



## Prophylactic Risk-Reducing Salpingo-Oophorectomy in Women with BRCA1 or BRCA2 Mutations: A Systematic Review and Meta-Analysis

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### Abstract:

**Introduction & Objective:** Prophylactic risk-reducing Salpingo-oophorectomy (RRSO) refers to surgical removal of both fallopian-tubes and ovaries in women not thought to have cancer prior to surgical procedure but have a high lifetime risk. Despite previous studies, the role of RRSO in reducing breast and High-grade Serous Cancer (HGSC) of ovarian, tubal and peritoneal origin are uncertain. This study assesses benefits and harms of prophylactic RRSO in women with BRCA1 or BRCA2 mutations.

**Method:** We searched Cochrane Central Register of Controlled Trials, MEDLINE /Embase Ovid and trial registries, and abstracts with no language restrictions up to July 2017. We included non-randomized trials that used statistical adjustment analyses comparing RRSO versus no RRSO in women without a previous/coexisting gynecological malignancy and in women with a Risk-reducing Mastectomy (RRM). We extracted data and performed meta-analyses of Hazard

Ratios (HR) for time-to-event variables and Risk Ratios (RR) for dichotomous outcomes, with 95% Confidence Intervals (CI). We used ROBINS-I 'Risk of bias' assessment tool and quantified inconsistency using I2 statistic. We used random-effects models.

**Results:** Ten cohort studies were included comprising 8087 BRCA1/BRCA2 mutation carriers (2936 surgical and 5151 controls). GRADE assessment certainty of evidence was very low. Overall survival was longer with RRSO compared with no RRSO (HR 0.32, 95% CI 0.19 to 0.54;  $P < 0.001$ ; 3 studies, 2548 women; very low-certainty evidence). HGSC cancer mortality (HR 0.06, 95% CI 0.02 to 0.17;  $I^2 = 69%$ ;  $P < 0.0001$ ; 3 studies, 2534 women; very low-certainty evidence) and breast cancer mortality (HR 0.58, 95% CI 0.39 to 0.88;  $I^2 = 65%$ ;  $P = 0.009$ ; 7 studies, 7198 women; very low-certainty evidence) were lower with RRSO compared with no RRSO. No study reported adverse events.

**Conclusion:** There is very low-certainty evidence that RRSO may increase overall survival and lower HGSC and breast cancer mortality for BRCA1/BRCA2 carriers. Very low-certainty evidence suggests that RRSO reduces the risk of death from HGSC and breast cancer in women with BRCA1 mutations. Evidence for the effect of RRSO on HGSC and breast cancer in BRCA2 carriers was very uncertain due to low numbers. Further research is warranted to explore differential effects for BRCA1 or BRCA2 mutations.

### Biography:

George Eleje is currently working as a Senior Lecturer at the Nnamdi Azikiwe University, Nnewi Campus, Nigeria and a Consultant Obstetrician-Gynecologist at the Nnamdi Azikiwe University Teaching Hospital, Nigeria. He is also Research Coordinator at the Effective Care Research Unit, Nnamdi Azikiwe University, Nigeria.