Is there a demand for PGD and/or PND among healthy BRCA1/2 carriers at a reproductive age? A contingent valuation survey.

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Abstract

Breast cancer is one of the most common neoplasms in women and 2-5% are due to high-risk penetrance genes, such as BRCA1/2. Carriers are estimated to have a risk of 65–80% of developing breast cancer and 20–45% of developing ovarian cancer at a younger age. Few options are available to avoid transferring their mutation to the next generation (transmission risk=50%): adopting, ovum or sperm donation, preimplantation genetic diagnosis (PGD) and prenatal diagnosis (PND). PGD and PND for BRCA1/2 mutations are offered differently according to the countries. In France they are allowed based on the severity and non curability of a condition. Hereditary cancers could therefore be considered as indications; however no authorization has yet been reported. Exploring expectations of French BRCA carriers is necessary to incorporate these preferences into clinical care.

The national GENEPSO cohort gives us the opportunity to elicit the existence of a demand toward PGD and PND; and to elicit preferences toward these two diagnoses. In this objective we have used the contingent valuation (CV) method to elicit respondents' willingness to pay (WTP). Eligible subjects were women (18 - 49 years) and men (18 - 69 years) having been disclosed the test result for more than one year, carriers of a BRCA1/2 mutation, unaffected by cancer.

Among the 460 respondents 28% declared that, in the context of a theoretical next pregnancy, they would wish to beneficiate neither from PGD nor from PND. Multivariate adjustment shows that probability to be in this refusal group increases with education, prior knowledge of the existence of PGD/PND, considering PND and PGD equivalent, considering termination of pregnancy (TOP) for BRCA1/2 unacceptable, the importance attached to the risk of miscarriage implied by PND and to the increasing risk of cancer implied by hormonal stimulation. It decreases when considering information on PGD/PND should be given systematically, the importance attached to the fact that, with PGD, the fetus will be free from BRCA1/2 mutation and to the fact that after PND the question of TOP will be raised. Among the 330 respondents to whom the CV exercise was proposed, 64% have given a value to PGD or PND. WTP_{PGD} and WTP_{PND} were closed (1952€ *vs.* 1808€). WTP_{PGD} increases with income, when therapeutic ToP was considered acceptable, knowledge of the risk of transmission and certainty of wishing to beneficiate from PGD. WTP_{PGD} decreases when maternity project was not influenced by results of the test and when TOP was experienced. WTP_{PND} was mainly determined by WTP_{PGD}, but also increases with income, being a male and certainty of wishing to beneficiate from PND.

Debate around PGD/PND for BRCA1/2 carriers came from the fact that a mutation "only" predisposes to cancer. Our survey shows that BRCA carriers support the use and access to PGD/PND and challenges the recommendations to be made to onco-geneticians.

Introduction

Breast cancer is one of the most common neoplasm in women and between 2 and 5% are due to high-risk penetrance genes, such as BRCA1 and BRCA2 (Fortuny et al 2009). Carriers of mutations in these genes are estimated to have a lifetime risk of 65–80% of developing breast cancer and up to 20–45% of developing ovarian cancer (Antoniou et al 2003). Breast cancer in BRCA1/2 carriers may develop at a younger age than in the average population and women may also have a higher risk of bilateral disease or multiple neoplasms (Dekeuwer & Bateman 2013; Metcalfe et al 2004). Male BRCA2 mutation carriers also face a higher lifetime risk of breast and prostate cancer (Levy-Lahad & Friedman 2007). The probability of transmitting the mutation to each offspring is 50% and it has been shown that one of the main reasons for undergoing genetic testing of BRCA1/2 reported by individuals is to know if their children are at risk (Pasacreta, 2003; Meiser et al., 2006). Few options are available for those who wish to avoid transferring their mutation to the next generation: avoid to having children, ovum or sperm donation, preimplantation genetic diagnosis (PGD) and prenatal diagnosis (PND).

Recently a debate has been raised about extending the use of PGD and PND to include lower penetrance, late onset cancer such as hereditary breast and ovarian cancer (Clancy 2010). As an answer, the UK Human Fertilization and Embryology (HFEA) undertook, in 2005 and 2006, a public consultation (Menon et al 2007), and two French public bodies (the Agency of bio medicine and the National Cancer Institut (INCa) (D. Stoppa-Lyonnet & al. 2008) set up, in 2007, a working party to report the use of PND and PGD for hereditary forms of cancer (Dekeuwer & Bateman In press).

PGD and PND for BRCA1/2 mutations appear to be offered differently according to the countries (Quinn et al 2009c; Sagi et al 2009). For instance, in United Kingdom access to PGD and PND was authorized since May 2006 and depends of the perception of the severity by the couple, in USA it depends of the financial capacity of the couple, it was forbidden in Germany and has been approved in Israel by the National Bioethics Council. In France PGD and PND are allowed based on the severity and non curability of a condition. Hereditary cancers could therefore be considered as potential indications for PND or PGD. However it has been shown that the acceptability of PGD/PND for BRCA1/2 carriers was low among the French professionals in charge of giving these authorizations (Dekeuwer & Bateman In press; Julian-Reynier et al 2009). As far as we know no such authorization for a BRCA1/2 PGD/PND has yet been reported in France (Julian-Reynier et al 2012).

Whatever is the rule, these practices are emerging in industrialized countries, and carriers' attitudes, decision or hypothetical behaviors begun to be documented. To date, PGD is often exposed as a preferable alternative to PND avoiding the difficult decision of whether to terminate an affected pregnancy (Vergeer et al 1998). Thus studies mainly dealt only with PGD (Ormondroyd et al 2012; Quinn et al 2009b; Quinn et al 2010a; Sagi et al 2009; Staton et al 2008; Vadaparampil et al 2009), less often with PGD and PND (Fortuny et al 2009; Menon et al 2007), and none only with PND. Among survey dealing with both PGD and PND, the trend was to observe a higher proportion of respondents which found PGD acceptable compared to PND; although a preference for PND over PGD has also been found (Alsulaiman et al). Acceptability of PGD among those different surveyed population has been shown to vary with the severity of the condition, and in particular for adult onset condition such as breast and ovarian cancer (Alsulaiman et al). However, (Menon et al 2007) reported that 75% of 52 women BRCA1/2 carriers felt that it was acceptable to offer PGD for BRCA carriers, but 33% would consider PGD and 15% would consider PND for themselves. Similarly, (Fortuny et al 2009) reported that 61% and 74% of 77 men and women just before BRCA1/2 testing found respectively PGD and PND acceptable; and that 48% and 55% would consider PGD and PND for themselves if they were carriers. Similar rate of intention of resort to PGD for themselves were obtained (third of the sample) among a web-based survey of 962 women concerned with hereditary breast and ovarian cancer (composed of 49% of BRCA1/2 carriers, 35% of non carriers, and 16% of others) (Vadaparampil et al 2009); a survey among 111 women personally affected by hereditary breast and ovarian cancer (70% of BRCA1/2 carriers) (Quinn et al 2009b); and a survey among 228 men BRCA carriers or having a partner or first degree relative carrier (Quinn et al 2010a). In one web

based survey among 213 women BRCA1/2 carriers only 13% of them declared they would consider using PGD (Staton et al 2008).
Further research is necessary to explore the expectation of BRCA carriers of reproductive age to incorporate these preferences into clinical care and to allow the adaptation of the law to the progress of the sciences. To give us the means of a rigorous thought, it was necessary to know the opinions of the directly concerned persons (Menon et al 2007) and to explore the values they attributes to PGD and PND. If previous survey gives some elements of discussion, they have used little sample size (from 52 to 228) (Fortuny et al 2009; Menon et al 2007; Quinn et al 2010b)except for the web-based survey (n=961), but performed among heterogeneous respondents, they have often interviewed only women, and to our knowledge, none of them have reported the monetary value of both PGD and PND.
The national French GENEPSO cohort, (GENe Etude Prospective Sein Ovaire).(Andrieu et al 2006) gives us the opportunity to firstly elicit the existence of a potential demand from healthy women and men BRCA carriers of reproductive age toward both PGD and PND and to explore their characteristics; and secondly, when a demand was expressed, to explore their preferences toward these two diagnoses. In this objective we have used the contingent valuation (CV) method to elicit respondents' willingness to pay (WTP). The CV method is a stated preference approach designed to directly estimate welfare gains. Respondents are asked to consider a hypothetical scenario where they are asked to imagine that a market exists for the public program at stake. The exercise proceeds on the hypothetical contingency that such a market exists(Frew 2010). The CV method allows taking into account the whole attributes and the heterogeneous nature of the amenities to be valued (Carson et al 2000; Mitchell & Carson 1989; Protière et al 2004; Ryan 1996). The third objective was to determine factors associated with the variation of these monetary values.

Materials and Methods:

Sampling

Eligible subjects were women aged between 18 and 49 years, and men aged between 18 and 69 years at time of the survey, carriers of a BRCA1/2 deleterious mutation, unaffected by cancer and having been disclosed the test result for more than one year at the time of the survey.

Recruitment

Participants were identified in the French GENEPSO cohort, (GENe Etude Prospective Sein Ovaire).(Andrieu et al 2006) The GENEPSO cohort consists of BRCA1/2 carriers recruited in a routine consultation context since 2000 among 29 cancer genetic clinics belonging to the French National Federation of Cancer Centers' Cancer Genetic Network.

Questionnaire

The questionnaire was developed by a multidisciplinary working group of social scientists, clinicians, psychologists and a group of talks composed of women with a genetic predisposition to hereditary breast ovarian cancer (BRCA1/2 mutations).

Sociodemographic characteristics

Respondents were asked usual socio-economic characteristics (age, sex, marital status, professional activity, level of education, monthly income of the household and number of children) and if they were religious believer.
As the sample was better educated and then had a higher level of income compared to the general population (Table 1), those two variables were dichotomized to compare the highest class to the rest of the sample (Master or doctoral degree vs. other, and monthly household income > 5000 € vs other).

Maternity project

Respondents were asked if they had a maternity project in the next few years (yes, you are (your spouse is) pregnant / yes, you are trying to get pregnant / yes, you have a present desire to have a child / perhaps latter / no / you cannot anymore / you don't know). A new variable was created by

grouping together respondents who have answered one of the three first propositions: maternity project (yes/no).
They were also asked whether the result of the genetic test had influenced their maternity project (yes, absolutely / yes, a little / no, not really / no, not at all / not concerned (family already made). A new variable was created grouping the positive negative answers to be compared to the other.

Perception of own health and family history

To evaluate respondents' perception of their own heath, they were asked the following question: "Compared to someone of your age and gender, how would you rate your health status?" (Excellent / very good / good / fair / poor / don't know). This measure was dichotomized opposing the respondents who perceived their health as excellent or very good to the others.
Family history of breast/ovarian cancer was collected during the cancer genetic consultation. It included the number of women first and second degree relatives having had breast and/or ovarian cancer.

Knowledge and perception of risks

Knowledge of the exact risk of transmission (50%) was evaluated by asking respondents: "According to you, the risk for a child to carry the BRCA1/2 mutation identified for her/his father is?" (Null / one of two (50%) /one of four (25%) / 100% / don't know). The same question was asked when the mutation was identified for the mother. In analysis, a new variable was used taken the value of 1 when respondents have given the exact answer (50%) for both the father and the mother and the value of 0 otherwise.
Perception of the own risk to develop a cancer was measured with the following question: "Compared to someone of your age and gender, you think your own risk of developing cancer is?" (very superior to average / superior to average / equal than average / inferior to average / very inferior to average). The measure was re-coded onto three categories: very superior to average / superior to average / equal or less than average.

Perception and behaviors toward PGD and PND

Acceptability toward Therapeutic Termination of Pregnancy (TOP) for Down's syndrome first and for BRCA1/2 mutation after was evaluated by asking respondents whether they felt therapeutic TOP acceptable for themselves (yes, certainly / yes, rather / it depends / no, not really / no, certainly not / I don't know). For Down's syndrome, the variable was recoded onto three categories: yes, certainly /yes rather / others. For BRCA1/2 mutation, the variable was also recoded onto three categories, but not the same: Yes / It depends and don't know /No.
To ensure a common knowledge, a description of PGD and PND was given to respondents (fig 1), they were then asked to quote the importance they give to five characteristics of PGD and three characteristics of PND using a ten points Likert scale (from 1, very low to 10, very high). These latest variables were entered as specific ones. Respondents were also asked whether they considered that information about the possibility to access to PGD and PND should be given systematically (yes, totally / yes, perhaps / not really / not at all). In the analysis, the measure was dichotomized opposing the respondents who have answered yes totally to the others.
As a low participation rate to the CV exercise was expected (firstly because of the assumption of a high level of refusal toward PGD and moreover toward PND, and secondly because of the sensible aspect of the programs to be valued), we have asked respondents which sentence best reflects their opinion: 'PGD is preferable to PND', PND is preferable to PGD' or 'PGD and PND are equivalent'.

Before initiating the CV exercise, the context at time of the survey was exposed: that is to say revision of the French bioethics law concerning, among other things, the question of access criteria to PGD and PND. We have first evaluated respondents' theoretical demand for PGD and according to their answer they were asked, or not, their WTP for PGD. The same procedure was repeated for PND (cf. flow chart in Figure 2). The question of PGD and PND being sensible, particularly because respondents were directly concerned, we have chosen to evaluate first PGD as it seems to be more acceptable than PND in the literature.

Theoretical demand toward PGD/PND for a next pregnancy

The theoretical demand of PGD/PND was evaluated by asking respondents the following question: "Imagine you wish to have a child and PGD/PND is accessible in France for men and women carriers of a *BRCA1/2* mutation. Would you want to benefit from it?" (yes, certainly / yes, probably / I don't know / no, not really / no, not at all). Respondents who give a negative answer were not asked the WTP question.

To distinguish respondents who have answered "yes" from respondents who have answered "I don't know", a dichotomous variable was created (sure/unsure). This variable was considered as a proxy of certainty of the wish to beneficiate.

CV exercise

All respondents from the CV group received the following explanation: "Now we take an interest in the value you give to PGD/PND. A way to evaluate the intensity of this value is to ask you the maximum amount you are willing to pay. "They were then asked: "Imagining this technique is not funded by the health system, would you be willing to pay to beneficiate of it?" (yes/no). All respondents who were willing to contribute were asked the following question: 'How much is the maximum you will be willing to contribute to beneficiate from PGD/PND? Please bear in mind that your contribution would reduce what you have left to spend on other things'. Because it was a mailed survey and to facilitate answers , the following pre-coded scale was used (€):1 to 10, 11 to 50, 51 to 100, 101 to 150, 151 to 300, 301 to 500, 501 to 1000, 1001 to 2000, 2001 to 5000, 5001 to 10000, 10001 to 20000 and more than 20000. The middle of each range was used to represent a respondent's value.

When there is a positive WTP value for one diagnosis and a missing value for the other, the missing value was replaced by a "zero", on the assumption that, if the respondent has given a value to one diagnosis, he could not be seen as a protestor and then could not be excluded of the sample. Respondents who have given a positive value to at least one diagnosis represented then the subsample of participants in opposition to protestors. A dummy variable was created to indicate when respondents have contributed to both diagnoses.

Statistical analysis

The analysis was composed of three steps (Figure 2).

In the first step, the group of respondents who refused both PGD and PND (refusal group) were compared to the others (CV group).

In a second step (among the CV group), participants were compared to protestors. This second step allowed us to estimate the participation equation used to control for potential selection bias using Heckman procedure (Heckman 1979).

For this two first steps, comparison were made in term of socio-demographic characteristics, maternity project, perception of own health and family history, knowledge and perception of risks, and perception toward PGD and PND. Univariate analyses were performed using χ^2 for qualitative data and Student's t-test and one way analysis of variance (ANOVA) for continuous data. Multivariate adjustments were performed using a Probit model, all factors related to the dependent variable in univariate analyses (entry threshold: $p<0.20$) were initially introduced in the multivariate model, and then a backward selection procedure was performed and variables that remained significantly related at the $p<0.05$ level were retained in the final models. To allow interpretation of the model, marginal effects (effect of a unit change of a variable on the probability $P(Y = 1|X = x)$, given that all other variables are constant) at the mean were presented. Goodness of fit was investigated based on the classification of observed and fitted values.

The third step concerned the WTP exercise. We first described mean WTP for PGD and PND. Following that, univariate analyses were performed to define eligible factors to be included in multivariate model. We performed first a three step procedure to take into account for the selection bias as well as the interdependence existing when several programs are evaluated in a joint CV study (Luchini et al 2003; Protière et al 2004; Protière et al 2003). This estimation method was proposed in (Lee et al 1980), who proved the consistency of the estimator and derived its asymptotic covariance

matrix, and is known as the 'Heckman-Lee estimator' (Greene 2002). As the results showed no evidence for selection bias (results not shown), we have finally retained a simultaneous equation recursive model specification (Blau & Duncan 1967) to take interdependence between the evaluations of the two programs into account[1]. As in (Luchini et al 2003) the order of evaluation being the same (PGD before PND) we only introduced the value given to PGD (WTP_PGD) as an endogen variable.

Analyses were performed with the STATA IC 10 software program.

To lighten the read of the tables, some of the variables that never presented significant statistical difference were only presented in Table 1. Three concerning PGD (PGD require a hormonal stimulation increasing the risk of cancer, PGD provided a 20% rate of success and PGD medicalized the pregnancy), two concerning socio-demographic characteristics (living with a partner and having a professional activity) and perception of own cancer risk.

Results

Among the 605 carriers surveyed, 490 agreed to participate and send back their questionnaire (rate: 80.9%); 30 respondents were excluded from the analysis because of missing values in the outcome variables studied, yielding a final total of 460 questionnaires available for analysis. The average age of the sample was 39.89 (±9.69) and it was composed of a lower proportion of men than women. It should be noted that because of the inclusion criteria men were significantly older than women (49.8 vs. 37.1 – $p<0.001$). The whole sample had a higher level of education and of resources compared to the general population.

First step: comparison between the refusal group and the CV group

Among the 460 respondents, 198 (43.0%) declared that, in the context of a theoretical next pregnancy, they would not wish to beneficiate from PGD and 158 (34.3%) from PND ($p<0.001$). A total of 130 (28.3%) declared that they would not wish to beneficiate neither from PGD nor from PND. This group of respondents, which were then not asked the CV exercise (refusal group), was compared to the remaining respondents (CV group) (Table 1).

Multivariate adjustment shows that the probability to be in the refusal group increase when respondents were highly educated (from 14.7% *ceteris paribus*), when they had prior knowledge of the existence of PGD and/or PND (11.3%), when they considered PND and PGD being equivalent (13.6%) and, quite logically when therapeutic TOP for BRCA1/2 mutation was considered as unacceptable (26.2%). The probability to be in the refusal group also increase with the importance placed on the fact that PND by amniocenteses implied a risk of miscarriage (an increase of 2.4% with an increase of a unit of the score, *ceteris paribus*) and PGD require an hormonal stimulation increasing the risk of cancer (2.1%).

On the opposite, the probability of being in the CV group increase when considering the information on PGD and PND should be given systematically (19.3%), but also with the importance accorded to the fact that PGD allows to initiate the pregnancy with the quasi certitude that the fetus will not have the mutation (4.1%) and that after PND the question of therapeutic TOP will be raised (2.6%).

Although they don't remain significant in the multivariate model, some variables of specific interest were significant in the univariate analysis. A significant higher proportion of respondents has a maternity project in the refusal group compared to the CV group (31.5% vs. 20.6%, $p=0.013$) suggesting that PGD and PND were less conceivable among respondents most directly concerned by the question. Respondents in the refusal group more often considered their health as excellent to very good (50.0% vs. 33.9%, $p=0.001$) and had more often prior knowledge of the existence of PGD

[1] The interdependence was confirmed by the high correlation of the error terms when independent regressions for each WTP values are performed (rho=0.9, $p<0.0001$).

and PND (67.7% vs. 51.5%, p=0.002) and they were more often believers (56.3% vs. 46.1%, p=0.051) compared to the CV group.
A surprising result is that in both groups PND is more often considered as preferable than PGD (a little more than one third of the sample), however a higher proportion of respondents from the CV group, compared to the refusal group, considered PGD as preferable than PND (28.5% vs. 17.7%, p=0.017).
The two groups of respondents do not statistically differ in term of age, number of children, marital status, having a professional activity and monthly household income, burden family (number of close relatives having had a cancer), perception of cancer risk or knowledge of the exact risk of transmission.

Second step: participation equation

Among the 259 respondents who declared that they don't know if or they would like to beneficiate from PGD, 154 (59.5%) have given a positive WTP value (46.7% of the CV sample and 33.5% of the whole sample). Among the 301 respondents who don't know if or would like to beneficiate from PND, 180 (59.8%) have given a positive value (54.5% of the CV group and 39.0% of the whole sample).
Among the 330 respondents to whom the CV exercise was proposed, 211 (63.9%) were participants and have given at least a value to PGD and/or PND (45.9% of the whole sample).
Table 2 shows that the probability of being participant increase when respondents were from the highest class of income (19.2%), with the certainty of wishing to beneficiate from PGD (14.4%) and from PND (25.8%) and with the importance given to the fact that PGD allows to initiate the pregnancy with the quasi certitude the fetus will not have the mutation (4.1%).
The probability of being protestor increase when respondents have experienced miscarriage (19.5%) and considered PGD and PND being equivalent (16.9%).

The following variables significant in the univariate analysis do not remain significant in the probit model. Compared to protestors, participants gave a higher importance to the fact that PGD allow to avoid a potential decision of therapeutic ToP (7.86±2.18 vs. 7.11±2.25, p<0.001). A smaller proportion of participants considered that results of the genetic test have not influenced their maternity project (44.1% vs. 55.5%, p=0.047), has experienced miscarriage (9.5% vs. 16.8%, p=0.050) and a higher proportion considered that PGD is preferable to PND (33.6% vs. 19.3%, p=0.006) compared to protestors.

Third step: WTP values

As shown in Table 3, WTP for PGD and PND were much closed (1952€ *vs.* 1808€, p>0.05). Fifty eight percent of respondents (n=123) have given a positive WTP value to both diagnoses, and in this case have generally given a similar or equal WTP value. A small part (n=88) has given a positive WTP to only one of the two diagnoses and, in this case has given a smaller WTP value compared to respondents who have given a positive value to both diagnosis. As expected this suggests the existence of interdependence between the two evaluated programs. Interestingly a higher proportion of respondents have given a positive WTP value to PND compared to PGD, a result that could be linked with the fact that PND is more often considered preferable than PGD (Table 1).

Let now turn to the explanatory variables of WTP for PGD and PND. Table 5 shows results of the simultaneous equation model. The WTP value for PGD increases when respondents were from the highest class of income which confirms the internal validity of our results and; quite logically when they considered that therapeutic TOP for Down's syndrome and BRCA1/2 mutation were acceptable. It also increases when respondents knew the exact risk of transmission of the BRCA1/2 mutation and; with certainty of wishing to beneficiate from PGD in the context of a theoretical future pregnancy. On the opposite, the WTP value for PGD decreased when respondents considered that the results of the genetic test had not influenced their maternity project and when they have experienced voluntary ToP.

The WTP value for PND, was mainly determined by the WTP value given to PGD, but also increased when respondents were from the highest level of income and with the certainty of wishing to beneficiate from PND in case of a future pregnancy. One additional variable that determines the variability of the WTP value for PND is the gender which could be explained knowing that men found ToP more acceptable than women (Julian-Reynier et al 2012).
Although they do not remain significant in the simultaneous equation model some of the variables significant in the univariate analysis (Table 4) deserved attention. Number of children was positively correlated with the WTP values given to both PGD ($p<0.05$) and PND (but only at the 10% level), which is a counter intuitive result; if we considered that the family is completed. Another counter intuitive result is the sign of the correlation between the value given to PND and the importance given to the fact that PND let the initiative of pregnancy to the couple (negative) and raised the question of therapeutic ToP (positive). In the first case respondents who have given a higher importance to the initiative of pregnancy most frequently preferred PND to PGD and have most often given a WTP value only for PND, and then have given a smaller WTP value (cf. Table 3). The opposite applied for the second case: respondents who have given a higher importance to the question of therapeutic ToP have given a value to both diagnoses.

Preliminary discussion

This survey was, to our knowledge, the first investigating both PGD and PND supply and values among a large national cohort of healthy male and female BRCA1/2 carriers at a reproductive age (Lin et al 2013). The high participation rate (81%) shows the interest raised by the topic of PGD and PND among respondents. A little more than a quarter of the sample (28%) is firmly opposed to both PGD and PND. This proportion of refusal is in line with results from (Fortuny et al 2009; Menon et al 2007) and less than (Quinn et al 2009c; Vadaparampil et al 2009). The reasons of refusal among this high educated and informed group are directly linked with the opposition to therapeutic termination of pregnancy and the risk associated with PGD (hormonal stimulation) and PND (risk of miscarriage).
Among the remaining respondents (who have declared that they don't know if or they would like to beneficiate to at least one of the diagnosis) a majority (60%) have given a positive WTP value. That is to say nonetheless BRCA1/2 respondents were concerned with PGD and/or PND, but they were willing to contribute to beneficiate of them (they represent one third of the whole sample). Then our hypothesis of a massive rejection of PGD and/ PND is rejected. It is worth noting that our sample is nearly separated into three equivalent part: one third in opposition and even sometimes shock by PGD and PND, one third in favor, and one third in a more mitigate position. In accordance with the internal validity of CV surveys, participants (the ones who have given at least a positive WTP value to PGD or PND, 64% of the sample) had higher level of incomes and were more often certain of their wish to beneficiate from PGD and/or PND. They also gave a high importance to the certainty to initiate a pregnancy with the quasi certitude the fetus will not have the mutation. More interestingly, refusing to participate is correlated with a lack of preference between the two diagnoses and with an experience of miscarriage, suggesting that the impact of such an experience decrease the value of both diagnoses.
The interpretation of the WTP values obtained for PGD and PND is not straightforward. Indeed, they had given very close values to both diagnoses (1952€ for PGD and 1800€ for PND, median 225). This result could be interpreted in several ways. First respondents, in average, considered PGD and PND of equal values. However, although the general population is not suppose to know the cost of PGD nor PND, we may assume the reasonable assumption that every one evaluate the cost of PGD higher than the cost for PND (in particular knowing we have given to respondents a description of each procedure). For information, PGD price is 6800€[2] and PGD price is 675€[3]. From this point of view, the

[2] This amount is the price paid by a couple not covered by the French social security, strangers for instance, and who pay the totality of the treatment. This evaluation came from one of the 6 centers allowed to perform PGD in France (source cf. Isabelle Coupier)

[3] Based on the French social security tariff.

second interpretation could be that respondents gave a higher value to PND. This interpretation is supported by a significant higher proportion of respondents refusing PGD (43%) than PND (34%) when they were considered separately, and by the higher proportion of respondents who have given a positive value to PND than to PGD (respectively 55% and 47% of the CV group) and by the higher proportion of respondents who have declared preferring PND to PGD (35%) than the opposite (25%).
The WTP values drawn from a CV survey are determined by the characteristics of the respondent and the characteristics of the contingent market. By their nature CV studies are only representations of the world, and it is highly unlikely that stated preferences will ever fully match revealed preferences (Smith 2003). However their purpose is to provide a structure to guide public decisions. We face here a clear limit of CV surveys used in the objective to discriminate between two amenities. A solution could have been to use the marginal approach who ask individuals to consider what program they prefer and then to reveal their maximum WTP (Shackley & Donaldson 2002). Because we have anticipated to obtain very few answer to the CV exercise, in part because of our assumption of a large rejection of PGD and PND, and moreover because of an assumption of a large rejection of the CV exercise itself, we have not retain this approach. Another limitation of our study is to have not randomly change the order of evaluation. The main reason of this choice was the feeling of some physicians that PND will not be seen as acceptable.
A third explanation could be that respondents have rather valued the idea of a potential access rather than each diagnosis separately perhaps because of the lack of knowledge about this relatively recent aspect of the subject. This third explanation is supported by the amount given according to the number of diagnosis for which a value was given. When a value was given to only PGD, the value is nearly 1827€ which is more than three time higher than the 556€ given for PND alone. In this case the value better match the amount expected given the nature of each diagnosis. When respondents have given a value to both diagnoses, the amount is around 2800€ for PGD and PND. This could be related to the anchor effect only. However, as already shown in the field of oncology in general (Protière et al 2011) respondents have expressed a high desire of information and a wish for divulging this information to the whole population at high risk of HBOC.
Another point has to be considered. If we consider WTP values as a measure of the strength of preferences, we also have to consider the consequences of each option. In the case of PGD, the risk is reported on the mother (risk of cancer increased by the hormonal stimulation) and the rate of success is relatively poor (20%). On the other hand, PND reported the risk on the fetus (termination of pregnancy, but also on the parents, because of the psychological burden associated with a termination of pregnancy). This another limit of our study and a qualitative follow up would have help to conclude. At this point it is interesting to observe that comparison of direct rank ordering (respondents were asked which of the two option they prefer) and indirect ordering is quite consistent (see table A1 in appendix). Respondents have given a higher mean WTP value to the preferred option (3051€ for PGD and 2439€ for PND when PGD is preferred and 819€ for PGD and 1121€ for PND, when PND is preferred) and equivalent mean WTP values when the two option are considered as equivalent (1684€ for PGD and 1517€ for PND). It is worth noting that the mean WTP for PND is higher when PGD is preferred (2439€) than the one when PND is preferred (1121€), because of the anchor effect.

Conclusion

Debate around the use of PGD and PND for BRCA1/2 carriers came mainly from the fact that a mutation predisposes to but does not guarantee the development of cancer and that most cancers would not develop until adulthood (Tung 2011). Our survey, consistently with previous one shows that BRCA carriers support the use of PGD (60% to 75%) and that fewer of them would personally consider the procedure for themselves (Fortuny et al 2009; Menon et al 2007; Quinn et al 2009a; Vadaparampil et al 2009), in particular, our results have shown a lower demand among directly concerned respondents (actual maternal project) as already shown by (Menon et al 2007). More specifically, our results show a demand for PGD and PND access. The demand seems to be not necessarily for themselves but rather for the availability of this option and that it should be

integrated in the process of decision. The larger demand and the higher proportion of respondents who have accepted to give a WTP value than expected (knowing the delicate nature of our purpose) should be integrated in future revision of the bioethics low.

Those results emphasized the difficult question of the recommendations which could be made to the onco-geneticians. Indeed in one hand a clear wish for a systematic information and for access to PGD and PND were observed, suggesting that they should answer to these demands, but on the other hand talking about the existence of PGD and PND whereas they were, in facts, not applied in France. The question is complicated by the existence if several genetics tests on the web.

Ethical objections toward PGD and PND have resulted in a wide range of acceptability and regulation rules in developed countries. Additional survey are needed among international populations and more specifically among younger population more in age to procreate.

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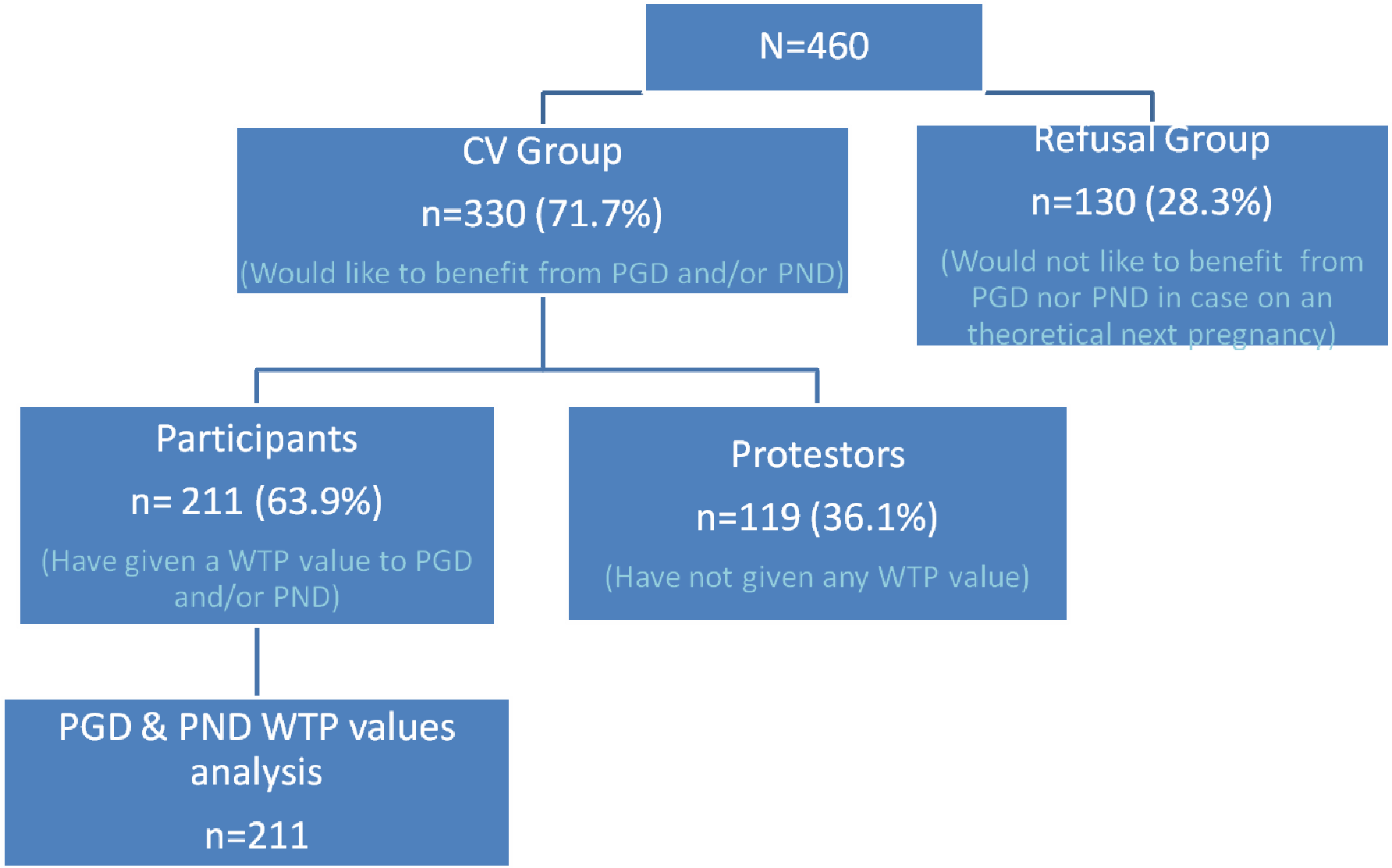
Figure 1: Description of PGD and PND

You will find below a short description of the procedures involved in Preimplantation Genetic Diagnosis (PGD) and Prenatal diagnosis (PND)

Preimplantation Genetic Diagnosis is an option when there is a high risk of parents transmitting a severe genetic disease to their offspring. A biological analysis carried out after in vitro fertilization (IVF) makes it possible to implant in the maternal uterus only healthy embryos not affected by the parental disorder.
IVF involves a hormonal method of ovarian stimulation which may increase the risk of cancer. Since this is a delicate intervention, only 20 women out of every 100 who undergo the PGD procedures will eventually give birth to a viable child.
In 5 to 10% of cases, PGD carries a risk of error. In view of this risk arising after a PGD, medical teams ***recommend*** amniocentesis as a means of prenatal diagnosis (PND) during the second trimester of pregnancy to make sure that the fetus is not affected by the genetic disease.
PGD enables parents to avoid having to think about the possibility of terminating pregnancy if the fetus is affected by the familial disease.

Prenatal Diagnosis (PND) makes it possible to determine during pregnancy whether or not the fetus is affected by a disease or by congenital abnormalities. When the disease is of a “particularly severe” kind and “no treatment is available”, a termination of pregnancy (TOP) can be proposed to the parents, provided the agreement of a Multidisciplinary Medical Team has been obtained.
When PND is carried out by performing an amniocentesis, the risk of spontaneous fetal loss is about 1%.
Prenatal Diagnosis enables couples to conceive their children in a natural (no medically assisted) way.

Figure 2: Flowchart



First step: theoretical demand for PGD and/or PND

Second step: participation equation

Third step: WTP analyses

Table A1 : Comparison of direct and indirect preferences

Direct preferences		WTP PGD			WTP PND		
	n	Mean	Sd	Median	Mean	Sd	Median
PND preferable to PGD	77 / 163	819	3602	0	1121	3677	225
PGD preferable to PND	71 / 117	3051	6555	750	2439	6499	125
PGD and PND equivalent	58 / 157	1684	4518	225	1517	4440	400

Table 1: Comparison between the CV group and the refusal group (n=460)

	Total (n=460)		CV group (n=330)			Refusal group (n=130)		Probit model (refuse=1)*		
								Coeff.	95% CI	dy/dx
	Mean	sd	Mean	sd	p	Mean	sd			
Age	39.89	9.69	40.32	9.77	ns	38.84	9.44			
Nber. of children	1.63	1.22	1.59	1.17	ns	1.73	1.36			
Nber. of close relatives with cancer	2.71	1.23	2.65	1.17	0.074	2.88	1.36			
PGD allow to initiate pregnancy with the quasi certitude that the fetus will not have the mutation	7.18	2.47	7.51	2.22	0.000	6.33	2.84	-.138	-.199 ; -.076	-.041
PGD allows to avoid a potential decision of TTP	7.28	2.47	7.59	1.13	0.000	6.51	2.87			
PGD requires an hormonal stimulation increasing the risk of cancer	7.27	2.54	7.18	2.48	ns	7.50	2.67	.072	.008 ; .135	.021
PGD provided a 20% rate of success	7.06	2.44	7.14	2.20	ns	6.86	2.95			
PGD medicalized the pregnancy	6.86	2.67	6.81	2.55	ns	6.98	2.97			
PND by amniocenteses implied a risk of miscarriage	6.45	2.9	6.27	2.88	0.049	6.88	2.96	.083	.028 ; .138	.024
PND let the initiative of pregnancy to the couple	7.05	2.70	7.04	2.67	ns	7.08	2.79			
After a PND the question of TTP will be raised	6.93	2.77	7.33	2.48	0.000	5.94	3.21	-.089	-.144 ; -.034	-.026
	n	%	n	%	p	n	%			
Male	102	22.2	82	24.8	0.028	20	15.4			
Living with a partner	386	83.9	274	83.0	ns	112	86.2			
Has a professional activity	370	80.4	260	78.8	ns	110	84.6			
Monthly household income					ns					
≤ 2000 €	107	23.3	83	25.2		24	18.5			
> 2000 € to ≤ 5000 €	265	57.6	188	57.0		77	59.2			
> 5000 €	88	19.1	59	17.9		29	22.3			
Educational level					0.003					
Less than baccalaureate	63	13.7	54	16.4	0.008	9	6.9	ref		
Baccalaureate to higher National Diploma	163	35.4	122	37.0	ns	41	31.5	ref		
First degree	112	24.3	76	23.0	ns	36	27.7	ref		
Master or doctoral degree	109	23.7	66	20.0	0.003	43	33.1	.459	.136 ; .783	.147
Being a believer	218	47.4	147	46.1	0.051	71	56.3			
Has a maternity project	109	23.7	68	20.6	0.013	41	31.5			

Consider that results have not influenced the maternity project (vs. yes and not concerned)	233	50.7	159	48.2	ns	74	56.9			
Health considered as excellent to very good	177	38.5	112	33.9	0.001	65	50.0			
Cancer risk					ns					
Very superior to average	130	28.3	86	26.1		44	33.8			
Superior to average	204	44.3	152	46.1		52	40.0			
Equal or less than average	126	27.4	92	27.9		34	26.2			
Knowledge of risk transmission for father and mother (vs. other)	297	64.6	205	62.1	ns	92	70.8			
Prior knowledge of the existence of PGD and/or PND (vs. other)	258	56.1	170	51.5	0.002	88	67.7	.393	.088 ; .699	.113
Consider TTP for Down's syndrome acceptable					0.001					
Yes, certainly	277	60.2	214	64.8	0.001	63	48.5			
Yes, rather	93	20.2	65	19.7	ns	28	21.5			
Other	90	19.6	51	15.5	0.000	39	30.0			
Consider TTP for BRCA1/2 mutation acceptable					0.000					
Yes	56	12.2	54	16.4	0.000	2	1.5	ref		
It depends, don't know	81	17.6	75	22.7	0.000	6	4.6	Ref		
No	323	70.2	201	60.9	0.000	122	93.8	1.080	.665 ; 1.496	.262
Has experienced miscarriage (vs. no)	61	13.3	40	12.1	ns	21	16.2			
Has experienced therapeutic ToP (vs. no)	6	1.3	4	1.2	ns	2	1.5			
Has experienced voluntary ToP (vs. no)	51	11.1	38	11.5	ns	13	10.0			
Preference					0.046					
PND	163	35.4	116	35.2	ns	47	36.2	Ref		
PGD	117	25.4	94	28.5	0.017	23	17.7	Ref		
Equivalents	157	34.1	105	31.8	0.096	52	40.0	.441	.139 ; .743	.136
Consider that information should be given systematically (yes, totally vs. other)	312	67.8	253	76.7	0.000	59	45.4	-.608	-.907 ; -.309	-.193

*The model correctly classifies 78.7% of cases

Table 2: Comparison between participants (participate to at least one diagnosis) and protestors (do not participate to any diagnosis) (n=330)

	Participants n=211			Protestors n=119		Participation equation Probit model (participe=1)		
	Mean	SD	p	Mean	SD	Coeff	95% CI	dy/dx
Age	40.25	9.82	ns	40.42	9.71			
Nber. of children	1.65	1.18	ns	1.47	1.15			
Nber. of close relatives with breast or ovarian cancer	2.60	1.17	ns	2.72	1.17			
PGD allows to initiate pregnancy with the quasi certitude that the fetus will not have mutation	7.87	2.02	0.000	6.87	2.43	.113	.046 ; .180	.041
PGD allows to avoid a potential decision of TToP	7.86	2.18	0.004	7.11	2.25			
PND by amniocenteses implied a risk of miscarriage	6.41	2.91	ns	6.03	2.84			
PND let the couple initiating the pregnancy	7.16	2.60	ns	6.82	2.80			
After a PND the question of TToP will be raised	7.42	2.53	ns	7.16	2.37			
	n	%	p	n	%			
Male	53	25.1	ns	29	24.4			
Monthly household income > 5000 €	45	21.3	0.029	14	11.8	.582	.151 ; 1.012	.192
Master or doctoral degree	51	24.2	0.012	15	12.6			
Being a believer	90	44.6	ns	57	48.7			
Has a maternity project	42	19.9	ns	26	21.8			
Consider that results have not influenced the maternity project	93	44.1	0.047	66	55.5			
Considered health as very good to excellent	79	37.4	0.074	33	27.7			
Knowledge of risk transmission for father and mother	133	63.0	ns	72	60.5			
Prior knowledge of the existence of PGD and;or PND	117	55.5	0.057	53	44.5			
TTP for Down's syndrome			ns					
Yes, certainly	143	67.8		71	59.7			
Yes, rather	40	19.0		25	21.0			
Other	28	13.3		23	19.3			
TTP for BRCA1;2			ns					
Yes	38	18.0		16	13.4			
It depends, don't know	46	21.8		29	24.4			
No	127	60.2		74	62.2			
Has experienced miscarriage	20	9.5	0.050	20	16.8	-.508	-.963 ; -.052	-.195
Has experienced VToP	25	11.8	ns	13	10.9			

Has experienced TToP	3	1.4	ns	1	0.8			
Preference			0.011					
PND	77	36.5	ns	39	32.8	Ref		
PGD	71	33.6	0.006	23	19.3	ref		
Equivalents	58	27.5	0.025	47	39.5	-.453	-.769 ; -.136	-.169
Consider that information should be given systematically (yes totally)	165	78.2	ns	88	73.9			
Should wish to access to PND (sure)	165	78.2	0.000	65	54.6	.686	.356 ; 1.015	.258
Should wish to access to PGD (sure)	125	59.2	0.000	43	36.1	.395	.084 ; .706	.144

*The model correctly classifies 71.7% of cases

Table 3: WTP values for PGD and PND

		PGD			p	PND		
	n	Mean	Sd	Median		Mean	Sd	median
WTP value	211	1952	5409	225	ns	1808	5337	225
Nb of values > 0 (n, %)		154	72.9			180	85.3	
WTP value when contribution for the two diagnoses	123	2888	6737	400	ns	2844	6783	400
WTP value when contribution for PGD only	31	1827	3068	750				
WTP value when contribution for PND only	57					556	912	225

Table 4: Comparison between the CV group and the refusal group (n=460)

	Total (n=460)		CV group (n=330)			Refusal group (n=130)		Probit model (refuse=1)*		
								Coeff.	95% CI	dy/dx
	Mean	sd	Mean	sd	p	Mean	sd			
Age	39.89	9.69	40.32	9.77	ns	38.84	9.44			
Nber. of children	1.63	1.22	1.59	1.17	ns	1.73	1.36			
Nber. of close relatives with cancer	2.71	1.23	2.65	1.17	0.074	2.88	1.36			
PGD allow to initiate pregnancy with the quasi certitude that the fetus will not have the mutation	7.18	2.47	7.51	2.22	0.000	6.33	2.84	-.138	-.199 ; -.076	-.041
PGD allows to avoid a potential decision of TTP	7.28	2.47	7.59	1.13	0.000	6.51	2.87			
PGD requires an hormonal stimulation increasing the risk of cancer	7.27	2.54	7.18	2.48	ns	7.50	2.67	.072	.008 ; .135	.021
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PND let the initiative of pregnancy to the couple	7.05	2.70	7.04	2.67	ns	7.08	2.79			
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	n	%	n	%	p	n	%			
Male	102	22.2	82	24.8	0.028	20	15.4			
Living with a partner	386	83.9	274	83.0	ns	112	86.2			
Has a professional activity	370	80.4	260	78.8	ns	110	84.6			
Monthly household income					ns					
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It depends, don't know	81	17.6	75	22.7	0.000	6	4.6	Ref		
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Has experienced miscarriage (vs. no)	61	13.3	40	12.1	ns	21	16.2			
Has experienced therapeutic ToP (vs. no)	6	1.3	4	1.2	ns	2	1.5			
Has experienced voluntary ToP (vs. no)	51	11.1	38	11.5	ns	13	10.0			
Preference					0.046					
PND	163	35.4	116	35.2	ns	47	36.2	Ref		
PGD	117	25.4	94	28.5	0.017	23	17.7	Ref		
Equivalents	157	34.1	105	31.8	0.096	52	40.0	.441	.139 ; .743	.136
Consider that information should be given systematically (yes, totally vs. other)	312	67.8	253	76.7	0.000	59	45.4	-.608	-.907 ; -.309	-.193

*The model correctly classifies 78.7% of cases

Table 5: Comparison between participants (participate to at least one diagnosis) and protestors (do not participate to any diagnosis) (n=330)

	Participants n=211			Protestors n=119		Participation equation Probit model (participe=1)		
	Mean	SD	p	Mean	SD	Coeff	95% CI	dy/dx
Age	40.25	9.82	ns	40.42	9.71			
Nber. of children	1.65	1.18	ns	1.47	1.15			
Nber. of close relatives with breast or ovarian cancer	2.60	1.17	ns	2.72	1.17			
PGD allows to initiate pregnancy with the quasi certitude that the fetus will not have mutation	7.87	2.02	0.000	6.87	2.43	.113	.046 ; .180	.041
PGD allows to avoid a potential decision of TToP	7.86	2.18	0.004	7.11	2.25			
PND by amniocenteses implied a risk of miscarriage	6.41	2.91	ns	6.03	2.84			
PND let the couple initiating the pregnancy	7.16	2.60	ns	6.82	2.80			
After a PND the question of TToP will be raised	7.42	2.53	ns	7.16	2.37			
	n	%	p	n	%			
Male	53	25.1	ns	29	24.4			
Monthly household income > 5000 €	45	21.3	0.029	14	11.8	.582	.151 ; 1.012	.192
Master or doctoral degree	51	24.2	0.012	15	12.6			
Being a believer	90	44.6	ns	57	48.7			
Has a maternity project	42	19.9	ns	26	21.8			
Consider that results have not influenced the maternity project	93	44.1	0.047	66	55.5			
Considered health as very good to excellent	79	37.4	0.074	33	27.7			
Knowledge of risk transmission for father and mother	133	63.0	ns	72	60.5			
Prior knowledge of the existence of PGD and;or PND	117	55.5	0.057	53	44.5			
TTP for Down's syndrome			ns					
Yes, certainly	143	67.8		71	59.7			
Yes, rather	40	19.0		25	21.0			
Other	28	13.3		23	19.3			
TTP for BRCA1;2			ns					
Yes	38	18.0		16	13.4			
It depends, don't know	46	21.8		29	24.4			
No	127	60.2		74	62.2			
Has experienced miscarriage	20	9.5	0.050	20	16.8	-.508	-.963 ; -.052	-.195
Has experienced VToP	25	11.8	ns	13	10.9			

Has experienced TToP	3	1.4	ns	1	0.8			
Preference			0.011					
PND	77	36.5	ns	39	32.8	Ref		
PGD	71	33.6	0.006	23	19.3	ref		
Equivalents	58	27.5	0.025	47	39.5	-.453	-.769 ; -.136	-.169
Consider that information should be given systematically (yes totally)	165	78.2	ns	88	73.9			
Should wish to access to PND (sure)	165	78.2	0.000	65	54.6	.686	.356 ; 1.015	.258
Should wish to access to PGD (sure)	125	59.2	0.000	43	36.1	.395	.084 ; .706	.144

*The model correctly classifies 71.7% of cases

Table 6: WTP values for PGD and PND

		PGD			p	PND		
	n	Mean	Sd	Median		Mean	Sd	median
WTP value	211	1952	5409	225	ns	1808	5337	225
Nb of values > 0 (n, %)		154	72.9			180	85.3	
WTP value when contribution for the two diagnoses	123	2888	6737	400	ns	2844	6783	400
WTP value when contribution for PGD only	31	1827	3068	750				
WTP value when contribution for PND only	57					556	912	225

Table 7: Univariate analysis for the variation of PGD and PND (n=211)

	PGD			PND		
	n	Pearson correlation	p	n	Pearson correlation	p
Age	204	0.154	0.028	204	0.178	0.011
Nber. of children	206	0.143	0.040	206	0.132	0.058
Nber. of close relatives with breast and;or ovarian cancer	204	0.016	ns	204	-0.016	ns
PGD allow to initiate pregnancy with the quasi certitude the fetus will not have the mutation	209	0.140	0.044			
PGD allow to avoid a potential decision of TToP	209	0.062	ns			
PND by amniocenteses implied a risk of miscarriage				206	-0.021	ns
PND let the initiative of pregnancy to the couple				205	-0.185	0.008
After a PND the question of TToP will be raised				204	0.172	0.014

	n	Mean	SD	p	n	Mean	SD	p
Sex				0.094				0.028
Male	53	3418.0	8025		53	3785	8229.0	
Female	158	1459.8	4103		158	1145	3730	
Monthly household income > 5000 €	45	5059	9531	0.009	45	5154	9530	0.005
Master or doctoral degree	51	3657	7603	0.049	51	3432	7484	0.057
Being a believer	90	1901	4963	ns	90	1802	5001	ns
Has a maternity project				0.003				0.001
Yes	42	705	1503		42	527	926	
Others	169	2262	5961		169	2127	5907	
Consider that results have influenced the maternity project								
No	93	1165	2599	0.041	93	1053	2491	0.046
Yes and not concerned	118	2572	6806		118	2403	6741	
Health considered as very good to excellent	79	2296	6144	ns	79	2416	6343	ns
Knowledge of risk transmission				0.001				0.001
For father and mother	133	2724	6631		133	2567	6566	
Other	78	636	1279		78	514	1048	
Prior knowledge of the existence of PGD and/or PND	117	1705	5473	ns	117	2083	5400	ns
TTP for Down's syndrome								

Yes, certainly	143	2504	6459	0.002	143	2338	6348	0.004
Yes, rather	40	929	1215	0.011	40	777	1441	0.012
Other	28	590	970	0.001		577	1430	0.005
TToP BRCA1;2								
Yes	38	4680	10104	0.052	38	4647	10106	0.043
It depends, don't know	46	1676	4692	ns	46	1702	4684	ns
No	127	1235	2851	0.044	127	997	2560	0.022
Has experienced miscarriage	20	2210	6629	ns	20	2145	6641	ns
Has experienced VToP	25	668	1128	0.003	25	652	1002	0.005
Has experienced TToP	3	3000	3897	ns	3	2542	4294	ns
Preference								
PND	77	819	3603	0.008	77	1121	3677	ns
PGD	71	3051	6555	0.060	71	2439	6499	ns
Equivalents	58	1684	4518	ns	58	1517	4440	ns
Consider that information should be given systematically				0.020				0.067
Yes, totally	165	2254	5948		165	2048	5860	
Other	46	868	2459		46	948	5860	
Should wish to access to the diagnosis				0.0				0.0
Sure	125	2985	6678	0.000	165	2147	5878	0.007
Unsure	42	923	2561	0.034	27	1014	2894	ns

Table 8: Factor associated with WTP variations (Three-stage least-squares regression, n=211)

Equation	Obs	Parms	RMSE	"R-sq"	chi2	P
PGD	211	8	4725	0.233	65.64	0.0000
PND	211	4	1805	0.885	445.59	0.0000

	Coef.	Std.Err	z	P>|z|	95% Conf.	Interval
WTP for PGD						
Highest level of income (monthly income > 5000€)	3217	820	3.92	0.000	1610	4825
Consider results have not influenced the maternity project	-1418	648	-2.19	0.029	-2689	-147
Knowledge of risk transmission for both father and mother	1544	674	2.29	0.022	222	2866
Acceptability of therapeutic ToP for BRCA mutation (yes)	1856	848	2.19	0.029	193	3518
Acceptability of therapeutic ToP for Down's syndrome (yes, certainly)	1466	691	2.12	0.034	111	2821
PGD sure	2795	647	4.32	0.000	1527	4063
Has experienced voluntary ToP	-2041	980	-2.08	0.037	-3962	-120
cons	-1825	856	-2.13	0.033	-3502	-148
WTP for PND						
Male	682	293	2.33	0.020	109	1256
Highest level of income (monthly income > 5000€)	1096	387	2.83	0.005	336	1855
PND sure	1376	293	4.69	0.000	801	1951
WTP_PGD	0.8	0.1	12.90	0.000	0.7	0.9
cons	-1239	274	-4.51	0.000	-1778	-701

Endogenous variables: wtp_pgd wtp_pnd

Exogenous variables: INC3 influen0 risk_mf ToPBRCA_y ToP21_ce PGD_sur VToP Male PND_sur