



HAL
open science

Malformations and pregnancy with schizophrenia – Authors' reply

Guillaume Fond, Damien Etchecopar-Etchart, Julie Blanc, Laurent Boyer

► **To cite this version:**

Guillaume Fond, Damien Etchecopar-Etchart, Julie Blanc, Laurent Boyer. Malformations and pregnancy with schizophrenia – Authors' reply. *The Lancet Regional Health - Europe*, 2021, 11, pp.100257. 10.1016/j.lanepe.2021.100257 . hal-03478199

HAL Id: hal-03478199

<https://amu.hal.science/hal-03478199>

Submitted on 13 Dec 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0
International License



Contents lists available at ScienceDirect

The Lancet Regional Health - Europe

journal homepage: www.elsevier.com/lanepe

Letter

Antipsychotics during pregnancy and increased risk of congenital malformation in offspring: toward a systematic use of real-world data

Guillaume Fond^{a,b,e,f}, Damien Etchecopar-Etchart^a, Julie Blanc^{a,d}, Laurent Boyer^{a,b,c,f}^a Aix-Marseille Univ., CEReSS - Health Service Research and Quality of Life Center, Marseille, France^b Department of Medical Information, Assistance Publique – Hôpitaux Marseille, Marseille, France^c Department of Epidemiology and Health Economics, Assistance Publique – Hôpitaux Marseille, Marseille, France^d Department of Obstetrics and Gynaecology, APHM, Nord Hospital, Marseille, France^e Department of Psychiatry, Assistance Publique – Hôpitaux Marseille, Marseille, France^f FondaMental Fondation, Creteil, France

ARTICLE INFO

Article History:

Received 28 September 2021

Accepted 11 October 2021

Available online xxx

In our study published in Lancet Regional Health Europe [1], we found no statistical difference between women with or without schizophrenia for the rate of congenital malformations (2.7% vs. 2.2%, $p=0.18$).

We agree that this result should be taken with caveat as rightly commented by Alain Braillon and Susan Bewley.

First, we agree that we cannot exclude congenital malformations being less coded in the French hospital database in case of medical abortions or stillborn children. This negative result may also be explained by our malformation codes being available only for the delivery stay. Many congenital malformations may be discovered later during early childhood. Other studies carried out in other countries have demonstrated that children of mother with schizophrenia had increased rates of mortality during the first year of life [2,3]. In the French hospital database, it is hardly possible to link children's outcomes during early childhood and those of their mothers.

Second, we mentioned in the limitations that the French Hospital Database has no treatment data. A recent review has concluded that there was no strong evidence for increased risk of congenital malformation after prenatal second-generation antipsychotic exposure [4] but a recent Finnish population-based study has concluded that olanzapine was associated with increased risk of musculoskeletal malformations [5]. As detailed in our discussion, it is probable that a high proportion of women with schizophrenia in our study were not treated by antipsychotics, as we found that an important proportion of them had insufficient contacts or no contacts with the psychiatric system during pregnancy.

DOI of original article: <http://dx.doi.org/10.1016/j.lanep.2021.100251>, <http://dx.doi.org/10.1016/j.lanep.2021.100209>.

E-mail address: guillaume.fond@ap-hm.fr (G. Fond).

<https://doi.org/10.1016/j.lanep.2021.100257>

2666-7762/© 2021 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Further analyses on population-based data are warranted to identify the risk factors of congenital malformations in the children of women with schizophrenia. All data published so far converge to conclude that the health of these children is threatened by many modifiable factors that should be actively prevented. Our future works are planned to focus on the French Healthcare database (SNDS) that combine hospital and out-of-hospital data, including drugs.

Author Contributions

Concept and design: Laurent Boyer, Guillaume Fond.

Drafting of the manuscript: Laurent Boyer, Guillaume Fond.

Critical revision of the manuscript for important intellectual content: All the authors.

Supervision: Laurent Boyer.

Declaration of Interests

We declare no competing interests.

References

- [1] Fabre C, Pauly V, Baumstarck K, et al. Pregnancy, delivery and neonatal complications in women with schizophrenia: a national population-based cohort study. *Lancet Reg Health – Eur* 2021 0. doi: [10.1016/j.lanep.2021.100209](https://doi.org/10.1016/j.lanep.2021.100209).
- [2] Nilsson E, Hultman CM, Cnattingius S, Olausson PO, Björk C, Lichtenstein P. Schizophrenia and offspring's risk for adverse pregnancy outcomes and infant death. *Br J Psychiatry J Ment Sci* 2008;193:311–5.
- [3] Liu CH, Keshavan MS, Tronick E, Seidman LJ. Perinatal risks and childhood premorbid indicators of later psychosis: next steps for early psychosocial interventions. *Schizophr Bull* 2015;41:801–16.
- [4] Wang Z, Brauer R, Man KKC, Alfageh B, Mongkhon P, Wong ICK. Prenatal exposure to antipsychotic agents and the risk of congenital malformations in children: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2021 published online March 27. doi: [10.1111/bcp.14839](https://doi.org/10.1111/bcp.14839).
- [5] Ellfolk M, Leinonen MK, Gissler M, Kiuru-Kuhlefelt S, Saastamoinen L, Malm H. Second-generation antipsychotic use during pregnancy and risk of congenital malformations. *Eur J Clin Pharmacol* 2021 published online June 8. doi: [10.1007/s00228-021-03169-y](https://doi.org/10.1007/s00228-021-03169-y).