From savvy consumers to informed risk managers: Shifting images of medical self-care

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Abstract

In February 1889, a 26 year-old Brooklyn woman, Ida Hunt, was told by a well-known surgeon, Mary Dixon Jones, that she suffered from an internal tumor that may burst and put her life in danger. Upon Dixon Jones's advice Hunt underwent an abdominal surgery, developed a peritonitis and died. The Brooklyn newspaper, *The Eagle*, used Hunt's death to mount a campaign against Dixon Jones, accusing her of being a knife happy, sadistic and corrupted practitioner, who persuaded naive women to undergo unnecessary and risky operations. In fact, Hunt was a savvy consumer of medical services, who consulted numerous doctors for her severe gynecological complaints, carefully evaluated her options, and in all probability elected Dixon Jones precisely because she advocated radical surgical solutions.

In 2008, the company *23andMe* included mutations in BRCA genes which predispose for breast and ovarian cancer in their "health package". The company's experts gathered testimonies from grateful clients who found out unexpectedly that they were BRCA mutation carriers and decided to undergo prophylactic surgeries (ablation of ovaries, and, for some, mastectomy). *23andMe* lost in 2013 the right to propose health information in the US, but in the same year the *American College of Medical Genetics and Genomics* (ACMG) recommended to include BRCA mutations among incidental findings that should be reported to patients. This recommendation, and the 2014 proposal to generalize the testing for BRCA mutations, were made in spite of lack of firm data on efficacy of preventive measures to reduce cancer deaths in mutation carriers, especially those without a family history of breast and ovarian malignancies. People, advocates of BRCA testing argue, have the right to know about their health risks in order to be able to make informed decisions about their management. This article takes these two cases as a starting point of reflections on continuity and change in self-care practices, with an accent on their gendering.

Keywords

Genetics, breast cancer, BRCA mutations, personal genomics.

Des consommateurs avides de savoir aux gestionnaires de risques éclairés : images changeantes du soin de soi dans le paysage médical

Résumé

Au mois de février 1889, Ida Hunt, une jeune femme du quartier de Brooklyn âgée de 26 ans, apprend par la chirurgienne de renom Mary Dixon Jones qu'elle est atteinte d'une tumeur susceptible de se propager et d'engager son pronostic vital. Sur les conseils de Mary Dixon Jones, Hunt subit une laparotomie, mais contracte une péritonite et meurt. *The Eagle*, le journal de Brooklyn, instrumentalise la mort de Hunt pour lancer une campagne contre Dixon Jones en l'accusant d'être une folle du scalpel et une chirurgienne sadique et corrompue ayant persuadé des femmes naïves de subir des opérations risquées et inutiles. En réalité, Hunt était une avide consommatrice de services médicaux qui avait consulté plusieurs spécialistes en se plaignant de sérieux problèmes gynécologiques ; elle avait ensuite envisagé soigneusement toutes les possibilités qui lui étaient offertes et avait vraisemblablement choisi Dixon Jones parce que celle-ci prônait précisément des solutions chirurgicales radicales.

En 2008, la société *23andMe* a intégré dans son « offre de santé » les mutations des gènes BRCA prédisposant aux cancers du sein et des ovaires. Les experts de cette société ont recueilli des témoignages de clientes reconnaissantes ayant pris la décision de subir une intervention prophylactique (ablation des ovaires, et, pour certaines, maséctomie) après avoir découvert, par hasard, qu'elles étaient porteuses de mutations des gènes BCRA. En 2013, *23andMe* a perdu le droit de proposer de l'information médicale aux États-Unis, mais, la même année, l'*American College of Medical Genetics and Genomics* (ACMG) a préconisé d'inclure les mutations BRCA dans les découvertes fortuites qui doivent être communiquées aux patients. Cette préconisation ainsi que la proposition de généraliser les tests sur les mutations BCRA, datant de 2014, ont été faites malgré l'absence de données précises sur l'efficacité de mesures préventives visant à réduire les décès suite à un cancer chez les porteuses de ces mutations ; en particulier en l'absence d'un historique familial sur les tumeurs malignes au niveau des ovaires ou du sein. Comme l'avancent les partisans des tests sur les BRCA, les personnes intéressées ont le droit de connaître les risques liés à leur santé afin de faire des choix éclairés pour mieux la gérer. Cet article prend appui sur ces deux études de cas pour proposer une réflexion sur les pratiques du soin de soi, entre rupture et continuité, en insistant sur leurs caractéristiques en terme de genre.

Mots-clés

Génétique, cancer du sein, mutation BRCA, génomique personnelle.

De consumidores inteligentes a gestores de riesgos informados: cambiando imágenes de auto-cuidado médico

Abstract

En febrero de 1889, Ida Hunt, una mujer de 26 años de Brooklyn, fue diagnosticada por una conocida cirujana mujer, Mary Dixon Jones, con un tumor interno que podría explotar y poner su vida en riesgo. Bajo el consejo de Dixon Jones, se le realizó una laparotomía a Hunt, quien desarrolló una peritonitis y murió. *The Eagle*, el diario de Brooklyn, utilizó la muerte de Hunt para montar una campaña contra Dixon Jones, acusándola de ser una médica entusiasta, sadística y corrupta que persuadía a mujeres ingenuas de realizarse operaciones innecesarias y riesgosas. De hecho, Hunt era una entendida consumidora de servicios médicos, que consultaba numerosos doctores debido a sus severas quejas ginecológicas, evaluaba cuidadosamente sus opciones, y en toda probabilidad había elegido a Dixon Jones precisamente porque advocaba por soluciones quirúrgicas drásticas.

En 2008, la compañía *23andMe* incluyó en su "paquete de salud" mutaciones para genes que predisponen al cáncer de mama y de ovario. Los expertos de la compañía recolectaron testimonios de clientes agradecidos que habían descubierto inesperadamente que eran portadores de la mutación de BRCA y habían decidido realizar cirugías profilácticas (ablación de ovarios y, en algunos casos, mastectomías). En 2013, *23andMe* perdió el derecho a ofrecer información médica en los Estados Unidos, pero el mismo año el *American College of Medical Genetics and Genomics* (ACMG) recomendó incluir las mutaciones BCRA entre los resultados incidentales que deberían ser reportados a los pacientes. Esta recomendación, y la propuesta de 2014 de generalizar el test para las mutaciones BRCA, fueron hechos a pesar de la falta de datos firmes respecto de la eficacia de las medidas preventidas para reducir las muertes por cáncer en los portadores de mutaciones, especialmente en el caso de aquellos sin una historia familiar de malignidades ováricas o de mama. Quienes argumentan a favor del test BCRA argumentan que las personas tienen derecho a conocer sus riesgos de salud para poder así tomar decisiones informadas sobre cómo gestionarlos. Este artículo toma estos dos casos como punto de partida de una reflexión sobre las continuidades y cambios en las prácticas de autocuidado, con acento en su generización.

Palabras clave

Genética, cáncer de mama, mutaciones BRCA, genómica personalizada.

1. Introduction: "Ida Hunt's last ride" as a case of medicalization of the female body?

In the night of February 14th, 1889, a carriage left the Women's Hospital of Brooklyn, bringing a recently operated 26 year-old housewife, Ida Hunt, to her home. The night was described as exceptionally cold, with a snow blizzard, and Ida Hunt was desperately sick. Hunt, who suffered from various crippling ailments, consulted Mary Dixon Jones (1828-1908), the hospital's director who was also a reputed surgeon – in a time where few women ventured into surgery. Dixon Jones diagnosed a tumor ready to burst, told Hunt that she was at risk of severe aggravation of her condition, and proposed an immediate operation. Hunt, who previously consulted several physicians, who were unable to help her, agreed. She underwent an abdominal surgery (laparoctomy), but alas developed peritonitis, at that time, an incurable condition. Her family insisted later that Dixon Jones expelled a dying woman to avoid a death on the ward. Dixon Jones strongly rejected this accusation and claimed that Hunt insisted on going back home despite Dixon Jones's advice against it (Morantz-Sanchez, 2000).

"Ida Hunt's last ride" became a rally cry of the campaign conducted by the newspaper *The Brooklyn Eagle*. Hunt was described in this campaign as a naïve young woman who had become a prey of a sadistic and knife happy female surgeon. A few weeks after the Eagle made Hunt's story public, Mary Dixon Jones was indicted for manslaughter. But when the criminal case went to trial a year later, the newspaper was compelled to re-examine the version of the story it published in 1889. Testimony revealed that Hunt had been chronically ill since early in her marriage, and the real cause of her poor health might well had been a venereal disease she contracted from her significantly older husband. After a brief deliberation, the jury pronounced the doctor not guilty, but Dixon Jones' reputation was severely harmed. The harm was aggravated by the fact that she lost her attempt to sue *The Brooklyn Eagle* for slander. Dixon Jones was obliged to abandon her job at the Women's Hospital, and left surgery altogether.

Regina Morantz-Sanchez fascinating book, *A Conduct Unbecoming for a Woman* focuses on Dixon Jones's trials. Morantz-Sanchez uses these trials to illustrate the tribulations of women pioneers of medicine (Morantz-Sanchez, 1999). This text focuses on different aspects of Dixon Jones/Hunt's story: patients' active role in seeking diagnoses and cures, and treatment of cancer. Regina Mordant Sanchez's historical study indicated that Ida Hunt was far from being a naïve victim of an aggressive female surgeon. She was a woman who could speak casually and without embarrassment about her illness, and who actively sought aid from referral networks of laywomen and a variety of professionals. Before addressing Dixon Jones, Hunt consulted a large number of male doctors, listened to their advice, took the prescribed medication – and did not

get better. Hunt might well have elected Dixon Jones precisely because the latter advocated radical surgical measures. Women like Hunt did not have to be told by Dixon Jones that an ablation of the ovaries or of the uterus was a possible treatment for "female complaints". They already knew it, and, some were anxious to have such a surgery. Moreover, in the case of Hunt, Dixon Jones proposed not only a cure, but also a preventive measure. Dixon Jones warned Hunt that she was at a great risk of aggravation of her ills, and proposed an operation that would eliminate this risk.

Treatment for risk was indeed the hallmark of Dixon Jones's brand of medicine, with a special focus on preventive therapy of female tumors. Dixon Jones had an unorthodox career. First trained in general medicine, homeopathy and hydrotherapy, she retrained as a surgeon in her late 40s. She then founded the Women's Hospital of Brooklyn, an institution specialized in surgical treatment of gynecological diseases. Mary Dixon Jones was the first US surgeon to perform (in 1888) a hysterectomy — an ablation of the uterus — for fibroids (benign tumors). Dixon Jones was persuaded that hysterectomy was the only acceptable treatment for cancer of the womb. This operation, she argued, should be proposed to all the women with operable tumors, but also to those with advanced cancers, because it could provide an efficient palliation for some of the most distressing symptoms of advanced uterine cancer such as uncontrolled blood loss and foul smelling secretions. This surgery should also be performed in borderline cases:

> The uterus should be removed on suspicion; where there is a doubt that cannot be solved, the patient should have the benefit of this doubt (...) Better remove a few organs with no malignant disease than to leave one cancerous uterus, and a patient with the awful risk of dying from a condition that the surgeon could have remedied (Dixon Jones, 1893).

In late nineteenth century surgical ablation of female reproductive organs — ovaries and the uterus — were alternatively seen as a "normal" way to treat women, or an illicit practice. Women were perceived as more disease-prone than men, and many of their health problems continued to be linked to their reproductive functions. It is also likely that some women might have viewed the loss of their ability to carry children as a welcome relief from the tyranny of repeated pregnancies. On the other hand, the "desexing of women" by surgeons was occasionally viewed as a shady, suspicious practice. It was criticized by some practitioners, but also by women who saw it as a manifestation of cruel and unfeeling attitude of gynecologists towards female bodies. The doubtful reputation of gynecological surgeries, coupled with a high

mortality from these surgeries, occasionally produced an explosive mix, strongly present in Dixon Jones's trial for manslaughter of Ida Hunt.

After she had lost her hospital job, Dixon Jones turned to the study of gynecological diseases. She focused on microscopic diagnosis of female malignancies. Data from her 1890's trials do not mention microscopic evidence that Hunt had a malignant tumor, or any other microscopically confirmed condition. In 1893 Mary Dixon Jones published a plea for the generalization of microscopic diagnosis of uterine tumors. Only such a diagnosis, she argued, could dispel doubts and prevent medical mistakes. It is possible that Dixon Jones subsequent interest in cytology of cancer and her strong defense of microscopic diagnosis of malignancies were linked with her (presumed) earlier incapacity to legitimate her therapeutic decision to operate on Hunt through the display of objective evidence of a strong indication for a laparotomy (Dixon Jones, 1893).

2. The ethnicization of genetic susceptibility to breast cancer

Let us move a hundred years ahead, to 1990 and the laboratory of Mary Claire King at Berkeley, which provided a first complete description of BRCA genes predisposing women to breast and ovarian cancer. King did not patent her findings: the company Myriad Genetics did, in 1994, after a "race" to clone the gene[1]. Myriad Genetics started in the late 1990s to propose testing for BRCA mutations to women with family history of breast and ovarian malignancies. If the mutation is unknown, it is necessary to sequence the whole BRCA gene. If the mutation was already detected in other family member, or if one is looking for a "founder mutation", present in a well defined group, the cost is much lower, since it is already known what parts of the gene have to be studied. The most striking example of the latter is testing for one of the three "Ashkenazi mutations" of BRCA genes shared by many women in the Ashkenazi Jewish population. Such testing is ten times cheaper than testing for other mutations of BRCA gene[2]. Among Ashkenazi Jews, Mary Claire King and her collaborators had shown in 2003, a family

[1] For details of the "patent fights" around BRCA genes, see e.g., Parthasarathy (2007). In 2013, the US Supreme Court invalidated Myriad's patent, ruling that "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated."

[2] A "founder" BRCA-2 mutation was also found in the Icelandic population; it is however limited to Iceland, and has a relatively low penetrance.

history of breast and/or ovarian cancer was not always sufficient to reveal risk, especially when the families are small or the family history is not well-known (King et al., 2003).

In the USA, the great difference in the price of testing for "private" and for Ashkenazi mutation, coupled with the observation that many Jewish women who carry BRCA 1 and 2 mutation are not aware of the existence of a family risk, contributed to the *de facto* transformation of these malignancies into a "Jewish disease". Higher incidence of breast cancer among Jews was reported from the early 20th century on, but definitive data were elusive. The higher prevalence was occasionally attributed to environmental factors: Jewish women often belong to an urban, educated population, they have a sedentary life style, and tend to have children late in life, all independent risk elements for breast cancer (Kushner, undated). On the other hand, statisticians did notice the presence of "breast cancer families" among Jews. The first reports on high prevalence of a specific mutation of BRC A1 gene found in many women of Jewish–Ashkenazi origins (185delAG) was published in 1995, and the first estimates were that approximately one percent of individuals in this community carry the mutated gene (Struewing et al., 1995). Another "Ashkenazi mutation" (5382insC) was described in the BRCA1 gene, and additional one (6174delT) in the BRCA2 gene.

The initial reaction of the Jewish community was very positive. Rabbi Mathew Simon, the president of the United Jewish Appeal (UJA) federation of the greater Washington, strongly supported a NIH sponsored study of follow up of about five thousand people of Jewish Ashkenazi origins in the Washington DC area and was reported to say that in history Jews have bleeds for negative reasons, and this was an opportunity for Jews to give blood for positive reasons (Rothenberg, 1997). Similar studies were conducted in NYC and in the Boston area. The National Breast Cancer Coalition protested against the design of these studies (for example, the participants in the Washington study did not receive individual results), but these studies continued to be supported by Jewish organizations and publications. In 1996, the *Jewish Week*, a popular Jewish newspaper, suggested to women who wanted more information about genetic testing that they should address the Genetics And In Vitro Fertilization Institute in Fairfax, Virginia, that commercialized a test for 185delAG in 1996 (for the relatively modest sum of $295). The *Hartford Jewish Ledger* published in the same year advertisement for competing services, that claimed that "if you carry damages breast genes and you live long enough you are almost sure to develop breast cancer" (Rothenberg, 1997, pp. 101-102). With the establishment of Myriad's monopoly, all the testing for Ashkenazi mutations was concentrated by this firm, and Myriad's "multisite 3 analysis" for the Ashkenazi mutations became one of its more popular products.

Today experts claim that the relative frequency of BRCA mutations is indeed higher in Jewish-Ashkenazi populations (the oft repeated estimate is one in 40 in Jewish population against one in 340 in the general population), but there is no proof that the overall frequency of breast cancer among Jews is very different from its frequency in other populations in the places they live. Nevertheless, higher frequency of the mutation induced higher frequency of "breast cancer families" and therefore more dramatic individual stories and a higher chance of a bias in small samples taken from limited geographic area. It also stimulated the rise of self help organization such as Sharsheret (The Chain), which deals with specific problems of women (especially young women) with hereditary risk of breast cancer[3].

In the USA, where ethnicity is perceived as a central issue by medical geneticists and genetic counselors, the Ashkenazi mutations rapidly acquired high level of visibility. They were widely discussed by experts, by cancer charities, by patients groups, and by Jewish women organizations[4]. For example, the Zionist women organization Hadassah developed a program "It's in the genes", which aimed "to cover the concerns related to the science of genetics, counseling psycho-social issues, discrimination and ethics from a Jewish perspective", and a "breast awareness" group, with activities targeted towards Jewish women, especially those with a family history of breast and/or ovarian cancer. This "ethnicization" of breast cancer may be linked to previous sensitization of the US Jewish community to Ashkenazi diseases, to the high percentage of Jews in medical and paramedical professions, and to the presence of many women of Jewish descent among breast cancer activists. It may also be related to the publicity given to Ashkenazi mutations by Myriad and, before 1997, also by other providers of BRCA tests.

The fact that the only important "founder mutations" for BRCA in the US were described in the Jewish population, coupled with the relatively high level of education and health awareness of this population, made Jews an excellent target for selling of specifically tailored services. The possibility to offer these services at a greatly reduced price is an additional marketing argument. Jewish women are invited by Myriad to check whether they are at enhanced hereditary risk to develop breast cancer even when their family history is not very evocative of this pathology. This marketing strategy reinforces in turn the association between Jewish origins and breast cancer. Being Jewish is indirectly presented as belonging to an

[3] Sharsheret (2015). Website. Retrieved April 9, 2015 from http://www.sharsheret.org/index.php.

[4] The prevalence of these mutations among Ashkenazi women is approximately 2.5% (one in forty women). This may sound impressive, but one should take into consideration that mutation carrier has 50-60% cumulative lifetime risk of breast cancer, and that the risk of breast cancer in the general population of women is 10-11%.

extended "high cancer risk" family, and breast cancer, a pathology with a very high prevalence in the general population, is partly transformed into a "Jewish disease".

Discussing the introduction of testing for the Ashkenazi mutations in the Jewish community, and the enthusiastic endorsement of such testing by some of the community leaders, the US law professor, Karen Rothenberg, pointed out to the dangers of the "geneticization" of health, a question that goes well beyond questionning whether the finding of "Jewish" genes of susceptibility to disease is good or bad for the Jews. Rothenberg was concerned about insurance discrimination and confidentiality issues, but above all about life in the shadow of a risk, and the implications of cancer surveillance and prevention strategies on the healthcare system. She concluded that:

> Until we have a better understanding of the benefits and risks of genetic testing and our strategies how to best protect the public, we must strive to resist a genetic "quick fix" mentality that promotes genetic testing in the healthcare market. Obviously there is no "quick fix" for the ethical, legal and social challenges (Rothenberg, 1997, p. 124).

Rothenberg's article appeared in 1997. At that time, the race for cloning and patenting BRCA1 and 2 genes ended, and Myriad Genetics was about to reach an agreement with Oncormed that left her a monopoly of the testing market in the US, and genetic tests were about to become a marketable commodity. Their distribution was driven by professional and commercial interests, but also by patients' demand, encouraged by important coverage of the race to clone the "breast cancer gene" in the media. Rothenberg's warning did not come at quarter to midnight, but at quarter past it, that is already too late. People at hereditary risk of cancer kept — in principle — their right not to know, but the presence of tests, and the new accent on the importance of preventive surgery in familial cancers (including those with no identified mutation) — transformed a preference not to be tested from a simple abstention from action into a difficult choice[5]. The decreasing costs of genetic testing, and gradual "normalization" of search for predisposition genes, accelerated this trend.

[5] On the "choice of no choice" introduced by new medical technologies, see Strathern (1992).

3. Enlarging the population deemed "at risk" for breast cancer predisposition

Women who learn about their increased risk of breast and ovarian cancer have two main preventive means at their disposal: preventive surgery – ablation of ovaries and/or breasts –, and the uptake of drugs such as tamoxifen (an inhibitor of estrogen receptors) expected to lower the risk of breast cancer (but not ovarian cancer). The latter recommendation, however, was seen for a long time as unproven. Studies in BRCA mutations carriers were inconclusive; the samples were often too small to allow statistically meaningful effects, and there were no randomized trials of the preventive effects of tamoxifen in that population (Teller & Kramer, 2010). Facing paucity of reliable data, an American Society of Clinical Oncology panel concluded in 2009 that "the current limited evidence precludes reliable assessment of tamoxifen effects in this setting and, this issue is unlikely to be resolved by further analyses of already completed trials" (Visvanathan, Chlebowski, Hurley & Temin, 2009).

A 2013 study, however, provided an indication that tamoxifen was able to reduce the incidence of breast cancer in BRCA gene carriers. This study has shown that in BRCA mutation carriers diagnosed with invasive cancer in one breast, uptake of tamoxifen reduces the risk of cancer in the contralateral breast (Phillips et al., 2013). Although this study did not deal with cancer-free mutation carriers, its results were seen as a strong indication that tamoxifen indeed prevents cancer in BRCA-positive women. One of the obstacles to the recommendation of preventive chemotherapy to carriers of BRCA mutations was the observations that the great majority of cancers in mutation carriers (75% to 80%) are estrogen receptors (ER) negative at the time of diagnosis. As a rule, tamoxifen — ER receptor inhibitor — is not prescribed to women with ER negative tumors. On the other hand, the ablation of ovaries, a surgery which drastically limits the level of estrogen in the body — reduces the risk of cancer in women with BRCA1 mutation. This observation hinted that estrogen may play a role in the development of ER negative tumors as well. The finding that tamoxifen reduced risk of cancer in contralateral breast in BRCA1 mutation carriers, was interpreted as an additional, and stronger indication that estrogen might play an important role in the advent of cancer in this population.

The logical next step or rather two steps was/were a) to offer tamoxifen to all the healthy women with BRCA mutations, and b) to broaden the scope of search for hereditary predisposition to cancer in order to uncover more women eligible for the new, relatively inexpensive preventive strategy. The four possible pathways for enlarging the scope of search for BRCA mutations are:

- systematic reporting on incidental finding of BRCA mutations during search for other genomic data;
- lowering the existing threshold for initiating search for BRCA mutations;
- population-based screening, through systematic offering of the test to everybody, independently of their stated risk;
- search for mutation that increase disease risk, including BRCA mutations through the use of personal genomics.

3.1. BRCA AND INCIDENTAL FINDINGS

In 2013, the American College of Medical Genetics and Genomics (ACMG) issued a statement about reporting of incidental findings uncovered by genetic testing. The recommendations provided a list of incidental findings that should be reported, among them mutations in BRCA genes. The rationale for this recommendation was that incidental genomic finding are not different from other incidental finding uncovered through physical examination, laboratory tests or medical imagery. In all these cases, if accidentally found condition can be cured, treated, prevented to be worse, or even when, in absence of cure, patients may plan their life differently, the doctors' duty is to report their findings. The same should be true for incidental genetic findings (Green, et al., 2013).

In a follow up article, Kurt Christensen and Robert Green, who were among the promoters of the ACMG declaration, argued that disclosure of genetic data on risk motivate individuals to change their behavior through psychological mechanisms that differ from typical risk assessment interventions. Individuals who learned that because they were carriers of specific variant of APOE gene were at increased genetic risk for developing Alzheimer disease in the future, were not only more likely to report modifying potential risk-reducing behaviors compared with those who learned that they did not have an increased genetic risk or did not receive a genetic risk of assessment, but they also were more likely to report changing their long-term care insurance coverage. The beneficial effects of revealing risk are even more obvious in cases such as BRCA mutations, where efficient preventive intervention—above all surgery—is possible. Disclosure of incidental information, Christensen and Green concluded, will be increasingly common, and practitionners should be carefully optimistic about its ability to motivate positive health changes (Christensen & Green, 2013).

3.2. Lowering the detection threshold

The UK officially (and other countries, unofficially) lowered the threshold of BRCA screening, mainly because the cost of testing went significantly down. In 2013 the National Institute for Clinical Excellence (NICE, UK) proposed to halve (from 20% to 10%) the threshold of risk of carrying a BRCA mutation necessary to initiate a genetic analysis of this mutation. Professor Gareth Evans, one of the authors of NICE's new recommendations on the management of breast cancer risk, explained in a NICE's press release that this was a cost-efficient option for the NHS, when weighed against the possibility of preventing breast cancer in high-risk women:

> Reducing the threshold for genetic testing will inevitably mean more men and women being seen but this is something that's already happening in some parts of the country. Testing unaffected relatives will also have an impact on services but genetic clinics are able to carry out testing much quicker nowadays - between four and six weeks in some cases - and the cost of genetic testing is dropping substantially.[6]

The NICE's list of elements in one's family history which denotes an increased risk of breast cancer is composed from finding specific to a given family – a bilateral breast cancer, male breast cancer, ovarian cancer, sarcoma in a relative younger than 45 years of age, glioma or childhood adrenal cortical carcinomas and complicated patterns of multiple cancers at a young age in a first degree relative or several second degree relatives – and a single "ethnic marker": Jewish Ashkenazi origins (NICE, 2013, p. 20).

3.3. Screening of all Ashkenazi women, or without ethnic distinction

In 2010, a group of Canadian experts headed by Stefan Narod first proposed to offer a screening for BRCA mutations to all the women of Jewish origins without bothering to calculate

[6] NICE (2013, June 23). Major shift in breast cancer care on horizon as NICE recommends preventative drugs for 'at-risk' women. *NICE Website*. Retrieved April 9, 2015 from https://www.nice.org.uk/news/press-and-media/major-shift-in-breast-cancer-care-on-horizon-as-nice-recommends-preventative-drugs-for-atrisk-women.

their individual risk (Metcalfe et al., 2010). The Canadian group reinforced their argument three years later. The transformation of all the women of Jewish Ashkenazi descent into a highrisk group, they affirm, will be a cost-effective step:

> Genetic testing of all Jewish women above the age of 25 years will greatly expand the number of BRCA mutation carriers identified without a commensurate increase in the number of hours required for counseling (Metcalfe et al., 2013a).

The proposal to screen all the Jewish Ashkenazi women for BRCA mutations is today a topic of heated debate among Israeli geneticists (Rabin, 2013)[7]. A group of Israeli geneticists, led by Efrat Levy–Lahad, one of the main advocates of population-based screening for BRCA mutations, published in 2014 an article that demonstrated that more than half of mutation carriers among Ashkenazi Jews, do not have a family history evocative of such a mutation - a finding that was already present, although on the basis of much smaller sample, in Marie-Claire King 2003 article (Gabai-Kapra et al., 2014). The time has come, the authors of this article argue, to propose screening for BRCA mutations to all Ashkenazi Jews.

> General screening would identify many carriers who are not evaluated by genetic testing based on family history criteria. Such a program could serve as a model to investigate implementation and outcomes of population screening for genetic predisposition to cancer in other populations (Gabai-Kapra et al., 2014, p. 14209).

The Ashkenazi mutations are but one example of "founder mutations" in BRCA genes, that is mutations found in well-defined populations. Numerous other populations also carry founder mutations in these genes. Testing for such origin-specific founder mutation, Stefan Narod and his colleagues proposed is relatively inexpensive—and can expand greatly the number of women diagnosed with a hereditary risk of breast or ovarian cancer (Narod, 2010). Mary-Claire King strongly agrees. In a text published in 2014 with the main authors of the Israeli study she argued that it had shown that the time had come for population-based screening for BRCA mutations (King, Levy-Lahad & Lahad, 2014). The authors of this text explain that:

[7] The proportion of BRCA positive Israeli women who elect to prophylactic mastectomy is much lower than that of US BRCA positive women; the rates of prophylactic ablation of ovaries in the two countries are similar (Metcalfe, Birendaum-Carmeli, Lubinski & Gronwald, 2008).

> Inherited mutations in BRCA1 and BRCA predispose to an extremely high risks of breast and ovarian cancer. But these risks are not immutable. Among women who carry mutations in BRCA1 or BRCA2, surgical intervention, in particular risk-reducing salpingo-ophorectomy, reduces risk of both ovarian and breast cancer and reduces overall mortality. However, many women with mutations in these genes are identified as carriers only after their first cancer diagnosis because their family history of cancer was not sufficient to suggest genetic testing. To identify a woman as a carrier only after she develops cancer is a failure of cancer prevention (King et al., 2014, p. 1092).

King and her collaborators accordingly propose:

> To offer genetic screening for these genes to every woman at about age of 30, in the course of a routine medical care. Women with cancer predisposing mutations in BRCA1 and BRCA2 are high risk group in who special screening and counseling should be focused (King et al., 2014, p. 1092).

3.4. USE OF PERSONAL GENOMICS

From 2008 on, *23andMe* included testing for BRCA mutations in their genetic disorder risk assessment. The $99 kit did not provide a diagnosis of a mutation, but it did supply an indication of increased risk of such mutation, followed by recommendation of a full-scale diagnostic test for those who want to know for sure whether they are mutation carriers.

Scientists linked with *23andMe* claim that such incidental and non-invited finding of these mutations is perceived by their clients as a positive thing. They studied 63 users of the *23andMe* kit (both males and females) who had chosen to learn whether they carried the Ashkenazi BRCA mutation: 32 positive cases and 31 negative ones (Francke et al, 2013)[8]. Out of the 32 people who received a positive diagnosis 29 of them claimed that knowing that they carry BRCA mutations was a good thing. Typical statements were:

[8] The authors of this article work all for *23andMe*; only the first author, Uta Francke has also an academic affiliation with Stanford University.

> While the results were shocking and a little stressful, ultimately I think this could potentially change my life, and it obviously made a difference for my aunt, who was able to catch pre-cancer early. So I think all in all, it's a positive thing. We would have never known, because there are no [affected] first and second-degree relatives. So until somebody ended up with breast or ovarian cancer I don't think we would have known. This way we're taking care of things prophylactically.
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> You know, if you get information that you can do something about, and I think particularly Ashkenazi Jewish women, it's certainly worth doing (…) I'm a proactive person, so it's hard to imagine someone not doing something.
>
> Even after I talked with genetic counselors, they never would have recommended me to be tested based on my family history that I knew of at the time. I feel like a genetic secret was found in my family. I feel like I may have saved my sister's life. I mean, nobody knows. That's a hard thing in our family because nobody had cancer early, but it makes a difference. You accept it. It's in your system and I'm lucky enough to know that it's there as opposed to finding out something too late. It increases your odds you're going to find something and find it earlier.
>
> I immediately had my children tested, finding that my daughter was predisposed (sic) to BRCA1 and she's now being treated because of this. In other words, 23andMe may very well have saved my daughter's life (Francke et al., 2013, pp. 14-15).

The reception of a positive result of BRCA testing led some of the women who received these results to undertake or consider preventive interventions, above all prophylactic surgery[9]. In addition, numerous relatives of mutant carriers - both males and females - were screened for BRCA mutations following an initial positive test in a relative. Several "secondary cases" (that is women who found out about their BRCA mutation following an initial testing of family member with *23andMe*) also underwent prophylactic surgeries or indicated that they were planning to have such surgeries in the near future (Francke et al., 2013, p. 13). Unsurprisingly, the *23andMe* researchers concluded that a direct access to BRCA mutation tests, provided clear benefits to participants but also, thanks to a cascade effect and identification of further mutation carriers, to their families[10].

[9] Among the 11 women who were found BRCA positive in that sample, one had prophylactic mastectomy and three others considered it, two had prophylactic ablation of ovaries (not clear if the same women had a mastectomy and ablation of ovaries) and four considered this surgery, and one planned to ask her oncologist for a prophylactic drug treatment (Francke et al., 2013, p. 12, table 6).

[10] *23andMe* researcher's conviction that the accidental revealing of the existence of BRCA mutation provides "clear benefit for participants" was not shared by the FDA. In a warning letter of 22 November 2013, and signed

In November 2013, the FDA condemned *23andMe* delivery of "health results", because the company was not licensed to provide medical information[11]. The interdiction was condemned by some experts, including Robert Green. Unsurprisingly. Green, together with co-author, Rita Farahany, a jurist, explained that:

> FDA's precautionary approach to *23andMe* is particularly troubling because it could presage similar actions against other consumer health products. In its recent guidance on mobile health applications, the FDA left open the possibility that it will regulate as medical devices information-based products such as questionnaires that evaluate the risk of a heart attack or the plethora of fitness trackers that help people to follow their weight, body temperature, heart rate, sleep patterns and more. Many operate as standalone or companion software for predicting risks including the likelihood of sleep disorders, seizures or heart attacks. Downloads and installations of these applications are expected to grow from 156 million in 2012 to 248 million in 2017 (Green & Farahany, 2014, p. 287).

They quoted the *23andMe* sponsored article on reaction of people who received information about the probability they carry BRCA mutations, adding that:

> 30 family members of those carrying a pathogenic mutation decided to get tested themselves; 13 of them tested positive for the high-risk mutation and so received

by James L. Woods, FDA's Deputy Director of Patient Safety and Product Quality Office, FDA strongly criticized 23andMe practices: "Some of the uses for which PGS is intended are particularly concerning, such as assessments for BRCA-related genetic risk and drug responses (…). For instance, if the BRCA-related risk assessment for breast or ovarian cancer reports a false positive, it could lead a patient to undergo prophylactic surgery, chemoprevention, intensive screening, or other morbidity-inducing actions, while a false negative could result in a failure to recognize an actual risk that may exist". See: Food and Drug Administration, US [FDA] (2013, November 22) Warning Letter. 23andMe, Inc. 11/22/13. *FDA*. Retrived April 9, 2015 from http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2013/ucm376296.htm.

[11] The "health services" provided by *23andMe* continues to be legal in Canada – and were recently introduced in the UK, although with smaller number of tested conditions. See: Gibbs, S. (2014, December 2) DNA-screening test 23andMe launches in UK after US ban, *The Guardian* [online]. Retrieved on April 9, 2015 from http://www.theguardian.com/technology/2014/dec/02/google-genetic-testing-23andme-uk-launch

In February 2015 the FDA allowed 23andMe to propose genetic tests for selected, well defined hereditary conditions, opening the way to new *modus vivendi* with this firm. Buhr, S. (2015, February 19), FDA Authorizes 23andMe To Market Genetic Testing For Bloom Syndrome, *TechCrunch*. Retrieved on April 9, 2015 from http://techcrunch.com/2015/02/19/fda-authorizes-23andme-to-market-genetic-testing-for-bloom-syndrome/.

> potentially life-saving information they might not have obtained otherwise (Green & Farahany, 2014, p. 287).

Green and Farahani concluded that:

> Consumer products could democratize health care by enabling individuals to make choices that maximize their own health. They follow the historical trend of patient empowerment that brought informed-consent laws, access to medical records and now direct access to electronic personal health data (…) The effects of these products should be monitored but, as long as emerging empirical data show no evidence of harm, we urge the FDA to let consumer genomics testing proceed (Green & Farahany, 2014, p. 287).

Green's and Farahani's proposal is, however, far from innocuous, nor are its costs limited to 99 dollars for the *23andMe* test and the additional cost of 300 dollars for Myriad BRCA testing for Ashkenazi mutation. An important increase in the number of women defined as being at a heighten risk of breast cancer, their monitoring, and their prophylactic treatment, may increase the overall costs of health care[12]. Expansion of the definition of being at risk may also hike up the non-monetary costs of "living with a *ticking bomb*" (Metcalfe et al., 2013b). As the only women in the *23andMe* group that was not happy to find out that she was BRCA positive put it:

> I would not do it again, because it is really not information I need to know. I don't think the cost in dollars was important, I think the emotional cost is more. The impact of the results to a greater extent was negative. It's just basically knowing that I have it, I might pass it on. And that's the main thing. Sometimes ignorance is better." (Francke et al., 2013, p. 15).

On the other hand, she expressed a minority opinion, one negative view among 31 (self-selected) participants, 28 of whom were very pleased to learn incidentally about their BRCA positive status. Social scientists had found out that nearly all the women who elect to undergo

[12] The majority of women who received an "accidental diagnosis" of Ashkenazi BRCA mutation increased considerably their consumption of medical resources: consultations with experts, medical imagery, additional tests (Francke et al., 2013, p. 12, table 6).

preventive surgeries, such as prophylactic ablations of breasts and ovaries, were very satisfied with their choices[13].

4. Conclusions

Pro-active users of health information and interventions are not an invention of the internet era. Historians like Regina Morantz-Sanchez, Ornella Moscucci or Judith Leavitt had shown that medicalization of childbirth and the rise of surgery for gynecological problems in the 19th century was not only a male doctors' assault against women's bodies and sexuality, but a mutual movement, driven by both physicians' *push* and users' *pull*. Women sought "medicalized childbirth" because some interventions (ergot, forceps) shortened long births, while anesthesia reduced suffering. They aspired to such medicalization despite that, as the historian of medicine Irvine Loudon had shown, these interventions were often dangerous. In the early 20th century affluent women who could afford the services of a physician had a greater risk to die in childbirth than those who relied exclusively on midwife's help, a difference attributed to catastrophic results of some of the physicians' interventions (Loudon, 1992).

In the late 19th century women actively sought surgical ablation of uterus and/or ovaries again despite the important risks attached to such interventions, because they had faith in "miracles" of surgery, but also because these operations sometimes did put an end to debilitating chronic gynecological problems such as endometriosis or ovarian cysts. Moreover, the elimination of their reproductive organs was the best possible contraceptive method, often highly sought after outcome, while the ablation of the uterus was a well-known abortive technique, popular until the 1970s. It is quite possible that if Ida Hunts's surgery had not ended with a fatal peritonitis, she would have been very happy with the choice she had made as an informed, pro-active patient.

[13] E.g., BRCA mutation carriers who underwent prophylactic salpingo-oophorectomy reported that their satisfaction with the decision to undergo this surgery remained high regardless of increased vasomotor symptoms and decreased sexual function (Finch et al., 2011).

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