PROTOCOL NAME:
Depo Provera Self-Administration Study:
Putting a Patient-Centered Practice to the Test at Planned Parenthood

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SUMMARY

This open-label, randomized parallel group clinical trial will study subcutaneous depot medroxyprogesterone acetate (DMPA sc) self-administration at two Planned Parenthood affiliates serving diverse patient populations. A total of 400 female patients (ages 15–44) requesting DMPA will be randomized to either self-administration of DMPA sc or clinic administration (usual care) in a 1:1 allocation. Subjects will be followed for one year to compare method continuation rates and patient satisfaction between arms. All subjects will receive reminders when their next injection is due. Follow-up surveys will be conducted at 6 and 12 months via secure email, phone, text messaging, or a combination to increase response rate. Adherence will be monitored by subject self-report and study outcomes will be ascertained by self-report and medical record review.

The primary study outcome is DMPA continuation at one year by self-report in both study arms. Secondary outcomes include patient-reported satisfaction with treatment; satisfaction with home use; and costs associated with contraceptive care. We hypothesize higher continuation rates among self-injection users compared to patients who receive standard care and have sufficient statistical power to detect an estimated 13% difference (80% power; one-sided α=0.05; allowing for 15% loss-to-follow-up). The study will include some minors (ages 15–17) — a population at high risk of unintended pregnancy — due to limited information available from previous studies (Williams et al. 2013). The proposed trial will be substantially larger than prior studies of self-administration.

The study is funded by a private grant from the Tara Health Foundation, with additional support requested from Pfizer in the form of one-year drug supply for all randomized study participants.

STUDY DESCRIPTION

Rationale

In the United States nearly half of all pregnancies are unintended and one-third are mistimed (Finer & Zolna 2011). Higher rates of unintended pregnancy persist in many of the subpopulations served by Planned Parenthood, including younger women ages 18–24, minorities, and low-income women. The most effective way to reduce unintended pregnancy is to increase consistent use of effective contraceptive methods. The best contraceptive method for any individual woman is the method that she is most likely to use consistently — the method that works best for her.

The National Survey of Family Growth (NSFG) estimates that approximately 4% of contraceptive users ages 15–44 in the U.S. rely on injectable contraception. This amounts to nearly 1.5 million women (Guttmacher Institute 2014). Among Planned Parenthood clients, use of injectable contraception is higher. In 2013, approximately 12% of female contraceptive clients were relying on DMPA — roughly 250,000 women and adolescents.

Recent studies demonstrate that DMPA self-injection is safe, effective, feasible, and acceptable to patients (Beasley et al. 2014; Prabhakaran & Sweet 2012; Cameron et al. 2012); however, we do not know whether self-administration results in better contraceptive continuation. Previous studies have been too small to have sufficient statistical power to detect clinically important differences between groups.

This study will build upon the strengths of prior studies to generate additional evidence on continuation of DMPA to assess whether this practice can increase continuation for both adult women and adolescents by removing barriers to care.

This study will make a contribution to the existing evidence on feasibility, satisfaction, and continuation of DMPA, with potential to immediately affect practice. If the findings are positive, the study will lead to a change to the *PPFA Medical Standards and Guidelines*, improving access and care for thousands of Planned Parenthood patients across the country. Study results will also likely influence practice outside of Planned Parenthood settings.

Objectives and Hypotheses

The primary study objective is to compare one-year method continuation rates between patients who self-administer DMPA sc outside of the clinic setting and those who receive in-clinic administration of DMPA sc. Secondary objectives are to: confirm the feasibility and acceptability of self-injection among adult and adolescent DMPA users; compare method satisfaction rates between patients who self-administer and those who receive in-clinic injections; and compare costs associated with contraceptive care across both groups.

Primary study outcome: DMPA sc continuation at one year by self-report in both the self- and clinic administration arms.

Secondary study outcomes: Patient-reported satisfaction with treatment; satisfaction with home use; cost differentials.

Primary research question: Will allowing for self-administration of DMPA sc outside of the clinic setting result in increased method continuation rates at 6 and 12 months?

Secondary research questions:

- Do adult and adolescents patients report that self-administration of DMPA sc is a feasible and satisfactory alternative to clinic administration of DMPA sc?

- What are the cost-related implications of self-administration of DMPA sc compared to clinic administration for patients, providers, and payers?

Primary Hypothesis: We hypothesize higher continuation rates among self-administration users compared to patients who receive in-clinic administration.

- Independent variable: Self-administered DMPA sc versus clinic administered DMPA sc.
- Dependent variables: DMPA continuation rates at 6 and 12 months, defined as having received 3 contraceptive injections by 26 weeks post-enrollment and 4 injections by 42 weeks post-enrollment.

Secondary Hypotheses:

Self-administration of DMPA sc is a feasible and satisfactory alternative to clinic administration of DMPA sc.

- Outcome variables: percent of patients able to successfully self-inject; participant satisfaction ratings with self-administration.

Self-administration of DMPA sc is cost effective compared to clinic administration of DMPA sc.

- Outcome variables: percent of dispensed DMPA sc used by participant; time and money spent on contracepting behaviors.

Additional Exploratory Questions:

Additional exploratory questions for which we will not specify hypotheses include:

- Do implementation challenges impact a clinic's ability to provide this option to DMPA users in the future?

- Are there other potential non-safety related harms associated with self-administration of DMPA sc compared to clinic administration? (e.g., forgoing other indicated health care services like STI testing in the event of a new sexual partner)

- Do satisfaction and/or continuation outcomes differ by age group or DMPA user status (i.e., continuers, first-time initiators, past users)?

Previous Similar Studies

Prior studies show that DMPA self-injection is effective, feasible, and acceptable to patients. Most recently, Beasley et al. (2014) conducted a randomized trial with 137 women to evaluate the feasibility, acceptability, and continuation of self-administration of DMPA sc versus clinical administration, and to confirm the therapeutic effect using trough serum levels. They found that 90 out of 91 women randomized to the self-administration group were able to correctly self-inject. Continuation rates were somewhat higher in the self-administration group (71% vs. 63%); however, this difference was not statistically significant (p=0.47) and the study did not have adequate statistical power to detect a difference of this magnitude (i.e., 8%). All of the women who reported continuous use of DMPA had serum levels in the therapeutic range, confirming the ability of women to learn self-administration, continue it successfully at home, and reliably self-report such use. This study required repeated visits in both groups to assess serum levels and therefore involved significant intervention with both groups, potentially attenuating the difference between groups.

A non-randomized study of 120 women by Cameron et al. (2012) found that 80% of self-injections were given on time, and that no injections were given beyond the acceptable 14-week interval. The authors also found that continuation rates were higher in the self-administration group than the clinic

administration group (88% vs. 72%); however, this difference was not statistically significant and again the study did not have statistical power to detect such a difference. Cameron et al. found that the majority of women who wanted to use Depo at home were able to do so; however, 20% experienced some difficulty with one or more of the self-injections due to either resistance to the medication passing through the needle (17%) or the needle detaching from the syringe (2%).

Prabhakaran and Sweet (2012) conducted a non-randomized pilot study to evaluate feasibility, continuation, and patient satisfaction with self-administered DMPA sc. This prospective study enrolled 50 women at Planned Parenthood health centers in Florida who were taught self-injection and provided with home injection kits. The continuation rate at one year was 74% and no pregnancies were reported. In addition, 87% reported self-injection to be "very easy" or "easy" and 94% said they would be likely to recommend self-injection to other women. The authors conclude that self-injection of DMPA is feasible, acceptable, and continuation is high.

Earlier studies confirm that women are interested in self-injection. Lakha et al. (2005) surveyed 176 women and found that two-thirds of those currently using DMPA expressed interest in self-administration. Of women who had discontinued DMPA in the past, 77% expressed interest in a method that would reduce the number of clinic visits and 40% would regain interest in DMPA if self-administration were an option. In a study of Lunelle, Stanwood et al. (2006) also concluded that self-injection is feasible and may result in greater satisfaction and contraceptive success.

Furthermore, the safety and feasibility of other self-administered subcutaneous injections is well documented with many different medications for both adults and adolescents (e.g., insulin, epinephrine, heparin, heparin, and methotrexate). Patient ability to learn how to safely perform subcutaneous injections and to do so with short (10-minute) teaching sessions has also been documented. Compliance and patient satisfaction with self-administration is similar to nurse-administered medications.

To our knowledge, only one study by Williams, Hensel, and Fortenberry (2013) examined self-administration with adolescent DMPA users (ages 14 and older) and found that the majority were interested in self-administration and nearly all were able to do so successfully with brief education and minimal assistance. We seek to ensure that this practice will be feasible and effective in real-world settings for a broader range of the patients we serve.

In sum, the findings of previous studies all point to greater continuation among DMPA self-administrators, but no studies have had sufficient statistical power to detect a clinically significant difference between self- and clinic administration. This study builds upon the strengths of prior studies to generate additional evidence on continuation and patient-centered outcomes to consider whether this practice is feasible and effective for both adult women and adolescents in Planned Parenthood settings.

STUDY DESIGN

This will be an open-label, randomized parallel group clinical trial to study DMPA sc self-administration at two Planned Parenthood affiliates serving diverse patient populations. A total of 400 female patients

requesting DMPA will be randomized to either self-administration of DMPA sc or clinic administration (usual care) in a 1:1 allocation. Subjects will be followed for one year to compare method continuation rates and satisfaction between arms. All subjects will receive reminders approximately two weeks before their next injection is due. Follow-up surveys will be conducted at 6 and 12 months via secure email, phone, text messaging, or a combination to increase response rate. Adherence will be monitored by subject self-report and study outcomes will be ascertained by self-report and medical record review.

We hypothesize higher continuation rates among self-administration users compared to those who receive in-clinic administration and have sufficient statistical power to detect an estimated 13% increase (80% power; one-sided α=0.05, allowing for 15% loss-to-follow-up). We project a 57% one-year continuation rate among the clinic administration group based on the findings of the CHOICE Project in St. Louis, which also provided free contraception for one year and included adolescents (Peipert et al. 2011). We project a 70% continuation rate among the self-administration group based on similar studies described above (though slightly lower due to the inclusion of adolescents in our study). Given our primary research question, and that all prior studies suggest higher continuation among women self-administering DMPA, a one-tailed hypothesis test is appropriate.

The study will include minors (ages 15–17) due to exceedingly limited information available thus far, but will not oversample adolescents. The proposed trial will be substantially larger than previous studies and the first to have adequate statistical power to detect a clinically relevant and plausible difference between self-administration and usual care. To permit some assessment of generalizability of the results, we will also calculate overall DMPA continuation rates for all DMPA users at each participating health center at the end of the study period.

Eligibility Criteria

The study will enroll females ages 15–44 requesting DMPA at participating health centers, including method initiators and continuers.

Inclusion Criteria

- Females ages 15–44
- Current or past users of DMPA or desires initiation of DMPA for contraception
- Can understand spoken and written English or Spanish
- Willing to consider/attempt DMPA self-injection
- Willing to be randomized to either self- or clinic administration of DMPA
- Do not want to become pregnant in the next 12 months
- Willing to provide contact information and to complete three surveys at baseline, 6 months, and 12 months
- Have consistent access to a working telephone, email, and Internet
- No contraindications to DMPA use

Exclusion Criteria

- Suspected or confirmed pregnancy
- Vaginal bleeding of unknown etiology
- Known or suspected breast cancer

- Acute liver disease
- High blood pressure (Systolic ≥ 160 mm Hg or diastolic ≥ 100 mm Hg)
- Known hypersensitivity to medroxyprogesterone acetate or any other components of DMPA
- Desire for pregnancy within one year

Subject Recruitment

Recruitment will begin in July 2015 and will continue for approximately six months until a combined total of 400 subjects have been enrolled (200 intervention; 200 control). Participants will be recruited from two Planned Parenthood affiliates: Planned Parenthood Gulf Coast (Houston, TX health center) and Planned Parenthood of Central and Greater Northern New Jersey (Elizabeth, NJ and Hackensack, NJ health centers).

Patients desiring DMPA will be invited to receive more information about the study. Patients who are already using DMPA or scheduled for a DMPA injection visit will be approached by a trained Research Coordinator or approved representative. Minors will be approached with their parent or guardian if present (see consent procedures below). Patients scheduled for a DMPA injection visit may also be introduced to the study by phone prior to their appointment. Existing DMPA users may also be introduced to the study using secure existing patient communications channels such as patient portals or message retrieval systems.

At both sites, patients who desire contraception but have not yet selected a method are typically seen by a health center assistant for contraceptive counseling prior to seeing a clinician. Women who present for a new contraception consultation may be invited into the study *only after they have decided to start DMPA*. Telling them about the study earlier may make them feel pressured to use DMPA given the free contraception and compensation they would receive and reduce the generalizability of study findings. Women choosing to initiate DMPA will be approached by the Research Coordinator. This may occur in counseling or exam rooms depending on clinic flow.

The Research Coordinator or approved representative will discuss the study with potentially eligible women, briefly summarizing the study in plain language and highlighting benefits of participation (See Appendix: Recruitment Talking Points & Tips). If a woman is interested in hearing more about the study, the Research Coordinator or approved representative will screen the patient for eligibility using the Eligibility Screening Checklist form (See Appendix). Patients who are ineligible or refuse to participate once screened will be tracked by the Eligibility Screening Checklist form, which will be completed for all women who are screened regardless of whether they proceed to consent and enrollment to track refusals and reasons for ineligibility. Patients who screen eligible and are interested in participating will undergo the informed consent process.

Informed Consent

The Research Coordinator or approved representative will review the appropriate consent forms with the patient. Patients should not enroll if they know they would not be interested in learning the self-administration procedure. As patient medical records may be reviewed as part of the follow up process, consent for this must be obtained. Combined Consent and HIPAA Authorization Forms will be located with the locked study materials. The Consent and HIPAA Authorization Forms (2 copies) will be reviewed

and signed after the patient has been given the chance to ask any additional questions. The person obtaining the consent will print and sign their name and fill in the date sections of the form. Patients will be offered a copy of the form.

Consent and Assent Procedures for Minors

Houston, TX Study Site. In the state of Texas minors (<18) require parental consent to participate in research unless they are pregnant, emancipated, or living apart from their parents and managing their own affairs (and age 16+) (Tex. Fam. Code. Ann. §32.003). Therefore, minors ages 15–17 will require parental consent to enroll in the study and will also assent to participate. Parental Consent and HIPAA Authorization forms and Assent Forms of a different color will be kept with locked study materials and used only for patients ages 15–17 (See Appendix). Williams, Hensel, and Fortenberry (2013) successfully enrolled 55 adolescents (≥14) in a similar study with parental consent procedures.

Requirements for parental consent will follow both IRB requirements and site-specific procedures in compliance with the applicable laws of the jurisdiction in which the research will be conducted [45 CFR 46.402(a)]. Given the low level of risk associated with the study procedures, we will request IRB approval for the consent of *one* parent or guardian. To obtain parental consent from two parents would require significant burden on study subjects and may prove difficult or impossible for many subjects depending on their home circumstances. It would also require subjects to disclose the use of contraception to both parents, which could create an additional burden and increased discomfort for adolescent subjects. Furthermore, because minors can consent on their own to family planning services (including Depo Provera), they typically do not attend appointments with their parents. Therefore, we will request IRB approval to conduct the informed consent process by telephone with one parent or guardian with written consent provided to a secure fax line or scanned email or delivered in person by the adolescent. We will also request IRB approval to introduce the research to minors by phone prior to their visit so that they can bring a parent if feasible or otherwise prepare for the consent process.

New Jersey Study Sites. In the state of New Jersey, minors ages 15 and older are not restricted in their legal rights to consent to participate in research on their own. Nevertheless, these sites will follow the same procedures outlined for the Houston site above.

Randomization and Assignment

Subjects who consent to participate will then be randomized to self-administration or standard clinic administration in a 1:1 allocation as follows. Before the study begins, the sequence for 1:1 group allocation will be predetermined stratified by study site. Separate randomization sequences will be generated for each site using randomly permuted number blocks.

Group assignments will be placed in sealed opaque envelopes and will be maintained by the Research Coordinator. The envelopes will be opened by the Research Coordinator or approved representative only after participant enrollment and informed consent. Study staff will complete and sign a Randomization Form for each randomized subject (See Appendix).

Crossover will be permitted from the self-administration arm to the clinic administration arm only. Any subject crossover will be documented by the Research Coordinator or approved representative with the subjects' ID number to permit later assessment of crossover and ITT analyses.

Due to the nature of the study, no blinding will be used.

Study Procedures

Once enrolled, all participants will be seen by a clinician. Based on study assignment, subjects will either be taught to self-inject or will be administered DMPA by qualified clinic personnel. Nurses who dispense DMPA sc (regardless of study arm) will record the name of each subject receiving the medication, her chart number, and the lot number of the medication distributed to the patient on a Study Drug Distribution Log to be maintained in the pharmacy.

Subjects who are randomized to self-administration will be taught self-administration by a clinic nurse (or other qualified personnel) following an instructions sheet based on the drug packaging insert. If willing, subjects will then self-administer DMPA sc under nurse supervision. Subjects who are able to correctly self-administer DMPA sc as assessed by the supervising nurse and who are interested in continued home self-administration will then be provided medication (3 doses of DMPA sc), a self-administration kit (includes alcohol swabs, cotton pads, bandages, mini sharps disposal container), and instructions to do so for the subsequent 3 injections along with a small calendar showing the appropriate dates for injection. The calendar will also indicate when the subject will be asked to complete each of the 2 follow-up surveys.

Subjects who are uninterested in self-administration either after the educational session or after correctly self-administering medication in the office will be permitted to crossover to the clinic administration group and remain in the study. They will be re-assigned to the clinic administration group and be followed accordingly. *Subjects will not be told ahead of time that they can opt out of their randomization assignment and remain in the study to discourage enrollment of subjects who are not actually willing to be in the self-administration group.*

Subjects new to DMPA will be started using the QuickStart protocol (per Planned Parenthood routine practice) and will be instructed to perform a provided pregnancy test in four weeks and report the result to clinic to be documented by the Research Coordinator in the subject correspondence log. Subjects who did not provide the result of the pregnancy test will be contacted by study staff to be documented in the correspondence log.

All subjects will complete an electronic baseline survey in the clinic (using tablets provided by the study) assessing demographics, sexual activity, reproductive history, and contraceptive use and satisfaction. Subject contact information will be collected for each participant including home, work, and mobile telephone numbers; home address; e-mail; and an alternate person to contact if they cannot be reached after several attempts. This information will be used for reminders and to contact the subject for follow-up surveys at 6 and 12 months following enrollment. After completing the survey, subjects will receive a re-loadable cash card (See Compensation section below).

Follow-Up Procedures
Subjects will either return to the enrollment clinic or perform self-injection every 12–14 weeks, depending on study arm. The appropriate date for injection will be indicated on the subject's instructions for injection/calendar. All subjects (both arms) will receive reminder emails and/or text messages two weeks *before* their next injection is due. Reminders will be generated by PPFA investigators using the secure Qualtrics electronic survey platform which enables programmable email and text message communications.

If a subject is uncertain if she was able to administer the entire dose of DMPA she should return to the enrollment clinic and have a complete dose administered. The event will be recorded and reported to the Pfizer Quality Complaints department. These subjects may continue to receive injections at the enrollment clinic or return to self-administration; this will be documented by the site Research Coordinator.

Subjects who are uncomfortable with self-injection at any point in the study may return to the enrollment clinic to receive their injection per usual clinic protocol (i.e. study arm crossover to usual care will be permitted and tracked). They will be asked to complete all surveys and follow-up activities and be included in the clinic administration group. Subjects should continue to complete all surveys regardless of the location at which she receives her injection.

Crossover will be permitted from the self-administration arm to the clinic administration arm only. Any subject crossover will be documented by the Research Coordinator with the subjects' ID number to permit later assessment of crossover and ITT analyses.

The Research Coordinator will provide the Principal Investigator with a list of subjects enrolled each month so that PPFA investigators can complete the appropriate follow up. Approximately two weeks *after* subjects' target injection dates, follow-up surveys will be emailed by PPFA investigators to all participants. If no survey is completed by 16 weeks after previous injection, study staff will contact the subject twice and at her alternate contact to remind them to complete the survey whether they administered DMPA or not.

Adverse Events
In the event of an adverse reaction, the Research Coordinator or approved representative will notify the Site Investigator and Principal Investigator. The subject will be provided appropriate treatment. In addition, the event will be reported to Pfizer and the FDA via the IIR SAE form. Participant surveys will also ask about difficulty or other reactions.

Compensation
Subjects will be compensated $20 via a re-loadable cash card after completing the baseline survey at the enrollment visit; $30 upon completion of the 6-month survey; and $40 upon completion of the 12-month survey, such that they can receive a total of $90 if they complete all three surveys. The initial cash card will be distributed and logged by the site Research Coordinator or approved representative upon completion of the baseline questionnaire; the remaining follow-up surveys and incentives will be managed by PPFA investigators.

Criteria for Discontinuation
All subjects will have the option to discontinue the study at any time. A subject will be discontinued from the study by the Principal Investigator only if she is unable to be contacted. There are no anticipated events that would lead to termination of the study.

Data Collection & Management
The Research Coordinator, Principal Investigator, and Data Manager who will collect, input, analyze, and otherwise handle study data, have been trained in Good Clinical Practice and HIPAA regulations. All medical records will be stored at the recruiting clinic per individual clinic protocol. All research data will be stored in locked file cabinets at the study sites. All electronic survey data will be stored on a password protected, fire-walled, secure server at PPFA. Only members of the study team will have access to this information.

Data Analysis
The Principal Investigator and Data Manager have access to a secure computer with Excel, SPSS, and STATA software. Analyses will be performed on an intent-to-treat basis. We will perform descriptive analyses of demographic variables to assess the success of randomization and characterize the study population. Chi-square and t-test analyses will be used to compare proportions and mean differences between groups. The primary analysis will compare DMPA continuation rates between the intervention and control groups at 6 and 12 months. Cox proportional hazards regression analyses will be used for survival analysis. Secondary analyses will compare satisfaction scores and time/money spent on contracepting behaviors between the two groups.

Number of Subjects and Statistical Power
The study sites will enroll a combined total N of 400 women. Individuals will be randomized to self-administration or clinic administration with a 1:1 allocation, such that 200 women will be randomized to self-injection, and 200 women to clinic administration. A 15% loss to follow-up rate will yield completed surveys from approximately 340 participants. Based on previous studies, we hypothesize greater continuation rates among self-injection users compared to patients who receive standard care and have sufficient statistical power to detect a difference of 13% or greater. While we will ask subjects about unintended pregnancies, given the high efficacy of DMPA, we will not have statistical power detect a difference between groups.

Given the primary study hypothesis that increased accessibility to DMPA through self-administration will result in higher method continuation rates and the results of prior studies, we estimate that the intervention group will have a 70% continuation rate at 12 months and the control group a 57% continuation rate. With a one-sided $\alpha=0.05$ and a $\beta=0.80$ and accounting for an approximately 15% dropout rate, completed follow-up from 338 subjects will be sufficient to detect the hypothesized difference. The study is not designed to detect statistically significant differences between adolescents and adults, or between method initiators and continuers.

STUDY DRUG

Description of drug to be studied

Subcutaneous depot medroxyprogesterone acetate will be utilized in this study. Subcutaneous DMPA is distributed by Pfizer as depo-subQ provera 104™. It is available in prefilled syringes (160mg/mL), containing 0.65 mL (104 mg) of medroxyprogesterone in sterile aqueous suspension. Each injection also contains 1.040 mg methylparaben, 0.098 mg propylparaben, 5.2 mg sodium chloride, 18.688 mg polyethylene glycol, 1.950 mg polysorbate 80, 0.451 mg monobasic sodium phosphate · H_20, 0.382 mg dibasic sodium phosphate · $12H_20$, 0.975 mg methionine, 3.250 mg providine, and water for injection. When necessary, the pH is adjusted with sodium hydroxide, hydrochloric acid, or both. Depo-subQ provera 104™ is manufactured by Pfizer Inc., 235 East 42nd Street, New York, New York 10017.

Management of study drug

Supply of Study Drug

The Sponsor (or designee) will ship study drug to the investigational sites. The initial study drug shipment will be shipped after site initiation (i.e., all required regulatory documentation has been received by the Sponsor and a contract has been executed). Subsequent study drug shipments will be made after site request for resupply. The site will confirm receipt of drug and account for each item listed on the shipping manifest.

Dispensing

The Site Investigator or designee will assume responsibility for dispensing study drug, self-administration kits, and instructions for use. They will account for each transaction on the Study Drug Accountability Log.

Storage

Study drug should be stored by the study site at controlled room temperature, 15 to 30ºC (59 to 86ºF) in a secure location. This will be monitored through a daily temperature log that captures minimum and maximum temperatures over time. If the temperature of study drug storage in the clinic/pharmacy exceeds or falls below this range, this should be reported to the Principal Investigator or designee and captured as a deviation. Subjects will be instructed to store the medication at room temperature.

Study Drug Accountability

An accurate and current accounting of the dispensing and return of study drug for each subject will be maintained on an ongoing basis by a member of the study site staff. The number of doses dispensed (and/or returned) by the subject will be recorded on the Study Drug Accountability Log. The Research Coordinator will verify these documents throughout the course of the study.

ETHICAL CONSIDERATIONS

Informed Decision-Making and Confidentiality

The investigators will ensure that the study is conducted in accordance with the International Conference on Harmonisation guidelines for Good Clinical Practice, and the Code of Federal Regulations on the

Protection of Human Subjects (45 CFR Part 46). All personnel involved in the conduct of this study have completed human subjects protection training.

The study protocol and all accompanying materials will be submitted to Chesapeake Institutional Review Board prior to initiation of the investigation. Efforts to maintain confidentiality have been outlined above and will reflect HIPAA standards.

Risks to subjects

The study involves minimal risk to participants. The safety and efficacy of the study drug is well established, as is the safety and efficacy of self-administration. The risks are commensurate with the alternative procedure which subjects are seeking, and prior studies described above demonstrated no increased risk associated with self-administration versus the available approach of clinic administration. The main risk to subjects is potential loss of confidentiality, which will be mitigated by study procedures.

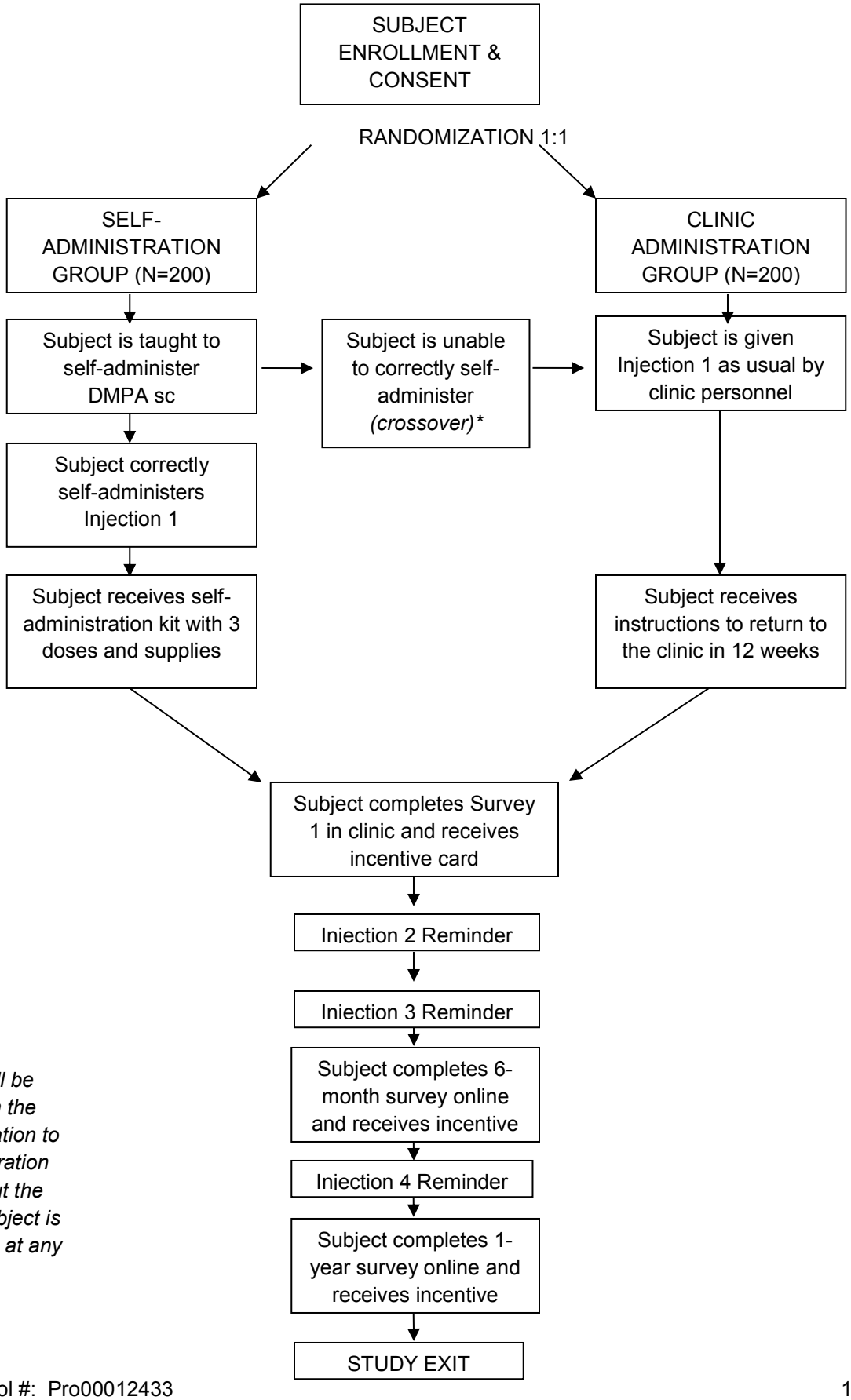
Benefits

Direct benefits include increased access to a highly effective contraceptive method to prevent unwanted pregnancy, including the possibility of reduced burdens and costs associated with contracepting behaviors. The study will also contribute to generalizable knowledge and may result in improved access to effective contraception and, therefore, reductions in unintended pregnancies and associated negative sequelae.

TIMELINE

Activity	**Q1 '15**	**Q2 '15**	**Q3 '15**	**Q4 '15**	**Q1 '16**	**Q2 '16**	**Q3 '16**	**Q4 '16**	**Q1 '17**
Develop Protocol, IRB, Training									
Recruitment and Enrollment									
Follow-Up Data Collection									
Data Analysis and Report									

STUDY SCHEMATIC



**Crossover will be permitted from the self-administration to clinic administration arm throughout the study if the subject is uncomfortable at any point.*

REFERENCES

Beasley A, White KO, Cremers S, Westhoff C. Randomized clinical trial of self versus clinical administration of subcutaneous depot medroxyprogesterone acetate. Contraception. 2014; 89(5): 352 - 356. http://dx.doi.org/10.1016/j.contraception.2014.01.026

Cameron ST, Glasier A, Johnstone A. Pilot study of home self-administration of subcutaneous depo-medroxyprogesterone acetate for contraception. Contraception. 2012; 85(5): 458 - 464. doi: 10.1016/j.contraception.2011.10.002

Finer LB, Zolna MR. Unintended pregnancy in the United States: Incidence and disparities, 2006. Contraception. 2011 November; 84(5):478–485.

Guttmacher Institute. 2014. Contraceptive Use in the United States. http://www.guttmacher.org/pubs/fb_contr_use.html. Accessed July 1, 2014.

Institute of Medicine. 2004. *Ethical Conduct of Clinical Research Involving Children.* The National Academies Press: Washington, DC.

Lakha F, Henderson C, Glasier A. The acceptability of self-administration of subcutaneous Depo-provera. Contraception. 2005; 72(1): 14 - 18. doi: 10.1016/j.contraception.2004.12.002

National Center for Health Statistics (NCHS). National Survey of Family Growth (NSFG).

Peipert JF, Zhao Q, Allsworth JE, Petrosky E, Madden T, Eisenberg D, Secura G. Continuation and satisfaction of reversible contraception. Obstet Gynecol. 2011 May;117(5):1105-13. doi: 10.1097/AOG.0b013e31821188ad.

Prabhakaran S, Sweet A. Self-administration of subcutaneous depot medroxyprogesterone acetate for contraception: feasibility and acceptability. Contraception. 2012; 85(5): 453 - 457. doi: 10.1016/j.contraception.2011.09.015

Stanwood NL, Eastwood K, Carletta A. Self-injection of monthly combined hormonal contraceptive. Contraception. 2006; 73(1): 53 - 55. doi: 10.1016/j.contraception.2005.05.02

Texas Family Code Ann. §32.003.

U.S. Code of Federal Regulations.

Williams RL, Hensel DJ, Fortenberry D. Self-administration of subcutaneous depot medroxyprogesterone acetate by adolescent women. Contraception. 2013; 88(3): 401 - 407. http://dx.doi.org/10.1016/j.contraception.2012.11.019