

regressed to CIN1 or less within 6 months after delivery (n=41), without CIN (n=16), CIN3 covering 3–4 quadrants (n=14) and randomly selected CIN3 (n=41). *FAM19A4/miR124-2* methylation analysis was performed blinded on first diagnosis.

**Results** All pregnant women with cervical cancer and with CIN3 progressing to cancer tested positive for *FAM19A4/miR124-2* methylation (100%, 22/22). In the regressing CIN3 group 47.5% and in the group without CIN 21.6% tested methylation positive. High-volume CIN3 and random selected CIN3 were methylation-positive in 91.7% and 82.1%. Methylation levels were significantly higher in progressive CIN3 and cancer compared to the controls ( $P < 0.0005$ ). The likelihood ratio of a negative methylation test (LR-) for progressive CIN3+ was 0 (95%CI:0–0.208).

**Conclusion** A negative *FAM19A4/miR124-2* methylation test can rule out progressive CIN disease in pregnant women diagnosed with CIN3. This can help the clinician by managing these pregnant women with conservative follow-up until after delivery. (Int J Cancer. 2022 Jun 6. doi: 10.1002/ijc.34153)

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#### QUALITY OF LIFE AFTER RISK-REDUCING SURGERY FOR BREAST AND OVARIAN CANCER PREVENTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

<sup>1</sup>Xia Wei, <sup>2</sup>Samuel Oxley, <sup>2</sup>Michail Sideris, <sup>2</sup>Ashwin Kalra, <sup>1</sup>Rosa Legood, <sup>2</sup>Ranjit Manchanda. <sup>1</sup>London School of Hygiene and Tropical Medicine, London, UK; <sup>2</sup>Wolfson Institute of Population Health, Queen Mary University of London, London, UK

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**Introduction/Background** RRS is the most-effective prevention for breast-cancer (BC) and ovarian-cancer (OC) in women with increased-risk. We aimed to assess the quality-of-life (QoL) impact of risk-reducing surgery (RRS) including risk-reducing-mastectomy (RRM), risk-reducing-salpingo-oophorectomy (RRSO) and risk-reducing early-salpingectomy and delayed-oophorectomy (RRESDO) through a systematic review and meta-analysis.

**Methodology** We searched major databases until December 2021 following a prospective protocol (PROSPERO-CRD42022319782). Qualitative-synthesis was performed to identify the impact of RRS on various QoL outcomes. Fixed-effects meta-analysis was performed to obtain pooled estimates of QoL outcomes.

**Results** Thirty-one studies were included (N=4151 post-RRS vs. N=3905 controls). 12/12 studies post-RRM (N=944) reported unchanged general-health QoL, and 10/16 (N=1911) post-RRSO reported unchanged/improved general-health QoL despite short-term deficits (N=578). 13/16 studies (N=1602) showed affected sexual-function post-RRSO. Meta-analysis showed a reduction (-1.21[-1.53,-0.89]; N=3070) in sexual-pleasure and an increase (1.12[0.93,1.31]; N=1400) in sexual-discomfort using the Sexual-Activity-Questionnaire. HRT in pre-menopausal RRSO was associated (on meta-analysis) with an increase (1.16 [0.17, 2.15]; N=291) in sexual-pleasure and

a decrease (-1.20 [-1.75, -0.65]; N=157) in sexual-discomfort. 4/10 studies post-RRM (N=236) showed impacted sexual-function, while 6/10 (N=572) showed stable sexual-function. 5/10 studies post-RRM (N=514) reported no body-image problems, whereas 5/10 (N=344) showed otherwise. 12/13 studies (N=1871) reported increased menopause symptoms post-RRSO with a reduction (-1.96 [-2.81, -1.10]; N=1745) in Functional-Assessment-of-Cancer-Therapy-Endocrine Subscale on meta-analysis. 5/5 studies (N=365) post-RRM and 8/10 (N=1223) post-RRSO reported unchanged/decreased cancer-related-distress. RRESDO (2 studies, N=413) resulted in better sexual-function and menopause-specific QoL.

**Conclusion** RRM/RRSO reduced cancer-related distress with unaffected general-health QoL. Women/clinicians should be aware of the negative impact of sexual dysfunction and menopause related symptoms from RRSO, along-with potential detrimental impact of RRM on body-image. Early salpingectomy does not appear to increase sexual dysfunction or impact menopause symptoms and RRESDO may be a promising alternative to mitigate QoL-related risks.

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#### COST-EFFECTIVENESS OF RISK-REDUCING SURGERY FOR BREAST AND OVARIAN CANCER PREVENTION: A SYSTEMATIC REVIEW

<sup>1</sup>Xia Wei, <sup>2</sup>Samuel Oxley, <sup>2</sup>Michail Sideris, <sup>2</sup>Ashwin Kalra, <sup>1</sup>Rosa Legood, <sup>3</sup>Ranjit Manchanda. <sup>1</sup>London School of Hygiene and Tropical Medicine, London, UK; <sup>2</sup>Wolfson Institute of Population Health, Queen Mary University of London, London, UK; <sup>3</sup>Wolfson Institute of Population Health, Queen Mary University of London, Charterhouse Square, London, UK

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**Introduction/Background** Risk-reducing mastectomy (RRM) and salpingo-oophorectomy (RRSO) are the gold standard preventative strategies for women at high-risk of breast cancer (BC)/ovarian cancer (OC). Risk-reducing early-salpingectomy followed by delayed-oophorectomy (RRESDO) is being trialled as an alternative to RRSO. Opportunistic bilateral salpingectomy (OBS) during gynaecological surgery has been proposed as a potential approach to prevent OC in general population. We performed a systematic review of the published evidence on cost-effectiveness of RRM/RRSO/RRESDO for BC/OC prevention in intermediate/high-risk women, and OBS in baseline-risk.

**Methodology** We searched major databases to December 2021. We included economic evaluation studies reporting on cost-effectiveness/cost-utility outcomes in women at high-risk of BC/OC undergoing RRM/RRSO/RRESDO, or baseline OC risk undergoing OBS.

**Results** Our search yielded 5801 citations; 22 studies were included. Eight studies concluded that RRM/RRSO individually or in combination were cost-effective compared to surveillance/no surgery for unaffected *BRCA1/2* carriers, while one study found that RRESDO was cost-effective. Two studies on women at low/intermediate OC-risk specified that RRSO was cost-effective at OC lifetime risks of  $\geq 4\%$  (pre-menopausal) and  $\geq 5\%$  (post-menopausal women). These results were partially sensitive to initial age, uptake rates, cancer risk-reduction, and disutility following surgery. Four studies concluded that the addition of OBS to hysterectomy was cost-effective for OC prevention in the general population. Similarly, OBS was cost-effective as an alternative to