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ORIGINAL ARTICLE

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The cooccurrence of heightened media attention and adverse drug reaction reports for hormonal contraception in the United Kingdom between 2014 and 2017

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Aim: The aim of this study was to examine the cooccurrence of heightened media attention after the publication of a paper by Skovlund et al in September 2016 on the link between hormonal contraception and depression or mood on adverse drug reaction (ADR) reports in the UK.

Methods: A quantitative analysis of relevant newspaper articles published between January 2014 and December 2017 was performed, as well as a content analysis. ADR reports were collected from the Medicines and Healthcare Products Regulatory Agency website and via a Freedom of Information request. A quantitative analysis was performed on ADR reports of hormonal contraceptives for all ADRs and for depressed mood disorders and disturbances.

Results: The publication of the Skovlund et al paper did not lead to a peak in relevant newspaper articles, but there was a change in the content of the newspaper articles, which focussed more on the link between hormonal contraceptives and depression or mood. There was an overall increase in ADR reports by women relating to hormonal contraceptives between 2016 and 2017, and for combined contraceptives this was due to an increase in ADR reports of depressed mood disorders and disturbances.

Conclusions: The content of media attention appears to affect ADR reporting by women for combined contraceptives. In general, patients report the majority of depressed mood disorders and disturbances ADRs as opposed to health professionals, who report other ADRs. Care providers can anticipate the effect of heightened media attention and help patients when they experience these ADRs.

KEYWORDS

adverse drug reaction reporting systems, depressive disorder, drug-related side effects and adverse reactions, hormonal contraception, mass media, pharmacovigilance

1 | INTRODUCTION

On 28 September 2016, a study by Skovlund et al entitled "Association of hormonal contraception with depression" was published in *JAMA Psychiatry*.[1] The findings were widely covered in the UK media, and it seems reasonable to ask if this media coverage could, in turn, have impacted on the behaviour of users of hormonal contraceptives, specifically on spontaneous adverse drug reaction (ADR) reporting.

Depression and/or mood changes have been associated with the use of hormonal contraceptives for some time, with oestrogen and

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progesterone both hypothesised to influence women's mental health.[2,3] However, it is accurate to say that, while summaries of product characteristics and the respective patient information leaflets of hormonal contraceptives have listed depression and mood disturbances as possible side effects for some time, the Skovlund et al paper was significant because it showed a scientific association between the use of such products and subsequent antidepressant use and first diagnosis of depression.[1]

In the UK, the Yellow Card Scheme (YCS), operated by the medicines regulator, the Medicines and Healthcare Products Regulatory Agency (MHRA), provides a process for collecting suspected ADR reports following the use of a medicine, vaccine or herbal or complementary remedy. Reports received are evaluated to identify new potential hazards or new information on known ADRs, resulting in changes to summaries of product characteristics and patient information leaflets, including to the recommended dose or even the withdrawal of a medicine, where appropriate.[4] Founded in 1964 after the **thalidomide** tragedy, the scheme was extended beyond health professionals to include patients and their representatives in 2005. Collecting these spontaneous reports sits within the field of pharmacovigilance and surveillance monitoring, which also encompasses anecdotal reports, observational studies, clinical trials, systematic reviews or even animal data.[5] Indeed, the Skovlund et al paper[1] itself, as an observational cohort study of prescribing registers, is a type of surveillance monitoring. The question is whether people's enhanced awareness of an ADR from one type of pharmacovigilance activity (ie, observational investigation), albeit via heightened media coverage, can impact on another, namely spontaneous reporting via the Yellow Card Scheme.

This question is important for two reasons. First, patient reports have been shown to strengthen ADR signal detection, while also highlighting the patient experience and perspective,[5] and are therefore to be encouraged. Second, while patients do now form the highest group reporting directly via the Yellow Card Scheme compared to any specific health professional group, 2018 saw a general decline in the reporting of suspected ADRs from other key reported groups such as general practitioners, pharmacists and hospital doctors. Understanding influences on suspected ADR reporting could then conceivably also help tackle potential under-reporting (as well as helping maintain patient reporting). Martin et al, asking a similar question, examined the impact of intense media scrutiny regarding **paroxetine** and suicidal behaviour on the subsequent prescribing of the drug and suspected ADR reports between 2001 and 2004 in England.[6] Their analysis of national prescribing trends and Yellow Card Scheme reports for the wider drug class of selective serotonin reuptake inhibitors (SSRIs) linked the media publicity with an increase in ADR reports for paroxetine, albeit in sharp and short-term peaks.[6] There was also a fall in SSRI prescribing after regulatory agencies in both the USA and the UK exposed the problem.[6] In 2012, Hernandez et al also showed changes in SSRI usage to be associated with the timing of media coverage and regulatory warnings about them in both the Netherlands and the UK.[7] Thus, certainly behaviours around SSRIs appear to be influenced by mass communication about them. Statins, a different type of drug, have also received heightened negative media coverage. Van Hunsel et al's paper examined the after-effects of the broadcast of a Dutch television programme, *Radar*, covering serious ADRs experienced by people taking statins, finding a peak in patient-reported (but not health-professional-reported) ADRs in the succeeding 3 months.[8]

What is already known about this subject

- People's usage of selective serotonin reuptake inhibitors and statins, and ADR reporting behaviours have previously altered following media sensationalising.
- Use of hormonal contraception has been linked to depression and mood changes.
- The cooccurrence of heightened media attention and the reporting of hormonal contraception ADRs, after a major study, remained unknown.

What this study adds

- The content, rather than the quantity, of newspaper articles has an effect on patient ADR reporting.
- Heightened media attention, predominantly, had an effect on ADR reports of combined hormonal contraceptives.
- Women report the majority of ADRs for hormonal contraception within the category “depressed mood disorders and disturbances”.

The media have has a great effect on what the mass audience thinks about important issues, such as health. There are several models to describe the effects of the media on public perception. Agenda setting is an example in which the media influence determines the importance of news for the public. When the media put more emphasis on a certain subject (eg, hormonal contraception and depression), it becomes more important to the public.[9] Where agenda setting shows an effect on what people are talking about, the model of framing suggests that the media can influence the feelings of people on an issue.[10] The frames used in a news story will predict the way in which the public reacts, eg, resulting in heightened reporting of ADRs after media attention.[11]

The general public is mainly informed on health news by the media, with newspaper articles being the key source for health information.[12] In recent years, social media platforms such as Facebook and Twitter have become popular too, especially among adults aged 18-29.[13] Health information is also available on these online platforms. However, a study by Mollema et al shows that traditional media predominantly determine what is said online, and that online and offline articles show a similar distribution of articles.[14]

In 2015, 81.3% of women in the UK used a form of contraception compared to 69.2% in Europe, with the majority using oral hormonal

contraceptive pills.[15] While there was intense media coverage of hormonal contraception and its effects on depression and mood changes after the publication of the Skovlund et al paper,[1] the cooccurrence of this media attention and changes in prescription numbers and ADR reports remains unexamined. The aim of this study was to examine the cooccurrence of media reporting, of the link between hormonal contraception and depression or mood changes, and Yellow Card Scheme reports submitted in the UK between 2014 and 2017 to encompass at least a year before and after the publication of the Skovlund et al[1] paper in September 2016.

2 | METHODS

2.1 | Data collection

2.1.1 | Newspaper articles

The Times, *The Guardian*, *The Telegraph*, *The Independent*, *The Sun*, the *Daily Mirror*, the *Daily Express*, the *Daily Star* and the *Daily Mail*, including their Sunday and online editions, were searched because of their status as the most circulated newspapers in the UK.[16,17] The databases ProQuest, using the search terms (depress*) AND ("the pill" OR contracepti* OR "birth control"), and LexisNexis, using the search terms (depress! OR mood!) AND ("the pill" OR contracepti* OR "birth control"), were used to extract all newspaper articles published between January 2014 and December 2017. A time period before the publication of the Skovlund et al paper in September 2016 was chosen to show the usual media coverage of the link between hormonal contraception and depression. A shorter study period was chosen after September 2016 to explore changes in coverage because previous studies have shown a short maintenance stage after the publication of key papers in which media coverage peaks and stays constant.[9,11,18]

The selected articles were read by LP and judged on relevance. Articles were considered relevant if a concrete link between hormonal contraception and depression or mood alterations was mentioned (eg, "The drugs [birth control] … are known to have side-effects in some adults, including nausea, depression, acne and headaches." [*Daily Express*, 2014]). Articles were excluded when considered irrelevant (eg, if the search terms were mentioned in the article, but discussed separately) or when depress*, mood! or "the pill" were used in a different context unrelated to the research question. The relevance of the selected newspaper articles was double-checked by PD. The inclusions and exclusion decisions were discussed between the two researchers to reach a consensus.

2.1.2 | Prescription items

Monthly data on the number of combined hormonal contraceptives/systems encompassing nine different formulations (British National Formulary [BNF] legacy, 7.3.1 drug class) and progestogen-only contraceptives encompassing nine other formulations (BNF 7.3.2 drug class), prescribed between January 2014 and December 2017, were extracted from OpenPrescribing.net[19] and maintained within an Excel spreadsheet.

2.1.3 | ADR reports

Suspected ADR reports made for hormonal contraceptives for the period 2014 to 2017 were extracted manually from the MHRA interactive Drug Analysis Profiles (iDAPs) on the Yellow Card website.[4] The total yearly number of suspected reactions and the number classed within the subset high level group term (HLGT) *Depressed mood disorders and disturbances* (encompassing *Depressive disorders* and *Mood alterations with depressive symptoms*) for each of 14 drug substances were extracted and recorded in Excel. Additional information (labelled type 1B data by the MHRA) on patient sex, age group, ADR reporter (woman or healthcare professional [HCP]), report submission route (direct to agency or indirect via industry), route of drug administration and ADR seriousness for the yearly reports was available and additionally retrieved.

Individual data points for **estradiol**, **ethinylestradiol** and **mestranol** were added together to create total reports for the combined contraceptives category. In the UK, combined oral contraceptives also contain a progestogen, therefore if a suspected ADR report is submitted for, say, the drug Logynon (which contains both ethinylestradiol and **levonorgestrel**), this is recorded twice on iDAPs under each constituent substance. Therefore, to eliminate double-counting, the total number of suspected reactions for progestogen-only contraceptives was derived by first adding together the number of reports for each of the 11 relevant substances (**medroxyprogesterone acetate**, **norgestimate**, **norethisterone**, **norelgestromin**, **nomegestrol**, levonorgestrel, **gestodene**, **etonogestrel**, **drospirenone**, **dienogest**, **desogestrel**) then subtracting the respective number for the combined contraceptives.

The relevant monthly data were obtained via a Freedom of Information request to the MHRA. Suspected ADR reports were chronicled according to the drug substance. Type 1B data for monthly ADR reports are not provided by the MHRA.

2.1.4 | Inclusion and exclusion criteria

Inclusion criteria for yearly suspected ADR reports were (a) women, (b) age groups 10-19 to 50-59, (c) reporter patient or HCP, (d) direct to agency (ie, reported directly to the MHRA), (e) all routes of administration, (f) all types of seriousness, (g) all suspected ADR reports and *Depressed mood disorders and disturbances* and (h) year received 2014 to 2017.

The oestrogens estradiol and ethinylestradiol can be given as monotherapy for indications other than contraception and therefore only suspected ADR reports for multiple active constituents of these oestrogens were included.[20,21] Suspected ADR reports of oral

single constituents of levonorgestrel were excluded because these are used as emergency contraception.[22] The routes of administration that were included for medroxyprogesterone were subcutaneous, intramuscular and parenteral because these routes are used for the purpose of contraception.[23] The active substances norethisterone and drosperinone also have other indications than contraception, but these could not be excluded.[24–26]

Although **cyproterone acetate** (Dianette) functions as a contraceptive pill, it is not licensed as a contraceptive in the UK and is only mentioned in BNF chapter 13.6.2. "Oral Preparations of Acne" of the BNF legacy,[22,23] so it was excluded from this study.

2.2 | Data analysis

2.2.1 | Newspaper articles

Quantification of relevant newspaper articles

The numbers of relevant articles appearing in the 4-month period September-December (in 2016, being the months directly ensuing the publication of the Skovlund et al paper[1]) for each of the 4 years 2014-2017 were compared using a one-way ANOVA test. The total numbers of relevant articles per year were also compared.

Content analysis of relevant newspaper articles

The frequency with which relevant newspaper articles appear on their own is not fully informative about the actual messages carried. For that reason, a quantitative content analysis was used to examine differences in headlines and content of relevant newspaper articles before and after September 2016. A coding frame was constructed by one author (LP) after scrutinising a subset of 14 randomly selected relevant newspaper articles to create thematic categories, shown in Table 1. Then PD coded the same 14 randomly selected newspaper articles using the categories, after which the inter-rater reliability was determined using Cohen's kappa. Then, the whole set of relevant newspaper articles was read and coded by LP in consultation with PD. Finally, χ^2 tests were used to examine specific differences between the newspaper articles published before and after September 2016 in the identified categories as detailed in the results.

Prescription items and ADR reports: Statistical analysis

Monthly prescription data for combined contraceptives and progestogen-only contraceptives between January 2014 and December 2017 were analysed to assess correlation using a Spearman's Rho. Because the number of prescriptions for combined contraceptives decreased between 2014 and 2017 (r_s = –0.740, P < 0.01), and prescriptions for progestogen-only contraceptives increased over the same period (r_s = 0.641, P < 0.01) (Figure 1), ADR reports were corrected for the respective number of prescription items by expressing the number of reports/100 000 000 items.

The monthly number of ADR reports/100 000 000 items for HLGT *Depressed mood disorders and disturbances* for combined contraceptives and progestogen-only contraceptives were compared to examine for differences before and after publication of the Skovlund et al paper in 2016, as follows.[1] ADR reports/100 000 000 items from September 2016-December 2016 and January 2017-April 2017 (accounting for a lag time) were compared to these same months in 2014, 2015, 2016 and 2017, respectively. A one-way ANOVA with Bonferroni post hoc test was used to determine any differences. Spearman's Rho was used to assess the correlation of monthly ADR reports/100 000 000 items between September 2016 and April 2017.

To test if media attention affected the number of woman-submitted ADR reports, χ^2 tests were used to examine differences in ADR reports/100 000 000 items for woman- versus HCP-submitted reports in 2016 versus 2017.

SPSS 24.0 was used for the statistical analyses (IBM Corp. in Armonk, NY, USA), and statistical significance was set at P < 0.05.

2.2.2 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in http://www.guidetopharmacology.org, the common portal for data from the IUPHAR/BPS Guide to PHARMACOLOGY.

3 | RESULTS

3.1 | Newspaper articles

3.1.1 | Identification of newspaper articles

A total of 987 newspaper articles, published between 1 January 2014 and 31 December 2017, was initially identified using the aforementioned search terms (Figure 2). From these, 891 articles were excluded and 96 articles were deemed relevant. Articles were mainly excluded because the search terms were mentioned within, but not linked together. The relevant articles were divided into two groups: appearing before publication of the Skovlund et al paper[1] in September 2016 (n = 41) or appearing after its publication (n = 55).

3.1.2 | Quantification of relevant newspaper articles

During September-December 2016, the 4 months after publication of the Skovlund et al paper, a total of 31 relevant newspaper articles were written (Figure 3).[1]

There was a statistically significant difference between this figure and the total number of relevant articles published in these same months in the other years, namely 2014, 2015 and 2017 (F(3, 15) = 5.893, 0.010). However, Levene's test indicated violation of the assumption of homogeneity (P < 0.05) and therefore the Games-Howell test was used as post hoc test to locate the difference. These comparisons showed no statistically significant difference between

TABLE 1 Content analysis of relevant newspaper articles

	Total (n = 96)		Before September 2016 (n = 41)		After September 2016 (n = 55)		
	n	%	n	%	n	%	χ^2 (before *vs* after)
Search terms mentioned in the headline of the newspaper article							
None	22	22.9	11	26.8	11	20.0	0.243
Contraception	53	55.2	28	68.3	25	45.5	0.001**
Depression/mood	1	1.0	1	2.4	0	0.0	0.497[a]
Both	20	20.8	1	2.4	19	34.5	0.000**
Theme of the newspaper article							
Acne treatment	7	7.3	5	12.2	2	3.6	0.027*
Male contraception	12	12.5	1	2.4	11	20.0	0.000**
Female contraception	29	30.2	18	43.9	11	20.0	0.000**
Blood clots	4	4.2	3	7.3	1	1.8	0.093[a]
Contraceptive app/natural contraception	12	12.5	6	14.6	6	10.9	0.318
Contraception and depression/mood	23	24.0	2	4.9	21	38.2	0.000**
Other	12	12.5	6	14.6	6	10.9	0.318
Contraception method mentioned in the link							
Hormonal contraception	26	27.1	10	24.4	16	29.1	0.377
Oral contraception	59	61.5	23	56.1	36	65.5	0.129
Contraceptive implant	7	7.3	5	12.2	2	3.6	0.041*
Dianette	5	5.2	4	9.8	1	1.8	0.020*
Kind of ADR mentioned in the link							
Depression	69	71.9	25	61.0	44	80.0	0.005**
Mood changes/swings	36	37.5	21	51.2	15	27.3	0.002**
Mood/moody	14	14.6	6	14.6	8	14.5	0.907
Kind of association of the link							
Statement	41	42.7	26	63.4	15	27.3	0.000**
Statement with scientific reference	39	40.6	6	14.6	33	60.0	0.000**
Personal story	31	32.3	16	39.0	15	27.3	0.105
Number of newspaper articles that (indirectly) referred to the Skovlund et al paper							
					30	54.5	

[a]Fisher's exact test.
*Statistically significant at the 0.05 level,
**Statistically significant at the 0.01 level.

the mean of relevant articles published in September-December 2016 and the same 4 months of 2014, 2015 and 2017.

The total number of relevant newspaper articles published per year in each of 2014-2017 was also not significantly different ($F(3, 47) = 0.885, 0.456$).

3.1.3 | Analysis of newspaper content

The headlines of the relevant newspaper articles were more likely to mention both contraception and depression or mood after September 2016 (n = 19, 34.5%) compared to before September 2016 (n = 1, 2.4%) (χ^2 (1) = 36.1113, P < 0.01) (see Table 1). Before September 2016, the retrieved newspaper articles mostly mentioned contraception only in the headlines.

The articles themselves were also more likely to focus specifically on associating contraception and depression or mood after September 2016 (n = 21, 38.2%) compared to before September 2016 (n = 2, 4.9%) (χ^2 (1) = 30.061, P < 0.01). *Note*. While articles were only included in the study if they mentioned both, this was no guarantee of a focus on linking the two. Articles, whether written before or after the Skovlund et al paper,[1] mostly mentioned hormonal contraception or oral contraception (versus, eg, implants) when associating the drug with the ADR, which was more likely to be referred to using the word "depression" after September 2016 (n = 44, 80.0%) compared to before September 2016 (n = 25, 61.0%) (χ^2 (1) = 7.796, P < 0.01).

In addition, the way in which the association between contraception and depression or mood was made changed so that it was less likely for this to be a standalone statement after September 2016 (n = 15, 27.3%) compared to before September 2016 (n = 26, 63.4%)

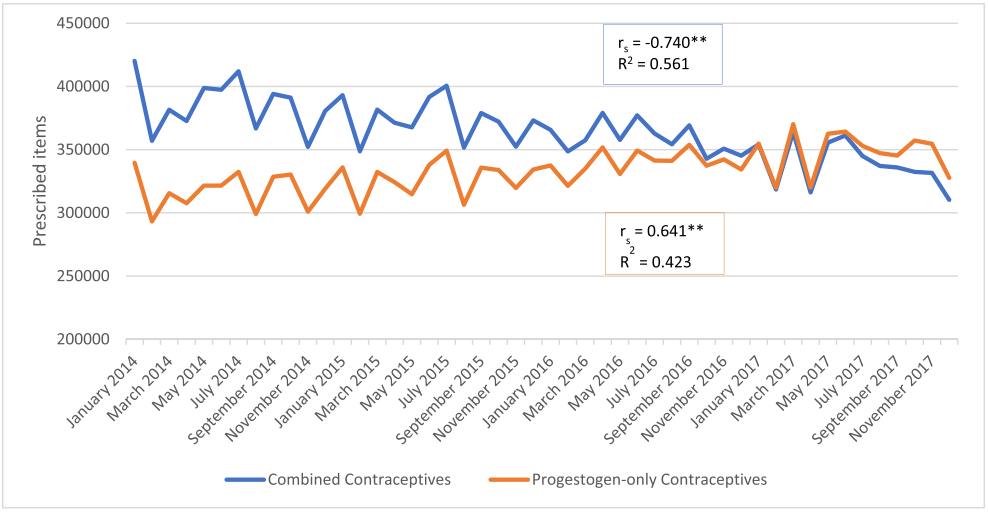


FIGURE 1 Prescribed items of combined contraceptives and progestogen-only contraceptives by month. *Statistically significant at the 0.05 level, **statistically significant at the 0.01 level

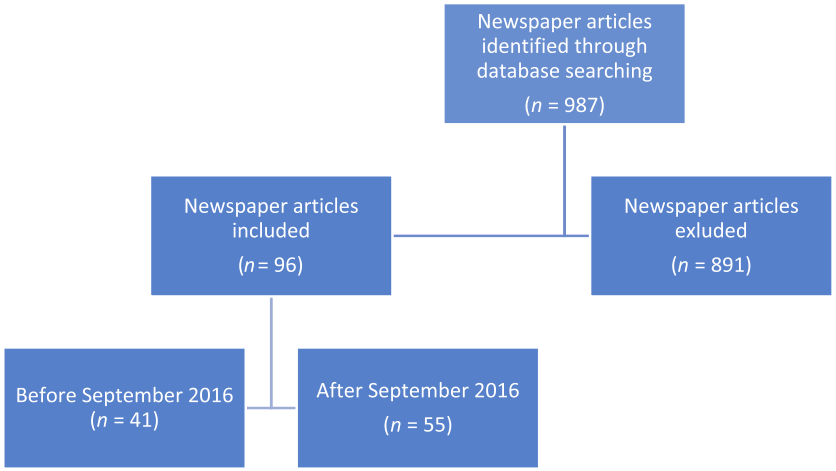


FIGURE 2 Flowchart of included and excluded newspaper articles found with the search terms in the databases ProQuest and LexisNexis

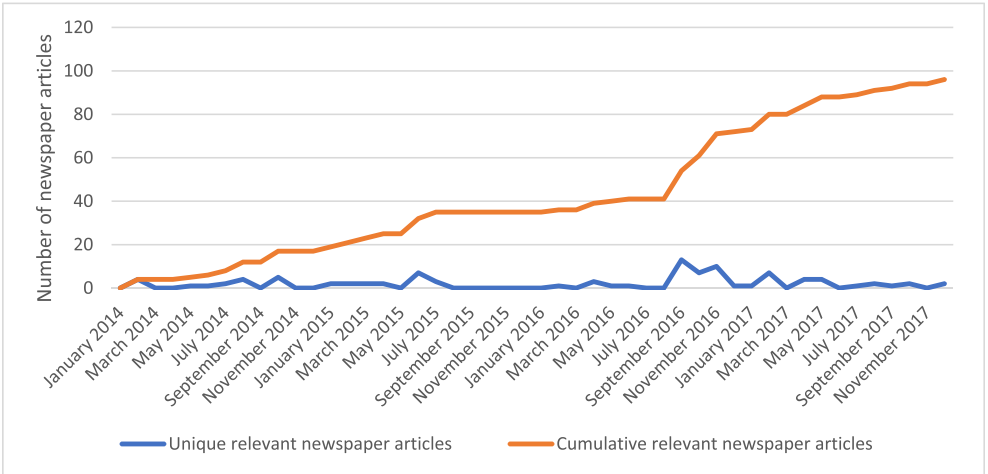


FIGURE 3 Number of relevant newspaper articles by month

(χ^2 (1) = 22.088, P < 0.01), whereas using a statement backed by scientific reference increased after September 2016 (n = 33, 60.0%) compared to before September 2016 (n = 6, 14.6%) (χ^2 (1) = 41.056, P < 0.01).

The inter-rater reliability for articles (n = 14, 14.5%) coded by LP and PD is shown in Table 2.

3.2 | ADR reports of hormonal contraceptives

The age distribution of ADR reports within the HLGT *Depressed mood disorders and disturbances* and all ADR reports for hormonal contraception between 2014 and 2017 is shown in Figure 4.

TABLE 2 Inter-rater reliability of content analysis

Category	Cohen's kappa	Level of agreement
Theme of the article	0.898	Strong
Contraception method	0.886	Strong
Side effect	0.770	Moderate
Association	0.891	Strong
Skovlund et al	1.000	Perfect

Value of κ (level of agreement) = 0.0-0.20 (none), 0.21-0.39 (minimal), 0.40-0.59 (weak), 0.60-0.79 (moderate), 0.80-0.90 (strong), >0.90 (almost perfect).[27]

3.2.1 | Monthly ADR reports for depressed mood disorders and disturbances before and after September 2016

There was a statistically significant increase in the number of ADR reports/100 000 000 items sent to the MHRA linking combined contraceptives with *Depressed mood disorders and disturbances* in January-April 2017 compared to the same 4 months in the previous 3 years (F (3, 15) = 4.545, 0.024), shown in Figure 5. Levene's test indicated no violation of the assumption of homogeneity ($P > 0.05$) and therefore the Bonferroni post hoc test was used to locate the difference, which was between the number of reports submitted in the first 4 months of 2017 versus the first 4 months of 2014 ($P < 0.05$). No such difference was found at all for reports relating to progestogen-only contraceptives (F(3, 15) = 0.882, 0.478). In addition, no differences were found between the respective reports submitted in September-December 2016 compared to the same 4 months in 2014, 2015 and 2017, either for combined contraceptives (F(3, 15) = 0.591, 0.633) or for progestogen-only contraceptives (F(3, 15) = 1.307, 0.317). Finally, reports submitted for combined contraceptives ($r_s = 0.690$, $P = 0.058$) and progestogen-only contraceptives ($r_s = -0.238$, $P = 0.570$) remained stable between September 2016 and April 2017.

3.2.2 | Women versus HCP ADR reports for hormonal contraceptives

There was an increase in *all* ADR reports for combined contraceptives between 2016 and 2017 whether submitted by women (2621/100 000 000 items *vs* 3397/100 000 000 items) or health professionals (1577/100 000 000 items *vs* 1846/100 000 000 items), with a similar pattern for all ADR reports for progestogen-only contraceptives submitted by women (3999/100 000 000 items *vs* 4286/100 000 000 items) but not health professionals. Women were generally more likely to have reported an ADR per se for a combined contraceptive than health professionals (65:35), whereas this figure was around 50:50 for progestogen-only contraceptives (see Figure 6).

Nearly all of the reports linking combined contraceptives with *Depressed mood disorders and disturbances* were made by women, with the figure being 9:1 for progestogen-only contraceptives. The wider trend across the four study years is shown in Figure 5. In addition, there was a statistically significant increase in the number of women reports linking combined contraceptives (but not progestogen-only contraceptives) with *Depressed mood disorders and disturbances* between 2016 (394/100 000 000 items) and 2017 (960/100 000 000 items) (χ^2 (1) = 10.185, $P < 0.01$).

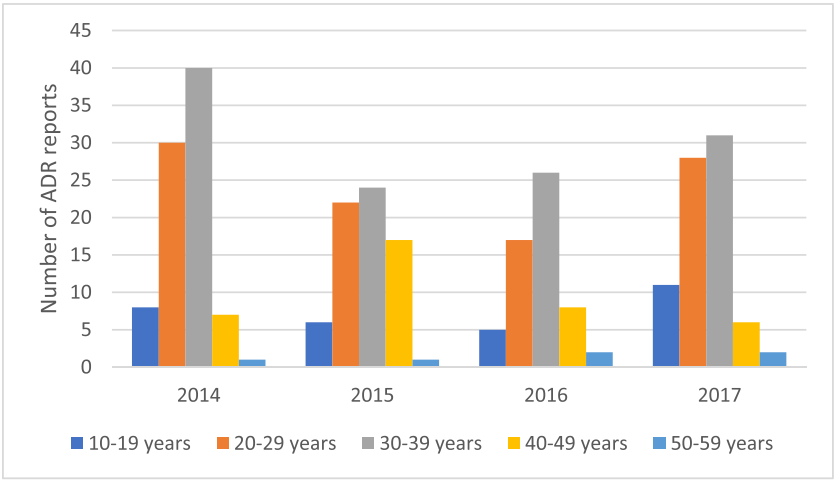
4 | DISCUSSION

While the number of newspaper articles mentioning contraception and depression or mood changes in the 4 months following the publication of the Skovlund et al paper[1] did not significantly increase, the number of headlines that mentioned both themes after September 2016 did increase, and more articles published after this time also focused on the causative relationship between the two as the major theme in the body of the article, backed by reference to science. The overall reporting of all ADRs by both women and HCPs also increased between 2016 and 2017 for both drug categories. However, for the category of combined contraceptives this increase was due to reports by women of *Depressed mood disorders and disturbance*s in 2017, while this was not the case for the progestogen-only contraceptives. This increase in reports by women for the combined contraceptives occurred predominantly in the first 4 months of 2017, suggestive of a lag period between the publication of the Skovlund et al paper and the reporting of depression or mood-related ADRs by women.[1] A final observation was that the vast majority of ADR reports relating to *Depressed mood disorders and disturbances* in general for both types of hormonal contraception were made by women rather than HCPs.

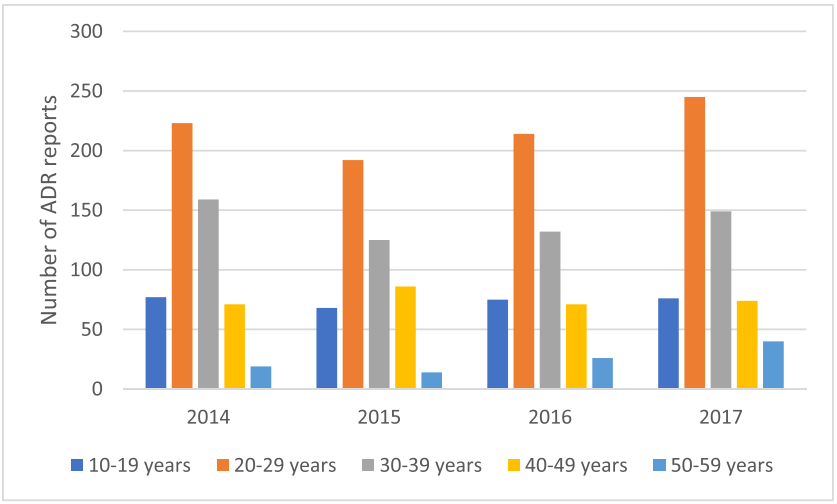
This study suggests media reporting of the link between hormonal contraception and depression or mood changes increases ADR reports by women relating to combined contraceptives. The frames of the newspaper stories changed from being mainly focussed on female contraception to mainly focussing on the link between hormonal contraceptives and depression or mood, while giving scientific references to studies mentioning this link.[1] This suggests that if there is an effect on patient reporting of ADRs, it is the frame in which the stories are presented rather than the quantity of media attention which acts as the causative agent.

Monthly data on *Depressed mood disorders and disturbances* showed an increase in ADR reports of this subset for combined contraceptives in January-April 2017 compared to the same months in 2014. This, in combination with the fact that ADR reports did not increase in September-December 2016, suggests a lag time between the publication of the Skovlund et al paper,[1] the heightened media attention and actual ADR reporting by women. This lag time is not in line with the findings of Martin et al and Van Hunsel et al.[6,8] Their results show a short peak in ADR reports of respectively paroxetine and statins directly after the media coverage about these drugs. An explanation of the lag time in this study could be that the media coverage in newspapers here did not show a peak after publication of the Skovlund et al paper[1] and was spread over a couple of months, which could have led to the lag time in ADR reports.

Overall, an increase in ADR reports by women was seen for all hormonal contraceptives when comparing 2016 to 2017, suggesting



(A)



(B)

FIGURE 4 (A) Age distribution of HLGT depressed mood disorders and disturbances reports for hormonal contraceptives between 2014 and 2017. (B) Age distribution of all ADR reports for hormonal contraceptives between 2014 and 2017

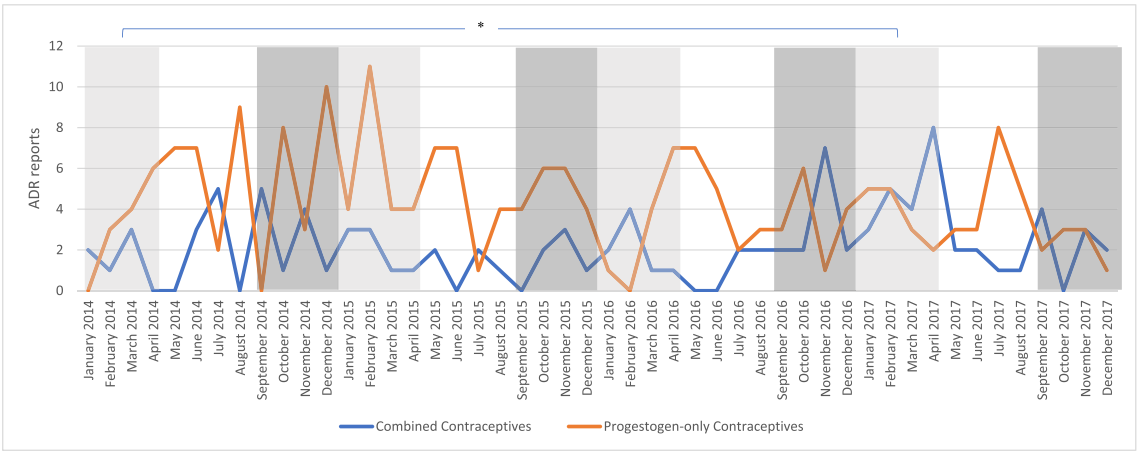


FIGURE 5 Monthly ADR reports of the HLGT depressed mood disorders and disturbances

women were generally more aware of the possibility to report ADRs themselves. This is in line with the findings of a study by Banovac et al, who found that women were more likely to report ADRs for hormonal indications than HCPs and reports by women were expected to increase more over time.[28] The increase in ADR reports for combined contraceptives was because of a significant increase in the reporting of *Depressed mood disorders and disturbances* by women. This finding could suggest that women using combined contraceptives were more

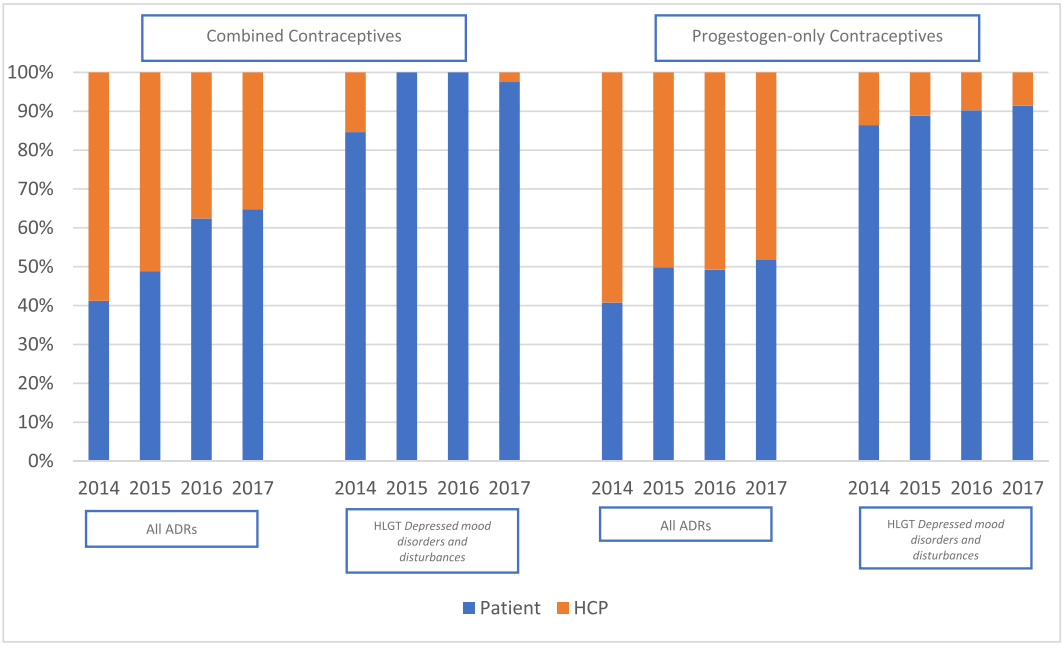


FIGURE 6 Proportions of ADR reports by women *vs* HCP for combined contraceptives and progestogen-only contraceptives in 2014-2017

likely to show agency and take it upon themselves to report these ADRs.

A notable difference was seen in the proportions of ADR reports by women versus HCPs for combined contraceptives and progestogen-only contraceptives when comparing all ADR reports and the reports for *Depressed mood disorders and disturbances*. The vast majority of reports for the subset was made by women. De Langen et al showed that depression is in the top 10 most frequently reported ADRs by patients, but is absent in the list of ADRs reported by HCPs.[29] Another finding of De Langen et al is that HCPs do not take a suspected ADR seriously in 50% of the cases and did not want to report the ADR. A possible explanation for the difference in proportions for all ADRs and ADRs of *Depressed mood disorders and disturbances* could be therefore that HCPs do not take the suspected ADR seriously because of the psychiatric nature of depression and, therefore, women had to report the ADRs themselves.

This study has several strengths and limitations. The main strengths of this study are the long time period in which newspaper articles, prescription items and ADR reports are compared, and that a comparison is not only made between the number of articles before and after publication of the Skovlund et al paper,[1] but also between the content of the newspaper articles, with data on combined contraceptives and progestogen-only contraceptives analysed separately. The data showing the monthly numbers of ADR reports for depressed mood disorders and disturbances are somewhat overestimated in this study because it was not possible to exclude some reports relating to other hormone treatments such as emergency oral contraception, and no distinction could be made between women and HCPs for these reports. This limitation arose due to lack of 1B data for this category of ADR reports received directly from the MHRA. Therefore, the short-term effects of heightened media attention, as suggested by Hernandez et al, Van Hunsel et al and Martin et al, could not be examined for women and HCPs separately.[6,8] Nonetheless, it was possible to compare women *vs* HCP reports in the year that followed the publication of Skovlund et al paper to the year before.[1]

5 | CONCLUSION

Heightened media attention after publication of the Skovlund et al paper[1] in September 2016 appears to have increased the number of ADR reports linking combined contraceptives with *Depressed mood disorders and disturbances* submitted to the MHRA in the following quarter (January-April 2017). The framing of the news story, and not necessarily the quantity of media attention, is likely to have led to the effect on women reporting ADRs for combined contraceptives. No effect was shown for the reporting of ADRs for progestogen-only contraceptives. A difference was shown in the proportions of reports by women and HCPs for *Depressed mood disorders and disturbances* compared to all ADRs. These findings confirm that HCPs and regulatory agencies can expect an increase in patient awareness of ADRs after media attention prompting them to respond to this by guiding patients at the time. Further research is necessary to examine the attitude of HCPs towards depression or mood changes as ADRs of hormonal contraceptives.

COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

L.P. and P.D. contributed to the design of the study, reviewing and revising the data collection and analyses, the manuscript and approving the final version to be published. L.P. was responsible for collecting and analysing the data and drafted the manuscript.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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REFERENCES

1. Skovlund CW, Mørch LS, Kessing LV, Lidegaard Ø. Association of Hormonal Contraception with Depression. *JAMA Psychiat*. 2016;73(11):1154-1162. https://doi.org/10.1001/jamapsychiatry.2016.2387
2. Joffe H, Cohen LS. Estrogen, serotonin, and mood disturbance: where is the therapeutic bridge? *Biol Psychiatry*. 1998;44(9):798-811. https://doi.org/10.1016/S0006-3223(98)00169-3
3. Inoue K, Barratt A, Richters J. Does research into contraceptive method discontinuation address women's own reasons? A critical review. *J Fam Plann Reprod Health Care*. 2015;41(4):292-299. https://doi.org/10.1136/jfprhc-2014-100976
4. MHRA. Yellow card scheme. https://yellowcard.mhra.gov.uk/faqs/. Accessed November 15, 2018.
5. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. *Lancet (London, England)*. 2000;356(9237):1255-1259. https://doi.org/10.1016/S0140-6736(00)02799-9
6. Martin RM, May M, Gunnell D. Did intense adverse media publicity impact on prescribing of paroxetine and the notification of suspected adverse drug reactions? Analysis of routine databases, 2001-2004. *Br J Clin Pharmacol*. 2006;61(2):224-228. https://doi.org/10.1111/j.1365-2125.2005.02527.x
7. Hernandez JF, Mantel-Teeuwisse AK, van Thiel GJMW, et al. A 10-year analysis of the effects of media coverage of regulatory warnings on antidepressant use in the Netherlands and UK. *PLoS ONE*. 2012;7(9):e45515. https://doi.org/10.1371/journal.pone.0045515
8. van Hunsel F, Passier A, van Grootheest K. Comparing patients' and healthcare professionals' ADR reports after media attention: the broadcast of a Dutch television programme about the benefits and risks of statins as an example. *Br J Clin Pharmacol*. 2009;67(5):558-564. https://doi.org/10.1111/j.1365-2125.2009.03400.x
9. McComb ME, Shaw DL. American Association for Public Opinion Research the Agenda-Setting Function of mass media. *Public Opin Q*. 1972;36(2):176-187. https://doi.org/10.1086/267990
10. Sotirovic M. Effects of media use on audience framing and support for welfare, mass communication and society. *Mass Commun Soc*. 2000;3(2-3):269-269. https://doi.org/10.1207/S15327825MCS0323_06
11. Price V, Tewksbury D, Powers E. Switching trains of thought: the impact of news frames on readers' cognitive responses. *Communic Res*. 1997;24:481-506.
12. Goodfellow NA, Almomani BA, Hawwa AF, McElnay JC. What the newspapers say about medication adherence: a content analysis. *BMC Public Health*. 2013;13(1):909. https://doi.org/10.1186/1471-2458-13-909
13. Bastos MT. Shares, pins, and tweets: news readership from daily papers to social media. *J Lesbian Stud*. 2015;16(3):305-325. https://doi.org/10.1080/1461670X.2014.891857
14. Mollema L, Harmsen IA, Broekhuizen E, et al. Disease detection or public opinion reflection? Content analysis of tweets, other social media, and online newspapers during the measles outbreak in the Netherlands in 2013. *J Med Internet Res*. 2015;17(5):1-12. https://doi.org/10.2196/jmir.3863
15. The Guardian. (n.d.). Prevalence of contraceptive use in the United Kingdom and Europe from 1970 to 2030. In Statista - The Statistics Portal. https://www.statista.com/statistics/663186/contraceptive-use-in-the-united-kingdom-europe/. Accessed November 14, 2018.
16. Top 10 U.K. newspapers by circulation - agility PR solutions. https://www.agilitypr.com/resources/top-media-outlets/top-10-uk-newspapers-by-circulation/. Accessed September 24, 2018.
17. Top 20 newspapers of England (UK) 2017. https://pakproreviews.com/top-20-newspapers-uk-2017. Accessed September 24, 2018.
18. Shih TJ, Wijaya R, Brossard D. Media coverage of public health epidemics: linking framing and issue attention cycle toward an integrated theory of print news coverage of epidemics. *Mass Commun Soc*. 2008;11(2):141-160. https://doi.org/10.1080/15205430701668121
19. EBM DataLab, University of Oxford. OpenPrescribing.net. https://openprescribing.net/. Published 2017. Accessed December 6, 2018.
20. BMJ group and the Royal Pharmaceutical Society. MedicinesComplete - Ethinylestradiol. doi:https://doi.org/10.18578/BNF.461442861
21. BMJ group and the Royal Pharmaceutical Society. Medicines Complete - estradiol. https://www.medicinescomplete.com/#/content/bnf/_558909765. Published 2018. Accessed December 10, 2018.
22. BMJ group and the Royal Pharmaceutical Society. Medicines Complete - Levonorgestrel.
23. BMJ group and the Royal Pharmaceutical Society. MedicinesComplet - BNF legacy. https://www.medicinescomplete.com/#/browse/bnf/legacy. Published 2018. Accessed December 10, 2018.
24. BMJ group and the Royal Pharmaceutical Society. Medicines Complete - Norethisterone. https://www.medicinescomplete.com/#/content/bnf/_661093734. Published 2018. Accessed December 10, 2018.
25. BMJ group and the Royal Pharmaceutical Society. Medicines Complete - estradiol with drospirenone. https://www.medicinescomplete.com/#/content/bnf/_803741938?hspl=drospirenone. Published 2018. Accessed December 10, 2018.
26. BMJ group and the Royal Pharmaceutical Society. MedicinesComplete - Ethinylestradiol with drospirenone. https://www.medicinescomplete.com/#/content/bnf/_789644950?hspl=Estradiol&hspl=with&hspl=drospirenone. Published 2018. Accessed December 10, 2018.
27. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med*. 2012;22(3):276-282. http://www.ncbi.nlm.nih.gov/pubmed/23092060. Accessed January 16, 2019
28. Banovac M, Candore G, Slattery J, et al. Patient reporting in the EU: analysis of EudraVigilance data. *Drug Saf*. 2017;40(7):629-645. https://doi.org/10.1007/s40264-017-0534-1
29. De Langen J, Van Hunsel F, Passier A, De Jong-Van Den Berg L, Van Grootheest K. Adverse drug reaction reporting by patients in the Netherlands three years of experience. *Drug Saf*. 2008;31(6):515-524. www.lareb.nl. Accessed March 11, 2019

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