

# **Bilateral oophorectomy and all-cause mortality in women with *BRCA1* and *BRCA2* mutations**

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## **Abstract**

**Importance:** Preventive bilateral salpingo-oophorectomy is offered to women at high-risk of ovarian cancer who carry a pathogenic variant (mutation) in *BRCA1* or *BRCA2*; however, the impact of oophorectomy on all-cause mortality has not been clearly defined.

**Objective:** To evaluate the association between bilateral oophorectomy and all-cause mortality among women with a *BRCA1* or *BRCA2* mutation.

**Design:** Information on bilateral oophorectomy was obtained via biennial questionnaire. Women were followed from age 35 to 75 years for incident cancers and deaths. Cox proportional hazards regression was used to estimate the hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality associated with a bilateral oophorectomy (time-dependent).

**Setting:** International, longitudinal study of *BRCA* mutation carriers.

**Participants:** Women with a *BRCA1* or *BRCA2* mutation, no prior history of cancer, and at least one follow-up questionnaire completed.

**Exposures:** Self-reported bilateral oophorectomy (with or without salpingectomy).

**Main Outcomes and Measures:** All-cause mortality, breast cancer-specific mortality and ovarian cancer-specific mortality.

**Results:** There were 4,322 women enrolled in the cohort, of whom 2,932 (67.8%) chose to undergo a preventive oophorectomy at a mean age of 45.4 years. After a mean follow-up of 9.0 years, 902 women developed cancer and 228 died; 57 died of ovarian or fallopian tube cancer, 58 died of breast cancer, 16 died of peritoneal cancer and 97 died of other causes. The age-adjusted HR for all-cause mortality associated with oophorectomy was 0.32 (95%CI 0.24-0.42;  $P < 0.0001$ ). The age-adjusted HR was 0.28 (95%CI 0.20-0.38;  $P < 0.0001$ ) for *BRCA1* and was 0.43 (95%CI 0.22-0.90;  $P = 0.03$ ) for *BRCA2* mutation carriers. For *BRCA1* mutation carriers, we estimate the cumulative all-cause mortality to age 75 for women who have an oophorectomy at age 35 to be 25%, compared to 62% for women who do not have an oophorectomy. For *BRCA2* mutation carriers, we estimated the cumulative all-cause mortality to age 75 to be 14% for women who have an oophorectomy at age 35 compared to 28% for women who do not have an oophorectomy.

**Conclusion and Relevance:** Among women with a *BRCA1* or *BRCA2* mutation, oophorectomy is associated with a significant reduction in all-cause mortality.

## **Summary**

*BRCA1* and *BRCA2* are notorious for their profound effects on a woman's life. In fact, in a recent study of 735,000 individuals, researchers showed that the *BRCA* genes were two of only four common genes that had a measurable impact on a woman's life expectancy at the population level. In this extension of our earlier report on the same topic, we have shown that the life span of women with a *BRCA1* or *BRCA2* mutation can be greatly enhanced by preventive bilateral oophorectomy. Moreover, the profound reduction in mortality confirms the clinical value of genetic testing of young women and the need to expand genetic testing programs around the world.