Research Plan, inclusive of Study Protocol and Statistical Analysis Plan

Project Title: Enhancing Male Participation in Interventions to Prevent Unintended Pregnancy (CHARM2)

NCT number: NCT03514914

Date of document creation: 2/13/2020

Date last approved by IRB: 3/31/2022

UCSD Human Research Protections Program
New Biomedical Application
RESEARCH PLAN INSTRUCTIONS

These are instructions are for completing the Research Plan that is available in MS Word format from the HRPP website.
The headings on this set of instructions correspond to the headings of the Research Plan.
General Instructions: Enter a response in for all topic headings.
Enter "Not Applicable" rather than leaving an item blank if the item does not apply to this project.

Version date: 11/15/2016

1. PROJECT TITLE

CHARM2 – Enhancing Male Participation in Interventions to Prevent Unintended Pregnancy

2. PRINCIPAL INVESTIGATOR

Anita Raj, PhD, Professor, Department of Medicine

3. FACILITIES

- UCSD, Department of Medicine, Division of Infectious Disease and Global Public Health: Project coordination from US side; **no access to identifiable data**
- National Institute for Research on Reproductive Health, Mumbai, India – **under jurisdiction of a separate IRB in India**
- Homes of study participants for survey assessments, intervention sessions take place in primary health center clinics, located in Maharashtra, India

4. ESTIMATED DURATION OF THE STUDY

The entire study duration is 5 years.

5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

Globally, 41% of all pregnancies are unintended, increasing risk for maternal and infant morbidities and mortality. Most unintended pregnancies occur in the context of contraceptive non-use or failure. Women with husbands not supportive of contraception are more likely to report contraceptive non-use, and women with sexually abusive husbands are more likely to report contraceptive failure. Such findings highlight the need for family planning (FP) interventions that engage both women and men, focus on eliminating marital sexual violence (MSV) and promote use of effective (low failure risk) spacing contraception including long-acting reversible contraception (LARC; e.g. intrauterine device or IUD). Rural India, with some of the lowest rates of contraception and highest rates of marital violence globally, offers an important context in which to test such interventions, with global implications. Prior research from this team documents promise of the original CHARM intervention, a gender equity (GE) FP intervention engaging men and delivered by male health providers over three months. This intervention improved contraceptive use and reduced likelihood of MSV, but demonstrated no reduction in unintended pregnancy; additionally, it demonstrated good participation from men (91%) but less from couples (51%), largely due to women's discomfort with a male provider. Poor reach to women and provision of only short-acting contraceptives (pill, condom) more vulnerable to contraceptive failure, likely compromised unintended pregnancy outcomes. Based on these findings, we propose CHARM2, which will include CHARM sessions for men AND parallel women-focused GE+FP sessions delivered by a female provider and inclusive of broader contraceptive options, including LARC, as well as a combined couples session. This study seeks a) to implement CHARM2, b) to evaluate its impact on contraceptive use, unintended pregnancy, and MSV with rural couples in India, and c) to assess its potential for sustainability in rural India, using implementation science methods. To evaluate the impact of CHARM2 on our outcomes of interest, a two armed cluster randomized controlled trial will be conducted with N=1200 married couples from 20 geographic clusters (n=60 couples per cluster) in rural Maharashtra, India. Participants will receive CHARM2 or the standard of care (SOC) control condition, which will involve community health workers offering pills/condoms and linking women to public health clinics. Outcomes for both intervention and SOC participants will be assessed via pregnancy testing and surveys at baseline and 9 & 18-month follow-ups. Implementation science methods will be used to assess the quality, scalability, and replicability of CHARM2 for uptake by rural health care systems (i.e., sustainability). Specifically, in-depth interviews (IDI) will be conducted with CHARM2 intervention couples (n=50), providers (n=20); 5-7 focus group discussions (FGDs) will be conducted with mother in laws (MILs) of couples that participate in IDIs, and key stakeholders from the family planning and rural health infrastructures at state, national and international levels (n=50), and we will implement a cost-effectiveness analysis of CHARM2.

6. SPECIFIC AIMS

1) To implement the CHARM 2 GE+FP intervention, comprised of CHARM sessions with men and parallel sessions with women, and inclusive of broader contraceptive options including LARC, as well as one combined couples session. Men's sessions will be delivered by male health providers; women's sessions will be delivered by public Auxiliary Nurse and Midwives (ANMs), or a trained provider/counselor. The couple's session will be delivered by an ANM, trained provider, or counselor.

2) To evaluate the impact of CHARM2 on spacing contraceptive use (including LARC), unintended pregnancy, and MSV via a two armed cluster RCT with N=1200 married couples from 20 geographic clusters (n=60 couples per cluster) in rural India. The control arm will receive SOC in the form of community health workers offering pills/condoms and linking women to public health clinics. Outcomes will be assessed via pregnancy testing and surveys at baseline, 9 and18-month follow-ups.

Hypotheses: We hypothesize that CHARM2 participants will be more likely than SOC participants to:
a) Use contraception (including LARC) at 9 &18-month follow-ups; effects on LARC will be explored
b) Be less likely to report marital sexual violence (MSV) at 9 &18-month follow-ups
c) Not have an unintended pregnancy over the 18-month follow-up period.

3) To assess the quality, scalability, and replicability of CHARM2 for uptake by rural health systems (i.e., sustainability), using implementation science methods including IDI with CHARM2 couples (n=50) and providers (n=20), 5-7 focus groups with MILs of couples that participate in IDIs, control condition couples (n=20), and key stakeholders from the FP and rural health infrastructures at state, national and international levels (n=50), survey of healthcare facilities in the study area (n approximately=250), and a cost-effectiveness analysis.

Should CHARM2 prove effective and sustainable, study findings will have broad implications for FP interventions for low resource settings in India and elsewhere.

7. BACKGROUND AND SIGNIFICANCE

India still faces high unintended pregnancy (3.3 million pregnancies, annually)[1] and unmet need for spacing (use of LARCs is <10% in rural India)[1,2,3]. Moreover, there is a gender-based barrier to accessing contraception, especially among the youngest (15-24 years) wives.[1,4,5] Though male engagement in FP is recommended,[6-8] there is little evaluated work in this area. The CHARM study effectively demonstrated impact of a GE+FP intervention on contraceptive use through counseling on gender equitable decision-making. CHARM2 is a brief GE+FP intervention that builds on the proven CHARM approach to engage husbands. CHARM2 aligns with recent policy efforts made by the Indian government to increase LARC use. These policies offer free provision of IUDs (Copper-T),[9,10] and more recently, injectables.[11] CHARM2 also supports recommended training of public health ANMs on IUD provision.[12] CHARM2 is significant as it uses a proven theoretical model that utilizes male engagement, to improve use of LARCs to address the unmet need for spacing in rural India.

8. PROGRESS REPORT

This application is a resubmission.

9. RESEARCH DESIGN AND METHODS

Overview: This study will involve 3 phases: Phase 1- the Preparatory Phase to map the project area and prepare communities for the planned research. Phase 2- Implementation and Evaluation of CHARM 2 (Aims 1&2), using a two-armed cluster randomized controlled trial (RCT) in 20 geographic clusters mapped in Phase 1. To assess treatment impact on contraceptive use, MSV and unintended pregnancy, clusters will be randomized to receive CHARM2 or the control program, which includes SOC public health FP services. Intervention effects will be assessed via surveys and pregnancy testing at baseline and 9 &18-month follow-up with n=1200 couples (wife 18-29 years). Phase 3- Implementation Science Assessments will include IDI with CHARM2 providers (n=20), select CHARM2 couples (n=50), MILs for those IDI couple participants that are comfortable with MIL participation, control condition couples (n=20), and key Indian stakeholders in FP & public health (n=50). Interviews with providers and couples will explore intervention delivery and perceived impact. Interviews with FP & public health stakeholders will obtain feedback on perceived feasibility to sustain and scale up CHARM2. A survey of all healthcare facilities in the study area (n approximately=250) will support understanding of the local healthcare context as well as access to and availability of family planning in the study communities. A cost-effectiveness analysis will also be done to support considerations of sustainability.

Procedures/Activities for Participants: Phase 1 of the study is preparatory stage for cluster randomization and training of providers. In phase 2 and phase 3, the participants will participate in the trial at the villages where they reside. NIRRH staff will conduct survey assessments with participants in the homes of the participants, after obtaining permission to do so. Intervention sessions with male providers and ANMs or trained providers/counselors will take place in at home, or in clinic settings. In Phase 2, the participants will complete survey assessments at baseline, and 9 &18-month follow-up. Female participants (wives) will also take urine pregnancy tests at baseline, and 9 &18-month follow-up. In phase 3 a subsample of CHARM2 couples (n=50) will participate in IDIs at 9 month follow-up to describe their experiences with the intervention and their views of its utility, as well as their perceptions related to its outcome effects. All CHARM2 providers (n=20) will be asked to participate in IDIs at their facility to assess their perceptions of CHARM2 quality, acceptability and utility. A subsample of control condition couples (n=20) will participate in IDIs at 18 month follow-up to describe their experiences with family planning and gender-based violence in the study area context but outside of the intervention. Healthcare facilities in the area will be mapped and information will be collected on whether the facility provides family planning, what methods they provide, and whether the facility participated in the CHARM2 intervention.

The CHARM2 Intervention: CHARM2 intervention will involve gender, culture and contextually-tailored FP+GE counseling sessions delivered individually to husbands by a trained male health provider (2 sessions), and, in parallel, delivered individually to wives by a trained female ANM or trained provider/counselor (2 sessions), as well as a combined couples session. CHARM2 differs from the original CHARM intervention by adding parallel sessions for wives, delivered by the ANM, and including LARC counseling for husbands and wives and opportunity for LARC provision in the sessions with women. The ANM or trained provider/counselor session will use GE counseling from the CHARM couple session with public health FP and LARC counseling. Sessions will be provided at the participants' home or within the clinical setting, as the husband and wife prefer. The 5 sessions will be delivered across 3 months with a minimum of 1 week between the men's sessions; the men's Session 1 must be delivered before the female session.

SOC Control Condition: Under India's public health system, ASHAs and ANMs provide household visits to women to increase awareness and use of FP services, with ASHAs incentivized to bring women to PHCs for FP services and ANMs rarely providing contraceptives. For those women or couples that reach the PHC, SOC FP counseling and services are delivered by a physician; free contraceptives are then offered, most often female sterilization and rarely LARC.[1,2] Control group female participants will be linked with ASHAs to support access to PHC FP services. ANMs will not provide LARC or GE counseling for control condition women. Men will receive no FP counseling.

Timeline: Phase 1 of the study preparation will take approximately 3 months. Phase 2 will be in month 4 to month 60, including enrollment and intervention start at month 4, 9 month follow up at month 13, and 18 month follow up at month 22. The outcome analysis will also be carried out in this phase at month 40. Phase 3, on sustaining the intervention, will overlap from month 7 to month 60.

Quantitative Data Collection:

Survey and urine pregnancy test data (from wives) will be collected from all enrolled couples in the CHARM2 RCT evaluation study. Both intervention and SOC arm participants will provide survey data at baseline and 9 & 18 month follow-ups. Survey data will be collected electronically on tablets using a unique identifier to link data between couples and across time. Wives in both the intervention and the SOC arms will be tested for pregnancy using a urine specimen at baseline and at both post-test timepoints; these data will directly be entered into the password protected electronic survey system at the time of survey data collection. Urine samples for pregnancy testing will not be retained for the study, but will be disposed of in disposal facilities upon completion of the test. Survey and pregnancy test results data will be stored locally on the tablet and, when internet is available, uploaded to the password-protected server. Separately, a list of contact names with unique identifiers will be maintained for tracking purposes; a hard copy form of this list will be kept in a locked file in Dr. Begum's locked office at NIRRH. Baseline and follow-up surveys will be collected from couples using measures from the original CHARM study, which was based on India's Demographic and Health Survey (DHS/India's NFHS-3)[1] and other validated measures. Couples must meet the eligibility criteria outlined below.

Eligible couples will be:

- Young wives (aged 18-29 years) and their husbands
- couples fluent in Marathi and both willing to participate
- no sterilization or infertility indicated (infertility is defined as having no pregnancy for 1+ years despite non-use of traditional or modern contraception)
- no pregnancy or female/male surgical sterilization planned for the next 18 months, and no reported use of consistent use of modern contraceptives in the past three months, and
- residing in the village for at least 2 years and residing together for at least 3 months, to facilitate follow-up tracking

The primary analyses will use an intent-to-treat approach and analyze all subjects according to randomized group. For subjects missing month 9 or 18 endpoints, these will be multiply imputed from the lower (worse) half of the distribution from their arm (conservative approach). Additional analyses will be conducted using a per protocol approach that includes only those subjects who complete the full intervention. Analyses will use women's data only; however, men's data will be used to validate outcomes a) increased contraceptive use, and b) reduced unintended pregnancy. Exploratory analyses using outcomes of contraception by type (e.g., LARC) may be conducted if numbers are sufficient across time-points.

At 18 month follow-up, healthcare facilities in the study area will be surveyed to assess provision of FP counseling and methods, availability of FP methods, approximate FP method client volume, provider type/qualifications, and participation in the CHARM2 intervention. Healthcare facility location GPS will be collected for mapping of healthcare services in the study area; no personally identifying information regarding the providers will be collected.

At 18 month follow-up, participants' location data will be re-collected in the form of GPS coordinates; this data will be used to examine distances to healthcare facilities in the study area. GPS data will be collected in a separate survey form to be accessed only by NIRRH in-country study staff. In-country study staff may use this location data, in conjunction with healthcare facility location data, to calculate participant-level distance to healthcare providers. Geolocation data will **not** be shared with UCSD or any other external sources; any maps produced which visualize healthcare facility location and access will **not** include participant locations. Calculated distances **only** may be shared with UCSD analysts, to be summarized and utilized in adjusted regression models to better understand drivers of and barriers to health care services generally, and family planning services specifically, in the study area.

Qualitative Data Collection:

In-depth interviews with CHARM2 providers and participants, as well as control condition couples, described as part of Aim 3, will assess perceived outcomes of the intervention, for triangulation with quantitative findings.

At 9 month follow-up, a subsample of CHARM2 couples (n=50 couples; 5 per CHARM2 intervention cluster) will be randomly selected to participate in IDI to assess how the program altered their relationship and behaviors, including FP, MSV and sexual communication. Interviews will be 45-60 minutes in length and conducted in Marathi. Interview participation may influence responses at 18 month follow-up but delaying qualitative feedback to 18 month follow-up may affect participant recall. Thus, we will compare these individuals at 18 month follow-up with those intervention participants who did not participate in interviews, and if significant differences are seen, we will drop them from further analyses. MILs of couples (mother's of the young married men) that participate in IDIs will also be invited for interviews *only* through the couples themselves, and with the couples knowledge that we will be describing the CHARM2 intervention to them. FGDs with MILs will assess family dynamics of young couples with regard to husband's parents, family planning attitudes, and their perceptions of the CHARM2 program.

All CHARM2 providers (n=20 providers/ANMs/counselors) will be asked to participate in IDIs to assess their perceptions of CHARM2 quality, acceptability and utility. NIRRH staff will conduct the 30 minute open-ended interviews with providers. As is standard in India, no monetary incentives will be offered.

At 18 month follow-up, a subsample of control condition couples (n=20 couples, 2 per control cluster) will be randomly selected to participate in IDI to understand FP counseling and access and gender-based violence in the study area outside of the CHARM2 intervention.

Data Analysis: The primary comparison of the binary outcomes between intervention groups at 9 & 18-months will use mixed-effects longitudinal logistic regression, with random effects for the individual (couple) and for geographical clusters, over time. Baseline will be included as a time point (Aims 2a, 2b only). A categorical time effect will be used (profile model). A "difference-in-differences" analysis will compare the treatment arms. Statistically, this amounts to testing for an interaction between time and treatment arm in the longitudinal model. In addition, the intervention groups will be compared via a generalized estimating equations (GEE) logistic regression analysis. The GEE models will use a nested exchangeable working correlation matrix that takes into account geographic clusters and the individual (couple) within the cluster. No other covariates will be included in the primary analysis. Since the treatment assignment is at random this "un- adjusted" analysis will provide a causal effect of the intervention. However, we will also conduct secondary analyses, adjusting for potentially relevant covariates (e.g., age, current pregnancy, past year child- birth, etc.), in addition to time and treatment arm, using backward model selection at the α=0.15 threshold level. These secondary analyses may improve precision (power) of estimating the treatment effect and reduce any bias due to random imbalances between arms.

Implementation Science: Subsequent to the efficacy trial, brief (30-60 minute) IDI with key stakeholders (n = 50) from FP and rural and public health at multiple levels (local, state, national, international) will be conducted, as will a cost-effectiveness analysis of CHARM2. IDI stakeholder participants will be identified by community leaders and advisors at multiple levels, including the villages in which the study will be undertaken, the District Health Office partnering with us for this study, and the Technical Advisory Committee who will guide and support our proposed work. NIRRH research staff will contact stakeholders via phone or email, to conduct the 30 minute interviews in English, Hindi or Marathi in-person or via phone, to share CHARM2 approach/findings and to ask whether and how this could be used to support FP programming in rural India. Interviews will be audio recorded unless the participant refuses, in which case detailed notes will be taken. Transcripts will be saved as text documents and imported into ATLAS.ti®, software that helps to organize and facilitate analysis of qualitative data.[14] Dr. Saggurti will guide data analysis using a grounded theory approach, in which there is a continuous interplay between data collection and analysis to iteratively generate themes and adapt interview guides.[15-17] Analysis will be initiated upon completion of the first wave of data collection, by site, using the following approach: (1) Data Immersion- Dr. Saggurti and the research staff will read and reread transcripts and associated field notes to familiarize themselves with the narratives and create memos to guide theme development; (2) Theme Generation- the team will develop a list of emergent key themes seen across narratives; (3) Framework Development- themes and their intersections will be reviewed and discussed with the investigator team to create a framework to understand the issues of focus; revisions to protocols or extensions of data collection may result in order to better support framework creation; (4) Codebook Development- a codebook will be developed based on the framework themes and any resultant subcodes, to guide further data analysis; and (5) Coding and Iterative Analysis- two coders will code and analyze all data using themes generated in steps 2-4. Coders will code separately and codes will be analyzed for inter-coder reliability based on Cohen's Kappa.[18] Coding discrepancies will be reviewed to reach consensus. If new codes are identified, the codebook will be expanded, and data will be re-coded. Additional participants may be recruited to reach saturation.

Cost Effectiveness: To further inform utility of CHARM2, a cost-effectiveness analysis will be conducted under the direction of Dr. Bharadwaj using WHO-CHOICE methodology,[19] an internationally accepted standard of economic analysis of health programs. Costs will be collected prospectively and include capital costs (e.g., equipment, space) and recurrent inputs (e.g., FP supplies, administrative costs). Given an expected outcome of improved contraception, costs of increases in non-CHARM2 FP services will be included as partner costs. Costs will be discounted at a rate of 3% per year, per WHO-CHOICE recommendations, varying from 0% to 6% in the sensitivity analysis. Drivers of variation in the total program cost will be assessed using multivariate linear regression. Cost-effectiveness will be calculated by dividing the total program costs by total health outcomes achieved over intervention duration. Outcome measures will include number reached by the CHARM2 and unintended births averted (based on outcome analyses). Based on prior research,[20] we will use an estimate of 3.8 DALYs averted per unintended birth averted. We will also include quantitative measurements of other benefits from unintended pregnancy prevention (e.g., household savings and assets) to capture some of the spill over effects of when unintended pregnancies are prevented. Following WHO benchmarks, the intervention will be categorized as 'very cost-effective' if the cost per DALY averted is <1x the country's per capita GDP.[19,21] We will undertake a probabilistic sensitivity analysis, sampling each cost and outcome from an appropriate distribution to determine mean incremental cost-effectiveness, and assess drivers of uncertainty using ANCOVA. Findings will be used to support sustainability and scale up of CHARM2 for use in rural India and elsewhere.

Sample size considerations: Treatment effects detectable with 80% power given the 2-armed design with 20 clusters of 48 measurable couples (assuming 80% retention) per arm, or n=960 observed couples. Power calculations took into account multiple levels of clustering, both within-village and within-sub center variance.

a) Based on CHARM,[13] we expect the proportion of women using modern contraception in the control group to be 40% at 18 month follow-up. This study will have 83.3% power to detect an absolute difference of 12% or more between treatment groups at follow-up, or 40% vs 52% in the two groups, with total kappa [variance]=0.10, assumed to be split equally between within-village variance and within-cluster variance . These values were found in the CHARM study.[13]

b) Based on CHARM, [13] we expect that 89.2% of women in the control group will report no recent MSV at 18 month follow-up. We have 91.5% power to detect an absolute difference of 6% or more between treatment groups (89.2% vs. 95.2%) with kappa=0.036,

assumed to be split equally between within-village variance and within-cluster variance. The effect size of 6% difference and the kappa=0.036 were observed in the CHARM study. [13]

c) Based on CHARM, [13] we expect the proportion of women with no unintended pregnancy over 18 month follow-up to be 90% in the control group. This study will have 89.5% power to detect an absolute difference of 5.5% or more between groups (90% vs. 95.5%), with kappa=0. The effect size of 5.5% difference is based on a meta-analysis of cluster RCTs evaluating impact of FP interventions on unintended pregnancy (with comparable measures to this study). The study showed a 50% reduced risk for intervention participants with no unintended pregnancy in the CHARM group, or 5.5%.[22] The kappa=0 is based on the CHARM study, where no significant intra-cluster correlation was found for this outcome.[13]

While we will use longitudinal mixed effects logistic regression methods in our analyses, for power calculations we considered only the 18-month time point in a model similar to those to be used in the analyses. Power for the prescribed longitudinal analyses will be higher. Power calculations for each hypothesis used statistical simulations with 10,000 iterations. The conversion from kappa to the random cluster effect was done using the delta method, and was confirmed through the simulation.

10. HUMAN SUBJECTS

NOTE: All subjects will be enrolled at Non-UCSD sites.
All participants will be of Indian heritage, and enrolled into the study in India.

Inclusion of Pregnant Women: Pregnant women will be included in this study, as the methods meet criteria for their inclusion, including posing no increased risk for the pregnant women or the fetus, beyond that seen for non-pregnant women. Additionally, study findings can support the health of pregnant women, and the study is in no way designed to influence the woman with regard to her choices for the index pregnancy. No additional protections for pregnant women are included, as the existing protections for all wives address risks for pregnant wives (e.g., risk for partner violence).

Inclusion of Children: Adolescent wives or husbands included in this study meet the federal definition of children, as they may be under age 21 years. Due to heightened vulnerability in households, very young wives (<18 years) will not be included in this study. We include this population of children as part of our research, but do so without parental consent as they are married and recognized as adults able to provide consent on their own. Study findings specifically support the health and safety of this young population. Existing protections outlined for all wives consider the heightened vulnerabilities young wives face in marriage. Thus, no additional protections are provided beyond that described above. Nonetheless, we have not included wives < 18 years, as the assessments used in this study are not necessarily tailored to the unique needs, sensitivities or cognitive capacities of these younger wives. Further, they are a more vulnerable group that may require greater support than is provided in this study. Our original CHARM study did not identify any wives this young in recruitment.

Inclusion of Pregnant Children: Although 18-21 year old pregnant wives may be included, their marital status makes parental consent inappropriate in this context. Research efforts conducted by NIRRH, University of California, San Diego or Population Council will not involve inducements, monetary or otherwise, for pregnancy termination. No members of the research team, including NIRRH research staff members conducting field research, will have any part in decisions related to pregnancy termination. No members of the research team, including NIRRH research staff members conducting field research, will have any part in determining the viability of a neonate.

11. RECRUITMENT

This study involves randomization at the geographic cluster rather than individual level. While individual randomization is more powerful, cluster randomization allows us to reduce risk for contamination that may occur if both treatment conditions were offered in the same geographic area. Participating couples will be recruited from geographic clusters of approximately equal size mapped for randomization. Clusters are geographically distinct areas with administrative boundaries, natural borders and appropriate distance from other study clusters to reduce risk for contamination. Clusters will be created based on geographic boundaries, population density (approximately 5000 population per cluster), and proximity to ANMs and health providers. Clusters will be selected based on minimum number of eligible couples (at least 60 eligible couples); clusters will then subsequently be randomized to intervention or control conditions using computer-generated random numbers. Households within each cluster will be screened sequentially for eligibility. Research staff are not to be blinded to the treatment condition assignment to clusters. Recruitment of eligible households will be n = 60 per cluster. In a small cluster if the total number of eligible couples is equal to 60, all couples are approached for recruitment. In a larger cluster if the eligible couple number is more than 60, the required number of couples will be selected through systematic random sampling (selecting every nth participant).

Trained NIRRH survey research teams (1 male & 1 female) will approach selected households for screening and recruitment. Three attempts to reach the couple will be made for each selected household. If an eligible household has two or more couples meeting eligibility criteria, a Kish Grid[23,24] will be used to determine the participants.[1] Couples selected from eligible households will be asked to join the study and will be informed that the study focuses on FP. Data will be collected to assess participation rates and biases by

age, and contraceptive use. Recruitment/enrollment and intervention delivery will occur over 2.5 years on a rolling basis.

PLEASE NOTE: No identifiable information will be collected from those screened and found to be ineligible or unwilling to participate, across study phases.

12. INFORMED CONSENT

Recruitment and written consent (hard copy) will be implemented by trained Masters-level research staff for all phases of study; research staff and participants will be gender-matched. For every source of primary data collection, written informed consent will be acquired prior to data collection. For RCT study participants, consent will be obtained prior to screening, survey, and, for women, urine pregnancy testing; consent will include follow-up data collection. For IDI participants, written informed consent will again be provided prior to interviews; all IDIs are 1-time events. Stakeholders providing IDI (Aim 3) will provide verbal informed consent prior to participation; verbal consent will be used to facilitate use of phone interviews since no personal questions will be included in these interviews.

It must be noted that issues of literacy are a major concern in rural India, particularly for women. Dr. Begum and other Co-Is on this study have years of experience obtaining written informed consent with both illiterate and literate men and women in rural India. In the case of illiterate men/women, the consent form will be read in the presence of a trusted literate adult (18 years or older) of the participant's choosing, and then the individual will be asked in the presence of that adult whether they are willing to participate. Research staff will provide explanations to all queries, and anything that cannot be answered in the field will be addressed via telephone contact with Dr. Begum.

The consent forms and survey forms will be prepared in Marathi language. Written consent will be required, as our in-country research partner NIRRH prefers written informed consent, rather than verbal consent, in behavioral studies involving sensitive research questions, such as those used in the current study. Although females aged 18-21 years will likely be included in this study, parental consent for their participation will not be obtained, as all of these females will be wives and are thus recognized as adults capable of providing consent for themselves in the Indian context.

13. ALTERNATIVES TO STUDY PARTICIPATION

There will be no required alternative treatments or procedures for study participants or those ineligible or declining participation. However, all husband and wife participants will be provided with information regarding local antenatal services and primary health center family planning services, available through the state public health system and National Rural Health Mission.

14. POTENTIAL RISKS

Questions included in qualitative and quantitative assessments with men and women may be embarrassing or emotionally upsetting to participants as they assess sexual and contraceptive behaviors, and for women, physical and sexual violence from husbands. Embarrassment is reduced by the brevity of the research tools and the use of matched-gender and well-trained research interviewers. Also, assessments of abusive or controlling behavior from husbands are asked of wives confidentially, and not from husbands. Wives and husbands will be recruited from the same households, but in accordance with the World Health Organization's "Ethical and Safety Recommendations for Research on Domestic Violence Against Women",[25] only wives will be assessed for domestic violence. These recommendations guide against asking husbands about perpetration or informing husbands of what wives are being asked, to reduce risk for violence. Husbands will be asked about their attitudes toward domestic violence, including marital sexual violence (MSV), a targeted outcome of the CHARM2 intervention. Wives will be asked about their marital sexual experiences including MSV as part of intervention sessions with ANMs or trained providers/counselors; again, this can create discomfort or potential vulnerability to violence if the husband learns of this disclosure. Wives will be discouraged from sharing both the nature of the questions and their responses in surveys and intervention sessions, with their husbands or others, and researchers will not share this information with husbands. To further protect wives, we will follow protocols used in our prior intervention studies on domestic and sexual violence to reduce risk for wives; these protocols are consistent with the World Health Organization's "Ethical and Safety Recommendations for Research on Domestic Violence Against Women."[25]

It is possible that some participants may become anxious, depressed, or angry due to study or intervention content, and there is a small possibility this may result in their becoming a risk to themselves or someone else. Our previous work in rural and urban Maharashtra, inclusive of wives and husbands and assessing similar items and using a similar approach, elicited no such responses. However, to ensure the safety of our participants and staff, precautions will be taken to minimize participants' risk of emotional distress. Prior to assessment, participants will be reminded that they are free not to answer a question and may terminate their participation at any point. If indications of distress are observed in an individual, the participant will be privately debriefed and screened for emotional distress: "These questions (or discussions) can make some people feel sad, anxious, or angry. How are you feeling now?" If it is determined that the participant is in need of immediate assistance, the individual will be immediately escorted to a mental health provider at the closest available health center. In addition to this debriefing, all participants will be provided with referrals, in the form of a list of local programs for family planning and, for wives only, domestic violence.

Loss of Confidentiality: There is the potential that researchers may be required to breech participants' confidentiality if participants disclose any intentions to hurt themselves or others, report child or elder abuse, or report homicidal intention or perpetration. Our research instruments do not ask this information, so there should be minimal risk about eliciting such a response from the participant. However, it is possible that participants may disclose this information during an intervention session or following survey completion

and during our debriefing which involves screening for emotional distress. The consent form will clearly outline for each participant conditions under which such a breach of confidentiality may occur; and will be covered prior to any survey assessment or interview.

In addition to risks to wives, there are also risks to CHARM2 providers and stakeholders participating in this study, as any criticism they provide can make them vulnerable to the public health system in which they may work or intersect. We will work to compile questions that are more objective than opinion in nature, with regard to care provision, health care and government infrastructures, and CHARM2 implementation and supervision, to reduce this risk. We also will assure confidentiality to participants. For anyone who is no longer comfortable participating in the study, they may withdraw from participation without penalty. CHARM2 providers who withdraw from the study lose no financial support from this discontinuation, as financial support is not given to providers for their participation in CHARM2.

15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

In addition to the protections against risks briefly outlined in the Potential Risks section above, additional precautions have been outlined to reduce risk for violence to wives, given the vulnerability of this population. These protocols and procedures were developed based on WHO guidelines for domestic violence research,[25] and based on existing NIH-funded projects Drs. Raj and Silverman have or have had in both India and the US. These protocols include (but are not limited to) the following efforts:

If women at any point in the study report life-threatening violence from husbands, these women will be withdrawn from the study and provided with supported referral (assistance with transport and accompaniment) to a state domestic violence agency (CEHAT) by research or program staff. Research staff, ANMs, and trained providers/counselors will be trained on how to work with women in these situations in accordance with WHO guidelines for domestic violence research.[25] For example, this includes using "dummy" questions if privacy is breached during an interview or an ANM or trained provider/counselor visit, and training staff to identify when women are distressed and need debriefing or immediate health attendance. They will also offer support to conduct a safety plan with woman reporting spousal violence to ensure she has thought through ways to safely escape her situation should she choose to do so.

Research and program staff will never disclose to any family member who participated in the study, what questions were asked of them, or what responses were given. Participants will also be asked not to share the questions and their responses with others, particularly if they think it could put them at risk for abuse. This is in line with WHO procedures for domestic violence research.[25]

Women will always be assessed for domestic violence in private places, with clarification that women can refuse to respond to items or questions, with supported referral and safety planning for identified victims, with validation that violence is never a woman's fault, with protocols and confirmation that all information provided is kept confidential, and with emotional debriefing subsequent to disclosure, in line with WHO procedures for domestic violence research.[25]

Participation in this study and programs is completely voluntary. If the participant feels uncomfortable or is upset by the interviews or surveys or intervention sessions, she/he may withdraw from the study as outlined by the consent form.

Only wives will be assessed for marital violence in the surveys and intervention sessions; they will be asked not to disclose participation in these items as it may put themselves or others at risk for violence as a consequence of study participation. Utmost confidentiality will be maintained by all research staff. Please see section below on "Protection from Loss of Confidentiality" for details. These protocols to protect women's confidentiality are in line with WHO guidelines on domestic violence research.[25]

It must be noted that there is no law against marital sexual violence/rape in India at this time. Dr. Raj works closely with many groups in India that work on issues of domestic and sexual violence, including Amnesty International India and CEHAT, allowing this team to be abreast of the most up to date laws and services to support victims who are identified and wish to seek services. Our experience from the original CHARM study as well as other studies is that women rarely wish to obtain formal support against domestic violence.

Protection from Loss of Confidentiality: As noted in the section on Potential Risks, security of confidentiality is a primary means of reducing risks for our research participants. Hence, every effort will be made to minimize participants' risk of a loss of confidentiality during this study. Participants will not have family members or others informed of their participation in the study unless they choose to tell them. Participants from the same household or institution will not be informed of the survey questions or responses for other members of their household or institution, or the nature of the interventions offered. Only unique identifiers will be used to label data collected in this study; only NIRRH staff and Co-Is will have access to the identifiable information linked with the unique identifiers. These research staff will be required to maintain the confidentiality of all research participants, and will have signed a pledge to do so upon joining the research team.

All participants will be informed, via written informed consent that any disclosure requiring our mandated reporting (e.g., perpetration of homicide, child abuse, or elder abuse; suicidality; homicidal intentions) will require that we contact authorities and provide them with identifiable information about the participant if we have it. We will also immediately escort them to mental health services care available at the community health center if they disclose that they are suicidal or homicidal; that may result in them involuntarily being made an inpatient in a psychiatric facility. If the participant informs us of abuse of children (exclusive of minor aged wives) or elders or perpetration of homicide, the authorities will also be contacted. This will be outlined in the informed consent. No procedures included in this study will involve assessment of any of the above concerns except suicidality.

Protections for Research Staff: The research and program staff will be trained not to provide judgment regarding participants' sexual behavior, parity, marital age or circumstances, victimization from violence, substance use or other stigmatized behaviors; as described above, all participants will receive referrals for relevant health and social services related to family planning and, for wives only, domestic violence programs. Standard provision of referrals to all participants, and clarity via consent forms regarding this standard provision, allows us to safely offer information without increasing our staff's vulnerability. To further help protect staff, both program and research staff will be trained in security protocols regarding how to reach nearby police or other staff members on short notice, if an issue becomes apparent; all staff will have cell phones to make such contact. Participants will be given the NIRRH PI's name and work phone number on the consent materials. Research and program staff will be trained on how to stay alert to participant distress and signs that the participant is becoming irritated by the questions or discussion. In addition to providing support and information to participants as described above, all research staff will be trained to end the participant's involvement if they (the staff) have any concerns for their own safety. If a situation of mandated reporting arises, research staff will be well trained to manage the situation. They will first contact the authorities to inform them of a potential security issue; this contact will be made in a way that does not alert the participant that the authorities have been contacted. Once the authorities arrive, the staff member will inform the participant that a mandated reporting issue has arisen, identify the issue for the participant, and remind the participant that this requires study termination and that authorities be contacted. All staff will be trained in these procedures by Dr. Jay Silverman, an expert on violence and ethics in research, as well as Drs. Begum and Saggurti, who have expertise conducting sexual and reproductive health research in India.

Importance of the Knowledge to be Gained
Data collected from this project will be used to create program efforts that can be integrated into national rural health and family planning policies and initiatives, with the goal of improving family planning and reducing unintended pregnancy at a population level.

Interim Safety and Efficacy Review. Study risks are low. However, we will convene a Data and Safety Monitoring Board (DSMB) to review safety on a yearly basis. The study will be stopped early if there are serious safety concerns or early evidence of a large beneficial treatment effect. An interim efficacy analysis will be conducted after half of subjects (n=10 geographical clusters) have completed the 18 month visit. The O'Brien-Fleming stopping rule for efficacy will be used.[26] Because validation of the proposed CHARM2 intervention is scientifically important independent of statistically significant results, there will be no futility analysis. The DSMB will consist of experts on FP, MSV and clinical trials in India.

Confidentiality and Security. Data security and confidentiality are critically important due to the sensitive subject matter of this study. All participant identifiers such as name, address or telephone number will be maintained on separate forms in locked storage at NIRRH and kept separately from the analytic database. Data shared among NIRRH, Population Council, and UCSD will be maintained on password-protected and secure servers at each site. The data will be backed up nightly on the UCSD server.

Data and Safety Monitoring Plan. Data safety monitoring of study participants will focus on two major safety aspects:
1. assurance that no harm comes to participants as a result of survey or program participation and
2. assurance that all data collected from this project, including process and quality assurance data as well as outcome data, maintain the privacy of research participants. Dr. Begum will oversee project staff to ensure that the data safety monitoring plan is being properly adhered to within India.

Measures to ensure that no harm comes to participants as a result of survey participation are described above under the sections on Potential Risks and Protections against Risks

In terms of data management, all hard data (e.g., paper surveys if a tablet malfunctions in the field) collected from this study will be brought to the lead field site (NIRRH) for transcription and translation; tapes will be locked away until transcription and then destroyed. Electronic files created from this transcription/translation will be compiled and analyzed at NIRRH. Hard data safety will be assured by locking the consent forms, contact numbers and addresses in separate securely locked cabinets in a locked office that is only accessible to NIRRH. All research staff who collect and have access to data from this study will sign a certificate in which they agree to maintain absolute confidentiality of all participants within this research project. If any security arrangement is violated, either through physical tampering or breach of confidentiality, the individual making the discovery will notify the Principal Investigators and the NIRRH and UCSD IRBs. Data analysis will occur at UCSD; electronic files will be kept on a password protected project drive within the school's network. Access to this data will only be made available to investigators and research staff from the project; the data will be password protected. Data files at UCSD are backed up nightly to minimize the likelihood of lost files.

This study has moderate risk. The risks are reasonable in relation to benefits/knowledge gained. Serious risk is unlikely. Major risk is attached to the study's focus on sensitive topics such as family planning and sexual violence. As noted, a number of efforts have been undertaken to reduce risks for study participants. In addition, we have developed both internal and external data safety and monitoring procedures, and a plan to determine if halting of study procedures are required. These are as follows:

16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

Every effort will be made to minimize participants' risk of a loss of confidentiality given the sensitive issues covered by this study. Research staff and village health providers will be required to maintain confidentiality of all research participants, and will have signed

a pledge to do so upon joining the research team. All data collected from this study will be identified only by the unique identifier, so it will be difficult to trace an individual's participation or study data in this project without the unique identifier list linked with identifier information, and that list that will be kept under lock and key at NIRRH. Further, data transmitted to the larger team will be de-identified or labeled only with the unique identifier, to reduce risk for breach of confidentiality in transference of data for this international research study. All NIRRH staff with access to identifiable information will sign a confidentiality agreement to ensure they maintain the confidentiality of all study subjects; if there is any indication of a breach of this confidentiality, Dr. Begum will take immediate efforts to identify the breach and terminate employment of anyone directly causing it.

There are some circumstances in which confidentiality will be breached by the researchers. If the participant directly informs a researcher of his/her perpetration of abuse against children (those under age 18 years) or elders (those 65 years or older), or his/her intentions of homicide or suicide, the researcher will immediately contact authorities (police or mental health) to help address the issue. However, as part of informed consent we will let all participants know this, and we do not directly assess any of these questions via our data collection processes. These procedures have been used in the past on diverse projects within India conducted by Drs. Begum and Saggurti, and there have been no issues that have arisen.

17. POTENTIAL BENEFITS

All study participants will receive referrals to or information regarding local health and social service programs, including family planning services and domestic violence program referrals, of which they may have otherwise been unaware. They are also provided with information and skills to approach their marital relationships in a more gender-equitable way. Furthermore, awareness and linkage to family planning services and domestic violence programs may improve their sexual and reproductive outcomes. Given that the potential benefits of the study would allow for the development of an intervention to improve maternal health and child survival and that there are multiple mechanisms in place to manage potential risks from study and intervention involvement, we believe the benefits outweigh the risks for this proposed study.

18. RISK/BENEFIT RATIO

The potential risks for male and female participants may be different. Questions asked in the interviews and surveys to men may be embarrassing as they assess their gender ideologies, attitudes and norms about reproductive choices and contraceptive use, while the questions asked to women may be embarrassing and upsetting as they assess husbands' gender ideologies and abusive or controlling behaviors, her knowledge and intentions about fertility and contraceptive behavior. Embarrassment among both male and female participants is reduced by the brevity of the research tools and the use of trained, gender-matched interviewers or demographers. Nonetheless, it is possible that some participants may become anxious, depressed, or angry due to this content, and there is a small possibility this may result in their becoming a risk to themselves or someone else. Efforts will be made to link those to care immediately if such concerns arise. Our previous work in India using similar items (including items of abuse, substance use and sexual infidelity) and a similar approach (e.g., one-on-one rather than couple survey implementation) has elicited no such responses. An additional risk in the pilot and efficacy phases is related to reactions to pregnancy test results; some could be upset by positive test results. To maintain optimal safety for wives, we will only inform wives of the test results in this study. They will then have the option of reporting those results accurately, inaccurately or at all to their husbands. Interviewers will not dispute women's reports, and marking of the test result will be conducted in a way that cannot be assessed by participants. Additionally, all women will be provided with verbal referrals for ASHAs (village women's health outreach workers) and the closest Primary Health Center (a facility which provides antenatal and family planning services), regardless of these test results.

With recognition of the high rates of male-perpetrated partner violence among young couples in rural India, special efforts will be made to prevent study involvement from inciting violence against wives. We will only include couples in which wives are allowed to participate and to participate in accordance with study design (private survey administration with wives). Male abuse and control behaviors will only be asked of wives and men will not be informed that wives will be assessed on these items; wives will be asked not to disclose survey questions and their responses to their husbands unless they feel very safe. The informed consent of the men serves as an agreement that the information researchers obtain from both men and their wives will remain confidential and would not be shared between investigators as well as between participants. In addition, the survey tools will be piloted to understand their sensitivity administering to both men and their wives; if any issues are identified, items will be revised or dropped accordingly. Notably, survey items and procedures proposed are similar to those used in the NFHS-3 and previous couples research from Drs. Begum and Saggurti; these efforts assessed partner violence in couples and no adverse outcomes were observed. This approach also follows WHO guidelines for Domestic Violence research. To provide greater support for participants, both husbands and wives in each phase of study will receive referrals to health workers known for having good sensitivity on issues of partner violence and family planning options. If, despite all these precautions, we find that there is a violence happening as a result of study participation, we will make efforts to stop through the use of local village committees and health care workers. If we see an inability to stop the violence even after our efforts, a highly unlikely scenario, the study will be terminated. Identification of such issues will be noted as adverse events and reported accordingly to all investigators, NIRRH, UCSD, Population Council.

Based on the above rationale and the knowledge that is expected to result from this study to inform intervention practices and policy implications around family planning approaches in rural India, and our belief that the risks associated with this study are minimal in relation to the possible benefits to the broader community, we feel that there is an appropriate risk/benefit ratio for this study.

19. EXPENSE TO PARTICIPANT

Subjects will not incur any expenses during the course of, and as a result of their participation in the study.

20. COMPENSATION FOR PARTICIPATION

Subjects will not be compensated financially for their participation.

21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Our binational team has over 10 years of experience working in Maharashtra, India, with multiple Indo-US projects. This team includes:

UCSD:

- Dr. Anita Raj, PhD (U.S. - PI) is a professor within the Division of Global Public Health, Department of Medicine at UCSD, and a developmental psychologist with over 20 years of experience conducting research on sexual and reproductive health among women, girls and men in the U.S., Russia and India. She has been PI on multiple Indo-US projects with this team.
- Dr. Jay Silverman, PhD (Co-I) is a professor within the Division of Global Public Health, Department of Medicine at UCSD, and a public health researcher whose work focuses on the improvement of practice in the prevention of violence against adolescent and adult women (e.g., intimate partner violence, sexual assault, sex trafficking) in the U.S. and internationally. He is a Co-Investigator on this project, and has also been PI on several other Indo-US projects with this team, as well. Given Dr. Silverman's expertise in domestic violence, he will help lead the project in terms of protections for women involved in this study.
- Dr. Sarah Averbach, MD, MAS (Co-I) is an assistant professor and clinician at UCSD's Division of Family Planning at the Department of Obstetrics, Gynecology and Reproductive Sciences. She has led and supported multiple research projects related to family planning and gender equity. She will be leading the development of the CHARM2 curriculum and training protocol for providers and offers expertise on LARC methods.
- Jennifer Yore, MPH will work as the Program Manager on the U.S. side of this project. She has worked with this team on previous projects in this capacity. She will work closely with both U.S. and Indian teams to ensure that all IRB protocols that have been approved by the UCSD IRB are followed.
- Florin Vaida, ScD, a UCSD, is a Professor, at the Division of Biostatistics and Bioinformatics, UCSD. He is a biostatistics Professor and clinical trials expert.
- Prashant Bharadwaj, PhD, is an Assistant Professor of Economics at UCSD. He is a development economist with expertise in cost effectiveness.
- Anvita Dixit, MSc, will work as the Graduate Research Assistant on this study, as a doctoral student training under Dr. Anita Raj at UCSD. She will assist with survey development, and coordination of monitoring & evaluation for the intervention. She has previous reproductive health research experience via her employment with the Population Council in India for four years prior to the PhD program.
- Gennifer Kully, MSc, has experience working on various reproductive health focused projects and will support the US-based CHARM2 team, with regard to study material standardization and survey testing.
- Nicole Johns, MPH will work as the Research Analyst with the U.S. team. She will design and implement the statistical analysis plan for the study, and develop a system to catalogue procedures, routines, programs, and output to build a log documenting the analytic progression over time.
- Dr. Mohan Ghule, PhD will work as a UCSD consultant based in India for this effort. He has previously worked with this Indo-US team in field implementation. He will work to implement the project in the field, and ensure quality of implementation as well as help maintain relationships with the health functionaries as well as other key field project staff.
- Namratha Rao, MPH is a UCSD consultant based in India. She will assist with coordination and collection of qualitative data collection for this project. She has previous experience with field data collection in India.
- Grace Chen, is a UCSD medical student. She will assist with cross-sectional baseline data cleaning, preliminary analyses and results tabling.
- Morgen Chalmiers, is a UCSD medical student. She will assist with cross-sectional baseline data cleaning, preliminary analyses and manuscript development.
- Anuja Sahane will work as a UCSD consultant based in India. She will conduct, transcribe, and translate in-depth interviews with study participants.
- Yogesh Kudale will work as a UCSD consultant based in India. He will conduct, transcribe, and translate in-depth interviews with study participants.
- Saniya Bonde is a UCSD medical student who will work as an intern based in India. She will assist with qualitative data analysis and manuscript development.
- Nicole Economou is a UCSD Family Planning Fellow. She will assist with preliminary analyses and manuscript development.

NOTE: All staff at UCSD will only have access to de-identified data for secondary data analysis purposes.

National Institute for Research in Reproductive Health (Maharashtra, India)

- Dr. Shahina Begum, PhD is a Scientist D in Biostatistics at the National Institute for Research in Reproductive Health (NIRRH), Mumbai, within the Indian Council of Medical Research (ICMR). Dr. Begum is a statistician trained in reproductive health and clinical trials work, with 15+ years of experience conducting research on reproductive health, gendered issues, and male involvement in reproductive health in both rural and urban areas. She will serve as in-country Co-Investigator for the proposed effort.

Population Council:

- Dr. Niranjan Saggurti, PhD (Co-I) is Senior Associate and Country Director at the Population Council, New York, stationed in New Delhi, India. Dr. Saggurti has more than a decade of research experience in the fields of sexual health/HIV, alcohol, gender, and reproductive health/family planning. For this project, he will lead efforts on data analysis and monitoring.
- Dr. Madhusudana Battala, PhD will serve as data coordinator on the Indian side. He will make sure that data for this project are transferred to the NIRRH server on a regular basis, as well as help facilitate that data are sent to the US team in a timely fashion.

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23. FUNDING SUPPORT FOR THIS STUDY

This project is funded through the National Institute of Health, National Institute of Child Development. This grant is an R01, Funding Number: R01HD084453. The grant funding period is 04/01/2017 – 03/31/2022. This grant is going through UCSD.

Fiscal contact person: Andrew Mucha, Fund Manager. Mr. Mucha can be reached at 858-822-1933.

24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT

There will be biological materials collected for this study, as urine samples will be collected from women in the study. However, the material will be moved from our local field site to a laboratory that is part of our partnering institution (NIRRH) as part of the study. Therefore, we don't believe that a Biological Materials Transfer Agreement (BMTA) is necessary.

25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER

This study does not involve any investigational drugs.

26. IMPACT ON STAFF

There is no need for additional training of UCSD staff for the purposes of this study.

27. CONFLICT OF INTEREST

Neither the PI nor any key personnel associated with this study have any financial interests or other "conflicts" related to this study.

28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES

This project does not qualify under the California Clinical Trial Law.

29. OTHER APPROVALS/REGULATED MATERIALS

Approval from other UCSD review committees is not necessary for this project.

30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

Not Applicable.