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## New Strategies in Ovarian Cancer: Uptake and experience of women at high risk of ovarian cancer who are considering risk-reducing salpingo-oophorectomy

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### Abstract

This paper reviews factors associated with uptake of risk-reducing salpingo-oophorectomy by women at increased hereditary risk for ovarian cancer, as well as quality of life issues following surgery. Forty one research studies identified through PubMed and PsychInfo met inclusion criteria. Older age, having had children, a family history of ovarian cancer, a personal history of breast cancer, prophylactic mastectomy, and *BRCA1/2* mutation carrier status increase the likelihood of undergoing surgery. Psychosocial variables predictive of surgery uptake include greater perceived risk of ovarian cancer and cancer-related anxiety. Most women report satisfaction with their decision to undergo surgery and both lower perceived ovarian cancer risk and less cancer-related anxiety as benefits. Hormonal deprivation is the main disadvantage reported, particularly by premenopausal women who are not on hormonal replacement therapy (HRT). The evidence is mixed regarding satisfaction with the level of information provided prior to surgery, although generally women report receiving insufficient information regarding the pros and cons of HRT. These findings indicate that when designing decision aids, demographic, medical history, and psychosocial variables need to be addressed in order to facilitate quality decision making.

### Keywords

ovarian risk; prophylactic oophorectomy; patient decision making; quality of life

### Background

Women at increased putative hereditary risk for ovarian cancer are faced with complex information that needs to be cognitively and emotionally processed in order to make a high quality decision about their risk management options<sup>1</sup>. The two main options available to women are increased surveillance and the uptake of risk-reducing salpingo-oophorectomy

(RRSO), that is, the surgical removal of noncancerous ovaries and fallopian tube<sup>2</sup>. There is considerable evidence that simply screening for ovarian cancer (testing for CA125 levels and transvaginal ultrasound) is both inefficient (with multiple false positives) and ineffective (the majority of screen-detected cases are diagnosed at a late stage)<sup>2</sup>. RRSO is the alternative approach and has increasingly been shown to be an efficient and effective strategy for reducing cancer risk<sup>2</sup>. The guidelines for ovarian cancer risk management now recommend RRSO at the completion of childbearing or by age 35–40<sup>3</sup>. For premenopausal women who test *BRCA1/2* positive, RRSO has been associated with an 85–90% reduction in ovarian cancer risk and with a 50–68% reduction in breast cancer risk, provided the surgery is performed before the age of 50<sup>4,5,6</sup> for reviews see<sup>7,8</sup>.

Patients considering RRSO must also weigh the potential disadvantages of the procedure, including the risks associated with surgery, the effects of hormonal deprivation, and the residual breast, ovarian, and peritoneal cancer risk after removal of the ovaries<sup>2,4,9,10,11</sup> (see Table 1). The risks associated with hormonal deprivation are reportedly higher for women who undertake RRSO before the age of 45 and some premenopausal women take hormone replacement therapy (HRT) in order to reduce these risks<sup>12,13</sup>.

The percentage of women who opt for surgery varies considerably across studies<sup>14,15,16,17</sup> (Table 2) and reflects the heterogeneity of samples across studies with respect to the influence of specific demographic, medical, and psychosocial variables on the decision-making process regarding RRSO. These factors are discussed in detail in the next section. The majority of women who opt for surgery do so within a year after undergoing genetic risk assessment<sup>5,18,19,20,21,22,23,24</sup> although the timing of the surgery seems to be, in part, a function of the participants' age<sup>25,26,27</sup>. In this paper, we review studies that examine the patient factors involved in decisions about whether or not to undergo RRSO as well as the impact of that decision on quality of life (QOL) after surgery. We searched PubMed and PsychInfo to identify relevant articles published in English between 2000 and March 2010. The following search terms were combined: prophylactic oophorectomy, preventive oophorectomy, decision making, predictors, and quality of life. Additional sources of articles were references cited in identified papers. Studies were included if they were based on women at high or moderate risk due to a family history of ovarian cancer and if the findings focused on: 1. predictors of RRSO or 2. QOL issues following RRSO. We excluded abstracts of presentations, book chapters, and studies that focused exclusively on self-reported attitudes and intentions to undergo surgery. Regarding factors associated with RRSO uptake, we examined 24 empirical studies and we report only statistically significant findings. Regarding QOL we included 13 quantitative studies. In addition, we report information from four qualitative studies<sup>28,29,30,31</sup>.

## On the Horizon

### Factors associated with RRSO uptake

A number of predictors and correlates of RRSO have been identified (Table 2). In terms of demographic variables, both prospective and retrospective studies show that older women and women who have children are more likely to undergo surgery<sup>20,32,33,34,35,36–38</sup> (Table 2). Indeed, if one compares uptake rates of RRSO across similar age groups, the differences across studies are not as pronounced (Table 2). Presumably younger women are less likely to have completed their childbearing and are more concerned about their menopausal status and that may be why younger age and not having had children are associated with delaying surgery among mutation carriers<sup>18,27,26</sup>. This is not surprising since premenopausal women who undergo surgery (as opposed to surveillance) have to deal with the sudden onset of menopause, which is not only associated with infertility but also with medical and psychological symptoms<sup>39</sup>. Finally, less educated women are more likely to undergo

surgery<sup>19,40</sup>. A possible explanation for this finding is that less educated women prefer a more definitive solution (surgery) in order to gain a higher sense of control<sup>28, 41</sup>.

Among medical correlates of RRSO uptake, prospective and retrospective studies have found that family history of ovarian cancer<sup>22,41,27,36,42,43</sup> and personal history of breast cancer<sup>16,18,20,34,21,44,45</sup> are associated with higher rates of RRSO (Table 2). In addition, carriers of a *BRCA1/2* mutation<sup>19,37,33,34,38,42</sup> are more likely to have RRSO, with several recent studies showing that rates are highest among women with a *BRCA1* mutation<sup>26, 43</sup>. Prophylactic surgery is more likely to appeal to women who want to decrease uncertainty and maintain a high sense of control over their lives<sup>29</sup>. Thus women who opt for risk reducing mastectomy (RRM) choose to undergo RRSO as well<sup>18,33,34,44,46</sup>.

Psychosocial factors, both cognitive and affective, are also predictors of RRSO uptake<sup>22,30,32,40,44</sup> (Table 2). Among cognitive factors, the importance of perceived risk is highlighted in one study where both baseline perceived risk and perceived risk after receipt of a genetic test result (positive, negative and uninformative) were explored as predictors of surgery among familial high risk women participating in genetic testing<sup>22</sup>. It was the former that predicted RRSO uptake, indicating that pre-existing notions about personal risk continue to influence one's decisions, even after receipt of genetic counseling and testing feedback. This is an important issue given that women tend to overestimate their perceived risk for breast and ovarian cancer<sup>8,47</sup>. Other predictive factors include personal values and beliefs, such as perceiving one's personal health as poor, viewing ovarian cancer as an incurable disease, believing that surgery is beneficial, and believing that surgery will provide a greater sense of certainty about controlling one's ovarian cancer risk<sup>40</sup>. In addition, in a qualitative study, the majority of women reported their sense of obligation to their family to manage their personal cancer risk as a reason for undergoing RRSO<sup>30</sup>. Affective factors, in the form of worry and intrusive ideation, also play a significant role in decision making<sup>32,40</sup>. For example, in a retrospective study, women rated both risk-reduction for ovarian cancer and reduction of cancer worry as important reasons for undergoing surgery, but it was cancer worry that uniquely differentiated the women who underwent surgery from those who relied on surveillance<sup>32</sup>. Similarly, in a qualitative study, many women who had witnessed a relative die from ovarian cancer were convinced to have surgery<sup>30</sup>. In contrast, fear of surgery was associated with the decision to forego RRSO<sup>30</sup>.

## RRSO and QOL

The effect of RRSO on QOL has been examined in a few studies. Although the findings are not universal<sup>48</sup>, women who undergo RRSO report positive changes following surgery, such as lower perceived risk about ovarian cancer (particularly among younger women), less impact of cancer worry on their daily functioning, less anxiety about developing ovarian cancer<sup>8,33,36,39,47,49,50</sup> and a higher sense of control over their lives<sup>29</sup>. Qualitative studies have confirmed that the reduction of worry is a major benefit of the surgery and many women reported feeling content that they have fulfilled their family obligations as a benefit<sup>28</sup>. Long-term QOL seems to be unaffected<sup>51,33,47,9,45</sup> as women may be adjusting their QOL expectations to take into account the physical changes that result from hormonal deprivation, a cognitive process termed response shift<sup>52</sup>. The overwhelming majority of women are satisfied with their decision to undergo surgery (86.4–97%)<sup>33, 36</sup> and report that RRSO had minimal impact on their lives (93%)<sup>29</sup> (Table 2). In a qualitative study, some premenopausal women who took HRT felt more conflicted about their decision to undergo RRSO and expressed guilt about their inability to tolerate the symptoms associated with menopause, particularly when their physician was not committed to the surgery<sup>29</sup>.

The majority of women report that RRSO did not have a negative impact on their sense of femininity, presumably because there is no external bodily change<sup>45</sup>. In a qualitative study, only a minority reported that they felt older and less feminine following surgery<sup>28</sup>. However, both prospective and retrospective studies comparing women who had RRSO with women who relied on surveillance for risk reduction show that those who underwent RRSO reported an increased number of symptoms, such as hot flashes, vaginal dryness, a reduction in sexual interest, a decrease in pleasure and satisfaction with sexual activity, and painful intercourse<sup>33,34,45</sup> particularly among women who were not taking HRT<sup>33,34,50</sup>. Most of these symptoms appear to subside with time elapsed since surgery, although the impact of surgery on sexual discomfort<sup>9</sup> and perceived health<sup>50</sup> seems to be greater in younger women. Even so, a small number of quantitative<sup>50,48</sup> and qualitative<sup>29,30,31</sup> studies identify a subset of women for whom distress is high after surgery.

The findings are contradictory regarding satisfaction with the information provided prior to the procedure, with some women reporting that they felt that they were fully informed and have participated in the decision process<sup>47</sup>, while others report that they would have preferred to have had more information<sup>41</sup>. Several qualitative studies reported that after the surgery, many women felt they had inadequate information to make decisions regarding HRT<sup>28,29,31</sup>, an important QOL issue for those who are premenopausal<sup>11,12,53</sup>.

### Decision aids

Because of the complexity of the information that needs to be conveyed to women to enable them to make informed decisions that are consistent with their values, studies have begun to explore the role of decision aids<sup>19,23</sup>. Most decision aids aim to provide patients with medical information and help them to systematically integrate that information with their personal values in order to reach a quality decision, consistent with their personal preferences<sup>54</sup>. Although helpful, these tools do not take full account of the affective states of women that interact with their cognitive states to influence decision making<sup>54,55,56</sup>. One randomized study<sup>23</sup> examined the impact of an intervention aimed at maximizing information processing and promoting informed and deliberate, value-based, decision making among women who had received a positive genetic test result. Although the intervention had no effect on their choice, women who had not had surgery at the time of questioning and who had received the intervention had stronger treatment preferences and experienced less decision uncertainty<sup>23</sup>. In a second randomized controlled study, the intervention was administered prior to the receipt of the test result and was designed to facilitate cognitive and affective processing of risk information provided<sup>19</sup>. Over four times as many women underwent prophylactic surgery in the intervention group as in the control group (which received provision of general health information)<sup>19</sup>. To the extent that early adoption of risk-reduction strategies, such as RRSO, has a significant impact on lowering medical morbidity, interventions that help women fully process the pros and cons of different strategies may be useful in enhancing decision making.

### Conclusions

A number of factors have been identified that are positively associated with RRSO uptake. (Figure 1) These include demographic variables (older age, having had children, lower educational level), medical variables (*BRCA* mutation carrier status, family history of ovarian cancer, personal history of breast cancer, having undergone RRM), and psychosocial variables (e.g., greater perceived ovarian cancer risk, elevated cancer-related distress). (Table 2) Post-surgery, the majority of women are satisfied with their decision to undergo RRSO and report positive QOL-related changes, including reduced perceived ovarian cancer risk, reduced cancer-related distress, and an increased sense of control<sup>36, 47, 50</sup>. (Figure 1) Women who report the most surgery-related problems (e.g.;

impact of surgery on sexual activity and hot flashes) were for the most part premenopausal at the time of the surgery and did not take HRT<sup>34, 50</sup>.

The evidence is contradictory regarding level of satisfaction with the information provided prior to surgery and generally women feel inadequately supported with regard to their decision concerning HRT<sup>47</sup>. (Figure 1) Two randomized studies evaluated the impact of interventions on decision making and found that interventions have positive effects on the quality of decision-making<sup>19, 23</sup>. In the future it will be important to design decision aids that adequately address the cognitive-emotional sequelae of RRSO, particularly for the subset of women who remain distressed regarding their cancer risk following the surgery<sup>48, 50</sup>.

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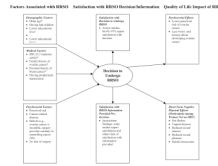


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**Figure 1.** Factors associated with RRSO uptake, satisfaction with RRSO decision and pre-decision information, and QOL impact of RRSO. Findings marked with an asterisk (\*) have strong support in the literature based on number of studies ( $\geq 5$ ) and aggregate sample size ( $\geq 1000$ ).

**Table 1**

## Advantages and Disadvantages of RRSO versus Surveillance

	<b>Advantages</b>	<b>Disadvantages</b>
<b>RRSO</b>	Most effective form of ovarian cancer risk reduction	Risks associated with the surgical procedure
	Associated with reduction in breast cancer risk, if performed prior to menopause	Adverse effects of hormonal deprivation (sudden onset of menopausal symptoms, increased risk of osteoporosis, increased risk of metabolic syndrome)
		Residual breast, ovarian and peritoneal cancer risk
		Concern about adverse effects on sexuality
		Concern that HRT may increase breast cancer risk, and thus reverse the beneficial effects of the surgery on breast cancer risk
<b>Surveillance</b>	Noninvasive	Multiple false positives
	May reduce cancer mortality	Majority of detected cases are diagnosed at late stage
		Does not reduce risk of ovarian cancer
		Adherence issues

Table 2

Studies Reporting Significant Predictors of the use of RRSO

Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>Antill et al. (2006)</li> <li>Retrospective</li> <li>Clinic based</li> <li>Multisite</li> </ul>	<ul style="list-style-type: none"> <li>Moderate or high risk women for ovarian cancer or <i>BRCA1/2</i> carriers (unaffected)</li> <li><math>N = 52</math></li> <li>Median age = 45 (22–74)</li> </ul>	<ul style="list-style-type: none"> <li>17.3%</li> <li>Varies across centers (12–41%)</li> </ul>	<ul style="list-style-type: none"> <li>Mean follow-up time: 3.73 years.</li> <li>Mean time from consultation to surgery: 3.36 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– &gt; 40 yrs (+)<sup>d</sup></li> <li>– <i>BRCA1/2</i> (+)</li> </ul> </li> <li><b>Impact:</b> <ul style="list-style-type: none"> <li>– Lower perceived risk</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>Beattie et al. (2009)</li> <li>Prospective</li> <li>Clinic based</li> <li>Multisite</li> </ul>	<ul style="list-style-type: none"> <li><i>BRCA1/2</i> carriers (affected and unaffected)</li> <li><math>N = 240</math></li> <li>Median age = 45 (20–79)</li> </ul>	<ul style="list-style-type: none"> <li>51% (no significant differences across sites)</li> </ul>	<ul style="list-style-type: none"> <li>Median follow-up time: 3.7 years.</li> <li>Median interval from receipt of test result to surgery: 4 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– Age (+) for women less than 60</li> <li>– <i>BC<sup>b</sup></i> (+)</li> <li>– <i>RRM<sup>c</sup></i> (+)</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>Botkin et al. (2003)</li> <li>Prospective</li> <li>Clinic based</li> <li>Single site</li> </ul>	<ul style="list-style-type: none"> <li>K2082 kindred - <i>BRCA1/2</i> carriers (affected and unaffected)</li> <li><math>N = 26</math></li> <li>Mean age = 43.45 (27–72)</li> </ul>	<ul style="list-style-type: none"> <li>46% among all carriers</li> </ul>	<ul style="list-style-type: none"> <li>Follow-up time: 24 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– Appears to be an effect for age (&gt;40: 78%; &lt;40: 29%) (+), but significance level not reported.</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>Bradbury et al. (2008)</li> <li>Retrospective</li> <li>Clinic based</li> <li>Single site</li> </ul>	<ul style="list-style-type: none"> <li><i>BRCA1/2</i> carriers (affected and unaffected)</li> <li><math>N = 88</math></li> <li>Median age = 42 (23–71)</li> </ul>	<ul style="list-style-type: none"> <li>70%</li> <li>26% of those had surgery before receipt of genetic test result</li> </ul>	<ul style="list-style-type: none"> <li>Median interval from receipt of test result to surgery: 12.5 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– Age (+)</li> <li>– <i>CH<sup>d</sup></i> (+)</li> <li>– <i>BC</i> (+)</li> <li>– Being white (+)</li> <li>– <i>RRM</i> (+)</li> <li>– <i>FH<sup>e</sup></i> (+)</li> </ul> </li> </ul>

Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>▪ Evans et al. (2009)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Single site</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>BRCA1/2</i> carriers (unaffected).</li> <li>▪ <math>N = 211</math></li> <li>▪ <math>Age \geq 18</math></li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>BRCA1</i> mutation carrier: 52%</li> <li>▪ <i>BRCA2</i> mutation carrier: 28%</li> </ul>	<ul style="list-style-type: none"> <li>▪ Median follow-up time: 4.19 years.</li> </ul>	<p><i>Multivariate</i></p> <ul style="list-style-type: none"> <li>- Age</li> <li>- CH</li> <li>- Being white</li> <li>- FH</li> </ul> <p><b>Predictors:</b></p> <p><i>Univariate</i></p> <ul style="list-style-type: none"> <li>- <i>BRCA1</i> (+)</li> </ul>
<ul style="list-style-type: none"> <li>▪ Fry et al. (2001)</li> <li>▪ Retrospective</li> <li>▪ Clinic based</li> <li>▪ Single site</li> </ul>	<ul style="list-style-type: none"> <li>▪ Affected and unaffected women at moderate or high risk based on family history</li> <li>▪ Women were operated on 1 to 5 years earlier</li> <li>▪ Comparison group also at moderate to high risk registered 1 to 5 years earlier</li> <li>▪ Surgical group <math>N = 30</math></li> <li>▪ Control group: <math>N = 28</math></li> <li>▪ Mean age = 50.1 (35–66)</li> </ul>	<p>NA</p>	<p>NA</p>	<p><b>Predictors: Differences between surgical and non-surgical groups in importance rating for each decision-making factor:</b></p> <p><i>Univariate</i></p> <ul style="list-style-type: none"> <li>- Age (+)</li> <li>- Reducing risk (+)</li> <li>- Reducing worry (+)</li> <li>- Recovery time (-)<sup>a</sup></li> <li>- Worry about effectiveness of screening (+)</li> <li>- Loss of periods (+)</li> </ul> <p><i>Multivariate</i></p> <ul style="list-style-type: none"> <li>- Reducing worry</li> </ul>
<ul style="list-style-type: none"> <li>▪ Kauf et al. (2002)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Single site</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>BRCA1/2</i> carriers (affected and unaffected)</li> <li>▪ Excluded women younger than 35 and women who had RRSO prior to genetic testing</li> <li>▪ <math>N = 170</math></li> </ul>	<ul style="list-style-type: none"> <li>▪ 58%</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean follow-up time: 24.2 months</li> <li>▪ Median interval from receipt of test result to surgery: 3.6 months</li> </ul>	<p><b>Predictors:</b></p> <p><i>Univariate</i></p> <ul style="list-style-type: none"> <li>- More likely to have had BMF before the start of the follow-up</li> </ul>

Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>▪ Kram et al. (2006)</li> <li>▪ Retrospective</li> <li>▪ Clinic based</li> <li>▪ Single site</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean age = 46.65 (35–78)</li> <li>▪ Affected and unaffected women who underwent testing for founder mutations based on the ethnic origin of the patient</li> <li>▪ Included women who had BSO<sup>8</sup> prior to genetic testing for various reasons</li> <li>▪ <i>BRCA1/2</i> carriers: <math>N = 43</math></li> <li>▪ Non-carriers: <math>N = 56</math></li> <li>▪ Mean age = 53.75</li> </ul>	<ul style="list-style-type: none"> <li>▪ 78% of carriers</li> <li>▪ 11% of those had surgery prior to receipt of genetic test result</li> <li>▪ 18% of non-carriers (40% of those prior to receipt of genetic test result)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Follow-up time: 1–4 years after receipt of genetic test result</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Reasons for having surgery:</b> <ul style="list-style-type: none"> <li>– Reduction of risk</li> <li>– Reduction of anxiety</li> <li>– Lack of trust in surveillance methods</li> </ul> </li> <li>▪ <b>Predictors:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– <i>BRCA1/2</i> (higher percentages are found in age group &gt; 50 (89%) when compared to &lt; 50 (44%))</li> <li>– More women with BC found among non-carriers who had RRSO, but significance levels not reported</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>▪ Madalinska et al. (2005)</li> <li>▪ Cross-sectional</li> <li>▪ Clinic based</li> <li>▪ Multisite</li> </ul>	<ul style="list-style-type: none"> <li>▪ High risk women (affected and unaffected) who had RRSO (<math>N = 369</math>)</li> <li>▪ High risk women (affected and unaffected) who had surveillance (<math>N = 477</math>)</li> <li>▪ Mean age = 47.87 (30–75)</li> </ul>	<p>NA</p>	<p>NA</p>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– Age (+)</li> <li>– BC (+)</li> <li>– <i>BRCA1/2</i> (+)</li> <li>– RRM (+)</li> </ul> </li> <li>▪ <b>Impact:</b> <ul style="list-style-type: none"> <li><i>Univariate</i></li> <li>– 97% satisfied with decision</li> <li>– Less anxiety</li> <li>– Lower perceived risk</li> <li>– Negative impact on sexual functioning</li> </ul> </li> </ul>

Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>▪ Madalinska et al. (2007)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Multisite</li> </ul>	<ul style="list-style-type: none"> <li>▪ BRCA1/2 carriers (affected and unaffected)</li> <li>▪ Greater than 35</li> <li>▪ Completed childbearing</li> <li>▪ <math>N = 160</math></li> <li>▪ Mean age = 47.51</li> </ul>	<ul style="list-style-type: none"> <li>▪ 74% within 12 months of initial genetic testing consultation</li> </ul>	<ul style="list-style-type: none"> <li>▪ Median interval from consultation to surgery: 2.8 months</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Univariate</i></li> <li>- Age (+)</li> <li>- Married (+)</li> <li>- Education (-)</li> <li>- Menopausal status (+)</li> <li>- Distress (+)</li> <li>- Perceived health (-)</li> <li>- Perceived risk (+)</li> <li>- Ovarian cancer is incurable (+)</li> <li>- Surgery will increase certainty (+)</li> <li>- Benefits of surgery (+)</li> </ul> <p style="text-align: center;"><i>Multivariate</i></p> <ul style="list-style-type: none"> <li>- Education</li> <li>- Perceived health</li> <li>- Ovarian cancer is incurable</li> <li>- Benefits of surgery</li> </ul>
<ul style="list-style-type: none"> <li>▪ Meijers-Heirboer et al. (2003)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Single site</li> </ul>	<ul style="list-style-type: none"> <li>▪ BRCA1/2 affected carriers</li> <li>▪ Age greater than 35</li> <li>▪ <math>N = 95</math></li> <li>▪ <u>59 women &lt;50</u></li> <li>▪ <u>36 women ≥50</u></li> </ul>	<ul style="list-style-type: none"> <li>▪ 49%</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean time from genetic test result to surgery: 8 months.</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Univariate</i></li> <li>- Women with BC at stage I more likely than those at stage II or III</li> </ul>
<ul style="list-style-type: none"> <li>▪ Meijers-Heirboer et al. (2000)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> </ul>	<ul style="list-style-type: none"> <li>▪ BRCA1/2 unaffected carriers</li> <li>▪ <math>N = 60</math></li> <li>▪ <u>Age range 30-80</u></li> </ul>	<ul style="list-style-type: none"> <li>▪ 64% of eligible women &gt; 35.</li> <li>▪ 35-40: 41%</li> <li>▪ 40-54: 90%</li> <li>▪ &gt;54: 50%</li> </ul>	<ul style="list-style-type: none"> <li>▪ Median follow-up time: 26 months.</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Univariate</i></li> <li>- Higher percentages in age group 40-54 than in 35-40</li> </ul>



Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>▪ Multisite</li> </ul>		<ul style="list-style-type: none"> <li>▪ &lt;35: 47%</li> </ul>		
<ul style="list-style-type: none"> <li>▪ Metcalfe et al. (2008)</li> <li>▪ International</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Multisite</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>BRCA1/2</i> carriers (affected and unaffected)</li> <li>▪ Did not distinguish between surgeries performed for risk reduction and those performed for other reasons</li> <li>▪ <math>N = 2677</math></li> <li>▪ Mean age: 45.6 (25–80)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Range varied from 34.9% (Poland) to 73% (Norway)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean follow-up time from genetic test result: 3.9 years.</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Univariate</i></li> <li>▪ – BC (+)</li> </ul>
<ul style="list-style-type: none"> <li>▪ Metcalfe et al. (2007)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Multisite</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>BRCA1/2</i> carriers (affected and unaffected)</li> <li>▪ Did not distinguish between surgeries performed for risk reduction and those performed for other reasons</li> <li>▪ <math>N = 672</math></li> <li>▪ Mean age = 46.9 (25–79)</li> </ul>	<ul style="list-style-type: none"> <li>▪ 54% (range: 38.9–67.3%)</li> <li>▪ (41% of those prior to receipt of genetic test result)</li> <li>▪ 25–35: 22%</li> <li>▪ 36–40: 45%</li> <li>▪ 41–60: 64%</li> <li>▪ 61–70: 59%</li> <li>▪ &gt;70: 47%</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean follow-up time from genetic test result: 4 years</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Univariate</i></li> <li>▪ – BC (+)</li> </ul>
<ul style="list-style-type: none"> <li>▪ Metcalfe et al. (2008)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Multisite</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>BRCA1/2</i> carriers (affected and unaffected)</li> <li>▪ <math>N = 517</math></li> <li>▪ Mean age for total sample = 46.8 (25–79)</li> </ul>	<ul style="list-style-type: none"> <li>▪ 67% (age greater than 35)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean follow-up time from genetic test result: 4.5 years</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Multivariate</i></li> <li>▪ – Age (+)</li> <li>▪ – FH (+)</li> <li>▪ – <i>BRCA1</i> (+)</li> </ul>
<ul style="list-style-type: none"> <li>▪ Miller et al. (2005)</li> <li>▪ Prospective</li> <li>▪ Clinic based</li> <li>▪ Single site</li> </ul>	<ul style="list-style-type: none"> <li>▪ High risk women tested for <i>BRCA1/2</i> (affected and unaffected). <math>N = 77</math></li> </ul>	<ul style="list-style-type: none"> <li>▪ 60%</li> </ul>	<ul style="list-style-type: none"> <li>▪ Mean follow-up time from genetic test result: 6 months</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Predictors:</b> <i>Multivariate</i></li> <li>▪ – Intervention (+)</li> <li>▪ – <i>BRCA1/2</i> (+)</li> <li>▪ – Education (–)</li> </ul>

Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>Scheuer et al. (2002)</li> <li>Prospective</li> <li>Clinic based</li> <li>Single site</li> </ul>	<ul style="list-style-type: none"> <li><i>BRCA1/2</i> carriers (affected and unaffected)</li> <li><math>N=179</math></li> <li>Mean age = 47.7 (24.1–79.0)</li> </ul>	<ul style="list-style-type: none"> <li>50.3%</li> </ul>	<ul style="list-style-type: none"> <li>Median interval from genetic test result to surgery: 3.4 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b></li> <li><i>Univariate</i></li> <li>– Age (+)</li> <li>– BC (+)</li> </ul>
<ul style="list-style-type: none"> <li>Schmeler et al. (2006)</li> <li>Prospective</li> <li>Clinic based</li> <li>Single site</li> </ul>	<ul style="list-style-type: none"> <li><i>BRCA1/2</i> carriers (affected and unaffected)</li> <li><math>N=106</math>.</li> <li>Mean age: 43.37 (19.6–71.1)</li> </ul>	<ul style="list-style-type: none"> <li>61.3%</li> <li>&lt;35: 10.77%,</li> <li>36–40: 16.92%,</li> <li>41–45: 26.15%,</li> <li>&gt;45: 46.15%</li> </ul>	<ul style="list-style-type: none"> <li>Median interval from genetic test result to surgery: 4.6 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b></li> <li><i>Univariate</i></li> <li>– Age (+)</li> <li>– CH (+)</li> <li>– BC (+)</li> </ul>
<ul style="list-style-type: none"> <li>Schwartz et al. (2003)</li> <li>Prospective</li> <li>Clinic based</li> <li>Single site</li> </ul>	<ul style="list-style-type: none"> <li>High risk women tested for <i>BRCA1/2</i> (affected and unaffected)</li> <li><math>N = 289</math></li> <li>Mean age: 47 (&gt;25)</li> </ul>	<ul style="list-style-type: none"> <li>Carriers: 27%</li> <li>Uninformatives: 5%</li> <li>Non-carriers: 2%</li> </ul>	<ul style="list-style-type: none"> <li>Follow-up time from genetic test result: 12 months</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b></li> <li><i>Univariate</i></li> <li>– <i>BRCA1</i> (+)</li> <li>– Perceived risk (+)</li> <li>– Worry (+)</li> <li>– FH (+)</li> <li><i>Multivariate</i></li> <li>– <i>BRCA1</i></li> <li>– Perceived risk at baseline</li> <li>– FH</li> </ul>
<ul style="list-style-type: none"> <li>Skytte et al. (2010)</li> <li>Retrospective</li> <li>Population based</li> </ul>	<ul style="list-style-type: none"> <li><i>BRCA1/2</i> carriers (unaffected)</li> <li><math>N=306</math></li> <li><u>265 women &lt; 50</u></li> <li><u>41 women ≥ 50</u></li> </ul>	<ul style="list-style-type: none"> <li>75%</li> </ul>	<ul style="list-style-type: none"> <li>Follow-up time from genetic test result: 10 years</li> <li>Median interval from genetic test result to surgery: 34 months (13 months for women over 35)</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b></li> <li><i>Univariate</i></li> <li>– Age (+)</li> <li>– CH (+)</li> </ul>

Study	Study Population	Percent who had RRSO	Follow-up	Predictors/ Impact
<ul style="list-style-type: none"> <li>Tiller et al. (2002)</li> <li>Prospective</li> <li>Clinic based</li> <li>Multisite</li> </ul>	<ul style="list-style-type: none"> <li>Unaffected high risk: 91%</li> <li>Unaffected moderate risk: 9%</li> <li>N=68</li> <li>Median age: 40 (19–75)</li> </ul>	<ul style="list-style-type: none"> <li>23.2% of total</li> <li>40% of women recommended for RRSO</li> </ul>	<ul style="list-style-type: none"> <li>Mean follow-up time from genetic test result: 3 years</li> </ul>	<ul style="list-style-type: none"> <li><b>Predictors:</b> <ul style="list-style-type: none"> <li>Univariate                             <ul style="list-style-type: none"> <li>Age (+)</li> <li>FH (+) (trend)</li> </ul> </li> </ul> </li> <li><b>Impact:</b> <ul style="list-style-type: none"> <li>86.4% satisfied with decision</li> <li>Greater reduction in cancer anxiety when compared to surveillance group</li> <li>Women not on HRT reported negative impact on sexual functioning</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>Uyei et al (2006)</li> <li>Retrospective</li> <li>Clinic based</li> <li>Singel Site</li> </ul>	<ul style="list-style-type: none"> <li>Women tested for BRCA1/2 (affected and unaffected)</li> <li>Risk level of participants unclear</li> <li>Unclear whether surgeries were performed for risk reduction or for other reasons</li> <li>N= 554</li> <li>36 women &lt; 50</li> <li>29 women &gt;=50</li> </ul>	<ul style="list-style-type: none"> <li>14.8% had RRSO.</li> </ul>		<ul style="list-style-type: none"> <li><b>Predictors:</b> <ul style="list-style-type: none"> <li>Univariate                             <ul style="list-style-type: none"> <li>BRCA1/2 (+)</li> <li>BC (+)</li> <li>Lower stage disease (+)</li> <li>FH (+)</li> <li>HRT (+)</li> <li>OCP<sup>h</sup> (+)</li> <li>Total mastectomy as part of treatment for breast cancer (+)</li> </ul> </li> </ul> </li> <li>Multivariate                             <ul style="list-style-type: none"> <li>BRCA1/2</li> </ul> </li> </ul>

<sup>a</sup>+,+': positive effect and '-,-', negative effect

<sup>b</sup>BC: personal history of breast cancer

<sup>c</sup>RRM: risk reducing mastectomy

<sup>d</sup>CH: has at least one child

<sup>e</sup>FH: family history of ovarian cancer

<sup>f</sup> BM: bilateral mastectomy

<sup>g</sup> BSO: bilateral salpingo-oophorectomy

<sup>h</sup> OCP: use of oral contraceptive pills