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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 6632

**Title:** Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations

**Reviewer code:** 00006071

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-10-27 11:20

**Date reviewed:** 2013-11-29 01:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ Y] Major revision
		[ ] No records	

## COMMENTS TO AUTHORS

The review by Wong and Ahmed addresses the issue of ethnic influence among Asian populations on the association of obesity and NAFLD. The subject is clearly of interest, and the review is well written and documented. After carefully reading the manuscript, some questions arise: Major questions: . Ethnicity is clearly a factor related to differences in the association of obesity and NAFLD between Asians and other human populations, but other factors are surely playing a role. By tradition and culture, Asians consume higher amounts of carbohydrates than other human population in their daily diet. Carbohydrates are highly lipogenic through the activation of the transcription factor ChREBP, favoring, when consumed in excess, the development of fatty liver. As in other parts of the world, Asian countries have improved the access to food of their populations over the years, thus favoring the intake of hypercaloric diets enriched in carbohydrates in wide segments of their inhabitants. Clearly, this issue should be properly addressed in the present revision. . The two last paragraphs of the review “NAFLD and HCC”, and “NAFLD and liver transplantation”, should specifically include and comment data on these issues obtained from Asian populations. Minor questions: Please correct: . Abstract: “Asians continue to demonstrate significant prevalences of hypertension”, prevalence . Introduction: “Non-alcoholic fatty liver disease (NAFLD) spans a spectrum of liver disease that ranges”, diseases . Please, every time a reference is cited, such as “western countries.[6-12]”, move the point mark to the end “western countries[6-12].” . Obesity disparities, page 7: “Cognizant of these disparities” for “Acknowledging these disparities” . The sentence “Shao et al demonstrated that a waist-hip ratio of 0.50 achieved an area under the receiver operating curve of 0.794 for men and 0.901 for women, both significantly better at



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predicting risk of metabolic syndrome than BMI or waist circumference alone” is difficult to understand, please rewrite. . Natural History of NAFLD in Asians, page 10, substitute “However, simple steatosis is not always benign, and progression of disease, while slow can occur.” For “However, simple steatosis is not always benign, and progression of disease, while slow, can occur. “. NAFLD and HCC, page 12, substitute “the risk of HCC among patients with NASH are less well known” for “the risk of HCC among patients with NASH is less well known” . References: Please correct references 26, 46, 77, 78, 80, 83, 85, 86, 88, and 94. . Figure 2: Please, change “Diabtese” for “diabetes”.



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**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 6632

**Title:** Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations

**Reviewer code:** 02861131

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-10-27 11:20

**Date reviewed:** 2013-12-26 04:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Manuscript Number: 6632 Manuscript Title: Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations Comments To Authors GENERAL COMMENTS

(1) The importance of the research and the significance of the research contents; Against a background of increasing rates of obesity worldwide, Non-Alcoholic Fatty Liver Disease (NAFLD) has become the commonest cause of liver disease in many developed countries, affecting up to a third of the population<sup>1</sup>. Increased waist circumference is probably the best single clinical predictor of underlying insulin resistance and the presence of NAFLD<sup>2</sup>. Asians as a group generally have lower BMI and lower prevalence of obesity compared to other ethnic groups. Despite lower obesity prevalence, higher rates of metabolic syndrome have been reported in Asians compared to other ethnic groups at similar BMI levels. These findings demonstrate that BMI thresholds for defining overweight and obesity should not be applied uniformly to all ethnic cohorts<sup>3</sup>. (2) The novelty and innovation of the research; This study has reported on ethnic disparities in the prevalence of obesity as well as the impact of weight gain on overall risk of obesity-related diseases. Despite lower obesity prevalence, higher rates of metabolic syndrome have been reported in Asians compared to other ethnic groups at similar BMI levels. The Wong group has performed an in-depth analysis of ethnic disparities in obesity and obesity-related diseases with a focus on Asian populations (using data from the California Department of Public Health and the U.S. Centers for Disease Control and Prevention). They created a multivariate logistic regression model to assess the effect of each one unit increase in BMI on the risk of hypertension or diabetes mellitus. This data suggest that despite having lower BMI, weight gain as measured by BMI disproportionately affects Asians to a greater degree. (3)



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Presentation and readability of the manuscript; and Review is well organized, and systematic theoretical analyses and valuable conclusions are provided. This review is a classically presented scientific article. (4) Ethics of the research. Not relevant for this article (authors used official data from the California Department of Public Health and the U.S. Centers for Disease Control and Prevention) Bibliography 1. Argo CK, Caldwell SH. Epidemiology and natural history of non-alcoholic steatohepatitis. Clin Liver Dis 2009;13:511-31. 2. Dyson JK, McPherson S, Anstee QM. Non-alcoholic fatty liver disease: non-invasive investigation and risk stratification. J Clin Pathol. 2013 Dec;66(12):1033-45. 3. Robert J. Wong , Aijaz Ahmed. Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations. World J Hepatol 2014 in press

**SPECIFIC COMMENTS** Title: accurately reflects the major topic and contents of the study. Abstract: it gives a clear delineation of the research background, objectives and main point presented in this review. Significant ethnic disparities in central adiposity and visceral fat distribution have been hypothesized to contribute to the prevalence of obesity and the progression of hepatic histologic damage associated with NASH. Review is well organized, and systematic theoretical analyses and valuable conclusions are provided. Introduction: present relevant information about significant difference in epidemiology of obesity and NAFLD, dependent of ethnic group. Obesity Disparities: present original analysis of ethnic disparities in obesity and obesity-related diseases with a focus on Asian populations, performed using data from the California Department of Public Health and the U.S. Centers for Disease Control and Prevention in period 1985 to 2011. These data suggest that despite having lower BMI, weight gain as measured by BMI disproportionately affects Asians to a greater degree. Disparate Association of NAF



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**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 6632

**Title:** Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations

**Reviewer code:** 00002726

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-10-27 11:20

**Date reviewed:** 2014-01-02 10:04

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The article is intended as a review of the differences in NASH in Asians. The topic is of potential interest but much of the article really does not deal with the topic. 1. The opening pages are very repetitive as for example the points that there is an obesity epidemic and Asians have a high prevalence of NASH despite a lower rate of obesity are made several times. 2. the authors state that a disparity in insulin levels has been noted in Asians but then only figures on prevalence of the metabolic syndrome are provided. Have insulin levels by BMI been documented to be different in Asians? This should be clarified in the review. 3. It is not clear what data Fig. 1 is based on. 4. The Wong study cited on progression of simple steatosis to NASH had a very high rate of progression that is not consistent with other studies. The extensive discussion on progression is on NASH in general and not related to differences in Asians. 5. The HCC section is also not really focused on differences between Asian and non-Asian populations. Same for transplantation section. 6. Pages are not numbered so it is difficult to cite all of the examples, but there are a number of typographical/grammatical errors. Page 2, line 7 should be "exhibit" not exhibits. Page 2, line 9 "prevalences" is not a word, it should be singular, and the sentence should be reworded, "...continue to have an increased prevalence of..." Wordage and style is very repetitive and should be improved upon. One sentence has "in addition" and "additionally" twice. The statement that differences in Asians may be due to their fat distribution is repeated multiple times. Too much actual numerical data is cited from the papers when more summary and interpretation is needed. Fig. 2, lower panel title "Diabetes" is misspelled. Manuscript title should really read between Asian and non-Asians not among Asians which means among various types of Asians.



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**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 6632

**Title:** Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations

**Reviewer code:** 00070635

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-10-27 11:20

**Date reviewed:** 2014-01-03 05:21

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

The review is important and interesting and very well written. I have few minor comments: 1. Page 4, "from 1985 to... (...), all details in parentheses are not needed if it's all described in figure 1. 2. End of page 4: was interaction tested between ethnicity and weight gain (with regard to risk of DM)? There seems to be one but is it significant? 3. Natural history of NAFLD- is NAFLD appearance really more recent in Asian countries or is the possible that the awareness and screening for nafld are more recent? 4. How would ethnic disparities in central obesity may alter the natural history of NAFLD? To which direction?



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**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 6632

**Title:** Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations

**Reviewer code:** 01562153

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-10-27 11:20

**Date reviewed:** 2014-01-04 13:21

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

The prevalence of obesity and progression of hepatic damage associated with nonalcoholic steatohepatitis (NASH) exhibits significant ethnic disparities. Asians demonstrate significant prevalences of hypertension, diabetes, metabolic syndrome, and NASH, despite significantly lower body mass index (BMI) and lower rates of obesity. In this manuscript, the authors reviewed and discussed the epidemiology of obesity and NASH, disparate association of non-alcoholic fatty liver disease (NAFLD) and BMI, and natural history of NAFLD in Asians. This is a comprehensive review on the obesity and NAFLD in Asian populations. The manuscript was well prepared. Although the major etiologies of liver diseases in Asia are hepatitis B virus and hepatitis C virus, NAFLD also plays an important role. This review may provide useful information to the clinicians in Asia.



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### ESPS Peer-review Report

**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 6632

**Title:** Obesity and Non-Alcoholic Fatty Liver Disease: Disparate Associations Among Asian Populations

**Reviewer code:** 02541859

**Science editor:** Ma, Ya-Juan

**Date sent for review:** 2013-10-27 11:20

**Date reviewed:** 2014-01-05 14:23

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

File attached.