All hormone therapy—regardless of the formulation, estrogen dose, progestin type, dose regimen, route of administration, or duration of use—appears to raise the risk of ovarian cancer, according to a new report. If the association between HT and ovarian cancer proves to be causal, it would mean that as many as 5% of such malignancies could be attributable to the treatment. “Even though this seems low, ovarian cancer remains highly fatal, so accordingly this risk warrants consideration when deciding whether to use [HT],” said Lina Steinrud Mørch of Copenhagen University and her associates (JAMA 2009;302:298-305).

They assessed ovarian cancer using data from the Danish Sex Hormone Register Study, a national 10-year cohort study of nearly 1 million Danish women. Ms. Mørch and her colleagues restricted their analysis to the 909,946 women who were perimenopausal or postmenopausal at study entry, 575,881 women who had never used HT and 334,063 who had. Among the current users of HT, nearly half had been taking the hormones for more than 7 years.

A total of 3,068 incident ovarian cancers developed during the study period, including 2,681 that were epithelial tumors. Compared with women who had never taken HT, those who had showed a relative increase of 30%-58% in their risk of developing ovarian cancer, according to Ms. Mørch and her colleagues. The risk did not differ significantly by duration of use, with women who took HT for up to 4 years showing similarly increased risk as those who took it for 5 years or more. Similarly, women who took estrogen alone had approximately the same risk as did those who took combined estrogen plus progestin.

Women who took cyclic HT had increased risk similar to that in women who took continuous HT. And ovarian cancer risk was elevated regardless of HT dosage and whether it was delivered by oral tablet, patch, or gel. “If the difference in risk between never users and current users is due to hormone therapy, these results imply that use of HT resulted in about 1 extra case of ovarian cancer for roughly every 8,300 women taking HT each year,” the investigators wrote.

In commenting on the study, Dr. Wulf Utian, executive director of the North American Menopause Society, said, “The possibility of a very slight increase in ovarian cancer risk [with HT] should be added to the risk-benefit discussion between the doctor and the patient. Women who have severe vasomotor symptoms negatively affecting their quality of life are likely to take the risk, he added.

Although Dr. Utian said the Scandinavian figures are probably “as reliable as you can get in a public health system,” he said the investigators included in the progesterin category drugs that are not progesterone similar such as cyproterone acetate, an antianabolic agent, and medroxyprogesterone acetate, a progestin used in contraceptive pill formulations. “What they’ve got here is fruit salad,” he said. “They’ve got all different kinds of products lumped together, and they haven’t adequately broken them out.”

The CGH technique is considered an excellent alternative to conventional PGS, because it does not require sequential embryos be biopsied and frozen for analysis of only about half of the chromosomes in a 3-day embryo, the new technique, known as comparative genomic hybridization (CGH), can evaluate all chromosomes, including sex chromosomes, and is capable of detecting minute genetic variations, or mosaics in embryos. Using CGH, Dr. Fragouli and her associates found chromosomal abnormalities in 64% of 473 screened zygotes, including abnormalities in chromosomes that are not examined in conventional PGS. “With standard screening, 39% of these abnormalities would not have been detected, and 16% of abnormalities would have been incorrectly diagnosed as normal.”

Only healthy zygotes were allowed to mature, resulting in 73 embryos, which were transferred to 35 patients. The CGH technique is considered less invasive than regular PGS, because it does not require a day 3 biopsy of embryonic cells, which some experts consider damaging to the embryo. Instead, CGH involves the removal and examination of polar bodies, which are by-products of fertilization and not necessary for embryo development.

Dr. Fragouli did not declare any conflicts of interest. ■