The Health Policy Partnership

Genetic testing for *BRCA* mutations:

country profile for France

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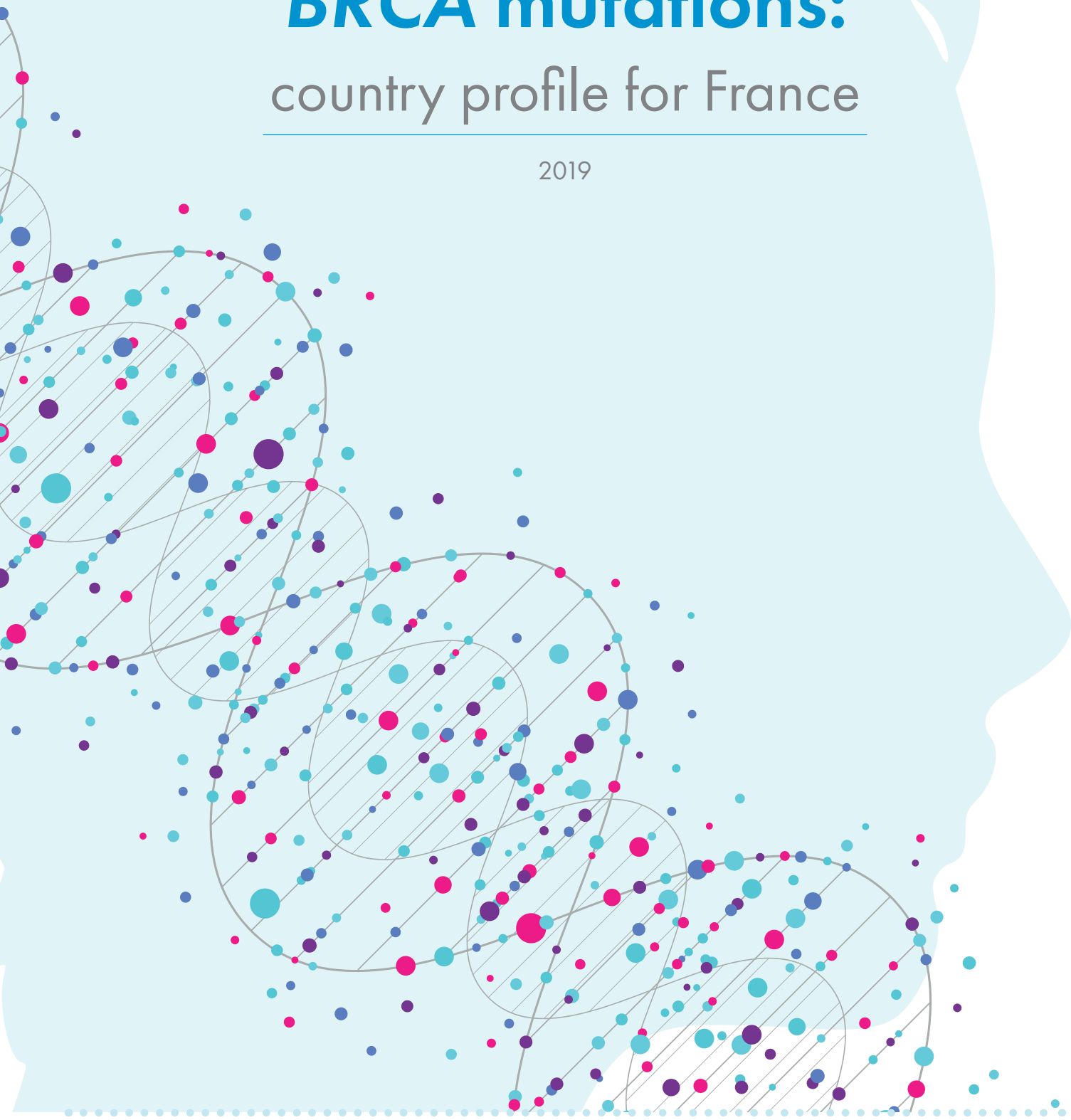

Pfizer Oncology

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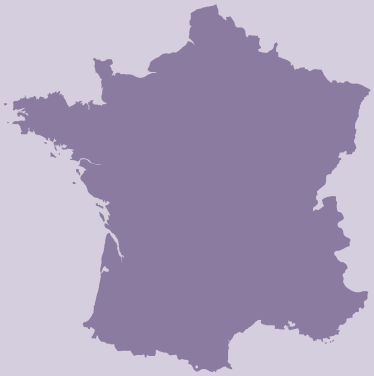
Key facts and figures on breast cancer and *BRCA* mutations in France

- 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]



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.[8-10] Breast cancers related to *BRCA1* mutations are more likely to be triple-negative breast cancer, which is difficult to treat.[11]

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.[12]

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.[13] 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 France 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

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,[14] while a national plan for rare diseases has also been developed.[15]

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.[16]

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.[17] 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.[17] 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[18] via their doctor.[19]

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

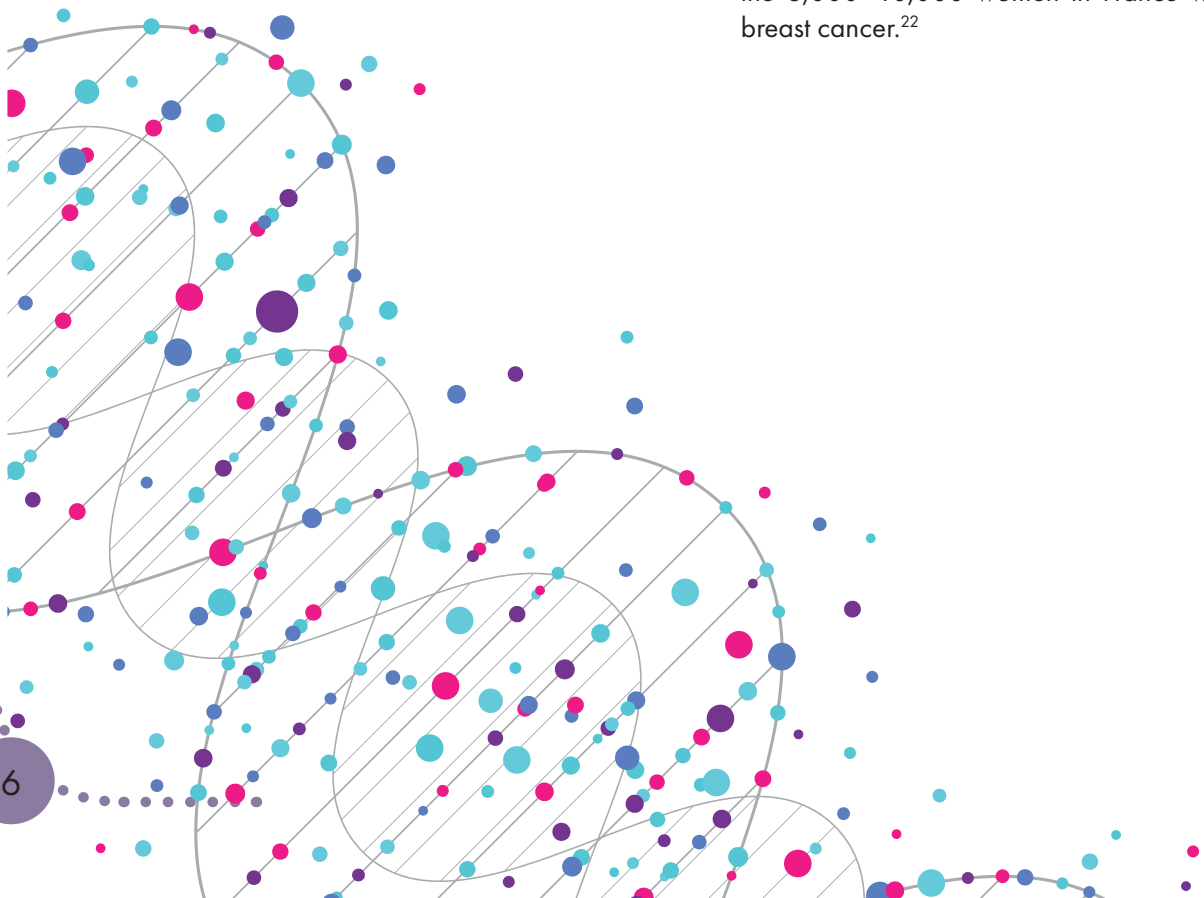
A number of patient organisations are working to raise awareness of *BRCA* mutations and advocate for improvements in care.

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.[20]

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.[21]

***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.[22]



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.[23] 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.[24]

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.[25]

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.[26]

Supporting oncologists to take a more active role in prescribing genetic tests for cancer patients may streamline this pathway and reduce waiting times.[24] 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.[27] Guidance is being developed and shared with these healthcare professionals to ensure the advice of geneticists is included in the genetic testing pathway.[24 26]

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.[28] This network has developed a set of guidelines for screening, prevention and genetic counselling for multigene panel testing for breast and ovarian cancer.[29] 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.[30]

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.[24 26]

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.[31]

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.[32] This gives the role more credibility as it is defined by its own governance structure, rather than by overarching healthcare professional governance.[33]

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,[34] although discussions are underway to potentially double this capacity.[26]

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:[25 35]

- 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.[36] Conversely, the uptake of prophylactic salpingo-oophorectomy is similar to other countries.[37]

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.[26]

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.[37] 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.[26]

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.[39] In addition, a DIU (diploma interuniversity) dedicated to cancer predispositions has been established to train students who are mainly oncologists, geneticists and genetic counsellors.[40]

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.[23 35] 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.[24]

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,[26] including those who are not genetic specialists, such as GPs and gynaecologists.

References

1. European Cancer Information System. 2018. Estimated of cancer incidence and mortality in 2018, for all countries. Available from: https://ecis.jrc.ec.europa.eu/explorer.php?$0-0$1-All$4-2$3-29$6-0,14$5-2008,2008$7-8$2-All$CEstByCountry$X0_8-3$X0_19-AE28E$X0_20-No$CEstRelative$X1_8-3$X1_9-AE28$X1_19-AE28E$CEstByCountryTable$X2_19-AE28E [Accessed 26/11/18]
2. Institut national du cancer. n.d. Prédispositions génétiques. Available from: https://www.e-cancer.fr/Patients-et-proches/Les-cancers/Cancer-du-sein/Facteurs-de-risque/Predispositions-genetiques#toc-mutation-des-g-nes-brca1-et-brca2 [Accessed 30/10/18]
3. Institut national du cancer. 2019. *Oncogénétique en 2017/consultations et laboratoires.* Boulogne-Billancourt: Institut national du cancer
4. Bredart A, Anota A, Dick J, *et al.* 2018. Patient-Centered Care in Breast Cancer Genetic Clinics. *Int J Environ Res Public Health* 15(319): 1-16
5. Institut national du cancer. 2017. *Femmes porteuses d'une mutation de BRCA1 ou BRCA2 / Détection précoce du cancer du sein et des annexes et stratégies de réduction du risque.* Boulogne-Billancourt: Institut national du cancer
6. Janavicius R. 2010. Founder BRCA1/2 mutations in the Europe: implications for hereditary breast-ovarian cancer prevention and control. *EPMA J* 1(3): 397-412
7. Stanford Health Care. Founder's Effect - Cancer Genetic. Available from: https://stanfordhealthcare.org/medical-conditions/cancer/hboc/founders-effect.html [Accessed 11/06/2018]
8. National Cancer Institute. 2017. BRCA1 and BRCA2: Cancer Risk and Genetic Testing. Available from: https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet [Accessed 08/04/19]
9. Ovarian Cancer Action. 2017. *Acting on BRCA: Breaking down barriers to save lives.* London: Ovarian Cancer Action
10. The Royal Marsden. 2016. *A beginner's guide to BRCA1 and BRCA2.* London: The Royal Marsden NHS Foundation Trust
11. Bayraktar S, Gutierrez-Barrera AM, Liu D, et al. 2011. Outcome of triple-negative breast cancer in patients with or without deleterious BRCA mutations. *Breast Cancer Research and Treatment* 120(1): 145
12. McCarthy AM, Armstrong K. 2014. The Role of Testing for BRCA1 and BRCA2 Mutations in Cancer Prevention. *JAMA Internal Medicine* 174(7): 1023-24
13. Cavanagh H, Rogers KMA. 2015. The role of BRCA1 and BRCA2 mutations in prostate, pancreatic and stomach cancers. *Hereditary Cancer in Clinical Practice* 13(1): 16-16
14. Institut National du Cancer. 2014. *National Cancer Institute: Driving progress in cancer control.* Boulogne-Billancourt: Institut National du Cancer
15. Ministère des Solidarités et de la Santé. 2018. Les maladies rares. Available from: http://solidarites-sante.gouv.fr/soins-et-maladies/prises-en-charge-specialisees/maladies-rares/article/les-maladies-rares [Accessed 23/05/2018]
16. Alliance Nationale pour les Sciences de la Vie et de la Santé. 2016. *Genomic Medicine France 2025.* Paris: Alliance Nationale pour les Sciences de la Vie et de la Santé
17. Eisinger F, Fabre R, Lasset C, *et al.* 2012. Spontaneous disclosure of BRCA1/2 genetic test results to employers: a French prospective study. *Eur J Hum Genet* 20(9): 981-3
18. BRCA France. 2018. Cancer du sein ou de l'ovaire, gène, risque et suivi BRCA. Available from: https://www.brcafrance.fr/suivi-brca/ [Accessed 29/05/2018]
19. Bignon Y-J. 2015. Questions éthiques choisies en oncogénétique. *Journal international de bioéthique et d'éthique des sciences* 26(3): 215-25
20. BRCA France. Homepage. Available from: www.brcafrance.fr [Accessed 15/05/2018]
21. Geneticancer. Home page. Available from: http://geneticancer.org/ [Accessed 17/12/18]
22. Le Figaro. 2017. Cancer du sein: pour un dépistage génétique. Available from: http://sante.lefigaro.fr/article/cancer-du-sein-pour-un-depistage-genetique/ [Accessed 22/05/2018]
23. Haute Autorite Sante. 2014. *Dépistage du cancer du sein en France : identification des femmes à haut risque et modalités de dépistage Volet 2.* Saint-Denis: HAS
24. Pujol P. 2018. Interview with Sandra Evans at The Health Policy Partnership [Telephone]. 03/07/18
25. Institut National du Cancer (INCa). 2017. *Le dispositif national d'oncogénétique - Oncogénétique et plateformes de génétique moléculaire.* Boulogne-Billancourt: INCa
26. Stoppa-Lyonnet D. 2018. Interview with Sandra Evans at The Health Policy Partnership [Telephone]. 23/07/18
27. Colas C, Golmard L, de Pauw A, *et al.* 2019. "Decoding hereditary breast cancer" Benefits and questions from multigene panel testing. *The Breast* DOI: 10.1016/j.breast.2019.01.002:
28. Unicancer. Cancer and Genetic Group. Available from: http://www.unicancer.fr/en/cancer-and-genetic-group [Accessed 26/02/2019]
29. Moretta J, Berthet P, Bonadona V, *et al.* 2018. The French Genetic and Cancer Consortium guidelines for multigene panel analysis in hereditary breast and ovarian cancer predisposition. *Bulletin du Cancer* 105(10): 907-17
30. Beroud C, Letovsky SI, Braastad CD, *et al.* 2016. BRCA Share: A Collection of Clinical BRCA Gene Variants. *Human Mutation* 37(12): 1318-28
31. Institut National du Cancer (INCa). 2017. *Un suivi adapté - Oncogénétique et plateformes de génétique moléculaire.* Boulogne-Billancourt: INCa
32. Cordier C, Taris N, De Pauw A, *et al.* 2013. French professionals in genetic counselor careers. *J Genet Couns* 22(6): 844-8
33. Cordier C, Lambert D, Voelckel MA, *et al.* 2012. A profile of the genetic counsellor and genetic nurse profession in European countries. *J Community Genet* 3(1): 19-24
34. Abacan M, Alsubaie L, Barlow-Stewart K, *et al.* 2018. The Global State of the Genetic Counseling Profession. *Eur J Hum Genet* 27(2): 183-97
35. Institut National du Cancer. 2017. Dépistage du cancer du sein : orienter vos patientes en fonction de leur niveau de risque - Dépistage du cancer du sein. Available from: http://www.e-cancer.fr/Professionnels-de-sante/Depistage-et-detection-precoce/Depistage-du-cancer-du-sein/Orienter-vos-patientes [Accessed 11/06/2018]
36. Julian-Reynier CM, Bouchard LJ, Evans DG, *et al.* 2001. Women's Attitudes toward Preventive Strategies for Hereditary Breast or Ovarian Carcinoma Differ from One Country to Another Differences among English, French, and Canadian Women. *American Society of Human Genetics* 92(4): 959-68
37. Julian-Reynier C, Mancini J, Mouret-Fourme E, *et al.* 2011. Cancer risk management strategies and perceptions of unaffected women 5 years after predictive genetic testing for BRCA1/2 mutations. *European Journal of Human Genetics*19(5): 500-06
38. Ministre des solidarités et de la santé. 2015. Order of December 8, 2015 establishing the list of national orientations for the continuous professional development of health professionals for the years 2016 to 2018. Available from: https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000031632884&categorieLien=id [Accessed 08/04/19]
39. Universite Montpellier. Diagnostic de précision et médecine personnalisée. Available from: https://du-diu-facmedecine.umontpellier.fr/diplome-diagnostic-de-precision-et-medecine-personnalisee-162 [Accessed 17/12/18]
40. Universite Paris Descartes. Oncogenetic IUD. Available from: http://www.scfc.parisdescartes.fr/index.php/descartes/formations/medecine/oncologie-hematologie/diu-oncogenetique/(language)/fre-FR [Accessed 16/01/19]