Re: Polycystic ovary syndrome and risk of stillbirth: a nationwide register-based study a nationwide register-based study a nationwide register-based study. BJOG. 2021 Aug 29

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April 05, 2024

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LETTER TO THE EDITOR

in response to

Valgeirsdottir et.al., Polycystic ovary syndrome and risk of stillbirth: a nationwide register-based study a nationwide register-based study a nationwide register-based study. BJOG. 2021 Aug 29. doi: 10.1111/1471-0528.16890.

From

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Disclosure of Interests

I have no conflicts of interest to declare.

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20th September 2021.

Dear Editor,

Re: Polycystic ovary syndrome and risk of stillbirth: a nationwide register-based study a nationwide register-based study a nationwide register-based study. BJOG. 2021 Aug 29

The aims of my letter are to comment on some of the methodological aspects of your recent article on the association between polycystic ovary syndrome and stillbirths[1] and make an urgent call for further research to validate the findings.

An important confounding variable that wasn't addressed, was the authors did not control for smoking which is a known risk factor for stillbirths[2]. They argued that "*Information on the effect of smoking on PCOS is scarce in the literature, and therefore smoking was not considered as a confounder* ". PCOS is however associated with depression[3] and depression is associated with smoking[4]. Women with anovulatory infertility were also classed as PCOS without objective verification and a diagnosis of PCOS was not objectively excluded in the control group.

More studies are therefore urgently required to validate the findings in the article and provide some insights into the possible mechanistic links between PCOS and stillbirths. Ideally this would be a large international prospective study with PCOS women properly diagnosed and classified into the different phenotypes. However, the logistics of organising a study like this might be a challenge. Other studies using established cohorts of women with PCOS might address this challenge. Some possible solutions include using women with PCOS recruited into the UK Biobank or identified from the UK's Clinical Practice Research Datalink (CPRD). Although the use of these cohorts may also present some similar challenges with phenotyping, present in the article published in your journal, they might, offer the opportunity for independent validation in cohorts of PCOS women of different demographics and provide the opportunity to address some of the confounders not addressed in the study published in your journal.

Best wishes

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