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Bilateral Salpingo-Oophorectomy Versus GnRh Analogue in the Adjuvant Treatment of Premenopausal Breast Cancer Patients: Cost-Effectiveness Evaluation of Breast Cancer Outcome, Ovarian Cancer Prevention and Treatment

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ABSTRACT

Background: there are no available evidences to recommend GnRH analogue based ovarian suppression versus bilateral salpingo-oophorectomy (BSO) in the adjuvant treatment of early breast cancer, since the two approaches are considered equivalent in terms of oncologic outcome. The role of surgical ovarian ablation has been revitalized based on the advances of minimally invasive surgery, and a better understanding of clinical and molecular basis of hereditary breast/ovarian cancer syndromes. The aim of this study is to analyze the cost-effectiveness of laparoscopic BSO and GnRH analogue administration in patients with hormone-sensitive breast cancer, aged 40-49 years.

Methods: A probabilistic decision tree model was developed to evaluate costs and outcomes of ovarian ablation through laparoscopic BSO, or ovarian suppression through monthly injections of GnRH analogue. Results were expressed as incremental costs per quality-adjusted life years gained (QALY).

Results: laparoscopic BSO strategy was associated with a lower mean total cost per patient than GnRH treatment, and considering the difference in terms of QALYs, the incremental effectiveness did not demonstrate a notable difference between the two approaches. From the NHS perspective and for a time horizon of five years, laparoscopic BSO was the dominant option compared to GnRH treatment; laparoscopic BSO resulted less expensive than GnRH, € 2,385 (CI 95%= 2,044, 2,753) *versus* € 7,093 (CI 95%= 3,409, 12,105) respectively, and more effective.

Conclusion: Surgical ovarian ablation is more cost-effective than GnRH administration in the adjuvant treatment of hormone sensitive breast cancer patients aged 40-49 years, and the advantage of preventing ovarian cancer through laparoscopic BSO should be considered.

Key Points

- A cost-effective analysis to compare BSO and GnRH analogue in breast cancer is proposed
- Laparoscopic BSO resulted less expensive and more effective than GnRH analogue
- Laparoscopic BSO reported a mean cost per patient of € 2,385 and a mean QALY of 4,245

1. INTRODUCTION

Ovarian ablation through bilateral salpingo-oophorectomy (BSO) has been recognized since 1896 as a valid method of endocrine manipulation in hormone-sensitive advanced breast carcinoma. [1-4]

Even though there are still debated issues relative to the limited number and quality of studies comparing GnRH analogue based ovarian suppression versus BSO in the adjuvant treatment of early breast cancer patients, [5-7] there are no available evidences to recommend medical instead of surgical ovarian ablation since the two approaches are considered equivalent in terms of oncologic outcome. [8] Nonetheless, pharmacological ovarian suppression has progressively replaced BSO over time, because of the potential advantage to avoid surgery-related complications as well as the consequences of irreversible menopause. In this context, current guidelines suggest the use of monthly doses of GnRH analogue for two-three years in combination with tamoxifen for five years, or alternatively, the association of both drugs for two-three years with subsequent replacement of tamoxifen with an aromatase inhibitor. [8,9]

Recent results from the SOFT and TEXT randomized phase III studies in hormone receptor positive, HER-2 negative breast cancer patients have provided relevant clinical issues; in particular, the data from the SOFT trial have reported no significantly different 5-year disease-free survival rates in patients treated with tamoxifen plus GnRh analogue versus tamoxifen alone [10, 11]. On the other hand, in the low risk subpopulation (women>40 years with small and lymph node negative. tumors of low to intermediate grade) tamoxifen alone can be considered the standard treatment. On the other hand, in a pre-planned analysis of patients who remained premenopausal after chemotherapy, and had high risk features, exemestane plus GnRh was shown to provide longer 5-year breast cancer free interval compared to tamoxifen plus GnRh (82.5%) and tamoxifen alone (78.0%), thus underlining the need of more individualized approaches according to patient features. [10,11] In recent years the role of surgical ovarian ablation has been revitalized based on the advances of minimally invasive surgery, which nowadays provides excellent results in terms of cosmetic outcome, short operating times, hospital stay, and return to normal activity, as well as low rates of complications. [12-14] Moreover, a better understanding of clinical and molecular basis of hereditary breast/ovarian cancer syndromes has resulted in a larger awareness by breast cancer patients of their lifetime risk of developing primary ovarian carcinoma. [15-18] Indeed, ovarian cancer represents one of the most common malignancies among

BC survivors, especially when breast cancer diagnosis is done at younger age; [16] in particular, the observed number of ovarian cancer documented among estrogen receptor (ER)-positive breast cancer survivors aged <50 years is on average 21% higher compared to the expected number of ovarian cancers in the general population. [17] Since prophylactic BSO has been shown to dramatically reduce (up to 80-90%) the risk to develop ovarian cancer in women endowed with personal/familial risk factors as well as *BRCA* 1/2 gene mutation, [18,19] it could represent a valid clinical and cost-effectiveness option in the adjuvant treatment of pre- and perimenopausal hormone sensitive breast cancer patients, and an effective strategy for ovarian cancer prevention.

Few studies have already addressed the cost-effectiveness issues of laparoscopic BSO versus GnRh ovarian ablation in pre- and perimenopausal breast cancer patients: [20-22] evidences have shown the cost-effectiveness superiority of surgical versus medical (i.e. GnRH or tamoxifen) ovarian ablation. However, only one of these studies has applied a decision tree model and analyzed the results in terms of quality-adjusted life years. [21] Moreover, it has also to be emphasized that, to our knowledge, no formal analysis has investigated in this specific setting, the cost-effectiveness performance of the two strategies in terms of prevention of ovarian cancer, a very aggressive disease endowed with intrinsic and treatment-related high levels of morbidity and mortality, with consequently heavy social, and health care costs.

The aim of this study is to analyze the cost-effectiveness of laparoscopic BSO and GnRH analogue administration in patients with hormone-sensitive breast cancer, aged 40-49 years. A decision tree model has been developed, and results have been expressed in terms of quality-adjusted life years gained, based on the utilities related to breast cancer outcome, ovarian cancer prevention and treatment outcome.

2. METHODS

Model structure

A probabilistic decision tree model was developed in order to evaluate costs and outcomes of ovarian ablation through laparoscopic BSO, or ovarian suppression through monthly injections of GnRH analogue in patients with hormone-sensitive breast cancer, aged 40-49 years.

We chose on purpose to focus the attention on the 5-year time horizon, based on the data obtained from the Surveillance, Epidemiology, and End Results program (1973 to 2008) published by Schonfeld et al [18]; indeed, this study reported the standardized incidence ratio for the occurrence of a second primary ovarian cancer among ER-positive premenopausal BC patients within 5 years since breast cancer diagnosis. In this context, considering a time horizon of 5 years (short term), the decision tree model would represent the best choice for simulating the disease evolution without data transformation and assumption needed. In fact, in this case we can apply the risk parameters derived from the two studies without any assumption referred to the transformation of 5 years probabilities in one year, or less, lag probability (needed in case of a Markov Model). Furthermore, considering that the data from the literature represents cumulative risks in 5 years' time horizon, Markov Model approach probably would not add information, or change significantly the results, while it complicates the model and adds many assumptions.

Figure 1 represents the model structure that simulates natural history of the selected cohort of breast cancer patients proceeding through the different treatment strategies and disease outcome.

The model was structured considering the possibilities for patients triaged to the two treatment arms to survive or die during a five-year horizon. If patients survive, the model considers the opportunity to experience breast cancer relapse or survive in health. A second step has considered the risk of developing primary ovarian carcinoma, and the consequent risk of developing ovarian cancer relapse.

For each treatment strategy, costs associated with surveillance and treatment procedures were calculated. A five- year horizon and National Health System perspective were considered.

The National Health Service administers the functions belonging to the Government for the protection of human health, coordination of national healthcare services, veterinary health, protection of health in the workplace, hygiene (including disease prevention) and food safety. The fundamental ideas underlying the NHS are the following: a] health services should be available to everyone on the basis of need, free of charge, without differentiation or

discrimination among citizens and without barriers at the point of use (universalism); b] the system should be subject to popular democratic control at national, regional, and local level (participation). [24]

Epidemiological parameters and utilities

Epidemiological and clinical estimates were obtained from the available literature; in particular, the review of English language literature was performed through PubMed, and Medline by using the following terms "breast cancer [TITLE] AND ovarian ablation [TITLE]".

Efforts have been made to utilize data originated from Phase III trials, or meta-analyses; however, when these data were lacking, data from phase II or clinical experience were used. Criteria for inclusion included year of publication within 2005 and March 2015.

Supplementary Figure 1 shows the flow chart of literature search, and number of selected studies included in the final analysis, according to predefined criteria: a] we included the full text articles published within 2005 and March 2015, with complete information, and b] we excluded full text articles focused on selected groups like specific ethnic groups, different age intervals or population with other clinical features different from the study population.

Data about the five-year overall survival, and the five-year relapse free survival rates after BSO and GnRH were extracted from the literature, thus selecting a minimum and a maximum value and calculating an average. Table 1 summarizes all clinical and epidemiologic parameters that were used to generate the transition probabilities, and shows mean values, and the 95% confidence intervals (95% CI). Utilities for survival and recurrence were obtained from the available evidences. [6,13,18,19,25-28]

Table 1. Epidemiologic parameters and utility

Probability of transition	Base Case	Minimum	Maximum	Reference
5-year BC overall survival with GnRH (%)	83.40	80.00	87.00	6
5-year BC overall survival with BSO (%)	83.40	80.00	87.00	6
5-year BC relapse free survival with GnRH (%)	26.70	17.00	29.30	6
5-year BC relapse free survival with BSO (%)	26.70	17.00	29.30	6
Probability of developing primary OC with GnRH (%)	0.020	0.015	0.025	18,19
Probability of developing primary OC with BSO (%)	0.004	0.002	0.006	18,19
3-year probability of OC relapse with GnRH (%)	50.00	40.00	60.00	18
3-year probability of OC relapse with BSO (%)	50.00	40.00	60.00	18
UTILITY				
No relapse	0.90	0.79	1.00	13,25-28
BC relapse	0.70	0.50	0.85	13,25-28
Primary OC	0.65	0.45	0.86	13,25-28
OC relapse	0.55*	0.45	0.65	**assuming the mean value between the minimum value and the base case for primary ovarian cancer*

BC: breast cancer; BSO: bilateral salpingo-oophorectomy; OC: ovarian cancer

The model was calibrated using data on the age-specific (40-49 years) rate of the five-year breast cancer survival and relapse after BSO or GnRH analogue, and on the incidence of primary ovarian cancer as well as the three-year probability of ovarian cancer relapse after the two strategies, respectively.

Economic parameters

All direct medical costs associated with each of the two strategies were compared. Costs of all medical-surgical procedures have been defined on the basis of the so-called "Diagnosis-Related Group" (DRG, version 24th)[29]; in this model the direct costs have been estimated through the tariffs associated with specific DRG. The 14th DRG system identifies a considerable number of diagnoses associated with hospital admissions, which were selected to be significant and homogeneous both in terms of clinical profile and economic resources absorbed (isoresources).

Therefore, DRGs can be defined as an iso-resources system describing the complexity of the assistance given to patients, on the basis of the assumption that similar diseases in similar hospitals are treated with the same level of resources (including any type of drug, materials, and personnel, excluding physicians). This macro-system, aggregating all activities, measures the healthcare provided by hospitals and predicts the relative amount of economic resources needed as a proxy. Therefore, to each specific diagnosis is assigned a reimbursement tariff corresponding to the sum of whole interventions provided.

For each DRG cost, an average score was calculated balanced by the rates specified in the 21-regional resolutions found: Abruzzo, Basilicata, Bolzano, Calabria, Campania, Emilia-Romagna, Friuli Venezia Giulia, Lazio, Liguria, Lombardy, Marche, Molise, Piedmont, Puglia, Sardinia, Sicily, Tuscany, Trento, Umbria, Valle d'Aosta, Veneto.

Estimated economic parameters are presented in Table 2.

Table 2. Economic parameters

Costs	**Base case (€)**	**Range (€)**		**Reference**
GnRH	6,443.10	4,295.40	6,443.10	DRG tariff
BSO	1,787.86	1,520.91	2,054.82	DRG tariff
No BC relapse *(5-year follow up)*[a]	810,34	410,36	1,210.32	DRG tariff, NCCN guidelines, Institutional references
3-year BC relapse[b]	566,04	359,72	772,36	
OC	9,017.0	8,273.0	9,759.00	
No OC relapse *(2 years follow up)*[c]	1,235.28	669,48	1,030.88	
OC relapse[d]	6,759.52	3,049.52	11,953.52	

BSO: bilateral salpingo-oophorectomy, OC: ovarian cancer; BC: breast cancer

a] follow up surveillance was estimated to include: 5 clinical examinations, pap-smears, abdominal ultrasounds (US), breast ultrasounds, mammograms, and chest x-ray exams; tumor marker assay was estimated to be done 14 times

b] follow up surveillance in cases experiencing breast cancer relapse includes: 3 clinical examinations, pap-smear, abdominal US, breast US, mammograms and chest x-ray exams; tumour marker assay was estimated to be done 10 times

c] follow up surveillance for ovarian cancer patients not experiencing relapse: gynaecological examination, pelvic ultrasound and tumour marker blood test for 12 times and 3 CT-scans.

d] treatment of relapse has been estimated to include during an interval of 0-5 years, an average of 4 chemotherapy lines (4 cycles each) per patient (i.e. DRG 410 for each outpatient access, N=16) plus gynaecological examination, pelvic US, tumour marker assay for 8 times, and 2 CT-scans.

Concerning GnRh analogue, we considered a monthly administration of one drug unit for a maximum period of 36 months in the absence of disease relapse; further details are provided in Supplementary Table 1.

For laparoscopic BSO strategy, the DRG 359 has been considered (hysterectomy and/or adnexectomy for non-malignant conditions, no complications). Further details are reported in Supplementary Table 1. For breast cancer and ovarian cancer management, costs have been estimated based on DRG tariffs, international guidelines, and institutional references) (see Table 2). In particular, for primary ovarian cancer management, we identified the following two therapeutic paths:

a] radical surgery (generally feasible in 60-70% of cases) followed by six cycles of adjuvant chemotherapy with carboplatin and paclitaxel every three weeks; b] diagnostic laparoscopy or laparotomy with biopsies in patients with unresectable disease at primary effort, followed by three cycles of neoadjuvant chemotherapy interval debulking surgery and three additional cycles of chemotherapy.[28, 30-32]

For radical surgery, the DRG code 357 has been considered (hysterectomy and/or adnexectomy plus additional surgeries for ovarian carcinoma) (see Supplementary Table 1). For costs of antiblastic chemotherapy, the DRG code 410 was used (antiblastic chemotherapy not associated with a diagnosis of hematological malignancies) (see Table 2, and Supplementary Table 1).

Final costs were obtained by summing the individual costs weighted by the probability of each event.

Economic and statistical analysis

Cost results (€) are reported as the total sum of costs attributable to each patient undergoing each of the two different treatments.

Efficacy results are reported in terms of QALYs (Quality-adjusted life-years) [33] gained during the five-year horizon considered in the model. QALYs were estimated considering the utilities associated to each disease state and weighted considering the transition risks and the time spent in each state. The cost-effectiveness comparison between the different treatment options was expressed as incremental cost-effectiveness ratio (ICER), which corresponds to

the result of the cost differences between the two treatments, divided by the differences between their respective efficacy. In the absence of an Italian official threshold, a willingness-to-pay value of €25,000 to €40,000 per QALY gained was used. [34]

In order to verify the uncertainty of the model results, a deterministic one-way and probabilistic sensitivity analysis (DSA and PSA, respectively) was performed. [35]

Univariate sensitivity analysis was conducted modifying baseline costs and probabilities within the range reported in Table 1 and 2. In particular, the following scenarios were investigated: five-year survival with BSO, primary ovarian cancer with BSO, utility of ovarian cancer, cost of GnRH, cost of BSO, cost of primary ovarian cancer.

Probabilistic sensitivity analysis provides a useful technique to quantify the level of confidence of a decision maker in drawing conclusions from an economic evaluation. [35]

A probabilistic distribution was associated for costs parameters (gamma distribution) and epidemiological parameters (beta distribution) and 1,000 Montecarlo simulation were performed to define Cost-Effectiveness Plan and 95% CI (calculated considering mean and standard deviation derived from the simulations). [36].

Considering the short time horizon no discount rate were applied for both costs and outcomes. Two-tailed t-test was performed for estimating differences between BSO and GnRH group, and p-values less than 0.05 were considered as statistically significant.

The model and the sensitivity analysis were developed in Microsoft Excel® (Microsoft, Redmond, WA, USA).

3. RESULTS

As shown in Table 3, under baseline assumptions, the model estimates for GnRH treatment a mean cost per patient of € 7,093 (CI 95%= 3,409, 12,105), and a mean QALY per patient of 4,239 (CI 95%= 3,861, 4,617); conversely, laparoscopic BSO strategy was associated with a mean total cost per patient of € 2,385 (CI 95%= 2,44, 2,753), and a mean QALY per patient of 4,245 (CI 95%= 3,878, 4,612). Results in terms of incremental costs showed that laparoscopic BSO carries out a mean reduction of cost of € 4,708 (CI95%= € -9,104, € -312) with respect to GnRH administration.

Table 3. Cost-effectiveness results

	COST (€)	QALY	Incremental Cost (€)	Incremental QALY	ICER
GnRH	7,093	4,239	-	-	-
CI 95%	*3,409, 12,105*	3,861, 4,617	- -	- -	- -
BSO	2,385	4,245	-4,708	0.006	BSO Dominant
CI 95%	*2,044, 2,753*	3,878, 4,612	-9,104, -312	-0.312, 0.324	BSO dominant, 548,447

BSO: bilateral salpingo-oophorectomy

Therefore, in the same hypothetical cohort of patients incremental QALY favored laparoscopic BSO with an increase of 0.006 (-0.312, 0.324).

Considering the cost per QALY analysis, this model estimated €1,673.27 per QALY (€7,093/4,239) for GnRH, and € 561,83 per QALY (€2,385/4,245) for laparoscopic BSO.

From the NHS perspective and for a time horizon of five years, laparoscopic BSO was the dominant option (more effective and less expensive) compared to GnRH treatment.

Costs associated with ovarian cancer management, accounted for 0.33% of the overall costs estimated for GnRH, and for 0.06% of the costs estimated for BSO (data not shown); therefore, as far as costs of ovarian cancer management only are concerned, BSO resulted in 81% reduction compared to GnRH.

As shown in Table 4, univariate sensitivity analysis showed a good robustness of the model: indeed, laparoscopic BSO resulted less expensive and more effective than GnRH in 13 out of 14 possible scenarios analyzed; the exception refers to the case in which the survival probability was 0.80 versus the base case of 0.834.

Table 4 – Univariate DSA

	MIN (%)	MAX (%)	ICER MIN (€)	ICER MAX (€)
5-yr OS with BSO (%)	0.80	0.87	4,906	BSO Dominant
Probability of primary OC with GnRH (%)	0.015	0.025	BSO Dominant	BSO Dominant
Probability of primary OC with BSO (%)	0.002	0.006	BSO Dominant	BSO Dominant
Utility for OC	0.45	0.86	BSO Dominant	BSO Dominant
Cost of GnRH **(€)**	€ 4,295	€ 6,443	BSO Dominant	BSO Dominant
Cost of BSO **(€)**	€ 1,521	€ 2,055	BSO Dominant	BSO Dominant
Cost of primary OC **(€)**	€ 8,273	€ 9,759	BSO Dominant	BSO Dominant

OS: overall survival; OC: ovarian cancer; BSO: bilateral salpingo-oophorectomy

After applying probability sensitivity analysis, the model demonstrates that the difference in terms of costs was so wide as to be of important relevance (Fig 2); 99.9% of Monte Carlo simulations estimate the cost of BSO lower than cost of GnRH; number of simulations below the x-axis). However, considering the difference in terms of QALYs, incremental effectiveness did not demonstrate a notable difference between the two approaches (51.0% of Monte Carlo simulations estimated efficacy of BSO higher than GnRH; number of simulations at the right side of y-axis). Analysis shows that there is an 82.0% probability the BSO strategy is cost-effective at a willingness to pay of €30,000 (82.0% of Monte Carlo simulations are below the red line).

4. DISCUSSION

This cost-effectiveness analysis showed that laparoscopic BSO is more cost effective than GnRH administration in the adjuvant treatment of breast cancer patients aged 40-49 years. This was confirmed by univariate analysis, which favoured laparoscopic BSO in all but one of the scenarios analyzed, thus demonstrating a good robustness of the model. Moreover, probability sensitivity analysis resulted in 82% probability of laparoscopic BSO being more effective than GnRH at a willingness to pay of € 30,000.

Although this issue has been addressed by other studies, our analysis seems to provide novel information: in particular, it represents the first example of a decision tree model developed in the context of a European National Health System perspective utilizing the direct costs estimated through the tariffs associated with specific DRGs. Indeed, the only available formal cost-effectiveness analysis of LPS BSO versus medical ovarian suppression in premenopausal breast cancer patients has utilized direct costs obtained from the literature or from hospital billing records in a US country. [23] The achievement of the same conclusions despite the differences in health care systems and modalities of cost calculation, further sustain the reliability of current results.

Costs of complications associated with each approach (e.g. peri-operative complications of laparoscopic BSO or moderate/severe injection site reactions for GnRH) have been not included in the analysis because considered as occurring at negligible rates [12-14,37]; conversely, we carefully considered the issues of medical morbidities associated with menopause induction, and planned to focus on the group of hormone responsive breast cancer patients aged 40-49 years. Besides the advantage to reduce the impact of different cohorts in terms of population heterogeneity, the choice of the 40-49 year interval was made in order to restrict the analysis to patients closer to the age of physiologically occurring menopause, and likely expected to better face the anticipated menopause (especially the irreversible one associated with BSO), with its burden of fear of a longer period of estrogen deprivation and related morbidities. As recognized earlier, [23] the implications of emotional distress from surgically induced menopause are generally hardly quantifiable, and are expected to vary across different clinical settings: for instance, in women at high heredo-familiar risk of developing breast and ovarian cancer, the unfavourable impact of surgically induced menopause on quality of life is overcome by the decrease of anxiety. [19,38,39] On the other hand, the utilities developed in high risk, but still healthy women, unlikely reflect the utilities of patients who have already faced breast carcinoma, as in our model.

Therefore, with the aim to provide a really individualized counselling, efforts should be made to develop more specific utilities for each clinical setting.

Finally, our study first analysed in this specific setting of patients the cost-effectiveness of laparoscopic BSO in terms of primary ovarian cancer prevention.

The costs associated with ovarian cancer management contributed to only 0.33% and 0.06% of the overall costs estimated for GnRH and laparoscopic BSO, respectively; this has to be ascribed to the relatively high risk of ovarian cancer development (about 21%) in hormone sensitive breast cancer patients compared to general population. [18] However, if we consider the costs of ovarian cancer management only, laparoscopic BSO resulted in 81% cost reduction compared to GnRH. Moreover, the ethical implications inherent in the prevention of a very aggressive disease, even in a limited number of patients, adds further value to the choice of surgical approach to ovarian ablation.

Some limitations of the study have to be taken into account: first, the studies selected for the extraction of outcome figures and utilities, although being mainly represented by meta-analyses and large trials, were not so recent, and consequently could not take into account the novel clinical and molecular acquisitions related to the acknowledgement of the key role of *BRCA* gene system in breast and ovarian cancer natural history. [16] Such information could have intuitively played a role in a better discrimination of hormone sensitive BC patients at higher or lower risk of ovarian cancer development: for instance, breast tumors with mutation of the *BRCA*2 gene, which carries out a lower risk of ovarian cancer development compared to mutation of *BRCA*1, are more frequently estrogen receptor positive. [40]

It is noteworthy that for young women carrying a germ mutation of BRCA1 and BRCA 2 genes, the prophylactic bilateral salpingo-oophorectomy is indicated by the age of 40 or at the end of the reproductive age. This approach would reduce the risk of ovarian cancer by 80-90% and the risk of breast cancer by 50%, with an improvement of global and psychological woman health. In fact, the possible worsening of quality of life and endocrine symptoms related to surgical menopause are counterbalanced by the improvement of the anxiety associated with the risk of developing an ovarian malignancy [19,20,41]

Therefore, it should be highlighted that women indecision to undergo a surgical procedure due to aesthetic effects, complications or functional compromises, has been greatly minimized by modern mini-invasive surgical approaches development. [42]

We did not take into consideration the costs related to the management of breast cancer recurrence; however, it has to be acknowledged that treatment options may show an excess of variation in this clinical setting, and sometimes expenses relative to the supportive care/cure are administered outside the Hospital, and are not easily quantifiable.

5. CONCLUSIONS

In conclusion, we showed that surgical ovarian ablation is more cost-effective than GnRH administration in the adjuvant treatment of hormone sensitive breast cancer patients aged 40-49 years.

The advantage of preventing ovarian cancer through laparoscopic BSO should not be underestimated. Despite the reduction of ovarian cancer, management costs contribute minimally to the overall costs.

The need to identify, within hormone sensitive breast cancer patients, those who can be offered surgical ovarian ablation should be individualized according to familiar risk, reproductive history and counselling about side effects of anticipated menopause as well as alternative strategies to the relief of them. Indeed, the issues related to prevention of ovarian cancer risk, as well as the potential worsening of quality of life due to surgical menopause, represent a very delicate and private aspect conditioning patient's choice; in this context, efforts should be made to identify conditions and supportive approaches able to facilitate and support high risk patients to make their choice. Therefore, beside the results from cost-effectiveness analysis useful to better set up health care interventions and equitable resources, the physician's judgement and patients' preferences still remain the ultimate determinants in the choice of treatments.

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Compliance with Ethical Standards:

The Authors declare that they have no competing or financial interests. In the past five years the authors confirm that they have not received any reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future. No organization has financed this manuscript (including the article-processing charge). The Authors do not hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future; and they do not hold or are not you currently applying for any patents relating to the content of the manuscript, and they have not received any reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript. The Authors do have not any other financial competing interests.

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