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Comment on the grouping of patients with polycystic ovary syndrome based on body mass index

Sir,

Recently, I read the article by [Chen et al. \(2021\)](#) with interest. They explored the risks of offspring obesity and diabetes until 22 years of age concerning maternal polycystic ovary syndrome (PCOS) by conducting a cohort study of all live births during 1996–2014 in Finland. The authors concluded that maternal PCOS/anovulatory infertility was associated with an increased risk of obesity in male and female offspring from an early age. Although I appreciate and agree with most of the content of the article, after intensively reading and studying, a few following points I would like to propose.

I noticed that the authors describe 'For offspring Type 2 diabetes, the number was too small for a subgroup analysis. Pre-pregnancy body mass index (BMI) (three strata: <25, 25–29, ≥30 kg/m²) ' in the section of Statistical Analyses, and they also stratified the pregnant women by pre-pregnancy BMI according to the classification of above BMI. In my view, it is not a good choice to divide patients into three groups according to BMI value (<25, 25–29, ≥30 kg/m²). In general, people are divided into four groups according to the World Health Organization classification ([Parr et al., 2010](#)): BMI <18.5, 18.5–24.9, 25.0–29.9, and ≥30 kg/m². Therefore, I do not recommend dividing patients into three groups according to BMI value. If patients were divided into four groups in the subgroup analysis, the results would be more reliable and interesting.

Conflict of interest

None.

References

Chen X, Koivuaho E, Piltonen TT, Gissler M, Lavebratt C. Association of maternal polycystic ovary syndrome or anovulatory infertility with obesity and diabetes in offspring: a population-based cohort study. *Hum Reprod* 2021;**36**:2345–2357.

Parr CL, Batty GD, Lam TH, Barzi F, Fang X, Ho SC, Jee SH, Ansary-Moghaddam A, Jamrozik K, Ueshima H, et al.; Asia-Pacific Cohort Studies Collaboration. Body-mass index and cancer mortality in the Asia-Pacific Cohort Studies Collaboration: pooled analyses of 424,519 participants. *Lancet Oncol* 2010;**11**: 741–752.

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Reply: Association of maternal polycystic ovary syndrome or anovulatory infertility with obesity and diabetes in offspring: a population-based cohort study

Sir,

We would like to thank Dr [Wei \(2021\)](#) for the interest in our paper ([Chen et al., 2021](#)) and are happy to respond.

In the letter to the editor, Dr Wei states their appreciation for the paper and they agree with most of the article content. Dr Wei correctly notices that maternal pre-pregnancy BMI is categorized into three strata: <25, 25–29 and ≥30 kg/m². Dr Wei states that this is not recommended given that, according to the World Health Organization (WHO) classification ([Parr et al., 2010](#)), BMI is generally divided into four categories: <18.5, 18.5–24.9, 25.0–29.9 and ≥30 kg/m².

WHO has recommended classification of bodyweight including degrees of underweight and excess weight based on BMI, calculated as weight in kilograms divided by height in meters squared (kg/m²). However, the BMI distribution differs between ethnic groups. According to the WHO regional office for Europe, BMI falls into one of the following categories for adults over 20 years old: (i) underweight: below 18.5, (ii) normal weight: 18.5–24.9, (iii) pre-obesity: 25.0–29.9, (iv) obesity class I: 30.0–34.9, (v) obesity class II: 35.0–39.9 and (vi) obesity class III: above 40 kg/m² ([Office WER, 2019](#)).

BMI groups are not distributed equally in the population. Generally, there are a few people in the underweight and obesity class III groups, and the majority of people have normal-weight, pre-obesity, or obesity class I or II. In order to have a good statistical power, the underweight

group is often combined with the normal weight group, while persons with BMI over 30 kg/m² are often combined in an obesity group. Specifically, in our study, there were 419 (1.7%) mothers with polycystic ovary syndrome (PCOS) who had BMI <18.5 kg/m² before pregnancy. They were too few for a subgroup analysis for offspring diagnosis of obesity or diabetes. Therefore, they were combined with the normal-weight group.

Women with PCOS are more likely to be overweight or obese, and our results and others' also suggest that increased BMI at early ages might predict the development of PCOS (Brower *et al.*, 2019; Koivuaho *et al.*, 2019; He *et al.*, 2020). By focusing on the independent and interactive effects of maternal PCOS and higher BMI, our results would have implications on preventative interventions for offspring born to mothers with PCOS, particularly those with BMI over 25 kg/m².

Therefore, in this study, we classified pre-pregnancy BMI into three strata in the analysis. However, we acknowledge that it would be better to categorize groups in more detail wherever the sample size is large enough. Also, there might be a pathophysiological heterogeneity in PCOS, dependent on BMI (Escobar-Morreale, 2018). For underweight or normal-weight women with PCOS, the defect in androgen synthesis is severe enough to trigger PCOS with absence of other factors such as obesity; for PCOS with overweight or obesity, a mild defect in androgen secretion is amplified by the coexistence of adiposity and/or insulin resistance to manifest as PCOS. It would be interesting to further examine offspring obesity and diabetes risks in the underweight group.

Conflict of interest

None.

References

Brower MA, Hai Y, Jones MR, Guo X, Chen YI, Rotter JI, Krauss RM, Legro RS, Azziz R, Goodarzi MO. Bidirectional Mendelian randomization to explore the causal relationships between body mass index and polycystic ovary syndrome. *Hum Reprod* 2019;**34**: 127–136.

Chen X, Koivuaho E, Piltonen TT, Gissler M, Lavebratt C. Association of maternal polycystic ovary syndrome or anovulatory infertility with obesity and diabetes in offspring: a population-based cohort study. *Hum Reprod* 2021;**36**:2345–2357.

Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. *Nat Rev Endocrinol* 2018;**14**: 270–284.

He Y, Tian J, Blizzard L, Oddy WH, Dwyer T, Bazzano LA, Hickey M, Harville EW, Venn AJ. Associations of childhood adiposity with menstrual irregularity and polycystic ovary syndrome in adulthood: the Childhood Determinants of Adult Health Study and the Bogalusa Heart Study. *Hum Reprod* 2020;**35**:1185–1198.

Koivuaho E, Laru J, Ojaniemi M, Puukka K, Kettunen J, Tapanainen JS, Franks S, Järvelin MR, Morin-Papunen L, Sebert S *et al.* Age at adiposity rebound in childhood is associated with PCOS diagnosis and obesity in adulthood-longitudinal analysis of BMI data from birth to age 46 in cases of PCOS. *Int J Obes (Lond)* 2019;**43**: 1370–1379.

Office WER. BMI in Europe. <http://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi>. 2019.

Parr CL, Batty GD, Lam TH, Barzi F, Fang X, Ho SC, Jee SH, Ansary-Moghaddam A, Jamrozik K, Ueshima H *et al.* Body-mass index and cancer mortality in the Asia-Pacific Cohort Studies Collaboration: pooled analyses of 424,519 participants. *Lancet Oncol* 2010;**11**:741–752.

Wei J. Comment on the grouping of patients with polycystic ovary syndrome based on body mass index. *Hum Reprod* 2022;**1**:193.

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