The Health Policy Partnership

Genetic testing for *BRCA* mutations:

country profile for Israel

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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]

Introduction

Mutations in the *BRCA1* and *BRCA2* genes put women at significant risk of developing breast cancer. Based on international data, it is thought that most women have a 12.5% risk of developing breast cancer in their lifetime. This risk increases to 60–90% among women with a *BRCA1* mutation and 45–85% among women with a *BRCA2* mutation.[7-9] Breast cancers related to *BRCA1* mutations are more likely to be triple-negative breast cancer, which is difficult to treat.[10]

It is important for women to know whether they carry a *BRCA* mutation. *BRCA*-mutation carriers who are asymptomatic can be supported to make an informed choice to reduce their risk of developing breast cancer through, for example, preventive surgery and, in some countries, chemoprevention. They can also reduce their chance of breast cancer mortality through regular monitoring which can pick up earlier cases of the disease. Knowing whether a woman with breast cancer carries a *BRCA* mutation can also help to inform decisions around treatment and surgery. In addition, identifying *BRCA*-mutation carriers allows for family members to be tested.[11]

Men can also benefit from knowing they carry a *BRCA* mutation. *BRCA* mutations can increase the risk of prostate and other cancers, so men with identified mutations can be closely monitored for early signs of the disease.[12] In addition, men who carry a *BRCA* mutation can pass it on to their daughters.

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

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

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

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

National 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,[13] 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.[14 15]

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.[16]

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.[17] 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*).[18]

Box 1 | BRACHA: Israel's patient education and advocacy organisation[5 14 18 19]

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.[20-22] This may be a reflection of the stigmatisation of breast cancer within some sections of these communities.[23 24] Understanding and knowledge seem to be rising, however,[21 22 25] with non-profit organisations such as BRACHA and the Mariam Foundation, which works with Arab communities, raising awareness and addressing misconceptions surrounding cancer.[14 26]

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.[27] 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.[28]

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.[29] 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.[14]

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;[30] it is estimated that this would identify around an additional 24,000 *BRCA*-mutation carriers compared with current criteria.[31] 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.[14 32]

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.[33] Despite this, waiting times for genetic tests can be long, with some people waiting up to a year for their test.[34]

***BRCA* genetic testing was expanded in 2013 to include testing for the 14 most common mutations among the Israeli population.**[35] 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.[36] 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.[14]

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 have some bearing on this.[24 25] However, women in these communities do seem to be increasingly accessing *BRCA* genetic testing services.[14]

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.[22] 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.[37] 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.[14]

Access to genetic counselling

Pre- and post-test genetic counselling is supposed to be offered to all those who undergo *BRCA* testing in Israel.[37] After they have received their result, a genetic counsellor – either working under the supervision of a medical geneticist,[38] 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.[37] 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.[14]

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.[38] 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.[38]

Genetic counsellors in Israel are licensed and regulated by the Ministry of Health but must work under the supervision of a medical geneticist.[38] This limits their ability to act independently and may contribute to a perception of low status by other healthcare professionals.[14]

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[39] and include periodic examination, annual magnetic resonance imaging (MRI) in addition to ultrasound or mammography, blood tests and clinical consultations.[40]

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.[17] [41] [42] 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.[43]

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.[44] 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.[43]

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[45] and bone loss (among women who have undergone risk-reducing salpingo-oophorectomy).[46]

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 17] which is lower than the average for Western Europe.[47] 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.[14] Other factors such as a women's age at study entrance, family history, personal experiences and other subjective data may also be relevant.[36]

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.[48] Evidence from other countries suggests that knowledge among non-genetic specialists is often low and that this contributes to low referrals for testing.[49 50] Experts suggest this situation also applies in Israel,[14] 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.[14] 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.[14]

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.[33] Furthermore, people in Israel who are considering genetic testing are supported by BRACHA, a dynamic and active patient support and advocacy organisation.[18] 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,[28] 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.[49 50] 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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