COLORADO MULTIPLE INSTITUTIONAL REVIEW BOARD
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Protocol #: 22-1037
Project Title: Counseling among gender diverse adolescents who use depot medroxyprogesterone

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I. Hypotheses and Specific Aims:

Recommendations regarding contraceptive counseling and reproductive health differ amongst transgender and gender diverse (TGD) youth compared to cis-gender youth. TGD youth face unique health disparities including increased risk of sexually transmitted infections, sexual abuse and violence, and unwanted pregnancies. TGD youth also face inequities within the healthcare system including lack of access to providers and delay or avoidance of care. Both patients and providers also have misconceptions around pregnancy risk in transgender individuals assigned female at birth (AFAB) who are sexually active with people assigned male at birth. Limited existing literature demonstrates the need for contraceptive counseling that moves beyond cis- and heteronormative assumptions that start with pregnancy prevention and addresses concerns at the intersection of gender identity.

Our qualitative study will focus on creating best practices regarding equitable contraceptive counseling for TGD youth. We will recruit transgender youth who are AFAB, and currently or interested in using depo medroxyprogesterone (DMPA). Through focus groups (FG) and semi-structured interviews, we hope to gain the perspectives of and experiences of TGD youth with self- and clinic- administered DMPA. We hope the results of this study can guide providers in creating best practices and more equitable contraceptive counseling for TGD youth.

With this exploratory study, we aim to

1. Understand the perspectives of, and experiences with previous contraceptive education and counseling among transmasculine youth and young adults;
2. Understand what drives interest in, and initiation or discontinuation of DMPA among transmasculine youth and young adults;
3. Understand why transmasculine youth and young adults choose in office or self-administrated DMPA;
4. Explore the acceptability and satisfaction of office or self-administered DMPA;
5. Identify the unique patient-centered communication considerations when counseling and prescribing contraceptives at the intersection of gender identity in transmasculine youth and young adults

II. Background and Significance:

The Society of Family Planning, American Academy of Pediatrics, the World Professional Association of Transgender Health (WPATH), the American Society of Reproductive Medicine (ASRM), and the Endocrine Society have all recommended counseling on contraception and reproductive health specific to transgender and gender diverse (TGD) youth. [1,2] TGD youth face disparities related to sexual health such as increased risk of STIs, HIV, sexual abuse and violence, unintended and unwanted pregnancies, and are less informed about their sexual health when compared their cisgender counterparts. [1,3,4] Further, underlying structural inequities, such as

discrimination within health care settings, and difficulty finding health systems and providers who offer gender affirming care have resulted in unmet healthcare needs, delay or avoidance of care, and persistent disparities for TGD youth, particularly within sexual health. [5,6]This is particularly illuminated by a national survey showing 71% of national OBGYN providers stated they were uncomfortable caring for TGD patients assigned female-at-birth, [7]and 50% of TGD people report having to teach their clinicians about their own health care needs, including reproductive health concerns.

Possessing baseline competency in care that is both gender-affirming and recognizes the unique needs of TGD patients can play an influential role in creating opportunities for equitable health care experiences and sexual health outcomes of TGD youth. Transgender and gender diverse youth who were assigned female-at-birth (AFAB) should receive counseling regarding contraceptive options when seeking hormone replacement therapy or gonadotropin releasing hormone for menstrual suppression, pregnancy prevention, or both.[8] However, there is minimal literature on counseling regarding the specific use of hormonal contraception in TGD youth, most focusing on fertility preservation and pregnancy prevention.[9] While these topics are important to address, reasons for hormonal contraceptive use also includes menstrual suppression. Menstrual periods may be associated with significant anxiety, worsened dysphoria, and social barriers to menstrual hygiene such as concerns of personal safety while using public restrooms.[10,11] Both patients and providers also have misconceptions around pregnancy risk in transgender AFAB individuals who are sexually active with people assigned male at birth.[8] Obtaining contraception can be difficult without invasive and potentially traumatic examinations.[12]Further, services for adolescents are constrained by issues of consent, assent, and parental support of their child's transitional or reproductive decisions.[13] This literature, though limited, demonstrates the need for contraceptive counseling that moves beyond cis- and heteronormative assumptions that start with pregnancy prevention and addresses concerns at the intersection of gender identity.

Patient-centered contraceptive counseling (PCCC) is essential in achieving equitable sexual and reproductive health and is a prominent aspect in the Quality in Family Planning Guidelines.[14] PCCC is measure of patient centeredness and language that evaluates how a patient feels they were respected as a person, were able to say what mattered most to them, if their preferences about contraceptive choice were taken seriously, and whether they were given enough information to make the best decision about their preferred methods. Despite the broader documented importance of patient-centered counseling, best practices for working with TGD youth within a patient-centered framework does not exist.[15] PCCC offers a framework to better understand the unique experiences and needs concerning contraceptive counseling in TGD youth despite its cis-normative and heteronormative underpinnings. Application of this framework to gender expansive populations also offers opportunity to assure PCCC can be more equitably framed for all populations.

Given the persistent disparities in sexual and reproductive health within TGD youth, it is crucial to investigate the unique views, experiences, beliefs, attitudes, language preferences, and desires about communication regarding contraceptive use— particularly at the intersection of gender identity. For this project, we respond to the call in the literature to center voices of TGD youth, [15] address direct patient experiences,[16] and move beyond previous work which has primarily investigated this topic through surveys and secondary data sources. Within this qualitative study we will use the underlying principles of PCCC to interview TGD adolescents and young adults about perspectives of and experiences with self- and clinic- administered DMPA. We hope the results of this study can guide providers in creating best practices and more equitable contraceptive counseling for TGD youth.

II. Preliminary Studies/Progress Report:

Limited data exists on contraceptive counseling of TGD youth. It a study of 231 TGD adolescents, 58% reported current use of contraception. The most reported method was DMPA at 35%. Although this study showed that DMPA was most reported, it did not measure the perspectives or experiences with TGD youth during contraceptive counseling. Previous studies show that TGD individuals may have their gender dysphoria worsened by repeatedly taking medication that is associated with cisgender women. [17] Additionally, TGD individuals may prefer contraception that does not require a pelvic exam and are more likely to choose a contraceptive method which suppresses menstruation. [17] Use of DMPA does not require a pelvic exam and studies have shown it suppresses ovulation. This makes DMPA a potential preferred method of contraception for TGD youth. DMPA can be prescribed as an intramuscular (IM) injection or as a subcutaneous (SC) injection. The CDC adopted the WHO recommendation for self-administered DMPA-SC in 2021. [18] Compared to the DMPA-IM dose, DMPA-SC has been proven to be associated with fewer side effects while still providing equal efficacy. [19] DMPA-SC has not approved for self-administration use by the FDA. Self-administration of DMPA-SC has been proven to result in longer continuation rates and higher satisfaction.

IV. Research Methods

A. Outcome Measure(s):

1. Understand the perspectives of, and experiences with previous contraceptive education and counseling among transmasculine youth and young adults;
2. Understand what drives interest in, and initiation or discontinuation of DMPA among transmasculine youth and young adults;
3. Understand why transmasculine youth and young adults choose in office or self-administrated DMPA;
4. Explore the acceptability and satisfaction of office or self-administered DMPA;
5. Identify the unique patient-centered communication considerations when counseling and prescribing contraceptives at the intersection of gender identity in transmasculine youth and young adults

B. Description of Population to be Enrolled:

We will recruit up to 40 transmasculine adolescent and young adult participants from two clinic sites that provide care for gender-diverse patients in the Denver metro area. Clinic sites include: (1) a centralized pediatric gender services clinic in a university-based medical center; and (2) a decentralized safety-net hospital system that sees gender diverse patients in an integrated primary care clinic setting and/or at school-based health centers. Among our clinic sites, approximately 100 out of 800 gender diverse patients have used DMPA-IM within the last year. Self-administered DMPA-SC is not currently offered at either of these clinic sites.

Inclusion criteria includes participants with fluency in English, between ages 15-21, currently receiving care at one of the clinic sites, assigned female-at-birth, identify as transgender or gender diverse (we use these terms for ease of communication in this proposal, with recognition that patients may have a range of terms and identities to describe themselves), and currently using or are interested in using DMPA. We limit our participants to English-speaking to make focus group discussion more feasible given the small sample size. Young adults up to age 21 are still seen in the pediatric clinic. For participants under 18 years of age, we will obtain a waiver of parental consent from the IRB. This is available because reproductive services are confidential for all adolescents in the state of Colorado. The University of Colorado IRB recognizes that requiring consent for studies which involve the same risks as routine contraceptive care is biased against adolescent participation. Furthermore, we anticipate that a large proportion (>50%) of the potential participants will arrive at the clinic without a parent or guardian. Hence, a requirement of parental

consent for participation is apt to differentially exclude participants, thereby biasing the findings by including only those that are supported by and can discuss contraceptive choices and sexual health with their parent/guardian and may further exclude the perspectives an already marginalized population.

C. Study Design and Research Methods

After the participant has been consented, research staff will collect clinical and demographic information from each participant.

We will collect data for this phenomenological study using focus groups and semi-structured interviews to explore the perspectives and experiences of transmasculine adolescents and young adults using DMPA and contraceptive counseling. Phenomenology, like much of qualitative inquiry, privileges the voices of participants, allowing for in-depth exploration into the significance, structure, and meaning they ascribe to their lived experiences. While they are many approaches to qualitative inquiry, hermeneutic phenomenology excels at situation persons back into the context of their unique lives and aligns with tenants of PCCC which aims to center individual experiences, intersecting identities, structural injustices, and experiences within sexual and reproductive health care.[20]

We will use purposive sampling to recruit (up to 30) participants, specifically with criterion and chain-referral strategies[21] to participate in focus groups and interviews. While the final number will depend on the adequate depth of responses to create experientially rich accounts, we are limited by the feasibility of funding for compensation and availability of participants. Purposeful sampling with a criterion strategy is appropriate because (1) it aligns with tenets of phenomenology where selected individuals represent those who have experienced the central phenomenon under study; and (2) because TGD adolescents and young adults who are interested in or using DMPA represent a relatively small proportion of the population. We will employ a chain referral strategy by collaborating with providers who will help identify and help distribute study information through virtual and/or direct communication such as emails, clinic newsletter, and use of a flyer while youth are in the clinic for appointments. Study recruitment material will have information about the project, and contact information for the study team (email, phone). Members of the study team may also be in the clinics during appointment hours to speak directly with interested participants, or answer questions about the study. We will collect contact information including a reliable preferred method of contact (telephone number and/or e-mail address). A member of the study team will offer each participant a date for an online focus group or ask about availability for interviews via an online platform.

We will collect data for this study through focus groups with participants who are already using clinic-administered intramuscular (IM) and participants who are initiating DMPA (IM or SC). At the end of the FG, all participants will be offered the opportunity to switch to self-administration of subcutaneous (SC) DMPA. If they elect initiate self-administered DMPA-SC, a trained member of our research staff will follow-up with self-injection instructions and a care kit (2 doses of DMPA-SC, a sharps container, alcohol swabs, and a calendar with the next injections). Participants will be asked to participate in a semi-structured interview after 2 self-administered injections. Semi-structured interviews will be conducted with participants who initiate self-administered DMPA-SC or change from in-clinic administration of DMPA-IM to self-administration of DMPA-SC during the study period. In this study, self-administration may also include administration by another individual outside of the clinic setting (e.g. parent/guardian).

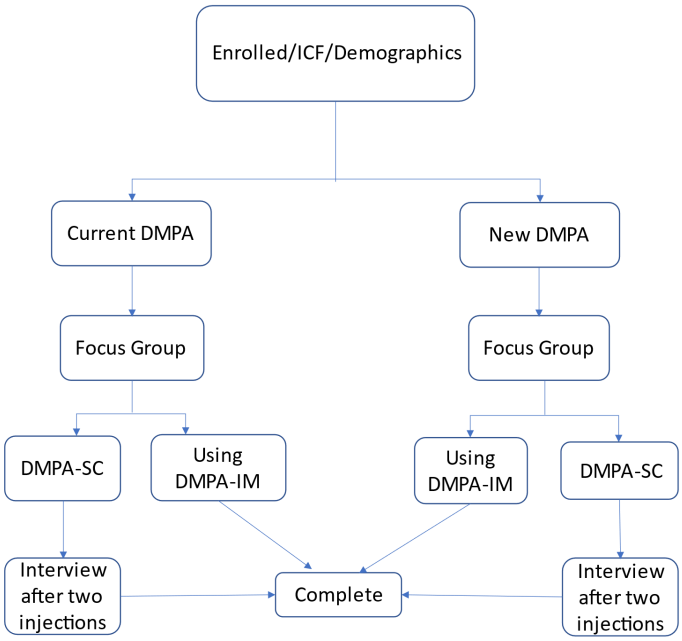
Focus Groups

Focus groups and individual interviews will be led by a member of the trans-masculine young adult community who will be trained on interviews and focus group procedures. Guides will be developed from a collaboration between experts in gender affirming care (N. Nokoff), qualitative community-based research and transgender health (R. O'Connell), community advocate (L. Dunbar) and family planning (N. Fang). Before finalization, we will conduct two short interviews with (community partners, youth, providers) to review interview guide and make recommendations with a member of the research team.

Focus groups are used for generating information on collective views and follow the tenets phenomenology to help highlight the meanings that lie behind those views. Focus groups capitalize on communication between participants, and explicitly use group interaction to generate a rich understanding of participants' experiences. For youth, and anyone who may be reluctant to be interviewed on their own, FG are useful in creating group process that generating conversation that may not come up in 1-1 interviews, and help to examine not just what participant think, but how and why and often allow for communication that resembles more day-to-conversation rather than response to direct questions. We will conduct online focus groups, which can provide adolescents a more permissive and less intimidating environment to share their experiences.[22] An online platform is also preferable given the continued COVID-19 pandemic and encourages limited in-person interaction. Focus group guides will be structured with primary questions about perspectives of, and experiences with DMPA. Questions will include experiences around contraceptive counseling, language and communication about contraceptive use, their reasons for initiation and choice of contraception and administration, Focus groups will be conducted with participants who are continuing DMPA-IM and initiating DMPA (either IM or SC). Focus groups will be composed of 4-6 participants and a facilitator. All focus groups will be conducted over an online platform (Zoom).

Interviews

For those participants who participated in the FGs and who switch to self-administration, we will ask them to also participate in a semi-structured interview after 2 injections. For those initiating DMPA during the study period and choose the SC formulation, they will participate in an individual interview after 2 injections. Interviews will focus on experience of home administration, side effects, satisfaction, and acceptability. Study participants will be compensated $50 ($100 total) for participating per focus group or individual interviews.



Optional Study Procedures.
At-home administration of DMPA-SC

Both DMPA-IM and DMPA-SC are FDA-approved for use in humans and therefore do not have an IND or IDE. Both drugs are FDA-approved for administration by a health care provider. DMPA-SC is not FDA-approved for self-administration by patients, however the 2021 update to the CDC Selected Practice Recommendations advises that DMPA-SC be made available for self-administration.[18] Self-administration of DMPA-SC in this research study should be considered exempt from IND requirements under Category #1 - Lawfully Marketed Drugs (21 CFR 312.2(b)(1)) or Biologics, because a) it is lawfully marketed in the United States; b) the research is not intended to be reported to the FDA in support of a new indication for use nor intended to be used to support any other significant change in labeling for the drug; c) the research is not intended to support a significant change in advertising for the drug; d) the research does not involve a route of administration, dosage level, use in a patient population, or other factor that significantly increases the risk (or decreases the acceptability of the risks) associated with the use of the drug; and e) the research is conducted in compliance with the marketing limitations described in 21 CFR §312.7. In particular, as outlined above, extensive data exists documenting that self-administration of DMPA-SC is associated with similar or lower rates of adverse effects compared to health care provider-administration of DMPA.

Each participant will be given the opportunity to initiate or switch to a 6 month trial of at-home administration of DMPA-SC (104 mg). For those interested in initiating or switching to this method, we will provide a 6 month supply for at-clinic pick-up or ship to their preferred location. We will also offer a telehealth visit for teaching, video, and written instructions on how to administer the medication. DMPA-SC is currently not offered at the clinical sites we are recruiting from. However, our clinical staff have been prescribing and shipping DMPA-SC to adolescents through another clinical site (BC4U) within the same hospital system. Additionally, both recruitment sites offer self-administration of other medications, including subcutaneous testosterone, as part of clinical practice.

D. Description, Risks and Justification of Procedures and Data Collection Tools:

Risk of loss of privacy and/or confidentiality: There is a risk that people who are not on the research team may see the research information. All research documentation will be stores in a locked cabinet behind two locked doors that only the research staff will have access to. All electronic information will be stored in REDCap. We will complete all necessary steps to protect all information, but confidentiality cannot be guaranteed.

Risk of DMPA use: The most common adverse reactions experienced with DMPA are changes in menstrual periods, weight gain, nausea, stomach cramping or pain, bloating dizziness, headache, tiredness, drowsiness, irritability, breast tenderness, decrease in breast size, acne, hair loss, decreased sex drive, hot flashes, joint pain, or injection site reactions.

Risk of Pregnancy: There is a rare risk, 4% chance that DMPA injection could fail, leading to an unintended pregnancy. DMPA has a failure rate of over one year of use. All participants will be counseled on this potential risk of pregnancy[23].

Injection site reactions: There is an increased risk of injection site reactions with self-administered DMPA-SC. Injection site reactions are typically mild to moderate and resolve without sequalae.

E. Potential Scientific Problems:
We anticipate some limitations in our qualitative study, given that the population may not want to engage in additional research activities beyond their gender-affirming medical care. Participants may be not representative of greater community of transgender and transmasculine adolescents since we are restricting participants to those who present to well-known gender-affirming care centers and providers, as well as restricting participants to English speakers only. Lastly, TGD youth may discontinue DMPA for a variety of reasons, including menses suppression secondary to testosterone or no longer engaging in penile/vaginal intercourse. Therefore, satisfaction and acceptability of DMPA-SC should be framed in the context of aligning with the goals of the participants rather than continuation rates or rates of unintended pregnancy.

Data Collection Tools: As each subject completes the study, we will enter all data into REDCap, which is a password-protected database that will allow us to de-identify subject-specific data. The only personnel that will have access to this data will be the PI, co-investigator, and any trained research staff on the protocol. All study-related documents including the informed consent forms will be stored in a locked cabinet in a locked room. The only people who will have access to the documents will be the PI, co-investigator, and any trained research staff on the protocol.

F. Data Analysis Plan:

All focus groups and interviews will be audio-recorded and transcribed into NVivo for coding and analysis. We will provide descriptive statistics for demographic information and code interviews accordingly to isolate any demographic difference in experience which may suggest future research questions. Data analysis of focus groups and interviews will be ongoing and iterative, allowing the team to make any changes to interview questions reflecting changes or emerging themes that may appear as data collection progresses. Thematic analysis in phenomenological research seeks to uncover the essential components of a particular experience. We will use three steps to isolate themes: (1) holistic, (2) selective, and (3) detailed. In the holistic approach the goal is to find one phrase that can capture the "fundamental or main significance of the text as whole."[17] In the selective approach, the goal is to find a number of specific phrases that stand out that seem to be thematic of the experience. In the detailed approach, a line-by-line analysis occurs with the goal of asking what each sentence or group of sentences might reveal about an experience. During this process we will begin to link themes together that have common characteristics and patterns and develop a codebook while ensuring concepts stay close as possible to participants' own words. We will also examine themes across focus groups and interviews.

G. Summarize Knowledge to be Gained:

We need a better understanding of the contraceptive practices among gender diverse patient populations. We plan to build upon this study to explore acceptability and satisfaction with different contraceptive methods for those desiring menses suppression and/or pregnancy prevention. We also aim to develop counseling aids with the goal of improving care provision for gender diverse adolescents.

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