High-risk sexual behaviors while on depot medroxyprogesterone acetate as compared to oral contraception

Deborah Bartz¹,²,⁴*, Rie Maurer³, Jessica Kremen², Jennifer M. Fortin², Elizabeth Janiak¹ and Alisa B. Goldberg¹,²

Abstract

Background: Depot medroxyprogesterone acetate (DMPA) contraceptive use is associated with an increased risk for Chlamydia infection. However, prior studies inadequately account for potential differences in sexual behavior between users of DMPA and users of other contraceptive methods. In this study we compare sexual risk-taking behavior in women using DMPA to women using oral contraceptive pills (OCP) to assess risk of Chlamydia trachomatis infection.

Methods: In this cross-sectional study of 630 reproductive-aged women seeking routine gynecologic care (449 OCP and 181 DMPA users) sexual risk-taking was evaluated by use of the Safe Sex Behavior Questionnaire, a validated measure of sexual behaviors and attitudes. All women were screened for Chlamydia. Logistic regression estimated the association of contraceptive choice, sexual behaviors, and Chlamydia infection.

Results: Oral contraceptive pill users differed from DMPA users in age, race, marital status, education level, and pregnancy history (p-values all <0.05). Oral contraceptive pill users had used their method of contraception for longer average duration (p < 0.01) and reported greater frequency of condom use (p < 0.01). Eleven (2.5%) OCP and 2 (1.1%) DMPA users had Chlamydia (p = NS).

Conclusions: Oral contraceptive pill and DMPA users differed with respect to both demographic factors and frequency of condom use. Odds of current Chlamydia infection did not differ between OCP and DMPA users when controlling for sexual risk-taking or demographic factors, though due to low Chlamydia rates in our population, this study was underpowered to detect this difference.

Keywords: Sexual behavior, Depot medroxyprogesterone acetate, Oral contraceptive pills, Chlamydia

Background

The injectable hormonal contraceptive depot medroxyprogesterone acetate (DMPA) is currently used by over 41 million women worldwide [1]. The ease of administration, high efficacy, lack of estrogen and duration of action make DMPA an attractive contraceptive for many women around the world.

Chlamydia trachomatis is the most commonly reported sexually transmitted infection (STI), and its incidence continues to rise by 3.3–4.9% per year for US women [2].

Three prospective human studies suggest that use of DMPA for contraception increases a woman's risk for Chlamydia infection, with hazard ratios (HR) for Chlamydia infection reported as high as 3.6 when compared to oral contraceptive pill users [3, 4] or contraceptive non-users [3, 5]. The authors of these studies have primarily posited physiologic changes induced by exogenous hormone administration, such as changes in the immune system or vaginal and cervical epithelia, as the cause of higher Chlamydia acquisition among users of DMPA [3, 5]. However, follow up analysis and investigation of functional change of cervical ectopy [3, 5, 6], vaginal pH [5], or cervicovaginal flora [7] have not demonstrated a difference in DMPA users as compared to non-hormonal contraception users.

* Correspondence: dbartz@partners.org

¹The Department of Obstetrics, Gynecology, and Reproductive Biology, Brigham and Women’s Hospital, 75 Francis St, Boston, MA 02115, USA
²Planned Parenthood League of Massachusetts, 1055 Commonwealth Ave, Boston, MA 02115, USA

Full list of author information is available at the end of the article

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These previous studies that have focused on a physiologic mechanism to explain the association of DMPA use and *Chlamydia* acquisition have inadequately controlled for sexual behaviors that may put DMPA users at risk for sexually transmitted infections [3–5]. Depo medroxypregesterone acetate users may differ from users of other methods or from non-contraceptors because DMPA is a simple-to-use method well-suited to women with busy schedules, chaotic lives, or intermittent access to health care. These life characteristics may be associated with higher-risk sexual behavior.

We therefore sought to investigate whether the apparent association between use of DMPA and heightened risk for *Chlamydia* acquisition could be an artifact of uncontrolled confounding variables, particularly sexual risk-taking. We chose to compare DMPA users to oral contraceptive pill (OCP) users because both methods are reversible hormonal methods that afford excellent protection against pregnancy, no protection against *Chlamydia* acquisition, and both are frequently used by young women, a population at risk for *Chlamydia* infection [8].

**Methods**

Consecutive women presenting for routine gynecologic care at a high-volume, urban reproductive health clinic were recruited to participate if they met the following criteria: were 18–49 years old, had initiated use of either DMPA or OCPs at least 1 week prior to the study visit, and could speak and read either English or Spanish. Women who were pregnant, had a prior total hysterectomy, or a recent cervical procedure (such as a colposcopically directed biopsy or cone), a potential non-behavioral risk factor for cervical infection, were ineligible. Participants may or may not have been presenting for STI testing as part of their care; the reason for the visit of all subjects was recorded. We compared categorical variables using Chi-square tests and analyzed in the exact manner as all *Chlamydia* tests performed in this clinic outside of the study during this same time period [12]. At enrollment, all participants were given a copy of their personal study number and a phone number to call a study nurse for *Chlamydia* results. This was the only way subjects could access their anonymous study results; those patients who did not call study nurse with their study number did not receive their culture results. Subjects who called and were found to be positive were required to identify themselves over the phone in order to be prescribed antibiotic therapy. Subjects who desired or had clinical indications for routine STI testing and follow-up by clinical staff had been offered additional testing under normal procedures at the clinic on the day of their visit before study enrollment. Therefore, some subjects had two *Chlamydia* cultures sent, one from their clinic visit and one from the study protocol. The IRB approved these *Chlamydia* reporting procedures.

We compared numerical variables, including the summed SSBQ score, between the two birth control groups using either t-tests or Wilcoxon Rank-Sum tests. No pattern in missing SSBQ responses was apparent and because omissions appeared to be randomly distributed in the sample, median substitution method was used for the analysis where applicable.

We compared categorical variables using Chi-square or Fisher’s exact tests. *Chlamydia* infection rates were reported with exact 95% confidence intervals. We performed logistic regression to assess the relationship between contraceptive method and *Chlamydia* infection adjusting for potential confounding variables. *P*-values and odds ratios with 95% confidence intervals are reported. All analyses were performed with SAS v9.2 statistical software (SAS Institute, Cary, NC).

**Results**

Over the course of 12 months of May 2007 to May 2008 we approached 1,869 patients. Nine hundred thirty-five were not current OCP or DMPA users and thus, did not
meet eligibility. Six hundred thirty-one of 934 eligible patients elected to participate, for a participation rate of 67.6%. The study was closed before full recruitment of the DMPA exposure arm was completed (225 intended participants) because the lower than expected *Chlamydia* rates would require an unfeasibly large sample size to detect a difference between groups. One OCP participant who did not complete half of the survey data pertaining to sexual risk-taking was excluded from analysis; the final analytic sample includes 630 study participants, 449 OCP and 181 DMPA users. Overall response rate for each question was very high with fewer than 3% of responses missing for all scale items except one, “I avoid sexual intercourse when I have sores or irritation in my genital area” (9.8% missing).

Demographic characteristics of OCP and DMPA users are summarized in Table 1; the two exposure arms differed in all demographic measures. The overall mean sexual risk-taking score as assessed by the SSBQ was not significantly different between subjects using OCPs (55.7 ± 6.9) versus DMPA (54.5 ± 7.8) (*p* = 0.09). Table 2 summarizes associations between contraceptive method and selected items on the SSBQ. Oral contraceptive users reported longer duration of current contraceptive method use (*p* < 0.01) and greater condom use (*p* < 0.01). Age of first sex was found to be earlier in DMPA users (*p* < 0.01) and fewer DMPA users co-habited with their current partners compared to OCP users (*p* < 0.01). Oral contraceptive users more frequently stated that their primary reason for visiting the clinic at the time of study enrollment was to get tested for STIs due to symptoms or suspected exposure (*p* < 0.01). Subjects who presented for STI testing in either group were more likely to test positive for *Chlamydia* (*p* < 0.01). However, the relationship between contraceptive method and *Chlamydia* infection remained non-significant after adjusting for the reason for the visit.

Eleven OCP users (2.5%, 95% CI: 1.4–4.3%) and two DMPA users (1.1%, 95% CI: 0.3–3.9%) tested positive for *Chlamydia* (*p* = NS). The mean sexual risk-taking score was not statistically different between subjects with (53.9 ± 6.9) and without (55.4 ± 7.2) *Chlamydia* infection. The lack of significant difference in the odds of *Chlamydia* infection according to contraceptive method persisted after adjusting for sexual risk-taking scores.

### Table 1 Baseline subject characteristics by birth control method used (*n* = 630)

| Characteristic                        | OCP Users (*n* = 449) | DMPA Users (*n* = 181) | P value |
|---------------------------------------|-----------------------|-------------------------|---------|
| Age in years, mean [range]            | 23 [21, 26]           | 24 [22, 27]             | 0.04    |
| Race                                  |                       |                         | <0.01   |
| White/European American               | 347 (77.3)            | 103 (56.9)              |         |
| Black/African American                | 19 (4.2)              | 38 (21.0)               |         |
| Latina                                | 23 (5.1)              | 24 (13.3)               |         |
| Other                                 | 60 (13.4)             | 16 (8.8)                |         |
| Marital Status                        |                       |                         | <0.01   |
| Single                                | 201 (44.8)            | 59 (32.6)               |         |
| Married                               | 15 (3.3)              | 15 (8.3)                |         |
| Divorced                              | 2 (0.5)               | 3 (1.7)                 |         |
| In a relationship                     | 231 (51.5)            | 104 (57.5)              |         |
| Education                             |                       |                         | <0.01   |
| High school or less                   | 24 (5.4)              | 29 (16.0)               |         |
| Some college                          | 133 (29.6)            | 72 (39.8)               |         |
| College graduate                      | 206 (46.0)            | 54 (29.8)               |         |
| Graduate or professional school       | 86 (19.2)             | 26 (14.4)               |         |
| Income (personal, annual)             |                       |                         | <0.01   |
| $9,999 or less                        | 187 (41.8)            | 50 (27.8)               |         |
| $10,000–34,999                        | 162 (36.2)            | 80 (44.4)               |         |
| $35,000 or more                       | 98 (21.9)             | 50 (27.8)               |         |
| Number of Prior Pregnancies           | 0 [0, 0]              | 1 [0, 2]                | <0.01   |
| Mean [range]                          | 89 (19.9)             | 92 (50.8)               | <0.01   |

Categorical variables are presented with frequency counts (%). Numerical variables are presented with mean [range] as noted.
Lastly, there was no significant association between the frequency of \textit{Chlamydia} infection and contraceptive method after adjusting for race and marital status.

\textbf{Discussion}

We sought to assess whether women who chose a short-term, high-maintenance contraceptive method, the daily OCP, differ in risk-taking behavior from women who chose the long-acting, low-maintenance DMPA injection. We found that DMPA and OCP users did differ in both sexual risk-taking behaviors and in demographics, such as relationship status, that may influence \textit{Chlamydia} acquisition risk. However, due to unexpectedly low \textit{Chlamydia} infection rates within our population, this study was underpowered to detect a difference in infection prevalence.

The hypothesized physiological pathway for an association between DMPA and \textit{Chlamydia} is challenged by other investigations that have found a possible protective effect [13] or no effect [14, 15] of hormonal contraception use on risk of \textit{Chlamydia} acquisition. Furthermore, while a recent meta-analysis demonstrated an increased acquisition of another sexually transmitted infection, HIV, among DMPA users, the evidence suggests that there is a behavioral component to this risk. The risk of HIV was higher in all women who use DMPA (pooled

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|p{1cm}|}
\hline
Question & OCP Users (n = 449) & DMPA Users (n = 181) & \textit{P} value \\
\hline
Condom use: & & & <0.01 \\
\hline
Never or 0% of the time & 43 (9.6) & 30 (16.7) & \\
Vary rarely-25% of the time & 129 (28.7) & 65 (36.3) & \\
25-75% of the time & 140 (31.2) & 40 (22.4) & \\
Almost always -100% of the time & 137 (30.5) & 44 (24.6) & \\
\hline
When did you start using current BC method? & & & <0.01 \\
\hline
Less than 12 months ago & 110 (24.5) & 77 (42.8) & \\
12–23 months ago & 92 (20.5) & 31 (17.2) & \\
24–48 months ago & 96 (21.4) & 39 (21.7) & \\
More than 48 months ago & 151 (33.6) & 33 (18.3) & \\
\hline
Sexually Transmitted Infection & & & 0.88 \\
\hline
Have you ever been diagnosed with a sexually transmitted infection? & & & \\
\hline
Yes & 75 (16.7) & 31 (17.2) & \\
No & 374 (83.3) & 150 (82.8) & \\
\hline
How old were you when you had sex very first time? & 17.5 ± 2.2 & 16.9 ± 2.3 & <0.01 \\
\hline
How many men have you had sex with? & 6 [3, 11] & 6 [3, 10] & 0.82 \\
\hline
Are you monogamous? & & & 0.28 \\
\hline
Yes & 365 (81.5) & 157 (86.7) & \\
No & 37 (8.2) & 11 (6.1) & \\
Not sexually active & 46 (10.3) & 13 (7.2) & \\
\hline
Are condoms effective? & & & 0.72 \\
\hline
Not at all & 6 (1.4) & 4 (2.2) & \\
Somewhat & 151 (33.6) & 61 (33.9) & \\
Very & 292 (65.0) & 115 (63.9) & \\
\hline
Have you ever been treated for a sexually transmitted infection? & & & 0.69 \\
\hline
Yes & 5 (1.1) & 3 (1.7) & \\
No & 444 (98.9) & 178 (98.3) & \\
\hline
Are you currently living with a sexual partner? & & & <0.01 \\
\hline
Yes & 133 (30.0) & 80 (44.2) & \\
No & 316 (70.4) & 101 (55.8) & \\
\hline
Reason for appointment & & & <0.01 \\
\hline
Vaginal itching/STI & 136 (30.3) & 10 (5.5) & \\
\hline
\end{tabular}
\caption{Selected Safe Sex Behavioral Questionnaire responses by birth control method used (n = 630)}
\end{table}

Categorical variables are presented with frequency counts (%). Numerical variables are presented with mean ± SD or median [Q1, Q3].
STI have behavioral risk factors that increase their risk for
Our findings suggest that women who choose DMPA may
contraceptive method for many women around the world.
Depot medroxyprogesterone acetate is an important
Conclusion
1.37 –
styles (HR 1.73, 95% CI 1.28 –
were higher from studies of women with high-risk life-
95% CI 1.10 –
uated when analysis was restricted to the eight studies
1.40, 95% CI 1.16 – 1.69) compared with use of non-
Departments recruiting from the general population (pooled HR 1.31,
5% CI 1.10 – 1.57), excluding studies from populations with high-risk sexual lifestyles such as commercial sex-
workers [16]. Estimates for HIV risk with DMPA use were higher from studies of women with high-risk life-
styles (HR 1.73, 95% CI 1.28 – 2.34 [17] and HR 3.93
1.37 – 11.2 [18]).
Our low Chlamydia rate may in part reflect bias intro-
duced by self-selection into the study population. While
we took measures to reassure patients of the anonymous
nature of data collection, given the sensitive nature of the sexual behavior questions that were queried and the
resulting patient-directed Chlamydia result reporting, it
is possible that women who considered themselves to be at
higher risk for infection chose not to participate, bias-
ing our sample towards a non-infected population. Since
our study inclusion criteria excluded patients initiating a
new contraceptive method, it is also possible that we
recruited women who had recently started their contra-
ceptive method at the clinic and who had been previ-
ously screened, diagnosed, and treated for Chlamydia as
part of a relatively recent contraceptive initiation visit.
The reliability and validity of patient-reported sexual
history data has been studied with conflicting results
[19, 20]. Our use of a validated survey instrument and
anonymous study design was intended to minimize
reporting bias and promote accuracy of behavioral self-
reports. However, only a randomized controlled trial of
contraceptive methods would be sufficient to resolve all
potential behavioral confounders in exploring the
relationship between hormonal contraception and STI
acquisition, including reporting bias that is potentially
differential with respect to predictors of interest. Several
studies have randomized subjects to hormonal versus
non-hormonal contraception and found discontinuation
and pregnancy rates similar to the general population
using these contraceptive methods [21 – 23], discounting
concerns that randomization to contraceptive method is
unethical. Furthermore, Hubacher and colleagues [24]
conducted a cross-sectional survey to assess the feasibil-
ity of randomizing women to an intrauterine device or
DMPA in order to assess STI risk in DMPA users, and
found that 70% of respondents stated they would accept
randomization into one of these treatment arms.

Conclusion
Depot medroxyprogesterone acetate is an important
contraceptive method for many women around the world.
Our findings suggest that women who choose DMPA may
have behavioral risk factors that increase their risk for
STIs, however, composite sexual risk-taking scores did
not differ between DMPA and OCP users. This study was
underpowered to detect a difference in Chlamydia rates
between users of these two contraceptive methods.
Interventions should be directed towards improved safe-sex be-
behavior amongst DMPA users. Experts at the World Health
Organization have recently reviewed the data on DMPA
and STI risk and agree that prior work suggesting an asso-
ciation between progesterone-only injectable contracep-
tion and STI acquisition have important methodological
limitations that hinder interpretation, that DMPA is still a
good method of contraception for women, and that
instead of directing patients away from this method in
order to decrease STI risk, clinicians should promote STI
preventative measures, such as male and female condoms
among DMPA users [25].

Abbreviations
DMPA: Depot medroxyprogesterone acetate; HR: Hazard ratio; OCP: Oral
contraceptive pills; SSBQ: Safe sex behavior questionnaire; STI: Sexually
transmitted infection

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Author’s contributions
DB contributed to the development of study design and survey instrument, IRB
preparation, data analysis plan and manuscript development. RM assisted with
development of data analysis plan and conduction of data analysis. JK lead
study recruitment and data collection and management. JMF contributed to
the development of study design and data collection and management. EJ
assisted with literature review, analysis planning, manuscript development. ABG
led the study question idea, development of study design and data analysis
plan, and mentorship and guidance during manuscript development. All
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Competing interests
The authors declare that they have no competing interests. The findings and
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Author details
1Department of Obstetrics, Gynecology, and Reproductive Biology, Brigham
and Women’s Hospital, 75 Francis St, Boston, MA 02115, USA. 2Planned
Parenthood League of Massachusetts, 1055 Commonwealth Ave,
Boston, MA 02115, USA. 3Center for Clinical Investigation, Brigham and
Women’s Hospital, 75 Francis St, Boston, MA 02115, USA. 41620 Tremont St,
OBC-3, Boston, MA 02120, USA.
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