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Since publication of his article, the author reports no further potential conflict of interest.

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Shared Genetic Predisposition in Peripartum and Dilated Cardiomyopathies

TO THE EDITOR: Ware et al. (Jan. 21 issue)¹ describe a very similar distribution of presumably causative genetic variants in *TTN* and other genes in women with peripartum cardiomyopathy and in persons with idiopathic dilated cardiomyopathy. The clinical outcome of peripartum cardiomyopathy is highly variable, ranging from full recovery to rapid progression to end-stage heart failure,² and the appropriate duration of therapy is controversial. I therefore wonder whether analysis of the data of Ware et al. can shed light on whether *TTN*-truncating variants are associated with late recovery or persistent left ventricular dysfunction in patients with peripartum cardiomyopathy.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Ware et al. report a striking similarity of the presumed genetic causes of peripartum and idiopathic dilated cardiomyopathies in a large series of women. In our recent analysis of data from a large administrative U.S. database (the Healthcare Cost and Utilization Project National Inpatient Sample), we found remarkable similarity between patients with dilated cardiomyopathy and those with peripartum cardiomyopathy in terms of demographic and clinical

characteristics and patient outcomes in pregnancy during the hospitalization for delivery.¹ Approximately 30% of the women in each cohort were black, and the two cohorts had similarly elevated rates of death, heart failure, arrhythmias, and pre-eclampsia spectrum disorders. Perhaps some of the patients (mis)classified as having peripartum cardiomyopathy were women with an asymptomatic dilated cardiomyopathy before pregnancy, and the hemodynamic demands of pregnancy worsened the degree of left ventricular dysfunction, leading to clinical heart failure. Have the authors considered whether the overlap in the reported genetic variants is consequent to the same disease presenting differently owing to pregnancy?

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No potential conflict of interest relevant to this letter was reported.

1. Lima FV, Parikh PB, Zhu J, Yang J, Stergiopoulos K. Association of cardiomyopathy with adverse cardiac events in pregnant women at the time of delivery. *JACC Heart Fail* 2015;3:257-66.

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THE AUTHORS REPLY: In response to Biteker: we agree that there is an important need for prognostic indicators for women with peripartum cardiomyopathy. Our study was not powered to test whether genetic variants correlate with clinical outcomes, nor did we have information on clinical outcomes for all patients. We did, however, have information for 1 year after enrollment on the 83 women in the Investigations in Pregnancy Associated Cardiomyopathy (IPAC) study. We noted that women enrolled in that study who

bore truncating variants in *TTN* had a significantly lower average left ventricular ejection fraction 1 year after enrollment than did the women with no truncating variants (mean [\pm SD], $44\pm 17\%$ vs. $54\pm 8\%$; $P=0.005$). The burden was largely seen in women of African descent. The results thus suggest that the presence of a truncating variant in *TTN* may presage persistent left ventricular dysfunction. However, these post hoc results must be interpreted with caution, and larger prospective studies are needed.

In response to Stergiopoulos et al.: we agree that peripartum and idiopathic dilated cardiomyopathies share many characteristics, including a high burden of truncating variants in *TTN*. We do not have data to directly address the question of whether women classified as having peripartum cardiomyopathy had cardiomyopathy before pregnancy. However, dilated cardiomyopathy typically manifests decades later than peripartum cardiomyopathy. In addition, in our study, women with *TTN* variants and those without such variants had similar numbers of previous pregnancies without development of the disease (mean, 2.9 ± 2.3 and 2.8 ± 1.9 pregnancies, respectively; $P=0.84$). Together, these observations do not support pregnancy-induced clinical expression of a preexisting condition, though we cannot rule out

this possibility. With respect to the question of whether peripartum and idiopathic dilated cardiomyopathies are the same disease presenting differently owing to pregnancy, we agree that this appears likely, at least for a subset of each disease. In that context, we note that nearly all *TTN* variants in the IPAC cohort occurred in women without a hypertensive disorder, despite the 46% prevalence of hypertension in the cohort. Peripartum cardiomyopathy may thus have two different causes — genetic variation in genes associated with dilated cardiomyopathy such as *TTN* and preeclampsia. As noted above, these post hoc results must be interpreted with caution, and larger prospective studies are needed.

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Weekly vs. Every-3-Week Paclitaxel for Ovarian Cancer

TO THE EDITOR: Chan et al. (Feb. 25 issue)¹ found a marginal benefit of dose-dense (weekly) chemotherapy over standard chemotherapy in a group of 112 women with ovarian cancer who did not receive bevacizumab, a subgroup that represents a mere 16% of the whole. The use of progression-free survival, instead of overall survival, in trials of ovarian-cancer therapies will exaggerate the benefit of a therapy that delays progression but has no effect on survival. The degree of exaggeration is greatest for trials, such as this one, in which the overall survival is poor, because the worse the survival is, the farther the hazard ratio associated with the intervention will fall below unity. In the present study, the 4-year survival rate was 44%; the high mortality can be attributed to the low rate of acceptance of neoadjuvant chemotherapy (13%) and the far lower rate of microscopic residual disease than gross residual

disease (24% vs. 63%) after surgery. These two treatment factors are of far greater importance than is any minor modification to the chemotherapy regimen,² and improving these should be our goal.

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No potential conflict of interest relevant to this letter was reported.

1. Chan JK, Brady MF, Penson RT, et al. Weekly vs. every-3-week paclitaxel and carboplatin for ovarian cancer. *N Engl J Med* 2016;374:738-48.

2. Narod S. Can advanced-stage ovarian cancer be cured? *Nat Rev Clin Oncol* 2016;13:255-61.

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TO THE EDITOR: Chan et al. report that weekly paclitaxel and carboplatin, as compared with