Potential Bias due to Excluding Oral Contraceptive Users When Estimating Menstrual Cycle Characteristics

Ganesa Wegienka¹,² and Donna Day Baird²

¹ Department of Biostatistics and Research Epidemiology, Henry Ford Health System, Detroit, MI.
² Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, US Department of Health and Human Services, Research Triangle Park, NC.

Received for publication February 25, 2003; accepted for publication May 23, 2003.

Women take oral contraceptives for contraception but also for menstrual dysfunction treatment. This raises the question of whether or not women with menstrual dysfunction are underrepresented in analyses of menstrual function because oral contraceptive users are excluded. To explore this, the authors examined the history of oral contraceptive use among 1,322 Black women and White women, aged 35–49 years, who had been randomly selected from a large health plan's membership in Washington, DC, between 1996 and 1999. The women reported whether they took oral contraceptives during their teens, twenties, and thirties, and if so, the reason they took them (prevent pregnancy, medical problem, or both). They also reported their usual menstrual cycle length when not using oral contraceptives during these decades. The prevalence of oral contraceptive use strictly for medical problems was low for both Black women and White women (4–9% of women), and the distributions of usual cycle length were similar for women who did and did not take oral contraceptives. Thus, there was little evidence of substantial bias of estimates of cycle characteristics caused by excluding oral contraceptive users from analyses of menstrual function. However, our data indicate that, with only a few additional questions, information on usual menstrual cycle characteristics can be collected and used to evaluate bias in any given study.

bias (epidemiology); contraceptives, oral; menstrual cycle

Menstrual dysfunction has financial costs including lost work time, medical consultations, and prescription and over-the-counter medications. It also can reduce the quality of life because of pain, embarrassment from menstrual overflow, and interruption of daily and sexual activities (1, 2). One important methodological issue in the study of menstrual function is the exclusion of oral contraceptive users. Because oral contraceptive formulations determine bleeding patterns, menstrual data from oral contraceptive users must be excluded. Excluding oral contraceptive users can lead to biased estimates of cycle characteristics when oral contraceptive users are different from nonusers in their normal menstrual functions. Differences seem likely since some women take oral contraceptives in order to treat menstrual dysfunctions such as hypermenorrhea and menometrorrhagia. Oral contraceptive users have been described by various studies as being more educated, of higher income, and more likely to be single and smokers compared with nonusers of a similar age (3, 4). Although there may be assumptions based on anecdotal evidence, no data have been published comparing usual menstrual characteristics for users and nonusers or on the percentage of women that use oral contraceptives to treat medical problems. Without these data, there is no way to gauge the potential impact that excluding oral contraceptive users might have on estimates of menstrual cycle characteristics. We present data from a group of Black women and White women, aged 35–49 years, who had been randomly selected from membership rolls of a prepaid health plan in Washington, DC, to explore questions about why women use oral contraceptives and what happens to estimates of menstrual cycle characteristics, specifically menstrual cycle length, after excluding oral contraceptive users.

MATERIALS AND METHODS

The data for this research come from the National Institute of Environmental Health Sciences’ Uterine Fibroid Study.

Correspondence to Dr. Ganesa Wegienka, Department of Biostatistics and Research Epidemiology, 1 Ford Place, 3 E, Detroit, MI 48202 (e-mail: gwegien1@hfhs.org).
We obtained a random sample of 2,384 health plan enrollment records from the George Washington University Health Plan (a health maintenance organization) for women who were aged 35–49 years and had telephone numbers. Of those women, 129 (5 percent) were not reachable, 150 (6 percent) declined eligibility screening, and three were not contacted as a result of error. Of 2,102 women screened, 316 (15 percent) were found to be ineligible (not female, not aged 35–49 years, not currently enrolled in the health plan, did not obtain care in Washington, DC), the majority of whom no longer obtained care at the Washington, DC site. Of the 1,786 eligible, 335 (19 percent) declined participation, and four (0.2 percent) who agreed to participate but became unreachable before a telephone interview could be completed. Thus, 1,430 (80 percent of the eligible) women participated in the study. We analyzed the responses of the Black women and White women (n = 1,322). We did not analyze the responses of women who were neither Black nor White because of small numbers (n = 108). Details about the study population’s demographic characteristics have been published elsewhere (5).

Women were asked if they had ever used birth control pills and how old they were when they started. Starting with their teen years, women were then asked at which ages they took oral contraceptives. For each decade, they were also asked: “Were you using the pill to prevent pregnancy or to treat some medical problem or both?” In addition, women were asked about their usual menstrual cycle length when they were in their twenties and when they were in their thirties, considering only the times when they were not pregnant, breastfeeding, taking birth control pills, or taking other medication that could affect their periods. Data were collected in the following categories: “26 days or less, 27–32 days, more than 32 days, or too variable to estimate.” Women were not asked about the specific oral contraceptive formulations that they used.

A small percentage of the women reported that they did not have any naturally occurring periods (because of pregnancy, nursing, hormone use, and so on) during a decade (7 percent in their twenties and 5 percent in their thirties), and these women had to be excluded from the descriptive menstrual cycle data. We did not collect information on the specific reason women did not have a naturally occurring period during a decade. We calculated the proportion of Black women and White women who used oral contraceptives to treat medical problems, and we compared usual menstrual cycle length for oral contraceptive users and nonusers.

**RESULTS**

Of the 504 White women, 82 percent reported ever using oral contraceptives, while 92 percent of the 818 Black women did. Of those who ever used oral contraceptives, the vast majority started using them before the age of 25 years, and among these early users 13 percent of Black women and 14 percent of White women reported use for a medical problem at some time during their first decade of use (table 1). Use for a medical problem was more common (approximately 27 percent) among those who started pill use after the age of 24 years, but few women started that late (table 1). Black women tended to have a younger age at first use compared with White women (table 1).

Table 2 shows the breakdown, by ethnicity, of the rates of pill use and the reason for pill use during each decade among all women (oral contraceptive users and non-oral contraceptive users). The proportion of women who took the pill strictly for a medical problem never exceeded 5 percent of women during any decade, and the proportion of women who took the pill for both a medical problem and to prevent pregnancy was similarly low (6 percent). Patterns of use for a medical problem were similar for Black women and White women. However, White women were less likely than Black women to have reported pill use during their teens and twenties, while the rates were similar when the women were in their thirties.

<table>
<thead>
<tr>
<th>Age (years) at first use</th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prevent pregnancy (%)</td>
<td>Medical problem (%)</td>
</tr>
<tr>
<td>&lt;19</td>
<td>472</td>
<td>85</td>
</tr>
<tr>
<td>20–24</td>
<td>221</td>
<td>90</td>
</tr>
<tr>
<td>25–29</td>
<td>38</td>
<td>76</td>
</tr>
<tr>
<td>30–34</td>
<td>12</td>
<td>58</td>
</tr>
<tr>
<td>35–39</td>
<td>3</td>
<td>67</td>
</tr>
</tbody>
</table>

* Percentages are for that reason within that age group and ethnicity.
group of women had little impact on the overall comparison of all oral contraceptive users with nonusers. The distribution of reported usual cycle lengths for women who took oral contraceptives was similar to the distribution for those who did not take oral contraceptives for those in both their twenties and their thirties (table 4).

### DISCUSSION

Women are prescribed oral contraceptives for not only contraception but also irregular menstrual cycles, to reduce menstrual flow, to prevent ovarian cysts, and to treat symptoms of perimenopause (6–8). Because some women take oral contraceptives to treat menstrual dysfunction, one might
expect the prevalence estimates for these conditions, estimates that are by necessity based on data from nonusers, to underestimate the true prevalence. However, our data showed that only small proportions of women took oral contraceptives strictly for noncontraceptive reasons, and the usual menstrual cycle lengths were similar for users and nonusers. Although our data are from one health care plan and do not represent the full diversity among women, the health plan membership was both ethnically and socioeconomically diverse (the health plan membership included individuals with great income and those on Medicaid; about half the membership was Black). Furthermore, the large study sample was randomly selected from the membership. However, assessing the impact of excluding oral contraceptive users in any given study is prudent. We were able to study only cycle length, but other types of menstrual dysfunction (heavy bleeding, prolonged bleeding, dysmenorrhea) could also be studied in this way.

We did not study the potential bias of analyses of risk factors for menstrual dysfunction. Excluding oral contraceptive users from risk factor analyses could create selection bias. If the relevant information is collected, adjustments can be made as prescribed by Rothman and Greenland (9).

Some researchers focus on menstrual cycle characteristics as exposures (a proxy measure for underlying endocrine function) and explore their associations with subsequent outcomes (i.e., usual menstrual cycle length and breast cancer). Our work focused on rates of menstrual function as the outcome of interest and should not be applied to analyses using menstrual cycle characteristics as proxy measures of underlying ovarian/hormonal function. However, in such cases, seeking additional information on the reasons for oral contraceptive use could also aid in evaluating the associations with subsequent disease. Perhaps the women who take the pill for irregular menses (as opposed to those taking the pill merely for contraception) have an underlying hormonal milieu that is a risk factor for a particular disease/health event. By asking the reason for their oral contraceptive use, researchers might more easily identify women with probable hormonal abnormalities.

Our data suggest that, when estimating menstrual dysfunction risk, researchers can evaluate the potential bias due to the exclusion of oral contraceptive users in future studies with the addition of only a few more questions. Data on general menstrual characteristics can be collected from both oral contraceptive users and nonusers by decade (as done in our study) or by 5-year age interval (if more detailed data are desired). Such data can be used to evaluate the potential bias from excluding oral contraceptive users.

ACKNOWLEDGMENTS

This research was funded by the intramural program at the National Institute of Environmental Health Sciences with support from the Office of Research on Minority Health, National Institutes of Health.

REFERENCES