YEAR 7 SEMI-ANNUAL REPORT
OCTOBER 1, 2021 – MARCH 31, 2022

SUBMITTED BY:
Family Health International (FHI 360)

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Transforming Contraception to Expand Access and Choice
Family Planning and Reproductive Health Methods to Address Unmet Need


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Introduction

The objective of Envision FP is to develop, introduce, and expand understanding of contraceptive technologies and approaches to enhance choice and reduce unmet need. The proposed research agenda aligns with the three specific aims outlined in the original USAID Annual Program Statement: 1) refine existing methods; 2) respond to product-related issues that arise from the field and impact provision; and 3) develop new methods to fill gaps. Envision FP focuses on key challenges and opportunities significant for users and programs in an effort to achieve the overall goal of broadening choice of and access to quality, affordable, and acceptable contraceptives to meet the changing needs and desires of women and girls throughout their reproductive lives.

The following sections define the activities, accomplishments and challenges for the first half of Year 7 (October 1, 2021 - March 31, 2022). Plans through award close-out are included. Year 7 budgets and expenditures through March 2022 are provided in Appendix 1.

AIM 1: REFINE EXISTING CONTRACEPTIVE METHODS

Lower-dose injectable contraception
Lead: Vera Halpern, MD

Goal: Develop and receive regulatory approval for a low-cost, lower-dose, three-month subcutaneous depot-medroxyprogesterone acetate (SQ DMPA) injectable contraceptive.

Significance and Impact: Over 40 million women worldwide use injectable contraceptives, particularly intramuscular (IM) DMPA (150 mg every 3 months). Despite its popularity, this dose is unnecessarily high. An alternative, Sayana Press (SP), provides 104 mg MPA subcutaneous (SQ) for 3 months, but also provides more drug than is likely needed. A lower-dose SQ DMPA product would offer a highly effective and safer contraceptive option for women. Reduced side effects would enhance acceptability and increase continuation.

Approach: The team used a marketed DMPA IM formulation (Pfizer) to determine the potential of developing a lower-dose SQ product. A partially-blinded randomized trial was conducted to assess pharmacokinetics (PK) and pharmacodynamics (PD) of three doses of Pfizer’s current DMPA formulation (45 mg, 75 mg, and 105 mg) compared with Depo-subQ 104. MPA levels and ovarian activity were evaluated after a single injection and women were followed for 7.5 months. The 105 mg arm provided a direct comparison with the marketed Depo-subQ 104,
allowing the study to control for formulation differences between DMPA IM and SQ, with the possibility of pursuing a lower-cost generic SQ product. The team also leveraged documentation from our other PK/PD studies funded by the Gates Foundation to accelerate protocol development, investigational new drug (IND) preparation and study start-up.

**Activities, accomplishments, and challenges in past 6 months:** The datasets for this study were submitted to the USAID Data Development Library (DDL) in Oct. 2021. In Feb. 2022, the secondary manuscript based on the PK/PD data from this study (in combination with PK/PD data from the ESS trial) was accepted for publication in *Contraception X*.

**Plans until award closure:** We will conduct a secondary analysis of the supportive PD data from this study to explore the role of secondary mechanisms of contraceptive action of MPA and provide information on potential biomarkers of contraceptive effectiveness (in addition to ovulation) for future contraceptive studies. A manuscript based on this analysis will be drafted.

**Extending the reinjection interval of Sayana Press (SP)**

**Lead: Vera Halpern, PhD**

*This study was co-funded by the Bill & Melinda Gates Foundation, under the Contraceptive Technology Innovation Initiative (CTII) and Advancing priority CT leads to meet user needs (CTII-2). The return to ovulation sub-study was co-funded by Envision FP and the Children’s Investment Fund Foundation (CIFF).*

**Goal:** Determine effectiveness, safety, and acceptability of extending the reinjection interval for Sayana Press (SP) and to determine the appropriate grace period for re-injection.

**Significance:** Evidence suggests that SP is effective for four months or longer but is currently indicated for three months. Extending SP duration by one month would reduce commodity costs for a year of protection by 25%. Given the same commodity budget, countries could serve 33% more women annually. Less frequent reinjections would also reduce drug exposure, provide greater convenience to women, and lower overall health system burdens.

**Approach:** The team developed a 12-month, single-arm clinical trial to determine the effectiveness, safety, and acceptability of SP given every four months, and to determine the appropriate grace period for re-injection. Women were enrolled in three countries to assess one-year pregnancy rates, adverse events and side effects, and discontinuation rates. Key informant interviews were conducted with FP providers and MOH decision-makers on the acceptability of extending SP intervals to four months.

**Activities, accomplishments, and challenges in past 6 months:** Final tables, figures and listings were completed in Nov. 2021. The primary effectiveness manuscript was accepted by the journal and published in *eClinicalMedicine Jan. 2022*. Open data submission (Harvard Dataverse and USAID Data Development Library) occurred in Jan. 2022 and final results were submitted for posting on clinicaltrials.gov in Jan. 2022. The CSR was published and shared with USAID in Feb. 2022. With co-funding from CIFF, a secondary manuscript based on return to ovulation data and PK/PD modeling was submitted to Contraception X in Mar. 2022, and a related abstract was submitted to the International Conference on Family Planning (ICFP). The team also responded to the survey by WHO SPR, suggesting that issues around delayed return to
ovulation and strengthening the existing recommendation on the 4-week reinjection window be included on the agenda for the next WHO SPR steering committee meeting.

The acceptability paper was drafted, reviewed by USAID and then submitted to Contraception in Dec. 2021. In Feb. 2022, Contraception responded with comments to revise and resubmit and revisions were completed in Mar. 2022.

**Plans until award closure:** eTMF archival is expected to be completed by May 2022. The team will continue dissemination efforts including but not limited, to publishing a commentary in a peer-reviewed journal and engaging with Pfizer regarding adding upper arm and a possibility to extend re-injection window from 1 to 4 weeks on the label of Sayana Press. We will continue collaborating with CIFF, DMPA-SC Access Collaborative and other stakeholders on finding proper and efficient channels for broader dissemination of our findings.

On Apr. 1, 2022, the acceptability manuscript was re-submitted to Contraception and they responded with a few minor changes required for acceptance. The revisions were made and the manuscript was re-submitted. The paper was accepted for publication on Apr. 15, 2022.

**Year 7 Implementation Timeline**

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**Phase I Clinical PK/PD study of DMPA XT— the Early Start Study (ESS)**

**Lead:** Vera Halpern, MD

This study was co-funded by two grants from the Bill & Melinda Gates Foundation: the Contraceptive Technology Innovation Initiative (CTII) and Advancing Priority CT Leads to Meet User Needs (CTII-2). Envision FP funds were not used for any site activities.

**Goal:** Develop and receive regulatory approval for a low-cost, 6-month subcutaneous depot-medroxyprogesterone acetate (SQ DMPA) injectable contraceptive.

**Significance and Impact:** Over 40 million women worldwide use injectable contraceptives to prevent pregnancy. In sub-Saharan Africa, more than one-third of modern method contraceptive users rely on injectable contraceptives. Depending on the formulation, currently available injectables are effective for one to three months, requiring women to return to their provider monthly, every other month or quarterly. A longer-acting injectable would facilitate use, improve continuation, possibly increase effectiveness, and provide women with greater choice. Adaptation of existing methods for novel uses is an appealing, cost-efficient approach to expedite availability of new contraceptive options.
**Approach:** The team used a marketed DMPA IM formulation (Pfizer) to support the development of a 6-month SQ product. A partially-blinded randomized trial was conducted to assess pharmacokinetics (PK) and pharmacodynamics (PD) of one injection of either 150mg/mL or 300mg/2mL of Pfizer’s current DMPA formulation compared with two cycles of Depo-subQ 104. MPA levels and ovarian activity were evaluated and women were followed for up to 18 months.

**Activities, accomplishments, and challenges in past 6 months:** In Feb. 2022, the secondary manuscript based on the PK/PD data from this study (in combination with PK/PD data from the LD DMPA trial) was published in *Contraception X*. The publication link is: [Contraception X](#)

**Plans until award closure:** Dr. Vera Halpern and Ms. Neha Mehta attended the NICHD 2022 Contraception and Development Meeting in Apr. 2022 and gave an oral presentation, “Clinical development and regulatory pathways for new contraceptives”. Dr. Halpern will attend the European Society of Contraception (ESC) Congress on May 25-28, 2022. Dr. Halpern will serve on a joint USAID/FHI 360 panel, "From pipeline to reality: development of new contraceptive products for worldwide impact." In addition, Dr. Halpern has an accepted poster, ““Everything new is a well-forgotten old”: innovative path towards 6-month contraceptive injectable”. Data from the DMPA XT Phase 1 study is included in the poster and presentations.

**Transforming postpartum IUD (PPIUD) insertion**

*Lead: Markus J. Steiner, PhD*

**Goal:** Stimulate interest and facilitate sustained postpartum IUD (PPIUD) services through registration, introduction, and evaluation of an easy-to-use PPIUD inserter.

**Significance and Impact:** Many women in the extended postpartum period have unmet need for contraception. Postpartum IUD insertion is safe and effective, and USAID has made investments in expanding access to such services across Africa. However, PPIUD insertion can be technically challenging, and the current copper IUD inserter cannot be used postpartum. Pregna International, Ltd. has developed and is testing a simple, inexpensive, easy-to-use pre-loaded, pre-sterilized PPIUD inserter that could increase convenience, simplify insertion, reduce expulsions, and enhance safety. In countries where access to PPIUD services is limited, this new inserter has the potential to spark sustained interest and dramatically increase uptake.

**Approach:** FHI 360 has provided technical assistance to Pregna in preparation for submission to obtain CE Marking, achieving UNFPA/WHO Prequalification, and qualifying for USAID procurement. In discussion with USAID, after learning that over 60,000 units have been distributed to 13 countries, we expanded the approach to include an assessment of initial experiences with the device. Since the initial assessment, over 250,000 units have been distributed with numerous countries reordering the device (Congo, Cote d’Ivoire, Ethiopia, Indonesia, Guatemala, Myanmar, Nigeria, Senegal, South Africa).

**Activities, accomplishments, and challenges in past 6 months:** Instead of the promised final decision by the end of 2021, Pregna received additional requests to edit the instructions for use (IFU) on Mar. 15, 2022. Pregna and Drs. Blumenthal and Steiner had a series of email exchanges and telephone calls to finalize the IFU. Pregna provided the updated document to UNFPA and is awaiting the final decision.
**Plans until award closure**: If/when UNFPA grants prequalification of the PPIUD, FHI 360 staff will help design the PMCF study/quality assurance activity.

**AIM 2: RESPOND TO PRODUCT-RELATED ISSUES WITH EXISTING CONTRACEPTIVE METHODS**

**Contraceptive drug-drug interactions (DDIs)**

**Lead: Kavita Nanda, MD**

Hormonal contraceptives (HCs), when used with antiretroviral (ARV) or anti-TB drugs, may be subject to PK interactions that could lead to decreases in efficacy or increases in toxicity. WHO’s updated guidance on HCs and HIV note that women taking ARVs can use all HC methods, but special consideration may be needed (Category 2) for those who use progestin-only contraceptives with certain ARVs. Since then, more data have become available and the knowledge base is rapidly changing.

**Technical leadership**

**Goal**: Support efficient, consistent, and thorough study of issues related to contraceptive DDIs that will inform global and local policies.

**Significance and Impact**: Engaging partners working in the rapidly emerging area of contraceptive DDI research will support efficient research design and evaluation while facilitating a faster application of results to policy and practice in the field.

**Approach**: FHI 360 staff engaged groups conducting research around this topic, providing technical assistance as needed. FHI 360 staff provided peer review for a DDI manuscript. FHI 360 staff also collaborated with researchers at UW on DDI research, which led to two published papers.

**Activities, accomplishments, and challenges in past 6 months**: Literature searches were conducted through Feb. 2022 to further update papers included in the systematic review. The protocol registered on the International Prospective Register of Systematic Reviews (PROSPERO) has been updated and final review data abstraction and synthesis completed, with draft manuscript sent to authors Mar. 2022. Work on a revised manuscript continued with plans for Envision FP senior management review in Apr.

**Plans until award closure**: FHI 360 review of the manuscript will be completed in Apr. We plan for submission to USAID for review in May 2022 and then to the Journal of the International AIDS Society once USAID approvals are received.

**DDI Database**

**Goal**: Develop a comprehensive, evidence-based, up-to-date, publicly available online database of information on contraceptive DDIs, to be housed on FHI 360’s Contraceptive Technology Innovation Exchange platform (ctiexchange.org).

**Significance and Impact**: A centralized resource to inform clinical practice and policy specifically related to contraceptive DDIs is lacking. Such a tool would improve clinical practice across FP and disease areas, enable policy makers to strengthen guidelines to ensure that women can use
the best contraceptive options given other needed treatments, and offer guidance for the design of new contraceptive and multipurpose prevention technologies.

**Approach:** FHI 360 has led reviews of HC DDIs for the WHO MEC for over a decade. The team’s existing review of current HC products and ARVs was updated and supplemented with other reviews of HCs interactions with anti-TB drugs and antibiotics. Information on PK DDIs, relevant clinical data, and current guidance was compiled into a custom online database that will allow users to easily obtain information on interactions between HC methods and non-HC drugs.

**Activities, accomplishments, and challenges in past 6 months:** The database has been maintained. It had 40 unique users over 46 sessions from Oct. 2021 to Mar. 2022.

**Plans until award closure:** The database will remain posted online through the end of Envision FP. There will be no additional updates to the database.

**Supporting scale-up of the hormonal IUD**

**Lead:** Kate Rademacher, MHA

**Goal:** Implement and evaluate best practices in the global introduction and scale-up of the hormonal IUD as a highly effective method of contraception.

**Significance and Impact:** The hormonal IUD is one of the most effective forms of reversible contraception available and is increasingly popular among women worldwide. The hormonal IUD offers a number of advantages including reduction of menstrual cramps and blood loss, fewer side effects compared to some other hormonal methods, and possible alleviation of anemia in some populations. All of these characteristics could provide substantial benefits to women in developing countries. Recent assessments have indicated that in settings where unmet need for family planning is high, the hormonal IUD could play an important role in helping to reduce unintended pregnancies and improve maternal health. To date, the high cost of the method has been a barrier to making it widely available; however, the approval of a lower cost hormonal IUD by the FDA in 2015 has helped revitalized discussions around expanding access to this method in developing countries.

**Approach:** The team engaged in global technical leadership activities to promote the evaluation, introduction and scale-up of the hormonal IUD. Note: In 2021, the nomenclature for the LNG IUS was changed to hormonal IUD to align with WHO guidance. This new term is used in the activity title and below.

**Activities, accomplishments, and challenges in past 6 months:** During the past six months, we made substantial progress with work related to (1) the hormonal IUD and (2) contraceptive induced menstrual changes as summarized below.

1. **Global- and country-level updates regarding the hormonal IUD**

During this period, FHI 360 continued to serve as co-Secretariat (along with CHAI) of the Hormonal IUD Access Group. This included supporting a refresh of the governance structure that was approved by the Steering Committee in Feb. 2022. FHI 360 continued to manage and expand the Hormonal IUD Access Portal website including content in the resource library and blog. The team also led development of two editions of the global e-newsletters that were sent in Dec. 2021 and Feb. 2022 to over 1000 subscribers. FHI 360 continued to
partner with CHAI, PSM-GHSC, and Medicines360 on the supply-side workstream and contributed to a draft of an investment case that will be submitted to SEMA in Apr. 2022. In collaboration with government and NGO partners, FHI 360 continued to support coordination for broader method introduction in several countries including Nigeria, Kenya and Uganda. We led development of a new country ‘briefing book’ that summarizes the introduction status in each country; this tool will be shared with the Steering Committee and finalized in Apr. 2022. In addition, the refreshed global learning agenda was finalized and posted online. In addition, a synthesis manuscript entitled, “Five Years Later, What Have We Learned? Implementation of a Global Learning Agenda for the Hormonal Intrauterine Device” was submitted to Global Health: Science and Practice. The manuscript is currently being revised based on reviewer comments and will be resubmitted in Apr. 2022. We also submitted a joint panel abstract to ICFP in collaboration with the DMPA-SC Access Collaborative and the Implants Access Collaborative.

The HIP strategic planning guide on Contraceptive Method Introduction to Expand Choice was finalized and published in Mar. 2022; dissemination efforts are underway including plans for a global webinar (date TBD).

2. Contraceptive-induced menstrual changes

Two national dissemination events were held in Nairobi in Jan. and Feb. 2022 to share results from the NORMAL study. During the second event, the group aligned on final edits to the NORMAL job aid based on MOH feedback including a request to add the national MOH logo. Plans are underway to integrate NORMAL into the national package of counseling materials for community health volunteers. In addition, a manuscript was developed entitled, ‘‘Before it was like we were in darkness’ – Field testing the NORMAL job aid with community health workers in Kenya to address contraceptive-induced menstrual changes.’’ The paper was submitted to Frontiers Research for inclusion in a series focused on Global Menstrual Health Literacy. We also submitted an abstract to ICFP with the results from the NORMAL assessment in Kenya.

**Plans until award closure:** FHI 360 will continue to serve as co-Secretariat of the Hormonal IUD Access Group, and manage content on the Hormonal IUD Access Portal website and the global e-newsletter. FHI 360 will contribute to an investment case that will be submitted to SEMA to support a potential technology transfer of Medicines360’s Avibela product. The country ‘briefing book’ will be finalized and shared with the Steering Committee. Revisions to the synthesis manuscript will be submitted. FHI 360 will also support dissemination of the new HIP brief (e.g.,) contributing to a global webinar. Technical assistance will be provided to the Kenya MOH and/or other countries to support adaptations of the NORMAL tool, as requested, and the manuscript with research findings from the assessment of NORMAL will be finalized, following peer review.
### AIM 3: DEVELOP NEW METHODS TO ADDRESS METHOD-RELATED NONUSE OR FILL GAPS

**Development of an intradermal (ID) biodegradable microneedle patch loaded with LNG/ENG/NES** (IAA-NICHD FY17 $84,091, FY18 $50,000 & Additional funding transferred from completed projects $40,834)

**Lead:** Jennifer Ayres, PhD

**Activities, accomplishments, and challenges in past 6 months:** This activity closed under Envision FP as of Sep. 2021 and further work is being implemented under Innovate FP. The final subaward payment to Georgia Tech was issued and the subagreement was closed.

**Development of biodegradable contraceptive implants**

**Lead:** Jennifer Ayres, PhD

**Activities, accomplishments, and challenges in past 6 months:** This activity closed under Envision FP as of Sep. 2021 and further work is being implemented under Innovate FP. The final subaward payment to Yale University was issued.

**Plans until award closure:** The subagreement will be closed by end of Apr. 2022.

### PROJECT MANAGEMENT AND MONITORING & EVALUATION

In an effort to ensure that Envision FP project activities are completed on time and within budget, FHI 360 has a centralized hub of operations for project management as well as monitoring & evaluation. These functions work together to serve as a feedback loop for the status of individual activities in support of project planning and reporting requirements as well as to identify opportunities for learning and project efficiency.

**Project management**

**Lead:** Amanda Troxler, BA

Project management support is provided at both the specific activity and overall project levels. Envision FP project management staff are responsible for ensuring that all reporting
requirements to USAID are met and serves as a liaison between USAID and the activity-level project managers, communicating issues related to timeline and budget.

**Monitoring and evaluation**  
*Lead: Amanda Troxler, BA*

The monitoring and evaluation (M&E) staff focus on implementing the Performance Monitoring Plan (PMP) in close collaboration with project management, the full team, and USAID. The M&E approaches include the indicators, outcome mapping, learning, and evaluation, and builds on what was developed and implemented for the CTI Initiative. M&E staff also assist with the Key Results Reporting, Management Reviews and regular reporting, coordinating closely with the project management team.

**OTHER ACTIVITIES AND INTERAGENCY AGREEMENTS (IAAS)**

The *Envision FP* team also manages the following portfolio of activities supported through additionally obligated funds and Interagency Agreements:

**Technical Assistance for FP-HIV Integration** *(GH-C-POP FY15 $90,000, FY19 $15,000)*  
*Lead: Irina Yacobson, MD*

**Goal:** To support providers in both HIV and FP settings in offering integrated HIV/FP care.

**Approach:** A job aid was developed that offers practical guidance to providers in family planning settings on counseling clients about their HIV prevention options, including PrEP, as well as on initiating PrEP in FP settings. Another FP/HIV integration tool was planned to offer guidance to providers in HIV settings on assessing their clients’ reproductive intentions and counseling on available family planning options. Remaining funds in this account will be used to complete Evidence for contraceptive options and HIV outcomes (ECHO) Study-related work.

**Activities, accomplishments, and challenges in past 6 months:**

**FP/PrEP integration job aid/resource package**

- Per USAID request, the background section for the planned resource package was developed.
- For final approval, USAID involved additional reviewers from the Office of HIV/AIDS as well as from the MOSAIC project. Based on their feedback, additional revisions to the job aid were made. However, the job aid was not finalized as WHO is planning to release new PrEP guidelines in April/May and the job aid will have to reflect any applicable changes.
- Per USAID request, the overview of some of the integration tools developed over the course of the project will be presented at the webinar in May 2022.

**FP/HIV integration tool**

After discussions with USAID, it was decided not to proceed with the development of this tool as there is not enough time left until the end of the project to facilitate a thorough review process and complete the development.
Plans until award closure:

FP/PrEP integration job aid
- Final changes will be made to the job aid based on any applicable new WHO guidance.
- The job aid will be submitted to USAID for approval (we do not anticipate a lengthy review process at this point as any changes are not expected to be significant).
- A dissemination plan will be developed in consultation with USAID, which may include presentation to USAID missions.

FP/HIV integration tool
No activities are planned.

Remaining funds will be used to complete ECHO manuscripts. See the ECHO activity section for additional details on manuscripts.

Longitudinal study of LARC acceptors in Senegal
Lead: Marga Eichleay, MPH

Goal: To better understand the factors related to LARC continuation in low resource settings in order to provide guidance that will improve routine family planning service delivery.

Significance and Impact: Long-acting, reversible contraceptives (LARCs) including subdermal implants and intrauterine devices (IUDs) have begun to show their potential to radically change voluntary family planning (FP) in Africa. LARCs have taken on greater importance in the contraceptive method mix in many countries, with implants in particular seeing marked increases in users. While failure rates of LARCs are low, discontinuation is an important concern that can leave women vulnerable to pregnancy if they do not adopt another method. Effectively meeting the current (and increasing) demand for LARCs requires responsive and effective strategies to ensure expanded access as part of a broad method mix that also includes related services such as follow-up, management of side effects and removals. There is a dearth of information—from the client’s point of view—on how to help women effectively manage side effects associated with LARCs and on how service delivery factors may affect a decision to continue or discontinue the method. Enhanced understanding of these factors and their interplay is important, as it could inform guidelines and approaches to routine service delivery.

Approach: This longitudinal study of long-acting, reversible contraceptive users began as part of a five-year, USAID-funded project implemented by Marie Stopes International (MSI) and its partners, one of whom was FHI 360. Referred to as the SIFPO (Support for International Family Planning and Health Organizations) 2 project, the goal was to deliver high quality family planning services at scale by providing access to and expanding method choice globally. Funding from MSI was discontinued prior to project completion; however, the project received funding through Envision FP beginning in March 2018. Under Envision FP, the study goal and focus remained the same as the initial SIFPO2 funding. The quantitative component consisted of surveys of LARC acceptors who will be interviewed at service delivery sites, then re-interviewed 1, 3, 6 and 12 months after accepting an implant or an IUD. The qualitative component included formative cognitive interviews and mid-term in-depth interviews (IDIs) with a subset of survey participants reporting experiences with side effects. The formative
cognitive interviews were conducted prior to the beginning of the survey activities to refine the latter’s content and development. This process was expected to result in surveys that not only capture the information needed, but in a way that reflects participants’ understanding and experiences with LARC methods. The mid-term interviews were conducted after the six-month survey follow-up to provide richer details and a deeper understanding of women’s experiences coping with side effects.

Activities, accomplishments, and challenges in past 6 months: The manuscript was published in Frontiers in Global Women’s Health in Jan. 2022. This activity is complete.

ECHO continuation
Lead: Rebecca Callahan, PhD

Goal: To assess contraceptive experience, including method continuation and access to removal services, among a subset of women exiting the ECHO trial.

Significance and Impact: The ECHO study offers a rare opportunity to follow a relatively large cohort of women using long-acting reversible contraceptive (LARC) methods and DMPA in Sub-Saharan Africa, for which continuation rates are extremely limited, especially beyond one year of use. Similarly, little is known about LARC users’ access to and experiences with method removal. Most of the women exiting ECHO will have been using their method for 12-18 months in the context of the trial. Following them after study exit allowed for documentation of method experience beyond one year.

Approach: This was a prospective observational longitudinal study including a phone survey every 6 months up to 24 months with a sample of women who have exited the ECHO trial in South Africa and Zambia. The study was conducted in collaboration with MatCH Research Unit (MRU) of the University of the Witwatersrand in South Africa and the University of North Carolina (UNC) Kamwala Research Clinic in Zambia. The primary study objective was to document contraceptive status over at least 24 months following exit from the ECHO trial and measure method-specific and overall continuation rates. Secondary objectives were to describe reasons for contraceptive discontinuation and to describe implant and IUD removal outcomes, including success or failure at obtaining removal and number of removal attempts. Additionally, to delve deeper into decisions around continuation/discontinuation and experience accessing LARC removal, sites conducted 20 in-depth interviews during the second year of data collection. In response to the COVID-19 pandemic, which began during the course of the CUBE study, we added questions to both the survey and IDIs to assess the effect of the pandemic on participants’ access to and use of contraceptive services. We also added IDIs with 15-20 FP providers and other stakeholders in each country to explore service delivery perspectives on COVID’s impact on contraceptive use.

Activities, accomplishments, and challenges in past 6 months: The primary manuscript was submitted to Studies in Family Planning on Jan. 15, 2022 and is currently under review. Another manuscript, detailing experiences with family planning access in the context of the COVID-19 pandemic, was submitted to USAID for review on Jan. 30, 2022 and after incorporating feedback, was submitted to Global Health: Science and Practice on Mar. 22, 2022. The subaward with MatCH was closed.
**Plans until award closure:** Two additional manuscripts, one examining HIV testing frequency led by our research partners at MatCH, and another on self-care, will be submitted to USAID for review in early May 2022 and then to be submitted to journals by late May/early Jun. 2022.

Our research partners at the University of the Witwatersrand in South Africa will also lead dissemination activities on the CUBE results, including preparing a webinar in consultation with FHI 360, to which national and provincial Department of Health participants will be invited.

The subaward with UNC will be closed out.

**Evidence for contraceptive options and HIV outcomes (ECHO) Study (GH-C-POP FY16 $1,250,000, FY17 $3,850,000; OHA FY16 $2,500,000, FY16 $280,000 (transfer), FY17 $1,250,000)**

**Lead: Tim Mastro, MD, DTM&H (as co-PI)**

*This study was co-funded by the Bill & Melinda Gates Foundation.*

**Goal:** To evaluate whether there is a link between use of hormonal contraception and increased risk of acquiring HIV infection.

**Significance & Impact:** As the HIV epidemic spread, it became important to explore risk factors for HIV, and particularly whether there was an association between use of specific contraceptives and HIV acquisition. A number of observational studies have examined this issue. Some of these studies suggest that injectable methods, particularly DMPA, might increase a woman’s risk of acquiring HIV infection, while other studies show no association. The lack of definitive data from observational studies makes it difficult to offer guidance on contraceptive use in settings where women have a high risk of acquiring HIV and where many women use progestin-only injectable methods such as DMPA, often due to limited options for contraception.

**Approach:** Designed to address this critical evidence gap, the ECHO Study randomized women to DMPA, the copper IUD, and Jadelle to evaluate whether there is any difference in the risk of acquiring HIV infection among users of these methods. The study also compared side effects, pregnancy rates, and how well women stayed on each of the three contraceptive methods. A total of 7,830 sexually active HIV-negative women ages 16 to 35 were enrolled across 12 study sites in four countries (Kenya, South Africa, Swaziland, and Zambia). The first participant enrolled on Dec. 9, 2015, and enrollment was completed on Sep. 12, 2017. The total duration of the study in the field was almost 35 months, and the results were published and presented on Jul. 13, 2019.

**Activities, accomplishments, and challenges in past 6 months:** We continued to manage ECHO Management Committee review of manuscripts on secondary analyses of ECHO data and ancillary studies. Four manuscripts were published, two others were accepted for publication, and another seven were submitted to journals. The following manuscripts were published:

- *Incidence of herpes simplex virus type 2 among African women using depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a nested randomized trial* in Clinical Infectious Diseases
Daily oral pre-exposure prophylaxis (PrEP) continuation among women from Durban, South Africa, who initiated PrEP as standard of care of HIV prevention in a clinical trial in AIDS and Behavior

The effect of contraception on genital cytokines in women randomized to copper intrauterine device, intramuscular depot medroxyprogesterone acetate or levonorgestrel implant in The Journal of Infectious Diseases

Contraceptive method preference and reasons for discontinuation among women randomized to intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant: findings from Durban, South Africa in Contraception

Plans until award closure: We will continue to: convene calls with the ECHO Management Committee as needed to address various issues, including working with the sites to try to obtain waivers of informed consent so ECHO data can be shared on a public website; overseeing destruction of the South Africa lab specimens; helping team members comply with USAID publication policies; and overseeing Management Committee review of the manuscripts.

FHI 360 staff will complete the following ECHO manuscripts. Funds from the Technical Assistance for FP-HIV Integration activity will support this work.

- Contraceptive method continuation and factors associated with method discontinuation in the ECHO trial
- Comparative PID risk associated with contraceptive method provision in high STI settings: the ECHO trial experience
- Skill-based IUD insertion outcomes following providers’ training: ECHO trial experience

Southern Africa method mix technical assistance (OHA FY17 $500,000)
Lead: Elena Lebetkin, MPH

Goal: Provide technical assistance to up to five Southern African countries to support method choice analysis and technical/advocacy efforts to foster method choice expansion.

Significance and Impact: In many countries with high HIV prevalence, the family planning method mix is heavily skewed to the injectable contraceptive, DMPA. In Southern Africa, namely South Africa, Namibia, Botswana, Swaziland, and Lesotho, both HIV prevalence and the use of DMPA is high. As the international community awaits the ECHO trial results, working with countries in Southern Africa to expand the method mix is important not just in terms of method choice, but also in the event that there is a link between HIV acquisition and DMPA use. This funding presents the unique opportunity to work in Southern Africa, where family planning funding is minimal, but the need to foster method choice expansion is present.

Approach: FHI 360 worked in collaboration with USAID to conduct individual country assessments in order to identify country-specific gaps in method choice and develop and implement a technical assistance plan in order to help the target countries expand method choice.

Activities, accomplishments, and challenges in past 6 months:
Lesotho: The dissemination meeting was held on Oct. 25, 2021 and was chaired by a MOH representative and attended by MOH representatives, stakeholders, and USAID/Washington and Lesotho and included a presentation of results and discussion on next steps. The MOH decided at the meeting that they would set up an HIV prevention/FP task team that includes multiple MOH departments, namely Health Planning and Statistics Department and Family Health, in order to have a forum to discuss integration. The work under the subaward with Jhpiego was completed and the subaward was closed out in Dec. 2021. The team is drafting a manuscript for submission to a journal. The study team submitted an abstract in Feb. 2022 for consideration for an oral presentation at the International Conference on Family Planning to be held in Nov. 2022.

Namibia: The MOH in Namibia hired a new FP Advisor to take over for the former Advisor who retired more than a year ago. The new FP Advisor contacted USAID Namibia for assistance locating FP guidance and materials developed by FHI 360. The FHI 360 team prepared a brief summary of the work undertaken in Namibia and consolidated all materials in a shared drive for dissemination to the MOH.

Botswana: The MOH in Botswana rolled out the FP Procedures Manual, FP training curriculum, job aids, and tools that FHI 360 adapted for Botswana from the Namibia materials.

Plans until award closure: The team will continue drafting the Lesotho manuscript, share with USAID for review, and submit to Frontiers in Reproductive Health for consideration.

Preparing for Ring Opportunities through Market Introduction Support and knowledge Exchange (PROMISE)

Lead: Kristine Torjesen, MD/MPH

Goal: To shape the market and establish a family planning service delivery platform for future multipurpose vaginal rings (VR) through the provision of early product introduction support for the dapivirine vaginal ring (DVR). The intent is for this work to create an enabling environment for the introduction and sustainability of VR products for pregnancy and HIV prevention, such as segesterone acetate-ethinyl estradiol VR (Annovera), 90-day DVR, and dapivirine-levonorgestrel VR.

Significance: Given the high burden of unintended pregnancies and sexually transmitted infections, including HIV, among women in sub-Saharan Africa, research efforts have focused on the development and implementation of female-initiated drug-delivery methods, such as the VR, particularly for low- and middle-income countries (LMIC). Improving options for prevention products in sexual and reproductive health is critical to address women’s diverse and dynamic preferences. Yet access to currently approved VRs is limited in LMIC, primarily due to high product cost and lack of investment in their market introduction in these countries. VRs remain a relatively unfamiliar formulation to most women in LMIC. Pending regulatory approval, IPM’s dapivirine ring for HIV prevention will be the first VR to be primarily marketed in sub-Saharan Africa. This presents a market shaping opportunity to build awareness, acceptance, and demand for VRs as an additional method choice to meet women’s sexual and reproductive health needs, as well as a health systems opportunity to strengthen family planning services to support VR delivery. Successful market introduction of the DVR will pave
the path for accelerated introduction and uptake of future VR products in sub-Saharan Africa, including longer-acting and MPT VRs for both contraception and HIV prevention.

**Approach:** Work was conducted by a consortium of partners, across countries prioritized for regulatory approvals and early introduction efforts. Partners included: AVAC, Avenir Health, LVCT Health, Afton Bloom, Columbia University, the Public Health Institute (PHI), International Partnership for Microbicides (IPM) and Wits RHI. The geographic focus of this work will be in South Africa, Kenya, Uganda, and Zambia. The work was conducted in close collaboration and coordination with the IPM, who are the market authorization holder for the DVR, as well as the product developers of the dapivirine-levonorgestrel VR currently in Phase 2 trials.

**Activities, Accomplishments, and Challenges in past 6 months:**

**Activity 1** (Service delivery channels strategy): In this period of performance, PROMISE completed the last of the Activity 1 work by formally launching **PrEP-it 2.0**. Through the support of the PROMISE Activity, PrEP-it is now a more user-friendly web-based tool which includes multiple PrEP methods (e.g., pill, PrEP ring, CAB PrEP and includes an embedded user-guide. In October, UNAIDS hosted a webinar that reviewed the recent updates made to the WHO consolidated guidelines as well as PrEP-it 2.0 and PROMISE hosted a satellite session at ICASA in Dec. 2021 showcasing PrEP-it 2.0. The session was entitled: Launching PrEP-it 2.0 – a multi-functional online tool for planning, monitoring, and evaluation of all forms of PrEP.

**Activity 2** (National planning and programming): The final set of PROMISE tools for the PrEP ring were completed during this period. These tools are the PrEP ring templates for the situation analysis, rollout scenarios and service delivery channel analysis; facility readiness assessment tool; considerations for health care provider training; demand creation lessons learned and design guide for the PrEP ring; and M&E considerations. All tools will be made available on PrEPWatch.org in the next reporting period. Stakeholder dialogues were conducted and completed in Zambia, South Africa and Kenya. The purpose of these dialogues was to gather information from providers and potential end-users to inform PrEP ring introduction alongside oral PrEP. The results of these dialogues were developed into briefs for Kenya and South Africa. Information from the Zambia dialogues are undergoing analysis; a brief will be developed under the MOSAIC project (a new USAID-funded project to support the rollout of new biomedical prevention products, including the PrEP ring) when that analysis is complete.

**Activity 3** (Demand Creation and Market Shaping): Work under activity 3 concluded in this period of performance. The final outputs for this activity include the following:

- The PROMISE team launched the **PrEP Ring Demand Creation Design Guide**, a step-by-step process intended to guide program teams and managers of social and behavior change programs as they design and implement an integrated demand creation strategy for the PrEP ring.
- A digital landscape analysis was completed to support the planning for the introduction of the monthly PrEP ring in sub-Saharan Africa. This resource provides an overview of existing virtual channels that can be used to increase awareness and access to the ring. This analysis identified countries where virtual channels are best placed for demand creation and distribution of the PrEP ring and related products for the specified audience(s).
• The **HIV Prevention User Journey Tool** was completed. The Journey Tool is a digital tool that provides clients with information on the available and future HIV prevention methods and is designed to support clients in their journey to select their most appropriate combination of HIV prevention methods. The journey tool is publicly available in South Africa and will be adapted across countries through MOSAIC.

• The **HIV Prevention Ambassador Training Package**, updated under PROMISE to incorporate the PrEP ring, was developed to support AGYW to play a meaningful role in the rollout of PrEP in their communities was update. This update to the package was completed and is publicly available.

• The work led by IPM to prepare for PrEP ring market introduction in Eswatini was completed during this period of performance. The results of this work will assist the Eswatini government and implementers to develop their own outreach strategies. This activity was conducted using human-centered design to ensure end users, their influencers and key stakeholders are co-creating approaches that address their core barriers/levers to uptake. The final report will be publicly available on [PrEPWatch.org](http://PrEPWatch.org).

• The Story Map activity, **Word on the Street: African Women Share Their Reproductive Health Stories**, was completed. This is an interactive, web-based tool that captures the authentic narratives of adolescent girls and young women, key influencers (male partners, grandmothers/mothers), and technical experts in “hot spot” areas of South Africa, Uganda, and Zimbabwe regarding prevalent issues of HIV, other STIs, and unintended pregnancy. By amplifying the diverse voices, needs and lived experiences of these stakeholders, “Word on the Street” serves as an advocacy tool for fostering enabling environments for female-initiated HIV prevention and family planning options, including multipurpose technologies as potential game-changers in addressing these issues.

• The PROMISE team created a series of video vignettes that amplify the voices of potential end-users of the PrEP ring and former ring trial participants to inform the introduction of the ring as an additional HIV prevention method alongside oral PrEP for women. The PROMISE team interviewed women in Zimbabwe (supported by the CHOICE Activity), Zambia, South Africa and Kenya and key topics explored included the needs of potential end-users and former ring trial participants, support and desire for choice, and perceptions of benefits of the ring as a HIV prevention option for women. The videos were edited into country specific clips as well as a summary video which included the voices across all the countries. The videos are in the process of being uploaded to PrEPWatch.

**Activity 4 (Knowledge Management):** In the previous period of performance, AVAC carried out a User Experience (UX)/User Interface (UI) consultation which sought to better understand the needs of PrEPWatch users and provided recommendations for the new structure. In this period of performance, AVAC implemented the recommendations of the report and, through a consultative process, designed the new structure of the site and developed the wireframes, which will provide the backbone for the new site. These wireframes were finalized and approved in Mar. 2022. The PrEPWatch redesign will be built out and finalized under MOSAIC.

PROMISE published a manuscript in *Current HIV/AIDS Reports*. This work, “**Introducing the dapivirine vaginal ring in sub-Saharan Africa: What can we learn from oral PrEP?**”, highlights how evidence from oral PrEP introduction and scale-up can help inform and expedite ring
introduction. In addition to the introduction to PrEP-it described above, PROMISE also hosted a satellite session entitled Meet the Ring, which provided an overview of the PrEP ring and provider/user perspectives on the dapivirine vaginal ring.

**Plans until award closure:** All PROMISE activities concluded on Mar. 31, 2022 with the exception of the delivery of the dapivirine ring demonstration rings. This work is being managed by IPM. The dapivirine ring demonstration rings will be delivered by Apr. 30, 2022. At that point, the PROMISE activity will be complete. All PROMISE subawards will be officially closed out.

**Year 7 Implementation Timeline**

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Appendix 1: Year 7 Budget and Expenditures through March 2022

See attached.