriers to save lives*. London: Ovarian Cancer Action
5. The Royal Marsden. 2016. *A beginner's guide to BRCA1 and BRCA2*. London: The Royal Marsden NHS Foundation Trust
6. Bayraktar S, Gutierrez-Barrera AM, Liu D, et al. 2011. Outcome of triple-negative breast cancer in patients with or without deleterious BRCA mutations. *Breast Cancer Research and Treatment* 120(1): 145
7. McCarthy AM, Armstrong K. 2014. The Role of Testing for BRCA1 and BRCA2 Mutations in Cancer Prevention. *JAMA Internal Medicine* 174(7): 1023-24
8. Cavanagh H, Rogers KMA. 2015. The role of BRCA1 and BRCA2 mutations in prostate, pancreatic and stomach cancers. *Hereditary Cancer in Clinical Practice* 13(1): 16-16
9. Boccia S, Federici A, Colotto M, et al. 2014. Le policy di genomica in sanità pubblica in Italia: le sfide nella implementazione delle linee guida nel sistema sanitario nazionale. *Epidemiologia e prevenzione* 38(6 Suppl 2): 29-34
10. Ministero della Salute. 2014. *Piano nazionale della prevenzione 2014-2018*. Roma, Italy: Ministero della Salute
11. Osservatorio nazionale sulla salute della donna (Onda). 2017. *Call to action per la prevenzione e cura del carcinoma ovarico e della mammella*. Milano, Italy: Onda
12. Bonanni B. 2018. Interview with Kirsten Budig and Rodolfo Catena at The Health Policy Partnership [Telephone]. 27/07/2018
13. Mancuso AM. 2018. Interview with Rodolfo Catena at The Health Policy Partnership [Telephone]. 02/08/2018
14. Mancuso AM. 2019. Personal communication by email: 06/03/2019
15. Presidente del Consiglio dei Ministri. 2017. *Definizione e aggiornamento dei livelli essenziali di assistenza, di cui all'articolo 1, comma 7, del decreto legislativo 30 dicembre 1992, n. 502*. Roma, Italy: Gazzetta Ufficiale
16. Alleanza Contro il Tumore Ovarico. Il test BRCA oggi in Italia. Available from: <http://www.actoonlus.it/domande-e-risposte-cosa-si-deve-sapere/test-brca-oggi-in-italia> [Accessed 5/10/2018]
17. Salute Donna Onlus. Mozioni al senato sul tumore al seno [online]. NEWSLETTER N 1/2017 – 17 FEBBRAIO 2017. Available from: http://www.salutedonnaonlus.it/media/1318/newsletter_n1_2017_feb2017.pdf [Accessed 13/06/2018]
18. Cervi E, Gualandri G, Strozzi L. 2016. Tumore, come ottenere l'esenzione totale dal pagamento del ticket. Available from: http://www.repubblica.it/oncologia/diritti/2016/03/20/news/tumore_esenzione_totale_dal_pagamento_del_ticket_come_ottenerla-135929902/ [Accessed 10/09/2018]
19. Tonutti S. 2016. *Dottorato di ricerca in diritto e nuove tecnologie*. Bologna, Italy: Alma Mater Studiorum-Università di Bologna
20. Salute Donna Onlus. Tumore ovarico e tumore alla mammella: come i test genetici BRCA1 e BRCA2 hanno rivoluzionato la storia dei tumori femminili. Available from: <http://www.salutedonnaonlus.it/it/chi-siamo/le-news-di-salute-donna/tumore-ovarico-e-tumore-alla-mammella-come-i-test-genetici-brca1-e-brca2-hanno-rivoluzionato-la-storia-dei-tumori-femminili> [Accessed 04/07/2018]
21. Salute Donna Onlus. n.d. *Accordo Di Legislatura 2018/2023 Fra Le Associazioni Pazienti La Commissione Tecnico-Scientifica L'intergruppo Parlamentare Nazionale Gli Intergruppi Regionali Aderenti Al Progetto "La Salute: Un Bene Da Difendere, Un Diritto Da Promuovere*. Rome: Salute Donna Onlus
22. Doxapharma, Alleanza contro il tumore ovarico (ACTO). 2015. *Carcinoma ovarico rischio genetico e test genetici. Ma cosa ne sappiamo?* Milano, Italy: ACTO Onlus
23. Associazione Italiana di Oncologia Medica. 2017. *Linee guida neoplasie della mammella*. Milano, Italy: AIOM
24. Fin M, Carola Finarelli A, Naldoni C, et al. 2013. *Familiarità per il tumore della mammella - Informazioni sul percorso di valutazione del rischio familiare o ereditario e su eventuali interventi di diagnosi e cura*. Anzola dell'Emilia: Servizio Sanitario Regionale Emilia-Romagna
25. Salute Donna Onlus. n.d. Lombardia in prima linea con l'intergruppo consiliare per la lotta contro il cancro. Available from: <http://www.salutedonnaonlus.it/it/chi-siamo/le-news-di-salute-donna/lombardia-in-prima-linea-con-l-intergruppo-consiliare-per-la-lotta-contro-il-cancro> [Accessed 06/03/19]
26. Boccia S, Simone B, Gualano MR, et al. 2012. La genomica in sanità pubblica - Sintesi delle evidenze e delle conoscenze disponibili sull'utilizzo della genomica ai fini della prevenzione. *Ital J Public Health* 9(1 Suppl 1):
27. Moriconi Tiziana. 2015. Rischio familiare per il tumore al seno: ecco dove rivolgersi. Available from: <https://la.repubblica.it/saluteseno/news/rischio-familiare-di-tumore-al-seno-e-alle-ovaie-ecco-dove-rivolgersi/4892/> [Accessed 27/06/2018]
28. Conferenza permanente per i rapporti tra lo Stato, le Regioni e le Province autonome di Trento e Bolzano. 2004. *Linee guida per le attività di genetica medica*. Roma, Italy: Gazzetta Ufficiale
29. Tavolo Associazione Italiana di Oncologia Medica (AIOM) - Società Italiana di Genetica Umana (SIGU) Tumori Ereditari (eds). 2014. *Consulenza genetica e test genetici in oncologia: aspetti critici e proposte di AIOM - SIGU*. Milan: AIOM, SIGU
30. Toss A. 2016. Consulenza Hub: criteri di eleggibilità, percorso di counseling e presa in carico. Modena, Italy: Convegno - La medicina di laboratorio nella prevenzione oncologica...ma non solo
31. Marzuillo C, De Vito C, Boccia S, et al. 2013. Knowledge, attitudes and behavior of physicians regarding predictive genetic tests for breast and colorectal cancer. *Preventive medicine* 57(5): 477-82

