PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Paediatrics Open. The paper was subsequently accepted for publication at BMJ Paediatrics Open.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Variation in the management of SSRI-exposed babies across England
AUTHORS	Peacock, Phil; Thomas, Eliza; Bates, Sarah

VERSION 1 - REVIEW

REVIEWER	Sie, SD VU University Medical Center, Amsterdam, The Netherlands Competing interests: Neonatology, Pharmacology, Psychiatry during pregnancy
REVIEW RETURNED	06-May-2017

GENERAL COMMENTS	The subject itself is very interesting. Th results are very concised for such a big survey. I would suggest to the authors to describe more in detail the answers to the survey and make use of graphs to show the results of the survey. They can anwer every survey question seperately in the results and give more statistics. Also, for the discussion, they could use several papers of N. Kieviet about this subject (for example her study about interventions used in exposed neonates).

REVIEWER	Smith-Collins, Adam Regional Neonatal Intensive Care Unit, St Michael's Hospital, Southwell Street, Bristol, UK Competing interests: None
REVIEW RETURNED	10-May-2017

GENERAL COMMENTS	The authors address and important issue with this article, and give a useful overview of the lack of consensus on how to manage infants exposed to SSRIs in utero. I do think, however, that the article could be improved in a few areas. In general terms, some reference to physiology/pharmacology would be beneficial. whilst this is a clinically focused paper, it is appropriate to note, for example, evidence of EEG changes in infants exposed in utero to SSRIs (Viden et al, 2016). In the discussion about the variance in choice of pharmacological treatments, some reference to drug effects, and that the target in treatment of SSRI withdrawal is

	on symptom control (as opposed to replacement and weaning e.g. with opiates) would be worthwhile. In some areas, expanded discussion would frame the article better. For example, the authors quote the Levison-Castiel et al (2006) paper showing ~30% of infants had symptoms (13% severe). However, there is no discussion that these infants all had prolonged exposure and to a heterogenous group of agents, including paroxetine which is now much less widely used in pregnancy following concerns from the US FDA of associations with increased rates of congenital heart disease. It is worth citing other studies, some of which have shown much lower levels of symptomatology (e.g. Forsberg et al, 2014 - severe withdrawal in ~3% of infants) The authors note that NICE do not provide specific recommendations regarding the regime for assessing withdrawal following SSRI exposure. This is accurate, but it is also worth noting that national guidance does exist elsewhere, notably the 2011 recommendation from the Fetal/Neonatal branch of the Canadian Paediatric Society for 48h of observation (A. Jeffries). The authors mention the Rivers and Finnegan scoring systems. While the Finnegan scoring system was not initially designed for assessing SSRI withdrawal, it has been widely used, and there is also an adapted abbreviated Finnegan score for antidepressant withdrawal available. Overall, I feel this is an important issue and I would like to see this article published, but feel it would be improved by consideration of the points raised above.

REVIEWER	Moses-Kolko, L University of Pittsburgh USA Competing interests: None
REVIEW RETURNED	22-May-2017

GENERAL COMMENTS	1. For an original article, this seems short and lacking some depth. It might be better received as a letter to the editor or brief report, if there is such a mechanism. 2. There has been rigorous examination neurodevelopmental correlates of in-utero SSRI exposure through 1 month of life (Salisbury et al AJP 2015). The authors describe a complex pattern of neurobehavioral outcomes in relationship to drug of exposure and maternal depression severity. This challenges the notion that altered neonatal adaptation is due to SSRI withdrawal or toxicity that must be addressed with medication treatment of the neonate. It would be important for the authors to note this research. 3. I am not aware of research on this topic recommending prolonged inpatient observation or treatment of neonates with in utero SSRI exposure, except in cases of medical instability. While it does not seem probable that prolonged hospitalization will be accommodated in medically stable, SSRI-exposed neonates, the authors could advocate for neurodevelopmental assessments on an outpatient basis in this group of infants. Indeed in the state of Pennsylvania, there is legislation pending to include maternal depression as a

	condition that entitles offspring to close neurodevelopmental monitoring over the first few years of life.

VERSION 1 – AUTHOR RESPONSE

Reviewer 2

We appreciate the reviewer's comments that this is an important issue which they would like to see published, and also their suggestions as to how to improve the paper.

- In the discussion, we have added to our previous statement around withdrawal vs toxicity. As suggested, we have highlighted the different aims of treatment (symptoms not weaning). We have also discussed research showing longer-term effects of SSRIs including EEG changes as recommended by the reviewer.

- We have expanded the discussion section, and included mention of the different estimates of prevalence from different studies, including the paper suggested by the reviewer.

- The reviewer quite rightly points out that although there is no UK guidance, guidance does exist in other countries. We have referenced the Canadian guidelines when discussing the lack of UK guidance.

- The reviewer helpfully mentioned the adapted Finnegan scoring system. Although none of the units in this study reported using this adapted score, we agree it is important to mention it, and have added this to the first paragraph of the discussion.

Reviewer 3

1. The reviewer has highlighted the length of this article – this was originally submitted as a Short Report to Archives of Disease in Childhood, and then automatically transferred to BMJ Paediatrics Open, which does not have a specific Short Report option. However, we feel that with the revisions following review that this paper holds sufficient depth as an Original Article.

2. The discussion section has been expanded, and now includes discussion of longer-term neurodevelopmental effects of SSRIs, including reference to the paper the reviewer suggests.

3. The reviewer mentions a lack of research recommending inpatient observation. We have added to the discussion reference to the Canadian guideline for 48 hours inpatient observation following SSRI exposure.

We have not specifically discussed longer neurodevelopmental follow-up as this study has sought to examine neonatal management, and we do not feel able to make any recommendations of this nature based on our findings.