PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Continuation rates of oral hormonal contraceptives in a cohort of first
	time users: a population based registry study, Sweden 2005-2010
AUTHORS	Brynhildsen, Jan; Josefsson, Dr Ann; Wiréhn, Ann-Britt; Lindberg,
	Malou; Foldemo, Annika

VERSION 1 - REVIEW

REVIEWER	Dr Gerry Molloy
	Lecturer in Psychology
	School of Psychology
	National University of Ireland, Galway
	Ireland
REVIEW RETURNED	12-Jul-2013

THE STUDY	1. A fundamental issue in this paper is the use of undefined terminology that is critical to the manuscript. In particular the authors do not define or distinguish between poor compliance and low adherence which they appear to consider as separate phenomena. In relation to this it would be useful to specify what precisely is meant by 'discontinuation' and if switching is always used interchangeably with this term. It is generally agreed that adherence refers to the extent to which a person's behaviour corresponds with agreed recommendations from a health care provider (See World Health Organization Report here:
	http://www.who.int/chp/knowledge/publications/adherence_Section1.pdf). Therefore it does not seem appropriate that 'patterns of adherence' is used in the title or in the paper to refer to this data, as this is not what is measured. It is also worth noting that the term compliance is falling out of favour. See here: http://www.nejm.org/doi/full/10.1056/nejmra050100
	2. Another important issue that emerges early in the manuscript concerns the focus on 'intentional non-adherence' due to side effects. Evidence suggests the majority of non-adherence may be unintentional e.g. forgetting to take the pill, however this is not adequately acknowledged in the paper. This indicates that the behavioural science of taking oral hormonal contraceptives is not adequately considered. See this paper for some discussion of these issues: http://www.biomedcentral.com/1471-2458/12/838
	3. It would be interesting to have some comment on the extent to which combined oral contraceptive pills are used as a treatment for acne, as not all users will be prescribed these medications for contraception purposes only. Is this practice common in Sweden? Might this explain a proportion of the switching? See here for details: http://www.ncbi.nlm.nih.gov/pubmed/22786490
GENERAL	The primary problem with this paper is that it is data rich and theory poor.
COMMENTS	This data-set is an excellent resource that can provide many important
	findings for health care professionals that prescribe oral hormonal
	contraceptives, however there needs to be greater precision with the
	terminology that is used (adherence, compliance, dicontinuation and

switching) and a greater appreciation of the behavioural science of taking
medications. This report may be useful in this respect:
http://www.netscc.ac.uk/hsdr/files/project/SDO_FR_08-1412-076_V01.pdf

REVIEWER	Joseph E. Potter
	Professor
	Population Research Center and Department of Sociology
	University of Texas at Austin
	USA
REVIEW RETURNED	17-Jul-2013

THE STUDY	A concern is the definition of women who were not dispensed OCs during the 7/2005- 12/2006 period, but who were dispensed pills during 2007-2009, as first time users. Some of these women could have been previous users who were trying to get pregnant, were pregnant, using some other method or abstaining during that period (or some combination of those states).
RESULTS & CONCLUSIONS	A possible difficulty of interpretation arises if there is an association between breastfeeding and use of POPs. If POPs are more likely to be dispensed when a woman is breastfeeding, and if postpartum use accounts for a substantial share of all POP use, then one might expect lower continuation of POPs as women switch to COCs following the termination of breastfeeding. In this case, the lower continuation of POPs might not be the result of side effects.
GENERAL COMMENTS	Might there be an association between physician prescription and switching before 6 months? If so the lower switching rates for ethinylestradiol + drospirenone might be the result of the higher proportion of those pills prescribed by physicians.

VERSION 1 – AUTHOR RESPONSE

1. A fundamental issue in this paper is the use of undefined terminology that is critical to the manuscript. In particular the authors do not define or distinguish between poor compliance and low adherence which they appear to consider as separate phenomena. In relation to this it would be useful to specify what precisely is meant by 'discontinuation' and if switching is always used interchangeably with this term. It is generally agreed that adherence refers to the extent to which a person's behaviour corresponds with agreed recommendations from a health care provider (See World Health Organization Report here:

http://www.who.int/chp/knowledge/publications/adherence_Section1.pdf). Therefore it does not seem appropriate that 'patterns of adherence' is used in the title or in the paper to refer to this data, as this is not what is measured. It is also worth noting that the term compliance is falling out of favour. See here: http://www.nejm.org/doi/full/10.1056/nejmra050100

Reply:

a/We thank the reviewer for these valuable comments and fully agree. What we actually have studied are continuation rates and the title of the manuscript as well as the text has now been changed. The terms compliance and adherence (except from where we refer to other studies) have now been replaced by "continuation rates".

b/ "Discontinuation" and "switching" are used as separate terms

2. Another important issue that emerges early in the manuscript concerns the focus on 'intentional

non-adherence' due to side effects. Evidence suggests the majority of non-adherence may be unintentional e.g. forgetting to take the pill, however this is not adequately acknowledged in the paper. This indicates that the behavioural science of taking oral hormonal contraceptives is not adequately considered. See this paper for some discussion of these issues: http://www.biomedcentral.com/1471-2458/12/838

Reply

As we now have abandoned the terms compliance and adherence and only are talking about continuation rats we believe that this comment is not relevant anymore.

3. It would be interesting to have some comment on the extent to which combined oral contraceptive pills are used as a treatment for acne, as not all users will be prescribed these medications for contraception purposes only. Is this practice common in Sweden? Might this explain a proportion of the switching? See here for details: http://www.ncbi.nlm.nih.gov/pubmed/22786490

Reply

This is now commented in the discussion, last paragraph, page 12, and a new reference has been added.

4. A concern is the definition of women who were not dispensed OCs during the 7/2005- 12/2006 period, but who were dispensed pills during 2007-2009, as first time users. Some of these women could have been previous users who were trying to get pregnant, were pregnant, using some other method or abstaining during that period (or some combination of those states).

Reply

A comment on this matter has been added in the discussion, page 13, first paragraph

5. A possible difficulty of interpretation arises if there is an association between breastfeeding and use of POPs. If POPs are more likely to be dispensed when a woman is breastfeeding, and if postpartum use accounts for a substantial share of all POP use, then one might expect lower continuation of POPs as women switch to COCs following the termination of breastfeeding. In this case, the lower continuation of POPs might not be the result of side effects.

Reply

As seen in table 1, the age group with the highest use of POPs is women 16-19 years old. This group of women have the highest risk of switching and approximately the same probability of having a second prescription compared to the women in the older age groups.

The mean age for giving birth to the first child is in Sweden almost 30 years. Consequently, the majority of the women in the youngest age group can be considered as nulliparae. Thus, we consider the risk of use during breastfeeding as a source of bias as low.