



## Reply to: “NAFLD and beneficial effects of lifestyle intervention: Defining the meat of the matter”

### To the Editor:

We thank Drs Alferink and Murad for their interest and comments on our study.<sup>1</sup> We agree that body mass index (BMI) is an imperfect measure of adiposity. A number of studies have shown that waist circumference or waist-hip ratio, as surrogates of central obesity, may predict histological changes in patients with non-alcoholic fatty liver disease (NAFLD) and the presence of metabolic diseases in the general population.<sup>2,3</sup> In our study, the change in waist circumference among patients with baseline BMI <25 kg/m<sup>2</sup> was 1.9 ± 5.6 vs. 0.2 ± 5.0 cm at Year 1 ( $p = 0.11$ ) and -0.4 ± 9.3 vs. -0.2 ± 5.4 cm at Year 6 ( $p = 0.93$ ) in the lifestyle intervention and control groups, respectively. The change in waist circumference among patients with baseline BMI ≥25 kg/m<sup>2</sup> was -4.0 ± 6.9 vs. 1.9 ± 5.8 cm at Year 1 ( $p < 0.001$ ) and 2.2 ± 6.2 vs. -0.5 ± 6.6 cm at Year 6 ( $p = 0.32$ ) in the lifestyle intervention and control groups, respectively.

In response to Alferink and Murad's request, we repeated the multivariable analysis using percentage of weight reduction in place of absolute weight reduction as a covariate. As expected, percentage change in body weight remained a strong independent factor associated with remission of NAFLD at Year 1 in patients with baseline BMI <25 kg/m<sup>2</sup> (Table 1). Compared with Table 3 of our original article,<sup>1</sup> the adjusted odds ratios of the other factors were almost unchanged in this new analysis. Participation in lifestyle intervention now has only borderline statistical significance, supporting the notion that the benefit of lifestyle intervention was reflected by improvements in anthropometric parameters. We did not include both absolute and relative weight reduction in the same model because of collinearity.

Finally, Alferink and Murad discussed the accuracy of fatty liver index (FLI). We agree that FLI and similar simple prediction scores have modest accuracy for the diagnosis of NAFLD.<sup>4</sup> While they have important roles in epidemiological research using large cohorts, they are not accurate enough for the clinical management of individual patients. We thank Alferink and Murad for sharing their data comparing FLI and ultrasonographic fatty liver in the Rotterdam study.<sup>5</sup> Since BMI and waist circumference are components of FLI, the score may perform differently

in patients with different BMI. We did not perform c-statistics for FLI in our study because all patients had NAFLD at baseline.<sup>1</sup> Rather, FLI had modest correlation with intrahepatic triglyceride content (IHTG) by proton-magnetic resonance spectroscopy in the overall population ( $r = 0.20$ ,  $p = 0.028$ ). The correlation was weaker when stratified by BMI ( $r = 0.11$ ,  $p = 0.41$  for BMI <25;  $r = 0.19$ ,  $p = 0.12$  for BMI ≥25 kg/m<sup>2</sup>). The latter probably reflects the effect of narrow spectrum. As such, we would emphasize that IHTG was the robust primary outcome in our study, and data based on FLI should be considered exploratory.

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### Conflict of interest

V.W. has served as a consultant or advisory board member for Allergan, Center for Outcomes Research in Liver Diseases, Gilead Sciences, Janssen, Perspectum Diagnostics, Pfizer, TARGET-NASH and Terns, and a speaker for Echosens and Gilead Sciences. H.C. has served as an advisory board member for Gilead Sciences, and a speaker for Echosens and Gilead Sciences.

### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2019.02.008>.

### References

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Vincent Wai-Sun Wong<sup>1,2</sup>  
Henry Lik-Yuen Chan<sup>1,2,\*</sup>

<sup>1</sup>Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

<sup>2</sup>State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

\*Corresponding author. Address: Department of Medicine and Therapeutics, 9/F, Prince of Wales Hospital, 30-32 Ngan Shing Street, Shatin, Hong Kong. Tel.: +852 35051506; fax: +852 26373852.

E-mail address: [hlychan@cuhk.edu.hk](mailto:hlychan@cuhk.edu.hk)

**Table 1. Multivariable analysis of factors associated with remission of NAFLD at Year 1 in patients with baseline BMI <25 kg/m<sup>2</sup>.**

Factors	Adjusted odds ratio	95% CI	p value
Lifestyle intervention group	5.332	0.972–29.245	0.054
Baseline IHTG (%)	0.745	0.602–0.922	0.007
Percentage change in body weight from baseline to Year 1	0.649	0.510–0.825	<0.001
Change in waist circumference from baseline to Year 1 (cm)	0.792	0.662–0.948	0.011

BMI, body mass index; IHTG, intrahepatic triglyceride content; NAFLD, non-alcoholic fatty liver disease.

Binary logistic regression analysis was performed to identify factors associated with remission of NAFLD.

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