than a delay in diagnosis and greater tumor burden at presentation.

SANDRA M. BROWN
Concord, North Carolina, USA

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Reply to Comment on: Racial, Ethnic, and Socioeconomic Disparities in Retinoblastoma Enucleation: A Population-Based Study, SEER 18 2000–2014

REPLY

WE ARE THANKFUL FOR THE OPPORTUNITY TO RESPOND TO the issues raised in Dr Brown's letter. We would also like to thank Dr Brown for these comments and for expressing interest in our work.[1]

Dr Brown raises concerns regarding the validity of SEER stage data. Dr Brown notes SEER Extent of Disease (EOD) does not fully correspond with the International Classification of Retinoblastoma (ICRB). SEER historic stage, used in our study, is based on EOD and categorized as localized, regional, or distant. Therefore, Dr Brown's point further implies SEER staging may be insufficiently granular, as all ICRB categories will correspond primarily to "localized" SEER staging. In such case, one would expect SEER stage to not statistically qualify as a confounder in regression modeling. However, in our analysis, SEER stage not only met criteria, but subsequent adjustment showed an independently significant association between race, ethnicity, socioeconomic status (SES), and enucleation.

When discussing the validity of SEER stage data, Dr Brown notes that pathologic staging takes precedence over clinical staging in the EOD system. However, SEER historic stage used in our study combines EOD data with clinical data, representing a more wholistic perspective.

We appreciate and acknowledge that differences between ICRB and SEER staging is a limitation of our study, particularly when evaluating delayed diagnosis as an etiology of racial, ethnic, and socioeconomic disparities. However, the primary objective of our study was first and foremost to examine whether disparities are present at all, which both our descriptive and regression results confirm. To evaluate delayed diagnosis as an etiology, we examined for effect modification between stage and race, ethnicity, and SES but observed none. Granted, specific staging, chemotherapy, and primary vs secondary enucleation data are integral to fully understanding treatment courses. These are important limitations, which we acknowledge in our manuscript.[1] Therefore, though it is difficult to definitively exclude delayed diagnosis as a driver of treatment disparities, factors like geographic practice patterns and healthcare access should not be overlooked.

Of note, SEER is an epidemiologic registry aimed at capturing oncologic data across various institutions,[2,3] some of which lack expertise in ocular oncology and retinoblastoma and therefore may not use ICRB. With this context, the racial, ethnic, and socioeconomic differences in SEER become even more meaningful.

Dr Brown finally comments that statistical significance between enucleation and racial, ethnic, and socioeconomic groups was described as "largely not met." However, the statement Dr Brown is referring to specifically addresses treatment trends over time. Enucleation differences in both descriptive and regression analyses were statistically significant. Furthermore, although statistical significance was not met in our treatment trend analysis, nonwhite, Hispanic, and socioeconomically disadvantaged children were consistently enucleated in greater proportions from 2000 to 2014, despite overall decreases in enucleation rates.

Overall, we believe the strengths of our study outweigh the limitations. Although further research is certainly required to better delineate why racial, ethnic, and socioeconomic disparities in treatment patterns occur, our manuscript is an important start, highlighting that other factors beyond delayed diagnosis should be considered and addressed.

NITYA RAJESHUNI
ALICE S. WHITTEMORE
Stanford, California, USA
CASSIE A. LUDWIG
PRITHVI MRUTHYUNJAYA
DARIUS M. MOSHFEGHI
Palo Alto, California, USA

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