Removal of All Ovarian Tissue at the Time of Hysterectomy for Benign Conditions: Change in Practice Following Evidence of Negative Health Effects

Felicity Evison (Principal Research Informatician), Jemma Mytton (Information Analyst), Kelly Schmidtke (Assistant Professor), Peter Chilton (Research Fellow), Richard Lilford (ARC WM Director)

Tens of thousands of applied health research articles are published every year. Few of these lead directly to a change in practice, especially if they are not based on an experimental design. We published an observational study in the BMJ in 2017 on the health effects of removing versus conserving ovarian tissue at the time of hysterectomy for benign disease.(1) The study was by an order of magnitude the largest ever performed, with a mean follow up of nine and a half years. The study showed that there was an increase in admissions for cardiovascular disease, deaths from cardiovascular disease and overall deaths in the bilateral oophorectomy group when compared to propensity score matched controls where ovarian tissue was retained. There was no countervailing benefit and the expected reduction in ovarian cancer had not materialised over the follow-up period. We thought it would be interesting to track the use of oophorectomy during hysterectomy over the time of publication of our papers. We conduct an interrupted time series analysis to test for any discontinuity around the year in which our paper was published. We hypothesised that there would be no discontinuity in the data.

To replicate the sampling strategy in the previous paper we selected patients undergoing a hysterectomy for benign disease. This means, we only included patients aged 35-45, whose age and sex were both recorded, who were resident in England and who were undergoing an elective hysterectomy.

We performed an interrupted time series analysis to examine for any interruption in the proportion of bilateral oophorectomies accompanying eligible hysterectomies. Two change points were selected - the first to reflect the time of publication of our paper in Q1, 2017; the second to reflect a pattern in the earlier data where there is an apparent upturn in the proportion of hysterectomies accompanied by bilateral ovary removal at Q2, 2012/13.

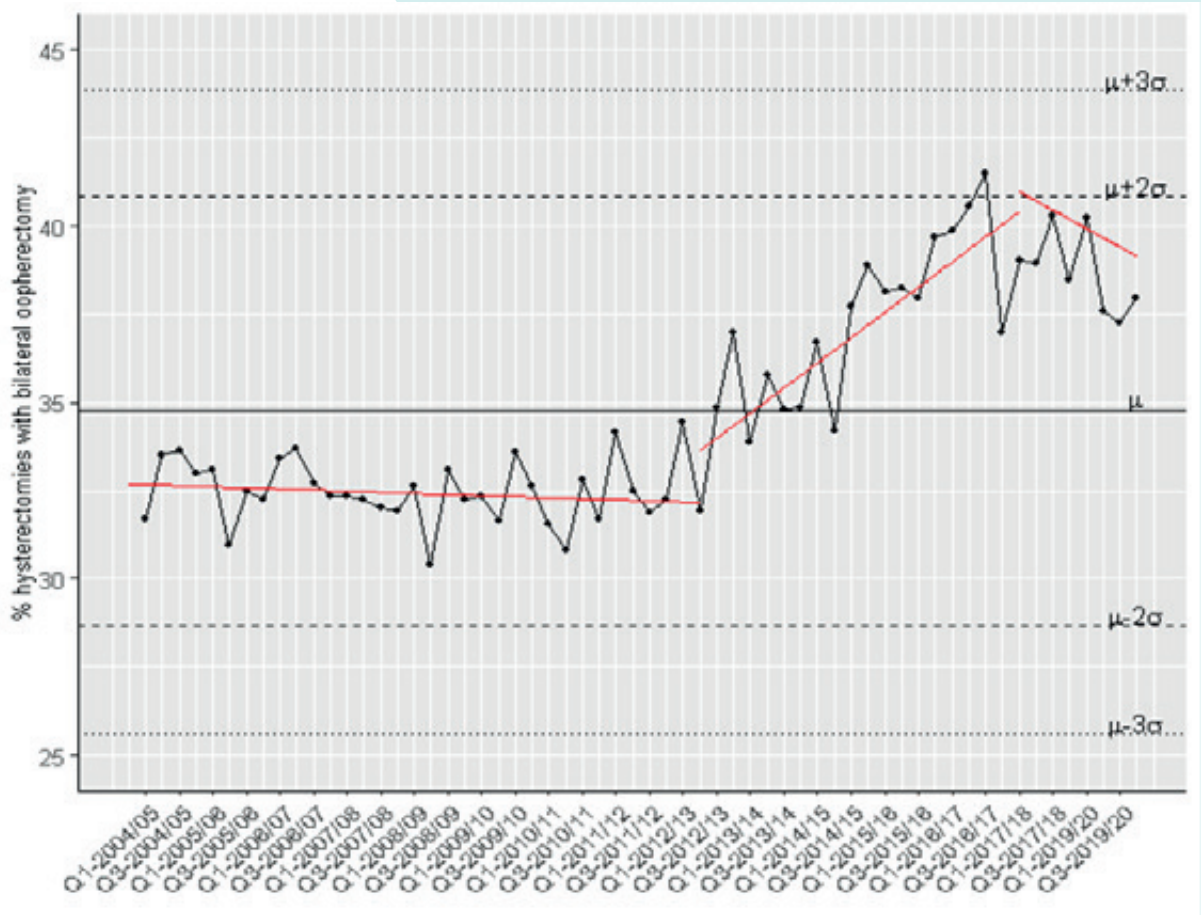
After exclusions we identified 158,619 eligible hysterectomy procedures between 1st April 2004 and 31st March 2020. These were split into two groups of ovary conservation (104,168 [65.7%]) vs no ovaries remaining (54,451 [34.3%]). The mean length of follow up has increased from 6.2 (SD 2.84) years in our previous study, to 9.5 (SD 4.49) years. The total number of hysterectomies per year has maintained its downward trajectory as observed in the original paper from 13,047 in 2004/05 to 6,217 in 2019/20.

Prior to Q2 2012/13 there appears to be a slight (but non-statistically significant) decrease in the percentage of hysterectomies with bilateral oophorectomy β_1 = -0.015 (95%CI: -0.0537 - 0.023, p= 0.432). In Q2 of 2012/13 there appears to be a significant step-change in the percentage of bilateral operations α_2=1.47 (95%CI: 0.44-2.50, p=0.007), along with a significant upward change in the direction of the slope β_2 = 0.372 (95%CI: 0.281 - 0.462, p<0.001). Then, at Q2 2017 there is a non-significant step-change α_3 = 0.947 (95% CI: -1.27-3.16, p=0.4055), but there is a significant downward change in slope direction β_3 = -0.618 (95%CI: -0.957 - -0.279, p=0.0007). This is displayed in the figure overleaf.

We were surprised to see such a clear statistical result but, aware that correlation is not causation, we remain sceptical. On the one hand our findings were published in an influential journal. On the other hand, changing clinical practice often requires more than just publication of evidence, and our publication may have coincided with a random high (although such an observation was not the motivation for the study).

Impactful as the *BMJ* is, we think that at least one of two antecedents would be necessary to change practice in such a short space of time; there would have had to be some form of professional endorsement from a respected organisation or from patients. Our article was accompanied by a press release, but it attracted only local attention and we think this muted response was insufficient to drive a change in practice.

On the other hand, the subsequent issue of *BJOG: the International Journal of Obstetrics and Gynaecology* (dated 21 April 2017) carried a resume of our article in their '*Research Snippets*' section.(2) We will never know whether our article had an influence on practice. And, of course, the operation is a matter for personal choice where increased risk of cardiovascular disease and colon cancer must be traded against a numerically smaller, but for some people more salient, decreased risk of ovarian and breast cancer if the ovaries are removed. We like to think that our findings have usefully informed this decision.



Percentage of hysterectomies with bilateral ovary removal over time (by quarter)

References:

1. Mytton J, Evison F, Chilton PJ, Lilford RJ. Removal of all ovarian tissue versus conserving ovarian tissue at time of hysterectomy in premenopausal patients with benign disease: study using routine data and data linkage. *BMJ*. 2017; **356**: j372.
2. Kent A, Kirtley S. Insights from outside BJOG - Hysterectomy-with or without BSO? *BJOG*. 2017;**124**(6):850.

This article originally appeared in *ARC WM News Blog. 28 Jan 2022; 4(1): 13-14.*