




# Reply to ‘Paracetamol use in pregnancy — neglecting context promotes misinterpretation’




Ann Z. Bauer, Shanna H. Swan, David Kriebel, Zeyan Liew, Hugh S. Taylor, Carl-Gustaf Bornehag, Anderson M. Andrade, Jørn Olsen, Rigmor H. Jensen , Rod T. Mitchell, Niels E. Skakkebaek  and David M. Kristensen 

We would like to thank O’Sullivan and colleagues for their Correspondence on our Consensus Statement (Bauer, A. Z. et al. Paracetamol use during pregnancy — a call for precautionary action. *Nat. Rev. Endocrinol.* **17**, 757–766 (2021))<sup>1</sup>, in which they raise some important issues on our recommendations over a precautionary approach for paracetamol (*N*-acetyl-*p*-aminophenol (APAP), otherwise known as acetaminophen) use in pregnancy (O’Sullivan, J. et al. Paracetamol use in pregnancy — neglecting context promotes misinterpretation. *Nat. Rev. Endocrinol.* <https://doi.org/10.1038/s41574-022-00656-9> (2022))<sup>2</sup>.

We believe that APAP-specific risk communication is warranted for pregnant women due to the widespread accessibility of this over-the-counter medication and the common perception of negligible risk<sup>1</sup>. We agree with O’Sullivan et al. that more well-designed studies of APAP use in pregnancy are required; for example, exposure misclassification, confounding by indication for use and the potential influences of other endocrine disrupting chemicals require further investigation. However, given the large amount of new data and the high degree of consistency between the human and experimental studies<sup>1</sup>, we believe that it is prudent to recommend a

precautionary approach, while conducting further studies and exploring alternative strategies for treatment. Our recommendations, which are consistent with those of agencies such as the European Medicines Agency<sup>3</sup> and the US Food and Drug Administration<sup>4</sup>, are for pregnant women to use APAP only when clinically indicated; to consult with a physician or pharmacist if they are uncertain whether use is indicated and before using on a long-term basis; and to minimize exposure by using the lowest effective dose for the shortest possible time<sup>1</sup>.

O’Sullivan and colleagues are concerned that informing pregnant women of the potential adverse effects of APAP could increase their anxiety. We completely understand this concern but it is our belief that pregnant women and their health professionals deserve to be informed of the potential risks in order to make the best possible decisions regarding use. We therefore reiterate that until proven safe for use in pregnancy by further studies, APAP use in pregnancy should be minimized. At the same time, we recognize that when medically indicated for high fever and/or moderate to severe pain, APAP use in pregnant women might be the course of action with the lowest risk for both the pregnant individual and their fetus.

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1. Bauer, A. Z. et al. Paracetamol use during pregnancy — a call for precautionary action. *Nat. Rev. Endocrinol.* **17**, 757–766 (2021).
2. O’Sullivan, J. et al. Paracetamol in pregnancy — neglecting context promotes misinterpretation. *Nat. Rev. Endocrinol.* <https://doi.org/10.1038/s41574-022-00656-9> (2022).
3. European Medicines Agency. PRAC recommendations on signals: adopted at the 12–15 March 2019 PRAC meeting. [https://www.ema.europa.eu/en/documents/prac-recommendation/prac-recommendations-signals-adopted-12-15-march-2019-prac-meeting\\_en.pdf](https://www.ema.europa.eu/en/documents/prac-recommendation/prac-recommendations-signals-adopted-12-15-march-2019-prac-meeting_en.pdf) (2019).
4. Food and Drug Administration. FDA Drug Safety Communications: FDA has reviewed possible risks of pain medicine use during pregnancy. <https://www.fda.gov/media/90209/download> (2015).

## Competing interests

The authors declare no competing interests.