Response to Reviewers' Comments

We were most delighted to learn that our manuscript **ESPS manuscript NO** 28299 has been subject to opportunity of revision for publication in ***World Journal of Gastroenterology***. We have carefully considered the valuable comments and suggestions provided by referees and the editor, and made great efforts to improve the manuscript accordingly. The followings are point-by-point answers to specific questions raised by the reviewer (The modifications in the manuscript are highlighted in Red Bold).We hope that the revised version of manuscript could meet the priority required for the publication.

Reviewer: 1

This manuscript presented models to predict development of HCC in patients with chronic HBV infection. The prediction of HCC is important in clinical practice to determine regular surveillance. The models are presented in detail, however, significance of each model was not clear. Most of the models were based on China and Korea. HBV infection and HCC are popular in the areas, but the models seemed localized and limited to China and Korea. Were there any models in the United States or European countries?

Response) We fully agree with the reviewer's keen comment. Existing prediction models were mostly developed in Asia. There were limited data about HCC risk models for people at high risk in the United States or European countries (Guyot E et al. PNPLA3 rs738409, hepatocellular carcinoma occurrence and risk model prediction in patients with cirrhosis. J Hepatol 2013; Abu Dayyeh BK et al. A functional polymorphism in the epidermal growth factor gene is associated with risk for hepatocellular carcinoma. Gastroenterology 2011). We described these modes briefly on Page 13 subtitled "Other HCC risk models".

Reviewer: 2

Dear author Liver biopsy is currently considered the gold standard for assessing hepatic fibrosis or cirrhosis. However, it is an invasive procedure, with rare but potentially life-threatening

complications.1 In addition, the accuracy of liver biopsy in assessing fibrosis has limitations because of well-known sampling errors and interobserver variability. Transient elastography [FibroScan(FS)] is a rapid, noninvasive, and reproducible method for measuring liver stiffness. FS examination can be performed in about 95% of patients but is problematic in those with ascites or a body mass index above 28 kg/m. A strong association of liver stiffness measured by FS and the degree of liver fibrosis could be demonstrated in patients with chronic hepatitis. According to your data, liver stiffness value from transient elastography is a valuable tool to detect the fibrosis in chronic liver disease. I ask some question. Please tell me the what kind of procedure in Transient elastography do you perform in ascites and obesity patients?

Response) We appreciate the valuable comment. Previous studies reported that the use of XL probe could be helpful to check liver stiffness for patients with ascites or high BMI (Kohlhaas A et al. Transient elastography with the XL probe rapidly identifies patients with nonhepatic ascites. Hepat Med 2012; Sasso M et al. Liver Steatosis Assessed by Controlled Attenuation Parameter (CAP) Measured with the XL Probe of the FibroScan: A Pilot Study Assessing Diagnostic Accuracy. Ultrasound Med Biol 2016). However, we have few data about XL probe. Because XL probe has been used from February 2016 in our hospital. More data and further validation is needed.

Reviewer: 3

This review summarizes recent prediction models of HCC development in CHB patients systematically. Based on the progression in antiviral therapy and the application of liver stiffness measurement, the authors introduced two new HCC prediction models: LSM-HCC and mREACH-B. By comparison with the traditional models, mREACH-B model has been shown better prediction advantage. Undoubtedly, making a HCC prediction model in CHB patients is a very meaningful work. It not only has the value of primary prevention and early diagnosis of HCC, but also obtains a benefit in clinical cost-effectiveness. However, HCC heterogeneity related to race, cause and region has been a mainly obstacle in making a consistent prediction model for all the CHB patients. In addition, the

use of antiviral therapy, new biomarkers and test methods for liver related disease will also continuously promote the development of HCC prediction models. Therefore, many new prediction models for HCC in CHB patients are being searched for. The authors has done a lot of work in this field in recent years. Based on their work, they summarized the progression about these models exhaustively and comprehensively. I think it is a very important work and should be published priority.

Response) We appreciate the valuable comment. We tried to revised the manuscript according to reviewer's keen comment.

Reviewer: 4

The article is very interesting and useful for clinicians. The authors have made an objective synthesis of the possibilities of predicting the evolution of chronic hepatitis B toward hepatocellular carcinoma. Their comments on scores and their value are correct. There are several grammatical errors that must be corrected (for example: have be proposed).

Response) We appreciate the valuable comment. The English in this document has been checked by at least two professional editors, both native speakers of English.