

# Depot Medroxyprogesterone Acetate Use and Periodontal Health in 15- to 44-Year-Old US Females

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**Background:** It has been suggested that progestins may have an inflammatory component and/or increase in prostaglandin synthesis. Thus, extended progestin use may be associated with higher risk of periodontal diseases. This study investigates the association between depot medroxyprogesterone acetate (DMPA) injectable contraception and the prevalence of periodontal diseases among US premenopausal females.

**Methods:** Data for this cross-sectional analysis comes from the 1999 to 2004 National Health and Nutrition Examination Surveys. This analysis includes 4,460 US females (15 to 44 years of age) with complete DMPA usage and periodontal status data.

**Results:** Current and past DMPA use was 4.1% and 12.0%, respectively. The prevalence of gingivitis was 53.9% for females who reported having used DMPA compared with 46.1% for DMPA never-users. Females taking DMPA were more likely to be young, single, and non-white, have a history of smoking, have lower levels of education and income, and have  $\geq 1$  live births and were less likely to visit the dentist. Using logistic regression, DMPA use was associated with an increased risk of gingivitis (odds ratio [OR] = 1.7; 95% confidence interval [CI] = 1.09 to 1.67) and periodontitis (DMPA, OR = 1.49; 95% CI = 1.01 to 2.22) after adjusting for age, race, education, poverty income ratio, dental care use, and smoking status. A significant interaction between smoking status and DMPA use was also found ( $P = 0.029$ ).

**Conclusions:** This study suggests that DMPA use may be associated with periodontal diseases. Additional investigation is warranted as a result of the disproportionate usage of DMPA among low-income populations who are at an increased risk for poor dental health. *J Periodontol* 2012;83:1008-1017.

## KEY WORDS

Epidemiology; gingivitis; medroxyprogesterone acetate; periodontitis; public health; women's health.

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Hormonal contraceptives have been reported to impact the oral health of females.<sup>1,2</sup> Oral contraceptives primarily containing estrogen have been associated with increased gingival inflammation and periodontitis, although a consensus has not been reached in the literature.<sup>3-6</sup> Although less studied, progestin-only contraceptives, which contain a synthetic version of the sex hormone progesterone, may also impact periodontal tissues.<sup>1,7,8</sup> Progesterone has been associated with changes in gingival and other intraoral tissues in females, especially during life periods such as pregnancy.<sup>9-11</sup> Furthermore, progesterone has been shown to reduce corpuscular flow rate, allowing for accumulation of inflammatory cells, increased vascular permeability,<sup>1,12</sup> and increased vascular proliferation.<sup>13,14</sup>

Depot medroxyprogesterone acetate (DMPA) injectable contraception<sup>||</sup> is a highly efficacious long-lasting progestin-only injectable contraceptive. DMPA is administered by intramuscular injection every 3 months. A national study reports that 3.0% to 12.0% of females in the United States, 15 to 44 years old, use DMPA.<sup>15</sup> The contraceptive action of DMPA results from its suppression of gonadotropin secretion, which in turn inhibits ovarian estradiol production and prevents ovarian follicular maturation and ovulation. In addition to prescribing

|| Depo-Provera, Pfizer Pharmaceutical Group, New York, NY.

DMPA for contraception, DMPA is used in the management of abnormal uterine menstrual bleeding through the prevention of the overgrowth of the uterine endometrium.<sup>16,17</sup> After 1 year of DMPA use (four injections), 50% of females experience amenorrhea.<sup>16</sup>

Females using this contraceptive method have high levels of synthetic progestins and low circulating endogenous estradiol levels, comparable to those seen in the early follicular phase of a menstrual cycle or postmenopause.<sup>18</sup> With the suppression of ovarian estradiol production, declines in bone mineral density (BMD) at the hip and spine of DMPA users has been shown to decrease by 0.5% to 3.5% after 1 year and 5.7% to 7.5% after 2 years of use compared with non-users.<sup>19-22</sup> Because of the skeletal health concerns, a black box warning was issued by the US Food and Drug Administration (FDA) stating that use should be no longer than 2 years.<sup>23</sup>

Progestin-only contraceptive use has been associated with periodontal changes in adult females.<sup>1,7,24</sup> Tilakaratne et al.<sup>8</sup> observed that females who used a progestin-only injectable contraceptive (DMPA) for >2 years had significantly higher levels of gingival inflammation and clinical attachment loss (AL) compared with non-users. In a clinical study by Seck-Diallo et al.,<sup>7</sup> females using injectable progestin-only contraceptives demonstrated more gingival inflammation, periodontal pocketing, and AL than non-users. More recently, in a prospective 6-month clinical study examining the effect of the levonorgestrel implant on the periodontium,<sup>1</sup> females using the progestin implant contraceptives exhibited a statistically significant increase in gingival probing depths (PDs) over the study period compared with non-users. However, these studies have important limitations, such as low number of DMPA users, reporting DMPA use and oral contraceptive use together, and lack of control for important periodontal disease-associated confounders.

A suggested mechanism for the effect of DMPA on periodontal tissues is that progestins in an active form may stimulate the synthesis of prostaglandins, thereby contributing to increased vascular permeability within the chronically inflamed periodontium. Another possibility is that progestins may promote tissue catabolism, possibly resulting in increased AL.<sup>25,26</sup> Because DMPA suppresses estradiol concentrations, and estrogen deprivation has been associated with tooth loss, alveolar bone loss, and AL, there is a possibility that the drug could adversely affect the periodontal structures.

Many females of all social economic backgrounds and ages use DMPA because of the convenience of the method and contraceptive efficacy.<sup>15,27-29</sup> However, approximately twice as many black females use DMPA compared with white females.<sup>27</sup> In addition, the majority of DMPA users are females of low socioeconomic status who are already at risk for in-

creased levels of gingival disease.<sup>30</sup> Given that DMPA use is common among high-risk females, it is important to learn more about potential deleterious effects on periodontal tissues. The objective of this analysis is to determine if a progestin-only contraceptive<sup>¶</sup> was associated with increased periodontal disease among females 15 to 44 years of age in the US population.

## MATERIALS AND METHODS

### Data Source

Data for this study were obtained from the 1999 to 2004 National Health and Nutrition Examination Surveys (NHANES) public use datasets. The NHANES are cross-sectional studies designed to obtain information on the health and nutritional status of the non-institutionalized population of the United States conducted by the National Center for Health Statistics. The sampling plan of each of the NHANES followed a highly stratified multistage probability design in which a sample of the US civilian, non-institutionalized population was selected to provide national estimates. Methods for the standardized interviews, dental examinations, and procedures for human protection and consent have been described in detail previously.<sup>31</sup> The number of records available for analysis varied depending on the variables used.

### Population

From the initial sample of 4,988 non-pregnant, premenopausal females (aged 15 to 44 years), 4,462 received periodontal examinations and had complete DMPA use data. This age range was used for comparability of data to existing National Survey of Family Growth data. Data were excluded for females who indicated the current use of oral contraceptives ( $n = 2$ ). Menopausal status was ascertained based on a respondent's report that her menstrual periods had not occurred within the past 12 months or stopped entirely (excluding females who were reported to be breastfeeding or pregnant). In addition, 1,812 participants had missing data in relation to other variables used in the analysis; therefore, regression analyses models were based on 2,648 females.

### DMPA Use (Exposure to Sex Steroids)

The main exposure variable, DMPA use, was determined from two questions from the reproductive health section of the examination interview conducted at the mobile examination centers (MECs).<sup>31</sup> The questions were as follows: "Have you or respondent ever used DMPA or injectables to prevent pregnancy?" and "Are you/or the respondent now using DMPA or injectables to prevent pregnancy?" The NHANES survey did not

¶ Depo-Provera, Pfizer Pharmaceutical Group.

ask respondents about duration of DMPA use or age of initiation of the contraceptive.

### **Measurement of Periodontal Conditions**

All dental examinations were conducted by trained and standardized examiners in dental units located in MECs. The periodontal status of individuals in NHANES was assessed using randomly assigned half-mouths (one maxillary and one mandibular quadrant) for each individual using a periodontal probe.<sup>#</sup> There were slight differences in the periodontal examination data between the different NHANES. The data from the 1999 to 2000 survey included AL and PD assessments at two sites per tooth, and the gingival sweep was used to assess gingival bleeding at the quadrant level. For the 2001 to 2004 survey, periodontal assessments were taken at three sites per tooth and were assessed for PD, AL, and periodontal bleeding.<sup>32,33</sup> For this study, gingival bleeding was defined as the presence or absence of gingival bleeding in  $\geq 1$  quadrants or  $\geq 1$  sites. Periodontal disease was defined as  $\geq 2$  sites with AL = 4 mm and a PD  $\geq 4$  mm following previously published reports.<sup>6,34</sup>

### **Sociodemographic Covariates**

Sociodemographic and behavioral factors that have been shown to be associated with DMPA use were evaluated for confounding and effect modification. Variables obtained from the face-to-face interviews included age, which was specified as both continuous and categorical, with six age categories. Race/ethnicity was defined as non-Hispanic black, Hispanic, and non-Hispanic white to allow comparisons with the National Survey of Family Growth.<sup>15</sup> Other race/ethnicities were excluded from the analysis. Marital status was defined as married (married or living together as married) or not married. Poverty income ratio is the ratio of reported family income category divided by the poverty income threshold. Using the suggested cut points from the NHANES III Analytic Guidelines,<sup>35</sup> three categories, low, medium, and high, were created for poverty index level in both datasets: 0.00 to 1.350, 1.351 to 3.500, and  $\geq 3.501$ . Parity was collected from the question "How many live births have you had?" Parity was coded as a categorical variable with categories being 0, 1 to 2, and  $\geq 3$  live births. Smoking status was defined as never smoked (<100 cigarettes in lifetime), former smoker (a positive answer to ever smoked but do not smoke cigarettes now), and current smoker (a positive answer to smoke now and have smoked  $\geq 100$  cigarettes in a lifetime). Education level was reported as <12 years of education, 12 years of education, or >12 years of education.

### **Statistical Analyses**

The NHANES involve complex sampling designs; therefore, all statistical analyses were performed tak-

ing into account the effect of the study design as well as incorporating the examination sampling weights. The dependent variables for this analysis were gingival bleeding and periodontal disease.

Univariate statistics were calculated for all variables to describe the variables and their distributions along with measures of unadjusted association between the periodontal outcomes (gingival bleeding/periodontitis) and other covariates of interest for the total sample. The bivariate relationships between categorical variables were assessed with the Pearson  $\chi^2$  test. The relationships between continuous and categorical variables were assessed with simple (unadjusted) linear regression models. Multiple logistic regression analysis using the manual backward selection method was used to assess the relationship between DMPA use and periodontal outcomes while controlling for other covariates. Because level of education and poverty index were highly correlated, only poverty index was used when generating the regression models.

Potential interactions between DMPA use and smoking history were also examined. Because of the complex interpretation associated with a three-level variable (current, past, and never use) for both DMPA exposure and smoking status, the interaction term was recategorized into a cross product of a dichotomous variable of smoking history (ever versus never) and DMPA use (ever versus never). The interaction term was not significant for the gingival bleeding model; therefore, only the main effects model is reported.

All analyses were conducted using a software package\*\* that can account for complex sampling design and gives adjusted variance estimations. Therefore, in all tables, the number of participants per category is unweighted, whereas all means, percentages, and odds ratios (ORs) are weighted to reflect the target population and standard errors, and 95% confidence intervals (CIs) are adjusted for sampling design.

## **RESULTS**

The study sample included 4,460 non-pregnant, premenopausal females, 15 to 44 years old, as shown in Table 1. The distribution of the subpopulation was estimated to be 65.6% white, 51.4% well-educated (more than a high school degree), and well-represented in each of the poverty index levels; >57% were not married, and 27.2% have never had a child. Approximately 4% were current DMPA users, whereas 12.1% indicated a past history of DMPA use. Nearly one third of the respondents indicated current smoking, 59.5% indicated

# NIDCR periodontal probe, National Institute of Dental and Craniofacial Research, Bethesda, MD.

\*\* Stata Data Analysis and Statistical Software v.11, StataCorp, College Station, TX.

**Table 1.****Demographic Characteristics of Females (aged 15 to 44 years) by DMPA Use: 1999 to 2004 NHANES**

Variable	Weighted % DMPA Use (mean ± SE)			
	Current (n = 157)	Past (n = 553)	Never (n = 3,750)	Total (n = 4,460)*
Gingival bleeding				
Yes	3.6 ± 0.4	14.0 ± 0.9	80.4 ± 1.0	53.9 ± 1.9
No	2.5 ± 0.4	10.0 ± 0.8	87.5 ± 1.1	46.1 ± 1.9
Periodontitis				
Yes	2.3 ± 0.4	12.3 ± 1.0	85.4 ± 1.1	10.6 ± 1.7
No	3.3 ± 0.5	8.1 ± 0.9	88.6 ± 1.0	89.4 ± 1.7
Age (years)				
15 to 19	4.2 ± 0.8	5.0 ± 0.7	90.8 ± 1.0	16.3 ± 0.4
20 to 29	4.7 ± 0.7	17.6 ± 1.4	77.7 ± 1.5	30.9 ± 0.9
30 to 39	1.8 ± 0.4	11.8 ± 1.3	86.4 ± 1.5	34.2 ± 0.8
40 to 44	1.4 ± 0.4	5.6 ± 1.3	92.0 ± 1.3	18.5 ± 0.6
Race				
Non-Hispanic white	2.7 ± 0.5	8.7 ± 0.7	88.6 ± 0.9	65.6 ± 1.6
Hispanic	3.0 ± 0.5	15.4 ± 2.0	81.6 ± 1.9	17.1 ± 1.5
Non-Hispanic black	4.0 ± 0.7	18.0 ± 1.8	78.0 ± 1.9	17.3 ± 1.2
Education				
Less than high school	4.3 ± 0.6	13.2 ± 1.2	82.5 ± 1.4	26.1 ± 0.7
High school	3.5 ± 0.8	14.9 ± 1.6	81.6 ± 1.8	22.5 ± 0.8
More than high school	2.1 ± 0.5	8.9 ± 0.8	89.0 ± 0.9	51.4 ± 1.0
Family poverty level				
0 to 1.3	4.9 ± 0.8	18.0 ± 1.7	76.1 ± 1.9	26.3 ± 1.2
1.31 to 3.49	3.3 ± 0.5	11.0 ± 1.1	85.7 ± 1.2	36.9 ± 1.1
≥3.5	1.2 ± 0.3	5.8 ± 0.8	93.0 ± 0.8	36.8 ± 1.4
Marital status				
Not married	3.7 ± 0.4	11.5 ± 0.9	84.8 ± 0.9	57.2 ± 1.1
Married/cohabitating	1.9 ± 0.3	11.4 ± 0.8	86.7 ± 1.1	42.8 ± 1.1
Parity (live births)				
0	3.1 ± 0.9	4.5 ± 1.0	92.4 ± 1.2	27.2 ± 1.2
1	6.1 ± 1.0	18.4 ± 1.6	75.5 ± 2.1	21.8 ± 0.9
2	2.2 ± 0.4	14.0 ± 1.1	83.8 ± 1.2	43.6 ± 1.4
≥3	1.7 ± 0.6	18.0 ± 2.2	80.3 ± 2.3	7.4 ± 0.6
Dental visit <2 years				
Yes	2.5 ± 0.3	9.0 ± 0.6	88.3 ± 0.7	59.5 ± 0.9
No	3.9 ± 0.5	15.9 ± 1.3	80.2 ± 1.5	40.5 ± 0.9
Smoking status				
Current	3.6 ± 0.9	17.4 ± 1.3	79.0 ± 1.7	30.2 ± 1.0
Past	2.7 ± 0.8	12.9 ± 2.3	84.4 ± 2.4	15.4 ± 0.7
Never	2.4 ± 0.3	10.6 ± 0.9	87.0 ± 0.9	54.4 ± 1.2

All demographic factors differed significantly between the three DMPA user groups using a  $\chi^2$  test for association ( $P \leq 0.003$ ).

\* Total sample weighted percents in column format.

a dental visit within the past 2 years. Using the study definitions of periodontal disease, 54% had gingival bleeding, whereas 10.6% had periodontitis.

Figure 1 shows the prevalence of DMPA use by age and ethnicity. Of the three ethnicity groups, non-Hispanic

black females demonstrate the highest use at 22.9%. When examining the ethnicity by age groups, young non-Hispanic black females, 18 to 35 years old, reported the highest use of the DMPA. For females >35 years old, a higher percentage of Hispanic females

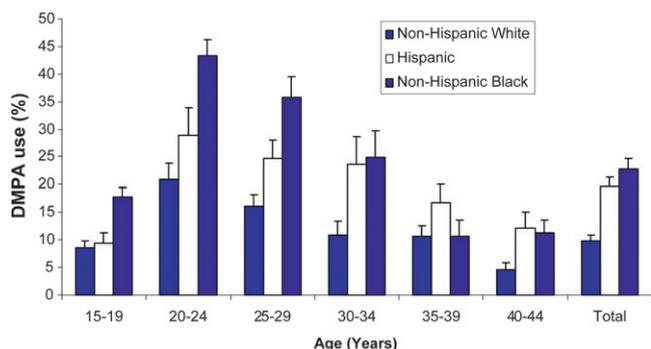
indicated use of DMPA, especially among the oldest age group of 35 to 39 years.

Table 1 shows a summary of characteristics of the sample by DMPA use. DMPA users were significantly more likely to be young, non-white, among lower education and poverty levels, and have ≥1 child and were less likely to have a dental visit within the past 2 years. The prevalence of gingivitis was significantly associated with DMPA use. Current DMPA users were more likely to have gingivitis (3.6% versus 2.5%), as were past DMPA users (14% versus 10%). Past users of DMPA were more likely to have periodontitis (12.3% versus 8.1%), whereas current users were less likely to have periodontitis.

Table 2 outlines the results from simple linear regression analyses for periodontal conditions among premenopausal adult US females, 15 to 44 years of

age, stratified by DMPA use. DMPA users were significantly younger than non-DMPA users (mean ± SE, 25.1 ± 0.58 versus 30.0 ± 0.23 years; *P* = 0.001). Gingival bleeding and PDs were significantly increased among current and past DMPA users compared with never-users. There was no significant difference in the mean number of teeth among the contraceptive groups.

The results of the logistic regression analyses presented in Table 3 indicate that, in general, females using DMPA have increased odds of poor gingival health. In the unadjusted analysis, compared with non-DMPA users, current users (OR = 1.91; 95% CI = 1.20 to 1.83) and past users (OR = 1.43; 95% CI = 1.19 to 3.02) had greater odds of gingivitis. After adjusting for covariates, including race, age, and dental use, these associations remained significant for current DMPA use (OR = 1.73; 95% CI = 1.09 to 1.67). Comparing past users and non-users, the prevalence was higher (logistic OR = 1.34; 95% CI = 0.98 to 2.67) for past users but did not reach statistical significance. Hispanic and non-Hispanic black females were estimated to have 39% to 50% higher odds of having any periodontal disease compared to non-Hispanic white females. In addition, both lower poverty index levels and not having a dental visit within the past 2 years resulted in an increased odds of having gingivitis. Smoking history was not significantly associated with a higher odds of having gingivitis. The interaction between smoking status and DMPA did not have a significant relationship with gingivitis (*P* = 0.46). Therefore, the main effects model is presented without the dichotomous recategorization



**Figure 1.** Females, aged 15 to 44 years, who reported ever using DMPA by age and race/ethnicity: 1999 to 2004 NHANES.

**Table 2.** Periodontal Characteristics of Females (aged 15 to 44 years) by DMPA Exposure (n = 4,460)

Periodontal Measure	Current Use	Past Use	Never Use	<i>P</i> value*
Number of females	157	553	3,750	
Mean age (years)	25.1 ± 0.58	28.6 ± 0.29	30.0 ± 0.23	0.001
Gingival bleeding (%)	5.2 ± 0.97	3.54 ± 0.38	2.9 ± 0.23	0.01
PD >4 mm (%)	33.6 ± 3.0	36.8 ± 1.7	27.2 ± 0.7	0.01
Max AL (mm)	1.6 ± 0.06	1.7 ± 0.04	1.3 ± 0.02	0.04
Mean AL (mm)	0.40 ± 0.04	0.46 ± 0.02	0.44 ± 0.02	0.35
Max PD (mm)	2.2 ± 0.09	2.4 ± 0.06	2.0 ± 0.04	0.04
Mean PD (mm)	1.0 ± 0.06	0.96 ± 0.03	0.90 ± 0.02	0.04
Mean number of teeth	27.7	27.8	27.3	0.43

Results are shown as mean ± SE; Max = maximum.  
\* Comparisons were performed using simple unadjusted linear regression.

**Table 3.****Logistic Regression Model for Gingival Bleeding: Odds of Having Gingival Bleeding Among US Females (aged 15 to 44 years) 1999 to 2004 NHANES (n = 2,648)**

Variable	Unadjusted OR	95% CI	Adjusted OR*	95% CI
DMPA use				
Current	1.91	1.20 to 1.83	1.73	1.09 to 1.67
Past	1.43	1.19 to 3.02	1.34	0.98 to 2.67
Never	1	NA	1	NA
Age (years)				
15 to 19	0.95	0.83 to 1.13	1.02	0.69 to 1.50
20 to 29	0.87	0.73 to 1.10	0.95	0.66 to 1.37
30 to 39	0.96	0.66 to 0.96	0.89	0.61 to 1.30
40 to 44	1	NA	1	NA
Race				
Non-Hispanic black	1.50	1.08 to 2.07	1.50	1.08 to 2.07
Hispanic	1.39	1.04 to 2.19	1.39	1.04 to 2.19
Non-Hispanic white	1	NA	1	NA
Poverty index level				
0 to 1.3	1.81	1.45 to 2.26	1.50	1.10 to 2.08
1.31 to 3.49	1.25	1.07 to 1.45	1.01	0.59 to 1.73
≥3.5	1	NA	1	NA
Dental visit <2 years				
Yes	1.91	1.59 to 2.11	1.80	1.59 to 2.11
No	1	NA	1	NA
Smoking status				
Current	0.90	0.69 to 1.18	1.00	0.76 to 1.32
Past	1.06	0.90 to 1.25	1.15	0.77 to 1.71
Never	1	NA	1	NA

\* Model adjusted for age, race, poverty income level, dental visit, and smoking status.

of smoking, and DMPA use as the collapsed variables did not show differences between current and past DMPA users with respect to increased risk of gingival inflammation.

The results of the logistic regression model examining the association of DMPA use with periodontal disease are presented in Table 4. A significant interaction between smoking status and DMPA use was found using the collapsed categorization of the two variables discussed above. There was a significant association between periodontal disease and race (specifically, non-Hispanic blacks compared with non-Hispanic whites), poverty index levels, age, and not having a dental visit within the past 2 years.

The interaction between smoking status and DMPA use is shown in Table 5. For those females who indicated never smoking, ever (current/past) use of DMPA was associated with an increased odds of having periodontal disease compared with females who indicated never use of DMPA (OR = 1.49; 95% CI = 1.01 to 2.22). For females that never used DMPA, respondents who indicated ever (current/past) smoking

have an increase odds of having periodontal diseases compared with those who never smoked (OR = 1.71; 95% CI = 1.26 to 2.38). For those females with a history of ever smoking and a history of ever DMPA use, the odds of having periodontal diseases decreased (OR = 0.55; 95% CI = 0.32 to 0.93).

## DISCUSSION

In 2004, the FDA added a “black box” into the package labeling for the injectable contraceptive DMPA warning about bone health, indicating that use of DMPA for >2 years may increase bone loss and put females at risk for osteoporotic fractures.<sup>36</sup> Furthermore, there is evidence that progestin-only contraceptives may affect periodontal health.<sup>1,7,8</sup> Hence, the aim of this study is to investigate the association between DMPA and periodontal diseases using a representative sample of US females 15 to 44 years of age. This study suggests that DMPA use may be associated with an increase in adverse periodontal changes: gingival bleeding and periodontitis.

A significant association between current DMPA use and gingival bleeding was observed after controlling

**Table 4.****Logistic Regression Model for Periodontitis: Odds of Having Periodontitis Among US Females (aged 15 to 44 years) 1999 to 2004 NHANES (n = 2,648)**

Variable	Unadjusted OR	95% CI	Adjusted OR*	95% CI
DMPA use				
Ever	1.62	1.27 to 1.92	1.49	1.01 to 2.22
Never	1	NA	1	NA
Race				
Non-Hispanic black	1.51	1.17 to 1.82	1.45	1.00 to 2.11
Hispanic	1.34	1.06 to 1.71	1.39	0.96 to 2.01
Non-Hispanic white	1	NA	1	NA
Age (years)				
20 to 29	1.71	1.36 to 2.15	1.65	1.00 to 2.62
30 to 39	3.52	2.81 to 4.54	2.43	1.89 to 3.18
40 to 44	5.82	4.61 to 7.52	4.38	3.20 to 6.01
15 to 19	1	NA	1	NA
Poverty index level				
0 to 1.3	2.32	1.33 to 3.20	1.70	1.16 to 2.47
1.31 to 3.49	1.86	1.66 to 2.55	1.51	1.19 to 1.91
>3.5	1	NA	1	NA
Dental visit <2 years				
Yes	1.59	1.38 to 1.83	1.44	1.18 to 1.76
No	1	NA	1	NA
Smoking status				
Ever	1.67	1.43 to 1.93	1.71	1.26 to 2.38
Never	1	NA	1	NA
DMPA use × smoking interaction <sup>†</sup>	0.49	0.30 to 0.79	0.55	0.32 to 0.93

\* Model controls for age, race, poverty index level, smoking status, and dental visits.

† Interaction term model for DMPA use (ever/never) and smoking (ever/never).

**Table 5.****Odds of Periodontal Disease Associated With Smoking History According to DMPA Use Among US Females (aged 15 to 44 years) 1999 to 2004 NHANES**

Variable	Adjusted OR*	95% CI
Never DMPA use and no smoking	1	NA
Ever DMPA use and no smoking	1.49	1.01 to 2.22
Never DMPA use and smoking <sup>†</sup>	1.71	1.26 to 2.38
Ever DMPA use and smoking <sup>†</sup>	0.55	0.32 to 0.93

\* Model controls for age, race, poverty index level, smoking status, and dental visits.

† Smoking is defined as ever (current/past).

for potential confounding variables (OR = 1.73; 95% CI = 1.09 to 1.67). A similar trend was observed for past DMPA users but failed to reach the significance level of  $P < 0.05$  ( $P = 0.057$ ). To the best of our knowledge, this is the first study to examine DMPA use and periodontal conditions using multivariable modeling to control for potential confounders, providing additional evidence of an association between DMPA use and gingival changes.

Using clinical periodontal measures, the study found significant differences in PDs, gingival bleeding, and AL between DMPA users and non-users. The increased PDs among DMPA users is similar to previous small clinical studies<sup>1,7</sup> that found females using the progestin implant contraceptives exhibited a statistically significant increase in gingival PDs compared with non-users. As in the study by Tilakaratne et al.,<sup>8</sup> the present study found statistically increased AL in DMPA users compared with non-users. Interestingly, for our population, the mean PDs were much lower compared with the abovementioned studies. Users of DMPA in this sample may be younger, but because the above

studies did not disclose the age of their population, it is difficult to make comparisons.

As the adjusted logistic regression model from Table 4 indicates, DMPA use has a modest association with the increased odds of periodontal disease. High systemic progestin levels associated with the use of DMPA have been shown to reduce skeletal BMD levels.<sup>22</sup> Recent reports<sup>37,38</sup> suggest that the BMD deficits are completely reversed within 1 to 3 years after discontinuation of the contraceptive. Because the majority of DMPA users are very young, this may allow for bone recovery without deleterious effects occurring in the periodontium.

The current analysis suggests that there is a strong interaction between smoking status and DMPA use on the prevalence of periodontal disease among females. Surprisingly, among DMPA users, smoking appears to decrease the risk for periodontitis. Because smoking is considered a risk factor for periodontal diseases, these results are puzzling. DMPA use and smoking may not synergistically increase the risk of periodontitis, and it can be speculated that smoking and DMPA may mask each other's effect on periodontitis. Accurate clinical diagnosis of periodontal disease has been shown to be difficult in smokers because of decreased gingival inflammation, bleeding on probing, and obstruction of periodontal probe penetration at the pocket base during examination.<sup>39</sup> Additional studies are needed to clarify this relationship and the possible effect modification of smoking on DMPA use and periodontal disease.

The sociodemographic composition of DMPA users in our study is similar to the National Survey of Family Growth estimates for contraceptive choices in females 15 to 44 years old in the United States.<sup>28</sup> The majority of DMPA users are young, non-white females of low socioeconomic status, who are more likely to smoke. Our prevalence estimates are consistent with those of Brunner Huber and Huber,<sup>40</sup> who showed that Hispanic females have a higher prevalence of DMPA use among those 35 to 44 years old. Furthermore, we found that females who use DMPA were more likely to smoke than females who had never used DMPA contraception. Females who smoke have been shown to be more likely to use implants, injectable contraceptives, and hormonal patches compared with non-smokers.<sup>40</sup> These same groups are disproportionately at higher risk for gingival bleeding and other periodontal diseases.<sup>30,41</sup> Significantly fewer current DMPA users reported visiting a dentist within the past 2 years compared with non-users (2.5% versus 4.0%), thus potentially increasing the risk of poor oral health among these females.

Compared with previous studies of this association, strengths of the current study include a large nationally representative sample that provides greater generalizability of findings across race/ethnicity and age

groups compared with periodontal-based samples and detailed covariate information. Furthermore, the use of multiple logistic regression models allowed us to control for potential confounders, increasing the validity of our outcomes.

Although the logistic model examining the increase in the prevalence of periodontitis with DMPA use demonstrated only a modest association, an increased risk attributable to the use of an injectable contraceptive requires additional evaluation. Eke et al.<sup>42</sup> reported recently that the partial-mouth periodontal examinations used in the NHANES produce underestimation of the prevalence of periodontal disease resulting in disease misclassification. The small number of DMPA users coupled with the young age of the population and the ensuing small number of periodontal cases may have affected our ability to effectively capture the association between DMPA use and periodontal disease. Furthermore, progestins, synthetic versions of the hormone progesterone, are used for both contraception and to treat dysfunctional uterine bleeding. Therefore, females using DMPA for uterine bleeding may have different population characteristics than younger females who use DMPA for contraceptive purposes. These factors could lead to non-differential misclassification among those who use DMPA and those who do not, thus attenuating the strength of the association identified in the analysis and therefore suggesting that the associations identified in this study may be even stronger than reported here.

This study was subject to another limitation. NHANES did not ask questions about the duration of DMPA use or age of initiation of the contraceptive. Consequently, we cannot determine the dose response between DMPA duration and periodontal diseases. Another limitation was the cross-sectional nature of the data. Because DMPA use and periodontal status were measured at one point in time, it is impossible to know whether the use of DMPA causes adverse periodontal changes. Furthermore, unmeasured variables related to oral health (oral hygiene measures, time since last pregnancy) or other non-contraceptive use of DMPA use may have influenced the results. Despite these limitations, this study demonstrates that poor gingival health is associated with a progestin-only contraceptive.

## CONCLUSIONS

Our study confirms and expands on the findings of previous research to suggest that DMPA use influences periodontal health. In addition, females who use DMPA may be at increased risk for poor oral health as a result of sociodemographic and lifestyle behavior factors. Future clinical studies, including oral health behaviors and duration of DMPA use, are required to evaluate the relationship between DMPA use and the incidence of periodontal diseases.

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