UC San Diego

Pharmacist Provision of Medication Abortion Pilot Study

Protocol Number: 210175

National Clinical Trial (ClinicalTrials.gov) Identifier Number: NCT04956731

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1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Pharmacist Provision of Medication Abortion Pilot
Study Description:	A pilot study will be conducted among 2 pharmacists providing start to finish medication abortions to 10 patients utilizing a previously created toolkit. Following completion of the pilot, in-depth semi-structured interviews will be performed with the participating patients and pharmacists to understand their experiences with pharmacist provision of medication abortion. In addition, feedback will be elicited about ways to refine the toolkit to support the scale-up of pharmacist provision of medication abortion in the future.
Aims:	1. To pilot a toolkit for pharmacist provision of medication abortion. 2. To understand patient and provider satisfaction with pharmacist provision of medication abortion.
Study Population:	Patients desiring a medication abortion
Description of Sites Enrolling Participants:	University of California, San Diego (UCSD)
Study Duration:	1 year
Participant Duration:	6 weeks

2 INTRODUCTION

2.1 STUDY RATIONALE

We will conduct a pilot study among 2 pharmacists providing start to finish medication abortions to 10 patients utilizing a previously created toolkit. Following completion of the pilot, we will perform in-depth semi-structured interviews with the participating patients and pharmacists to understand their experiences with pharmacist provision of medication abortion. In addition, we will elicit feedback about

ways to refine the toolkit to support the scale-up of pharmacist provision of medication abortion in the future.

2.2 BACKGROUND

Approximately 90% of counties in the United States do not have a single clinic offering abortion care, and 39% of women ages 15-44 living within those counties.[1] Travel required for patients to access abortion leads to increases of out-of-pocket costs for the patient, including child care, lodging, food and lost wages in addition to delays in care.[2] In contrast, more than 90% of Americans live within 2 miles of a community pharmacy.[3] Pharmacies commonly have expanded evening hours and are open to patients on the weekends. Although the overall abortion rate in the United States has decreased, the proportion of abortions that are medication abortion has increased from 5% of all abortions in 2001 to 39% of all abortions in 2017.[1]

With the goal of increasing access to medication abortions, a sample protocol for "no touch" medication abortion was recently published, which includes recommendations for appropriate patient selection, Rh evaluation, treatment regimen and follow up care.[4] A prospective case-series conducted from 2015-2016 in the United States, Mexico and Moldova demonstrated the safety of medication abortion without pretreatment ultrasound or pelvic exam among 365 women.[5]

A previous study among 11,487 patients demonstrated the safety of abortion care provided by advanced practice clinicians. The study showed abortion complications were clinically equivalent between the newly trained advanced practice clinicians and physicians, demonstrating that expanding the pool of clinicians who can provide abortion is feasible and may increase access without compromising safety.[6]

Pharmacists have safely provided care in other aspects of reproductive health in the U.S. including provision of hormonal contraception.[7] Pharmacy dispensing of medication abortion drugs from pharmacies in Australia has led to improved access to medication abortion, specifically in rural areas.[8] Pharmacists regularly review prescriptions to ensure safety and efficacy in addition to providing patient counseling.

Recently a study in California and Washington states, including UCSD as a site, investigated the feasibility, acceptability, and effectiveness of pharmacy dispensing of mifepristone. This study used qualitative surveys to explore pharmacists' perspectives on dispensing mifepristone.[9] The researchers also evaluated the clinical outcomes of participants and satisfaction with pharmacist provision of medication abortion. The data demonstrates that pharmacists can safely dispense mifepristone safely and effectively and patients are satisfied with this care.[10] Additionally, a systematic review published in 2018 evaluated medication abortion provision in pharmacies and drug shops in low and middle-income countries by pharmacy workers and drug sellers. The review found the knowledge and counseling provided by the pharmacy workers was poor when unregulated and there was a wide variation in the advice given regarding complications. In the three studies included in the review that included a training intervention however, the results were all positive with increases in knowledge and information provision demonstrating the need for structured support for pharmacists when implementing medication abortion care.[11]

Provision of medication abortion in pharmacies could lead to increased access to medication abortion in the United States especially in rural areas without physician or other abortion providers.[12]

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Potential medical risks to medication abortion patients participating in the study are the same as those they would incur by undergoing a medication abortion outside of the study. However, this study will determine eligibility of gestational age by the patient's last menstrual period without confirmation by pelvic exam or ultrasound. This is sometimes done in clinical practice and supported by society guidelines. However, there is a risk that any patient who does not complete an ultrasound could undergo medication abortion beyond 70 days gestational age. However previous studies have discovered that less than 1% of patients who are certain of their last menstrual period present at gestational ages beyond their reported dating by last menstrual period.[16] Additionally, the mifepristone and misoprostol regimen included in this protocol has been shown to be safe and effective to 77 days gestational age, allowing for the possibility of a small underestimate in dating.[17] In addition, there is potential risk of loss of confidentiality.
Other risks to consider include:

1. Pain experienced during medication abortion
2. Heavy vaginal bleeding
3. Known side effects of mifepristone/misoprostol including nausea, vomiting, diarrhea and headache
4. Unknown risks

These risks are related to the medication abortion and not unique to provision by pharmacists or expected to be affected by pharmacist provision

During the post abortion interviews, there is a risk of emotional discomfort. Interviews will be performed in a private room. Patients and pharmacists will have the option to decline to answer any questions or to stop the interview at any point. Additionally, patients will be offered additional mental health and wellbeing resources such as social work referral or connection to the All-Options support line.

2.3.2 KNOWN POTENTIAL BENEFITS

Participants may not experience direct benefit from participation in this study. However, we are hopeful this research will begin to provide preliminary data about a novel model of medication abortion provision that has potential to greatly increase access nation-wide. We hope the findings of our proposed project will lead our audience to continue investigating additional models for abortion care. Our goal in the piloting of a created toolkit for pharmacist provision of medication abortion is to provide the support tools necessary for a larger pilot of this model. The current political climate in the United States requires that we continue to explore and investigate alternative methods to provide care to our patients. Now, more than ever, these new models can make large impacts. With further research and investigation into this model of abortion care, pharmacist provision of medication abortion has the potential to increase abortion access, especially for patients in counties without current abortion providers.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

The benefit of the proposed research potentially increasing abortion access nation-wide outweighs the minimal increase in risk of medication abortion within our pilot compared to the risk incurred by undergoing a medication abortion outside of the study.

3 OBJECTIVES AND ENDPOINTS

1. To pilot a toolkit for pharmacist provision of medication abortion.
2. To understand patient and provider satisfaction with pharmacist provision of medication abortion.

4 STUDY DESIGN

4.1 OVERALL DESIGN

We will conduct a 'proof of concept' pilot study among two pharmacists providing start to finish medication abortions utilizing a previously created toolkit[4], followed by in-depth interviews with the patients and the pharmacists providing their care to understand their experiences. We will be adapting an existing toolkit, created by the University of Washington, to assist primary care providers in their provision of medication abortion[13]. The toolkit will be finalized following analysis of pharmacist interviews assessing the acceptability and feasibility of pharmacist provision of medication abortion. These interviews and subsequent toolkit adaptations will take place under a separate IRB application. The final toolkit is expected to contain the no test protocol to be followed; medication abortion basics, such as information on mifepristone restrictions and appropriate patient criteria and selection; tools to assist in setting up abortion care clinics; implementation guidance, such as guidance on dispensing and distributing medications; protocols for follow up of patients receiving abortion care; and additional considerations, such as local abortion laws and restrictions. We will recruit patients calling to schedule medication abortion at the University of California, San Diego (UCSD) Family Planning Clinics. We have one central scheduler for the Division of Family Planning at UCSD, who has been trained in and is responsible for phone recruitment for studies. This scheduler has experience discussing patients' preferred method of abortion. Patients will be offered participation in the pilot study with provision of medication abortion with a pharmacist. The visits with the pharmacist will take place in a private room within the hospital-affiliated outpatient clinical pharmacy at the UCSD outpatient clinic in the same building as the family planning physicians provide medication abortion in the Women's Health clinic. The goal for recruitment is 10 participants. Inclusion criteria include last menstrual period less than 70 days prior to planned mifepristone administration, regular menses and no symptoms or risk factors of ectopic pregnancy.

Patients who meet the inclusion criteria will provide written informed consent with a research assistant experienced in consenting patients for abortion care prior to the start of their visit with the pharmacist. Patients who provide consent to participate will be further counseled about pregnancy options by a pharmacist. If a patient decides they do not want a medication abortion or would like to proceed with a visit with a physician first, they will be scheduled within 3 days to see a physician.

If a patient decides to proceed with a medication abortion and the participating pharmacist assesses that they are an appropriate candidate, the patient will be provided Mifepristone 200 mg. Two doses of 800 mcg of Misoprostol will also be dispensed at the visit. Patients will be instructed to take the

mifepristone within 24-48 hours and the 800 mcg of misoprostol buccally 24-48 hours after their Mifepristone. Patients whose estimated gestational age is between 64 and 70 days will be instructed to take the additional dose of 800 mcg of misoprostol 4 hours after the first dose. Patients who estimated gestational age is 63 days or less will be instructed to take the additional dose of 800 mcg of misoprostol if they do not experience at least moderate bleeding within the first 24 hours following their first misoprostol dose. For pain control, 20 tablets of 600 mg Ibuprofen will be dispensed and 20 tablets of 650mg Acetaminophen will be provided. Patient's will be instructed to alternate the Ibuprofen and Tylenol, with each medication take each medication 6 hours apart from itself.

In congruency with a "no test" protocol published by the Society of Family Planning, Rh typing and administration of anti-D immunoglobulin will not be performed if the patient reports a positive Rh type, if the patient does not desire future childbearing or if the patient declines. For all other patients, they will be offered Rh typing and administered anti-D immunoglobulin as indicated. The blood typing and Rhogam administration will be ordered and administered by the participating pharmacists. Patient participants will be provided with two high sensitivity urine pregnancy tests to be used four weeks after the abortion as well as a patient instruction sheet that will include symptoms for which to call their abortion provider. These symptoms will include severe pain, pain not responsive to provided analgesics, bleeding soaking 2 maxi pads an hour for two consecutive hours, multiple clots the size of an egg or greater, dizziness or vomiting lasting more than 2 hours, an increase in bleeding or pain 24 hours after taking the misoprostol, fever of 100.4°F or higher 24 hours or more after taking the misoprostol and vomiting within 30 minutes of taking the misoprostol. The patients will be provided with written instructions about when to call and the emergency phone numbers to reach a UCSD provider. The participating pharmacist will provide a pager number and will be the initial provider available for questions and concerns with immediately available support from the UCSD family planning physicians as indicated. The family planning fellow will also be available to the pharmacists and patients at all times via the paging system for concerns or questions. Post-abortion contraception will be available to the patient by prescription from the pharmacist for oral contraceptive pills, contraceptive rings, the contraceptive patch or Depo Provera. Patient electing for intrauterine devices, contraceptive implants or sterilization will be scheduled for an appointment with a physician. Participants will be reimbursed a $40 electronic gift card for their time and participation.

Following completed visits with the participating pharmacist, but prior to administration of Mifepristone, the patients will complete a brief 5-10 minute telehealth visit with a registered physician Mifepristone prescriber. This will allow the prescriber to confirm dating and will also offer an additional opportunity for the patient to ask questions and to review signs and symptoms for which to be concerned and how to reach a provider should they have concerns. The standard Mifepristone consent form will be signed at this time and the patient will then be instructed to take the Mifepristone orally. This will allow the pilot to meet the FDA REMs requirement on mifepristone.

Participants will be contacted one week after receiving treatment by the providing pharmacist to evaluate symptoms and bleeding. If the participant history suggests any concern for a continuing pregnancy, ectopic pregnancy or worrisome bleeding they will be referred to the UCSD Family Planning Division where they will be scheduled for an ultrasound in clinic with a physician and further evaluation as indicted in a timely fashion. If the participant does not indicate any concern for a continuing pregnancy or ectopic pregnancy and is having appropriate bleeding, they will be instructed to use the high sensitivity urine pregnancy test four weeks after taking their misoprostol. This is a standard method for follow up supported by the American College of Obstetricians and Gynecologists.[14] If the participant's first high sensitivity urine pregnancy test is positive but they have no symptoms concerning

for ongoing pregnancy, they will be instructed to perform a second, high sensitivity urine pregnancy test in one week. If the second, high sensitivity urine pregnancy test is also positive, the patient will be evaluated by a physician and ultrasound or serial serum HCGs will be utilized if indicated.

The study participants will have the option to exit the pilot and proceed with a medication abortion or procedural abortion or consultation visit with a physician at any time. Should any questions, concerns, or abnormal symptoms arise, the UCSD family planning fellow will be responsible for facilitating a timely evaluation and treatment of patients if needed, either on the phone or in the clinic. The fellow and the overseeing Family Planning attending will decide if further treatment or evaluation is warranted according to standard of care.

Pharmacists' involvement in this pilot project will be conducted under a collaborative practice agreement (CPA). UCSD has an established history of CPAs across a variety of clinical services including HIV care, anticoagulation and transplant medicine. Under the agreement with a supervising physician, pharmacists can prescribe provide care for specified conditions. CPAs are utilized in some form in all states except for Delaware, and 36 states are currently allowing pharmacists to initiate patient medications in outpatient setting via CPAs.[15] The pharmacists providing the medication abortions are not investigators nor research team members on this study.

Following completion of study recruitment and patient visits, we will continue our study by performing in-depth semi-structured interviews with the participating patients and pharmacists to understand their experiences. In addition, we will elicit feedback about ways to refine the toolkit to support the scale up of pharmacist provision of medication abortion in the future. We will follow a prepared interview guide (See Appendix A and Appendix B) The interviews will be analyzed using directed content analysis.

4.2 END OF STUDY DEFINITION

A participant is considered to have completed the study after she has completed all phases of the study including verifying completion of the medication abortion and completion of the post pilot survey and interview.

5 STUDY POPULATION

We plan to recruit 10 patients who are calling to schedule a medication abortion.

There will be no limitations of gender identity or ethnic background for the patients recruited. Only people assigned female at birth who have a uterus, regardless of current gender identity, can become pregnant and, therefore, will be included.

5.1 INCLUSION CRITERIA

In order to participate in the pilot study, the patients must meet the following inclusion criteria:

1. Age 18 or older
2. Pregnancy must be confirmed by either patient report of a positive urine pregnancy test, serum pregnancy test or ultrasound
3. Patient's last menstrual period (LMP) must be less than 70 days before the anticipated date of mifepristone administration
4. Patient must be certain of their LMP within 7 days and have regular menses
5. Patient has no symptoms or risk factors for ectopic pregnancy including bleeding or spotting in the week before their visit, prior ectopic pregnancy, significant pelvic pain the last week, prior

permanent contraception or tubal surgery, current intrauterine device (IUD) in place or IUD in place at time of conception.

5.2 EXCLUSION CRITERIA

Patients may not participate in the proposed pilot if they meet any other following exclusion criteria:

1. Any contraindications to medication abortion, as reported on their medical history. These contraindicated include:
   a) Hemorrhagic bleeding disorder
   b) Current anticoagulation therapy
   c) Chronic adrenal failure
   d) Long-term systemic corticosteroid therapy
   e) Inherited porphyria
   d) Allergy to misoprostol or mifepristone
2. Any patient with complex medical conditions will also be excluded from this initial pilot. These medical conditions include:
   a) Poorly controlled hypertension as defined a history of systolic blood pressure >160 or diastolic blood pressure >110 or patients requiring two or more antihypertensive medication to control their blood pressure. This will be exclusion criteria for the study but it not a standard exclusion criteria for medication abortion
   b) Poorly controlled diabetes as defined by a known history of Type 1 or Type 2 diabetes with history of finger stick blood sugar >200 or HbA1c>10 in the last 6 months. This will be exclusion criteria for the study but it not a standard exclusion criteria for medication abortion
   c) Hepatic or renal failure
   d) History of solid organ transplant
   e) 4 or more cesarean sections
   f) Allergy to NSAIDs.

5.3 SCREEN FAILURES

For individuals who do not meet the criteria for participation in this trial (screen failure) due to not meeting eligibility requirements, they will be schedule within one week in a UCSD Family Planning physician clinic for pregnancy evaluation and options counseling. No identifying information will be collected from screen failures.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION

Pharmacist provision of medication abortion.

6.2 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

This pilot study will not be randomized or blinded.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

If a participant chooses not to move forward with pharmacist provision of medication abortion, she will be offered scheduling in either a UCSD Family Planning clinic for abortion care or in an obstetric clinic for ongoing obstetric care.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants may withdraw voluntarily from the study at any time. The PI or study team will not withdraw anyone from the study without specific request from the participant. Medical care will be provided by the patient's clinician as standard of care in the case of study withdrawal.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if she fails to return for any scheduled visits or fails to complete her post pilot survey and interview and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to respond to surveys or return for the required study visit:

- The research coordinator will attempt to contact the participant, re-send surveys and reschedule the missed visit within one week and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant, including 3 telephone calls or texts. These contact attempts should be documented in the participant's study file.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 EFFICACY ASSESSMENTS

Participants will be contacted one week after receiving treatment by the providing pharmacist to evaluate symptoms and bleeding. If the participant history suggests any concern for a continuing pregnancy, ectopic pregnancy or worrisome bleeding they will be referred to the UCSD Family Planning Division where they will be scheduled for an ultrasound in clinic with a physician and further evaluation as indicted in a timely fashion. If the participant does not indicate any concern for a continuing pregnancy or ectopic pregnancy and is having appropriate bleeding, they will be instructed to use the high sensitivity urine pregnancy test four weeks after taking their misoprostol. This is a standard method for follow up supported by the American College of Obstetricians and Gynecologists.[14] If the participant's first high sensitivity urine pregnancy test is positive but they have no symptoms concerning for ongoing pregnancy, they will be instructed to perform a second, high sensitivity urine pregnancy test in one week. If the second, high sensitivity urine pregnancy test is also positive, the patient will be evaluated by a physician and ultrasound or serial serum HCGs will be utilized if indicated.

8.2 SAFETY AND OTHER ASSESSMENTS

A Data Safety and Monitoring Board (DSMB) is not planned for this small pilot study.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

The FDA definition of an Adverse event is any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

An adverse event (AE) or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Related** – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.

- **Not Related** – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

OR

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study intervention administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the study intervention (DE challenge) should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge procedure if necessary.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.
- **Potentially Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study intervention) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

8.3.3.3 EXPECTEDNESS

The PI will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, by communication from the participant to the study team, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.5 ADVERSE EVENT REPORTING

All adverse events will be reported to th UCSD IRB. The management of information that is relevant to the protection of participants including adverse events, UPRs, protocol violations/deviations, interim results and protocol modifications will be the responsibility of the PI.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

All serious adverse events will be reported to th UCSD IRB. The management of information that is relevant to the protection of participants including adverse events, UPRs, protocol violations/deviations, interim results and protocol modifications will be the responsibility of the PI.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

The UCSD IRB provide guidance to the PI on informing participants regarding AEs and SAEs as needed.

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS (UP)

Unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEM REPORTING

The investigators will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the lead principal investigator (PI). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported to the IRB within reasonable timing of the investigator becoming aware of the problem.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

The IRB at each site will provide guidance to PIs on informing participants regarding UPs as needed.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Not applicable

9.2 SAMPLE SIZE DETERMINATION

The sample size (N=10) was chose as a sample of convenience as this was a proof concept pilot

9.3 POPULATIONS FOR ANALYSES

All patients (N=10) will be included in the single sample

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

Participants will be contacted one week after receiving treatment by the providing pharmacist to evaluate symptoms and bleeding. If the participant history suggests any concern for a continuing pregnancy, ectopic pregnancy or worrisome bleeding they will be referred to the UCSD Family Planning

Division where they will be scheduled for an ultrasound in clinic with a physician and further evaluation as indicted in a timely fashion. If the participant does not indicate any concern for a continuing pregnancy or ectopic pregnancy and is having appropriate bleeding, they will be instructed to use the high sensitivity urine pregnancy test four weeks after taking their misoprostol. This is a standard method for follow up supported by the American College of Obstetricians and Gynecologists.[14] If the participant's first high sensitivity urine pregnancy test is positive but they have no symptoms concerning for ongoing pregnancy, they will be instructed to perform a second, high sensitivity urine pregnancy test in one week. If the second, high sensitivity urine pregnancy test is also positive, the patient will be evaluated by a physician and ultrasound or serial serum HCGs will be utilized if indicated.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Following completion of study recruitment and patient visits, we will continue our study by performing in-depth semi-structured interviews with the participating patients and pharmacists to understand their experiences. The interviews will be analyzed using directed content analysis.

9.4.4 SAFETY ANALYSES

AEs and SAEs will be recorded by the study team when they become aware. Adverse events leading to premature discontinuation from the study intervention and serious treatment-emergent AEs will be presented in a table.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Not applicable

9.4.6 PLANNED INTERIM ANALYSES

Interim analyses are not planned during this short pilot study.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator and funding agency. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants

- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor and/or IRB.

10.1.2 STUDY GOVERNANCE

The name and contact information of the Principal Investigator:

Sarah Averbach, MD, MAS, Associate Professor
University of California, San Diego
9500 Gilman Drive, La Jolla, CA, 92093
858-329-4464
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10.1.3 SAFETY OVERSIGHT

Safety oversight will be monitored by the study PI.

10.1.4 CLINICAL MONITORING

Data verification will take place periodically. This will ensure data completeness and monitor safety of participants.

10.1.5 DATA HANDLING AND RECORD KEEPING

10.1.5.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

10.1.5.2 STUDY RECORDS RETENTION

Study documents will be retained for 2 years after the formal completion of the study.

10.1.6 PROTOCOL DEVIATIONS

It is the responsibility of the PI to use continuous vigilance to identify and report deviations. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

11 REFERENCES

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