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INTRODUCTION

MOST CLINICIANS involved in genetic counselling adopt a non-directive approach. The role of a genetic counsellor is to ensure that correct diagnosis and risk estimate have been made and that those being counselled have correctly understood the situation [1]. It is not the duty of a genetic counsellor to recommend a particular line of action if a genetic risk has been identified. Dr Klijn and I were asked to take positions as if we were acting paternalistically when counselling and we accepted playing the role of a ridiculous counsellor who possesses the infallible scientific truth and who always gives the same authoritative solution to a very complex human problem. The aim of this unrealistic role game is, of course, not to persuade the audience that one of us is right

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while the other is wrong, but to animate this difficult debate. As a result of a draw, the role of the counsellor who knows that prophylactic surgery should never be counselled fell to me.

THE CONTRA POSITION BASED ON ESTABLISHED FACTS ABOUT BREAST CANCER, ITS TREATMENT AND ITS PREVENTION

Most oncologists would surely acknowledge that one of the greatest achievements of the last 20 years has been the recognition that breast conservation is a safe alternative in the surgical treatment of most stage I and II primary breast cancers. In the face of this reality, does it not seem excessive to propose mastectomy when neither invasive nor *in situ* carcinoma has even been diagnosed? How is it possible to accept a prophylactic procedure that will be in most cases more invasive and disfiguring than the treatment of the disease it seeks to prevent? Does a cumulative risk of breast cancer reaching 80% at the age of 80 years justify such a radical measure?

What the high risk really means

Does the proposition of prophylactic mastectomy rely on the certainty that a deadly breast cancer is about to strike the patient unless you remove her breasts? The prediction we can make with available genetic tests is fortunately much less frightening. If a 25 year old woman has a deleterious *BRCA1* germ-line mutation, we know that her cumulative risk of developing breast cancer is 80–90%, but the temporal definition of the risk is very poor [2]. If this young woman wants to know when the cancer will strike, we cannot say whether she will get cancer in one month, one year, 10 years, 20 years or 40 years or not at all. Of course, we can give rough estimations: the risk of developing cancer is maximum between the ages of 35–50 years, although 30% of at-risk women develop cancer later in life. Some unfortunate women also get it before the age of 30 years. This knowledge is very difficult to use in making a choice and perhaps we can help by giving a rough estimate of the risk of cancer each year (cumulated risk divided by the number of years she would be expected to live). This would give an average risk of getting breast cancer roughly equal to 2% each year up to the age of 50 years (50/50−25) and 1% afterward (30/80-50). Who would immediately undergo prophylactic bilateral mastectomy with a risk presented this way?

Breast cancer is often a curable disease and some data suggest that genetic predisposition might be an independent factor of breast cancer good prognosis

A large population-based case–control study suggests that the risk of dying of breast cancer among young women (age range 21–45 years) with a first-degree family history of breast carcinoma is half that of women with no family history of breast cancer carcinoma (RR = 0.5; CI = 0.3–0.9) [3]. Since the comparison between the groups was made after adjustment for tumour size and stage, age, year of diagnosis and treatment, the observed difference in survival does not appear to be attributable to differences in screening or treatment. Other studies have also reported a better survival among breast cancer patients with a family history of breast cancer [4, 5].

According to the Knudson's hypothesis, cancers occurring in cancer-prone individuals should be identical to their sporadic counterparts. Knudson suggested that the risk of cancer-prone individuals could be explained by assuming that they had inherited a mutation involved in the genesis of sporadic cancers [6]. This hypothesis definitely does not apply to breast cancer: no sporadic breast cancer with mutations inactivating both alleles of *BRCA1* has been reported to date, while these 'two hits' appear to be constant in the genesis of breast cancer in the context of germ-line *BRCA1* mutation [7]. With regard to their *BRCA1* mutation status, sporadic breast cancer cases can never be assimilated with those associated with germ-line *BRCA1* mutations. Because of these genotypic differences, it would not be surprising if future studies confirm that breast cancers associated with germ-line *BRCA1* mutations have a less aggressive nature than their sporadic counterparts.

Screening can be expected to reduce the risk of breast cancer

Population-based incidence and mortality figures show that roughly 50% of breast cancers can be cured. Of course, this figure is likely to overestimate substantially the risk of dying from breast cancer in a very particular subpopulation of cancer-prone women, well informed of their risks and extremely conscious of the importance of regular screening strategies (monthly self-examination, frequent clinical examination and yearly mammography).

We know that systematic mammographies once every 2 to 3 years in the general population aged 50–70 years reduce the risks of dying from breast cancer by 30%, but we cannot extrapolate this data to the at-risk subpopulation. The usefulness of screening in women younger than 50 years has long remained a controversial issue, but data accumulating now suggest that screening is a useful life-saving strategy in younger women. A meta-analysis combining seven population based trials has shown that screening results in a statistically significant reduction of mortality of 24% in women younger than 50 years [8]. Moreover, a recent Swedish study suggests that screening may be as effective in women younger than 50 years as in older women [9]. Pessimists will suggest that the benefit will be lower than in the general population, because mammography screening will be started at a much younger age where the natural breast density surely may diminish sensitivity to screening. Pessimists will also raise the doubt that repeated X-rays may favour the development of breast cancer. Optimists will suggest that screening in a limited at-risk population could be more effective because the interval will be shorter and because the radiologist as the physician aware of the high risk will scrutinise the mammograms very attentively.

The risk of dying from breast cancer may appear acceptable to some people

It is unfortunately unavoidable that a small proportion of the at-risk women undergoing regular high-quality screening will die of breast cancer. This is due to the fact that screening will sometimes miss the early and still curable cancer, or because a kind of cancer will develop that is unfortunately very aggressive and turns out to be incurable even when detected at the preclinical stage. Will this proportion of fatal breast cancer cases be closer to 10% or closer to 30%? An accurate prediction is impossible from the available data. Assuming the pessimistic estimate, the average mortality from breast cancer can be estimated to be roughly 0.6% each year (30/80–25). Assuming the optimistic estimate, breast cancer mortality would fall to 0.2% each year. Who would immediately undergo prophylactic mastectomy knowing that this figure might turn out to be the closest to reality?

It is very difficult to accept the idea of a decision threshold of risk

Evolution of the state of the art makes us realise that the bulk of prophylactic mastectomies done in the past were based on indications that would be considered irrelevant today, and would warrant nothing more than a regular clinical and mammographic follow-up [10]. Not so long ago, bilateral mastectomy was proposed for healthy women having only a 50% probability of being at risk, meaning that their cumulative risk was close to 40% [11]. Recent progress in genetic testing still does not allow us to recognise who is really going to develop cancer among the cancer-prone women. It is worrying that some 10–20% of the women carrying a deleterious *BRCA1* mutation may undergo an unjustified mutilation by accepting bilateral mastectomy when they simply would never have developed breast cancer during their life, even if they were to reach the age of 70 years.

It is very difficult to define the right age to mastectomise

Counselling a 25-year-old woman to undergo prophylactic mastectomy means that we do not want to take the few-percent risk that the disease will develop in the next five years. Referring to the anticipation phenomenon that has lately been recognised in genetic predisposition to breast cancer [12, 13], the risk for this young woman may be sensibly higher than the one estimated from pooled data mixing women born before 1930 with women born after 1950. However, no precise individual prediction can be made. Even if the risk, taking the anticipation phenomenon into account, was to reach 20% at the age of 30 years, it would still mean that the vast majority of cancer-prone women can safely live with breast conservation until the age of 30 years. Moreover, if we admit the anticipation phenomenon and assume that our goal is zero risk, we are obliged to accept the absurd conclusion of advising prophylactic mastectomy among teenagers.

No data are available today on the long-term outcome of the mastectomised women

Although prophylactic mastectomies have been applied for more than 30 years, the true preventive value of this procedure cannot be precisely defined. Breast cancer has been reported after subcutaneous [14, 15] and after total [16] mastectomies, but these failures are rare and prophylactic surgery probably reduces the risk in high-risk women below the average woman's lifetime risk [17]. Of more concern is the lack of information about the long-term satisfaction or dissatisfaction with this procedure. In a small series of women at increased risk because of family history, satisfaction was reported by all women at a minimum of six months after completing surgery, but the author stressed that these women ($n = 14$) received a strong family and friend support following in-depth genetic counselling [18]. Moreover, it is reported that a high level of self-reported anxiety may have influenced their decision of undergoing prophylactic surgery. Curiously, repercussions of bilateral mastectomy on sexual relations is rarely if ever mentioned, as if breasts were not so important in sexual life. From the available data, I think the most unquestionable evidence is that mastectomy is for many an effective way of dealing with the fear of cancer.

THE CONTRA POSITION BASED ON PHILOSOPHY

We are supposed to base our practice on the knowledge of the state of the art. Facing a medical decision, it may come as a relief when a gold standard consensus has been reached after days of debate between experts. Consensus recommendations may sometimes smack of dictatorship, but using the standard treatment does not need to be justified and so we can serenely turn to other problems. Without guidelines, it is not so comfortable to make a decision. When scientific information is inadequate, when the right decision cannot be substantiated on available published data, we have to be guided in our decision by a philosophy of responsibility.

Dr Klijn and I have many things in common: we are both clinical oncologists, have experience in treating breast cancer, have the same knowledge of predisposition to breast cancer and we both know the effectiveness (or lack of) of the present means of preventing breast cancer. However, the preventive strategies we propose are totally different (in this role game). Our opinions do not differ because of any noticeable difference in the analysis of the situation. To state it clearly, I am also convinced that the most effective way of preventing death by breast cancer at the present time is prophylactic bilateral mastectomy. The main reason why Dr Klijn and I differ on how to deal with the risk lies in philosophical differences in the way we consider the same available data, because we do not have the same ideas about life and death and about health and medicine.

According to the World Health Organisation (WHO), health is 'a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity' [19]. Dr Klijn and I are familiar with this definition and both wish to preserve health. My opponent pretends that a young woman will remain healthy if she has bilateral mastectomy. I pretend the contrary because we do not have the same conception of health. Although we agree on an objective definition of health, we surely do not mean the same thing when we say 'healthy'. First of all, it seems to me that the conception of health of my opponent encompasses a long period of life and projects way ahead in the remote future, while my idea of health is restricted to the present and near future. I am unable myself to make plans more than 2 or 3 years ahead. For this reason, I would refute the idea of a prophylactic mastectomy in the absence of any demonstrable immediate threat.

Although we agree on the various components in the definition of health (physical, mental and social), I suppose we would not balance these components in the same way. It seems to me that the mental part of the definition comes first in Dr Klijn's idea of health. He may assume the cancer-prone young woman is not in a state of mental well-being (and therefore not healthy) because of a pervading fear of getting breast cancer (a disease she intimately knows because she has suffered so much from its devastating effects in her close family). Obviously, bilateral prophylactic mastectomy can be looked upon as a deliverance in such a case, and bring the woman closer to a state of mental well-being through an overwhelming sense of relief. In my view, physical well-being takes precedence in the definition of health (as in the WHO definition) and breasts are of paramount importance to the feeling of physical well-being. Breasts are the most visible elements of feminity and can convey and receive a wealth of emotions. Although I am not aware of studies exploring these problems (although they are sometimes very briefly alluded to), I suppose bilateral mastectomy can have a devastating impact on the emotional and sexual life of young women. Loss of sensibility of the areolar areas (which are removed in total mastectomy) can surely impede the sexual arousal and fulfilment of a woman. It has been reported that the sexual functions of the breast are significantly reduced even after subcutaneous mastectomies [20]. A less obvious but potentially greater problem could be that the scars of the mastectomies or the unnatural shape or firmness of the reconstructed breasts could block the partner, because of a spontaneous fear of the disease or fear of hurting. It is possible that partners in a stable relationship will overcome this problem, thanks to their maturity and understanding of each other. However, a stable partner may not even exist at the age of 25 years. Our society no longer associates childbearing with success or no children with failure, but individuals may suffer severely from not having children. Although many women do not breast-feed their children nowadays, breastfeeding surely remains in our imagination a very important element of the tenderness and love a mother can give to her child. I therefore fear that bilateral mastectomy could also hinder plans of motherhood.

Thanks to breast reconstruction, the outward body image of a cripple is often replaced by the one of a very nice-looking woman. Feeling confident towards the outer world is very important for a successful life in society, but a near-normal life in society is neither a guarantee nor a prerequisite to a successful intimate life. Instead, I think that the reverse is true for many, for whom a successful intimate life will be a prerequisite to a successful public life.

For all these reasons, I think it could be wiser to counsel intensive screening rather than prophylactic surgery. Of course, this choice means accepting a certain risk of dying from breast cancer and it is our duty to make this clear when counselling. My opponent could argue that my position is not compatible with regard to our responsibility of combating disease and death. I categorically refute the argument that I have to implement bilateral mastectomy because it is a life-saving measure: it is not valid because it confuses truth and value.

Truth and value

A true scientific statement does not prove anything and does not justify anything. 'Bilateral mastectomy is a life saving measure' is a true statement but it is neither good nor bad because nobody has to undergo prophylactic surgery. The value associated with this statement can only be decided at an individual level, because it raises an ethical question, namely 'How should I live to be happy?' According to Spinoza, it is a mistake to think one has to desire something because it is good: the reality is that one thinks something is good because one desires it [21]. In this ethical debate about the value of prophylactic surgery, I defend the point of view that it is a bad solution, because I defend a certain idea of the quality of life. I certainly share the conviction of my opponent about the efficacy of the strategy he advocates, but I definitely do not want to go on a crusade aimed at saving lives at any price. I think many persons seeking advice accept the idea that quality of life is not synonymous with increased security or a hypothetical longer life. Hell is paved with good intentions. Considering the intention of saving lives thanks to prophylactic mastectomies, I suggest hell could be hidden in two basic considerations.

(1) As I have previously shown, the life-saving prophylactic mastectomy is not an absolute truth, but a statistical certainty which applies only to a subgroup of cancer-prone women. The knowledge that I will have to mastectomise a whole group of women to benefit only a few (those who would otherwise have died from breast cancer) appears unacceptable to me. The hell to me is the knowledge that I would in the future be able to have group statistics showing I am right, while I would be obliged to acknowledge in front of each woman that I may be wrong in her particular case. My own thoughts would also torment me: 'Is this woman really going to die of breast cancer if I do not convince her to accept this irreversible mutilation? Perhaps she will be unhappy all her life although she never would have got cancer, or would have been cured thanks to a breast-sparing strategy, or would have got cancer only in one breast and I unnecessarily remove the other one...' In our era of evidence-based medicine and of sophisticated statistics, I want to cling to the simple *primum non nocere* I was taught. I see no reason why the principle of non-maleficence in relation to one individual should be discarded in favour of a new principle of beneficence in relation to the group. This new principle may be defended when the harm caused to each individual is an acceptable transient discomfort (i.e. the one caused by an adjuvant chemotherapy in breast cancer), definitely not when it may have everlasting devasting consequences I have tried to imagine above.

(2) Hell would be to accept the idea that medicine is a religion whose god is Life. I do not want to sacrifice young women's breasts on the altar of Life, because I do not worship Life. I am not a servant of Life but a servant of Health, which supposes life but cannot be reduced to life. If I were to become haunted by the idea of preventing death, I know I could forget that my job is to help people live. this point has been very acutely expressed by Theodore Fox: 'People differ in their attitude to life. Some cling to it as a miser to his money, and to as little purpose. Others wear it lightly—ready to risk it for a cause, a hope, a song, the wind on their face. When so many people think of it (life) as a means, the doctors, surely, would be wrong to insist that it is always the first of ends. Life is not really the most important thing in life' [22]. It is so obvious that life has to be preferred to death that one may not realise that lives are sometimes ruined trying to avoid death. The French philosopher André Compte-Sponville made this point very clear: 'the *right to life* does not mean that death is a crime... To pretend to ban death not only means to be mistaken about death, but also to lie to oneself about life... Courage and philosophy should be enough (to live). No one fully accepts life without accepting death too' [23].

CONSEQUENCES OF THE DISTORTED PERCEPTION OF THE REALITY OF MEDICAL POWER

People almost always have a distorted perception of the reality when they come to the oncogenetic consultation. If they belong to a family with multiple cases of cancer, they very often overestimate their risk of getting cancer [24] and the first task of the genetic counsellor is to educate about the facts, which is a very efficient way to reduce anxiety [24]. Reduced anxiety in turn enables the patient to understand their situation much better. Patients' expectancies about our power may also be exaggerated, a tendency which is unfortunately very often supported by unrealistic claims in the press about some medical breakthroughs related to new discoveries in cancer genetics.

We reluctantly accept the idea of erasing the distance of knowledge and of power of decision that separates us from our patients, because this distance is a protection both to our patients and to us. We may want to spare our patients the anxiety of sharing the uncertainties and difficulties of our decision process. Perhaps more egoistically, this distance may enable us to avoid the hardship of spending an enormous amount of time, patience and psychological commitment required to explain all the reasons leading to the choice of one treatment instead of another. Keeping this distance may often be a condition to a good practice of cancerology (as long as the proposed treatment is not a trial). However, in the practice of genetic counselling, we have to share our knowledge and renounce our power over people, because some decisions are beyond the scope of medicine. Genetic counselling may mean shaking the unrealistic faith some have in our power, because there is no medicine without trust and trust cannot be based on a lie (that a personal decision can be taken by someone else—even if this someone is a good doctor). Experience shows that patients can understand and accept the limits of medicine. While they can be very grateful to doctors taking the time necessary to explain how delicate the problems are, they can be very disappointed when they discover that—knowingly or not—their doctor did not tell them the truth.

Many people believe that medicine has the solution to their problem. This desire creates the illusion that the doctor's conclusions are necessarily good for them, which makes them extremely vulnerable to the advice given by the benevolent genetic counsellor. If a person is convinced that the expert knows the facts and knows how to use this knowledge in the right way, she will follow the advice given to her. A consequence of this faith in the doctor's words has been described as the process of 'anticipated decision regret' [25]. This process will make the cancer-prone woman accept bilateral prophylactic mastectomy, even if she is repelled by this idea. Acceptance of the intolerable is made possible by the illusion that refusing would be misbehaviour. Since the doctor knows what lies in the future, the patient is forced to accept by the tormenting thought that the disease will develop in the future if she refuses to follow the advice. Her illness and possibly her death would thus be her fault. This process of 'anticipated decision regret' puts an enormous weight on the doctors' advice. We sometimes have to play on this sensitive chord, in face of an emergency for example, but an emergency situation is totally incompatible with the process of genetic counselling.

When a genetic counsellor authoritatively decides what's good and counsels accordingly, he is exerting an unjustifiable tyrannical authority over people who have to accept his decision because he is the expert. It is our responsibility in genetic counselling to separate clearly knowledge from beliefs, even if it means dismantling the faith people have in the power of medicine. We are still ashamed of the atrocities caused in the name of medicine during the era of eugenics utopia. Hundred of thousands of healthy people were sterilised in order to reduce the societal burden of supposedly inherited disorders. Geneticists decided the fate of their patients because their aim was not to help individuals, but to implement a scientifically-based political decision for the betterment of mankind [26, 27]. Let's hope that the oncogeneticists will refuse exerting any dictatorial power in the name of a 'happy cancer-free' utopia.

CONCLUSIONS

Dr Klijn and I have tried in this debate to defend an ethics of conviction. Now the game is over, and I think that the best doctor would be none of the characters we tried to play, because we have to defend the ethics of responsibility, which states that prudence is a cardinal virtue in the practice of medicine and would advise to weigh out all possible consequences of our plans before acting. The ideal doctor would not follow any dogma but adapt every decision to each cancer-prone woman. This ideal doctor is very wise and patient, spending as much time as is needed to educate each individual person seeking advice about genetics, about risks and about ways of avoiding the risks. He is not carried away by the success of molecular genetics, as he knows how difficult it is to apply it in the patients' interest. He knows that success or failure in genetic counselling cannot be evaluated by any effect on the frequency of a disease or on its mortality, but has to be evaluated by the extent to which it has helped solve individual problems (which is much more difficult to measure). He respects the autonomy principle and clearly dissociates the facts from the values they may have. He accepts enduring inner conflicts when his own convictions differ from the patients' philosophy of life. He discloses the many pitfalls lying in an excessively simplistic idea of the role of a genetic counsellor, and when he is asked: 'Doctor, what would you do if you were in my place?', he knows he has to spend more time counselling. When counselling healthy people, we have to remain conscious of the fact that 'health is not happiness and medicine is not a philosophy—and not treatment can substitute for wisdom' [28].

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It has been known for many years that a family history of breast carcinoma is, along with increasing age, the most important risk factor for the development of breast cancer. The elevated incidence of breast carcinoma and its genetic heterogeneity have limited, until recently, the understanding of its mechanisms of inheritance. Approximately 30% of patients with breast cancer have some degree of family history of breast carcinoma. Twelve per cent have two affected relatives, and 6% have three or more relatives.

Recently, the contribution of some genes to the predisposition of developing breast carcinoma has been demonstrated, the most important of which seem to be the genes *BRCA1* and *BRCA2*. *BRCA1* is a gene located in chromosome 17, that is linked to approximately 45% of hereditary, early-onset breast cancers and approximately 85% of cases of the hereditary breast and ovarian cancer syndrome. It has recently been estimated that the frequency of *BRCA1* mutation in the general population is 0.0006, and that the proportion of breast cancers due to *BRCA1* is 5% below 40 years of age. This relationship diminishes with age and *BRCA1* is associated with 2% of breast cancers between 40 and 49 years and 1% between 50 and 70 years. The cumulative risk of developing contralateral breast cancer in breast cancer patients who are *BRCA1* carriers seems to be very high: 87% by the age of 70 years (with 95% confidence limits from 72% to 95%). Specific mutations for particular population groups have been described, such as Ashkenazi or Sephardic Jews or Icelanders. It is remarkable that *BRCA1*-related breast cancers have a more favourable clinical course than other hereditary breast carcinomas. The *BRCA2* gene is localised in chromosome 13. Its contribution to hereditary breast carcinoma may be as high as 40%, although genetic testing is not as developed as in the case of *BRCA1*. Other genes with marginal contributions to hereditary breast cancer are *p53* and the ataxia-telangiectasia gene.

Several questions arise in relation to genetic testing in patients with breast cancer and their relatives.

Is the appropriate test available now or should we wait for new diagnostic developments? It is clear that the difficulties of detecting mutations in *BRCA1* are quite important, since *BRCA1* is a large gene with non-clustered mutations, which makes the available DNA testing very time-consuming and expensive. Perhaps the development of a biochemical (functional) test that detects the enzymatic activity of the *BRCA1* protein will allow a more precise and certainly less expensive massive testing.

Who should be tested? The number of relatives with breast cancer is a known marker for developing breast cancer. Many centres now accept genetic testing for only those families with three or more affected members. Age is also used as a selector for testing. Since the genes *BRCA1* and *BRCA2* are linked especially to early-onset breast cancer, usually only members of less than 40 years of age are tested to assess their risk.

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