Arch Womens Ment Health
DOI 10.1007/s00737-014-0453-4

ORIGINAL ARTICLE

Oral contraceptive use and psychiatric disorders in a nationally representative sample of women

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Received: 20 February 2014 / Accepted: 30 July 2014
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Abstract The purpose of this study is to examine the association between oral contraceptive use (any current use, duration, and type) and major depressive disorder (MDD), generalized anxiety disorder (GAD), and panic disorder (PD) in a nationally representative sample of women in the USA. Data were drawn from 1,105 women aged 20–39 in the National Health and Nutrition Examination Surveys from 1999 to 2004. The associations between self-reported use of oral contraceptives in the past year and DSM-IV diagnosed and subthreshold MDD, GAD, and PD in the past year were assessed comparing oral contraceptive users to all non-users, former users, and former long-term users. Women using oral contraceptives had a lower past-year prevalence of all disorders assessed, other than subthreshold MDD. When adjusted for confounders, women using oral contraceptives in the past year had significantly lower odds of subthreshold PD, compared to former users (odds ratio (OR)=0.34, 95 % CI 0.14–0.84). Effects estimates were strongest for monophasic (versus multiphasic) oral contraceptive users. Hormonal contraceptive use was associated with reduced risk of subthreshold PD. A potential mental health benefit of hormonal contraceptives has substantial public health implications; prospective longitudinal studies are needed to confirm whether hormonal contraceptive use improves mental health.

Keywords Generalized anxiety disorder · Hormonal contraceptives · Major depressive disorder · Oral contraceptives · Panic disorder

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Introduction

Approximately 82 % of sexually active women in the USA use oral contraceptives (OCs) sometime during their reproductive years (Mosher and Jones 2010). In addition to the prevention of unintended pregnancy, OCs provide health benefits including decreased risk of ovarian, endometrial, and colorectal cancers; and preservation of bone mineral density (Burkman et al. 2001; Jensen and Speroff 2000). There is also some evidence that OCs provide mental health benefits, including decreases in depressed mood and irritability (Schultz-Zehden and Boschitsch 2006; Short 2009) and alleviation of premenstrual dysphoric disorder (PMDD) symptoms (Lopez et al. 2012), although these findings have not been completely consistent (Greco et al. 2007; Natale and Albertazzi 2006). Conversely, OC users cite perceived side effects, including negative changes in mood, as a common reason for discontinuation (Moreau et al. 2007; Stuart et al. 2013; Westhoff et al. 2007). Despite self-reported psychological effects of OCs, systematic research on their role in outcomes such as major depressive disorder (MDD), generalized anxiety disorder (GAD), and panic disorder (PD) remains limited. This is a significant oversight given lifetime prevalence estimates of 22.1, 7.7, and 7.0 % for these disorders, respectively, among women aged 18–65 (Kessler et al. 2012). Subthreshold levels of these disorders are of higher prevalence and also associated with significant functional impairment and medical comorbidity (Rucci et al. 2003).

Combined OCs contain synthetic forms of the ovarian hormones estrogen and progesterone, suppressing natural production of these hormones and eliminating variability over the menstrual cycle (Fleischman et al. 2010). Variation in symptoms of mood and anxiety disorders over the female life course coincides with natural changes in ovarian hormone levels during puberty (Halbreich and Kahn 2001), pregnancy and postpartum (Altshuler et al. 1998), and menopause (Payne

Published online: 13 August 2014

et al. 2007), suggesting hormonal influence on these symptoms. Additionally, elevations in these symptoms (Kaspi et al. 1994; Payne 2003) and peak admissions to inpatient psychiatric facilities and suicide attempts (Logue and Moos 1986; Targum et al. 1991) coincide with the late luteal phase of the menstrual cycle, when levels of estrogen and progesterone are rapidly decreasing. Lower levels of estradiol have been found among depressed versus non-depressed women (Young et al. 2000) and differences in progesterone and its metabolites, varying by phase of the menstrual cycle, in women with PD versus controls (Brambilla et al. 2003).

Despite substantial evidence that ovarian hormones influence the development and course of mood and anxiety disorders, few population-based studies have investigated the psychological effects of exogenous hormone intake via hormonal contraception including OCs. Two of these studies found no associations between OC use and general or premenstrual depressive symptoms (Duke et al. 2007; Joffe et al. 2003). In contrast, a population-based Finnish study found OC use to be associated with lower depressive symptoms, but not significantly associated with anxiety (Toffol et al. 2011). A study of US women found use of hormonal contraceptives including the pill, patch, or ring to be associated with significantly lower depressive symptoms and risk of past-year suicide attempts (Keyes et al. 2013).

At least three factors may account for the findings of association between OC use and reduced psychiatric symptoms in some studies but not others. First, former OC users may differ from women who never used OCs, creating heterogeneous comparison groups. One study reported that reduced risk of depression was associated with current but not previous use of hormonal contraception (Keyes et al. 2013). Second, variation in findings may partly be due to effect modification by duration of OC use. Two prior studies reported inverse associations between duration of OC use and depressive symptoms (Duke et al. 2007; Toffol et al. 2011). This may be due to a "survivor bias," whereby women with neutral or positive reactions to OCs continue use, while those experiencing negative symptoms are more likely to discontinue. Finally, OC formulation varies between users. Some research has indicated that monophasic OCs, which contain a constant dose of hormones in active pills, might have a stronger positive effect on mood than multiphasic OCs, in which active pills vary in hormone dosage across the menstrual cycle (Oinonen and Mazmanian 2002), although other studies have found no significant differences (Abraham et al. 2003; Walker and Bancroft 1990). This potential heterogeneity has not yet been explored in population-based research.

In the current study, we used data from the National Health and Nutrition Examination Survey (NHANES) to (a) determine the associations between OC use during the past year and full and subthreshold MDD, GAD, and PD during the past year; and (b) determine whether these associations are confounded by history of OC use in the comparison group, or duration of former OC use, or vary by OC formulation. We hypothesized that OC use would be associated with lower prevalence of these mental health outcomes and that the associations would vary by OC formulation. This adds to the existing literature by specifically examining PD, as well as MDD and GAD, and by assessing possible heterogeneity by OC formulation in a population-based, nationally representative sample.

Materials and methods

Data and population

Data were drawn from NHANES participants enrolled from 1999 to 2004. These years were selected based on availability of psychiatric diagnosis measures (described below). NHANES is a series of cross-sectional surveys combining interviews and physical examinations to assess the health and nutritional status of the US population. It enrolls a nationally representative sample of about 5,000 people per year (National Center for Health Statistics (a)). Analyses were limited to the half-sample of participants, ages 20–39 years, who received questionnaire modules on psychiatric disorders. Unweighted response rates for the portion of the survey including these modules were 76, 80, and 76 % for the 1999–2000, 2001–2002, and 2003–2004 waves, respectively (National Center for Health Statistics (b)). The study sample was further restricted to 1,171 women who had data available on OC use and covariates (Fig. 1). Participants were not excluded based on use of prescription medication other than OCs. Data was publicly available, and the study received a waiver of approval from the institutional review board of Columbia University.

Exposure

The primary exposure of interest was past-year OC use, in order to cover the same time period as the psychiatric diagnosis measures (below). Women were considered past-year OC users if they reported currently taking birth control pills or previously taking birth control pills, stopping at an age equal to or 1 year lower than their current age. Women reporting lifetime, but not past-year, OC use were considered former OC users. Duration of OC use was the total in years as reported by women. Continuous use could not be distinguished from intermittent use.

For 204 of 349 past-year OC users, information was available on the name of contraceptive taken. Drug names were used to classify exposure to combined (estrogen and progestin) OCs as monophasic or multi (bi- or tri-)-phasic. The multiphasic category was composed of primarily (97 %) triphasic formulations. One woman for whom the drug could not

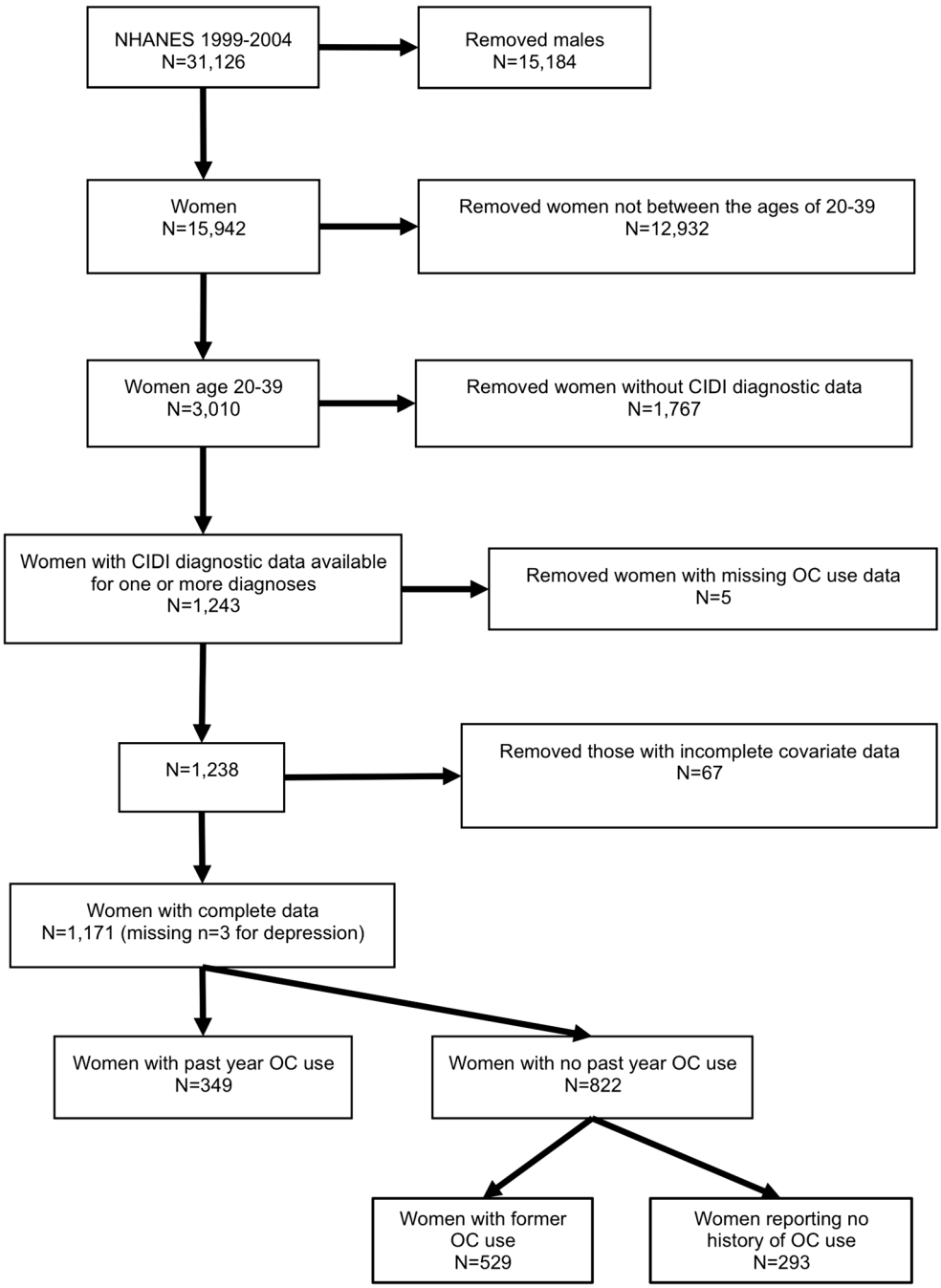

Fig. 1 Selection of population for inclusion

be classified and three women reporting use of progestin-only OCs were excluded from these analyses.

Hormone exposures other than combined OCs (injectable birth control, progestin-only OCs, or non-contraceptive estrogen/progestin medications) were reported among 4.4 % (n=51) of subjects. There was no significant difference in these exposures, as a group, between past-year OC users and non-users (p=0.32). Bivariate analyses indicated that they were not associated with any of the outcomes examined (p>0.2).

Outcomes

Outcomes included past-year GAD and PD at levels meeting a minimum of subthreshold criteria (here forth referred to as "diagnostic/subthreshold") and past-year MDD and any of the three disorders at diagnostic and subthreshold levels (considered separately). The diagnostic and subthreshold levels for GAD and PD were combined due to low numbers of observations in individual strata. The outcomes were determined based on responses to an NHANES version of three modules

from the automated WHO Composite International Diagnostic Interview (CIDI) 2.1 (WHO 1997). The CIDI is a comprehensive diagnostic interview designed for assessing mental disorders according to criteria of the ICD-10 and DSM-IV with good test-retest and inter-rater reliability (Peters et al. 1998; Wittchen 1994).

Variables for meeting full diagnostic criteria for GAD, PD, and MDD over the past year were used as provided in the NHANES CIDI modules. To operationalize subthreshold psychiatric disorders based on responses to the CIDI, we used criteria adapted from Rucci et al. (2003). The criteria used to define each outcome used in the study are listed in Table 1. For all subthreshold disorders, as with disorders themselves, participants were not considered to have met criteria if symptoms were due to direct physiological effects of a substance or medical condition. Diagnostic/subthreshold GAD and PD were treated dichotomously while MDD and disorders combined were three-level variables (diagnosis, subthreshold, and no disorder).

Covariates

Covariates considered as potential confounders included participant age, number of male sex partners in the last year, education, race/ethnicity, family poverty-income ratio, marital status, number of live-birth pregnancies, and current or recent pregnancy. Recent pregnancy was defined as reporting an age at last live birth equal to or 1 year less than the participant's current age. Information on past pregnancies with outcomes other than live birth (e.g., still birth) was not available. To address potential confounding by access to health care and the "healthy user effect," whereby women with more positive health behaviors are more likely to use hormonal contraceptives (Keyes et al. 2013), variables for continuous past-year health insurance, cigarette smoking (ever versus never smoked at least 100 cigarettes), diagnosis with chronic hypertension or diabetes, BMI category, and self-assessed level of physical activity compared with others of the same age were also examined. Categories for covariates are shown in Table 1.

Statistical analysis

To account for the sampling design, survey procedures in Stata/IC 10.1 (College Station, TX) were used for all analyses. Analytic weights were created for the 6-year sample by taking 2/3 of the 4-year CIDI subsample weight for each sampled person in 1999–2002 and 1/3 of the 2-year CIDI subsample weight for each sampled person in 2003–2004. All results used the survey weights unless otherwise specified.

To assess potential confounding, covariates were compared between past-year OC users and non-users and those with and without each outcome, using Pearson chi-squared tests. The percentages and standard errors of women with each outcome were estimated within categories of past-year OC use. To determine whether past-year OC users had different risks of full/subthreshold GAD or PD in the past 12 months relative to non-users, we used logistic regression models to estimate unadjusted and adjusted odds ratios (ORs). For MDD and any disorder, we used multinomial logistic regression to allow for three levels of outcome (diagnosis, subthreshold, or no disorder). Adjusted models included covariates that were associated with both past-year OC use and the outcome with

Table 1 Definitions of outcomes used in the presented study

Outcome	Definition
Full/subthreshold generalized anxiety disorder	• Excessive anxiety and worry for a duration of at least 1 month • Associated with at least three of six symptoms • Not exclusively about a mental disorder, weight gain, or multiple physical complaints • Diagnosis additionally required a duration of 6 months, report that the subject found it difficult to control the worry, and that anxiety causes clinically significant distress or impairment
Full/subthreshold panic disorder	• Report of panic attack (intense period of fear or discomfort) with four or more symptoms, during which the problems begin or sometimes begin suddenly and get worse in the first few minutes • Attacks have not always occurred in life-threatening situations • At least one lifetime attack must have occurred "out of the blue" • Diagnosis additionally required that >1 attack occurred "out of the blue," that the number of lifetime attacks with symptoms was reported as >1, and avoidance of situations due to fear of another attack or its consequences
Subthreshold major depressive disorder	• An episode of a minimum of 2-week duration of depressed mood or diminished interest with most days affected • Associated with at least four of nine total symptoms, including depressed mood or diminished interest
Major depressive disorder	• Subthreshold symptoms above plus • The symptoms cause clinically significant distress or impairment • The symptoms are not better accounted for by bereavement
Any disorder, subthreshold	• Reaches subthreshold criteria for at least one disorder above • Does not meet full diagnostic criteria for any disorder above
Any disorder	• Meets full diagnostic criteria for at least one disorder above

Table 2 Characteristics of US women aged 20–39 in 1999–2004, by past-year oral contraceptive use

	OC users (%)	Non-users (%)	*p* value
Age in years, mean (SD)	29.1 (0.3)	30.7 (0.3)	<0.01
One or more prior live births	49.4	67.5	<0.01
Education			
<9th grade	2.0	3.9	<0.01
9–11th grade	9.2	14.4	
HS graduate/GED	16.3	27.2	
Some college or AA degree	34.9	32.3	
College graduate or above	37.5	22.2	
Race/ethnicity			
Non-Hispanic White	71.7	60.3	<0.01
Non-Hispanic Black	8.4	16.2	
Mexican-American/other Hispanic	15.1	19.2	
Other	4.8	4.3	
Poverty-income ratio (%)			
<100	10.9	24.2	<0.01
100–199	18.7	23.7	
200–299	13.5	17.4	
300–399	13.9	15.7	
≥400	43.0	19.0	
Number of male sex partners in the past year			
None	4.4	16.1	<0.01
One	77.2	69.6	
Two or more	18.4	14.3	
Marital status			
Married	51.3	48.6	0.63
Never married	27.5	31.4	
Other	21.2	20.1	
Ever smoker	37.3	41.7	0.25
Less active than others your age	24.0	30.2	0.02
Body mass index category (%)			
Underweight (<18.5)	5.0	3.7	<0.01
Normal (18.5–24.9)	49.9	38.1	
Overweight (25.0–29.9)	23.4	24.3	
Obese (≥30.0)	21.8	33.9	
Constant health insurance past year (%)	77.5	66.0	<0.01
Chronic disease	6.9	11.2	0.06
Pregnancy status (%)			
Not pregnant	77.9	77.9[a]	0.98
Pregnant in the past year	11.9	12.2	
Currently pregnant	10.2	10.0	

[a] Assessed among all women with non-missing data for each specific variable

$p<0.2$, which was selected as a conservative threshold for the identification of potential confounders. All covariates were entered simultaneously into the model.

To account for the possibility of unmeasured differences between women who never versus ever used OCs, additional adjusted models were estimated restricting the unexposed group to former OC users and to never OC users, respectively. We adjusted models comparing past-year to former OC users for duration of use by including continuous (linear) and categorical (quartile) terms for years of OC use. To assess whether there were differences in OC-mental health outcome associations dependent on formulation of OC used, adjusted logistic regression models including indicator variables for type of past-year OC use (monophasic/multiphasic/non-exposed) were fit and formulation types compared using adjusted Wald tests.

Table 3 Prevalence of past 12 months mental health disorders by past-year oral contraceptive use among US women aged 20–39 in 1999–2004

Outcome	% (SE) with outcome			
	Past-year OC users	Past-year non-users		
		All non-users	Never users	Former users
Anxiety				
Generalized anxiety disorder, diagnosis or subthreshold	5.7 (1.4)	8.2 (1.4)	4.9 (1.6)	9.7 (1.8)
Panic				
Panic disorder, diagnosis or subthreshold	2.6 (1.0)	6.7 (1.2)	2.6 (1.2)	8.7 (1.6)
Depression				
Major depression, diagnosis	8.3 (1.9)	9.8 (1.1)	4.9 (1.8)	12.2 (1.6)
Major depression, subthreshold	4.3 (1.3)	3.9 (0.9)	2.8 (1.2)	4.5 (1.1)
Disorders combined				
Any disorder, diagnosis	9.8 (1.9)	13.7 (1.3)	7.9 (1.8)	16.5 (1.9)
Any disorder, subthreshold	7.8 (1.6)	7.4 (0.9)	5.5 (1.2)	8.3 (1.3)

Results

Characteristics associated with past-year OC use

Thirty-two percent of women aged 20–39 reported past-year OC use. Characteristics of women by OC exposure status are shown in Table 2. Compared with non-users, past-year OC users were significantly younger; more likely to be non-parous, white, and college educated, have high family incomes, report one or more male sexual partners in the past year, report having constant health insurance coverage over the past year, and have lower BMIs; and were marginally less likely to have been diagnosed with hypertension or diabetes ($p=0.06$). The groups did not differ with respect to marital status or prevalence of current/past-year pregnancy. Sixty-seven percent of past-year OC non-users reported previously using OCs.

Association between past-year OC use and psychiatric disorders

Table 3 includes the percentage of past-year OC users and non-users (total and stratified by former versus never use) meeting diagnostic and/or subthreshold criteria for each disorder. In general, each psychiatric disorder was least common among never users of OCs and most common among former users, with past-year OC users showing intermediate prevalence. The exception was PD, which occurred at subthreshold or diagnostic levels among 2.6 % of both past-year and never OC users versus 8.7 % of former users.

Table 4 shows the results of unadjusted and adjusted regression models. In unadjusted models, past-year OC use versus all non-users was associated with a statistically significant ($p<0.05$) OR of 0.37 for diagnostic/subthreshold PD. Although the association was attenuated and only marginally significant after adjustment for confounders (OR=0.47; $p=0.07$), comparing past-year OC users only to former users strengthened the association between OC use and diagnostic/subthreshold PD (OR=0.34; $p<0.05$). Results were similar when controlled for duration of OC use (data not shown).

GAD and MDD were not significantly associated with past-year OC use, regardless of comparison group. The OR for meeting criteria for any disorder diagnosis was 0.52 (95 % CI 0.29, 0.92) for past-year OC users relative to former OC users, and the association remained after adjusting for duration of OC use (data not shown).

Association of psychiatric disorders with OC category

Given the reduced number of observations with available data, we examined differences in association of OC use and outcomes by OC formulation (mono- versus multiphasic) only for diagnostic/subthreshold GAD and for diagnostic and subthreshold MDD (Table 5). Comparisons were made to all past-year non-users. While none of the effect estimates for monophasic or multiphasic OCs were statistically significant ($p<0.05$) themselves, there was evidence for a difference between the association of monophasic versus multiphasic OCs with subthreshold and diagnostic MDD ($p<0.01$). Specifically, the OR for MDD diagnosis was below 1.0 for monophasic OCs and above 1.0 for multiphasic OCs, with the situation reversed for subthreshold MDD (multiphasic OCs protective) (Table 5).

Comment

In a nationally representative sample of US women aged 20–39, we found evidence for an inverse association between

Table 4 Associations of past 12-month mental health disorders with past-year oral contraceptive use among US women aged 20–39 in 1999–2004

Outcome	Compared to all OC non-users		Compared to never OC users only	Compared to former OC users only
	cOR (95 % CI)	aOR (95 % CI)	aOR (95 % CI)	aOR (95 % CI)
Generalized anxiety disorder, diagnosis or subthreshold[a]	0.67 (0.40, 1.15)	0.80 (0.46, 1.39)	1.57 (0.77, 3.18)	0.66 (0.37, 1.21)
Panic disorder, diagnosis or subthreshold[b]	0.37 (0.17, 0.84)	0.47 (0.20, 1.08)	1.28 (0.41, 3.96)	0.34 (0.14, 0.84)
Major depression[c]				
Diagnosis	0.83 (0.49, 1.42)	0.81 (0.47, 1.40)	1.30 (0.51, 3.33)	0.66 (0.36, 1.20)
Subthreshold	1.08 (0.46, 2.52)	1.23 (0.48, 3.13)	2.17 (0.53, 8.97)	0.96 (0.34, 2.67)
Disorders combined[d]				
Diagnosis	0.69 (0.43, 1.10)	0.64 (0.38, 1.08)	1.03 (0.50, 2.11)	0.52 (0.29, 0.92)
Subthreshold	1.01 (0.64, 1.60)	1.15 (0.70, 1.90)	1.96 (0.96, 4.01)	0.90 (0.51, 1.58)

Each model is adjusted for those variables that were associated with both OC use and the specific outcome, as follows:

[a] aORs adjusted for age, BMI category, physical activity, and number of sexual partners in the past year

[b] aORs adjusted for education, past-year health insurance, chronic disease, and physical activity

[c] aORs adjusted for race/ethnicity, physical activity, BMI, chronic disease, and number of sexual partners in the past year

[d] aORs adjusted for race/ethnicity, physical activity, BMI, chronic disease, and number of sexual partners in the past year

reported OC use and PD meeting at least subthreshold criteria in the past year. To our knowledge, this is the first population-based study reporting an association between OC use and reduced occurrence of PD diagnosis or symptoms. OC use was also associated with a non-significant trend toward reduced odds of MDD diagnosis and diagnostic/subthreshold GAD.

Past-year prevalences of PD, GAD, and MDD observed in the total study population (3.6, 3.4, and 9.4 %) were similar to those reported for females in the National Comorbidity Study-Replication (National Comorbidity Study). Similar to other recent studies (Duke et al. 2007; Joffe et al. 2003), we did not observe significant associations between OC use and risk of MDD diagnosis or subthreshold MDD or GAD. However, it is of note that the adjusted OR estimates for each of these outcomes, and for all disorders combined, were in the protective direction when compared to former OC users. Thus, the associations observed may be indicative of a more broadly protective effect of OCs, as opposed to one specific to PD. Moreover, the magnitude of association we report for MDD is similar to that found in a larger sample of US women (Keyes et al. 2013). The lower power for the present study where we had 80 % power to detect an OR of approximately 0.48 or less for MDD diagnosis may explain our non-significant result.

Another factor possibly contributing to differences in findings across studies is heterogeneity of effects by the formulation of OCs. We observed qualitative differences in associations between mono- versus multiphasic OCs, for

Table 5 Association between past-year oral contraceptive use, categorized as mono- or multiphasic, and mental health disorders in US women aged 20–39

OC formulation	GAD[a]	MDD[b]	
	Diagnosis or subthreshold OR (95 % CI)	Subthreshold OR (95 % CI)	Diagnosis OR (95 % CI)
No past-year OC use	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Monophasic	0.42 (0.11, 1.55)	1.79 (0.66, 4.90)	0.54 (0.21, 1.39)
Multiphasic	1.25 (0.57, 2.75)	0.40 (0.15, 1.10)	1.32 (0.60, 2.93)
p value (mono vs multi)	0.17	<0.01	

Reference group is all past-year OC non-users

[a] ORs adjusted for: age, BMI category, physical activity and number of sexual partners in the past year

[b] ORs adjusted for: race/ethnicity, physical activity, BMI, chronic disease and number of sexual partners in the past year

subthreshold GAD and MDD diagnosis, such that monophasic OCs were associated with a non-significant reduced risk and multiphasic OCs were associated with a non-significant increased risk. This suggests that the stabilizing effect of OCs on hormonal levels over the menstrual cycle may be behind any protective effect against symptoms of psychiatric disorders. OC users experience less affect variability over the menstrual cycle relative to non-users (Oinonen and Mazmanian 2002). However, data on hormonal variation across the menstrual cycle is necessary to further test this hypothesis. Investigation of additional sources of potential heterogeneity among OC exposures, such as progestin type or hormonal dose, may also be worthwhile.

Alternative explanations should be considered. Because the data were cross-sectional, reverse causality is possible. That is, women with psychiatric symptoms may have been more likely to discontinue ("healthy survivor effect") or choose against OC use, and health care providers may be less likely to prescribe OCs to such women. However, the findings that associations of the outcomes examined with past-year OC use were apparent relative to former OC users rather than never users and that adjustment for duration of OC use had little impact on the results suggest against this explanation. Future studies including longitudinal data would provide greater insight into the direction of the association between OC use and psychiatric outcomes.

Several biological mechanisms have been proposed linking hormonal changes to mood and anxiety symptoms. First, both estrogen and progesterone modulate neurotransmitter function, particularly serotonin, relative availability of which is linked to depression (Arpels 1996; Joffe and Cohen 1998). Second, progesterone metabolites exert effects on the $GABA_A$ receptor, which is thought to regulate anxiety (Nillni et al. 2011). Third, ovarian hormones have been implicated in shaping sensitivity to carbon dioxide, which may affect susceptibility to panic symptoms (Klein 1993). Fourth, ovarian hormones may influence stress responsiveness, and in turn susceptibility to disorder, through their impact on the hypothalamic-pituitary-adrenal axis (Young and Altemus 2004). Lastly, studies have suggested that estradiol affects neurological systems associated with fear extinction, such that it might play a protective function against elevated fear and anxiety among premenopausal cycling women (Taneepanichskul and Patrachai 1998; Zeidan et al. 2011). Alternatively, OC use could influence mood and anxiety through protection against life stressors, including unplanned pregnancy.

Limitations must be noted. Confounding by unmeasured factors is always a consideration in epidemiologic studies. OC use was associated with more health-promoting behaviors in general here as elsewhere (Keyes et al. 2013). The association observed here was somewhat weaker after controlling for covariates, but also was seen among women who all had a history of OC use. Because information on timing of OC use and pregnancy was reported by age rather than calendar date, misclassification of past-year exposure may have occurred for some women. However, any such misclassification would have occurred randomly dependent on birth date and would be expected to bias results toward the null. Information on the consistency of OC use, which may modify the effects of use, also was not available. Finally, power was limited for all analyses as reflected in wide confidence intervals.

In conclusion, the results of this study represent a significant step in understanding the potential influence of OC use on psychiatric symptoms, in particular those of PD, which have been understudied with respect to OC use. Strengths included use of a random nationally representative sample and of survey methods to adjust for sampling and non-response, increasing generalizability and limiting selection bias. Diagnostic/subthreshold PD was found to be significantly lower among past-year OC users relative to former users, even after adjusting for duration of use. Additional research is needed to deepen our understanding of the psychiatric effects of OCs given the high prevalence of use and the distress and dysfunction rendered by mood and anxiety disorders.

Acknowledgments The authors would like to acknowledge Michelle Haloossim for the literature review and writing assistance and Kirstin H. Heinrich for the assistance with literature review and figure preparation. At the time of manuscript preparation, Ms. Haloossim was a student in the Department of Sociomedical Sciences and Ms. Heinrich was a student in the Department of Epidemiology at the Columbia University Mailman School of Public Health. Funding for this study was provided by the National Institute of Mental Health (2-T32-MH-13043 to KCP and SRL and K01-AA021511 to KMK).

Conflict of interest The authors declare that they have no conflicts of interest.

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