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POPULATION TESTING AND PERSONALISED OVARIAN CANCER RISK PREDICTION FOR RISK ADAPTED TARGETED PREVENTION

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Introduction/Background The current approach to genetic-testing and risk assessment is based on family-history and misses the majority of people at risk. Unselected population-based testing can enable personalised ovarian cancer (OC) risk prediction combining genetic/epidemiology/hormonal data. This permits population risk stratification for risk adapted targeted screening and prevention. Such an intervention study has not previously been undertaken. We aimed to assess the feasibility of OC risk stratification of general population women using a personalised OC risk tool followed by risk management.

Methodology Volunteers were recruited through London primary care networks. Inclusion criteria: women ≥ 18 years. Exclusion criteria: prior ovarian/tubal/peritoneal cancer, previous genetic testing for OC genes. Participants accessed an online/web-based decision aid along with optional telephone helpline use. Consenting individuals completed risk assessment and underwent genetic testing (BRCA1/BRCA2/RAD51C/RAD51D/BRIP1, OC susceptibility single-nucleotide polymorphisms). A validated OC risk prediction algorithm provided a personalised OC risk estimate using genetic/lifestyle/hormonal OC risk factors. Population genetic testing (PGT) for OC-risk stratification uptake/acceptability, satisfaction, decision aid/telephone helpline use, psychological health and quality of life were assessed using validated/customised questionnaires over six months. Linear-mixed models/contrast tests analysed impact on study outcomes. Main outcomes: feasibility/acceptability, uptake, decision aid/telephone helpline use, satisfaction/regret, and impact on psychological health/quality of life.

Results In total, 123 volunteers (mean age = 48.5 (SD=15.4) years) used the decision aid, 105 (85%) consented. None fulfilled NHS genetic-testing clinical criteria. OC-risk stratification revealed 1/103 at $\geq 10\%$ (high), 0/103 at $\geq 5\%$ – $<10\%$ (intermediate), and 100/103 at $<5\%$ (low) lifetime OC risk. Decision aid satisfaction was 92.2%. The telephone helpline use rate was 13% and the questionnaire response rate at six months was 75%. The high-risk woman underwent surgical prevention. Contrast tests indicated that overall depression ($p=0.30$), anxiety ($p=0.10$), quality-of-life ($p=0.99$), and

distress ($p=0.25$) levels did not jointly change, while OC worry ($p=0.021$) and general cancer risk perception ($p=0.015$) decreased over six months. In total, 85.5%–98.7% were satisfied with their decision.

Conclusion Findings suggest population-based personalised OC risk stratification is feasible and acceptable, has high satisfaction, reduces cancer worry/risk perception, and does not negatively impact psychological health or quality-of-life. Larger implementation studies evaluating long-term impact and cost effectiveness of this strategy are needed.

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ATTITUDES TOWARDS RISK REDUCING EARLY SALPINGECTOMY WITH DELAYED OOPHORECTOMY FOR OVARIAN CANCER PREVENTION: A COHORT STUDY

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Introduction/Background With increasing evidence and acceptability of the central role of the fallopian-tube in the etiopathogenesis of epithelial ovarian cancer (OC), risk-reducing-early-salpingectomy-and-delayed-oophorectomy (RRESDO) has been proposed as a two-stage surgical alternative to risk reducing salpingo-oophorectomy (RRSO). RRESDO offers some level of risk reduction to women who decline/wish to delay RRSO whilst conserving ovarian function and avoiding detrimental consequences of premature-menopause. However, prospective outcome data for RRESDO are lacking. The aim of this study was to determine RRESDO acceptability and effect of surgical prevention on menopausal sequelae/satisfaction/regret in women at increased OC risk.

Methodology UK Multicentre, cohort, study (IRSCN:12310993). OC unaffected UK women ≥ 18 years, at increased OC-risk, with/without previous RRSO, ascertained through specialist familial-cancer/genetic-clinics and BRCA support-groups. High-risk women completed a 39-item customised questionnaire developed through literature review, expert clinician and patient support groups' involvement. Baseline characteristics were described using descriptive statistics. Logistic/linear-regression models analysed impact of variables on RRESDO acceptability and health-outcomes. Main outcomes were RRESDO acceptability, barriers/facilitators, menopausal-sequelae, satisfaction/regret.

Results 346 of 683 participants underwent risk-reducing salpingo-oophorectomy (RRSO) and 337 did not. 69.1% (181/262) premenopausal women who had not undergone RRSO found it acceptable to participate in a research study offering RRESDO. Premenopausal women concerned about sexual-dysfunction were more likely (OR=2.9, 95%CI=1.2–7.7, $p=0.025$) to find RRESDO acceptable. Women experiencing sexual-dysfunction after premenopausal-RRSO were more