April 10, 2016

To the Editor:

We appreciate the letter to the editor regarding our systematic review analyzing the impact of oral antivirals in preventing mother to child transmission of Hepatitis B. The author points out some of the limitations of systematic reviews of studies such as difficulty in accounting for and identifying overlapping populations from the same center and shortcomings due to limitations of the original studies, such as incomplete reporting, selection bias and loss to follow-up.

To overcome some of these limitations, we formed a multidisciplinary systematic review team of hepatologists, methodologists, a statistician and a native Chinese-speaking researcher. Nevertheless, we remain limited by the quality of data and adequacy of reporting of the primary studies. To explicitly address the challenges in the literature and the uncertainty around the estimate of effect, we used the GRADE approach and downgraded the quality of evidence when appropriate based on risk of bias, inconsistency, indirectness, imprecision or publication bias. The guideline writing group similarly downgraded the strength of the recommendations based on the quality of the evidence.

Our review shows that the majority of studies report that oral antiviral therapy in the third trimester for women with high HBV viral loads reduces the rate of mother to child transmission. Although, the magnitude of this difference and the risk of transmission without antiviral therapy in the mother may be debated, the transmission risk is certainly at least as high as 9%. Whether this transmission rate is

acceptable is a societal and patient-physician decision. Our systematic review demonstrates that antiviral therapy reduces the rate of transmission. Given that elimination of vertical transmission of Hepatitis B is a public health goal, we believe the data lead to a recommendation for this therapy, despite the limitations. A future trial would provide additional data, but potential information gained should be weighed against the already reported reduced risk with antiviral prophylaxis in women with high HBV viral loads, and thus whether such a trial would be ethical or feasible. Finally, the goal of systematic reviews and practice guidelines is to make the care recommendations with the currently best available evidence. Consequently, we continue to believe that we have provided the best inference from the data available at the present time and that the independent guideline committee appropriately phrased their recommendation.

Sincerely,

Robert S. Brown, Jr., MD, MPH

rsb2005@med.cornell.edu

Brian J. McMahon, MD

bdm9@cdc.gov

Anna SF Lok, MD

aslok@umich.edu

John B. Wong, MD

jwong@tuftsmedicalcenter.org

Ahmed T. Ahmed, MBBCh

Ahmed.Ahmed1@mayo.edu

Mohamed A. Mouchli, MD

Mouchli.Mohamad@mayo.edu

Zhen Wang, PhD

Wang.Zhen@mayo.edu

Prokop J Larry, MLS

Prokop.Larry@mayo.edu

Mohammad Hassan Murad, MD, MPH

Murad.Mohammad@mayo.edu

Khaled Mohammed, MBBCh, MPH

Mohammed.khaled@mayo.edu