TO THE EDITORS: The study titled “The association of obesity and type I uterine cancer—is this an oversimplification?” by Eakin et al.1 has been instrumental in raising a pursuit for analyzing the potential effect of obesity on the rising trend of type II endometrial cancer during the recent years. The classical teaching on obesity as a major risk factor for type I endometrial cancer is now being debated.1–3 We appreciate the authors for conducting this large-scale multicentric cohort study for a substantial period of 17 years. However, we wish to clarify certain observations that will further help in better comprehending the results.

Foremost, it would have been better if the analysis was performed as to whether the patients presenting with type II endometrial cancer being recruited in the study had a body mass index (BMI) of >30 kg/m². A correlation of BMI with the molecular classification of cancer will help to establish the hypothesis of the study. Moreover, a detailed analysis of other antecedent factors leading to endometrial cancer, such as familial history, nulliparity, assisted reproductive techniques, and exogenous hormonal therapy, needs to be evaluated in detail. These confounding factors need to be addressed before justifying our observations. Furthermore, certain modifiable risk factors for type I endometrial cancer might have been addressed by the changing lifestyles in recent years. In contrast, type II cancers are usually attributable to genetic non-modifiable risk factors.3 Therefore, further exploration into this aspect can help to uncover newer facts about the root cause of both types I and II endometrial cancers. This study will ultimately help in addressing the oncology team to delve into the matter and will probably stimulate researchers worldwide to provide a better classification of endometrial cancer.

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The oversimplification of uterine cancer classifications and risk factors

We appreciate Dr Sarkar and colleagues for their interest and thoughtful comments on our study titled “The association of obesity and type I uterine cancer—is this an oversimplification?” We agree with their comment that a direct analysis evaluating obesity in those presenting with nonendometrioid tumors is important. However, this would require a prospective, longitudinal cohort study over many years to accomplish. Our analysis focused on the use of population-level data over 2 decades to evaluate the association between obesity and the rising trend of high-risk, nonendometrioid tumors. Of note, one of the significant weaknesses of our study involved the use of 2 national databases that limited our ability to perform a direct correlation because of the lack of patient-level data. When patient-level data were available in smaller epidemiologic studies, evidence suggested overlapping risk factors between types I and II endometrial cancers, including obesity.1 Thus, our findings have added to the growing body of literature that suggests that obesity may play a role in high-risk, nonendometrioid tumors.

Given the rising incidence and mortality of endometrial cancer, we hope these findings will direct future research to explore the effect of obesity on the incidence of non-endometrioid tumors. Ideally, as Dr Sakar and colleagues noted, such a study would include an analysis of body mass index and its association with the types of endometrial cancer according to the molecular classification suggested by the Cancer Genome Atlas. Furthermore, it would ideally include a longitudinal, international analysis evaluating the effect of all other known and potentially unknown risk factors, such as demographic, socioeconomic, environmental, dietary, physical activity, family, hormonal, menstrual, parity, genetic, proteomic, metabolomic, epigenetic, and microbiomic factors. The role of obesity on type II tumors and the entirety of the traditional type I or II classification system may be
oversimplified in light of the molecular classification of endometrial cancer. Future studies should aim to validate a molecular classification system and determine associated modifiable risk factors to decrease the rising incidence and mortality associated with endometrial cancer.

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TO THE EDITORS: Husby et al1 investigated the risk of pelvic organ prolapse (POP) in women who underwent hysterectomy using the Danish National Patient Registry. The authors demonstrated that the risk of POP surgery was higher in women who had undergone hysterectomy than in those who still had their uterus.1 To eliminate bias in their analysis, the researchers used a 1:5 matching method based on age and calendar year. Despite these attempts, there are several issues with the study.

First, there is a problem with the composition of the subgroups. The authors argued that hysterectomy, excluding vaginal hysterectomy, was associated with POP (adjusted hazard ratio [aHR], 1.5; 95% confidence interval [CI], 1.0–2.4).1 However, excluding laparoscopic-assisted vaginal hysterectomy (LAVH) and vaginal hysterectomy from the subgroup analysis seems more reasonable. Furthermore, the authors explained that vaginal hysterectomy is difficult to perform when the vagina is narrow, and there is no descent of the uterus.1 This is a feature shared, in part, not only with vaginal hysterectomy but also with LAVH.2 In addition, the authors reported that total hysterectomy (aHR, 1.5; 95% CI, 0.9–2.4) and subtotal hysterectomy (aHR, 1.5; 95% CI, 0.6–3.5) were not associated with POP. Total hysterectomy and subtotal hysterectomy account for 95% of all hysterectomy cases. Therefore, it is overstated to claim that all hysterectomies are POP related. Moderately, it seems logical to claim that total hysterectomy and subtotal hysterectomy are unrelated to POP.

Second, there is a problem with target group selection. If POP was present in a patient before study selection, they should have been excluded from the target group or adjusted in the analysis. Patients with POP who had not undergone surgery were not excluded from the study group. For example, if a woman with mild uterine prolapse underwent a hysterectomy without colpopexy, this woman was assigned to the hysterectomy group. Therefore, among the finally selected women, women with POP before selection should have been excluded, regardless of whether they had undergone POP surgery.

Third, another bias that is present in the study was omitting pessary use from the primary outcome. Pessaries are so widely used that they are found in 19% of all POP treatments.3 In contrast, short vaginal length and previous pelvic surgery are risk factors for pessary failure.4 Because women who have undergone hysterectomy are more likely to experience pessary failure, they are more likely to need POP surgery. It is the same concept that a tubal pregnancy with a fetal heartbeat has a higher surgical risk than a tubal pregnancy without a fetal heartbeat. The reason is that a woman with a tubal pregnancy with a fetal heartbeat is more likely to experience methotrexate failure. Therefore, pessary use should be included in the primary outcome.

We respect the exciting work of the authors. Nonetheless, the conclusion of this study suggested that the POP risk associated with total and subtotal hysterectomy might be