1) **Protocol Title: Increasing early infant male circumcision uptake in Zambia: Like Father Like Son**
2) **Clinical Trials Number: NCT04119414**
3) **Version #: 1.2**

INSTRUCTIONS:

4) Protocol Title

Increasing early infant male circumcision uptake in Zambia: Like Father Like Son

5) IRB Review History*

This protocol is being submitted to another review board, the University of Zambia Biomedical Research Ethics Committee (UZBREC). *As an international study, it does not require single IRB review.*

*Objectives**

Objectives

Specific Aims: Voluntary medical male circumcision (VMMC) has proven to be effective in decreasing the risk of HIV infection for men in Southern and Eastern Africa by 51-60% (Bailey et al., 2007, Auvert, et al., 2005, Gray et al., 2007). Post-circumcision, long-term studies have reported increased levels of protection (up to 67-73%) (Bailey et al., 2010; Mehta et al., 2013, Gray et al., 2012; Siegfried et al., 2009). Zambia has high HIV prevalence (19.7% urban) and incidence (4% urban), and a low rate of male circumcision (23%). The Republic of Zambia Ministry of Health (RZMOH) established a National Operational Plan for the Scale-up of Voluntary Medical Male Circumcision (RZMOH, 2016-2020) with the goal of performing 2 million VMMCs by 2020. While most men surveyed in several sub-Saharan African countries expressed willingness to consider circumcision, (Westerkamp et al., 2007) over 80% of Zambian males expressed no interest in undergoing VMMC (Zambia Sex Behav Survey, 2010).

The Spear & Shield 1 (S&S1) comprehensive adult HIV risk reduction program conducted by this research team significantly increased VMMC rates among Zambian men who initially had no interest in undergoing the procedure. This clinical trial established that substantial increases in VMMC rates were attributable to the combination of the Spear & Shield behavioral intervention plus increased VMMC availability. Currently, the Spear & Shield 2 (S&S2; R01MH095539) dissemination and implementation program has expanded this Community Health Center (CHC)-based program to 96 CHCs in four Zambian Provinces with high rates of HIV and low prevalence of male circumcision. To date, ~20,000 men and women have attended the S&S2 program at 72 clinics since the study began almost 3 years ago.

The Government of the Republic of Zambia, as well as several other Sub-Saharan countries, has identified Early Infant Male Circumcision (EIMC) as an important component of the overall program to increase male circumcision at the population level. Consequently, as VMMC promotion progressed, the GRZ Ministry of Health (MOH) began development of an EIMC program as a long-term HIV prevention solution for the ~360,000 male neonates born yearly. EIMC is a safer, simpler and less expensive procedure than adult VMMC, with shorter healing times (Weiss et al., 2010; Binagwaho 2010; WHO/UNAIDS 2007). By increasing the availability and acceptability of both EIMC and VMMC, the overall population health benefit of male circumcision could be realized in less than one generation. In addition to offering lifetime protection from several diseases and disorders, EIMC is associated with improved penile hygiene and

fewer urinary tract infections, which are prevalent in uncircumcised infants. Yet, despite widespread agreement that EIMC would convey considerable short- and long-term health advantages, only about 0.3% of male infants have been circumcised (National VMMC Program Officer, 2018).

This study proposes to conduct a 3-year pilot to explore the barriers and facilitators associated with EIMC acceptability, and the feasibility and acceptability of providing a novel EIMC strategy, "Like Father, Like Son" (LFLS) plus S&S, in CHCs in Lusaka, the Zambian capital. This pilot study would expand the impact of S&S by adopting a family-oriented approach to encourage pregnant couples to consider both EIMC for their neonates and VMMC for fathers and other uncircumcised males in the household. This study proposes to 1) match 8 clinics on past 12 month VMMC/EIMC rates and catchment size and randomize to intervention (n = 4 clinics, S&S+LFLS + VMMC/EIMC training) or observation conditions (n = 4 clinics, VMMC/EIMC training only), 2) utilize collaborative input from community stakeholders (n = 144; CHC Community Advisory Boards, patient focus groups, EIMC experts) at the 4 Experimental CHCs to develop study protocol, assessments, and LFLS intervention sessions, 2) establish formative, process and outcome evaluation criteria to assess feasibility and guide the implementation of the LFLS sessions, 3) enroll 300 pregnant couples (75 per experimental clinic over 18 months recruitment), 3) conduct baseline, pre- and immediately post-partum and 6-month post-partum assessments, and 4) evaluate acceptability and feasibility of S&S+LFLS at the CHC level, and the effect of S&S+ LFLS on uptake of VMMC and EIMC. This study proposes to conduct a 3-year pilot study to explore the barriers and facilitators associated with early infant male circumcision (EIMC) acceptability, and the feasibility and acceptability of providing a novel EIMC strategy, "Like Father, Like Son" (LFLS) plus Spear & Shield (an evidence-based intervention), in community health centers (CHCs) in Lusaka, the Zambian capital. This pilot study would expand the impact of Spear & Shield by adopting a family-oriented approach to encourage pregnant couples to consider *both* early infant male circumcision (EIMC) for their neonates and voluntary medical male circumcision (VMMC) for fathers and other uncircumcised males in the household.

Aim 1. Develop, pilot and conduct formative, process and outcome evaluations to assess the CHC level feasibility and acceptability of S&S+LFLS.
Aim 2. Assess the intrapersonal, interpersonal, structural, and sociocultural factors relevant to the "Like Father, Like Son(s)" intervention, and develop program components to respond to these factors.

Hypothesis 2. Father's circumcision status, paternal grandparent's circumcision attitudes, peer circumcision attitudes, father's HIV status, and mother's HIV status will be indirectly related to the decision to elect EIMC through **the father's circumcision** attitudes. A mother's circumcision attitudes will be influenced by her HIV status, and her attitudes will also influence the father's circumcision attitudes.
Aim 3. Assess whether the combined S&S + LFLS pilot program will increase uptake of EIMC at the clinic level.

Hypothesis 3. The S&S + LFLS experimental condition clinics will have higher numbers of EIMC in comparison with observation condition clinics.

6) Background*

Voluntary medical male circumcision (VMMC). Randomized clinical trials involving over 11,000 adult men in Uganda, Kenya and South Africa have confirmed that voluntary medical male circumcision (VMMC) provides upwards of 60-73% protection for men from HIV infection (Auvert et al., 2005; Bailey et al., 2007; Gray et al., 2007; Weiss et al., 2000). Yet, despite these encouraging findings, the majority of Zambian men remain reluctant to circumcise (Weiss et al., 2015; Zulu et al., 2015; Republic of Zambia Ministry of Health (RZMOH, 2016). Zambia has the lowest level of MC acceptability among the 10 Sub-Saharan African countries with high HIV incidence. To attain the Zambian national goal of 2 million VMMCs by 2020, innovative "demand generation" strategies will be required to increase the acceptability of VMMC, and thereby, to reach the desired increases in the rates of circumcision nationally (RZMOH), 2016).

Zambia, population 17.61m, has a low rate of circumcision nationally (22%), even though cultural groups in the Northwestern and Western Provinces (the Luvale, Lunda, Luchazi, Chokwe), practice traditional male circumcision as a rite of passage for adolescent males (UNAIDS, 2018). The Government of the Republic of Zambia (GRZ) has demonstrated political will and support for VMMC services, but, as in Zimbabwe (Hatzold et al., 2014), challenges to VMMC uptake remain, e.g., fear of pain, adverse events, reduced sexual performance, misinformation about sexual abstinence during healing, MC-stigma associated with traditional circumcisers, and concerns regarding women's preferences for a specific circumcision status (Makawa, 2012). The Spear & Shield clinical trial conducted by this team from 2010-2015 (R01MH095539) found men who were better informed regarding VMMC protection, who perceived greater VMMC cultural acceptability, and who had female partners with greater VMMC acceptability were more likely to undergo VMMC (Jones, Cook et al., 2014; Redding et al., 2015; Weiss et al., 2015; Cook et al., 2015).

The Spear & Shield Program. Evidence-based community-level sexual risk reduction programs can increase VMMC acceptability and convince "hard to reach" uncircumcised Zambian men that VMMC is their best means of reducing risk of HIV infection if highly consistent condom use is not an option (De Cock et al., 2012). The original Spear & Shield program (S&S1; Weiss et al., 2015) was designed to increase both availability and acceptability of VMMC. Currently being disseminated and implemented in 96 community health centers (CHCs) in four Zambian Provinces, Spear & Shield 2 (S&S2) is a comprehensive sexual risk reduction intervention program that trains HIV Voluntary Counseling and Testing (VCT) counselors to conduct the S&S intervention and trains CHC biomedical staff to perform VMMCs. The intervention encourages use of multiple prevention strategies (Vermund & Hayes, 2013; de Bruyn et al., 2010) while emphasizing the unique lifetime HIV risk-reduction characteristic of VMMC, as well as other health-related benefits [(e.g., reduced HPV/cervical cancer risk for female partners, chancroid sexually transmitted infections (STIs), penile cancer) (Auvert et al., 2009; Gray et al., 2007; White et al., 2008; Weiss et al., 2006; Tobian et al., 2009; Sobngwi-Tambekou et al., 2009)]. The S&S1 program was effective in increasing the likelihood of men opting for VMMC by 2.5 times in comparison with the Control condition and by 8.5 times in comparison with an Observation-Only condition.

Increased condom use among the those in the Experimental group who underwent VMMC was also observed, countering concerns of behavioral disinhibition following VMMC (Weiss et al., 2015). If implemented on a nationwide scale, results could have a major public health impact on HIV prevention.

Women and VMMC. Men participating in S&S were encouraged to invite their female partners to participate, as the national Zambia Sexual Behaviour Survey found men viewed their partners' potential preference for an uncircumcised penis as an impediment to considering VMMC (Central Statistical Office, MOH, University of Zambia, and MEASURE Evaluation, 2010). The S&S intervention, with female participation of 80%, found a 6% increase in uptake of VMMC among Experimental participants attributable to positive shifts in women's preferences (see Preliminary Studies, Cook et al., 2015). To optimize women's influence on VMMC decision-making, the comparable women's intervention focused on VMMC attitudes and beliefs and highlighted VMMC health benefits for women (Westercamp et al., 2012; Lanham et al., 2012).

Early Infant Male Circumcision (EIMC, performed during the first 60 days of life). EIMC is a safer, simpler and less expensive procedure with shorter healing times than adult VMMC (Weiss et al., 2010; Binagwaho 2010; WHO/UNAIDS 2007). In addition to offering lifetime protection from several disorders/diseases, EIMC is associated with improved penile hygiene and fewer of the urinary tract infections (UTIs) that are prevalent in uncircumcised infants. By increasing the availability and acceptability of both EIMC and VMMC, the overall population health benefit of male circumcision could be realized in less than one generation. Consequently, as VMMC promotion began, the Ministry of Health began development of an EIMC program as a longterm HIV prevention solution for the ~360,000 male neonates born yearly in Zambia (GRZ Central Statistics Office, 2018). However, a study by Waters et al (2013) of 2000 Zambian pregnant women provided with information on EIMC, found although 97% agreed they would circumcise their infant if they had a boy, only 11% actually did so. More recently, the Zambia Operational Plan for VMMC 2016-2020 (RZMOH, 2016) reported that significantly lower uptake of infant MC had been achieved than originally targeted. In fact, as of October 1, only 1,181 of the 362,078 newborn males in 2018 underwent EIMC (GRZ Central Statistics Office, 2018; clinic data); in EIMC trained clinics in Lusaka, only ~0.02% of male infants were circumcised in 2018 (clinic data).

The proposed study seeks to address this discordance by developing and testing an innovative "father and son" biobehavioral demand generation strategy, providing on-site availability of EIMC and VMMC services embedded in the Spear & Shield behavioral intervention. The program, entitled "Like Father, Like Son" (LFLS), will evaluate the feasibility and acceptability of offering combined EIMC and VMMC services and behavioral interventions, building on successful implementation strategies utilized in S&S1 and 2.

Factors underlying EIMC Decision Making. Acceptability underlies uptake of both EIMC and VMMC (Sekhon et al., 2017) and the primary determinant of EIMC is

the father's MC status (Mavhu et al., 2011). Challenges to acceptability of EIMC have been identified among both women and men in Malawi, Zambia, Zimbabwe, Botswana, Uganda, South Africa, and Kenya. Barriers reported by men include availability of EIMC services, cultural/religious considerations, and lack of knowledge about EIMC (Chilimampunga et al., 2017; Mavhu et al., 2015); challenges to uptake identified by both women and men include religious/cultural issues, parental concern for son's autonomy, men as decision makers in the family (Jarrett et al., 2014), concerns regarding pain (Waters et al., 2012; Mavhu et al., 2011; Young et al., 2016), and access to services (Jarrett et al., 2014). Other barriers included skepticism regarding EIMC's protection against HIV, adverse side effects, and the perception that infant penises were too fragile for EIMC (Mavhu et al., 2012). Uptake increased when parents were reassured that infants could safely undergo EIMC (Waters et al., 2013). Women, including pregnant women, were generally receptive to EIMC (Chilimampunga et al., 2017; Waters et al., 2012; 2013; Mavhu et al., 2012; Plank et al., 2010; Kankaka et al., 2017). Women with more HIV knowledge were more receptive to EIMC, and women expressing high VMMC acceptability also endorsed high EIMC acceptability (Mavhu et al., 2011). Overall, women's MC perceptions were more positive than men's, both before and after receiving EIMC information, especially regarding younger boys (Albert et al., 2011). Following EIMC, mothers in Uganda and Zimbabwe reported satisfaction with the outcome (Mavhu et al., 2015; Kankaka et al., 2017).

Little research has evaluated the impact of demand creation on EIMC uptake. However, studies that evaluated uptake in response to information on EIMC (Waters et al., 2013; Mavhu et al., 2015; Mavhu et al., 2016; Kankaka et al., 2017; Plank et al., 2013) found EIMC uptake did not reflect reported acceptability. This discrepancy between theoretical acceptability and actual uptake has not been addressed. Barriers to EIMC suggest that poor uptake may arise from the bottleneck created by the final decision resting with husbands; 85% of women indicated that husbands' agreement is important, and only 10% of women identified as sole decision makers (Albert et al., 2011). Parents were more willing to accept EIMC if fathers were circumcised, if mothers were more educated, if couples were serodiscordant, or if parents were aware of the benefits of EIMC (Waters et al., 2013; Mugwanya et al., 2011; Young et al., 2016). While 83% of mothers in South Africa accepted EIMC, many refused the procedure as they were required to first discuss it with their husband and/or family (Young et al., 2016). Decisions governing sons are traditionally the purview of the father in most African societies, although the opinions of mothers and paternal family members may also be solicited (Mavhu et al., 2017). In addition, studies suggest that fathers "need to be provided with information directly, not just through their wives" (Mavhu et al., 2017; GRZ 2018). The proposed study will attempt to bridge the gap between hypothetical acceptability and low uptake by creating an intervention to increase acceptability and availability of EIMC and VMMC during the perinatal period, focusing on both parents and the option of a shared father-son circumcision experience. As such, pregnancy provides a "window of opportunity" to encourage the participation of both members of the couple in a culturally tailored informational/motivational HIV prevention program.

Based on the IMB Model (information, motivation, behavioral skills) and the theory of planned behavior addressing normative behaviors (Ajzen & Fishbein, 1980) this exploratory study will examine the factors (e.g., father's circumcision and HIV status, paternal grandparents' and peer circumcision attitudes, mother's HIV status and circumcision attitudes) that underlie the decision to engage in VMMC and EIMC, and tailor the LFLS intervention component to respond to these factors. The study will offer S&S + LFLS to pregnant couples, targeting the perinatal period to address MC for both father and son(s), and pilot test the biobehavioral program, assessing feasibility of offering S&S+LFLS in Lusaka Province CHCs, the acceptability of the pilot program, and the potential of S&S+LFLS to optimize both VMMC and EIMC uptake.

Innovation

This application includes a number of innovative components. Promoting the bonding component of the father-son relationship, this application simultaneously addresses both the short and long-term HIV risk reduction goals associated with increasing availability and acceptability of male circumcision. We are unaware of any evidence-based effort in sub-Saharan Africa to stimulate prospective parents to simultaneously consider both EIMC and VMMC. The S&S + LFLS intervention could stimulate both EIMC and VMMC to occur during the pre- and immediate postnatal period, prior to resuming sexual activities, which corresponds with both mother and father undergoing healing following childbirth and VMMC, respectively. (N.B.: Our previous research found approximately 25% of the men undergoing VMMC were unable to abstain from sexual activities for the 6-week healing period; this group accounted for the majority of adverse events and dissatisfaction with VMMC). As most Zambian men are uncircumcised, a combined VMMC/EIMC program could encourage prospective fathers choosing to undergo VMMC to circumcise their male neonates, as well as other sons, procedures that would render their penises identical. Among men already circumcised, the program provides additional support for EIMC and VMMC for other sons. Finally, this program includes community health center EIMC sensitization, training and behavioral interventions, optimizing the impact of demand generation on uptake.

Impact

There are several compelling reasons underscoring the potential impact of the combined VMMC/EIMC program. Combining availability of both circumcision services is cost-effective in terms of training of health care providers and equipping facilities to perform both procedures. The additional skills required for EIMC procedures can be added onto the skills of those trained in VMMC at a fraction of the cost of setting up EIMC training activities de novo. EIMC is safer, simpler and less expensive than adult VMMC with shorter healing times. It offers significant lifelong protection from HIV, chancroid STIs, penile cancer, HPV, and UTIs. The integration of the program within an evidence-based VMMC demand generation intervention would optimize sustainability (IIIE, 2013), establishing local capacity to provide a CHC-based VMMC/EIMC program, in contrast with externally supported "parachute in" programs. Finally, successful combined VMMC and EIMC programs would ultimately "sunset" the need for an adult program within a generation.

The National Operational Plan for VMMC In Zambia, 2016-2020 (RZMOH, 2016, pp.62-63) calls for EIMC demand creation similar to that needed for VMMC, yet "scale up has been slower than anticipated." The current application will apply demand generation strategies developed during formative work, utilizing CHC-tailored methods to optimize EIMC uptake. In addition, as noted above (RZ MOH, 2016, p.63), "the immediate postnatal period is too late to introduce [EIMC] to mothers/parents. Parents need sufficient time to discuss the issue among themselves, with their families and with health care workers before they are ready to authorize consent." Consistent with the National Plan, this study proposes to introduce EIMC to both parents prior to delivery, expanding male involvement during pregnancy to maximize the impact of the S&S+LFLS intervention.

VMMC and EIMC are high impact HIV prevention strategies: Successful outcomes of this study could provide a biobehavioral model to significantly increase the availability and acceptability of MC services within CHCs. With ~ 360,000 male newborns entering the population pool each year, combined EIMC/VMMC programs could ultimately have a major impact on the long-term health benefits conveyed by MC. Training existing health care staff to achieve an expanded scope of practice will leave a sustainable footprint by engaging both health care providers and leaders in the implementation and uptake of the VMMC/EIMC – S&S + LFLS Program.

Preliminary studies. This research team has been working in Zambia since 1999. The Zambian Spear & Shield team, led by Drs. Zulu and Chitalu, has established strong linkages and buy-in from the Ministry of Health, and Provincial and District Health leadership to promote risk reduction programs throughout Zambia (Chitalu et al., 2016; Jones et al., 2015; Weiss et al., 2011). Our previous translation and implementation studies in Zambia (e.g., Vamos et al., 2014, Chitalu et al., 2016), and the US (Jones et al., 2013, Weiss et al., 2011), have addressed the importance of engagement in achieving sustainable health care service programs. Drs. Weiss and Jones are co-creators of the Spear & Shield intervention (Weiss et al., 2015, Lancet HIV), and were co-investigators on Dr. Castro's two US studies promoting infant circumcision among Hispanic couples, and adult VMMC among high-risk Hispanic men, a population with low MC and disproportionately high HIV incidence (Castro et al., 2010; 2012). Dr. Mweemba is experienced in VMMC research (Chanda et al., 2012). Consultant Dr. Bowa is a world-renowned expert on EIMC and led the original Zambian study (Bowa et al., 2013; Waters et al., 2012, 2013); consultant Royd Kamboyi is the National VMMC Program Officer.

Spear & Shield 1 Project. Project aims were to increase both the availability and acceptability of VMMC among uncircumcised HIV- VCT participants who at study entry had no interest in VMMC for HIV prevention (Weiss et al., 2015; Jones, Cook et al., 2014). This four-year, cluster RCT enrolled 800 HIV-, uncircumcised men and 668 female partners. Experimental (S&S) group participants underwent more VMMC compared to Controls (40% vs. 24%; adjusted OR 2.45, 95% CI 1.24–4.90; p=0.02).

VMMC rates continued to increase in the Experimental condition between 6 to 12 months post-intervention, compared to the Control condition, which leveled off after 3-6

months (see Figure). Experimental group participants undergoing VMMC increased condom use (b = .055, 95% CI = (.01, .10), p = .027); no change was observed among Control participants who underwent VMMC, reinforcing the importance of "nesting" VMMC promotion in a comprehensive sexual risk reduction program (Rotheram-Borus et al., 2009; Alsallaq et al., 2013). Women's (n = 668) increased acceptance and preference for VMMC was noted in the Experimental condition (b = .390, p < .001), and mediated the relationship between the intervention and men's readiness to undergo VMMC at 12 months (indirect effect = .162, 95% CI = [.042, .318]) (Cook et al., 2015).

Increasing the Availability and Acceptability of Medical Male Circumcision in Zambia: The Spear & Shield 2 Project. PI. Weiss, Co-PIs R. Zulu, N. Chitalu, K. Bowa, D. Jones (NIH/NIMH R01MH095539). The Spear & Shield 2 program (S&S2) is currently disseminating and implementing the Spear and Shield 1 intervention, increasing the uptake of VMMC by training CHC staff in 96 CHCs in 4 Provinces to perform VMMCs and training CHC VCT staff to conduct the S&S program. S&S 2 has scaled up in Lusaka, Central, and Southern Provinces. CHC Staff have conducted VMMCs and have provided the Spear & Shield intervention to ~20,000 men and women at 68 clinics since the intervention began almost 3 years ago. Preliminary data indicate that sites receiving both VMMC plus Spear & Shield training had significantly higher numbers of VMMCs than the sites that initially received VMMC training only (F=5.23, p=0.028). Over the next two years, Spear & Shield 2 will be implemented and disseminated in the final 28 CHCs in Copperbelt Province. In addition to training ~300 qualified health care providers (e.g., physicians, clinic officers, nurses) in VMMC, the program ensures space, surgical supplies and administrative support are available at each CHC to accommodate VMMC and S&S services. The existing program infrastructure provides the ideal setting for the integration of the EIMC program.

Attitudes of Hispanics about male circumcision of their unborn children. PI, J Castro, Co-I, S Weiss & D Jones (El Centro, P60MD002266). This study was conducted with pregnant Hispanic women and their partners attending prenatal clinics in Miami and explored facilitators and challenges to promoting EIMC as an HIV prevention strategy. Participants (n = 148) attended gender concordant focus groups and interviews (n = 48) assessing EIMC attitudes. Results indicated high interest in EIMC among women, and a desire among men for infants to share their MC status (Castro et al., 2010).

Barrier Acceptability among Culturally Diverse HIV+/- Women and their Partners (The NOW/NOW2 Projects), PI S. Weiss, CoPIs N Chitalu, D Jones (RO1MH63630). The NOW risk reduction intervention (n=1080 HIV+/- women US/Zambia) study identified influences on sexual barrier acceptability and developed and tested strategies to improve acceptability and maintain barrier use (e.g., Jones et al., 2001; 2004; 2007).

Implementing HIV Risk Reduction in Zambia (Partner/Partner 2 Projects), PI D Jones, Co-PIs S Weiss, N Chitalu (R24HD43613; R01HD058481). The Partner Project (R24HD43613, Jones, PI) (Jones et al., 2009); found a high intensity sexual behavior intervention increased safer sex more than a low intensity condition (n=420 couples). Partner 2 (260 HIV+/- couples) successfully translated the original Partner couples intervention to community CHCs (Jones et al., 2009; Chitalu et al., 2016; Jones, Weiss, et al., 2014).

7) Inclusion and Exclusion Criteria*

- Men and women must be able to understand and sign the Informed Consent in English or local language.
- All participants must be adults able to provide consent
- Women participants may be pregnant
- Individuals not yet adults (infants, children, teenagers) are not eligible to participate
- Prisoners will not be eligible for recruitment

Study population.

Experimental sites only –participants are only recruited at experimental sites.

Clinic leaders and health care providers will be briefed on the study and study eligibility by the study team.

Potential patient candidates for couples and focus groups attending the clinic for HIV testing or pregnancy will be briefed on the study, and if interested, will be referred by clinic health care providers at the voluntary counseling and testing site and the antenatal clinic site (ANC) to the study staff.

Clinic leadership will provide referrals to CAB members to attend CAB meetings.

Participants will meet with study staff and will be verbally screened for eligibility based on the following criteria, by study staff at each clinic.

CAB participants: CABs operate in each CHC clinic and are comprised of community zone leaders in the clinic catchment area; as zone leaders, they educate their community on the study objectives and sensitize their community on study goals, risks and benefits. Eligible CAB members will be men and women aged >18, representing a ward within each experimental CHC site catchment area. Twenty Community Advisory Board (CAB) member participants will be recruited from CABs at each clinic (20 CAB members x 4 clinics, n = 80), and each attendee will be compensated ~$US10 per visit.

Focus Group participants. Stakeholder participants will be recruited from ANCs to attend gender specific focus group discussions (FGDs). A total of 8 pregnant couples from each of the 4 experimental CHC clinics (8 couples per clinic) will be recruited for this study [2 gender specific FGDs per clinic; (8 men and 8 women) x 4 clinics = 64 participants]. Both members of each couple must enroll to participate. Eligible participants will be pregnant couples (men and pregnant female partners) aged >18, attending the antenatal clinic of the experimental CHC. No personal, individually identifying information will be collected and no individual interviews or assessments will be conducted with FGD Members. Each attendee will be compensated ~$US10 per visit.

S&S+LFLS Participants. Pregnant couple participants (300 couples, n = 600 participants) will be recruited over 18 months via referral from ANC/VCT and enrolled as couples. A total of 75 pregnant couples will be recruited from each of the 4 clinics participating in LFLS (75 pregnant couples per clinic x 4 clinics = 300 couples = 600 individual men and women.) Both members of each couple must enroll to participate. Eligible women will be pregnant (up to 6 months pregnant), aged >18, any HIV status, and the partner of a male participant enrolling (neonates undergoing EIMC are receiving a clinical service approved by parents; only parents are study participants). Eligible men will be aged > 18, any HIV status [in accordance with Zambian and WHO/UNAIDS (2016) policy for MC eligibility], and the partner of the pregnant female participant enrolling. There is no upper age limit for participation, and each person will be compensated ~$US10 per visit.

8) Number of Subjects*

A total 744 individuals will be recruited; 300 couples (600 men and women) and 144 CHC Community Advisory Boards members, patient focus group members, and EIMC experts.

9) Study-Wide Recruitment Methods*

Participants will be recruited by the community health center staff by referral to the study staff at the clinic site and by word of mouth only. Clinic sites are in Lusaka Province, and were reviewed and approved by the Lusaka Provincial Health Officer leadership. Following guidelines for site VMMC accreditation (Health Professions Council of Zambia, 2010), the following criteria governed selection of 8 clinic sites: 1) a community clinic catchment area of >30,000; 2) 2 health care providers available at site for VMMC/EIMC training and provision; 3) >2 voluntary counseling and testing (VCT) counselors and antenatal clinic (ANC) staff available for S&S+LFLS training, 4) space for VMMC/EIMC, 5) > 150 births per month, 6) a maternity ward. Clinic selection (n = 8) focused on spatial separation between clinics to avoid clinic contamination. CHCs will be visited by the research team to introduce the study to relevant staff, and staff members will refer clinic patients (couples intervention and focus groups) based on study criteria from those attending the ANC and VCT clinics. Senior staff will refer CAB members for participation. EIMC experts are consultants on the project.

Experimental sites only –participants are only recruited at experimental sites.

Clinic leaders and health care providers will be briefed on the study and study eligibility by the study team.

Potential patient candidates for couples and focus groups attending the clinic for HIV testing or pregnancy will be briefed on the study, and if interested, will be referred by clinic health care providers at the voluntary counseling and testing site and the antenatal clinic site (ANC) to the study staff.

Clinic leadership will provide referrals to CAB members to attend CAB meetings.

Participants will meet with study staff and will be verbally screened for eligibility based on the following criteria, by study staff at each clinic.

No materials will be developed for recruitment flyers, etc. as this is not needed.

10) **Study Timelines***

LFLS TIMELINE: Activity & Month	**M1-3**	**M4-6**	**M7-9**	**M10-12**	**M13-15**	**M16-18**	**M19-21**	**M22-24**	**M25-27**	**M28-30**	**M31-33**	**M34-36**
Protocol development Identify 8 Lusaka CHCs Clinic sensitization Historical (1yr) data collection Monthly VMMC/EIMC data collect CAB meetings, FGDs, interviews Feedback & Prepare LFLS	X X X X X	X X X X X X	X	X	X	X	X	X	X	X		
Train 2 Providers at all 8 sites in EIMC/VMMC (n=16) Train 2 Providers (n = 8) at the 4 Experimental sites in S&S+LFLS		X X										
Experimental: Recruit & Assess n=300 Pregnant Couples			X	X	X	X	X	X				
Provide VMMC/EIMC Services Prenatal: S&S+LFLS Session 1			X X	X X	X X	X X	X X	X X				
Postpartum: LFLS Session 2 Postpartum Follow-up Assess				X X	X X	X X	X X	X X	X X			
6 mos post-partum: Assess EIMC/VMMC (father, sons, infant)						X	X	X	X	X		
Data Analysis. Manuscripts. Prepare R01 application											X	X X

Community Advisory Board (CAB) Members. CAB Members will meet for three formal group discussions in a private meeting room within their experimental clinic. CAB members will be asked to 1) provide input on cultural factors that influence attitudes, perceptions, and beliefs about EIMC within their communities and among the ethnic groups predominant in the Lusaka Province, and 2) provide input on the LFLS intervention and assessment content and information on community issues and concerns that could influence LFLS program uptake. CAB Members associated with each CHC will thereby facilitate the adaptation of the intervention strategies to the local culture and clinic culture, enabling LFLS to work with the community rather than imposing the program on the community. No personal, individually identifying information will be

collected and no individual interviews or assessments will be conducted with CAB Members.

Focus Group Discussion (FGD) Members. FGD members will meet in gender concordant groups in a private room within their experimental clinic site; members will provide input on cultural factors that influence attitudes, perceptions, and beliefs about EIMC among pregnant couples. They will provide guidance on cultural attitudes, ethnic preferences, beliefs and perceptions surrounding EIMC among pregnant couples in Lusaka. FGD members will inform the study on local issues or community concerns that could influence program uptake. No personal, individually identifying information will be collected and no individual interviews or assessments will be conducted with FGD members.

Pregnant Couple Members attending LFLS. All S&S+LFLS study participants will be followed from enrollment to six months post-partum (maximum ~ time of participation based on enrollment at ~3-4 months pregnant = 12 months). Participants will complete baseline, pre-and post-partum and 6-months post-partum assessments and attend the Spear & Shield and 2 LFLS intervention sessions (see below).

Enrollment will be conducted from month 7 – 24, a total of 18 months.

11) Study Endpoints*

Primary and secondary study endpoints.

Primary endpoints.

- EIMC uptake (infant)
- VMMC uptake (father and other sons)

Secondary endpoints.

- Father's and mother's circumcision attitudes

Primary or secondary safety endpoints.

This is a behavioral feasibility study, not requiring safety endpoints.

12) Procedures Involved*

Design.

Like Father Like Son(s) proposes to develop intervention materials and test the effectiveness of the intervention to enhance the uptake of early infant male circumcision (EIMC) and voluntary medical male circumcision (VMMC) in the community health center (CHC) setting.

The study utilizes a longitudinal repeated measures design [2 (condition) x 4 (time points)]. The pilot study intervention will expand the Spear & Shield (S&S) intervention to include the "Like Father Like Son" component (S&S + LFLS).

The pilot study will randomize 8 clinics to Experimental and Observation conditions; clinics will be matched on catchment area size and current EIMC and VMMC rates.

Experimental clinics (n = 4) will be trained to offer "S&S+LFLS"; Observation clinics (n = 4) will be "Observation Only" sites. Observation only sites will not recruit participants and will only be "observed" regarding the total number of VMMCs and EIMCs conducted at each individual clinic - Observation Only clinics will only provide clinic level aggregate data.

The study will train both Experimental and Observation Only clinic staff to conduct VMMC and EIMC procedures in order to provide equivalent services at all clinics, controlling for the availability of circumcision at all sites. Participants will only be recruited from experimental sites. The study will also assess the feasibility and acceptability of offering S&S+LFLS at the CHC level, and if successful, plan for a clinical trial of the S&S+LFLS intervention.

CAB Meetings & Focus Groups.

CAB Meetings & FGDs. FGDs and CAB meetings' discussion topics have been broken into smaller units within the context of the socio-ecological framework (from the individual to the context), using the PRECEDE model (Green & Kreuter 1999).

CAB and FGD activities will be led by Dr. Mweemba with support from study staff.

Focus group discussion stem items (see assessments attachment) explore intrapersonal, interpersonal and structural level factors associated with EIMC, and factors associated with each level. Stem items were derived from previous research (e.g., Albert et al., 2011; Amuri et al., 2016; Mavhu et al., 2012; Mavhu et al., 2016; Plank et al., 2010; Waters et al., 2012) and will be presented as open-ended questions; time will be provided to address additional topics as they arise. Prior to study onset, additional stems may be proposed using an iterative, collaborative process involving the University of Miami/University of Zambia (UZ) study team, which includes psychologists, social scientists, a pediatrician, surgeons, an infectious disease physician, and psychometricians. Final stem items will be reviewed and refined by the entire team prior to initiation of FGDs and CABs.

CAB meetings and FGDs will be approximately 1.5 hours in duration.

CAB meetings (1 per clinic, 3 meetings, n = 80 persons) and FGDs (2 per clinic, each gender concordant, 8 FGDs, n = 64) will be audio recorded and transcribed by trained study staff from the UZ into English; FGDs and CABs will be conducted in private areas in CHCs. Field notes will be made by staff during FGDs, CABs and study-related CHC staff meetings; meetings will be summarized from field notes. The project coordinator and study staff are social scientists and are experienced in conducting FGDs.

Community Advisory Board (CAB) Members. CAB Members will meet for three group discussions in a private meeting room within their experimental clinic. CAB members will be asked to 1) provide input on cultural factors that influence attitudes, perceptions, and beliefs about EIMC within their communities and among the ethnic groups predominant in the Lusaka Province, and 2) provide input on the LFLS intervention and assessment content and information on community issues and concerns that could influence LFLS program uptake.

CAB Members associated with each CHC will thereby facilitate the adaptation of the intervention strategies to the local culture and clinic culture, enabling LFLS to work with the community rather than imposing the program on the community.

No personal, individually identifying information will be collected and no individual interviews or assessments will be conducted with CAB Members.

Focus Group Discussion (FGD) Members. FGD members will meet in gender concordant groups in a private room within their experimental clinic site; members will provide input on cultural factors that influence attitudes, perceptions, and beliefs about EIMC among pregnant couples.

They will provide guidance on cultural attitudes, ethnic preferences, beliefs and perceptions surrounding EIMC among pregnant couples in Lusaka. FGD members will inform the study on local issues or community concerns that could influence program uptake. No personal, individually identifying information will be collected and no individual interviews or assessments will be conducted with FGD members.

Couples Assessments.
Assessments at baseline will be completed using audio computer-assisted self-interview (ACASI) software, with support from study staff as needed. Participants will be assessed individually in a private office in the CHC; ACASI headphones and touchscreen computers will provide confidentiality and privacy. LFLS session 2 will be scheduled to coincide with the post-partum neonatal clinic visit in the first week following birth.

Each assessment measure (see attachment) is related to the study theoretical model, outcomes (feasibility, acceptability, uptake) and associated factors (e.g., plans, knowledge, norms, attitudes/beliefs and cultural or religious values associated with EIMC/VMMC, family decision making, stage of readiness).

After each LFLS session, a brief paper-based questionnaire will be individually administered to assess Stage of Change. VMMC/EIMC uptake and the role of parents, family members, peers and HIV serostatus in decision-making will be assessed by telephone or office visit at 6 months post-partum.

Couples intervention.
S&S Intervention. The S&S program was developed and culturally tailored for men and women from qualitative data on VMMC attitudes, preferences and beliefs. This comprehensive risk reduction intervention consists of 4 weekly 90-minute manualized group sessions. Female partners of participants are invited to participate in 4 comparable sessions on women's VMMC-related issues (Martinez Perez et al., 2015).

Session One addresses HIV/STDs, safer sex, male condoms, male circumcision and sexual communication. Multiple strategies for protecting against HIV are discussed, emphasizing VMMC. The session addresses adult VMMC as a permanent method of risk reduction and provides a forum for discussion of the VMMC procedure, concerns, limitations and beliefs. Cognitive behavioral (CB) skill training heightens participants' awareness of reactions to VMMC, reframing thoughts that impede VMMC uptake, condom use, and sexual communication. Participants receive a week's supply of condoms after sessions 1-4.

Session Two addresses female condoms and their correct usage using female anatomical charts. CB skills are applied to sexual negotiation and improving communication techniques in relationships. Potential benefits of VMMC for female partners are addressed.

Session Three introduces novel products (e.g., PrEP, microbicides) and multiple protective strategies. The session includes sharing experiences, concerns and attitudes about female condoms, perceptions of partners' reactions to VMMC, role plays for problem solving and use of CB skills. A peer who has undergone VMMC shares experiences, abstaining from sex during healing (Hewett et al., 2012), and sexual satisfaction (Kigozi et al., 2008; Zulu et al., 2015), and answers questions about VMMC.

Session Four reviews personalized HIV risk reduction methods and includes a presentation on the VMMC procedure by a CHC VMMC provider, who discusses benefits and risks, post-VMMC recovery and resumption of sexual activities. High risk sexual behavior and alcohol/drugs are discussed, and CB skills are used to address conflict resolution, communication and sexual negotiation.

LFLS Intervention. The existing standard of care (RZMOH, 2016) outlines the need to ensure that parents and guardians need time to understand the importance of EIMC before bringing babies in for EIMC and should be sensitized before delivery. ANC and VCT staff are encouraged to sensitize ANC attendee mothers and men undergoing VMMC about EIMC, and fliers for family members have been developed. The LFLS program will be developed collaboratively by Drs. Mweemba, Jones, Weiss, Zulu, Chitalu, Bowa, Castro, and Dunleavy. The intervention will be culturally tailored for individual couples' sessions using qualitative data from FGDs and existing research.

The S&S manual will guide the first phase of the comprehensive HIV risk reduction program (i.e., four 90-minute weekly group sessions, audio recorded). After the S&S sessions, each pregnant couple will attend 2 private 90-minute LFLS sessions co-led by the male and female S&S facilitators, one couples session pre-delivery and one couples session immediately post-partum. Both sessions will explore issues relevant to parental decision making related to VMMC and EIMC. The gap between session 1 (antenatal) and 2 (postpartum) will provide opportunity for parents to consult with influential others (family members and peers who are decision makers, e.g., in-laws, aunts, uncles, grandfathers, brothers and sisters in law, friends).

Session 1 will focus on the immediate benefits associated with EIMC: Cost effective, faster wound healing, easier to circumcise, less chance of adverse events, easier to clean the penis, reduced urinary tract infections. Masculine cultural norms related to potential pain, sexual performance, and pleasure will be addressed during the S&S program; couples will learn that potential pain is diminished if the procedure is completed during infancy. Pregnancy heightens awareness of danger and safety for the infant, and the desire to protect the infant. Couples will be encouraged to weigh both present and future benefits and risks for the male child, utilizing a cost/benefit approach that incorporates cultural norms regarding the health and wellbeing of all family members. Session 1 will include a testimonial from a medical practitioner with EIMC experience, and at the end of the session, couples will be invited to return to Session 2 with an

influential other, if desired. EIMC brochures will be distributed and Stages of Change questionnaires will be administered prior to the session

Topics: Why undergo EIMC? What are the benefits? Why now? When is the best time for EIMC? Information: What happens? How long does it take? Is it painful, how is pain controlled? What happens next? How long is healing, cleaning during healing? What happens to the foreskin? What are the risks? Is it safe? Who should be involved in the decision? Any additional questions or concerns about EIMC?

Session 2 will include the opportunity for couples to bring a person culturally connected to making the EIMC decision to the session (e.g., paternal mother) (Mavhu et al., 2017). To enhance acceptability, LFLS sessions will be developed from CHC CAB members, focus group discussions, and health care staff. Content will be pertinent to the critical cultural, social and religious issues and beliefs affecting EIMC decision making, and will consider research in Zambia on this topic (e.g., Waters et al., 2012; 2013). The two LFLS sessions will be manualized, based upon the community input, and "fine-tuned" using feasibility pilot data. The preliminary outline, from focus discussions in Zambia, is proposed below.

Topics: Any new questions or concerns about EIMC? How does EIMC differ from VMMC? What is the religious view on EIMC? What does my culture say about MC? What was the purpose of the foreskin? (How long is it needed?) Will EIMC affect future sexual performance, functioning & potency? Final questions? Stages of Change questionnaires are administered prior to the session.

Location. All research procedures will be performed at the clinic sites, in private offices and meeting rooms.

Risks.

There are no drugs or devices used in this study; all procedures discussed (EIMC, VMMC) are available for uptake at the clinics and are evidence based practices.

Procedures to lessen the probability or magnitude of risks.

Source records used to collect data. All surveys, scripts, and data collection forms are being developed during the formative period of this study.

Proposed Assessments at baseline (see attachment for initially selected assessments):
Instruments will be adapted from S&S1 and previous VMMC/EIMC studies (~45 minutes).
1) Demographics, to include gender, age, marital status, male children MC status, education, income, father's MC status, HIV status (All public health facility users are required to undergo HIV testing per GRZ policy) (adapted, Kabwe, 2016 and Weiss et al., 2015).
2) Stages of Change EIMC items (Precontemplation, Contemplation, Preparation, Action, Maintenance) will be adapted from Redding et al. (2015).
3) EIMC knowledge, norms, attitudes/beliefs items (adapted from Castro et al., 2010; Chilimampunga et al., 2017; Kabwe, 2015; Mugyawana et al., 2011; Waters et al., 2013; Young et al., 2016).
4) VMMC knowledge, norms, attitudes/beliefs items will be evaluated using an adaptation of Kebaabetswe et al. (2003), Weiss et al. (2015)
5) EIMC/LFLS Intervention acceptability and feasibility at the clinic level will assessed using an adaptation of Chilimampunga et al. (2017) and Mavhu et al. (2015). Topics include review of the

S&S+LFLS model, and the incorporation of EIMC services in the clinic, advantages and/or disadvantages of the program, and changes or recommendations for the program. Staff and CAB members will participate in clinic meetings to evaluate feasibility and acceptability of the S&S+LFLS program.
6) EIMC decision making will be assessed using items adapted from the conceptual model developed by Mavhu et al. (2017).
7) EIMC/VMMC Individual level Uptake. EIMC outcome, male infant; VMMC outcome, fathers and sons in the household, sex of infant & birth status (M/F; Live/Lost). VMMC/EIMC uptake and the role of parents, family members, peers and HIV serostatus in the decision-making process will be assessed by telephone or private office visit at 6 months post-partum.
8) EIMC/VMMC Clinic level Uptake. CHCs will provide 12 months of historical VMMC/EIMC rate data prior to VMMC/EIMC and S&S+LFLS training. Clinics will also collect real-time comparative VMMC/EIMC monthly aggregate data for the duration of the study (Monthly EIMC/VMMC conducted following EIMC/VMMC training (M6) to M30). Historical period: Monthly CHC EIMC/VMMC conducted for 1 year prior to EIMC/VMMC training.

Following baseline assessments, couples will complete a brief Stages of Change questionnaire prior to each prenatal and one-week post-partum LFLS sessions. Couples will be assessed at 6 months post-partum to evaluate EIMC and VMMC uptake by father, sons and infant to examine the interactive influence of EIMC and VMMC uptake, as well as the role of both parents, family members, peers and HIV serostatus in the decision-making process (Montaño et al., 2018; Mavhu et al. 2017; Cook et al., 2015; Jones, Cook et al., 2014) (see Assessments).

13) Data and Specimen Banking* n/a

14) Data Management*

Analytic Plan and Power Analysis
Aim 1. Develop, pilot and conduct formative, process and outcome evaluations to assess the CHC level feasibility and acceptability of S&S+LFLS.

Aim 2. Assess the intrapersonal, interpersonal, structural, and sociocultural factors relevant to the LFLS intervention, and develop program components to respond to these factors.
Hypothesis 2. Father's circumcision status, paternal grandparents' circumcision attitudes, peer circumcision attitudes, father's HIV status, and mother's HIV status will be indirectly related to the decision to choose EIMC through the father's circumcision attitudes. A mother's circumcision attitudes will be influenced by her HIV status, and her protective attitudes toward the newborn which will also influence the father's circumcision attitudes.

Aim 3. Assess whether the combined S&S + LFLS pilot program will increase uptake of EIMC at clinic level.
Hypothesis 3. The S&S + LFLS experimental condition clinics will have significantly higher numbers of EIMC in comparison with observation condition clinics.

Hypothesis testing. The analyses for this feasibility pilot study will begin with examination of frequencies, means, skewness, and kurtosis across study variables (EIMC, VMMC, HIV status, attitudes) to assess normality. We will conduct 1) analysis of qualitative data, 2) a path model to explore undergirding sociocontextual factors of a father's decision to elect EIMC or VMMC for his male children, 3) a test of comparison between conditions.

H2. Assess factors relevant to the LFLS model. To investigate the indirect effects of the five main predictors (paternal grandparents' circumcision attitudes, peer attitudes surrounding circumcision, father's HIV status, father's circumcision status, and mother's HIV status) on infant circumcision, a path analysis (Kline, 2011) will be conducted. To estimate the indirect effects, it will be specified that the paths between the five main predictors on infant circumcision will act through father's circumcision attitudes. Mother's circumcision attitudes will be regressed on mother's HIV status, and a regression path between father's and mother's attitudes toward circumcision will be specified. When estimating the indirect effects, results will be adjusted for the effect of number of siblings circumcised.
All potential indirect effects will be estimated by a bootstrapping approach (MacKinnon et al., 2007). R-square of indirect effects will be used as measures of effect size (Fairchild et al., 2009). A sandwich estimator will be used to account for the nested data structure (e.g., individuals are nested by clinics). This estimator uses the Huber/White correction and adjusts for potential underestimated standard errors and bias in chi-square computation (Liang & Zeger 1986). Missing data will be handled using Full Information Maximum Likelihood estimation procedures (Enders & Bandalos 2001). For model fit evaluations, we will use well-established fit indices and cutoff values: A well-fitting model ideally will have a non-significant model $\chi 2$, a Comparative Fit Index / Tucker-Lewis Index greater than .95, a root mean square error of approximation less than .08, and a standardized root mean square residual less than .08 (Hooper et al., 2008). All analyses will be conducted in Mplus (V8; Muthén & Muthén, 2017).

H3. Effect of S&S + LFLS pilot. To compare the proportion of EIMCs in the experimental group to the proportion found in the observation group, a one-sample z-test will be conducted. The population proportion will be taken to be the midpoint of the findings from Waters et al. (2013) on neonatal circumcision and historical numbers of circumcisions from Zambian clinics and hospitals. Based upon this rationale, the percentage of EIMCs in the observation group is anticipated to be approximately 5.0%.

Exploratory analyses. To investigate change in EIMC attitudes, Stages of Change scores will be examined over time using an autoregressive modeling approach specifying the individual's stage at 1-week postpartum as the main outcome and individual's stage at baseline as a main predictor in the regression model (Hamaker et al., 2015). Variables from the previous path model will be included as potential covariates in attempting to explain stage movement. The estimated regression coefficient will reflect changes in EIMC attitudes over time. The model will use an ordinal logistic model to examine change over time. Odd ratios will be estimated as a measure of effect size (Chen et al., 2010).

Power. Using a two-tailed Z test to test the difference in proportions between two conditions at an α level of .05, this study has over 80% power to detect a difference of 6.0% in EIMC rate between the two conditions. This difference in proportion translates to an effect size of an odds ratio (OR) = 2.4, which is considered a small (OR = 1.68) to medium (OD = 3.47) effect size, according to Chen et al. (2010). This 2.4 OR is based on an effect size found in previous research examining circumcisions (Weiss et al., 2015). With these specified parameters, 80% power is achieved with 140 couples (out of ~151 couples with male infants).

Data Security. CAB and FGD participants will not provide any uniquely identifying information during participation in group discussion sessions. Pregnant couple participants in the intervention will be assigned a unique code upon entering the study. This number will identify all participant files, which will include no identifiable information. Access to the computer data files will be restricted by password codes. The list translating participant number to identifying information

will be maintained in a secure locked file in the Spear & Shield study office in Lusaka at the University of Zambia School of Medicine. Participants will be made explicitly aware at the time of the informed consent of the nature of the separate record that will be kept for them. CAB and focus group discussions will be audio-taped for review and summary of key discussion points; copies will be stored in a locked cabinet at the PI's Lusaka offices, and deleted following summarization.

Quality Assurance. The PI, Co-PIs, consultants, and study staff will train CHC staff in study protocols, including recruitment and intervention procedures. The US and Zambia will hold biweekly Skype calls to review the study progress. Semi-annual visits are made by members of the US team for protocol review, ongoing process monitoring and quality assurance; process evaluation is used to ensure fidelity to the study protocol and study instruments. All LFLS sessions will be recorded; 1) 10% of recordings will be randomly reviewed and rated for fidelity by the Project Coordinator, Ms. Banda (per existing random review system), and 2) feedback provided to the counselor within one week of the review; 3) all reviewed recordings will be entered in a spreadsheet detailing completed intervention components that 4) will be reviewed by the US Co-PI (Jones); 5) the Project Director and Dr. Jones will discuss the reviews to resolve fidelity issues collaboratively. ACASI assessment quality assurance will be conducted by US data manager biweekly. Quarterly meetings of CHC and S&S staff will be held to encourage team members to review study issues and discuss and resolve difficulties in a timely manner. Describe any procedures that will be used for quality control of collected data.

Data collection will be conducted at the Zambia site, and reviewed for quality control at the US site. Both sites will have access to the final dataset for analyses, and the US site will lead primary study analyses. Data will be reviewed at the Zambia office, and then transferred biweekly to the US site for review, feedback, and return for correction. Data will not include unique identifiers, and data will be stored on encrypted computers at both sites. Data transfer will be conducted on a secure site using BOX. Written materials (consent) will be stored in locked cabinets in the local PI office and destroyed after 3 years; only study staff will have access to the data. Transmission of data is conducted by Gibson Banda in Zambia to John Abbamonte in the US.

Following completion of the study, electronic data will be available per data sharing in accordance with NIH policies, such that de-identified data will be available for analysis following the publication of the primary outcomes manuscripts. Access to the database will be available under the supervision of the collaborators within the guidelines outlined by the NIH for data sharing. Given the small sample size from each clinic, any clinic and participant identifying information will be removed prior to data sharing. Data will be made available as a shared resource within the guidelines of the University of Zambia School of Medicine, UM and NIH.

15) Provisions to Monitor the Data to Ensure the Safety of Subjects*

LFLS Monitoring Plan: As a feasibility study, there is no data monitoring board or committee. However, the study staff will obtain monthly feedback from senior clinic personnel on adverse events as well as more general problems associated with study participation occurring among participants. During the consent process, participants are encouraged to report any problems associated with participation in the study to study personnel (see Risks, below).

Adverse events. As a behavioral study, adverse events are not anticipated that would be directly related to study involvement. However, if adverse events do occur, study procedures are in place

for study staff to contact the study PI, Dr. Weiss, within 24 hours of the event report. Dr. Weiss will ensure that the event is reported to the UM IRB and the UZ REC within 48 hours of the event report. Urgent issues arising will be discussed with senior clinic staff and the US/Zambia senior staff.

General problems will be reported during weekly staff meetings at the Zambia site and reported to the US site in biweekly conference calls. All issues are documented in biweekly study data reports. Semi-annual visits are made by members of the US team for review, monitoring, and quality assurance by senior study faculty.

Resolution. The US and Zambia teams hold biweekly Skype calls to review any study issues and resolve potential risks or problems arising. Quarterly meetings of CHC and S&S staff will be held to encourage team members to review study issues and discuss and resolve difficulties in a timely manner. CAB members will also provide support in problem solving problems arising during monthly meetings held by CHCs.

VMMC/EIMC. The proposed study will train health care providers to conduct VMMC and EIMC. All 8 CHC sites will be reviewed to determine their needs for training health care providers to conduct VMMC (dorsal slit) and EIMC (Mogen Clamp) training. A minimum of 2 CHC health care providers are needed at each clinic to provide MC services. Each site will identify 2 health care providers (physicians, Clinic Officers, nurses) who are already trained or have the requisite background to participate in the two week VMMC and one day EIMC training program of the University of Zambia School of Medicine, directed by Dr. Zulu, Zambia Co-PI, in accordance with guidelines for provision of VMMC (Health Professions Council of Zambia, 2010; RZMOH, 2012).

Training programs are conducted following the WHO MC training manual and recommendations by the Surgical Society of Zambia and MOH. The training in both dorsal slit and Mogen clamp procedures is conducted in 3 stages; Phase 1) theoretical training using the 10 WHO training modules, providing basic knowledge on VMMC/EIMC, VCT, infection prevention and M&E elements of VMMC/EIMC. Phase 2) classroom-based practicum in counseling, surgical skills and infection prevention. Phase 3) VMMC 5 days of supervised practicum, EIMC 5 days practicum; candidates perform 10 VMMC and 10 EIMC procedures under close supervision, including client assessment and post-operative reviews. Upon practicum completion, new VMMC providers will receive supervision by Dr. Zulu and trainers. EIMC requires training for qualified health care providers in the use of the Mogen Clamp for surgeons and non-surgeons in Zambia; 10 EIMCs must be successfully conducted and approved by the training team in order for the provider to receive a certificate of attendance. All EIMCs are documented in the EIMC register and are supervised within the CHC; after ~one-three months, providers are certified. Due to the rigorous training requirements, very few adverse events have been reported. In the event of an adverse event, providers may be directed to re-training, depending on the outcome of the review of the nature of the event.

Adverse events. The Government of Zambia has an established system for collection of data related to EIMC and VMMC adverse events.

This study is designed to make EIMC and VMMC available to those electing to undergo VMMC or to have their neonates circumcised. Currently, 16 clinics in Lusaka offer EIMC on a special day of the week when babies are circumcised, and they return for post-operative review after 7 days. Most babies are discharged at 7 days; those with adverse events (AEs, most typical have been insufficient skin removal, excessive skin removal, bleeding and infection) are reviewed and referred. Very low numbers of AEs have been reported. Staff at CHCs are provided with general information on EIMC management of complications and referral systems prior to onset of the program. EIMC surgical equipment and consumables are provided to all 8 CHCs to establish comparable availability of VMMC and EIMC services.

16) Withdrawal of Subjects*

Participants are advised during the consent process that participation in this study is voluntary. If they choose not to participate, they will not be denied any benefit to which they would be otherwise entitled and their employment will not be affected. They are free to withdraw from the study at any time, and if they do so, they will not suffer any penalty. If they decide to leave the study, they can contact the investigator or the study contact so that they will have no further contact. They are also advised that the investigators reserve the right to remove them from the study without their consent at such time that they feel that it is in the best interest for the participant medically or for administrative reasons. Finally, participants who lose their babies during or following pregnancy will be advised that they can drop out or attend sessions following a period of bereavement if they wish to continue. Information that has been collected during their participation in the study prior to their withdrawal will be retained by the investigator.

17) Risks to Subjects*

18) Potential Risks

Participants should incur no appreciable physical risks. Through participation in this study they may undergo psychological discomfort at times, including embarrassment, discomfort, or distress associated with discussion of sensitive topics which may lead some participants to experience mild, transient anxiety. Potential risks to participants in this study also include negative consequences that may be suffered if confidentiality of information obtained in the study were breached. Participants attending groups cannot be assured that another group member will not divulge information shared in the group format; group members will be encouraged to endorse confidentiality at the onset of the discussion sessions. A number of steps will be taken to protect the confidentiality of participant data and identity. Study staff will attend training sessions by the study investigators and receive ongoing supervision in areas related to ethical conduct, confidentiality protection, and other topics of human participant protection. We will ensure that study staff are trained to explain the purpose of the study to potential respondents, obtain informed consent, and inform respondents about their rights and benefits in a factual and neutral way without coercion to participate. We will also ensure that our interviewers and group leaders inform the potential respondents about the

confidentiality measures put in place to protect their privacy. The assessments are confidential and will be conducted in a private office area inside each clinic and all research data obtained from participants will be labeled with a respective unique code and not the participant's name. Only the unique code will appear on measures, data records, and computer files. A master list that includes participant identifying information and identifying codes will be kept in a locked file at the PI's Lusaka site office.

It is also possible that during the course of our contact with participants we may become aware of problems that fall outside of the scope of the proposed research but require intervention. As such, participants will be advised that there are certain ethical limits to confidentiality. Should any participant disclose that he/she is experiencing suicidal ideation, he/she will be immediately evaluated by a qualified physician or psychologist and actions may be taken to protect him or herself and others. If a participant tells the researcher that he or she plans to in any way physically or sexually harm an identifiable person including a spouse or partner, it will be required that the researchers take steps to intervene. If the participant tells the researcher that he or she believes an identifiable person is going to physically or sexually harm him or her, steps will be taken to protect him or her.

Although EIMC is the standard of care provided in Zambian antenatal clinics, participants will also be advised during the informed consent and the study intervention of the potential risks associated with early infant circumcision.

Protections Against Risk
Intimate Partner Violence.
Special considerations regarding the potential for intimate partner violence: Should participants experience extreme acute or persisting affective reactions at any point during the study period due to the risk or anticipation of intimate partner violence (IPV; see below for details), they will be referred to medical and/or human services professionals associated with the CHC for care. Following this evaluation, if necessary, the participant will be accompanied to the referral hospital for further assessment and/or hospitalization, or, if not in immediate danger of harming her/himself, will be referred for outpatient treatment. [N.B.: IPV has been a major concern in our HIV risk reduction studies in Zambia over the past 20 years. We are pleased to report that either a reduction or lack of increase in IPV has been observed post-intervention, despite the sensitivities of issues such as disclosure of status or use of sexual barriers among couples. We believe post-intervention improvement in couple communication and coping skills as well as anger management/assertiveness training have contributed to these reductions in IPV, even in venues with high rates of IPV].

Our previous Zambian studies utilized a gender-concordant group strategy and the proposed LFLS component utilizes a couples-based session format focused on joint decision making for EIMC. Our previous and ongoing couples-based studies in South Africa were sensitized to the potential for IPV when using a couples-based approach to reduce stigma (e.g., Peltzer et al., 2018) and promote healthy pregnancy practices (Jones et al., 2018). Our experiences with couple negotiation have contributed to our attention to

prodromal signs of IPV. However, although decision making discussions regarding adult and infant circumcision have not been typically associated with IPV, we will train counselors and staff to be aware of participant IPV and topics under discussion associated with its potential, and will apply elements from the existing standard of care for counselors to utilize a couples' voluntary HIV testing and counseling (CVCT) model based on the CVCT Intervention and Training Curriculum developed by CDC and the Rwanda Zambia HIV Research Group (CDC, 2011; Wu et al., 2018).

Procedures related to Intimate Partner Violence (IPV). In the event of a report of IPV, the CHC protocol for responding to reported IPV is 1) interview with offending partner (usually the husband), 2) medical examination of victim spouse and possible inpatient admission or 3) referral to the alternative community shelter for mother and children, provision of 4) medical treatment and counseling support. Based on the results of the medical examination, 5) a police report is also submitted by CHC staff and 6) police will then interview the domestic partner (husband). In the case of reported abuse of children, children are 1) assessed and as appropriate, 2) placed in the protective care. Following a report of IPV, all subsequent sessions and assessments will be conducted independently; no partners will attend sessions or assessments at coinciding times. In the event that both partners request to reunite, they will begin assessments at coinciding or overlapping times, if they prefer.

19) Potential Benefits to Subjects*

Risks to study participants related to attendance in the study are low, and the potential benefits to participants include discussion of information and experiences during assessments that may be helpful; participants may benefit from non-specific effects of discussing work experiences under the guidance of trained assessors.

20) Vulnerable Populations* pregnant women being enrolled.

21) Multi-Site Research*

This study is being conducted in Zambia and the US. The PI is located in Miami.

- Prior to study start, both sites will finalize the protocol, and both sites will have the most current version of the protocol, and consent document (there are no HIPAA authorizations required as there is no uniquely identifiable data being collected).
- Prior to study start, the required approval from the Zambia Research Ethics Committee will have been obtained.
- All modifications will be communicated to both sites, and approved (including approval by the site's IRB of record) before the modification is implemented.
- Both sites will safeguard data as required by local information security policies.
- All local site investigators will conduct the study appropriately.
- All non-compliance with the study protocol or applicable requirements will reported in accordance with local policy.

The following management structure is already in place and will be maintained at both the Miami and Zambia sites. Two project management teams (Miami: Weiss, Jones, Castro, Lee; Zambia: Zulu, Bowa, Chitalu, Mweemba) will ensure appropriate coordination, consistency and quality control in implementing the research protocol

across the two sites. The investigators will be responsible for the administration of the study at their respective sites, including Institutional Review / Ethical Review and approval, implementation of protocol and procedures, and oversight of issues related to human subject protections.

Fiscal and management coordination: Dr. Weiss is responsible for scientific direction and Drs. Weiss and Zulu will oversee fiscal management at their respective sites. Dr. Weiss will be responsible for the overall fiscal management as the University of Miami is the primary grantee.

Roles of Investigators and Process for Decision Making:
Dr. Weiss (PI) will provide guidance for overall study policy development, achievement of scientific aims, data analysis, publication and quality assurance for the study. Dr. Weiss will oversee the implementation of the aims of the study and maintain communication across both sites. Policy guidelines for the project and quality assurance include standards for staff training, assessment, treatment, quality control and maintenance procedures, as well as data review and analysis. Assessment and Intervention Manuals and Manual of Operations will be created in Miami and adapted to the Zambian context through consensus by both teams. "Like Father, Like Son" intervention manuals and assessments will be collaboratively developed by US and Zambia investigators with input from stakeholders. Publications and authorship will be collaboratively developed and shared between both sites.

Decisions on procedural issues and scientific management will be reached using a Project Executive Committee, chaired by Dr. Weiss, comprised of Drs. Weiss, Zulu, Bowa, Chitalu, Mweemba, and Jones. During semi-annual meetings, Dr. Bowa and Mr. Kamboyi will provide additional consultation on the project, providing guidance on the current standards on EIMC/VMMC and information on regional EIMC/VMMC uptake and acceptability. Dr. Jones will oversee quality assurance and training and chair the Publications Committee; Dr. Lee will oversee statistical issues and data review. The committee will meet twice a year in person during site visits, and twice per month on conference calls.

Dr. Zulu (co-PI) will chair the Project Steering Committee, comprised of Dr. Chitalu, Dr. Mweemba, Ms. Banda, and Mr. Mwanza, and oversee the scientific/operational arms of the study, and be responsible for site-specific program management, e.g., administration and site issues that may impinge on study conduct and/or outcome and operating procedures. Dr. Zulu will also organize and oversee the training of qualified healthcare providers from the 8 CHCs to perform VMMC and EIMC at the University Teaching Hospital. Decisions on procedures for recruitment, intake, assessment, treatment, maintenance and follow-up will be reached by the Project Steering Committee. The Committee will meet weekly, and minutes will be provided to the Miami site as a record of study progress.

Dr. Chitalu (co-Investigator) will oversee all administrative issues related to the project, including procedures for deployment of staff to clinics, behavioral training, and clinic

staff recruitment. Regular email communication and twice monthly conference calls over the course of the project will maintain a regular system of reporting on issues that may affect the conduct of the study.

Procedure for conflict resolution: The process for conflict resolution will, as in our previous collaborations, be designed to arrive at mutually agreeable solutions. In that rare instance when agreement cannot be resolved by discussion and simple vote, the chairperson of the respective committee will make the final decision, i.e., Dr. Weiss will make the final decision in the Project Executive Committee, Dr. Zulu will make the final decision in the Project Steering Committee.

Communication: Information sharing and project management will be facilitated by scheduled bi-monthly calls, and supplemented by email. The PI and Co-investigator (Jones) will travel to Zambia at the onset of the study to finalize all guidelines and protocols and train staff; Dr. Bowa and Mr. Kamboyi will travel to the main office for semi-annual meetings. Drs. Weiss and Jones will travel to the Zambia site twice yearly for the duration of the study (see Budget Justification), and hold monthly meeting with Miami investigators, consultant, statistician and staff.

Study Team and CHC staff roles: Zambia
Dr. Robert Zulu, Zambia senior co-Investigator
Dr. Kasonde Bowa, Zambia co-investigator
Dr. Ndashi Chitalu, Zambia co-investigator
Dr. Oliver Mweemba, Zambia co-investigator
Dr. Kasonde Bowa, Zambia consultant
Mr. Royd Kamboyi, Zambia consultant
Agatha Banda, Certified Project Manager,
Chileshe Mwanza, Administrator
Richard Msimuko, senior trainer and assessor
Mirriam Mwaba-Chisongo, senior trainer and assessor
Sharon Kalebaila, trainer and assessor
Rogers Mofya, trainer and assessor
Wazala Zulu, Driver
Gibson Banda, Data Management coordinator
TBA 8 Clinic sister/clinic officers (8 clinics, 1 per clinic)
TBA 16 EIMC Providers (8 clinics, 2 per clinic)
TBA 8 S&S LFLS Providers (4 clinics, 2 per clinic)

22) Community-Based Participatory Research*

CAB Meetings & Focus Groups (see above, PROCEDURES).

Content of CAB Meetings & FGDs. To address Aims 1&2, FGDs and CAB meetings' discussion topics have been broken into smaller units within the context of the socio-ecological framework (from the individual to the context), using the PRECEDE model (Green & Kreuter 1999). Activities will be led by Dr. Mweemba. Focus group discussion stem items explore intrapersonal,

interpersonal and structural level factors associated with EIMC, and factors associated with each level. Stem items were derived from previous research (e.g., Albert et al., 2011; Amuri et al., 2016; Mavhu et al., 2012; Mavhu et al., 2016; Plank et al., 2010; Waters et al., 2012) and will be presented as open-ended questions; time will be provided to address additional topics as they arise. FGDs will be approximately 1.5 hours in duration. Prior to study onset, additional stems may be proposed using an iterative, collaborative process involving the University of Miami/University of Zambia (UZ) study team, which includes psychologists, social scientists, a pediatrician, surgeons, an infectious disease physician, and psychometricians. Final stems will be reviewed and refined by the entire team prior to initiation of FGDs and CABs. CAB meetings (1 per clinic, 3 meetings, n = 80 persons) and FGDs (2 per clinic, each gender concordant, 8 FGDs, n = 64) will be audio recorded and transcribed by trained study staff from the UZ into English; FGDs and CABs will be conducted in private areas in CHCs. Field notes will be made by staff during FGDs, CABs and study-related CHC staff meetings; meetings will be summarized from field notes. The project coordinator and study staff are social scientists and are experienced in conducting FGDs.

Community Advisory Board (CAB) Members. CAB Members will meet for three formal group discussions in a private meeting room within their experimental clinic. CAB members will be asked to 1) provide input on cultural factors that influence attitudes, perceptions, and beliefs about EIMC within their communities and among the ethnic groups predominant in the Lusaka Province, and 2) provide input on the LFLS intervention and assessment content and information on community issues and concerns that could influence LFLS program uptake. CAB Members associated with each CHC will thereby facilitate the adaptation of the intervention strategies to the local culture and clinic culture, enabling LFLS to work with the community rather than imposing the program on the community. No personal, individually identifying information will be collected and no individual interviews or assessments will be conducted with CAB Members.

Focus Group Discussion (FGD) Members. FGD members will meet in gender concordant groups in a private room within their experimental clinic site; members will provide input on cultural factors that influence attitudes, perceptions, and beliefs about EIMC among pregnant couples. They will provide guidance on cultural attitudes, ethnic preferences, beliefs and perceptions surrounding EIMC among pregnant couples in Lusaka. FGD members will inform the study on local issues or community concerns that could influence program uptake. No personal, individually identifying information will be collected and no individual interviews or assessments will be conducted with FGD members.

23) Sharing of Results with Subjects*

No relevant information will be collected to share with participants.

24) Setting

Describe the sites or locations where your research team will conduct the research.

Proposed clinic sites (N=8) are to be drawn from n = 14 potential clinics in Lusaka Province, and were reviewed and approved by the Lusaka Provincial Health Officer leadership. Following guidelines for site VMMC accreditation (Health Professions Council of Zambia, 2010), the following criteria govern selection of 8 clinic sites: 1) a community clinic catchment area of >30,000; 2) 2 health care providers available at site for VMMC/EIMC training and provision; 3) >2 VCT counselors and antenatal clinic (ANC) staff available for S&S+LFLS training, 4) space for VMMC/EIMC, 5) > 150 births per month, 6) a maternity ward. Clinic selection (n = 8) will focus on spatial separation between clinics to avoid clinic contamination. Randomization. Clinics will be matched by catchment area size and historical EIMC/VMMC rates and randomized by a non-study member; statistician will be blinded to clinic assignment. Following site selection and randomization, CHCs will be visited by the research team to introduce the study to relevant staff. Sites will be reviewed for adequate space. Approval from the Research Ethics Committee and the Institutional Review Board will be obtained prior to any study activities.

Lusaka Province Community Health Clinics (CHCs). All CHCs identified in Lusaka Province for potential participation offer Voluntary Counseling and Testing (VCT) (Republic of Zambia Ministry of Health, 2013). All sites include qualified staff to provide leadership and to implement the Project, willingness to conduct sessions, adequate space to meet patients, and willingness to work with the Project to expand the delivery of VCT/ANC services to offer VMMC/EIMC services. CHC clinic doctors confirmed available staff, time, space and facilities, and required staff expertise and willingness for full participation in enrolling and assessing participants. Clinic sites acknowledged qualified VCT staff at all sites (i.e., having the minimum qualifications and experience to receive training), and a catchment area of at least 30,000 individuals. Finally, each site will establish special recruitment and follow-up efforts if necessary. Out of the available CHCs, all clinic sites have easy access by paved roads frequently traveled by local minibuses and taxis and with signs advertising the VCT program.

Lusaka Province & MC Attitudes & Culture. Lusaka Province has a population of 3,186,000. The provincial capital is Lusaka city, which is also the capital of Zambia. Lusaka Province is a link to all provinces, and people with different cultural backgrounds from other provinces and countries move to Lusaka looking for employment and other business ventures. The rate of traditional MC in Lusaka is estimated to be approximately 10.2% (Makawa, 2012), with an estimated HIV prevalence of 20.8%. Barriers to MC in Lusaka include fear of pain associated with the procedure along with the healing process. Fears related to the healing process have been perpetuated by reports of men who

indicate that the healing process did not go well for them. Others also report a fear that one could die from the procedure (Mwale & Jairos, 2009).

Zambia has many native languages which are spoken across Zambia in combination with English, which is the official language of the country. All languages are often used along with English in schools and government publications. In the 2010 census, 34% of Zambians reported speaking Bemba as their primary language, whereas 15% spoke Nyanja, 11% Tonga and 6% Lozi (Central Statistical Office, 2012). English is only natively spoken by 2% of the population but is commonly spoken as a secondary language by Zambians. *Bemba and Nyanja and English are spoken in Lusaka.*

Lusaka District (Urban). Lusaka is the largest city in Zambia, and is considered one of the fastest-developing cities in the Southern part of Africa. English is the official language of the city, but Nyanja and Bemba are also commonly spoken. Some of the sociocultural barriers to implementing HIV-risk reduction programs in Lusaka have been reported to be poverty and refugee status. In addition, the organizational structure in health care settings and HIV-related stigma have been identified as barriers to seeking care. Cultural characteristics, such as traditional gender roles combined with religious beliefs, are also factors that may inhibit men from considering undergoing VMMC (Auvinen, Kylma, Valimaki, Bweupe, & Suominen, 2013). Younger men in Lusaka assert they would be willing to consider circumcision if the services were more accessible and if more information was provided regarding the procedure (Chanda, Likwa-Ndonyo, Nzala, & Mweemba, 2012).

Kafue District. Kafue is in southern Lusaka Province located to the north of the Kafue River. According to the 2010 census, Kafue has a population of approximately 219,000 people. In some areas of Kafue, such as Nyimba and Namalyo, HIV prevalence is estimated to be 23.7% or higher (Lungu & Husken, 2010). Under a regional program, the WorldFish Center in Zambia conducted research in the Kafue Flats to investigate the accessibility of health care services, as well as to identify factors that may potentially explain the increased risk of HIV/AIDS among fishing communities (Lungu & Husken, 2010). Those working in the fishing industry are among the most vulnerable to HIV infection, and female fish traders often visit fishing communities in search of fish. Transactional sex ("fish-for-sex") is a common occurrence in the Kafue Flats, increased by the high demand for fish. Both male and female traders are at a higher risk of contracting HIV and STIs (Lungu & Husken, 2010).

Potential CHC study sites: Lusaka Province (8 to be selected)

- Bauleni (Lusaka District, large)
- Mtendere (Lusaka District, large)
- Chilanga (Lusaka District, large)
- Chongwe (Chongwe District, large)

- Karakantapa (Chongwe District, medium)
- Kriskatumba (Chilanga District, medium)
- Chainda (Chongwe District, small)
- Mwembeshi (Chilanga District, small)
- CHC study sites: Lusaka Province (alternates)
- Chalimbana (Chongwe District, small)
- *Makeni Konga (Chilanga District, medium)*Resources Available

Qualifications (e.g., training, experience, oversight) of US PI and team including experience and knowledge of local study sites, culture and society.

- Stephen M Weiss, PhD, MPH, PI, USA is Professor, Department of Psychiatry and Behavioral Sciences, University of Miami School of Medicine. Dr. Weiss is a clinical health psychologist with additional expertise in cultural anthropology (doctoral minor) and public health (MPH). He has extensive international experience in HIV research with a focus on sub-Saharan Africa, including being PI of the Spear & Shield studies, R01MH095539, "Increasing Availability and Acceptability of Circumcision in Zambia" and coPI of "Implementing Comprehensive PMTCT & HIV Prevention for South African Couples" (R01HD078187/R01HD078187-S1). He was PI of the US/Zambia multisite study "Reducing Risk for Multicultural HIV+/- Women & Partners" (R01MH63630), and Co-PI of "Implementing HIV Risk Reduction in Zambia" (R01HD058481). In the US, Dr. Weiss was Co-PI on US studies addressing infant and adult male circumcision, "Acceptability of Neonatal Circumcision among Hispanics" (P30AI073961; PI, J Castro), "Attitudes towards Circumcision among Hispanics: Avenues for HIV Prevention (P60MD002266; PI, J Castro), and "HIV Prevention Strategies Preferences" (P30AI073961; PI, J Castro). As the PI for the proposed study, Dr. Weiss will provide overall leadership and scientific guidance, including oversight of intervention training at the Zambian site.
- Deborah Jones, PhD, MEd, Co-Investigator USA, is Professor, Department of Psychiatry & Behavioral Sciences, University of Miami Miller School of Medicine. Dr. Jones is a clinical health psychologist with additional training in education (M.Ed.). She has extensive experience in conducting HIV/AIDS research and in developing psychosocial interventions for men and women living with HIV/AIDS in sub-Saharan Africa and the US. She is co-investigator and the co-creator of the intervention and assessments utilized in the Spear & Shield study, R01MH095539, "Increasing Availability and Acceptability of Circumcision in Zambia" and was Co-PI and Project Director on the US/Zambia study, "Reducing Risk for Multicultural HIV+/- Women & Partners" (R01MH63630) and was PI of "Implementing HIV Risk Reduction in Zambia" (R01HD058481). Dr. Jones was Co-PI on US studies addressing infant and adult male circumcision, e.g., "HIV

Prevention Strategies Preferences" (P30AI073961; PI, J Castro), "Acceptability of Neonatal Circumcision among Hispanics" (P30AI073961; PI, J Castro) and "Attitudes towards Circumcision among Hispanics: Avenues for HIV Prevention (P60MD002266; PI, JCastro), conducting qualitative data analysis for these studies. Dr. Jones has a long history in pregnancy-based interventions in the US/Southern Africa and is PI of the perinatal intervention "Implementing Comprehensive PMTCT & HIV Prevention for South African Couples" (R01HD078187/R01HD078187-S1) and was PI on "Pathways to Health Conception Practices" (U01 AI103397; PI Fischl; P30AI073961; PI Pahwa).

- Jose Castro, MD, MPH, Co-Investigator USA, is Associate Professor, Department of Infectious Diseases, University of Miami School of Medicine. Dr. Castro was PI of 3 studies addressing attitudes on infant and adult male circumcision among men, women and physicians, "Acceptability of Neonatal Circumcision among Hispanics" (P30AI073961; PI, J Castro), "Attitudes towards Circumcision among Hispanics: Avenues for HIV Prevention (P60MD002266; PI, JCastro), and "HIV Prevention Strategies Preferences" (P30AI073961; PI, J Castro). He is co-investigator on the Spear & Shield grant and will serve as the US medical consultant for the proposed EIMC study and provide guidance on the development of the study protocol
- Robert Zulu, MD, Surgeon, Co-Principal Investigator, ZAMBIA, is Honorary Lecturer, Department of Medicine, University of Zambia School of Medicine (UZSOM), Chainama College of Health Sciences, and Cavendish University. He is Director of Clinical services and Consultant Surgeon for the University Teaching Hospital (UTH) under the Ministry of Health. He is in-country co-PI of the previous (S&S1) and current Spear and Shield Projects (S&S2), and co-PI of 2 studies on MC devices (Shang Ring studies on male circumcision). He currently oversees all VMMC training for the study. Together with collaborative input from Drs. Bowa, Weiss, Jones, Chitalu and Castro, Dr. Zulu will be responsible for the implementation of the biomedical component of the revised application, specifically the recruitment and training of health care personnel from the selected district sites in Lusaka for EIMC training. He will oversee and provide the EIMC Clinical Circumcision Training to community health center (CHC) staff through mobilization of the Zambian Association of Surgeons training group, in collaboration with the EIMC consultant, Dr. Bowa. Dr. Zulu will supervise the implementation and execution of the biomedical component of the application, periodic review of EIMC trainees for quality assurance during the course of the study. He will be responsible, together with Dr. Chitalu and the Project Coordinator, for oversight of study activities at the 8 clinical sites.
- Ndashi W Chitalu, M.D., MPH, Co-Investigator ZAMBIA, is a Pediatrician and Senior Lecturer, Department of Medicine at the

University of Zambia School of Medicine, and Head of Emergency Care at the Paediatrics Unit of the University Teaching Hospital. Dr. Chitalu has extensive experience in the oversight and implementation of HIV/STD research in Zambia and is the Co-PI of the previous (S&S1) and current Spear and Shield Projects (S&S2). He was in-country co-investigator of "Implementing HIV Risk Reduction in Zambia" (R01HD058481), and of "Reducing Risk for Multicultural HIV+/- Women & Partners" (R01MH63630). Dr. Chitalu was a Fogarty Scholar at the University of Miami School of Medicine, and has served as an invited consultant for the Malawi Ministry of Health. He is the former National Director of the YMCA in Zambia and is trained in qualitative research methods. He will provide guidance on the pediatric component of the study, and will be administratively responsible to Dr. Zulu and the PI, Dr. Weiss. He will collaborate on the development and implementation of the intervention, behavioral research, and training.

- Oliver Mweemba, PhD, Co-Investigator ZAMBIA, is a Lecturer/Researcher in the Department of Health Promotion and Education, School of Public Health at the University of Zambia. Dr. Mweemba was a Fogarty Scholar in the African Bioethics Training Program (FABTP) at the Berman Institute of Bioethics, School of Public Health, Johns Hopkins University (JHU). His research addresses masculinity, gender, sexuality and health; ethical, legal, and social implications of advances in biomedical research and health systems; the link between public policy, health inequalities, and human rights; and life courses and health needs of vulnerable and marginalized groups and communities. He was co-PI on a Medical Research Council (MRC) MDP 301 multi-centre clinical trial assessing the effectiveness of candidate microbicides, PRO 2000, and was a site PI on an MRC multi-centre Top-up study, determining the feasibility of conducting a microbicide trial of the daily vaginal gel, and to inform the way adherence should be assessed. He has been co-Investigator on two NIH projects; 1) A dyad approach to combination HIV prevention in pregnancy for Zambia and Malawi, in which he was a Zambian site principal investigator for the formative phase, and 2) An assessment of capacity to prevent and manage major non-communicable diseases (NCDs) in primary care centres in Zambia using a health system approach. He is currently co-PI on a multi-centre collaborative research project with University of Oxford and Child Frontiers, funded by the Canadian International Development Research Centre, on Early Marriages and Parenthood, focusing on experiences of children who marry and become parents, the predictors of and motivations for child marriage and parenthood, and the wider implications for sexual and reproductive health, gender inequality and intergenerational poverty. He is also co-PI on an H3 Africa multi-centre and collaborative study with University of Oxford, London School of Hygiene and Tropical Medicine, and University of Cape Town, funded by Welcome Trust, aimed at developing a robust and supportive ethical and governance

framework for genomic research in Africa. Dr. Mweemba has taken an active role in the development of the formative elements of the study, the issues surrounding couples, families, and gender roles as they relate to early infant male circumcision. In collaboration with Drs., Weiss and Zulu, he will oversee the formative elements of the study, and in collaboration with Drs. Jones, Chitalu and Weiss, will provide training and oversight on the behavioral intervention and evaluation of the study outcomes.

- Kasonde Bowa, MD, MPH, Investigator, ZAMBIA, is Professor of Urology at the Copperbelt School of Medicine in Ndola, Copperbelt Province, and head of Urology at the Ndola Central Hospital. He is a Fellow of the Royal College of Surgeons in Glasgow, a Fellow of the American College of Surgeons, and a Fellow of the College of East and Central Africa in Urology. He was the founding Dean of the Copperbelt University School of Medicine. Dr. Bowa has been a leader in VMMC for HIV prevention and research for over a decade and was a collaborator on the WHO guidance documents on VMMC and EIMC training and on MC devices, is on the WHO committee of MC experts, and is a consultant on MC for numerous studies. He is a respected physician and local expert in cultural matters in the Copperbelt; he will assist in the planning of the training of healthcare personnel in adult and infant male circumcision according to current standards for the Like Father Like Son study, as well as advising the team on culturally relevant matters related to uptake and acceptability of VMMC/EIMC.
- Royd Kamboyi, MPH, Consultant, ZAMBIA, is the national VMMC Program Officer, Ministry of Health, Zambia with collaborative oversight of over 200 staff implementing VMMC nationally. Mr. Kamboyi was previously VMMC Provincial Coordinator, Society for Family Health Zambia, at Petauke District Hospital. He is a public health specialist and social scientist with experience in the Zambian health sector under the Ministry of Health and Non-Governmental Organizations, including the Centers for Disease Control and Prevention. Mr. Kamboyi is experienced in HIV/AIDs programming and implementation of interventions in the health sector, and has expertise in health systems strengthening in VMMC, PMTCT, HTC, ART services including general nursing care services. Mr. Kamboyi is a certified National Trainer in VMMC, ART and PMTCT.
- Recruitment. Our previous studies have recruited over 5,000 Zambian men and women within the agreed recruitment periods over the last 20 years. The study staff have access to ~50,000 eligible men per clinic. Our most recent Spear & Shield study recruited 800 eligible men in under two years.

Spear & Shield Project Offices. The UTH Pediatrics Wing at the Ridgeway Campus is the home to the NOW/Partner/WASH/Spear & Shield Projects, administered by the University of Miami Miller School of

Medicine through the SOM. The projects are housed in a dedicated 2000 sq. ft fully renovated building with computer systems offering wireless and fibre optic cable networks. Computers (24) are housed in 14 offices and include laptops (12) for ACASI data collection as well as desktops for on-site work. On site equipment includes desks, cabinets, computer projectors, air conditioners (6), freezers (2), photocopiers, television/VCR/Disk players (5), tape recorders (4), telephones and Skype capability.

Medical and/or psychological resources are available at both the community clinics and University Teaching Hospital to provide support for consequences of the human research, as outlined in the RISKS section.

All study staff have been working with the project for the last 4 years, and a system has been established of providing training on the study protocol, research procedures, and their duties and functions. Following training, all study staff review and sign off on the study SOPs.

25) Prior Approvals

Prior to study onset, the University of Zambia Biomedical Research Ethics Committee will need to provide an approval.

26) Recruitment Methods

Recruitment and Retention. Experimental Clinics Only

Community Advisory Board (CAB) Members.

Referral. CAB members will be approached for participation in study meetings by the study staff member, Sister in Charge or Clinic Officer at the experimental clinic sites (n = 4 clinics; n = 80 participants).

Overview. CAB members will be briefed on the nature of the study by the Sister in Charge or Clinic Officer.

Focus Group Discussion (FGD) Members.

Referral. FGD members will be approached for participation by a study staff member during antenatal clinic (ANC) days or at the VCT at the experimental clinic sites (n = 4 clinics, 64 participants). Women attending ANC are asked to bring their partners to ANC visits, and clinics will have both women and men in attendance. FGD participants will be couples (men and pregnant female partners). Couples participating in the FGDs will deliver following completion of the formative activities, and therefore will not be eligible to enroll in the LFLS program.

Pregnant Couple Members attending LFLS.

Referral. Pregnant couples, both members aged 18 or older, will be recruited over an eighteen month period from each of the 4 experimental clinics (75 pregnant couples per clinic x 4 clinics = 300 couples = 600

individual men and women.) Recruitment will be from both the VCT and the ANC; both men and women in pregnant couples will be eligible to participate with their partners. Women attending ANC are asked to bring their partners to ANC visits, and clinics will have both women and men in attendance. Those who participated in FGDs will not be eligible to enroll in the LFLS program.

No recruitment materials will be created.

Compensation. Participants are compensation $10 each for each study visit. Study visits are 1-2 hours per visit.

27) Local Number of Subjects

N=744 participants will be enrolled.

It is anticipated that N = 744 will be enrolled and will be needed to complete the research.

28) Confidentiality

Data Confidentiality. CAB and FGD participants will not provide any uniquely identifying information during participation in group discussion sessions. Pregnant couple participants in the intervention will be assigned a unique code upon entering the study. This number will identify all participant files, which will include no identifiable information. Access to the computer data files will be restricted by password codes. The list translating participant number to identifying information will be maintained in a secure locked file in the Spear & Shield study office in Lusaka at the University of Zambia School of Medicine. Participants will be made explicitly aware at the time of the informed consent of the nature of the separate record that will be kept for them. CAB and focus group discussions will be audio-taped for review and summary of key discussion points; copies will be stored in a locked cabinet at the PI's Lusaka offices, and deleted following summarization**.**

No specimens will be collected.

29) Provisions to Protect the Privacy Interests of Subjects

Prior to obtaining consent, study staff will review the environment in which the study will take place, and steps that will be taken to protect subjects' privacy interests. As the study uses group interventions, study participants will interact with other pregnant men and women. This is outlined in the consent.

Prior to beginning assessments, study staff traditionally, in Zambian culture, exchange general discussion to foster a positive environment. Participants are made to feel at ease during the entire research experience, and are welcome to ask questions and discuss the elements of the study at any time. When participants appear ill at ease, they are invited to return on another visit. Participants wishing to process difficult issues are invited to share

with the assessors, who are trained counselors, and can also be referred to support staff in the clinic.

The research team is only able to access study data; there is no potential for the study staff to access private health data at the clinic.

30) Compensation for Research-Related Injury

The research involves only Minimal Risk. The following is language relevant to compensation for research-related injury contained in the consent.
"Although risks are unlikely, if injury should occur, treatment will in most cases be available. If you have insurance, your insurance company may or may not pay for these costs. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay. Funds to compensate for pain, expenses, lost wages and other damages caused by injury are not routinely available."

31) Economic Burden to Subjects

N/A

32) Consent Process

Study Procedures – Informed Consent:

The informed consent will be reviewed in detail and read aloud to the prospective participant (CAB member, FGD member, or pregnant couple member) individually in their preferred language in a private room in the study offices at the CHC. The consent will then be reviewed section by section to ensure comprehension. Study candidates will be asked to recount the essential content of the informed consent back to the staff member using a consent comprehension test and agreeing to the terms of the consent before signing the form. Any items of confusion will be clarified by the study recruiter. Each study candidate will be asked to sign or provide their mark on the form after reading or having the contents read and explained, and if agreeing to its terms, and the signature of a witness will be obtained. [N.B. Neonates are not participants in LFLS, and are only potential recipients of a health care service provided by the clinics.] Our current consent process in Zambia is ~30 minutes in duration.

The following questions will be used to evaluate comprehension of Informed Consent.

- Purpose: Can you tell me in your own words what this project is all about?
- Procedure: Can you tell me how many visits you are expected to complete?
- Can you tell me how long a focus group will be?
- Risks: Can you tell me if there are any risks in participating in the study?
- Compensation: Can you tell me if there is any compensation?

- Confidentiality: Can you tell me how your records will be kept safe?
- Withdrawal: Can you tell me if you can drop out of the study?
- Summary: Do you have any questions or concerns about the study?
- Can you tell me how to get questions answered by the Zambia Research Ethics Committee?

Non-English Speaking Subjects

- Participants enrolled will be both English-speaking and non-English speaking. Local languages in the Lusaka area are Bemba and Nyanja, and all study materials will be translated into local language(s) in addition to English.
- Participants are in area are fluent in both Bemba and Nyanja, and all interventionists, group leaders, assessors and recruiters speak local language and English, enabling all participants to be enrolled, understand the materials. To ensure that the oral and written information provided to participants will be in their preferred language, and consent materials and assessment materials will be translated and back translated to local language.

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- N/A

Subjects who are not yet adults (infants, children, teenagers)

- N/A

Cognitively Impaired Adults

- Adults are eligible to enroll if they are able to understand the elements of the consent in the consent process.

Adults Unable to Consent

- Adults unable to provide consent will not be enrolled.

33) Process to Document Consent in Writing

- Consent will be documented in writing by signed or thumb print document on consent. Research presents no more than minimal risk of harm to subjects.
- Consent – following ZAMBIAN standard format – is attached.

34) Drugs or Devices

- N/A

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	*X*	*X*	
21 CFR 54	*X*	*X*	
21 CFR 210	*X*		
21 CFR 211	*X*		
21 CFR 312	*X*		
21 CFR 812		*X*	*X*
21 CFR 820		*X*	