

of both breasts.⁷ Risk-reducing prophylactic bilateral salpingo-oophorectomy, the surgical removal of both ovaries and Fallopian tubes, is generally recommended to women ages 35 to 40 with a *BRCA1* and *BRCA2* mutation.^{7,8}

Salpingo-oophorectomy has been cited as the cornerstone of this genetic clinical program, and Finch et al. have shown that preventive salpingo-oophorectomy in *BRCA* mutation carriers is associated with a 70% reduction in all-cause mortality until age 70.⁹ Preventive bilateral mastectomy has been documented to reduce breast cancer risk by approximately 95% in women with prior or concurrent preventive salpingo-oophorectomy and by approximately 90% in women with intact ovaries.¹⁰ A prospective multi-institutional study involving 2400 women positive for a *BRCA* mutation reported no cases of breast cancer following mastectomy (0/247) and a 7% (98/1372) incidence of breast cancer in those not treated with prophylactic bilateral mastectomy.¹¹ It is therefore notable that the uptake of these preventive surgical strategies by mutation carriers is lower in some countries.¹² The cost associated with these preventions is a likely factor influencing patient uptake and may vary significantly by country. Madalinska et al. documented that approximately three quarters

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of *BRCA* mutation carriers in the Netherlands who met eligibility criteria for preventive surgery had undergone preventive oophorectomy after the first gynaecologic consultation. The study acknowledged that this percentage of uptake was higher than that reported in studies in the United States, United Kingdom, and Australia (ranging from 23%–60%), with variability of patient insurance coverage as a possible limiting factor in these countries.¹⁶ All patients enrolled in the study in the Netherlands were

fully covered by health insurance policies. As an example of a similar disparity in outcomes, Skytte et al. reported a 10 year uptake of 50% for preventive bilateral mastectomy in healthy *BRCA* mutation carriers with no personal history of breast or ovarian cancer, while Julian-Reynier et al. reported an uptake rate of only 8%.^{14,17}

CANCER-RELATED DISTRESS

Given the high probability of mutation carriers developing potentially fatal cancers, it is important to understand the factors that influence risk-reducing behaviour, particularly preventive surgery. Metcalfe et al. conducted a two-year follow-up of Jewish women identified to carry a *BRCA* mutation who participated in population genetic testing.¹³ It was reported that 90% of this population of women accepted preventive oophorectomy, but only 11% opted for preventive bilateral mastectomy as a therapeutic option. These rates of uptake were interpreted to reflect cancer-related distress. It was suggested that the greater the psychological impact of a positive test result, the sooner the patient proceeded to a surgical solution; distress levels may decrease for those who undergo prophylactic interventions. It is not clear if elevated cancer-related distress is a transient phenomenon or if it persists over the long-term.

FAMILY-RELATED FACTORS

Time to risk-reducing prophylactic oophorectomy was also related to age and the completion of childbearing at the time of *BRCA* mutation testing.¹⁴ Evans et al. documented that younger women are more prone to delay preventive oophorectomy and the authors suggested that to more accurately measure the uptake of preventive surgery, longer-term follow-up is required.¹⁵ The highest rate of prophylactic oophorectomy occurred in post-menopausal women who were least likely to experience the possible adverse effects of surgically induced menopausal symptoms.¹⁴ In premenopausal women, outcomes of oophorectomy include infertility and onset of menopause.¹⁶ In contrast to natural menopause onset, surgical menopause may cause more unfavourable symptoms and decrease the patient's quality of life.

An association between the uptake of prophylactic surgery and a history of cancer in first-degree relatives has also been noted.¹⁴ It was established that having first-degree relatives with breast and/or ovarian cancer significantly influence the course of treatment and increase the acceptance of prophylactic bilateral mastectomy or prophylactic oophorectomy.