The Health Policy Partnership

Genetic testing for *BRCA* mutations:

A POLICY PAPER

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Executive summary

Genetic mutations in the *BRCA1* and *BRCA2* genes put women at significant risk of developing breast cancer. 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.[1-3] Furthermore, approximately 3–6% of breast cancer cases are due to mutations of the *BRCA1* and *BRCA2* genes.[4-7]

Women, when provided support with genetic counselling, may benefit from knowing if they carry a *BRCA* mutation. Asymptomatic women with *BRCA* mutations can reduce their risk of breast cancer mortality by being regularly monitored, and can reduce their risk of developing the disease by taking up interventions including preventive surgery and/or chemoprevention.[8] Knowing the *BRCA* status of women with breast cancer, meanwhile, can help to inform decisions around treatment and surgery.[8] Identifying *BRCA*-mutation carriers also allows for cascade testing of family members who can then be supported in accessing risk-reducing interventions themselves.[8]

Men can also benefit from knowing their *BRCA* status. *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.[9] In addition, men who carry a *BRCA* mutation can pass it on to their daughters.

Many people at high risk of developing *BRCA*-related breast cancer, however, cannot access a genetic test and are therefore not supported to decide how to act to reduce their risk of developing cancer. Numerous challenges exist across Europe which limit access to *BRCA* genetic testing, including a lack of knowledge among healthcare professionals, restrictive eligibility criteria and gaps in awareness among the population.

In addition, the genetic testing that is available is not always provided in the most appropriate or effective way. Genetic tests should be of high quality and delivered in line with the most up-to-date, evidence-based guidelines. These tests should be delivered as part of a comprehensive, multidisciplinary approach which ensures those being tested have provided informed consent and have access to clinical geneticists and genetic counsellors, services that should be available within breast units or breast cancer services.[10] Unfortunately, however, many women being tested do not benefit from such services.

Furthermore, many women who carry *BRCA* mutations face gaps in accessing ongoing care and support. Even in countries with robust infrastructure to support *BRCA* mutation carriers, such as Germany and the UK, many women have unmet needs and face barriers in accessing testing and ongoing care.

What do we need to strengthen access to genetic testing and improve care for people with *BRCA* mutations?

This report summarises four priority areas where policy change is needed to ensure *BRCA*-mutation carriers are provided with the care and support that they need along their entire genetic testing journey. This includes the time period prior to testing, during the testing process and, if they are found to carry a mutation, during ongoing monitoring and follow-up:

- Comprehensive, evidence-based policies for *BRCA* testing and the management of *BRCA*-related breast cancer
- Greater understanding among the public, *BRCA*-mutation carriers and patients
- Comprehensive care pathways
- Improved awareness and knowledge among healthcare professionals, including primary care physicians.

About this document

This document was developed for policymakers across Europe, and examines the situation in seven countries (France, Germany, Ireland, Israel, Italy, Sweden and the United Kingdom). This includes identifying the gaps and barriers which stand in the way of people at high risk of developing *BRCA*-related breast cancer accessing genetic testing in each country, and understanding where possible opportunities exist for policy change.

We have used this analysis to identify a set of concrete policy recommendations that aim to improve access for people across Europe to information, testing and care for *BRCA*-related breast cancer.

The report was developed based on a pragmatic review of published and grey literature from the seven countries and from European-level literature. This was supplemented by semi-structured qualitative interviews with national and European-level thought-leaders, including health professionals, researchers and patient organisation representatives.

The report is divided into two parts:

Part 1

A European report outlining key areas where action from European and national policymakers is needed to improve access to genetic testing and associated services for those at high-risk of *BRCA*-related breast cancer.

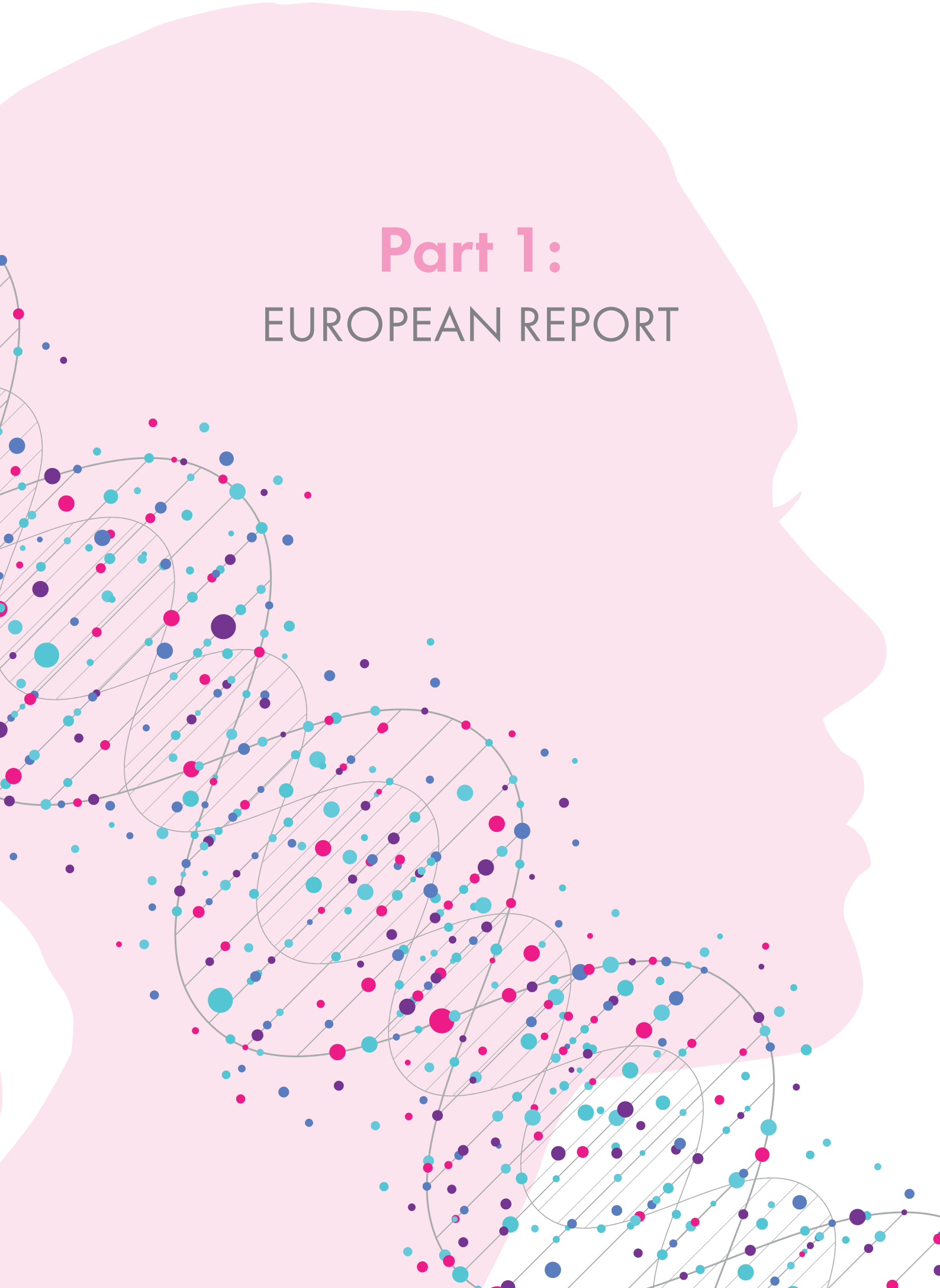
Part 2

Seven country profiles (for France, Germany, Ireland, Israel, Italy, Sweden and the United Kingdom) which provide more detailed information about challenges and opportunities around *BRCA* genetic testing and ongoing care in each country.

The following section sets out four areas that policymakers should focus on when looking to improve access to genetic testing and care for people with *BRCA* mutations. This includes the actions that need to be taken, the reasons they should be considered a priority and a snapshot of the current state-of-play in the selected countries.

Part 1:

EUROPEAN REPORT



1 Introduction: *BRCA* mutations and breast cancer

1.1 What are *BRCA* mutations?

Breast cancer is the most common cancer among women in Europe. Around 12.5% of women will develop breast cancer in their lifetime[1] and it is the second-highest cause of mortality for women among all cancers in Europe.[11] Estimates suggest that, in 2018 alone, more than half a million women in Europe were diagnosed with breast cancer and more than 130,000 died from the disease.[11]

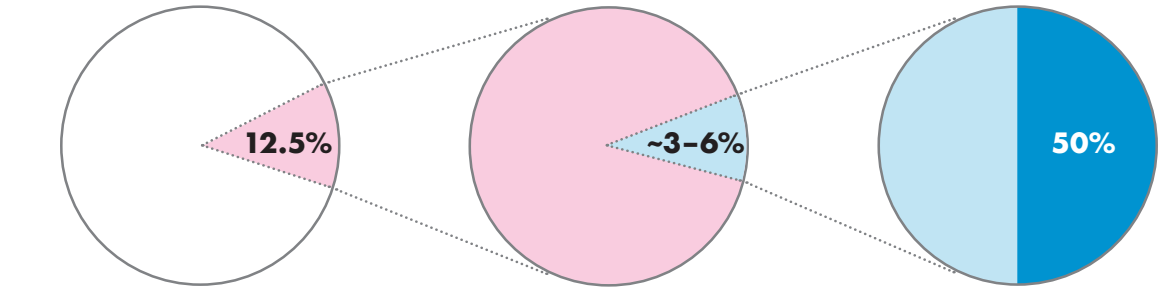
Table 1.
Estimates of breast cancer incidence and mortality per 100,000 women (2018)[11]

Country	Incidence	Mortality
France	166.6	35
Germany	150.4	36.8
Ireland	156.9	40
Italy	159.9	31.1
Sweden	160.1	27.9
UK	165.3	33.5
EU 28 average	144.9	32.9

Note: Comparable data for Israel are not available.

Genetic predisposition is responsible for up to 10% of breast cancers in Western countries.[12] Not all gene mutations which are associated with a higher risk of breast cancer have been identified, but two gene mutations, *BRCA1* and *BRCA2*, significantly contribute to the risk of developing breast cancer.

Figure 1. Epidemiology of *BRCA*-related breast cancer



12.5% of women in the general population have breast cancer[1]

~3–6% of all breast cancer cases are due to inherited mutations in *BRCA1* and *BRCA2*[4-7]

50% of cases are diagnosed and 50% go undiagnosed[13]

45–90% of women with a *BRCA* mutation will go on to develop breast cancer in their lifetime[1-3]

In Europe, approximately 3–6% of breast cancer cases are due to mutations of the *BRCA1* and *BRCA2* genes.[4-7] Observed variations between countries can partly be attributed to differences in genetic makeup. Populations that stem from a small number of individuals have a more homogenous gene pool, which explains the higher frequency of *BRCA* mutations found in some countries. This is known as the founder effect.[14] For example:

- In Israel, 9% of breast cancers among Ashkenazi Jewish women are due to inherited *BRCA* mutations – higher than the known rate among Israeli women from other ethnic backgrounds.[15] This is because 2.3% of Ashkenazi Jewish women carry one of three founder *BRCA* mutations which are known to be associated with a higher risk of developing breast cancer.[16]
- In Sweden, a country without a strong founder mutation, around 2% of breast cancer cases are estimated to be attributable to *BRCA* mutations.[17]

Women who carry *BRCA* mutations have a much higher risk of developing breast cancer than non-*BRCA*-mutation carriers. Between 60–90% of women with a *BRCA1* mutation and 45–85% of women with a *BRCA2* mutation will develop breast cancer during their lifetime,[1-3] compared with 12.5%[1] of women in the general population.

Furthermore, breast cancers related to *BRCA1* mutations have a higher chance of being triple-negative breast cancer, which is more difficult to treat.[18]

1.2 What are the benefits of genetic testing?

Genetic testing, which should be accompanied by genetic counselling, can identify *BRCA* mutations in women without breast cancer and allow them to make an informed choice about interventions to reduce their breast cancer risk. Predictive genetic testing for women without breast cancer means those identified as carriers can be closely monitored and/or they can choose risk-reducing strategies such as surgery or chemoprevention therapy.[8] Gaining this knowledge, however, while being empowering for some, may cause distress and anxiety among others. Furthermore, some women may simply prefer not to know if they carry a mutation.[8] Sensitivity in discussing genetic testing and the implications of the results, including the different risk-reducing options, must form an integral part of pre- and post-testing genetic counselling.[10]

Genetic testing of people already diagnosed with breast cancer can inform the appropriate management of their disease. Treatment for early *BRCA*-related breast cancer is currently the same as for other types of breast cancer. Surgical interventions, however, can be more aggressive as *BRCA* mutations are associated with a higher risk of contralateral breast cancer than other breast cancers, meaning bilateral mastectomy is more likely to be considered.[8] Recent advances are bringing new treatment options for *BRCA*-related breast cancer, however, and are currently being tested through clinical trials.[8]

Genetic testing can also enable the testing of a carrier's family members. Tracing and testing family members in this way is known as cascade testing, which should always be preceded by genetic counselling provided by an appropriately qualified professional. Cascade testing can be a cost-effective way of identifying those at higher risk of developing breast cancer, thereby offering an opportunity to prevent it.[19]

Early identification of breast cancer risk through genetic testing not only benefits individuals and their families but can also be cost-effective, reducing the need for future treatment.[8 19] It should be noted, however, that genetic testing should only be provided to those who are considered at high risk of developing *BRCA*-related breast cancer. Widening genetic testing to the population more broadly would increase both cost and the possibility of unnecessary fear and anxiety.[8]

Leaps in genomic medicine in recent decades promise to significantly advance screening and treatment for different types of cancer. Better understanding of cancer genetics has allowed us to identify a range of mutations linked to different cancers. This information can then be used to identify people at risk, implement preventive measures and devise personalised treatment plans for those diagnosed with cancer.[20] Recent advances in technology and increases in capacity in many countries mean that more people can access genetic testing than ever before,[20] and full panel tests which screen a larger number of genes could help identify new mutations.

As a result of these advances and potential possibilities to reduce costs to health systems, *BRCA* genetic testing is becoming more widely available. However, many people who may carry a *BRCA* mutation continue to lack access, either to counselling and testing or to necessary care and follow-up. For example, family history which is used to determine eligibility for *BRCA* genetic testing in many countries detects less than 50% of women with a *BRCA* mutation.[13] This means that more than half of all mutation carriers are currently unable to access genetic counselling from an appropriately trained professional, which could enable them to make informed decisions about testing and reducing their breast cancer risk.

It is therefore vital that policymakers gain a better understanding of the risks associated with *BRCA* mutations and the gaps in care that may exist, to ensure all people who are at high risk of *BRCA*-related breast cancer have access to the testing and care they need.

1.3 What are some of the challenges regarding *BRCA* genetic testing?

Across Europe, the demand for genetic testing is increasing,[21] [22] **yet the infrastructure to meet this demand is often not in place.** This jeopardises equitable and timely access to genetic testing for those at risk of developing *BRCA*-related breast cancer. There are several challenges:

- **An insufficient number of specialist staff, such as geneticists and genetic counsellors, and testing centres/equipment** causes bottlenecks and leads to long waiting times.[21-23] The quality and sensitivity of genetic testing can also be variable between countries and laboratories, leading to possible errors in how results are presented to those being tested.[24] [25]

- **Knowledge among non-genetic specialists such as GPs, gynaecologists and oncologists can be low** in some countries, presenting a barrier to providing accurate information to patients and making appropriate referrals. This is further complicated when non-genetic specialists are required to relay complex test results. These results may include difficult-to-interpret information regarding benign mutations and mutations for which the breast-cancer-related risk is as yet undetermined, known as variants of unknown significance (VUS).[25] [26] Misinterpreting test results could lead to a rise in unnecessary anxiety and, if the level of risk has been overestimated, the possibility of unnecessary interventions such as surgery.

- **A lack of data on *BRCA*-mutation carriers and the care they receive** hampers the ability of healthcare systems to plan and deliver services where and when they are needed.[4]

- **Eligibility criteria for *BRCA* genetic testing vary from country to country** – in some cases missing a significant proportion of people who may be carrying *BRCA* mutations.

- ***BRCA* genetic testing is often not incorporated into national (breast) cancer policies or strategies,** leading to a lack of strategic plans and fewer incentives to improve access to *BRCA* genetic testing for those at high risk of *BRCA*-related breast cancer.

This report analyses the reasons behind these and other challenges, and outlines some key policy priorities which should be in place to ensure that people who need to access genetic counselling and testing and those with *BRCA* mutations have access to the care and support they need.

2 *BRCA* genetic testing: what is most needed to improve the policy response?

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

What do we need?

- ✓ Include *BRCA* genetic testing and management of *BRCA*-mutation carriers in European and national plans and guidelines for cancer and genomics.
- ✓ Ensure EU and national health policies support access to appropriate genetic counselling, *BRCA* genetic testing and personalised follow-up care for those at risk of *BRCA*-related breast cancer, without imposing unaffordable costs on people.
- ✓ Strengthen existing collaboration between oncology and genetics at European and national level.
- ✓ Ensure *BRCA* genetic testing and care services are organised and delivered based on robust and locally relevant data which can also be used to measure and improve quality of care.
- ✓ Ensure *BRCA*-mutation carriers are protected through data protection and anti-discrimination legislation.

Why is this important?

- Access to *BRCA* genetic testing and care for *BRCA*-mutation carriers can be highly uneven within and between countries.
- Cost can act as a barrier to testing and to taking up preventive strategies such as monitoring and surgery in some countries.[27 28]
- Fears over the use of genetic data may inhibit some women accessing genetic testing.

How well are we doing?

There is currently no European framework for genetic testing that supports member countries in integrating genetic testing into cancer care, but efforts are underway aiming to raise awareness and address these gaps.[29] The European Joint Action on Cancer Control is developing guidance for genomics in cancer control and care.[30] The multi-stakeholder initiative Global Alliance for Genomics and Health set up the database *BRCA* Exchange to foster responsible use of information on *BRCA* for research,[31] and the International Quality Network for Pathology aims to improve quality for biomarker testing.[32] Furthermore, the recent call to action by the European Breast Cancer Council (EBCC) in its manifesto outlines priorities for genetic risk prediction testing in breast cancer.[10] *BRCA*-related breast cancer is also one of the priorities of the Advanced Breast Cancer Global Alliance.[33]

***BRCA* genetic testing is not always incorporated into national (breast) cancer or genetics policies or strategies.** Experts have highlighted that *BRCA* genetic testing is often not prioritised in national and pan-European policies.[29 34] Italy, however, has included genetic testing for *BRCA* mutations in its wider *Piano nazionale prevenzione 2014–2018* (National Prevention Plan 2014–2018), although the extent to which this plan has been implemented at the regional level is unclear.[35 36] Some countries, such as Ireland and France, include prevention of genetic cancers more broadly as a strategic priority.[23 37]

Across Europe, although some coordination and collaboration between geneticists, oncologists and other groups of health professionals is occurring, gaps remain. Experts suggest that there is no shared forum for pan-European professional societies in oncology and genetics.[29] This situation is mirrored at the national level in some countries.[38]

Great advances are being made in genomics, paving the way for improved access to personalised medicine. The UK, for example, is establishing the infrastructure to support greater access to genomic testing including through a national network of genomic laboratories and Genomic Medicine Centres which provide clinical services.[39] These are being established with the aim of embedding personalised medicine as part of routine clinical practice. Similar investments are being made in France,[40] Sweden[41] and Germany.[42] This could be of huge benefit to *BRCA*-mutation carriers as treatments for *BRCA*-related breast cancer become available in those countries.

In many European countries, comprehensive data on the incidence and prevalence of *BRCA* mutations are not routinely collected in national registries. As a result, frequency of *BRCA* mutations in the overall population and in women with breast cancer can often only be estimated,[43-45] hampering the development of an evidence-based policy response. In Germany, although data on *BRCA*-mutation carriers are collected, they are not routinely aggregated in a way that is accessible for policymakers.[46]

BRCA genetic testing is free of charge in most countries included in our analysis. However, in Italy and Germany a co-payment may be required.[27] In addition, in Germany, people with private insurance need to request a *BRCA* genetic test from their insurer and are not guaranteed to receive approval.[28]

Legislation to protect people from discrimination based on their genetic data exists in all countries, but differs in scope and requires updating in some cases to account for novel developments in genetic testing. The European Convention on Human Rights and Biomedicine protects individuals in European countries from discrimination based on genetic test results, and makes the individual's consent and right to be informed about genetic test results mandatory.[47] Among the countries included in our analysis, however, this convention has only been signed by Italy, France and Sweden. Most countries also have national anti-discrimination legislation in place. Israel was one of the first countries globally to enact legislation to protect against misuse of genetic information.[48 49] Other countries need to update their legislation. In the UK, for example, anti-discrimination legislation has not yet been extended to protect people with a known genetic mutation.[50]

2.2 Greater understanding among the public, *BRCA*-mutation carriers and patients

What do we need?

- Improve public awareness of *BRCA* mutations and their implications.
- Develop and ensure access to accurate and tailored information for people living with *BRCA* mutations, including the importance of providing informed consent, how to inform their families about their *BRCA* status, and what their risks and preventive options are. This should include information to support family members of *BRCA*-mutation carriers to access genetic testing following genetic counselling.

Why is this important?

- A lack of knowledge about *BRCA* mutations and their implications can create misconceptions and present a barrier to seeking genetic testing among those at high risk of *BRCA*-related breast cancer.[51] Furthermore, genetic testing among those who are not at high risk may create unnecessary anxiety.[8]
- Appropriate information can support and empower people and minimise their potential distress and fear.[52 53]

How well are we doing?

In many European countries, the demand for *BRCA* genetic testing has notably increased in recent years, suggesting that overall awareness has risen – although significant gaps have been noted for most countries. In France, for example, the number of genetic consultations increased more than sixfold from 2003 to 2017.[21] Experts suggest, however, that more needs to be done to improve awareness.[28 46 54 55] Furthermore, gaps in awareness do not seem to be evenly spread throughout populations, with differences by ethnic group being noted in Israel and the UK.[56-59]

European organisations engage in communication and advocacy activities to increase overall awareness and knowledge about genomic medicine, including genetic testing for *BRCA* mutations. Experts have noted low levels of health literacy for *BRCA* genetic testing, which can lead to fears and misconceptions.[29 34] The European Cancer Patient Coalition is one organisation working to address this by, for example, launching the advocacy campaign 'cracking the cancer code' to raise awareness about personalised medicine.[60]

The availability of patient and advocacy organisations for *BRCA*-mutation carriers in Europe varies, leading to gaps in the availability of locally appropriate support and information. Most of the countries we studied have active *BRCA*-related support and/or advocacy organisations.[61-65] In Ireland and Sweden, however, there are no national organisations devoted to supporting *BRCA*-mutation carriers, and in Sweden, the availability of locally tailored information to support people considering testing is limited.[55]

2.3 Comprehensive care pathways

What do we need?

- Develop national guidelines and well-defined care pathways to support healthcare professionals to provide consistent and high-quality care for people throughout the *BRCA* genetic testing journey as part of well-coordinated multidisciplinary teams. This should include the collection of informed consent, genetic counselling and medical supervision for all tests which could have high-risk implications.[10]
- Encourage greater collaboration between European member states to share best practice and resources on optimal care pathways for *BRCA* genetic testing.
- Ensure equitable, timely and affordable access to *BRCA* genetic counselling and testing for all those at high risk of *BRCA*-related breast cancer, through evidence-based and appropriate eligibility criteria. These services should be delivered in settings which provide access to specialists in clinical cancer genetics and genetic counselling prior to testing.
- Formally recognise genetic counselling within the medical profession and provide adequate resources to meet the demand for training and staffing.
- Ensure robust regulation of private-sector *BRCA* test providers in countries where they are active.

Why is this important?

- Care that is coordinated and delivered by multidisciplinary teams which include clinical geneticists and genetic counsellors can ensure people's physical and psychosocial needs are met along their whole genetic testing journey. Pan-European standards and care pathways for *BRCA*-mutation carriers could reduce variation between countries and support access to high-quality services.
- Strict, family-history-based testing criteria for *BRCA* mutations mean many people at high-risk of *BRCA*-related breast cancer are denied access to testing. By identifying women with *BRCA* mutations before they have cancer, we are more likely to be able to prevent the development of the disease.[8]
- Genetic counselling is an indispensable component of *BRCA* genetic testing as it ensures people are supported and can make informed decisions about their care and how to communicate their results to family members who may also be affected.
- As demand for private and direct-to-consumer (DTC) testing is growing in some countries,[10 66] adequate regulation is crucial to ensure providers adhere to quality and care standards.

Equitable and timely access to genetic testing

There is marked variation in *BRCA* services between European countries. Experts have highlighted significant differences among European countries in terms of *BRCA* testing and care offered.[25 29]

In some countries, a lack of comprehensive guidelines has led to variability in how services are organised and delivered. In Italy, for example, national guidelines are available only for oncologists managing breast cancer patients, while guidelines for other healthcare professionals are limited.[67] France, Germany and the UK, on the other hand, have well-defined guidelines which include eligibility criteria for testing, referral pathways and detailed guidance on the care which should be provided to women at high risk of *BRCA*-related breast cancer, at all stages of the genetic testing process.[68 69]

There are no European guidelines on *BRCA* genetic testing, and eligibility criteria vary across Europe. The European Society for Medical Oncology (ESMO) recommends countries use the eligibility criteria established by the UK's National Institute for Health and Care Excellence or the US National Comprehensive Cancer Network.[70] Most countries base their eligibility criteria on these recommendations, but some have stricter criteria, creating considerable variation in eligibility for genetic testing. For example, Ireland does not make genetic testing available to all asymptomatic women at high risk of familial breast cancer.[71] Germany and Italy have stricter cut-off points for the age of family members at the onset of cancer than Sweden and the UK.[68 69 72 73]

Eligibility criteria for genetic testing in many countries fails to include a significant proportion of *BRCA*-mutation carriers. Studies have shown that more than half of mutation carriers do not have a family history of breast and/or ovarian cancer before they are diagnosed with breast cancer themselves. This means that a large proportion of at-risk *BRCA*-mutation carriers do not fulfil current national guideline thresholds for genetic testing.[74-77] A study in one Swedish region found that only 18% of breast cancer patients who were identified as *BRCA*-mutation carriers had previously been tested for *BRCA* mutations.[78]

In most countries studied, availability of testing centres varies across regions, leading to inequalities in access. Sweden and Ireland have established specialist centres, but their clustered geographic distribution could lead to unequal access to the services provided, particularly in remote areas.[38] Unequal access has also been noted in Italy,[22] France,[21] Germany,[28 79] Israel and the UK.[80]

Inequalities in access based on ethnic or religious background have also been identified in some countries. In the UK, for example, factors such as lower awareness of testing, language difficulties, stigma of breast cancer and cultural beliefs act as a barrier to testing among people from ethnic minorities.[58 59] Similarly, uptake of genetic testing in Israel has traditionally been lower among ultra-Orthodox Jewish women compared to more secular women, but this now seems to be improving.[54 81 82]

Capacity constraints mean long waiting times for referrals and genetic tests are common, acting as a barrier to timely access. In Israel and Ireland, for example, waiting times can be up to a year.[71 83] In France, although waiting times are reducing, women still wait on average 12 weeks for a genetic consultation and 22 weeks for a genetic test.[21]

DTC testing is becoming increasingly popular but often lacks regulatory oversight.[10] Those who access a *BRCA* genetic test through DTC suppliers – who may not adequately interpret what can be a complex set of results, or provide access to genetic counselling – leave themselves open to the possibility of unwarranted distress and anxiety.[10] This is the case in Ireland, where people increasingly use private genetic testing[84 85] but concerns have been raised around the lack of regulation.[88]

Access to genetic counselling

While the importance of genetic counselling is acknowledged across Europe, it is not always a mandatory requirement when undergoing genetic testing.[10] In Germany, the UK, Israel and Sweden, genetic counselling is required by law as part of genetic testing.[16 68 69 87] In Ireland and France, genetic counselling is not mandatory, but is recommended and prioritised in national strategies.[37 88 89] In Italy, although genetic counselling is recommended as a part of wider multidisciplinary care, it seems that these services are not always available and many people do not have genetic counselling before a test.[22 35 90]

Furthermore, there are shortages in the genetics workforce in many European countries.[29 91] In proportion to their respective populations, the UK has the highest while Sweden and Ireland have among the lowest numbers of genetic counsellors and consultant geneticists in Europe, which results in bottlenecks in service provision and further delays people's ability to access testing.[17 23 92 93]

Standardisation, training requirements and formal recognition of genetic counsellors varies across Europe. The UK has pioneered the profession of the genetic counsellor, and has the highest number of genetic counsellors in Europe today.[91 92] The UK is also in the process of establishing genetic counselling as a statutory regulated profession, which will increase oversight and scrutiny of the profession. Many countries offer standardised training for genetic counselling, including master's courses which are available in Israel, the UK and France.[91] However, in countries such as Sweden, university-level courses are not available[91] and a lack of national standards, licensing and registration means practice varies between genetic centres.[38] Germany is unusual among the countries we studied in that genetic counselling can only be performed by physicians with appropriate training.[94]

The provision of psychosocial support both before and after genetic testing can be highly variable. It has been noted in the UK and Israel that many women receive either no counselling or inadequate support once they have received their test results.[2 54]

To meet the increasing demand for genetic counselling in light of sparse resources and the need to reach people in remote areas, novel forms of genetic counselling are being explored. Telemedicine and teleconsultation, when provided by appropriately trained healthcare professionals, could offer an effective alternative to face-to-face consultations[95] and have been trialled in countries including Sweden.[96]

Follow-up care and support for *BRCA*-mutation carriers

Despite the availability of European guidelines, some countries do not appear to have clearly defined responsibilities or protocols for follow-up care once a *BRCA* mutation is confirmed. This is the case in Ireland, for example, where little guidance is available and existing recommendations may not be implemented.[44] In Israel, where there are no national guidelines for those who have been identified with a *BRCA* mutation, support is offered through high-risk clinics but capacity constraints and a lack of awareness mean not all *BRCA*-mutation carriers can access them.[54] In Germany, *BRCA*-mutation carriers are monitored,[68] but risk-reducing surgery is not routinely reimbursed. Financial barriers in accessing intensive surveillance have also been noted in Italy.[67 97 98]

2.4 Improved awareness and knowledge among healthcare professionals

What do we need?

- ✓ Strengthen knowledge of *BRCA* mutations among healthcare professionals who are not genetics specialists, such as GPs, oncologists and gynaecologists. This includes being able to understand basic genetics and identifying when a woman is at high risk of *BRCA*-related breast cancer and eligible for referral to a specialist genetics centre.

Why is this important?

- Involving non-genetic-specialist healthcare professionals in the care pathway for genetic testing may provide an opportunity to ease the reliance on genetic specialists,[99] which is particularly important given the increasing pressure on healthcare budgets and the likely increase in demand for genetic testing.
- The introduction of panel tests offers the opportunity to identify more mutations associated with breast cancer. However, the interpretation of results is more difficult[100 101] and we need to make sure non-genetic healthcare professionals adequately interpret and communicate what are often complex results.[34] This would help to minimise anxiety and reduce the potential for unnecessary interventions such as surgery, which can in themselves carry risk.

How well are we doing?

Levels of genetic knowledge among non-genetic-specialist healthcare professionals, such as GPs and even oncologists, can be low in some countries, impacting on the level of appropriate referrals for testing.[34] In Ireland, for example, a survey among GPs found that 90% did not feel they had sufficient information about genetic testing to adequately advise and refer their cancer patients.[102] An Italian study found that 26.7% of healthcare professionals surveyed did not know about the implications of a *BRCA* mutation.[103] Similarly, experts in Germany[28 46] and Israel[54] suggested that GPs and gynaecologists do not have the knowledge needed to make adequate referrals and support people with *BRCA* mutations.

Furthermore, gaps in genetic knowledge among oncologists and breast surgeons can hamper their ability to appropriately interpret and communicate results to their patients. In the UK, a recent survey found that 71% of breast cancer specialists surveyed were unsure about the clinical implications of test results. This was compounded when there was no family history of breast cancer.[26] However, the UK, along with countries such as France and Germany, is delivering projects which aim to build genetic knowledge among healthcare professionals.[104-107]

Low understanding of preventive options for *BRCA*-related breast cancer among healthcare professionals can also hinder adequate follow-up care. A lack of structured follow-up care and information could contribute to women making decisions regarding risk-reduction which are not fully informed. For example, a European survey of GPs and breast surgeons found that only 27% of German GPs and 30% of French GPs thought prophylactic mastectomy should be an option for *BRCA*-mutation carriers, despite its proven role in reducing the risk of breast cancer among high-risk women. This is compared to 92% in the UK.[108]

Engaging these healthcare professionals in the genetic testing pathway and building their genetic knowledge can improve the care they provide for their patients. In Italy and Spain, a recent study showed that engaging trained oncologists in genetic counselling, when combined with genetic testing, led to high patient satisfaction and could reduce waiting times through more streamlined service provision.[99] Some countries such as France and Germany are already implementing this approach.[68 105]

3 Conclusion

Access to genetic testing and ongoing care for *BRCA*-mutation carriers varies widely, both within and between countries. While there are many examples of excellent practice across Europe, there are also significant gaps and unmet needs.

This report identifies a set of concrete recommendations in four key areas where policymakers looking to improve access, uptake and quality of *BRCA*-related services should focus. Prioritising efforts in these four areas has the potential to both prevent breast cancer and improve the quality of life of *BRCA*-mutation carriers.

Access to *BRCA* genetic counselling and testing and the prevention of *BRCA*-related breast cancer must be prioritised in cancer and genetics policies and strategies. This will require the availability of robust, up-to-date and locally relevant data on *BRCA*-mutation carriers and the infrastructure and workforce available to support them.

All people at high risk of *BRCA*-related breast cancer should have timely access to genetic counselling and testing and be supported throughout their genetic testing journey by a multidisciplinary team that meets their own, and their families', physical and psychosocial needs. Policymakers should ensure that geography, cost and ethnic background are not barriers to achieving this.

Efforts are urgently needed to ensure that people understand *BRCA* mutations and the potential risk of being a carrier. Awareness and understanding of *BRCA* mutations are highly variable, and this must be addressed.

Equally, knowledge gaps among non-genetic-specialist healthcare professionals, including primary care physicians, must be addressed. The healthcare professionals working with people considering testing and those interpreting and communicating results must be supported so that they can provide appropriate referrals, information and advice.

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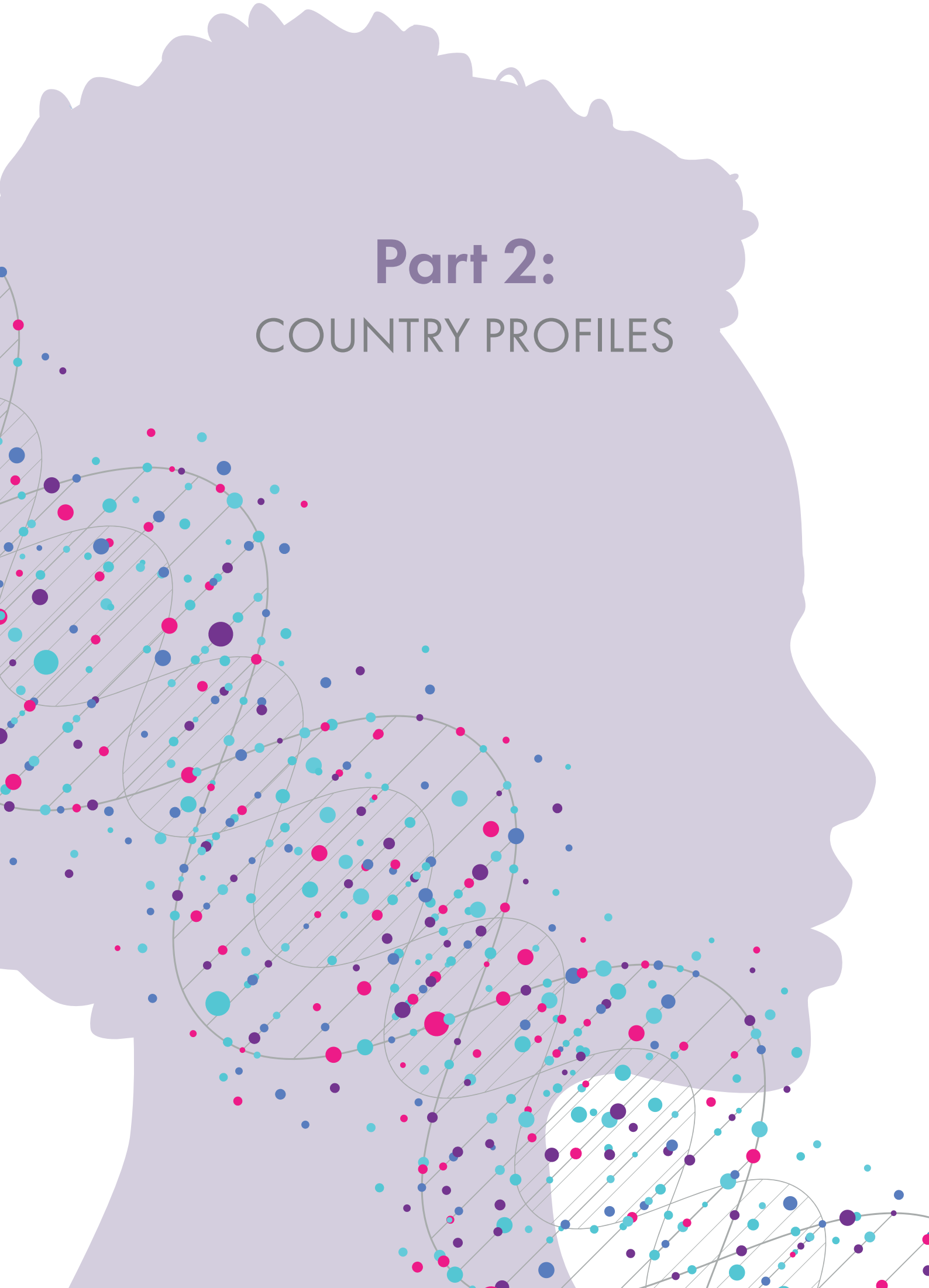


Part 2:

COUNTRY PROFILES

Genetic testing for *BRCA* mutations:

country profile for France

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

- France has the 4th highest incidence rate and the 14th highest mortality rate of female breast cancer in Europe.[1]
- It is estimated that around 2 in 1,000 women carry a *BRCA1* or *BRCA2* mutation.[2]
- In 2017, 2,084 women were found to carry a *BRCA1* mutation and 2104 a *BRCA2* mutation.[3]
- A woman in France has a lifetime risk of breast cancer of 51–75% if she has a *BRCA1* mutation and 33–55% if she has a *BRCA2* mutation, compared with 12% for the general population.[4 5]
- Geographical clustering of specific *BRCA1* mutations in the north-east and Alsace-Lorraine[6] suggests a founder effect, meaning that small groups of people have shared ancestors, giving rise to a higher prevalence of specific, rare mutations among these groups.[7]

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

France has well-developed policies and strategies in place for improving the prevention of hereditary cancers.

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

National policies and strategies include plans which support people with *BRCA* mutations. The French Cancer Plan (2014–2019) calls for the development of care pathways for people with rare and hereditary cancers,[8] while a national plan for rare diseases has also been developed.[9]

In addition, France is planning to develop a national plan on personalised medicine. 'Genomic Medicine France 2025', which was published in 2016, calls for healthcare and manufacturing firms to pilot genomic sequencing platforms that are integrated into healthcare pathways for diagnostic and therapeutic follow-up. By 2020 the aim is to establish a network of centres able to process around 235,000 samples for whole genome sequencing, whole exome sequencing or RNA sequencing per year. This will include the genomes of around 175,000 patients with metastatic tumours.[10]

Legal protection of *BRCA*-mutation carriers

Legislation is in place to protect people with *BRCA* mutations from discrimination. French legislation prohibits the use of genetic information by insurance companies and employers, even if the information is disclosed by the employee or the insurance applicant themselves.[11] However, a recent study found that one third of *BRCA*-mutation carriers surveyed disclosed their results to their employers. Women who had undergone preventive surgery and women of lower educational status were the most likely to disclose their test results.[11] Those with *BRCA* mutations and their families are also protected by legislation that allows carriers to inform their family members of their genetic test results anonymously[12] via their doctor.[13]

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

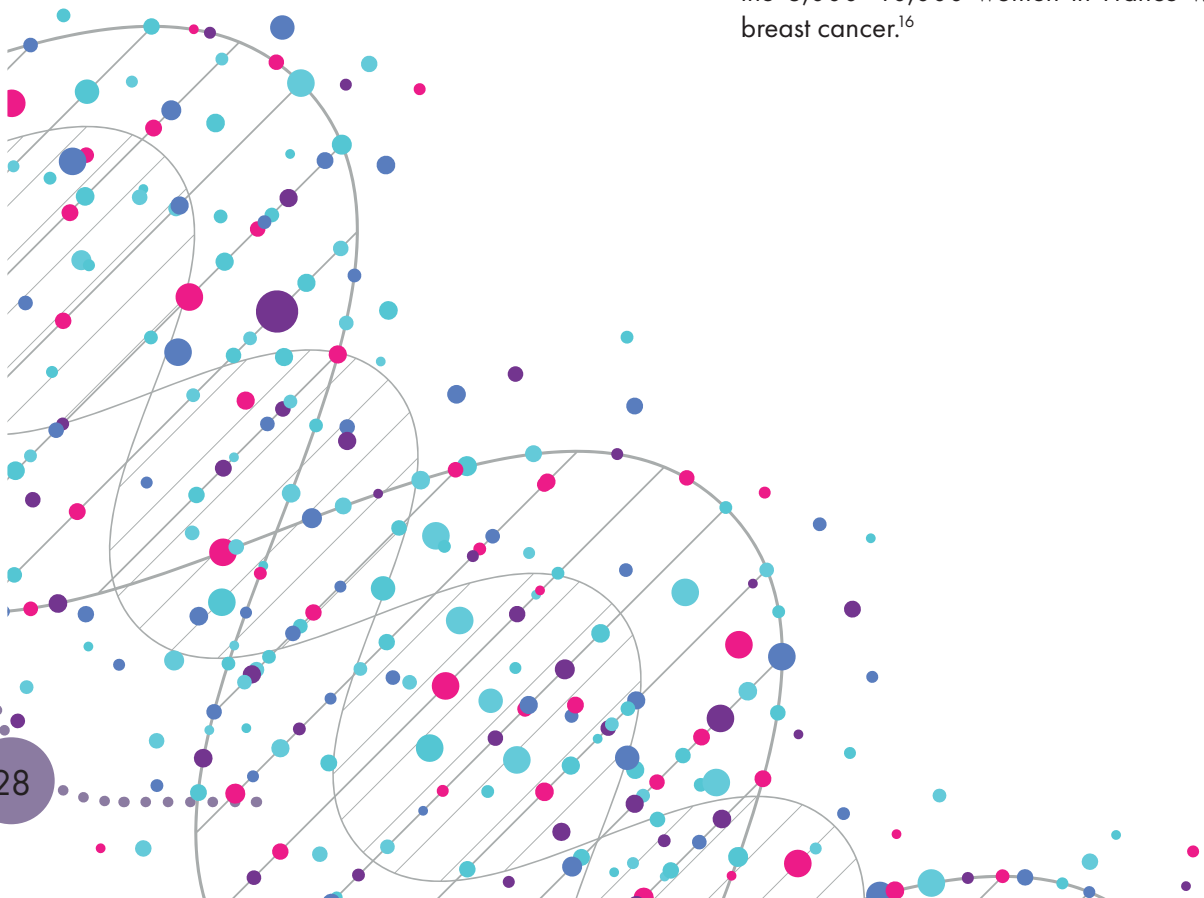
A number of patient organisations are working to raise awareness of *BRCA* mutations and advocate for improvements in care.

Data on levels of awareness and understanding of *BRCA* mutations in France are limited. The extent to which people understand their risk of carrying a mutation is unclear.

***BRCA*-France, established in 2015, is the only patient organisation focused on people with *BRCA* mutations or those who may be at risk.** It hosts an online community for those with *BRCA* mutations, along with information on *BRCA* diagnosis and strategies to reduce the risk of breast cancer among mutation carriers.[14]

Other, more general patient organisations advocate and raise awareness for *BRCA*, such as Geneticancer which publishes patient information on inherited cancers, focusing on genetic predisposition for breast and ovarian cancer.[15]

***BRCA*-France is also involved in public advocacy, aiming to expand genetic testing criteria.** It states that many who carry a *BRCA* mutation are being missed by current screening practices, as mutations carried by the father are currently missed in family-tree mapping used by geneticists. The organisation is also calling for genetic testing criteria to be expanded to include the 8,000–10,000 women in France with metastatic breast cancer.[16]



Comprehensive care pathways

The French National Cancer Genetics System supports people's access to genetic testing, but capacity constraints have led to bottlenecks and long waiting times.

Evidence-based national eligibility criteria and referral pathways for *BRCA* testing

Referral pathways for testing, diagnosis and management of people with *BRCA* mutations are well defined in national recommendations. The Haute Autorité de Santé (HAS) published recommendations on cancer screening in France which are based on family and personal history of cancer.[17] These are complemented by recommendations from the French National Cancer Institute (INCa).[5] Eligibility for genetic testing, which in France is undertaken through multi-gene panels that test for mutations in multiple genes at the same time, is likely to further expand in the coming years. INCa has convened an expert group which has been working to discuss how the anticipated expansion of *BRCA* testing to all women with metastatic breast cancer can be managed.[18]

Equitable and timely access to genetic testing

Infrastructure for comprehensive genetic testing is in place. Le dispositif national d'oncogénétique (national cancer genetics system), which was established following the National Cancer Plan, is organised around 147 consultation sites in 104 cities. It also has 25 laboratories responsible for carrying out genetic testing which are linked to genetic consultation sites.[19]

Genetic testing rates have increased due to greater awareness, more genetic consultations and improvements in gene sequencing techniques. The number of genetic consultations increased more than sixfold between 2003 and 2017 (from 12,696 in 2003 to 77,478 in 2017).[3] In 2017, 54,936 of these consultations were due to breast and/or ovarian cancer concerns, of which 18,180 women were tested for a *BRCA* mutation.[3]

Waiting times for genetic tests are relatively high, although they have decreased since 2012. On average, people currently wait 12 weeks for a first genetic consultation and 22 weeks to receive a complete *BRCA* genetic test – a 14-week reduction since 2012, largely due to advancements in genetic sequencing techniques.[3] However, major efforts are being made by public laboratories to reorganise and automate the analyses, which could reduce the result delays to a few weeks.[20]

Supporting oncologists to take a more active role in prescribing genetic tests for cancer patients may streamline this pathway and reduce waiting times.[18] Oncologists are currently able to prescribe genetic tests for patients with cancer, although often they do not. As multigene panel testing and *BRCA*-specific treatments become available, however, oncologists and surgeons are likely to increasingly request genetic testing of tumours to guide treatment decisions. This will require them to work closely with geneticists.[21] Guidance is being developed and shared with these healthcare professionals to ensure the advice of geneticists is included in the genetic testing pathway.[18 20]

Genetic consultation and testing are available in every region of France, but utilisation is uneven. Consultation rates vary from 65 per 100,000 inhabitants in the centre of France to 172 per 100,000 inhabitants in Pays de la Loire.[3] Diagnosis of breast and ovarian cancer-related mutations (predominantly *BRCA*) varies from 21.3% to 67.1% between laboratories.[3] This suggests variable implementation of national testing criteria at the referral and genetic consultation stages.

Clinics and laboratories providing cancer genetic services are organised by the Cancer Genetic Group of Unicancer, a network of private, non-profit hospitals.[22] This network has developed a set of guidelines for screening, prevention and genetic counselling for multigene panel testing for breast and ovarian cancer.[23] In addition, the Cancer Genetic Group has contributed to the classification of mutations which present an unknown risk of breast cancer, known as variants of unknown significance (VUS), especially for *BRCA1* and *BRCA2* genes.[24]

Role of private genetic testing providers

Some public-sector clinics are beginning to request genetic tests from private laboratories in an attempt to speed up the testing process and reduce costs. Experts have commented, however, that the continued role of university laboratories is critical in ensuring high-quality testing and the classification of rare or novel VUS mutations.[18 20]

Access to genetic counselling

Genetic counselling and psychological support are prioritised in national recommendations. INCa's 2017 *BRCA* recommendations emphasise the importance of genetic counselling and psychosocial support for people with *BRCA* mutations when making decisions on monitoring and risk-reducing strategies.[25]

Genetic counsellors are well established and hold important positions in multidisciplinary cancer care teams. France is one of just two countries in Europe, along with Norway, to have a legal framework for the profession.[26] This gives the role more credibility as it is defined by its own governance structure, rather than by overarching healthcare professional governance.[27]

Despite this, France has a relatively low number of genetic counsellors compared with some other countries in Europe. In 2017 there were 83 genetic counsellors, 187 genetic doctors and 64 psychologists employed in genetic consultations.[3] This equates to around three genetic counsellors per million people, which is lower than in countries such as Sweden and the UK. There is one master's programme in France which trains around 20 students per year,[28] although discussions are underway to potentially double this capacity.[20]

Follow-up care and support for *BRCA*-mutation carriers

People who have been found to carry a *BRCA* mutation, along with their close family members, are supported by a personalised monitoring system. This includes:[19 29]

- personalised, coordinated monitoring
- access to multidisciplinary skills and expertise for difficult cases
- clinical monitoring every six months from 20 years of age
- annual breast imaging from 30 years of age.

Uptake of preventive surgery in France is lower than in some other countries. According to international studies, French women are less likely to choose prophylactic mastectomy when testing positive for a *BRCA* mutation than their British or Canadian counterparts, opting instead for ongoing monitoring.[30] Conversely, the uptake of prophylactic salpingo-oophorectomy is similar to other countries.[31]

Improved awareness and knowledge among healthcare professionals

A number of professional development courses are available to address knowledge gaps among healthcare professionals.

Literature on the level of *BRCA*-related knowledge among both general practitioners (GPs) and oncologists is limited, although experts have indicated that it may be insufficient. *BRCA* and cancer genetics have only recently been included in medical curricula. Clinicians trained before this may therefore have insufficient knowledge of genetics.[20]

France has a national continuing professional development programme for healthcare professionals which includes modules on care for people with rare diseases, but this may be insufficient for managing genetic conditions. National orientation guidelines for healthcare professionals include 'organisation of care for someone suffering from a rare disease' and 'announcement of the diagnosis of a serious illness' but genetics is not included, other than for specialist genetic doctors.[32] Furthermore, it is not clear how well coordinated the programme is, nor the extent to which it addresses key genetic knowledge gaps among healthcare professionals.[20]

A diploma on precise diagnosis and personalised medicine has been developed to build knowledge in this area among oncologists, geneticists and genetic counsellors. This diploma includes information on genetics, the application of diagnostic data for treatment decision-making and ethics.[33] In addition, a DIU (diploma interuniversity) dedicated to cancer predispositions has been established to train students who are mainly oncologists, geneticists and genetic counsellors.[34]

Conclusions and recommendations

France has developed high-quality, monitored pathways for people with *BRCA* mutations. This includes well-defined and up-to-date referral and diagnostic systems and a national coordinated system for testing and monitoring those with BRCA mutations. There is also clear legislation to prevent genetic discrimination by employers or insurers. As this country profile has highlighted, however, there are several challenges which must be addressed in order for people with *BRCA* mutations to be able to access the comprehensive care they need.

Efforts are needed to ensure that women at high risk of *BRCA*-related breast cancer can access timely genetic counselling and *BRCA* genetic testing. The rising demand for cancer-related genetic consultation and testing has led to long waiting times,[3] which must be addressed. While investment in laboratory infrastructure is underway and should contribute to a reduction in waiting times, the role of oncologists in the genetic testing pathway should also be explored.[18]

Greater attention is needed to ensure that all women with a high risk of *BRCA*-related breast cancer have access to the genetic consultations and *BRCA* testing they need, regardless of where they live. While comprehensive infrastructure is in place to handle *BRCA* testing, utilisation varies greatly by region.[3] The reasons for this must be better understood and addressed.

All healthcare professionals supporting people with *BRCA* mutations must have access to high-quality information and guidance. This is urgently needed to address the significant and unacceptable knowledge gaps among some healthcare professionals,[20] including those who are not genetic specialists, such as GPs and gynaecologists.

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Genetic testing for *BRCA* mutations:

country profile for Germany

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

- Germany has the 15th highest incidence rate and the 9th highest mortality rate of female breast cancer in Europe.[1]
- 16% of women with triple-negative breast cancer in Germany carry a *BRCA* mutation.[2]

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

Germany's enabling policy environment has supported the development of a network of familial breast and ovarian cancer centres.

Inclusion of *BRCA* genetic testing in the national plan for cancer

Germany's national cancer plan, launched in 2008, aimed to advance early detection and provision of care for cancer patients in addition to the expansion of data registries, including for breast cancer.[3] The plan fostered the growth of a network of specialist familial breast and ovarian cancer centres in Germany and encouraged their certification.[3] Furthermore, data on treatment for breast cancer patients were incorporated into the national tumour registry, marking an important step towards comprehensive data collection and monitoring.[4]

The German Consortium for Hereditary Breast and Ovarian Cancer is active in implementing individualised, risk-adjusted prevention for hereditary breast cancer. It aims to ensure women with high genetic risk of breast cancer are legally entitled to intensified screening and risk-reducing options.[5] Consortium centres provide those women with access to care through multidisciplinary teams, working closely with the patient organisation *BRCA*-Network. They also collect and store data in a common database which allows them to share information for improved patient care. As part of this, the German Consortium is leading the European expert group RiskAP, which is developing a position paper on hereditary breast cancer prevention that accounts for genetic risk factors.[6]

To further improve care for people with rare diseases, including *BRCA*-related breast cancer, the Germany Ministry of Health initiated the National Action League for People with Rare Diseases (NAMSE), a multi-stakeholder coalition.[7] Partners include the patient advocacy group Allianz Chronischer Seltener Erkrankung (ACHSE), of which the *BRCA*-Network is a member.[8] In 2013, the league devised a National Action Plan for people with rare diseases, which aims to establish a network of referral centres, specialist centres and collaborative centres for patients with rare diseases.[8] Furthermore, several German genetic centres are part of the European Reference Network for Genetic Tumour Risk Syndromes (ERN GENTURIS), including the Munich Medical Genetics Centre, the Centre for Hereditary Tumour Syndromes (CHT) at the University Hospital in Bonn, and the Hereditary Cancer Syndrome Centre Dresden at the Faculty of Medicine of TU Dresden.[9]

National policies support cost-free access to *BRCA* genetic testing and personalised follow-up care

There are differences between statutory and private health insurance coverage, which could create difficulties in accessing *BRCA* genetic testing. While genetic testing is fully reimbursed by statutory health insurance, people with private insurance need to request the *BRCA* test from their insurer and are not guaranteed approval. Equally, prophylactic treatment may not be automatically covered.[10] Some private health insurers do not have contracts with the specialist centres, which may complicate or prohibit reimbursement for treatment in those centres.[11]

National registries to collect data on *BRCA* genetic testing

Germany benefits from a number of registries, although greater efforts are needed to aggregate data for policymakers. Cancer and tumour registries collect data on *BRCA*-mutation carriers, but an expert consulted for this research has highlighted that these data should be aggregated in order to validate clinical evidence and generate robust data for policymakers.[10]

Legal protection of *BRCA*-mutation carriers

German legislation is in place to protect those with *BRCA* mutations from employment and insurance discrimination. It guarantees every citizen the authority over their genetic information and appears to successfully prevent people from experiencing discrimination as a result of a positive *BRCA* test result.[12] An expert interviewed for this country profile, however, notes that some people do not request a test due to fear that it may affect their private insurance coverage.[13]

However, this legislation may present a barrier to testing family members of *BRCA*-mutation carriers. Unlike in some other countries, such as France, healthcare professionals in Germany are not allowed to contact family members of a mutation carrier regarding their potential genetic risk.[11]

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

BRCA-specific patient organisations and increased reporting in the media have contributed to growing awareness of *BRCA* mutations among the population.

Awareness of *BRCA* mutations has increased notably in recent years, largely due to advocacy from patient organisations and prominent cases in the media. Yet experts have highlighted that more needs to be done to increase knowledge about *BRCA* mutations and the benefit of genetic testing in the general population and among policymakers.[10 11]

The organisation Deutsche Krebshilfe funds specialist centres where people with familial breast cancer can seek information and receive adequate diagnosis and treatment. It also played a major role in funding and establishing the patient organisation *BRCA*-Network, which educates and supports those who may carry a *BRCA* mutation.[14 15]

The magazine *Mamma Mia!* – available online and in all breast cancer centres – also provides a range of information on *BRCA*. In 2013, it published a special edition with detailed information for mutation carriers about their options relating to *BRCA*. It also offered information on possible financial issues and available support programmes.[14] Updates are published regularly to improve knowledge among people with *BRCA* mutations of all aspects of medical care and living with cancer.[13]

Despite efforts to improve understanding and awareness, gaps remain. An expert interviewed for this country profile notes that some women continue to have low levels of knowledge about *BRCA* and the importance of multidisciplinary care in supporting women's physical and psychosocial needs.[13]

Comprehensive care pathways

Comprehensive guidelines provide detailed recommendations on care for *BRCA*-mutation carriers, while a network of specialist centres provides the infrastructure for delivery.

Evidence-based national eligibility criteria for *BRCA* testing

Updated comprehensive guidelines on breast cancer (S3 guidelines) were published in 2018 and provide recommendations for *BRCA*-related breast cancer. This includes eligibility criteria for genetic testing and recommendations regarding genetic counselling, long-term monitoring and risk-reducing strategies for mutation carriers.[16] Recommendations for *BRCA* genetic testing are also included in the guidelines from the working group for Arbeitsgemeinschaft Gynäkologische Onkologie (AGO).[17] To facilitate and promote guideline use in clinical practice, a checklist has been developed by the Consortium for Hereditary Breast and Ovarian Cancer to help healthcare professionals assess family history. The checklist is recommended for use by practitioners.[18 19]

Equitable and timely access to genetic testing

People can seek genetic testing for *BRCA* mutations either through one of the 18 certified specialist centres of the Consortium for Hereditary Breast and Ovarian Cancer, through Departments of Human Genetics at universities, or through private genetic testing providers. It is mandatory for physicians to assess the family history of all people requesting a genetic test and to inform them about all aspects of testing for genetic mutations associated with breast cancer. Genetic testing is offered to all who meet the eligibility criteria specified in the S3 guidelines.[16]

While specialist centres are located across Germany, there are fewer centres in some areas which may lead to geographic inequalities in access to *BRCA* genetic testing. People living in north-east Germany, for example, may face long travelling times to specialist centres.[11 20] The consortium of specialist centres is, however, building networks with other breast and gynaecological cancer centres in an attempt to ensure nationwide access.[21]

Waiting times for genetic test results from the specialist centres have reduced in recent years. In 2013, waiting times for genetic test results from one of these centres were between one and eight months, depending on medical urgency.[22] One expert interviewed for this country profile, however, indicated that this has now reduced to an average of one month.[21]

Role of other genetic testing providers

In addition to the specialist centres, genetic testing and counselling are also offered by human geneticists working in private practice. They may not provide the comprehensive, multidisciplinary care that is available through Consortium centres, but they may refer patients to these services.[14 22] Genetic counselling and *BRCA* genetic testing are also provided by all university-based Departments of Human Genetics.[13]

Access to genetic counselling

Genetic counselling is required following the results of diagnostic genetic testing. In the case of predictive genetic testing, genetic counselling is mandatory both before testing and once results are available.[23] People receive information on what it means to live with a *BRCA* mutation and about implications for other family members.[22]

As in several other European countries, genetic counselling in Germany is performed only by physicians. This includes those certified in human genetics and, in the case of diagnostic genetic testing, physicians with other specialties who have received the appropriate training.[23]

Follow-up care and support for *BRCA*-mutation carriers

As part of the care pathway for *BRCA*-mutation carriers, national breast cancer guidelines give guidance for long-term monitoring, prophylactic surgery and treatment options. Recommendations are frequently updated to incorporate emerging evidence and are implemented on a case-by-case basis and depending on the *BRCA*-mutation carrier's preferences.[16 24] However, risk-reducing surgery for asymptomatic women is not routinely reimbursed by all German health insurance, limiting access for some women.[25]

Improved awareness and knowledge among healthcare professionals

There are recognised gaps in *BRCA* knowledge among healthcare professionals who are not genetic specialists.

Non-genetic-specialist healthcare professionals, such as gynaecologists, breast surgeons and GPs, are often not adequately equipped to initiate referrals for *BRCA* genetic testing, make the right referral decisions or recommend appropriate risk-reducing interventions.[10 11 26] A survey from 2013 found that only 27% of GPs and 66% of breast surgeons in Germany were in favour of prophylactic mastectomy as a treatment option.[26]

The recent projects iKNOW and EDCP-*BRCA* aim to address this gap by supporting physicians to interpret and communicate *BRCA* testing results and provide accurate advice to *BRCA*-mutation carriers. The projects implemented by Charité – Universitätsmedizin, the Technische Universität in Berlin and the University of Cologne involve the development and roll-out of online tools, which will support doctors to discuss test results and breast cancer risk, and offer evidence-based prevention and treatment options in line with current guidelines.[27 28]

Conclusions and recommendations

Multi-stakeholder efforts at policy level in recent decades have significantly advanced the provision of care for women who have or are at risk of hereditary breast cancer.[3 14] The establishment of the German Consortium for Hereditary Breast and Ovarian Cancer and the foundation of its now 18 specialist centres has been an important step towards offering high-quality care in hereditary breast cancer.[21] Furthermore, the current national cancer plan aims to advance the risk-adjusted early detection of people at high risk of cancer, which includes women who may carry a *BRCA* mutation.[3 5] There are, however, a number of challenges and gaps which policymakers should address when considering ways to improve care for those with *BRCA* mutations.

Greater attention is needed to ensure that *BRCA*-mutation carriers and those with a high chance of carrying a mutation can access comprehensive, affordable care. This should cover the full range of services that people would be expected to access, including support and information before they are tested, and clinical and psychosocial support both during the testing process and, if they are found to have a mutation, following the test. This would address the geographical barriers and differences in insurance coverage which have led to inequalities in access to comprehensive *BRCA*-related care.[11 20]

GPs and gynaecologists must be supported with evidence-based guidance and up-to-date knowledge to enable them to make appropriate referrals of those at high risk of *BRCA*-related breast cancer. GPs and gynaecologists play a critical role in supporting women who may be carrying a *BRCA* mutation, but knowledge gaps among these professionals present a barrier to accessing high-quality care.[26]

Data from different registries, including hereditary tumour and cancer registries, should be aggregated for the validation of clinical evidence and the generation of robust data for policymakers. While Germany benefits from several registries which collect information on *BRCA* carriers and breast cancer patients, the data are not aggregated,[10] limiting the potential to support policymakers, researchers and clinicians.

Awareness of *BRCA* mutations among the general population must be improved. There is also a need to improve understanding of genetic testing in general and the importance of interdisciplinary care that supports the full range of physical and psychosocial needs of *BRCA*-mutation carriers.

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Genetic testing for *BRCA* mutations:

country profile for Ireland

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

- Ireland has the 11th highest incidence rate and the 3rd highest mortality rate of female breast cancer in Europe.[1]
- It is estimated that there were 3,334 new cases and 791 deaths from breast cancer in 2018.[1]
- There are no national data on the proportion of breast cancer cases which are due to *BRCA* mutations.

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

Significant gaps in hereditary cancer services have been identified by the Irish government, which has developed plans to boost access to comprehensive care for people with *BRCA* mutations.

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

There is no comprehensive national policy on genetics and genetic testing in Ireland, but there is a clear intention to scale-up access to these services.[2] In 2012, the National Cancer Control Programme (NCCP) established the Hereditary Cancer Programme to scale-up advanced diagnostics in genetics and meet increasing demand from healthcare professionals and patients for these services.[3] The programme is implemented in partnership with the Department of Clinical Genetics at Our Lady's Children's Hospital, Crumlin (OLCHC), with St James's Hospital acting as the National Clinical Lead for cancer genetics.[3]

The government has identified significant gaps in the Hereditary Cancer Programme and outlined a range of recommendations to improve access to genetic services as part of its National Cancer Strategy 2017–2026. The strategy recognises that the Hereditary Cancer Programme is underfunded and underdeveloped.[3] It plans to boost staffing by specialist healthcare professionals and training on cancer genetics among oncology graduates. It also calls for the Health Service Executive (HSE) to combine existing services under a coordinated National Cancer Genetics Service.[3]

National registries to collect data on *BRCA* genetic testing

There is a lack of data on *BRCA*-mutation carriers in Ireland, hampering the government's ability to make evidence-based policy decisions. There are no national registries which collect data on *BRCA* mutations and *BRCA*-related breast cancer.

Legal protection of *BRCA*-mutation carriers

Under Irish law, genetic data cannot be used for insurance, pension, mortgage or employment purposes.[4] However, there are no further anti-discrimination regulations with regard to genetic data.[5] In addition, Ireland has not signed the European Convention on Human Rights and Biomedicine, which protects individuals in other European countries from discrimination based on genetic test results and mandates the individual's consent and right to be informed about genetic test results.[6]

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

People in Ireland have access to a limited range of information on *BRCA* mutations and *BRCA*-related breast cancer, although national patient organisations are working to address this and raise awareness among the population.

Public awareness about hereditary breast cancer and genetic testing has increased, contributing to a significant rise in referrals for genetic testing.[3] Referrals to cancer genetics increased by 60% between 2000 and 2013, and testing for *BRCA* mutations is the most common reason for a request.[2] A large proportion of these referrals are healthy women worried about their genetic predisposition.[3]

A limited range of online and printed information from Ireland is available for people who are concerned about their risk of hereditary breast cancer.[7] Action Breast Cancer, a programme of the Irish Cancer Society, provides information about the likelihood of a *BRCA* mutation and the process of genetic testing.[8] Comprehensive information is also available from patient support organisations such as the Marie Keating Foundation.

There appear to be gaps in additional support available for those with *BRCA* mutations in Ireland. Until recently there were no peer-support groups for people with *BRCA* mutations, nor *BRCA*-specific patient organisations – but the Marie Keating Foundation has now developed a peer programme through which volunteers have been trained on topics including a patient's journey from genetic testing to surgery, and strengthening self-care and resilience. The programme, which was launched in April 2019, allows individuals to submit questions through the organisation's website, which are then answered in confidence by a trained volunteer or a *BRCA* expert.[9] The Foundation also offers workshops and seminars for those at high risk of breast cancer.[10] Furthermore, in 2016, Cancer Trials Ireland organised a *BRCA* conference for people with a family history of breast cancer.[11]

Comprehensive care pathways

Restrictive eligibility criteria for genetic testing and limited capacity have an impact on access to and uptake of *BRCA* genetic testing and follow-up care.

Evidence-based national eligibility criteria for *BRCA* testing

Ireland has established criteria for genetic testing for hereditary breast cancer, but these are more restrictive than in many other European countries.[7 12] The criteria, developed by the National Centre for Genetic Medicine (NCMG), define those who may be considered at high risk of carrying a *BRCA* mutation and are therefore eligible for referral by a specialist or their GP for a consultation. This may lead to either diagnostic genetic testing in patients with existing breast cancer, or predictive genetic testing in those without symptoms, to confirm whether they carry the *BRCA* mutation.

In contrast with many other European countries, Ireland does not make genetic testing available to all asymptomatic women at high risk of *BRCA*-related breast cancer.[12] The NCCP noted that, with the currently available resources, the introduction of testing for all women at high risk regardless of whether they are affected by cancer – as is practised in the UK – is not feasible.[2]

Equitable and timely access to genetic testing

Three public hospitals offer genetics services to people considering *BRCA* testing in Ireland. However, it has been noted that with current resourcing, these hospitals are not equipped to provide comprehensive genetics services on a national level.[3]

A lack of investment in cancer genetics has led to the low availability of oncologists with specialist training in cancer genetics. Such healthcare professionals are needed to lead on cancer genetics in their local cancer centres and to coordinate with NCMG.[3]

Consequently, waiting times for an initial consultation, genetic testing and counselling are high, placing a burden on people waiting for tests and potentially delaying initiation of necessary treatment.[3] People may have to wait up to 12 months to be seen in a cancer genetics clinic after the initial referral.[12] Only half of those referred have an initial appointment within the first six months of referral.[2]

Role of private genetic testing providers

Long waiting times and strict eligibility criteria have led some people to choose private *BRCA* genetic testing at high cost.[7] Private clinic-based and direct-to-consumer (DTC) testing for *BRCA* mutations are becoming increasingly popular.[5 7 13] The test costs between €1,400 and €1,800[14] and, although it is now covered by one private health insurance company,[15] cost is likely to be a barrier for some people.[7]

Furthermore, limited regulation and oversight have led to concerns about the quality of genetic testing services provided in the private sector in Ireland. There is a lack of standards to ensure the clinical and analytical validity of genetic test results, leading to the potential for misinterpretation. In addition, advertising of DTC genetic testing is not regulated under Irish law, and genetic counselling is often not provided. This may contribute to increased distress and anxiety among those being tested.[5]

Access to genetic counselling

Genetic counselling is not required by law but it is demanded by the Irish Medical Council and recognised as critical in the National Cancer Strategy.[5] The National Cancer Strategy also recognises the need for significant investment in the genetic counsellor and genetic nursing workforce.[2 3]

In proportion to its population, Ireland has one of the lowest numbers of genetic counsellors and genetic consultants in Europe. In 2011, Ireland had only six geneticists and six genetic counsellors; the recommended numbers, given the population size, would be 14 and 46, respectively.[16]

Novel forms of genetic counselling are being explored and could improve access and quality of cancer genetics services. The National Cancer Strategy proposes telemedicine services, which are already provided by some centres, as a possible option for genetics counselling.[3] A recent study showed that the majority of people surveyed value having the choice between different disclosure methods, and about 45% preferred to receive their results via post or telephone.[17]

Follow-up care and support for *BRCA*-mutation carriers

Recommendations for surveillance of *BRCA*-mutation carriers are in place but are not implemented on a nationwide basis. The Health Information and Quality Authority (HIQA) developed recommendations for surveillance of *BRCA*-mutation carriers as part of a comprehensive health technology assessment. Recommendations include breast cancer surveillance for women with an identified genetic breast cancer mutation and annual digital mammography for women aged 40–49 who have high familial risk but no identified genetic mutation. To ensure equity of access, the HQIA suggests establishing an organised surveillance programme at a national level.[18] Despite this, free annual breast checks are currently offered only to women aged 50–69 on a routine basis, regardless of their risk status.[19]

There is limited guidance available for the management of women with *BRCA* mutations. The National Clinical Guideline for breast cancer provides recommendations for women with *BRCA*-related breast cancer,[20] but guidance for reducing breast cancer risk among asymptomatic *BRCA*-mutation carriers appears to be lacking. This may be contributing to low uptake of preventive double mastectomy. One study found that only 12% of asymptomatic *BRCA*-mutation carriers in Ireland decided to take up this surgery.[21]

Improved awareness and knowledge among healthcare professionals

Knowledge gaps among GPs in Ireland limit their ability to facilitate access to genetic testing.

Non-genetic-specialist healthcare professionals, such as GPs, can request *BRCA*-mutation testing for their patients. NCMG has published guidelines for genetic testing and risk assessment for primary care practitioners.[22] These explain the process of genetic testing in Ireland. The NCCP has also developed a guidance document for non-genetics healthcare professionals.[23]

However, GPs may not be equipped to adequately respond to increased interest in testing for genetic cancer predispositions or to pre-assess their patients' risk. Patients may seek help from GPs to discuss potential genetic risks or query their test results from DTC genetic testing services.[3] In a national survey in 2016, around 90% of GPs who responded said they did not have sufficient information to discuss genetic testing with their cancer patients.[24] In response to the role of GPs as a gatekeeper for referrals to cancer genetics centres, the NCCP has called for an assessment service for GP referrals.[3]

Conclusions and recommendations

Ireland faces some significant challenges in meeting the needs of people who carry *BRCA* mutations. Eligibility criteria for *BRCA* genetic testing are more restrictive than in many countries in Europe, meaning that many people who may be carrying a *BRCA* mutation are not being identified.[7 11] In addition, the availability of specialist staff, including genetic counsellors, is too low to meet demand – contributing to long waiting times for genetic tests.[2]

Information and support for those with *BRCA* mutations must be improved. There are no *BRCA*-specific patient organisations in Ireland, although there are general cancer organisations providing information and limited support services for *BRCA*-mutation carriers.[8 10 11] Many non-genetic-specialist healthcare professionals, such as GPs, seem to lack the knowledge required to meet the needs of their patients.[24]

National guidelines which support access to comprehensive care for *BRCA*-mutation carriers are urgently needed. Access to genetic testing services for those at high risk of *BRCA*-related breast cancer is severely hampered by restrictive eligibility criteria. Recommendations on surveillance are not being adopted and there are no national guidelines on risk-reducing options for women with *BRCA* mutations who do not yet have breast cancer.

Ireland must follow through on its strategic commitments and urgently invest in the genetic testing infrastructure and workforce needed to improve access to timely *BRCA* genetic testing. This includes building staff numbers and streamlining current cancer genetic services.[3] Progress in relation to these commitments must be monitored to ensure that all those with *BRCA* mutations in Ireland have access to the care they need.

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Genetic testing for *BRCA* mutations:

country profile for Israel

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

- In 2012, Israel had the 16th highest incidence rate and the 8th highest mortality rate of female breast cancer in Organisation for Economic Co-operation and Development (OECD) countries.[1]
- 2.5% of Ashkenazi Jewish women in the population[2] and 9% of Ashkenazi Jewish women with breast cancer in Israel have a *BRCA* mutation.[3]
- As around 30% of the total Israeli Jewish population comprises Ashkenazi Jews,[4] Israel has a relatively high rate of *BRCA* gene mutations compared with other countries.[5]
- Rates of breast cancer among Arab women in Israel tend to be lower than among Jewish women, but breast cancer is responsible for 24.8% of cancer deaths among Arab women compared to 18.4% of cancer deaths among Jewish women. Furthermore, while deaths from invasive breast cancer have decreased since 1995 among Jewish women, they have increased among Arab women during the same period.[6]

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

National registries to collect data on *BRCA* genetic testing

Israel does not have a *BRCA* registry, limiting the availability of comprehensive published data on *BRCA* mutations. Although there is a well-established national cancer registry,[7] there are no registries systematically collecting data on *BRCA* mutations and much of the research in this field comes from studies on mainly Ashkenazi Jewish populations, although there are a limited number of studies on *BRCA* mutations in Sephardi Jewish, Arab and Druze communities.[8 9]

Legal protection of *BRCA*-mutation carriers

Israel was one of the first countries globally to enact legislation to protect against misuse of genetic information. The genetic information law was passed by the Israeli government in 2000. This law, along with subsequent amendments, aims to protect the confidentiality of genetic data and prohibit employers from discriminating against individuals based on their genetic information. It forbids health insurers from requiring individuals to undergo testing, demanding genetic test results, or refusing to cover a healthy individual or alter premiums based on the results of genetic testing. The law also covers the provision of genetic testing and counselling.[10]

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

Patient organisations, such as BRACHA, are working to raise awareness of *BRCA* mutations among different population groups in Israel.

In Israel, public awareness of *BRCA* mutations is increasing. Awareness-raising initiatives aiming to improve public understanding of *BRCA* mutations have been growing since the 1990s.[11] The non-profit organisation BRACHA is the only organisation in Israel specifically working on awareness-raising, education and advocacy for hereditary cancers and genetic testing (see *Box 1*).[12]

Box 1 | BRACHA: Israel's patient education and advocacy organisation[5 8 12 13]

BRACHA is the only organisation in Israel working solely to support people who carry genetic mutations which put them at risk of hereditary cancer. Its work is delivered entirely by volunteers and includes the following areas:

- **Advocacy**: BRACHA engages with policymakers to widen access to genetic testing and increase access to treatments available through the public health system.
- **Awareness and education**: BRACHA has run 20 medical conferences since 2009 in locations across Israel. It has also organised 12 'Ask the Expert' events, which provide private access to *BRCA*-specialist healthcare professionals for those carrying a *BRCA* mutation. These events are funded through voluntary donations with no support from the Ministry of Health. In addition, BRACHA has a monthly newsletter, has published books, organises awareness-raising art exhibitions, frequently engages with the media, and organises and delivers lectures to a range of audiences including, for example, Arab communities.
- **Support to those who have or may have *BRCA* mutations**: BRACHA provides face-to-face and online support in addition to telephone support in five languages.
- **Supporting access to testing and ongoing care**: BRACHA supports people who wish to access genetic testing, regardless of their family history. It also promotes and supports *BRCA*-mutation carriers to actively consider risk-reducing surgery.
- **Research**: the organisation also undertakes its own research on *BRCA* in Israel, collecting and analysing data on *BRCA*-mutation carriers and their experiences. It also maintains relationships with international researchers and lecturers.

Awareness is not evenly spread throughout the population, however, with lower but increasing awareness among ultra-Orthodox Jewish and Arab women. Although data are limited on awareness of *BRCA*-related breast cancer, research on breast cancer knowledge more broadly has found that some women from ultra-Orthodox Jewish and Arab communities appear to have lower levels of knowledge and lower uptake of screening than the general population.[14-16] This may be a reflection of the stigmatisation of breast cancer within some sections of these communities.[17 18] Understanding and knowledge seem to be rising, however,[15 16 19] with non-profit organisations such as BRACHA and the Mariam Foundation, which works with Arab communities, raising awareness and addressing misconceptions surrounding cancer.[8 20]

Comprehensive care pathways

Access to *BRCA* genetic testing and ongoing care is hampered by overly restrictive eligibility criteria and long waiting times.

Evidence-based national eligibility criteria for *BRCA* testing

Israel's Ministry of Health has published eligibility criteria for reimbursed *BRCA* genetic testing. These criteria are based largely on age at diagnosis and/or family history. They allow all healthy first- or second-degree relatives of known *BRCA*-mutation carriers to access the test. In addition, since January 2019 testing for common *BRCA1* and *BRCA2* mutations is reimbursed through the public health system for all patients with ovarian, breast or pancreatic cancer.[21] Patients with breast and ovarian cancer found to have at least 10% risk of carrying a mutation are eligible for full *BRCA1/BRCA2* sequencing if tested negative for the common mutations.[22]

However, the eligibility criteria may be insufficient to meet the needs of Israel's population. Global data suggest that over 50% of *BRCA*-mutation carriers do not meet family history criteria.[23] This means, as in many other countries, it is likely that large numbers of possible *BRCA*-mutation carriers in Israel are potentially being missed with current guidelines.[8]

This situation has led to calls for genetic testing to be much more widely available. Some are calling for extending genetic testing to all Ashkenazi Jewish women;[24] it is estimated that this would identify around an additional 24,000 *BRCA*-mutation carriers compared with current criteria.[25] In reality, however, mixed marriages are common and women are often uncertain about their ethnic heritage or family history.[2] Combined with concerns over ensuring equality in access to health services, this has led to some people calling for genetic testing to be expanded to all Israeli people regardless of ethnic background.[8] [26]

Equitable and timely access to genetic testing

Specialist infrastructure for genetic testing and counselling in Israel is well developed but waiting times can be long. Comprehensive medical genetics departments or units are available in 15 public and one private hospital. Most of these cover cancer genetics. Each department comprises at least one certified medical geneticist and one genetic counsellor.[27] Despite this, waiting times for genetic tests can be long, with some people waiting up to a year for their test.[28]

***BRCA* genetic testing was expanded in 2013 to include testing for the 14 most common mutations among the Israeli population.**[29] Previously, eligible people were tested only for the three mutations most commonly seen in Ashkenazi Jewish communities and, if relevant, for mutations commonly found in Iraqi and Yemenite Jews.[30] Despite this expansion, mutations are likely to be missed because, as noted previously, eligibility criteria restrict who can access the test. In addition, similarly to some other countries, genetic tests are not routinely conducted on the whole gene, limiting the identification of additional mutations.[8]

Uptake of *BRCA* genetic testing among some ultra-Orthodox Jewish women has traditionally been lower than among other population groups. Fears over the impact of genetic test results on future marriage prospects for women and their daughters seems to have some bearing on this.[18] [19] However, women in these communities do seem to be increasingly accessing *BRCA* genetic testing services.[8]

There do not seem to be any available data on non-Jewish women's uptake of *BRCA* genetic testing in Israel. Data on breast cancer screening, however, indicates that women in these communities are increasingly accessing genetic testing services.[16] Further research is needed to understand the true uptake of genetic testing among these women and the barriers they may face.

Role of private genetic-testing providers

Genetic testing and counselling are provided free at the point of use to all who are eligible, through Israel's comprehensive social insurance scheme.[31] Those who do not want to wait for the test, or who wish to be tested but do not meet eligibility criteria, may choose to take the test at a private centre.[8]

Access to genetic counselling

Pre- and post-test genetic counselling is supposed to be offered to all those who undergo *BRCA* testing in Israel.[31] After they have received their result, a genetic counsellor – either working under the supervision of a medical geneticist,[32] or a medical geneticist themselves – explains the result including the risk of developing cancer, potential preventive options available, how to discuss the result with family members and recommendations for follow-up.[31] An expert interviewed for this country profile, however, commented that these sessions do not always provide people being tested with the support that they need, and that a more person-centred approach should be consistently applied across the facilities involved.[8]

Israel has one of the highest numbers of genetic counsellors per person globally. In Israel there are 80 genetic counsellors for a population of 8.5 million people, a higher ratio than in countries including France, Sweden and the UK.[32] Three universities offer master's courses in human genetics or genetic counselling, which are required to practise the profession. These universities offer their courses to a total of around 20 students per year.[32]

Genetic counsellors in Israel are licensed and regulated by the Ministry of Health but must work under the supervision of a medical geneticist.[32] This limits their ability to act independently and may contribute to a perception of low status by other healthcare professionals.[8]

Follow-up care and support for *BRCA*-mutation carriers

There are no national clinical guidelines for the management of women who have been found to have a *BRCA* mutation, but the services available to these women as part of the social health insurance basket have been defined by the Ministry of Health. These services align to European guidelines[33] and include periodic examination, annual magnetic resonance imaging (MRI) in addition to ultrasound or mammography, blood tests and clinical consultations.[34]

Israel has several multidisciplinary, high-risk clinics specialising in care for those who carry a *BRCA* mutation – but not all people with *BRCA* mutations are aware of them. These clinics provide a range of services including regular breast cancer screening, genetic counselling and access to risk-reducing surgery.[11] [35] [36] Those who access genetic testing through a hospital are usually referred to the *BRCA* clinic at that facility. People who are tested in the community or at other hospitals, however, may not be aware of *BRCA* clinics, limiting their ability to access vital ongoing care. Furthermore, although the high-risk clinics are relatively well-spread geographically, there may not be enough capacity to meet demand; one expert interviewed for this profile commented that clinics throughout the country are at maximum capacity and not accepting new patients.[37]

Furthermore, some national health insurance providers do not provide access to these clinics. Israel's primary care services are delivered through four non-profit Health Plans which must provide their members with access to a basket of services defined by the Ministry of Health. There is, however, wide variation in how these Health Plans are organised and the additional services they provide.[38] It has been reported by an expert interviewed for this report that not all Health Plans support their members to access *BRCA* high-risk clinics.[37]

It has also been noted that the services provided at these clinics can sometimes be too limited. An expert interviewed for this country profile commented that although there are some centres providing comprehensive and multidisciplinary care, those visiting other centres may face gaps. Such gaps may be found, for example, in the provision of psychosocial support and in understanding and managing the additional risk that *BRCA*-mutation carriers have in association with conditions such as pancreatic cancer[39] and bone loss (among women who have undergone risk-reducing salpingo-oophorectomy).[40]

Uptake of risk-reducing double mastectomies among pre-symptomatic women with *BRCA* mutations in Israel is lower than in many other countries. Recent estimates suggest that uptake is around 13%,[5 11] which is lower than the average for Western Europe.[41] This may be, in part, a reflection of the level of support and information women receive. One small Israeli study has found that uptake of surgery was much higher among women whose physicians recommended surgery compared with those who recommended against it.[5] Further support and information is provided by BRACHA, which works with many women as they consider their choices, including taking up surgery.[8] Other factors such as a women's age at study entrance, family history, personal experiences and other subjective data may also be relevant.[30]

Improved awareness and knowledge among healthcare professionals

A lack of genetic knowledge among many healthcare professionals may have an impact on people's ability to access genetic testing.

Knowledge gaps among GPs and gynaecologists may be contributing to low referrals for genetic testing and gaps in comprehensive care. One study among families with significant previous incidence of breast or ovarian cancer found that only 35% had been previously referred for genetic testing.[42] Evidence from other countries suggests that knowledge among non-genetic specialists is often low and that this contributes to low referrals for testing.[43 44] Experts suggest this situation also applies in Israel,[8] with reports of misconceptions and misunderstandings regarding a woman's risk of breast cancer and thus her suitability for genetic testing.

It has been noted, for example, that some clinicians are unaware of the importance of family history along the male line, the possible association between *BRCA* mutations and pancreatic cancer in the family, or the possibility of *BRCA* mutations in non-Ashkenazi communities. This means women at high risk of *BRCA*-related breast cancer may not be identified or offered a test.[8] Conferences arranged by BRACHA are working to address these knowledge gaps, but the organisation argues that the Ministry of Health should take a more proactive role in supporting the professional development of its staff.[8]

Conclusions and recommendations

Israel has well-developed infrastructure for genetic testing and care of *BRCA*-mutation carriers but there are significant gaps, leaving many unsupported. Medical genetics departments provide genetic testing services, while high-risk clinics provide specialised ongoing care for those with *BRCA* mutations.[27] Furthermore, people in Israel who are considering genetic testing are supported by BRACHA, a dynamic and active patient support and advocacy organisation.[12] There are several significant gaps, however, meaning many are unable to access the range of comprehensive care services that they need.

Eligibility criteria must be evidence-based and support access to genetic counselling and testing for all women at risk of *BRCA*-related breast cancer. Despite recent changes,[22] eligibility for publicly funded *BRCA* genetic testing in Israel is based on criteria which are too limited, leaving many women who are at high risk without access to a test.

Greater attention is needed to build the knowledge of healthcare professionals to ensure they are able to support patients throughout the genetic testing process. Knowledge gaps and misconceptions among some healthcare professionals mean that some high-risk individuals are not being referred for a test, even if they meet current eligibility criteria.[43 44] This must be addressed urgently through educational activities.

High-risk clinics should expand the services they offer to ensure they provide access to comprehensive care for all carriers of *BRCA* mutations, regardless of the Health Plan they belong to. This should include ongoing psychosocial support and the management of risks associated with *BRCA*-related conditions.

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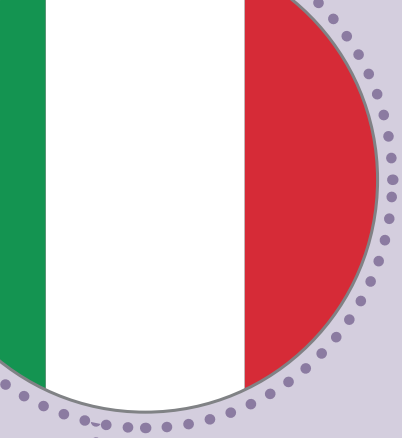

Genetic testing for *BRCA* mutations:

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]

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.[3 4] However, it is not clear whether all regions have achieved this.[5]

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.[3] 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.[3]

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 estalished.[6-8] There is also a lack of information on the centres that provide the test.[7] 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.[9] In addition, despite a national aspiration for free *BRCA* testing, access and eligibility criteria – including whether a co-payment is required – vary across regions.[10 11] Women who have had breast cancer, however, are exempt from paying a fee.[12]

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.[13]

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.[5] 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.[11 14] 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.[15]

Overall, despite these efforts, the quality and comprehensiveness of public information is insufficient.[5] A 2015 survey found that awareness of *BRCA* is low and that most women with some *BRCA* knowledge learn about it from their gynaecologist.[16] 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.[5]

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.[17] 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.[6]

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.[18] 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.[8 19]

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.[5] Testing is also available in private medical centres for people who do not want to wait for a test from a public facility.[20] 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.[5] 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.[21] Lombardia, however, had nine centres and Emilia-Romagna had four.[21]

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.[5]

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.[22] Guidelines also recommend involving a multidisciplinary care team – including oncologists, psychologists and geneticists – in the counselling process.[22 23] It has been noted by the women's health organisation Osservatorio Nazionale sulla Salute della Donna, however, that these services are not always available.[5]

In addition, there can be significant variability in genetic counselling services provided across the country.[3 23] 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.[3 23]

Genetic counselling centres are mainly available in research institutions such as university hospitals and research institutes.[23] There are, however, no clear guidelines on the skills and competences required by genetic counsellors.[20] This has limited the availability of training programmes to increase the number of professionals who can provide this service.[20]

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.[17] Around 10% of women seem to opt for prophylactic surgery, a proportion lower than in France but higher than in Spain.[24]

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.[6]

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 genetics[5] and do not seem to have the necessary knowledge to support those who need genetic testing.[25] 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.[25] In some cases, personal requests, rather than clinical need, seem to drive referrals for *BRCA* testing.[25] This could contribute to unnecessary tests which place additional costs on the healthcare system.[25] The number of trained geneticists also appears to be low,[5] 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[16 25] 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.[5] In addition, there is a lack of information about these facilities, leaving some people with significant barriers to access.[7] 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.[3 5 23]

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.[6 7] In addition, data are often unavailable on the centres that provide *BRCA* testing.[5 7]

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,[6 7] and personal requests may sometimes override clinical need in driving referrals.[25]

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.[6 7 10]

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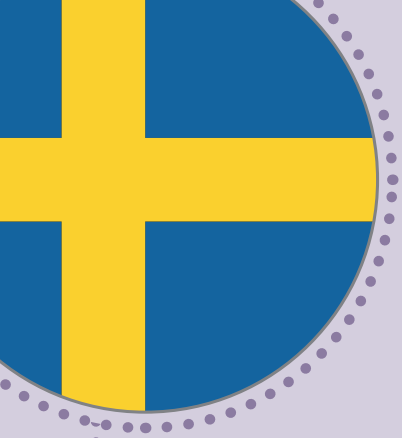

Genetic testing for *BRCA* mutations:

country profile for Sweden

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

- Sweden has the 6th highest incidence rate and the 26th highest mortality rate of female breast cancer in Europe.[1]
- Approximately 2% of breast cancer cases in Sweden are estimated to be associated with *BRCA* mutations.[2]
- Between 50–80% of Swedish women with a *BRCA* gene mutation will develop breast cancer.[3 4]

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

Sweden's national cancer strategy is being applied at the regional level with the aim of improving cancer prevention, while investments are being made on advancing genomic research.

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

In 2009, the Swedish central government launched a national cancer strategy prioritising improved primary prevention and quality of cancer care and equal access to care across the regions.[5] This led to the creation of six regional cancer centres with the aim of better responding to local care needs and encouraging care delivered by multidisciplinary teams.[5 6] These centres have developed activities in collaboration with healthcare providers and the regional health administrations, including breast-cancer-related activities and plans.[6]

Unlike many other European countries, Sweden has not yet implemented a national strategy for rare genetic diseases.[7] In 2011, Nationella Funktionen för Sällsynta Diagnoser (NFSD), the Swedish National Agency for Rare Diseases,[8] was founded. In conjunction with the National Board of Health and Welfare, it developed a national strategy for rare diseases – but this has not yet been officially adopted.[7]

Sweden has four designated centres of excellence which deal with rare and genetic disease, including hereditary breast cancer. Three of these centres are at the Karolinska University Hospital in Stockholm. They include the Centre for Rare Diseases, which is a member of the European Reference Network on Genetic Tumour Risk Syndromes (GENTRIUS), and an Expert Team for Rare Gynaecological Diseases, which is a member of the European Reference Network on Rare Adult Cancers (EURACAN).[9]

There are efforts to advance research and implementation of genomic medicine in Sweden. The multi-stakeholder initiative Genomic Medicine Sweden launched in 2017, with the aim of building new infrastructure to enable the use of novel diagnostics and precision medicine across Sweden. It focuses on people with rare inherited diseases and cancers.[10] In 2011, the large population-based cohort study LifeGene was launched, which aims to analyse biosamples from more than 500,000 participants and follow them up for more than 20 years.[11] Collected data will be used by various research groups, including a cancer working group.[12]

National registries to collect data on *BRCA* genetic testing

Although there are no *BRCA* or rare disease registries at national or regional level, Sweden has a range of disease-specific registries, including for cancer.[7] The National Breast Cancer Quality Register (NKBC) collates data from the regional cancer centres on quality and outcomes of breast cancer care. This includes information on preventive surgery but not on people with *BRCA* mutations.[13]

Legal protection of *BRCA*-mutation carriers

Legislation is in place to ensure data privacy and prevent discrimination based on genetic test results. Doctors are not allowed to talk to anyone about test results or pass them on without the permission of the person being tested. In addition, in most cases, insurance companies are not allowed to request information about pre-symptomatic testing from prospective customers. Genetic counsellors can advise those being tested on the kind of information on genetic testing that insurance companies may request or access. Furthermore, the Association of Swedish Insurers released a statement in 1998 clarifying that insurers would not enquire about genetic test results or use information from results when assessing risks below SEK 250,000 (€24,050 [05/19]).[14]

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

There are no national *BRCA*-specific patient organisations in Sweden and only limited information for people considering a *BRCA* genetic test.

Some information on *BRCA*-related breast cancer is available to those considering testing, but availability varies by region.[15] The limited information available includes a leaflet for people considering *BRCA* genetic testing, published by the Swedish Society of Medical Genetics and Genomics (SFMG) in collaboration with EuroGentest and Genetic Alliance. The leaflet advises on choosing the right time to get a genetic test, privacy rights and available support.[14]

A number of rare disease organisations engage in advocacy, patient information and support. These include Orphanet Sweden,[16] the national competence centre Ågrenska[17] and the patient organisation Riksförbundet Sällsynta diagnoser (Rare Disease Sweden).[18] However, there is no national patient organisation for hereditary breast cancer.[19]

Comprehensive care pathways

Sweden's national breast cancer programme provides comprehensive information for people with *BRCA* mutations at all stages of care. But geographic barriers may limit access to *BRCA* genetic testing, while a severe lack of genetic counsellors may leave some unsupported.

Evidence-based national eligibility criteria for *BRCA* testing

Comprehensive care pathways for those who carry *BRCA* mutations are well integrated in the national breast cancer care programme. This includes recommended criteria for genetic testing.[4] Eligibility criteria for *BRCA* genetic testing are mainly based on age at diagnosis and family history of cancer.[20] The criteria are more inclusive than they were in the past; for example, they now include women with breast cancer below the age of 40, rather than the previous cut-off age of 35, which means more women are now eligible. In addition, all women with ovarian cancer are also eligible for a *BRCA* genetic test.[21] While these recommendations are not mandatory, there seems to be national agreement and most clinicians and oncologists are familiar with them.[20] There may, however, be some regional variation in their implementation.[15]

Equitable and timely access to genetic testing

The Swedish government is investing in improving access to more consistent and timely care. In response to long waiting times for cancer diagnosis and treatment, in 2015 the Swedish government launched Standardised Care Pathways to achieve consistent, timely, high-quality diagnosis and care for cancer patients in all regions. This includes a care pathway for breast cancer which highlights the importance of understanding possible hereditary risk at the point of diagnosis.[22]

People considering *BRCA* testing are usually referred to genetic counselling by their GP, but self-referral is also common.[20 23] One study on referrals to a hospital in Stockholm found that 44% of people self-referred.[24] In these cases, people submit a personal assessment of their cancer-related family history.[24]

All main university hospitals have specialist genetic units that offer assessment, counselling and testing for hereditary cancer. These hospitals are located in Lund, Göteborg, Linköping, Uppsala, Umeå and Stockholm.[25]

Cost is unlikely to be a barrier to accessing genetic testing for *BRCA* mutations in Sweden. In most cases, referral, counselling and *BRCA* genetic testing do not impose any cost on the woman being tested or the clinic which referred her. Utilisation of private genetic testing is low, so the costs of testing should not present a barrier.[15 20]

People who carry *BRCA* mutations may, however, face other barriers in accessing *BRCA* genetic testing.[20] A small study in one region (undertaken before eligibility criteria were relaxed) found that only 18% of breast cancer patients who were retrospectively identified as *BRCA*-mutation carriers had previously been tested for *BRCA* mutations. Restrictive testing criteria, a failure to accurately report or assess family history, and women deciding not to be tested were all contributory factors.[20] The geographic spread of genetics units may also be an access barrier for some women, especially those in remote areas.[15]

Lack of coordination between some genetics and oncology clinics can be a further barrier. Genetics and oncology departments tend to work separately, with people usually visiting a genetics clinic only once or twice.[15] This may limit access to consistent and coordinated care.

Access to genetic counselling

Cancer genetics clinics have integrated genetic counselling into the management of hereditary cancer patients. Pre-test and post-test counselling is mandatory and provided during in-person sessions for individuals or families.[3 26] Post-test counselling includes psychological support by genetic counsellors and psychologists.[14 27] Those who are found to carry *BRCA* mutations are further encouraged to seek help from family members and patient groups.

There is variation between genetics centres in how genetic counselling is practised due to a lack of national standards, registration, licensing, or undergraduate or postgraduate training courses.[15] Genetic counsellors can, however, voluntarily register to be certified by the European Board of Medical Genetics (EBMG) and the SFMG.[26 28 29] The Swedish Professional Association for Genetic Counsellors (SFGV) aims to improve access to standardised training and accreditation,[28] and is developing national standards and a voluntary registration system together with SFMG. However, uptake of this registration scheme to date has been low.[15]

The limited number of genetic counsellors and high administrative workload can limit their ability to directly engage with people wishing to be tested, and cause bottlenecks.[15] The number of genetic counsellors per capita in Sweden is lower than in many other countries such as France, Ireland and the UK.[29]

Modifying the process of genetic counselling in Sweden, however, could help to meet the increasing demand of testing while maintaining quality of the service. Recent studies in Sweden show that new methods, such as telephone counselling or written pre-test information, reach similar satisfaction compared with the standard method of face-to-face counselling sessions before the test, and have the potential to reach more people.[24 30] Currently, however, telephone-based genetic counselling is is not believed to be commonly practised in Sweden.[15]

Follow-up care and support for *BRCA*-mutation carriers

The national breast cancer care programme provides detailed guidance on supporting women with *BRCA* mutations in line with current international best practice. It is, for example, current practice in Sweden to recommend risk-reducing salpingo-oophorectomy (RRSO) at the age of 35–40, depending on parenthood planning.[3] The uptake of RRSO among *BRCA*-mutation carriers has increased steadily, as has the uptake of prophylactic mastectomy, which is estimated to be around 50% in Sweden.[3] In addition to the population-wide mammography screening offered to all Swedish women over 40, carriers of a *BRCA* mutation are offered magnetic resonance imaging (MRI)-based screening from the age of 25 onwards.[3] Chemoprevention is not commonly used as a risk-reducing strategy for *BRCA*-mutation carriers in Sweden.[3]

Improved awareness and knowledge among healthcare professionals

The multidisciplinary SFMG and its cancer genetics working group play a role in training of healthcare professionals.

Hereditary cancers are a priority of the multidisciplinary SFMG, which supports training of healthcare professionals. It established a cancer genetics working group due to an increased demand for genetic tests and a rise in referrals. This group provides training for healthcare professionals and shapes the agenda of the SFMG.[31]

The role of regional patient process leaders (RPPLs) for hereditary cancer has also been established in some regions to improve genetic testing, diagnosis and treatment.[32] In the southern Swedish region, for example, a healthcare professional who is appointed as RPPL is responsible for advocating cancer-genetic health research, facilitating training in hereditary cancer for healthcare professionals and the general public, and reducing inequalities in access to cancer-genetic testing.[33]

Conclusions and recommendations

Sweden's national breast cancer care programme contains detailed guidance on supporting *BRCA*-mutation carriers. This includes clear recommendations on eligibility for *BRCA* genetic testing and for ongoing management and support of those who carry mutations.[4] While these recommendations are not mandatory, they seem to be well-accepted nationally. There are, however, some areas of development that policymakers in Sweden could take into account as they consider how to improve access to high-quality care for *BRCA*-mutation carriers.

Greater recognition and investment in genetic counselling is needed. There are no university-level training courses for genetic counsellors in Sweden, and no requirement for licensing or registration. Furthermore, there are not enough genetic counsellors practising to meet demand, leading to bottlenecks in access to *BRCA* genetic testing.[26] Greater emphasis on strengthening this profession is needed to ensure everyone who needs it has access to high-quality, standardised care. Widening access to innovative approaches such as the use of telemedicine could also play a role.

Robust and up-to-date national and regional data are needed on *BRCA*-mutation carriers to support effective planning. There is no dedicated registry for *BRCA*-mutation carriers, and *BRCA* is not included in the breast cancer registry. A comprehensive *BRCA* registry could be one way of collecting these data and making them available to policymakers as they work to understand the level of care needed for those who carry a *BRCA* mutation, and where gaps exist.

More comprehensive, locally relevant information would support *BRCA* mutation carriers and those considering *BRCA* genetic testing. There are no *BRCA*-specific patient organisations working nationally in Sweden. Although there are organisations providing support to *BRCA*-mutation carriers, this does not seem to be as well developed as in some other European countries. This is limiting the availability of tailored information and support for the general public and *BRCA*-mutation carriers in Sweden.

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Genetic testing for *BRCA* mutations:

country profile for the United Kingdom

Key facts and figures on breast cancer and *BRCA* mutations in the United Kingdom

- The UK has the 5th highest incidence rate and the 15th highest mortality rate of female breast cancer in Europe.[1]
- Between 1.5% and 2% of all breast cancer cases in the UK are due to *BRCA* mutations,[2 3 4] although this rises to around 3–7% among those under 35.[2 3]
- It is thought that 16% of all hereditary breast cancer cases in the UK are associated with *BRCA1* or *BRCA2* mutations.[5]
- 60% of women with a *BRCA1* mutation and 55% of those with a *BRCA2* mutation will develop breast cancer by age 70.[6] This compares to a risk of around 9% among all women by age 74.[7]

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

The UK has a clear strategic vision that recognises the importance of improving the prevention of hereditary cancers, including those related to *BRCA*.

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

The UK has committed to improving early diagnosis and care for patients with rare diseases, including hereditary cancers. In 2013, the Department of Health published a strategy for rare diseases, with input from all four UK countries. The strategy contains 51 commitments which aim to ensure that all people living with rare conditions, including hereditary cancers, have access to the high-quality care and treatment they need. These commitments include supporting and empowering patients, improving awareness and supporting effective coordination among healthcare professionals.[8] Scotland published its implementation plan for this strategy in 2014,[9] Northern Ireland in 2015[10] and Wales in 2017.[11] Scotland recently reported on progress in implementing its plan, highlighting progress in the availability of testing for somatic (acquired) *BRCA1* and *BRCA2* mutations.[12]

Unlike the UK's other countries, England only recently published its implementation plan, following an inquiry from the All-Party Parliamentary Group on Rare, Genetic and Undiagnosed Conditions.[13] The inquiry found that neither National Health Service (NHS) England nor the UK's Department of Health and Social Care was taking responsibility for implementing the strategy, leaving services poorly coordinated and patients unable to access the care they need. The plans for England have now been published[14] but patient support organisations argue that, with only two years until the strategy is due to end, it is time for it to be refreshed.[15]

Despite the lack of a rare diseases plan for England until recently, NHS England has invested heavily in advancing diagnosis for people with genetic disorders. It has, for example, been working in partnership with the private sector to provide quicker and more accurate diagnoses, including for people with hereditary breast cancer. The 100,000 Genomes Project established by Genomics England in 2012 forms part of this ambition. The project has sequenced 100,000 genomes from people with rare diseases and certain cancers, along with their families, in order to help with faster diagnosis and identify the most effective treatments.[16] Northern Ireland, Scotland and Wales have agreements in place so that their citizens can also take part in the project.[17-19]

NHS England is building on this investment by establishing the NHS Genomic Medicine Service, which aims to make genetic testing accessible to all in England. The service is establishing a national genomic laboratory network,[20] a National Genomic Test Directory, 13 Genomic Medicine Centres which provide a clinical service,[21] and a Genomics Unit within NHS England.[22]

National policies support cost-free access to *BRCA* genetic testing and personalised follow-up care

Genetic testing, care and follow-up for those eligible is fully funded by the NHS.[22] Cost is therefore unlikely to be a barrier for people considered at high risk.

National registries to collect data on *BRCA* genetic testing

There appear to be very few recent, national data on *BRCA* mutations, which may be hampering effective policymaking and planning. There seem to be no comprehensive registries collecting data on *BRCA* mutations. The Cancer Variant Interpretation Group (C-VIG), however, is an initiative delivered through Genomics England which draws on *BRCA*-mutation data from laboratories across England to discuss and classify specific variants.[23] In addition, there are plans to roll out the National Hereditary Cancer Registry in England, which would focus initially on *BRCA* mutations.[24]

Legal protection of *BRCA*-mutation carriers

Anti-discrimination legislation in the UK does not cover discrimination based on genetic predisposition for disease. In 2002, the statutory body charged with monitoring the Disability Discrimination Act (now absorbed into the Equality Act 2010) recommended the Act be extended to cover people who have a genetic predisposition. This would have made it illegal for an employer to require an individual to undergo a genetic test; however, the extension has not yet been adopted.[25] [26] The issue of genetic discrimination has continued to been debated, including during a seminar organised by the Human Genetics Commission, but a gap in legislation remains.[26]

Insurance companies in the UK have, however, signed up to a voluntary code of practice to protect people from genetic discrimination. The UK Government and Association of British Insurers have an agreement in place which features a number of commitments, including not treating an applicant differently based on test results or requiring an applicant to share results of a predictive test, except in certain cases, for example where life insurance cover exceeds £500,000. It also prevents insurance companies from imposing conditions, exclusions or disproportionate terms based on genetic test results.[27] The code does not, however, prevent insurance companies from requesting information regarding an individual's family history, or acting on this information.[28] Despite these gaps in legislation, an expert interviewed for this country profile noted that few, if any, cases of discrimination have occurred in the UK.[28]

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

Awareness of *BRCA* mutations has been raised through the efforts of patient organisations and media reporting.

A number of breast cancer advocacy groups have focused efforts on raising awareness about *BRCA* gene mutations, and support people who may be considering testing. *BRCA* Umbrella, for example, works to raise awareness of *BRCA* mutations and supports those who may be considering or undergoing testing. It provides an online community of *BRCA*-mutation carriers by encouraging conversation, support and information-sharing.[29] Other organisations that are active in promoting awareness include the National Hereditary Breast Cancer Helpline and Breast Cancer Now.

The media also have a powerful role in improving awareness – as was demonstrated when actress Angelina Jolie spoke openly about her *BRCA* test results. One study estimated that related media coverage led to a tenfold increase in calls to the UK's National Hereditary Breast Cancer Helpline. This, in combination with reporting on changes to eligibility criteria for testing, is thought to have contributed to a 2.5-fold increase in referral rates for *BRCA* testing compared with the same period in the previous year.[30]

Comprehensive care pathways

The UK has clear eligibility criteria and referral pathways for genetic testing, but inequalities in access persist.

Evidence-based national eligibility criteria for *BRCA* testing

The UK has comprehensive guidelines to support the diagnosis, care and management of women who carry a *BRCA* mutation. These guidelines, published by the National Institute for Health and Care Excellence (NICE) in 2013,[31] are used across the UK, are well regarded internationally and are referred to by the European Society for Medical Oncology (ESMO) 2016 guidelines.[32] The NICE guidelines include information on eligibility for genetic testing, referral pathways, taking a family history and providing information and support to those undergoing testing.[31]

Recommendations regarding eligibility for *BRCA* genetic testing have recently been expanded. Guidelines for the management of patients with early or locally advanced breast cancer were published by NICE in 2018. These recommend that all women in England with triple-negative breast cancer under the age of 50 are tested for *BRCA* mutations, regardless of family history.[33] In addition, in Scotland, all women with high-grade ovarian cancer, regardless of their age, have access to *BRCA* genetic testing.[34]

Equitable and timely access to genetic testing

Despite clear eligibility criteria, *BRCA* genetic testing is not being offered to all those in the UK who are eligible. Estimates suggest that there is a gap of over 3,000 women every year who undergo a risk assessment and are eligible for a *BRCA* test but are not offered it.[35] It is likely that, with advances in technology and the ability to identify personalised treatment based on genetic-testing results, the number of people accessing genetic testing will increase.[36]

These gaps in testing are compounded by lower referral rates for women from minority ethnic groups.[37] There are many reasons for this (see *Box 1*). Among South Asian communities, for example, some female patients have reported that discussing breast cancer with male practitioners was difficult and embarrassing. These women and their families may associate cancer with stigma and death, which may make them reluctant to raise the subject with other family members.[38 39]

Box 1 | What are the reasons for lower genetic testing rates among black and minority ethnic women?[37-39]

- Lack of awareness of testing
- Language difficulties and challenges around cross-cultural communication
- Limited awareness of support services available, including genetic counselling
- Culturally held beliefs about breast cancer and stigma related to the condition, which also influence communication with family members

There is also geographic variation in *BRCA* genetic testing throughout the UK. The number of *BRCA* tests performed is lower in England than in Scotland (see *Table 1*). There is also wide variation within England, with some regions such as Yorkshire and the Humber having particularly low rates of *BRCA* testing.[40] Understanding the reasons behind these differences will be critical in ensuring that access to genetic testing services is more evenly spread across the UK.

Table 1 | *BRCA* genetic testing provision across the UK

Country	Number of BRCA genetic tests per 100,000 women in 2016/17[40]	Number of laboratories offering genetic tests for familial breast/ovarian cancer[41]
England	54.2	16
Scotland	69.8	4
Northern Ireland	Data not available	1
Wales	Data not available	1

Two laboratories in the UK, both of which are in England, test samples against a panel of genes.[41] Panel tests for hereditary breast cancer test for mutations in 13 genes associated with an elevated risk of breast and ovarian cancer, using whole-gene sequencing. These laboratories provide results within 42–112 days depending on urgency.[42 43] Panel tests for known mutations in family members, however, take 14 days.[43]

Testing samples against a larger number of genes, however, runs the risk of leading to more uncertain results and greater anxiety. Genetic tests that identify mutations which are new or have an unknown association with cancer risk are referred to as variants of unknown significance (VUS). The VUS rate for *BRCA1/BRCA2* testing is less than 1%, but this increases to 14% when panel testing is used. This has implications for those being tested, who are likely to experience more stress and anxiety than with a more definite result.[44 45] In the longer term, however, more mutations will be identified and the proportion classified as unknown should reduce.

Role of private genetic-testing providers

Although genetic testing, care and follow-up for those who are eligible is fully funded by the NHS, private testing is also available, including for those who are not eligible for a test through the NHS or who do not want to wait. Although data are not available on the number of *BRCA* tests being delivered by private laboratories, experts suggest uptake of private *BRCA* genetic testing is low.[36] Private testing providers include those providing clinical genetic testing services and those that offer direct-to-consumer (DTC) testing. DTC testing is not regulated in the same way as genetic testing in clinical settings.[46] This can mean DTC providers test different, or fewer, mutations than the NHS and may not provide genetic counselling along with their results, potentially leaving people unsupported.[47]

Access to genetic counselling

Appropriate genetic counselling is an essential component of care for those eligible for *BRCA* testing. NICE guidelines recommend that all who are eligible for *BRCA* genetic testing are referred to genetic counselling teams for (preferably) two sessions of pre-test counselling.[31] Genetic counsellors provide support to those being tested as well as their families, to help them understand their breast cancer risk and options available to them.[31]

Psychosocial support following test results is critical. Despite this, psychological support may not always be provided as part of genetic counselling for those undergoing *BRCA* testing. In one survey undertaken by Ovarian Cancer Action, 42% of women who were tested and found to have a *BRCA* mutation received no counselling or support after they received their results.[48]

The UK has one of the highest numbers of genetic counsellors per capita globally. Currently there are around 310 genetic counsellors for the UK population of 60 million.[49] To support genetic counsellor development, the UK has three accredited master's programmes which train around 40 genetic counsellors per year and now include genomics.[50] This number includes 10–20 who are trained in England as part of the Scientist Training Programme (STP). Inclusion in the STP means they are included in NHS workforce planning, and will be awarded statutory regulation as clinical scientists when this is established in 2019.[49 51 52]

Unlike in many other countries in Europe, genetic counsellors in the UK are qualified to work independently or as part of a multidisciplinary team. Registration for genetic counsellors in the UK is voluntary and most work in regional genetics centres or associated outreach clinics.[49]

Despite the higher numbers of genetic counsellors compared with other countries, there are still not enough to meet demand and waiting times can be long in some areas.[36 48] This creates a significant bottleneck, slowing access to *BRCA* genetic testing.[53]

Follow-up care and support for *BRCA*-mutation carriers

Those who receive a positive result from a *BRCA* genetic test and do not have breast cancer have three main options available to them for reducing their risk of developing the disease: surgery, hormonal therapy, and changes to lifestyle coupled with surveillance. Although national data are not available on the extent to which different options are selected, studies have found that 34–40% of asymptomatic women who carry a *BRCA* mutation undertake preventive double mastectomies.[54 55] Uptake of chemoprevention in England is low, with a recent study suggesting that around 15% of women with a *BRCA* mutation initiate this therapy.[56]

Improved awareness and knowledge among healthcare professionals

The UK is investing in improving the genetics knowledge of healthcare professionals who are not genetics specialists.

Gaps in knowledge about *BRCA* testing among non-genetic-specialist healthcare professionals may play a role in lower-than-optimal referral rates and uptake of genetic testing. In a primary-care-driven health system such as the UK, GPs play an important role in addressing patients' initial enquiries and referring them to appropriate specialist genetic services to gather further information on family history, or for testing.[57] Yet a 2006 survey of GPs found that, while they felt genetics was an important topic for practice, they did not believe they had adequate knowledge to best guide their patients.[58]

Other factors may also impact on low rates of referral from primary care to specialist genetics services. These include time constraints and lack of experience in making a referral to a genetics specialist.[59] Poor communication between non-genetic-specialist healthcare professionals and people at risk of *BRCA* mutations may also create a barrier for people in seeking genetic testing, which is exacerbated in those who do not speak English as a first language.[38]

There is evidence that breast cancer specialists may feel uncertain about how to interpret *BRCA* test results or know what guidance to give their patients. For example, in a 2015 survey of 155 breast cancer specialists, 12% reported not having received any genetics training. In the same study, although 95% of the breast cancer specialists surveyed had referred patients for *BRCA* genetic tests, 71% felt unsure about the clinical implications of the test reports presented.[60] Clinicians seemed to particularly struggle to understand and communicate the clinical implications of results when there was no family history of breast cancer.[60]

Health Education England is aiming to address these knowledge gaps by developing the £20 million Genomics Education Programme (GEP) to build knowledge of genetics among healthcare professionals. The GEP is funding 500 master's places and additional healthcare science training places, and provides access to a range of genetics educational resources and tools for healthcare professionals, including for those working in primary care.[61]

Conclusions and recommendations

People with *BRCA* mutations in the UK are supported by comprehensive clinical guidelines, strong patient support organisations and well-developed services. Furthermore, existing policy initiatives seek to improve early detection for people with rare and genetic cancers.[8] Despite this, there are several gaps which must be addressed to ensure that all *BRCA*-mutation carriers have access to the comprehensive care and support they need.

Genetic testing services and information must be tailored to ensure they are accessible to all, regardless of location or ethnic background. Geographic and ethnic inequalities in awareness of and access to genetic testing[37-41] are a serious concern in the UK and must be addressed.

Plans are needed to manage the increasing demand for *BRCA* testing, to ensure that all *BRCA*-mutation carriers can access a timely genetic test and be supported as they manage their results. As treatments for *BRCA*-related breast cancer become available, demand for genetic testing is likely to increase, putting strain on existing infrastructure and workforce. Scrutiny is needed to ensure that services can keep up with this rising demand.

Greater efforts are required to ensure that everyone with a *BRCA* mutation is able to access the full range of care they need, including psychosocial care both before they are tested and following their results. The UK has one of the highest numbers of genetic counsellors per capita,[49] but waiting times vary and not all women receive the psychological support they need as part of their genetic counselling.[48]

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