clear statement of BMI classification and re-group the population based on correct BMI categories (<18.50, 18.5–24.9, 25.0–29.9, and ≥30.0 kg/m^2). If the population was divided into revised groups for analysis, the information obtained would be more comprehensive and the results would be more reliable.

Conflict of interest

The authors have declared no conflicts of interest.

References

Hernaez A, Rogne T, Skara KH, Haberg SE, Page CM, Fraser A, Burgess S, Lawlor DA, Magnus MC. Body mass index and subfertility: multivariable regression and Mendelian randomization analyses in the Norwegian Mother, Father and Child Cohort Study. *Hum Reprod* 2021;**36**:3141–3151.

Katsoulis M, Lai AG, Diaz-Ordaz K, Gomes M, Pasea L, Banerjee A, Denaxas S, Tsilidis K, Lagiou P, Misirli G *et al*. Identifying adults at high-risk for change in weight and BMI in England: a longitudinal, large-scale, population-based cohort study using electronic health records. *Lancet Diabetes Endocrinol* 2021;**9**:681–694.

Rao ACA, Ng ACC, Sy RW, Chia KKM, Hansen PS, Chiha J, Kilian J, Kanagaratnam LB. Electrocardiographic QRS duration is influenced by body mass index and sex. *Int J Cardiol Heart Vasc* 2021;**37**:100884.

WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;**363**:157–163.

Xuzhi Liang and Jiangtao Fan*

Department of Gynecology, Guangxi Medical University First Affiliated Hospital, Nanning, China

Correspondence address. Department of Gynecology, Guangxi Medical University First Affiliated Hospital, Nanning, Guangxi, China. Tel: +86-13737085001; Fax: +86-13737085001; E-mail: jt_fan2018@163.com

https://orcid.org/0000-0003-1308-4533

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Reply: The utilization of accurate body mass index classification is imperative for grouping based on BMI

Sir,

We read with interest the comments to our paper (Hernáez *et al.*, 2021) by Drs. Liang and Fan (Liang and Fan, 2022). They are correct that the BMI thresholds used in our article did not correspond to the standard values suggested by the World Health Organization (WHO). We have acknowledged this in the discussion of the study: 'Fifth, we were unable to use standard BMI categories for underweight (WHO threshold <18.5 kg/m^2), as this only included 2.69% and 0.14% of the female and male participants, respectively'. We decided to group all participants with BMI values below 20.0 kg/m^2 to obtain more robust odds ratios in the stratified analyses. For example, in Mendelian randomization, a 1 standard deviation increase in the genetically predicted BMI values was linked to 14% less odds of subfertility in all women with BMI values <20 kg/m^2 (odds ratio [OR] 0.86, 95% confidence interval [CI] 0.76–0.98). When we split this group to underweight women (<18.5 kg/m^2) and women with low-normal BMI values (18.5–19.9 kg/m^2), the direction and magnitude of the associations remained constant (18.5–19.9 kg/m^2: OR 0.86, 95% CI 0.75–0.99; <18.5 kg/m^2: OR 0.84, 95% CI 0.58–1.22), although the 95% CIs were wider due to the more limited sample size in each group. Something similar happened in men (<20 kg/m^2: OR 0.81, 95% CI 0.47–1.41; 18.5–19.9 kg/m^2: OR 0.84, 95% CI 0.43–1.63; <18.5 kg/m^2: OR 0.69, 95% CI 0.19–2.43). In any case, the J-shaped association curves suggest that there is an increase in the odds of subfertility in participants at the lower end of BMI distribution (Staley and Burgess, 2017). The 'low-normal' BMI category has also been used in previous studies following our same methodology (Sun *et al.*, 2019) and several other epidemiological works (Flegal *et al.*, 2014). Therefore, our conclusions are robust, even though this decision prevents us from establishing associations between clinically defined underweight and subfertility. Consequently, we have not used the term 'underweight' in the description of our results in the text; we systematically used 'participants with BMI values below 20.0 kg/m^2' to describe this group and indicated in the limitations of the study that further studies involving larger populations in the lower end of the BMI distribution are warranted.

Conflict of interest

The authors have no conflicts of interest to declare.

References

Flegal KM, Kit BK, Graubard BI. Body mass index categories in observational studies of weight and risk of death. *Am J Epidemiol* 2014;**180**:288–296.

Hernáez A, Rogne T, Skara KH, Haberg SE, Page CM, Fraser A, Burgess S, Lawlor DA, Magnus MC. Body mass index and subfertility: multivariable regression and Mendelian randomization analyses in the Norwegian Mother, Father and Child Cohort Study. *Hum Reprod* 2021;**36**:3141–3151.

Liang X, Fan J. The utilization of accurate body mass index classification is imperative for grouping based on BMI. *Hum Reprod* 2022;**37**:622–623.

Staley JR, Burgess S. Semiparametric methods for estimation of a nonlinear exposure-outcome relationship using instrumental variables with application to Mendelian randomization. *Genet Epidemiol* 2017;**41**:341–352.

Sun YQ, Burgess S, Staley JR, Wood AM, Bell S, Kaptoge SK, Guo Q, Bolton TR, Mason AM, Butterworth AS *et al*. Body mass index and

all cause mortality in HUNT and UK Biobank studies: linear and non-linear mendelian randomisation analyses. *BMJ* 2019;**364**:l1042.

Álvaro Hernáez[1,2,3,*] and Maria Christine Magnus[1,4,5]

[1]*Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway*
[2]*Instituto de Salud Carlos III, Consorcio CIBER, M.P. Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Madrid, Spain*
[3]*Blanquerna School of Health Sciences, Universitat Ramon Llull, Barcelona, Spain*
[4]*MRC Integrative Epidemiology Unit, University of Bristol, Bristol, UK*
[5]*Population Health Science, Bristol Medical School, University of Bristol, Bristol, UK*

*Correspondence address. Centre for Fertility and Health, Norwegian Institute of Public Health, PO 222 Skøyen, Oslo 0213, Norway. Tel: +47-955-23-51; E-mail: alvaro.hernaez@fhi.no
https://orcid.org/0000-0001-8593-1477

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