doi: 10.1093/jnci/djaa146 First published online September 21, 2020 Response

Response to Strassels and Durham

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We appreciate the opportunity to respond to the correspondence by Strassels and Durham regarding our brief communication entitled "Concurrent Opioid and Benzodiazepine Prescriptions Among Older Women Diagnosed With Breast Cancer." Below, we address each of the observations and questions raised in the correspondence.

First, we defined concurrent prescribing as greater than or equal to 1 day with overlap in opioid and benzodiazepine supplies. Strassels and Durham expressed concern that this threshold for overlap may be too low, hypothesizing that short periods of overlap are associated with a low risk of adverse events. The exposure-response relationship between concurrent opioid and benzodiazepine prescribing and overdose risk is not well understood; however, available data indicate that the risk of opioidrelated overdose is highest in the first days of overlap between opioid and benzodiazepine supplies (1). Our definition of concurrent opioid and benzodiazepine prescribing was based on prior research (2,3) and has demonstrated an association with an increased risk of emergency department or inpatient admission for opioid overdose (2). Moreover, in addition to reporting on this binary measure of concurrent opioid and benzodiazepine prescribing in our brief communication, we also described the extent of overlap in opioid and benzodiazepine prescriptions, measured as the count of overlapping days.

Second, Strassels and Durham raised a question regarding comorbidity burden among women in the study sample. In particular, they wondered why roughly one-half of women had a comorbidity score of 0 when the Charlson Comorbidity Index assigns a score of 2 for nonmetastatic cancer. As is standard in Surveillance, Epidemiology, and End Results (SEER)-Medicare studies, we used the National Cancer Institute–endorsed Klabunde modification of the Charlson Comorbidity Index, which excludes cancer diagnoses as comorbid conditions and does not attribute points based on patient age (4,5).

Third and finally, Strassels and Durham posed the question of whether women in the sample may have received palliative care services during the study period, offering the rationale that concurrent prescribing of opioids and benzodiazepines may be more common in the setting of advanced cancer. We agree; the risk-benefit ratio for opioid and benzodiazepine coprescribing may be fundamentally different for patients with advanced cancer. For that reason, our analysis was limited to patients with incident stage I-III disease. We did not attempt to exclude patients with palliative care encounters during the study follow-up period because we did not wish to exclude patients who, regardless of cancer stage at diagnosis, may have received ambulatory palliative care for symptom management alongside their curative-intent cancer treatment. Using the SEER-Medicare data, it was not possible to identify the source(s) of opioid and benzodiazepine prescriptions (ie, palliative care, oncology, primary care, or some combination). Understanding the source(s) of coprescribing is an important next step for identifying and reducing coprescribing of opioids and benzodiazepines that may be unintentional or otherwise avoidable.

References

- Hernandez I, He M, Brooks MM, Zhang Y. Exposure-response association between concurrent opioid and benzodiazepine use and risk of opioid-related overdose in Medicare Part D beneficiaries. JAMA Netw Open. 2018;1(2):e180919.
- Sun EC, Dixit A, Humphreys K, Darnall BD, Baker LC, Mackey S. Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis. BMJ. 2017;356:j760.
- Gellad WF, Zhao X, Thorpe CT, et al. Overlapping buprenorphine, opioid, and benzodiazepine prescriptions among veterans dually enrolled in Department of Veterans Affairs and Medicare Part D. Subst Abus. 2017;38(1):22–25.
- Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. J Clin Epidemiol. 2000;53(12):1258–1267.
- NCI Comorbidity Index Overview. National Cancer Institute Division of Cancer Control and Population Sciences website. 2019. https://healthcaredelivery. cancer.gov/seermedicare/considerations/comorbidity.html. Accessed August 26, 2020.

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