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ORIGINAL PAPER

Trends in oral contraceptive and intrauterine device use among reproductive-aged women in the US from 1999 to 2017

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Abstract

Purpose Since the 1960s, increasing oral contraceptive (OC) use has mirrored decreasing ovarian cancer incidence. The impact of intrauterine devices (IUDs) on cancer risk is less well established. With improved access and increased options, we must consider how changing usage can affect cancer risks.

Methods Nationally representative data from the National Health and Nutrition Examination Survey (NHANES, 1999–2016) and the National Survey for Family Growth (NSFG, 2006–2017) were used to evaluate contraceptive use over time in premenopausal women (NHANES $n = 13{,}179$; NSFG $n = 26{,}262$). Trends were assessed overall and by race, age, pregnancy history, education, and body mass index.

Results The average annual absolute increase in self-reported IUD use was 0.81% (NSFG), while OC use decreased 0.49% in NSFG and 0.47% in NHANES. This represents a significant decrease in OC use in NSFG [annual percent change (APC) − 2.2% (95% CI − 3.4, − 1.0%), $p < 0.01$]. Trends in OC use varied somewhat by pregnancy history in NHANES (p-interaction = 0.054). In contrast, IUD use increased 6.2% annually [(1.4, 11.2%), $p = 0.03$] and varied significantly by pregnancy history (p-interaction < 0.01). Nulligravid women increased IUD use 11.0% annually [(2.6, 20.1%), $p = 0.02$] compared to women with prior pregnancy at 5.2% [(0.4, 10.2%), $p = 0.04$]. In 2015–2017, IUD use was 76.5% hormonal (71.1, 81.8%) and 22.9% copper (17.4, 28.3%) with greater hormonal IUD use in obese women [89.4%, (82.9, 95.9%)].

Conclusion Increasing IUD use outpaced declining OC use in premenopausal US women. There may be a resulting decreased gynecologic cancer risk as more women gain access to potentially risk-reducing contraceptives.

Keywords Oral contraceptives · Intrauterine devices · Cancer risk · Gynecologic oncology · Women's health

Introduction

Since the 1960s, oral contraceptives (OCs) have been a major method of effective and easily reversible contraception [1]. In 1973, OC use appeared to peak in the United States (US), at 36% of women; however, survey data prior to 1982 only included married women [2]. The prevalence of reported OC use decreased by 2% overall between 1971 and 1980; this decline was 4% overall from 1982 to 1995 [3, 4].

OC use has been shown to influence the risk of certain cancers [5, 6]. A personal history of OC use is associated with a 30–50% reduction in ovarian and endometrial cancer risk [7, 8] that persists for over 30 years following cessation of use [5]. Evidence is mixed as to the effect that newer OC formulations have on breast cancer risk among women [6–11]. The risk of breast cancer has been found to be higher among women who currently or recently used contemporary hormonal contraceptives than among women who had never used hormonal contraceptives, with increased durations of use portending greater breast cancer risk. However, absolute increases in risk were small [11]. Associations between cancer risk and OC use should be continually evaluated as formulations evolve, patterns of use change, and populations age.

Intrauterine devices (IUDs) are an important form of long-acting reversible contraception that may also affect cancer risk. Prior to 1995 there was a steep decline in IUD

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use in the US from 7.1% in 1982 to 0.8% in 1995, likely due to reported pelvic inflammatory disease and other adverse effects linked with use of the Dalkon Shield IUD [4, 12]. When the copper IUD was first introduced in the US in 1998, it was originally contraindicated for women without a history of pregnancy, but was eventually approved for all women in 2005 [13]. In 2010, the Centers for Disease Control and Prevention began publishing the U.S. Medical Eligibility Criteria for Contraceptive Use and classified certain hormonal and copper IUDs as contraceptive methods that, for many women, offer "advantages that generally outweigh the theoretical or proven risks" associated with their use [14]. IUD use, like OC use, may be associated with reduced risks for ovarian cancer, but the consistency and magnitude of these risk reductions and the exact mechanisms through which they occur are not fully understood [15, 16]. This is in part, due to a lack of long-term follow-up in studies that collected information on IUD use. In addition to their use for contraception, hormonal IUDs are also used for treatment of complex atypical hyperplasia and low-risk endometrial cancer in women who desire future fertility due to the protective effects of progestins on the endometrium [17]. With the exception of recent studies reporting female cancer risk with hormonal IUD use in Finland [18], the association between hormonal IUD use and long-term cancer risk reductions has been largely unexplored. Additionally, there is some concern that the potential systemic absorption of hormones in IUDs may increase the risk of breast cancer, but this has been controversial [11].

In recent years, prescriptions from pharmacists and telehealth providers have increased access to many forms of contraception and many other countries have approved over-the-counter OCs [19]. Interestingly, the increased use of IUDs has corresponded with a decreased use of OCs in some countries [16]. Among women using contraception in the US, IUD use increased in recent years (2009–2012) [20, 21], but the rate of change over time in both IUD and OC use has not been elucidated. Using two nationally representative surveys conducted by the National Center for Health Statistics (NCHS), the National Health and Nutrition Examination Survey (NHANES), and the National Survey of Family Growth (NSFG), we examined trends in the current use of contraceptives over the last two decades and considered how these patterns of contraceptive prevalence may influence cancer risk.

Methods

Data sources and study population

NHANES is a nationally representative cross-sectional survey of the civilian, non-institutionalized US population [22]. Participants included in our analysis were premenopausal females aged 15–49 years during the nine most recent NHANES cycles ($n = 13{,}179$ individuals). Cycles included in our analysis were determined by data availability: 1999–2000 represented the first 2-year cycle of continuous NHANES with a cycle every two years up to 2015–2016, the most recent cycle for which data was available [23–25]. Women with a history of hysterectomy or bilateral oophorectomy were excluded due to lack of indication for standard contraception.

NSFG is a nationally representative survey of the civilian, non-institutionalized US population of women aged 15–44 years (15–49 years in 2015–2017 cycle used for current IUD use by type). We included information on current contraceptive (OC, IUD, surgical sterilization, implant, injectable medroxyprogesterone acetate) use among women from survey cycles 2006–2010, 2011–2013, 2013–2015, and 2015–2017. Eligible women for our analyses were premenopausal and without prior hysterectomy or bilateral oophorectomy ($n = 26{,}262$ individuals). Prior to 2011, IUD type was not included in the survey questionnaires; therefore, the 2011–2017 cycles were utilized when estimating current IUD use by type (copper vs. hormonal) [26–30].

Both surveys have complex stratified, multistage, and probability cluster sample designs. Each survey cycle was independent, and individual women were not followed longitudinally throughout either survey. NHANES oversampled low-income individuals, pregnant women, and certain racial/ethnic and age groups. NSFG oversampled persons identifying as black and Hispanic, as well as 15–19 year olds. Participants in both surveys were assigned weights to account for unequal sampling probabilities and differential nonresponse rates. For both surveys, age, race, ethnicity, height, weight, and reproductive health history were self-reported during an in-person interview. Body mass index (BMI) was calculated from self-reported height and weight (in kilograms divided by height in meters squared). All NHANES and NSFG participants provided written informed consent, and all analyses were performed using publicly available data [25, 26].

Assessment of oral contraceptive use

Prescription drug use in NHANES was obtained through the in-person interview. Participants reported prescription drugs taken over the past 30 days and presented containers/prescriptions when possible. Each drug was linked to the Lexicon Plus prescription drug database, which was updated each cycle to include new products. Contraceptive types were determined based on NHANES generic drug codes [25].

The 1999–2002 NHANES cycles asked about current use (yes/no) and "brand name" of contraception (Fig. 1). This information was cross-referenced with prescription

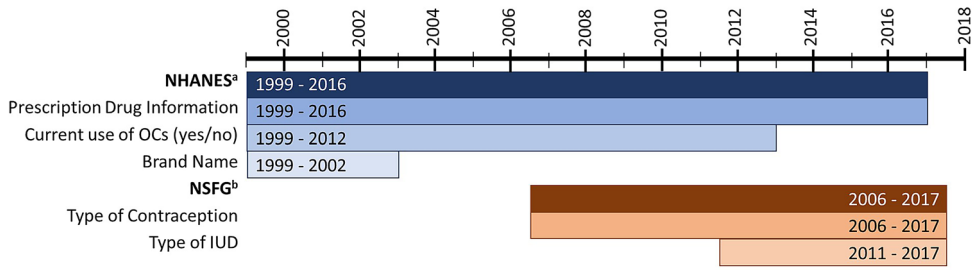

Fig. 1 Survey questions covered for NHANES and NSFG throughout the cycles covered by each survey. The letter "a" represents NHANES sampling began at the beginning of the calendar year and was stopped at the end of the calendar year. The letter "b" represents NSFG sampling started and ended in June of the years indicated

drug information to determine OC use. Cycles 2003–2012 included current use of OCs (yes/no), but not brand name. Questionnaire data was cross-referenced with prescription drug information to determine OC use. For years in which questionnaire and prescription data were present, an average of 29.4% of women did not have prescription drug information for OCs despite reported OC use in the questionnaire. These women did report other medication use in the prescription drug assessment, but did not include the specific prescription information for the OCs they reported taking in the questionnaire. Cycles 2013–2016 did not include a question about current use of contraceptives. Therefore, for these latter two cycles information on contraceptive use was limited to the prescription drug assessment. For all survey years prescription information was used to determine specific OC formulation. During the time frame of this study, generation of combined OC (1st–4th) was determined based on type of progestin [31]. In general, newer generations of combined OCs (3rd and 4th) have lower doses of both estradiol and progestin and contain progestins, such as gestodene and drosperinone [31]. Each generation was analyzed as the proportion of overall OC use by survey cycle. Trends in 4th-generation use excluded the first two survey cycles since they were not available to the general public at that time. The evaluation of patterns/trends in generation of progestin used was limited to the subset of users that reported data on OC formulation.

NSFG in-person interview questions about reproductive health included current and recent use of contraceptives in the past month. However, no information on prescription formulation was collected. For those who reported using multiple forms of contraception, all were included. Starting with the 2011–2013 cycle, a question was included about the type of IUD used [hormonal (brand examples of Mirena or Skyla), copper (brand examples of Copper-T or ParaGard), other, unknown, Fig. 1] [28–30].

Statistical analysis

OC prevalence was determined for each 2-year NHANES 1999–2016 cycle. NSFG cycles were also analyzed in 2-year increments (survey cycles started/ended in June, 2006–2008, 2008–2010, 2011–2013, 2015–2017) and included data on contraceptive use. All analyses used National Center for Health Statistics analytic guidelines to account for complex designs of NHANES and NSFG using strata, primary sampling units (counties or small groups of contiguous counties), and sample weights [23, 24, 27–30]. NHANES interview weights for cycles 1999–2000 and 2001–2002 were determined using 4-year interview weights (as recommended in analytic guidelines [23]) multiplied by 2/9. All other cycle weights were determined using 2-year interview weights multiplied by 1/9 to compare each cycle using a standardized weight across all cycles (nine total cycles) [23, 24].

We were interested in identifying changes in trends of contraceptive use over time within subgroups of women. Therefore, prevalence estimates were stratified by age, race/ethnicity, history of prior pregnancy, education level, BMI, and identification as religious. NHANES did not ask for religious identification; however, NSFG asked the current religious affiliation of each participant. We categorized women as either religious or non-religious. A recent paper showed that women with no religious affiliation were more likely to use short-acting, barrier, or LARC methods than women with a religious affiliation. Results for behavioral or surgical contraception were equivalent by the presence/absence of religious affiliation 32]. NHANES oversampled people identifying as Mexican American (prior to 2007) and Hispanic (2008–present). NHANES analytic guidelines recommend researchers use the Mexican American subgroup classification when estimating trends by ethnicity spanning the period covered in our analyses [23, 24]. The NSFG only queries women on whether they identify as Hispanic or non-Hispanic.

Participants with missing data for a given subgroup were excluded from analyses stratifying on or limiting to that subgroup. Information on age and race was available for both analytic populations. For covariates with missing information, this ranged from 7 (BMI) to 32% (education) within NHANES. BMI was the only covariate with missing information in NSFG (21%).

Logistic regression models were used to calculate least square means estimates of the adjusted prevalence (adjusting for age, race, pregnancy history, education, and BMI) of OC and IUD use over time. These adjusted prevalences were imported into Joinpoint Regression Program (version 4.7.0.0) to perform weighted least squares regression [33] to obtain the adjusted annual percent change (APC) and the corresponding 95% confidence intervals (CIs). In weighted least squares regression the independent variable was time and dependent variable was the natural logarithm of the percent of women using OCs or IUDs. Due to the small number of time points for each survey and no large changes in slope over time, all models were calculated using 0 joinpoints [34]. Average annual absolute percent change was calculated from the total change in contraceptive use from the first cycle to the last, divided by the total number of years analyzed for NSFG or NHANES, respectively.

In sensitivity analyses, we limited NSFG to the subpopulation of women identified as contraceptive users for comparisons with other published data from this survey. Our primary analysis focused on the larger group of reproductive-aged women at risk for ovarian and endometrial cancer as the proportion of use is more interpretable in the context of future cancer trends.

Differences across subgroups were characterized by Type 3/joint Wald test p values for model interaction terms between time and a given variable (e.g., race/ethnicity). A p value < 0.05 was used to determine statistical significance. Survey cycles were transformed by converting the year in which the cycle ended to time as the independent variable (i.e., NHANES cycle 1999–2000 is time = 0, 2001–2002 is time = 2, etc.) to analyze trends in per year increases/decreases. Analyses were conducted using the survey procedures in SAS version 9.4.

Results

Characteristics of the analytic populations are presented in Supplementary eTable 1. In both study populations, most participants identified as non-Hispanic white were under 35 years old and identified as religious. Participants not reporting current OC use were more likely to have a history of pregnancy than OC users within both NHANES and NSFG.

The average annual absolute increase in IUD use was 0.81% (NSFG), while the average annual absolute decrease in OC use was 0.49% (NSFG) and 0.47% (NHANES, Table 1). Surgical sterilization and injectable medroxyprogesterone acetate also decreased annually on average by − 0.28 and − 0.03%, respectively, while implant use increased 0.07% annually. For OC and IUD use this represents many women changing their contraceptive use patterns. For NSFG this average absolute percent change represents an increase of 506,204 women using IUDs annually and a decrease of 305,392 women using OCs annually (Table 1) [35].

Since 2006, self-reported OC use overall decreased annually in NSFG [APC − 2.2% (− 3.4, − 1.0%), $p < 0.01$] (Fig. 2, Table 2), while OC use was stable in NHANES [APC − 1.1% (95% CI − 2.6, 0.3%), $p = 0.10$] over the entire period evaluated (1999–2016). When restricting NHANES to 2007–2016 to make a direct comparison with NSFG, we observed an annual decrease in OC use of 4.4% [(− 6.8, − 1.8%) $p = 0.01$, Supplementary eTable 2]. In contrast to decreasing prevalence of OC use observed in NSFG, IUD use in NSFG increased by 6.2% annually [(1.4, 11.2%), $p < 0.03$] (Fig. 2, Table 2). Surgical sterilization decreased significantly to 10.2% of the population in 2017 [APC − 1.4% (− 2.2, − 0.6), $p = 0.013$]. Injectable medroxyprogesterone acetate use remained stable [APC 0.2% (− 3.1,

Table 1 Average annual absolute percent change of oral contraceptive (OC) and intrauterine device use (IUD) use for NHANES and NSFG

Overall use	Average annual absolute percent change	Population estimate[a]	Estimated number of additional women using method yearly
NHANES OC	− 0.47	73,368,515	− 345,566
NSFG OC	− 0.49	62,286,800	− 305,392
NSFG IUD	0.81	62,286,800	506,204
NSFG surgical sterilization	− 0.28	62,286,800	− 176,029
NSFG injectable medroxyprogesterone acetate	− 0.03	62,286,800	− 24,894
NSFG implant	0.07	62,286,800	43,815

[a]Population estimate based on the midpoint population estimate for the survey (NHANES—2008, women aged 15–49; NSFG—2012, women aged 15–44) using census predictions [33]

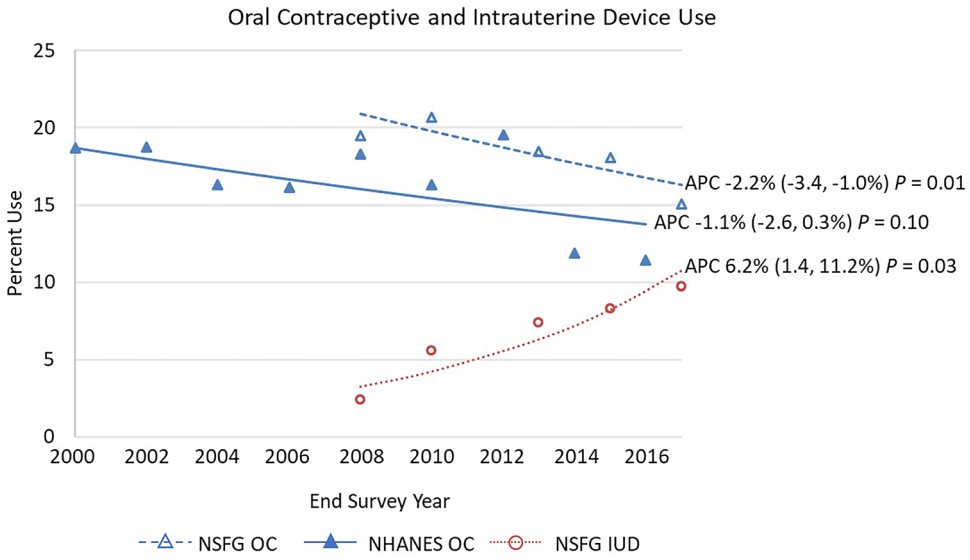

Fig. 2 Overall weighted oral contraceptive (OC) use (NHANES and NSFG) and intrauterine device (IUD) use (NSFG). Fit lines represent unadjusted models, while the corresponding adjusted annual percent change (APC) and 95% confidence intervals are reported

3.7), $p = 0.9$] and was used by 2.5% of the population in 2017. While implants increased in use [APC 12.6% (7.5, 18.1), $p = 0.004$], their overall use remained low at 3.5% in 2017. The proportion of OC use by generation of progestin was stable across all cycles (the 4th generation was limited to cycles from 2003 to 2016). In the cycle ending in 2016, 3rd-generation OCs were used by 41.1% of users, 1st generation by 38.8% of users, 2nd generation by 15.6% of users, and 4th generation by 4.5% of users.

We further analyzed trends in OC use over time by subgroups in NHANES and NSFG. We observed consistent trends in decreasing OC use over time by most subgroups analyzed (p-interaction > 0.05) in NHANES. There was a suggestion of heterogeneity in OC use trend by pregnancy history (p-interaction = 0.054). OC use was stable among nulligravid [APC − 0.2% (− 3.1, 2.8%) $p = 0.88$] women with a suggestive trend toward decreasing OC use over time for women with history of pregnancy [APC − 1.6% (− 3.4, 0.2%) $p = 0.08$, Table 2]. Trends in OC use over time did not vary by categories of race, age, pregnancy history, education, or BMI in NSFG.

Trends in IUD use varied significantly by pregnancy history in NSFG (p-interaction < 0.01). IUD use increased significantly for both women with and without history of prior pregnancy, but women without pregnancy history experienced a greater annual increase at 11.0% [(2.6, 20.1%), $p < 0.02$] compared to women with prior pregnancy at 5.2% [(0.4, 10.2%), $p < 0.04$, Supplementary eFig. 1]. Other groups evaluated showed consistent patterns of increased IUD use across categories. Prior to 2011 NSFG did not contain information on IUD type. The proportion of overall IUD use was 76.5% hormonal (71.1, 81.8%) and 22.9% copper (17.4, 28.3%) in cycle 2015–17 (Supplementary eFig. 2). Since 2011 US women had higher rates of hormonal IUD use and there was no significant change in the type of IUDs used in the general population (Supplementary eFig. 3). This ratio was consistent for most subgroups except obese women who reported a greater proportion of hormonal IUD use [89.4%, (82.9, 95.9%)] compared to women overall. Sensitivity analyses restricted to contraceptive users in NSFG demonstrated that the proportion of women using IUDs increased [APC 6.3% (1.5, 11.3%), $p < 0.001$], while the proportion using OCs decreased [APC − 2.5% (− 3.3, − 1.7%), $p < 0.001$]. This was similar to previously reported rates of change for this subgroup [20, 21]. Additional sensitivity analyses adjusting NSFG analyses for whether or not participants identified as religious did not qualitatively change the observed trends.

Discussion

In our evaluation of two nationally representative US surveys, OC use declined 2% annually and IUD use increased 6.2% annually (2006–2017). Women with prior pregnancy had patterns suggesting decreasing OC use with increasing IUD use, while women without prior pregnancy had stable OC use and greater increases in IUD use. Historically, being nulligravid would have been a contraindication to IUD use, but recent guideline changes have likely led to a particularly large increase in prescriptions for these women. Meanwhile, decreasing OC use among women with prior pregnancy are potentially driving the observed trends. Due to the cross-sectional nature of this study, it is unknown whether these women are choosing to utilize IUDs or other contraceptive methods over time or are stopping contraception altogether. A combination of patient choice and physician prescribing preferences likely accounts for these changes.

Table 2 Adjusted annual percent change (APC) in oral contraceptive (OC) and intrauterine device (IUD) use in two nationally representative US surveys: NHANES (1999–2016) and NSFG (2006–2017)

	NHANES Cycles 1999-2016				NSFG Cycles 2006-2017							
	OC use				OC use				IUD use			
	Adjusted joinpoint				Adjusted joinpoint				Adjusted joinpoint			
	Weighted percent use (2016)	APC	95% CI[a]	*p* value	Weighted percent use (2017)	APC	95% CI	*p* value	Weighted percent use (2017)	APC	95% CI	*p* value
Overall current use	11.5	− 1.1	(− 2.6, 0.3)	0.10	15.1	− 2.2	(− 3.4, − 1.0)	0.011	9.7	6.2	(1.4, 11.2)	0.026
Generation of progestin												
All generations		− 1.6	(− 3.2, 0.1)	0.07								
1st generation	38.8	− 1.4	(− 2.6, 0.0)	0.044								
2nd generation	15.6	− 1.8	(− 3.8, 0.4)	0.09								
3rd generation	41.1	− 1.9	(− 4.4, 0.7)	0.13								
4th generation[b]	4.5	− 2.8	(− 12.3, 7.7)	0.51								
Race/ethnicity												
Non-Hispanic White	15.4	− 1.0	(− 2.1, 0.1)	0.07	18.2	− 0.5	(− 9.5, 9.3)	0.87	10.3	7.1	(− 5.8, 21.9)	0.19
Non-Hispanic Black	6.7	− 2.9	(− 5.5, − 0.3)	0.032	10.7	− 2.2	(− 6.0, 1.7)	0.17	8.2	7.0	(3.4, 10.7)	0.008
Mexican American/Hispanic	3.3	− 1.0	(− 3.5, 1.6)	0.38	10.7	− 1.4	(− 4.1, 1.4)	0.20	1.03	4.0	(− 4.3, 13.1)	0.23
Other	7.6	− 1.0	(− 2.7, 0.7)	0.20	10.7	− 2.5	(− 3.8, − 1.2)	0.008	6.1	6.3	(1.1, 11.8)	0.031
p-interaction[c]			0.11				0.30				0.83	
Age												
15–24 years old	17.7	0.7	(− 1.7, 3.2)	0.51	21.7	− 2.6	(− 3.9, − 1.4)	0.007	4.1	7.3	(1.8, 13.0)	0.023
25–34 years old	13.3	− 1.3	(− 3.7, 1.2)	0.26	18.3	− 2.6	(− 3.9, − 1.3)	0.008	13.1	5.3	(− 0.8, 11.8)	0.07
35–44 years old	4.6	− 1.4	(− 3.8, 1.0)	0.21	8.5	− 0.7	(− 3.4, 2.0)	0.45	12.9	5.7	(− 2.7, 14.9)	0.12
p-interaction			0.20				0.17				0.19	
History of pregnancy												
No prior pregnancy	22.3	− 0.2	(− 3.1, 2.8)	0.88	22.9	− 1.6	(− 4.6, 1.5)	0.21	4.8	11.0	(2.6, 20.1)	0.024
Prior pregnancy	6.2	− 1.6	(− 3.4, 0.2)	0.08	10.1	− 2.6	(− 3.7, − 1.6)	0.004	12.8	5.2	(0.4, 10.2)	0.040
p-interaction			0.054				0.39				0.001	
Education level												
Less than 9th grade	4.0	− 1.0	(− 3.4, 1.5)	0.37	6.0	− 2.4	(− 3.3, − 1.5)	0.004	4.1	7.7	(2.2, 13.5)	0.021
9–11th grade (No HS diploma)	1.4	− 1.7	(− 2.8, − 0.5)	0.011	12.5	− 1.3	(− 3.6, 1.2)	0.20	4.0	6.7	(− 1.7, 15.8)	0.09
High school grad/GED equivalent	7.4	− 1.4	(− 4.3, 1.5)	0.28	11.1	− 3	(− 6.2, 0.3)	0.06	9.1	4.9	(0.6, 9.4)	0.035
Some college or AA degree	10.7	0.5	(− 3.0, 4.2)	0.75	17.1	− 3.3	(− 12.6, 7.1)	0.38	8.7	7.5	(− 7.5, 24.9)	0.22
College graduate or above	15.9	− 0.6	(− 4.9, 4.0)	0.78	19.1	− 1.3	(− 6.6, 4.3)	0.51	14.5	1.0	(− 12.6, 16.7)	0.84
p-interaction			0.40				0.61				0.34	

Table 2 (continued)

	NHANES Cycles 1999-2016				NSFG Cycles 2006-2017							
	OC use				OC use				IUD use			
	Adjusted joinpoint				Adjusted joinpoint				Adjusted joinpoint			
	Weighted percent use (2016)	APC	95% CI[a]	*p* value	Weighted percent use (2017)	APC	95% CI	*p* value	Weighted percent use (2017)	APC	95% CI	*p* value
BMI[d]												
< 18.5	17.8	− 0.2	(− 2.3, 2.0)	0.85	7.7	− 2.3	(− 4.4, − 0.1)	0.046	6.1	7.1	(0.7, 13.9)	0.038
18.5–24.9	12.4	− 1.9	(− 3.9, 0.1)	0.06	19.1	− 3.3	(− 6.3, − 0.2)	0.044	11.4	6.3	(2.0, 10.7)	0.018
25–29.9	10.8	− 1.2	(− 3.2, 0.9)	0.22	13.4	− 1.5	(− 2.7, − 0.2)	0.035	11.4	4.8	(− 1.5, 11.5)	0.10
> 30	10.3	− 2.7	(− 10.5, 5.9)	0.47	11.6	− 4.6	(− 14.1, 6.1)	0.25	10.4	14.0	(10.5, 17.6)	0.001
p-interaction			0.19				0.27				0.53	

[a]Confidence intervals (CI)

[b]Trends in fourth-generation progestin use excluded the first two survey cycles since they were not available to the general public at that time

[c]P values from type 3/Wald tests for a variable representing the interaction between time and a given characteristic. Significance level for individual test $p = 0.05$

[d]Body mass index (BMI) was calculated from self-reported height and weight (in kg divided by height in m^2)

Patterns of decreasing OC use were observed for most groups and all groups showed patterns of increasing IUD use. Given the difference in average annual absolute increase in IUD use compared with the decrease in OC use, it is likely that new IUD users are not limited to prior OC users. A proportion of the difference may be attributed to women who have been intolerant of OCs and are opting for IUDs. Ovarian cancer incidence rates, which have fallen since the introduction of OCs, are likely to stabilize and may even increase with changing risk factors including decreasing OC use [36]. However, given recent increases in IUD use, which may also reduce ovarian cancer risk [15, 16], the incidence in ovarian cancer may continue to fall as more women obtain access to risk-reducing contraceptives.

The particularly large increase of IUDs in obese women (14% annually) may be due to known thromboembolic and cardiac risks associated with OC use and altered pharmacokinetics in obese women, which may decrease effectiveness [37]. Additionally, obese women may benefit from protective effects of progestins on the endometrium given their increased endometrial cancer risk [17, 18]. This may explain why obese women are more frequently prescribed hormonal IUDs. Given the substantial increase in IUD use, and large proportion of hormonal IUDs, research is needed to determine effects of hormonal IUD use on gynecologic cancer risk.

Strengths of both NHANES and NSFG are the large nationally representative population-based nature of these surveys. NHANES collection of prescription data allowed the precise documentation of current contraceptive use and formulation. However, other reproductive factors, including current use of OCs in NSFG and NHANES, and IUD use in NSFG, are based on self-report and as such may be prone to underreporting. While OC use is stable in NHANES over the entire period evaluated, when restricted to the same period as NSFG, we note a consistent decrease in OC use across the two surveys, which suggests OC use has been declining since guideline changes increased access to IUDs (Supplementary eTable 2). Importantly, we utilized OC use data from two assessment methods in NHANES and demonstrated that OC use trends derived using the prescription data alone were consistent with OC use trends derived using the combined questionnaire and prescription data. The consistency of this comparison over time provided further support that trends were comparable when questionnaire data on OC use were no longer available in the last two cycles. Non-responders may represent a different population from those studied based on age, race, education, and other factors that could influence the patterns of use for these specific groups. However, both surveys attempt to account for nonresponse with sample adjustments. Sensitivity analysis in NSFG adjusting for religious vs. non-religious did not change our interpretation of the results; however, these data were not available in NHANES. Future surveillance

efforts should attempt to capture more detailed information on religious affiliation and practice to further assess potential confounding by this factor. Finally, recall of contraceptives used intermittently or not taken daily (i.e., IUDs, intermittent OC use) may be more prone to measurement error as participants may be less likely to list these as current methods. Response rates for recent cycles of NSFG and NHANES have been 69–78 and 63–84%, respectively [21, 25].

Conclusions

In these nationally representative surveys of reproductive-aged US women, significant decreases in OC use and increases in IUD use were observed. Overall, the absolute increase of IUD use outpaced declining OC use in recent years. The potential for both OCs and IUDs to decrease gynecologic cancer risk means there may be an overall benefit (decreased gynecologic cancer risk) as more women have access to these contraceptives. More research is needed to quantify cancer risk reductions of newer formulations of OCs and hormonal IUDs. It is important to continue monitoring contraceptive trends to assess how these varying risk factors may affect the future incidence of gynecologic, breast, and other cancers.

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Declarations

Conflict of interest The authors of this manuscript do not have any conflicts of interest to disclose.

References

1. Mosher WD, Jones J (2010) Use of contraception in the United States: 1982–2008. Vital Health Stat 1(29):1–44
2. Westoff CF (1976) Trends in contraceptive practice: 1965–1973. Fam Plann Perspect 8(2):54–57
3. Russel-Briefel R, Ezzati T, Perlman J (1985) Prevalence and trends in oral contraceptive use in premenopausal females ages 15–24 years, United States, 1971–1980. Am J Public Health 75(10):1173–1176
4. Piccinino LJ, Mosher WD (1998) Trends in contraceptive use in the United States: 1982–1995. Fam Plann Perspect 30(1):4–10
5. Collaborative Group on Epidemiological Studies of Ovarian Cancer, Beral V, Doll R, Hermon C, Peto R, Reeves G (2008) Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet 371(9609):303–314
6. Collaborative Group on Hormonal Factors in Breast Cancer (1996) Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Lancet 347(9017):1713–1727
7. Michels KA, Pfeiffer RM, Brinton LA, Trabert B (2018) Modification of the associations between duration of oral contraceptive use and ovarian, endometrial, breast, and colorectal cancers. JAMA Oncol 4(4):516–521
8. Havrilesky LJ, Moorman PG, Lowery WJ et al (2013) Oral contraceptive pills as primary prevention for ovarian cancer: a systematic review and meta-analysis. Obstet Gynecol 122(1):139–147
9. Beaber EF, Buist DS, Barlow WE et al (2014) Recent oral contraceptive use by formulation and breast cancer risk among women 20 to 49 years of age. Can Res 74(15):4078–4089
10. Marchbanks PA, McDonald J, Wilson HG, Folger SG, Mandel MG, Daling JR, Bernstein L, Malone KE, Ursin G, Strom BL, Norman SA, Wingo PA, Burkman RT, Berlin JA, Simon MS, Spirtas R, Weiss LK (2002) Oral contraceptives and the risk of breast cancer. New Engl J Med 346(26):2025–2032
11. Mørch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard Ø (2017) Contemporary hormonal contraception and the risk of breast cancer. N Engl J Med 377(23):2228–2239. https://doi.org/10.1056/NEJMoa1700732
12. Silvin I (1993) Another look at the Dalkon Shield: meta-analysis underscores its problems. Contraception 48(1):1–12
13. Nelson AL, Massoudi N (2016) New developments in intrauterine device use: focus on the US. Open Access J Contracept 7:127–141
14. Centers for Disease Control and Prevention (CDC) (2010) U S medical eligibility criteria for contraceptive use, 2010. MMWR Recomm Rep 59(RR-4):1–86
15. Wheeler LJ, Desanto K, Teal SB, Sheeder J, Guntupalli SR (2019) Intrauterine device use and ovarian cancer risk: a systematic review and meta-analysis. Obstet Gynecol 134(4):791–800
16. Balayla J, Gil Y, Lasry A, Mitric C (2020) Ever-use of the intrauterine device and the risk of ovarian cancer. J Obstet Gynaecol 12:1–6. https://doi.org/10.1080/01443615.2020.1789960
17. Trimble CL, Method M, Leitao M et al (2012) Management of endometrial precancers. Obstet Gynecol 120(5):1160–1175
18. Soini T, Hurskainen R, Grénman S, Mäenpää J, Paavonen J, Pukkala E (2014) Cancer risk in women using the levonorgestrel-releasing intrauterine system in Finland. Obstet Gynecol 124(2 Pt 1):292–299
19. Williams RL, Meredith AH, Ott MA (2018) Expanding adolescent access to hormonal contraception: an update on over-the-counter, pharmacist prescribing, and web-based telehealth approaches. Curr Opin Obstet Gynecol 30(6):458–464
20. Kavanaugh ML, Jerman J, Finer LB (2015) Changes in use of long-acting reversible contraceptive methods among U.S. women, 2009–2012. Obstet Gynecol 126(5):917–927
21. Hubacher D, Kavanaugh M (2018) Historical record-setting trends in IUD use in the United States. Contraception 98(6):467–470
22. Centers for Disease Control and Prevention (CDC) (2016) National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. U.S. Department of Health

and Human Services, Centers for Disease Control and Prevention, Hyattsville
23. Division of the National Health and Nutrition Examination Surveys (2018) The National Health and Nutrition Examination Survey (NHANES) Analytic and Reporting Guidelines, 2011–2014 and 2015–2016. https://wwwn.cdc.gov/nchs/nhanes/AnalyticGuidelines.aspx. Accessed 27 Oct 2020
24. Division of the National Health and Nutrition Examination Surveys (2013) National Health and Nutrition Examination Survey: Analytic Guidelines, 1999–2010. https://wwwn.cdc.gov/nchs/data/nhanes/analyticguidelines/99-10-analytic-guidelines.pdf. Accessed 27 Oct 2020
25. Centers for Disease Control and Prevention (CDC) (2016) National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Questionnaire (or Examination Protocol, or Laboratory Protocol). U. S. Department of Health and Human Services, Centers for Disease Control and Prevention, Hyattsville
26. The Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS). National Survey of Family Growth. https://www.cdc.gov/nchs/nsfg/index.htm. Accessed 27 Oct 2020
27. The Centers for Disease Control and Prevention (CDC) (2011) National Center for Health Statistics (NCHS). 2006-2010 National Survey of Family Growth User's Guide. https://www.cdc.gov/nchs/data/nsfg/NSFG_2006-2010_UserGuide_MainText.pdf. Accessed 27 Oct 2020
28. The Centers for Disease Control and Prevention (CDC) (2014) National Center for Health Statistics (NCHS). 2011-2013 National Survey of Family Growth User's Guide. https://www.cdc.gov/nchs/data/nsfg/NSFG_2011-2013_UserGuide_MainText.pdf. Accessed 27 Oct 2020
29. The Centers for Disease Control and Prevention (CDC) (2016) National Center for Health Statistics (NCHS). 2013-2015 National Survey of Family Growth User's Guide. https://www.cdc.gov/nchs/data/nsfg/NSFG_2013_2015_UserGuide_MainText.pdf.. Accessed 27 Oct 2020
30. The Centers for Disease Control and Prevention (CDC) (2018) National Center for Health Statistics (NCHS). 2015-2017 National Survey of Family Growth User's Guide. https://www.cdc.gov/nchs/data/nsfg/NSFG_2015_2017_UserGuide_MainText.pdf. Accessed 27 Oct 2020
31. De Leo V, Musacchio MC, Cappelli V, Piomboni P, Morgante G (2016) Hormonal contraceptives: pharmacology tailored to women's health. Hum Reprod Update 22(5):634–646
32. Lin CJ, Maier J, Nwankwo C, Burley C, deBorja L, Al Aaraj Y, Lewis E, Rhem M, Nowalk MP, South-Paul J (2020) Awareness and use of contraceptive methods and perceptions of long-acting reversible contraception among White and non-White women. J Womens Health. https://doi.org/10.1089/jwh.2020.8642
33. Joinpoint Regression Program, Version 4.7.0.0 (2019) Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute
34. Kim HJ, Fay MP, Feuer EJ, Midthune DN (2000) Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 19:335–351 (correction: 2001; 20:655).
35. Division of the National Health and Nutrition Examination Surveys (2018) NHANES population control tables. https://wwwn.cdc.gov/nchs/nhanes/ResponseRates.aspx#population-totals. Accessed 27 Oct 2020
36. Webb PM, Green AC, Jordan SJ (2017) Trends in hormone use and ovarian cancer incidence in the US white and Australian women: implications for the future. Cancer Causes Control 28(5):365–370
37. Edelman AB, Cherala G, Munar MY, Dubois B, McInnis M, Stanczyk FZ, Jensen JT (2013) Prolonged monitoring of ethinyl estradiol and levonorgestrel levels confirms an altered pharmacokinetic profile in obese oral contraceptives users. Contraception 87(2):220