

The Power of Women's Global Health:
A Comparison of Reproductive Multipurpose
Prevention Technologies

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To women finding their power in every corner of the world...

Forward

Whenever my family goes back to visit our home village near Allahabad, UP, India, I am always inspired by all of the young women in the village. They possess endless resilience and courage, as they always stand up for themselves and their right to an education. My grandfather helped build the first village school in 2006, and in 2018, it was the first time that enrollment of girls was higher than boys. After growing up in the United States with the privilege of unlimited education, I want to help all girls in our village receive the resources to have those same opportunities. As a sophomore, I became a research assistant for a global women's health research study called DIAL 3D. It was my first true introduction to women's health research. I was so excited to find a study with the same mission and dedication to help all women. There were so many new and exciting aspects of this project, but the most incredible is the multipurpose functionality of the DIAL 3D ring—not only will it provide contraception, it also will provide HIV and STI prevention, a purpose that few forms of technology have. After working on this project throughout undergraduate career, I have realized the true power of women's global health. From education to empowerment, it is amazing to think about the potential women have when they are given control of their lives and their own protection. I look forward to sharing this research as these technologies can provide a whole new life of opportunity for women to prioritize their rights to reproductive health and take control of their decisions.

Glossary

- Birth control: refers to procedures that prevent the birth of a baby
- Contraception: specific term for any procedure used to prevent fertilization of an ovum
- DIAL 3D (**D**eveloped for **I**ncreased **A**dherence to **A**RT with **L**ong-Acting **A**pplications using **3D** printing): This name refers to the project that serves to study the development of a 3D printed multi-purpose intravaginal ring with contraceptive and HIV/STI prevention purposes.
 - In coordination with the UNC NCSU Joint Department of Biomedical Engineering, UNC School of Medicine, and UNC Gillings School of Public Health
- Estrogen: A set of hormones emitted by the ovaries that affect a women's menstrual cycle and sexual development
- Family planning: term generally used to include timing and spacing of children
- HIV (Human Immunodeficiency Virus): Virus that attacks the body's immune system, transmitted through unprotected sexual interactions, needles, through blood contract, pregnancy
- IUD (Intrauterine device): Small contraceptive devices that are inserted into the uterus to prevent pregnancy
 - Four types: Liletta, Kyleena, Mirena, and Skyla
- IVRs (Intravaginal rings): Polymeric drug delivery devices designed to provide controlled release of drugs for intravaginal administration over extended periods of time for contraception, other purposes
- Microbicide: Compounds applied inside the vagina or rectum to protect against sexually transmitted infections (STIs) including HIV
- Millenium Development Goals (MDGs): United Nations' goals that UN Member States have agreed to try to achieve by 2015 that monitored progress from 2000
- MPTs (multipurpose prevention technologies): products designed to simultaneously prevent HIV, other STIs, and/or unplanned pregnancy
 - Examples: condoms, diaphragm with added microbicide, intravaginal rings, gels, films, patches, oral pills and injectables
- STI (sexually transmitted infection): Infection transmitted through sexual contact caused by bacteria, viruses, or parasites
 - Examples: HIV, herpes, chlamydia, gonorrhea, syphilis, human papillomavirus

- Sustainable Development Goals (SDGs): United Nations' 17 integrated global goals adopted in 2015 as a universal call to action by 2030
- Unplanned pregnancy: A pregnancy that is either unintended or mistimed, such that the pregnancy occurred when no children or no more children were desired or the pregnancy occurred earlier than desired

Chapter 1: Introduction of Women’s Reproductive Health

Women’s Health and UN Development Goals

Since 2000, there has been an improved dedication to global women's health through targeted public health clinical trials, United Nations' (UN) Millennium Development Goals (MDGs), HIV/AIDS research and support, and increased funding for reproductive health initiatives (Alexander et al., 2020). The momentum from the Millennium Goals highlighted the



significance of addressing women's health and promoting gender equality throughout the world, which catalyzed new goals in the UN Sustainable Goals (SDGs) for 2015-2030 (UN Goals

Figure 1. UN Sustainable Development Goals Analysis). The UN Women’s analysis shows that women and girls are the key to achieving each of the 17 goals proposed in the SDGs (**Figure 1**). While each of these goals is important to address, Goal 5: Achieve Gender Equality and Empower All Women is a vital goal to not only provide basic human rights, but to achieve a healthy, prosperous and progressive world as the UN strives to ensure universal access to sexual and reproductive health and rights (**Figure 2**).



Figure 2. UN Sustainable Development Goal 5: Gender Equality

As one of nine children growing up in Asosa, Ethiopia, Meaza Ashenafi was told by her village that she was so smart and had so much potential they said, “Too bad you’re not a boy,” they said. Her mother was illiterate and unsupported, but she believed in a better future for her daughter, and although Maeza’s mother did not have the resources to reach her full potential, she did everything she could to help her daughters reach theirs. Today, Meaza Ashenafi is a lawyer and leader in women’s rights advocacy and was appointed President of the Federal Supreme Court of Ethiopia. Women and girls like Meaza are recognized as the key to achieving worldwide development goals as gender equality will promote universal primary education, reduce child mortality, improve maternal health, and reduce vulnerability to HIV/AIDS (Sandler).

Universal access to women’s health includes resources for family planning, information and education on contraceptive methods, and integration of reproductive health into national strategy programs (Nour, 2008). Many efficacious forms of birth control and contraception already exist, such as the pill, a patch, a shot, condoms, spermicides, implants, IUDs, and a

vaginal ring. These effective means to prevent unplanned pregnancies enable women to exercise their rights to a higher quality of life. Alongside contraceptives, there are other forms of reproductive health technologies that serve multiple purposes, such as preventing sexually transmitted infections and HIV in addition to contraception. The DIAL 3D ring is one such multi-purpose technology.

In January 2020, UNC’S Dr. Rahima Benhabbour received a grant to create a 3D printed technology to prevent HIV, sexually transmitted infections, and unintended pregnancies. The increased functionality of contemporary reproductive health technologies goes beyond basic contraception to achieve new levels of drug delivery for women at risk for HIV. When asked about her inspiration and motivation behind this project, Dr. Benhabbour said, “I’m from North Africa. I’m a woman. The thought of helping women-some that don’t have a way of protecting themselves or controlling their lives– that’s my passion. It’s a dream for me to give back.”

After about three years of working on user perception and preference, we have completed the first two phases of the project. Dr. Benhabbour’s engineering team and our DIAL 3D qualitative team have worked in collaboration to develop the design of the ring for drug delivery (Innovate Carolina, 2020). From many female participants and 20 focus group and individual interviews, we have obtained an amazing amount of data to understand how this ring can be designed best to help women feel the most comfortable. I plan to use this data to analyze how the DIAL 3D technology serves to globally progress women’s health in comparison to other multipurpose prevention technologies.

With a strong understanding of these technologies, we can address how they serve as solutions for women’s reproductive health issues globally. This chapter focuses on the basics of women’s reproductive health and its barriers, along with a background on international practices

and the importance of providing women with access to family planning and contraception, HIV and STI prevention. I then include a literature review on user acceptability and adherence with multipurpose prevention technologies, specifically intravaginal rings. Following the literature review, I dive into the specifics of my DIAL 3D research and our results within the study, then compare the findings from the DIAL 3D study to international literature findings. Finally, I conclude with a discussion of my research and future use for these technologies, specifically DIAL 3D.

Barriers to Reproductive Health

The ability for women to protect themselves and control their bodies and reproductive functions are vital to maintain good health, good careers, and successful family lives. Throughout history, women all over the world have fought for control over their reproductive rights by fighting for various fertility options, specifically surrounding unwanted pregnancies (Nour, 2008). A little over 50 years ago, birth control pills were still illegal in some states within the United States. Barriers to reproductive health wellness include sociocultural, economic, and access considerations.

Attitudes towards family planning practices, birth control, and contraception widely vary based on culture, religion, and ethnicity (Jacobstein et al., 2013). A major barrier to these methods and practices include traditional and conservative households within male-dominant cultures. Economically, only some insurance plans cover the costs of contraceptives and birth control, as costs vary depending on the method (Singh, 2010). About one-half of pregnancies in the U.S. are unintended, often forcing women to bear the brunt of financial costs, particularly for low-income groups. Similarly, the burden of cost of contraception and birth control methods also

fall on women depending on their insurance coverage (Finer and Zolna, 2011). Additionally, the costs for STI and HIV screening and treatment are another financial barrier for many women.

In most developed countries, effective birth control and family planning practices are available to women. However, women in the developing world face extreme barriers to sexual and reproductive healthcare (Nour, 2008). Because of systemic gender inequalities, women in these countries may not know where the closest women's clinic is and may have to ask for permission from husbands or parents to receive care. If all women had access to care that met the standards of the WHO, unintended pregnancies would drop by 68%, unsafe abortions would

drop by 72%, and maternal deaths would drop by 62% (Sully et al., 2010). Many villages and rural communities are too remote to reach health service centers, clinics, and hospitals as the commute can be quite expensive. The opportunity cost to take time to go to these clinics often means losing valuable time or money that would be spent working or caring for family (Jacobstein et al., 2013). If they are able to get to these clinics, there is no guarantee

that the service providers are skilled and equipped to help them. Additionally,

these health professionals often face severe underfunding and supply shortages of medical supplies and contraceptives. Thus, expanding contraceptive technologies and services to these

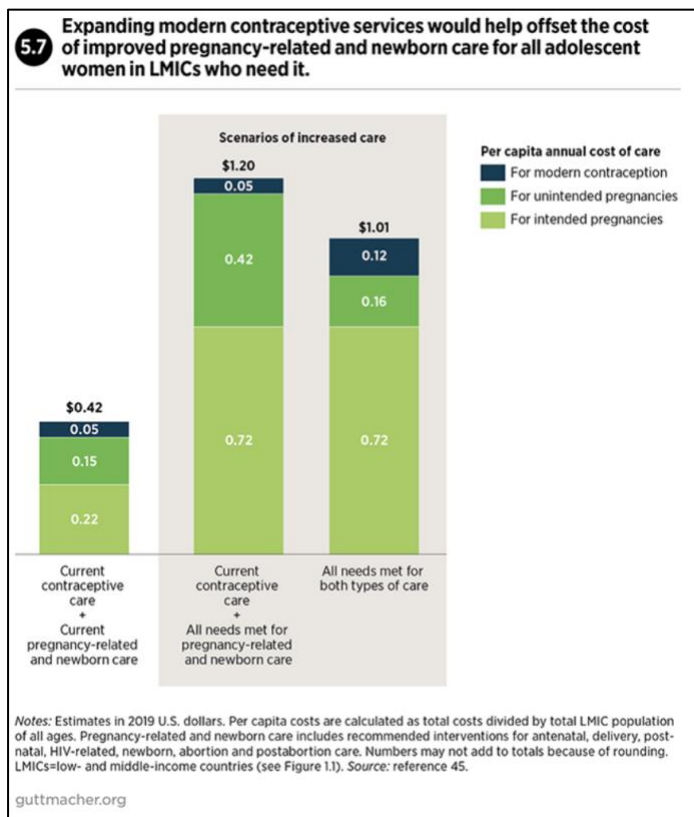


Figure 3. Gutmacher Institute on Contraceptive Services and Care (Sully et al., 2010).

areas could reduce costs and barriers to obtaining proper care as seen in **Figure 3** (Sully et al., 2010).

Family Planning and Contraception

Family planning is one of the most cost-effective ways to improve reproductive health and equity for women. As UN Millennium Development goals 3, 4, and 5 aim to do, increasing contraceptive use and increasing family planning are vital to improve overall maternal health (Jacobstein et al., 2013). Family planning gives women an opportunity to have fewer children which results in healthier mothers, infants, and children (Sonfield et al., 2014). Accessible family planning addresses needs far beyond maternal and infant mortality and morbidity, unintended pregnancy, unsafe abortion, and HIV risk (Jacobstein et al., 2013). These programs are useful in order to combat misinformation on contraceptives, as counseling tools help women feel more confident in discussing plans and future goals (Singh, 2010). Implementation can also focus on creating an environment for men to seek service and help their wives throughout their marriage. Globally, evidence suggests that improvement of family planning services and quality significantly increases the uptake, prevalence, and continuation of contraception (Sonfield et al., 2014).

In a study from the *Guttmacher Institute*, 222 million women expressed an unmet need for modern contraception, which equals about 1 in every 4 women globally (Sully et al., 2010). Consequently, 40% of the 210 million annual pregnancies worldwide are unintended (Singh, 2010). Contraception and birth control use are integral in keeping a woman safe physically and mentally. Researchers in this study found that women in the U.S. spend three years pregnant or trying to become pregnant, while they spend three decades trying to avoid pregnancy (Sonfield et al., 2014). Another 2014 multi-country analysis studied how many "sexually-experienced"

women had heard of emergency contraception, and the results ranged from less than 0.1% in Chad to 3.3% in Albania to 12% in Colombia (Palermo et al., 2014). 45 countries were considered, and in 36 of these countries, less than 3% of women had heard of or used emergency contraception.

Another major issue in the realm of contraception and women's is the occurrence of unsafe abortions (Brown et al., 2008). Contraception is the most effective way to prevent these abortions, as complications often arise yet there is rarely emergency treatment available (Palermo et al., 2014). Governments in multiple countries fail to make funding for reproductive health a priority, and there is still a stigma surrounding contraceptive use in many of these nations. Healthcare providers may impose implicit biases and barriers surrounding contraceptive services, based on a woman's age, marital status, and lack of partner support (Palermo et al., 2014).

HIV and Sexually Transmitted Infections (STI) Prevention

Along with family planning and contraception, lack of means to prevent HIV/AIDS and sexually transmitted infections (STIs) is a major issue that many women face due to a lack of protection and knowledge surrounding their reproductive health. Throughout the 1980s and 1990s, HIV spread at an alarming rate throughout the world and developing countries, like those in sub-Saharan Africa that were hit extremely hard (Simms, 2007). Over the past few decades, there have been major initiatives to increase access to HIV medications and treatments. However, as of 2010, a third of the 1.5 million women living with HIV did not have access to the antiretroviral care needed to save their lives and prevent transmission of HIV to their newborns (Singh et al., 2014). About 80% of HIV cases are transmitted sexually, and 10% are transmitted

during breastfeeding or perinatally (Simms, 2007). To treat populations at risk for HIV, countries have created prevention outreach plans through voluntary counselling, testing and screening services, education series, and increased awareness around contraception and family planning (Singh et al., 2014).

If women who wanted to avoid pregnancy used modern contraception and family planning methods, then the transmission of HIV from mothers to their newborns would be nearly eliminated with an estimated 93% reduction rate (Lester et al., 2010). STIs do not receive as much attention and action compared to HIV, but they also take an enormous toll on women's reproductive health. In developing countries, around 204 million women have one of the four curable STI's, but 82% do not receive those services (Askew and Berer, 2003) . By providing treatment for chlamydia and gonorrhoea, around 27 million women could prevent post-pelvic inflammatory disease and seven million could prevent the development of infertility. Likewise, meeting women's need for syphilis screening and treatment could reduce fetal deaths, stillbirths, and deaths among newborns (Lester et al., 2010).

Addressing these Barriers: Significance for Women

Throughout the past decade, the investment in maternal and reproductive health has been paying off as there is increased awareness and progress for women worldwide. The United Nations Millennium Development Goals 2, 3 4, 5, and 6 committed to promote gender equality and empower women, achieve universal primary education, reduce child mortality, improve maternal health, and combat HIV/AIDS by 2015. While there is still much work to be done, there is an elevated understanding that women must be given the power and ability to make their own choice to enact change and gain access to contraceptives and family planning.

By increasing access to contraceptives and family planning for women, there is potential for increased opportunity for education, reduced poverty, a higher income with paid employment, and the improvement of their children's cognitive development, behavior, and educational performance (Starbird et al., 2016). Given the above, it is vital that women gain access to new technologies such as DIAL 3D and other MPTs that could alter the trajectory of their lives through greater control over reproduction, disease prevention, and improvements in economic conditions.

Conversely, I also want to address that medical technologies may also negatively impact populations, especially those with particular social and cultural limitations. Technological determinism has changed the way we live, and it is important to note that technology can be misused and overly relied on, leaving a negative impact on the world, especially for populations with social and cultural vulnerabilities. An important limitation of technology is its reliance on human behavior before turning to technology, since technology will never make an impact without human adherence and acceptance.

Conclusion

In this modern day, the power lies in preventative technologies that alter the trajectories for women who suffer from a lack of control with their own reproductive rights. Creating technologies that address all of these issues at once is a robust way to give women control over their decisions that can empower them for the rest of their lives. In the next chapter, I dive into the historical progression of women's health technologies and the development of various contraceptives internationally beginning with the women's movements that started in the 1910s and spread throughout the world.

Chapter 2: History of Contraceptive Technologies

This section provides a history of contraceptive technology to provide a deeper understanding of why multipurpose prevention technologies (MPTs) were created. By explaining the main functions of MPTs and intravaginal rings (IVRs), I discuss the need for these technologies and the progress of their development-- the science behind them and the problems their producers are hoping to solve. To conclude this chapter, I will discuss their current uses and the modern approach, especially relative to the development of the DIAL 3D IVR.

History of Women's Reproductive Health Technologies

Modern methods of contraceptives, such as silk-based UDIs, were introduced in the 1920s when Margaret Sanger founded the first American birth control clinic in 1916, which eventually led to the invention of the birth control pill (Planned Parenthood, 2015). Sanger faced many obstacles and was arrested for violating the Comstock Act and state Comstock laws which outlawed the distribution of information about safe sex and use of contraceptives (Wardell, 1980). Sanger's arrest sparked birth control activism with numerous donors, who supported her founding of the first birth control league in America. Once she invented the pill with several collaborators in the 1950s, scientists discovered Mexican communities had used plants to prevent pregnancy for generations, to create the proper hormonal balances (Asbell, 1995). To create a functional pill to prevent ovulation, the team used progestin, a form of progesterone and hormone involved in the menstrual cycle and pregnancy (Planned Parenthood, 2015). Originally used by Mexican women to prevent pregnancy for many generations, the wild yam *Cabeza de negro* produced a plant-based progesterone that synthetically formed progestin, which was extracted to formulate the first birth control pill (Grimes, 2000). By 1957, the FDA approved the

pill to regulate menstruation then three years later, the FDA approved the sale of Enovid as an oral contraceptive (Asbell, 1995).

Globally, various birth control and reproductive health movements were gaining traction, as women became more educated about their bodies and reproductive freedoms. In Britain, in 1918, Marie Stopes established the first permanent birth control clinic and published a book, *Married Love*, with the help of Sanger (Grimes, 2000). The book was a success and gave Stopes and her husband a platform to open the Mothers' Clinic in Holloway, North London. Shortly after, they founded the *Society for Constructive Birth Control and Racial Progress*, making contraception and education more acceptable (Rose, 1992).

Movements were not only occurring in more developed areas of the world. In India, mathematics professor Raghunath Dhondo Karve opened India's first Birth Control Clinic in 1921 in Mumbai and published a monthly magazine titled *Samaj Swasthya* meaning "social health (Grimes, 2000)." In France, Italy, and Ireland, dissemination of birth-control literature was considered illegal until the loosening of restrictions, which legalized access to birth control information (Grimes, 2000). The Society Union also made birth control readily available as USSR commissar for public welfare, Alexandra Kollontai, promoted birth control education for adults to improve social and gender equalities between men and women (Barringer, 1991). In a study on Romania's governmental restriction from Decree 770 to promote higher birth rates, the surge of births was equivalent to the number of illegal abortions. Decree 770 restricted abortion and contraception for women under 40 with fewer than four children.

As the rates of illegal abortions continued to increase, governments were actively working to change policies to authorize contraception. Initially in 1957, the FDA approved the pill to only treat severely painful periods, but then many women began to report menstruation

problems and requested a prescription for the pill so by 1960, the FDA approved it for birth control purposes as well. In 1965, Planned Parenthood of Connecticut won the *Griswold vs. Connecticut* U.S. Supreme Court Case that allowed the use of contraception by married couples in outlawed states. In 1972, *Eisenstadt v. Baird* expanded the right to possess and use contraceptives for unmarried couples (Grimes, 2000). This was a major shift in the trajectory of reproductive rights, continuing momentum for the invention of new contraceptive products.

By 1967, about 13 million women worldwide were using the pill as multiple brands entered the market (Planned Parenthood, 2015). In 1984, the WHO approved the first birth control implant, the Norplant, then the FDA approved it in the U.S. in 1991. Around the same time, the Depo-Provera shot became available then was approved by the FDA in 1992. Around 1998, the first emergency contraception, Preven, was approved and widely approved, then a year later, Plan B was approved (Planned Parenthood, 2015).

In the 2000s, the contraceptive industry shifted towards more innovative, effective methods which gave women more options to choose what methods worked best with their bodies and reproductive systems (Planned Parenthood, 2015). The Mirena became available as the first hormonal IUD, then the NuvaRing was approved in 2001. The NuvaRing is a lightweight, flexible, plastic ring that is inserted into a woman's vagina once a month for three weeks at a time. It was the basis for which the DIAL 3D ring was created as an intravaginal ring; however, the NuvaRing solely provides contraceptive, while the DIAL 3D ring will also provide HIV and STI prevention. From 2002 to 2010, the first birth control patch, Ortho Evra, two birth control implants, Implanon which was replaced by Nexplanon, and a new type of emergency contraceptive, Ella, were approved for use.

Multipurpose Prevention Technologies (MPTs)

As of September 2021, 218 million women in lower- and middle-income countries reported an unmet need for contraception as roughly 817 women die each day globally from preventable pregnancy or child-birth causes (Boonstra, 2015). In regions of the world where women are at high risk of HIV, especially young women and girls in Sub-Saharan Africa, up to 71% of all new infections occur in adolescents (Hosek et al, 2016). With rates of STIs increasing and compounding the risk of HIV simultaneously, there is a need for new technologies to combine protection against unintended pregnancy. Multi-purpose technologies that simultaneously combine all three functions of contraception and HIV/STI prevention can, "improve uptake of and adherence to offer streamlined product delivery and eliminate the need for multiple, separate clinic visits to address family planning and other reproductive health needs (Abdool et al, 2014)."

Multipurpose prevention technologies (MPTs) are a new biomedical invention that will allow women to address many reproductive health issues within one product. An MPT is classified as a product that protects against at least two of the following risks: HIV, other STIs,

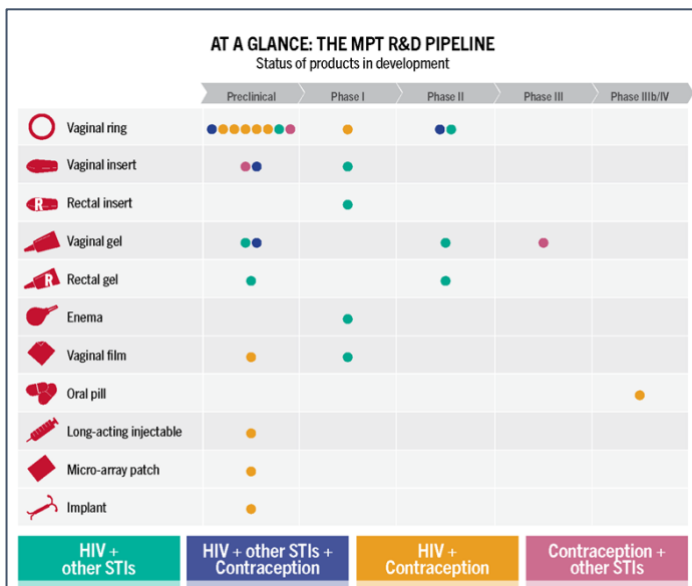


Figure 4. AVAC MPT Research & Development Pipeline

and unintended pregnancy (IMPT, 2021). These technologies include vaccines, contraceptives, microbicides, or devices that can be inserted such as diaphragms and intravaginal rings seen in **Figure 4** (WHO, 2017). While condoms are the only MPT currently available, there is a growing industry of new MPTs designed

to sustain the reduced risk of unintended pregnancy, STIs/HIVs, maternal mortality, and cost associated with treatment (IMPT, 2021).

The majority of "MPT candidates" are still in pre-clinical stages of development by academic labs and small biotechnology companies, like the DIAL 3D ring at UNC. There are many challenges with new drugs and technology options entering the "prevention pipeline," as years of intense testing and clinical trials are required to ensure approval and safety (Young Holt et al, 2021). However, promoting the development of a variety of products can advance the most promising products. The range of products currently in testing, from infused vaginal rings to injections, will help women choose the product that is most comfortable and fitting for their lifestyles (Young Holt et al, 2021). Women should be guaranteed a diverse mix of choices since there is not one type or design that fits all women as an array of products can maximize the prevention potential (IMPT, 2021). Different products will also be available worldwide. In fact, Dr. Benhabbour plans for DIAL 3D to impact women globally, while other companies are looking to only distribute in one or two countries. Along with women's MPTs, there are new studies looking at designs for men's MPTs that could protect men from risk of sexual diseases (IMPT, 2021).

Intravaginal Rings and DIAL 3D

Intravaginal rings (IVRs) are a promising approach to MPTs as they combine two to three functions of HIV prevention, STI prevention, or unintended pregnancy. IVRs are similar to NuvaRings but have the added component of infection prevention functionality through microbicide delivery. The NuvaRing is a flexible, plastic ring that is inserted into the vagina and releases a low dose of a progestin and estrogen over a period of three weeks to suppress ovulation and prevent pregnancy (NHS UK, 2021). If used correctly, the NuvaRing is more than

99% effective, and one ring provides contraception for a month. The United Kingdom's NHS suggests the use of condoms alongside the NuvaRing since it does not protect against STIs (NHS UK, 2021).

Thus, the potential for IVRs to have a high and effective success rate is quite promising. To prevent infection, intravaginal rings utilize microbicides, which are pharmacological agents and chemical substances that kill or destroy certain microorganisms that cause human infection, specifically STIs. While all IVRs except for the NuvaRing are still under review, some clinical trials have started to study the effectiveness of the microbicides in these rings. A large-scale clinical trial in uninfected women in South Africa, CAPRISA 004 Trial, showed a 44% reduction in HIV acquisition over a 1.2-year period (Baum et al, 2021). Along with microbicides, there are many components to creating an effective intravaginal ring, from the ring design and size to the execution of drug delivery. The DIAL 3D intravaginal ring combines all three functions and is currently under development for design and drug delivery.

Various biotechnology and engineering groups worldwide are creating their own process to engineer intravaginal rings. For DIAL 3D, we use 3D-printing to make our products, hence the name DIAL 3D! 3D printing allows us to control the flexibility and compression of the ring, giving us freedom to make changes without affecting the ring dimensions or material. The design and 3D printing also allow for more efficient drug release, preventing the drug from eventually getting stuck in the middle of the ring. The thin-walled design more efficiently diffuses drugs out of the ring because of the decreased thickness of the material compared to other cylindrical rings.

The design also fine-tunes drug release and its duration, the amount released per day, and enhance efficacy outcomes to ensure it protects women soon after insertion and after ring removal. The DIAL 3D ring aims to use two contraceptives, etonogestrel (ENG) and ethinyl estradiol (EE). ENG is a progestin used in FDA-approved contraceptive implants such as the Nexplanon and Implanon. EE is an estrogen widely used in birth control. The combination of both drugs is what is used in the NuvaRing. Alongside ENG and EE, the IVR will release an antiretroviral drug used in Pre-Exposure Prophylaxis (PREP) to prevent HIV.

The DIAL 3D ring is the first ring ever that is integrating color into designs. The color change on a microbicide is a big step in product development and has played a major role in behavioral studies. Integrating color into the design stage has been meaningful in our data analysis, as the material of the ring must be colored and cannot be clear, unlike the NuvaRing. The grey color has the least amount of dye compared to pink, purple, green, red, and white. I address participant color preference in chapter 4 of my thesis. The IVR will undergo rigorous testing and clinical trials to ensure there are no harmful side effects.

Progress of Development and Current Uses

About 10 years ago, the field of Multipurpose Prevention Technology was created to conceptualize and build upon the invention of microbicides for HIV prevention. Protection and prevention became a reality for many women with significant progress made in the field of technology and innovation. Since condoms are the only available method for sexual and reproductive health risks, they are not a sustainable with major barriers: ethnic and religious values, lack of access, misinformation and lack of knowledge about use, partner and relationship related lack of dialogue, financial and socio-economic vulnerability, alcohol consumption, gender inequalities, and personal aversions from prior use (Sarkar, 2008).

Condoms are a vital and necessary product for their multi-purpose functionality, but they do not provide a long-term guarantee of systemic protection or contraception (IMPT, 2021). They are not the optimal option for many women, as use can be difficult depending on partner preferences and access to education on use. MPTs provide a new option that ensure women have comprehensive choices to keep their bodies as protected as possible. In an article in *The New England Journal of Medicine*, Dr. Deborah Anderson discusses the need for multipurpose prevention technologies and writes that "they have the power to revolutionize the world of women's health" (Anderson, 2019).

MPTs were founded on the idea that a "suite of multipurpose prevention products would better meet a woman's needs throughout her life course (IMPT, 2021)." Incurable viral infections such as HIV and HPV have long-term effects of serious illness and suppressed immune systems which increase susceptibility to other diseases. MPTs designed to protect against these infections can address different needs for different countries. Creating rings that offer a single-step, cost-effective process, and are accessible to people who need them the most could make a huge impact on the rates of HIV, STI, and unintended pregnancies worldwide.

Conclusion

In the next chapter I present the results from a literature review I conducted which analyzes international studies on intravaginal ring acceptability. Worldwide, companies are working on the development of dynamic IVRs to meet women's needs in terms of contraception and HIV/STI prevention. In order to assess how DIAL 3D compares to international IVR studies, I must understand the progress of these studies and their findings in regards to user adherence and acceptability.

Chapter 3: Literature Review on effectiveness of Intravaginal Rings based on Acceptability Studies

Introduction

This chapter serves as a formal literature review to investigate how effective intravaginal rings (IVR) are based on the few studies that have been conducted. I synthesize the evidence on whether or not the technology has been successful for women's reproductive health in terms of efficacy, acceptability, and adherence. The goal of this review is to understand how DIAL 3D compares to existing ring technologies, so it is important to first look at how well the currently available IVRs worked for women worldwide based on comfort levels and initial impressions. This review will determine what is already known about how well IVRs work, along with the most salient concerns, difficulties, considerations, and thoughts of women worldwide. The studies represent a diverse group of participants from ages 15-50+, including women who are at high-risk for HIV, urban and affluent women seeking new forms of contraception, women who have used the NuvaRing, female sex workers, and male partners of female participants.

To identify these studies, I conducted the literature review with search terms including 'MPT acceptability,' 'IVR acceptability,' 'IVR studies,' 'IVR user perception.' I aimed to have a study from every region of the world, and was able to find some very dynamic and niche literature surrounding intravaginal rings in Brazil, the Dominican Republic, Kenya and Sub-Saharan African countries, India, and select regions of Australia, Europe, and North America.

Global Acceptance and Attitudes

The IVR has been a controversial topic for some women who are concerned about their partners' attitudes towards the ring, afraid that their partners will turn towards violence or anger if they disapprove (Griffin et al, 2019). Thus, it is important to gather data on how women truly

feel about the rings without any influence of what their partners may accept or approve. The IVR is meant to create a more sustainable and reliable form of contraception for women to utilize whether for their own empowerment and enjoyment, or for family planning purposes, so it is imperative to have their honest impressions. I will first provide global context on acceptability rates, then synthesize the findings on women's initial thoughts on IVRs. I will then present the significant concerns and difficulties that have been identified in studies that may prevent women from using the ring. Finally, I discuss future considerations and successful acceptability rates for IVRs.

In terms of global acceptability rates, studies from Europe and North America have indicated high levels of user and partner approval for the NuvaRing, which is seen to reflect the fact that acceptability has increased with duration of use and ring experience (Van der Straten et al., 2012). The Americas and Australia were associated with "less favorable comfort during sex and vaginal symptoms, but less frequent expulsions," so there is still potential to investigate acceptability levels in these areas of the world (Griffin et al, 2019). Studies in Asia have reported less favorable ease of use and more frequent vaginal symptoms, but this chapter will discuss a qualitative study exploring IVR acceptability in India that showcases increased interest in ring usage (Das et al., 2015). Multi-region studies and ring acceptability across regions and cultures are continuing to be assessed based on normative behaviors surrounding vaginal practices (Griffin et al, 2019).

Initial thoughts on IVRs

In 2019, a systematic review was conducted on vaginal ring acceptability and related user preference among women in low- and middle-income countries (Griffin et al, 2019). This study reported that when the trial initially began and users were first exposed to IVRs, the rates of ring

acceptability were quite low. Women were apprehensive to use an IVR and had many concerns about the logistics of insertion and removal, losing the ring in the body, and partner acceptability (Griffin et al, 2019). Over time, as women became more comfortable with the ring and multi-purpose technology functions, the study results indicated that 71-98% of the randomized-control trials and 62-100% of observational studies showed high vaginal ring acceptability rates among women (Griffin et al, 2019).

Women naturally express different preferences for the functions of contraceptive technology— some women prefer accessible, long-acting, and partner-approved methods that prevent both HIV and pregnancy while other women desire a method that can be used without partner approval that has no impact on sexual encounters and minimal negative side effects (Griffin et al, 2019).

Table 1. Sekhon acceptability model constructs and systematic review operationalization.

Construct	Operationalization	Corresponding outcomes
Affective attitude	Feelings about the intervention	Acceptability, liking or recommending; finding physical attributes acceptable
Burden	Perceived effort required to engage in intervention	Ease of use; ease of insertion and removal; cognitive and emotional burden of use
Ethicality	Intervention fit with an individual's value system; normative fit	Disclosure of use; use without partner/family knowledge; partner/family approval
Intervention coherence	Understanding of the intervention	We did not include studies reporting intervention coherence
Opportunity costs	Extent to which benefits, profits, or values must be given up engaging in the intervention	Impacts on sexual intercourse; vaginal discharge/irritation; expulsions; discomfort; and foreign body sensation
Perceived effectiveness	Extent to which the intervention is perceived to achieve its purpose	Perceived ability to prevent pregnancy/infectious disease/other VR outcomes; reduced risk of certain cancers
Self-efficacy	Confidence to perform the behaviors required for the intervention	Ability to support use

Figure 5. Participant Interest according to Acceptability Model (Griffin et al., 2019, pp.3).

This review utilized an acceptability model construct and systematic review operationalization to ultimately describe corresponding outcomes. Since acceptability is a multi-faceted concept, factors such as attitudes, tolerances, preferences, interests, and background play a role in understanding how women decide whether or not they are willing to try an IVR. **Figure**

5 above shows how participant interest and acceptability was evaluated according to the acceptability model.

It is important to note, not all IVR acceptability studies were conducted with the same methodology, since each study targeted a different way of identifying the success of the ring. Additionally, researchers designed their studies based on a region's societal and cultural implications as seen in the following cases in Africa and Latin America.

Africa

In a study comparing intermittent and continuous users of NuvaRing in Kigali, Rwanda, the results from early in the trial when women were first introduced to the ring showcased <1% of women would actually recommend the IVR to other women (Kesterlyn et al, 2018). This low percentage indicated reluctance to use the ring with low initial acceptability rates, which reduced over time once the trial allowed for physical ring usage, and women felt much more comfortable handling the ring, describing insertion and removal as "easy." The study was conducted from June 2013 to March 2014. By the end of the study, up to 98% of women reported that they would recommend the IVR since the majority said they could not feel the ring during daily use and appreciated the minimal side effects (Kesterlyn et al, 2018). The increase in acceptability indicated a promising solution that addresses a diverse number of preferences for women's contraceptive methods.

A 2008 study in Nairobi, Kenya assessed the potential acceptability of IVRs as an HIV prevention method for at risk women and men, mostly female sex workers (FSWs) and men who "frequent FSWS", in urban slum communities (Smith et al., 2008). This study was exceptionally interesting because of the role of male participants, who had an overall very positive impression of IVRs and were open to use. Within the "Impressions of the Intravaginal ring" section of the

paper, the authors provided direct quotes from female participants who voiced thoughts about the ring's functionality and physical features. Some women said the ring was too large in thickness and circumference, some liked the size and did not think it would be difficult to insert, while others were disoriented by how hard the texture felt (Smith et al., 2008). There were a few key impressions that will guide future considerations for the ring:

R1: I feel the doctor should insert it for me. I may insert it badly and it may bring problems to me. (Kenya Study Women's FG2, pg. 1030)

R2: If we are educated, we can insert it. Because if we can insert the female condom, even this one, if educated, we could insert it. (Kenya Study Women's FG3, pg. 1030)

R3: One year is good because once you insert it, you forget about it for a long time knowing that you are safe. You rest your head from worrying about HIV. (Kenya Study Women's FG3, pg. 1030)

As seen from these direct quotes, some participants preferred trained professionals help insert the ring for the first time, and other women voiced that with proper instruction, they felt confident and comfortable enough to insert the ring themselves. Many women also found that the ring's long-lasting formulation was especially appealing because their working conditions as female sex workers are often not conducive to the preparation and planning involved in successfully using a topical microbicide for HIV prevention.

In 2012, Ariane Van der Straten and other researchers conducted one of the first IVR studies in Africa to analyze the safety, acceptability, and use of a placebo ring for microbicide

delivery (Van der Straten et al., 2012). A study examining HIV prevention in ring use for 12 weeks in Tanzania and South Africa both qualitatively and quantitatively. When women in this study were initially introduced to the ring and asked about baseline interest, 69% said they were "very keen" to use the vaginal ring, 25% "a little keen", and 6% not "keen" at all (Van der Straten et al., 2012). Another descriptive study of young women in South Africa reported that 44% would "hypothetically try the VR [vaginal ring] as an HIV prevention product" (Routes2Results, 2017).

The authors of this study attribute the high rate of willingness to explore and try an IVR to the current state of women's reproductive health in Africa, as women continue to be disproportionately affected by HIV. The strong search for novel, simple, acceptable female-initiated methods gives the ring an advantage over applicator and gel approaches for HIV prevention. This advantage is attributed to initial pharmacokinetic studies and safety reviews that have indicated which IVRs are safe and sustainable delivery options for antiretroviral drugs to the body, especially with a proper introduction to the technology (Van der Straten et al., 2012).

Latin America

The cultural implications of finding a promising contraceptive product for women in Africa is similar to the need in Latin America. However, there are other cultural barriers that are considered in an older study on field acceptability of the CVR [contraceptive vaginal ring] in rural, small town and urban slum clinics in Brazil and in the Dominican Republic (Faundes et al., 1981). This study offered insight into initial thoughts surrounding the ring as women in this study were hesitant to participate due to Latin American cultural stigmas surrounding women using drugs or other products through or around the genital area. Thus, there was an overall

negative feeling surrounding this study when family planning programs administrators were asked to consult for the research team.

The study describes the CVR as a "method [that] requires the woman to manipulate her genitals, and to carry a foreign body in her vagina for three weeks each month (Hardy et al., 1983)." With this language, the researchers did not know to what extent female participants would accept a role in the study. The research team sought to utilize a comparative design that also tested acceptability of contraceptive pills and ensured participants that all ring testing would be offered in health clinics with professional medical personnel available to help in hopes that this would ease hesitancy surrounding cultural barriers and discomfort. Faundes and her colleagues attribute the success in acceptability rates of the ring study to the "advanced state of development" that progressed conversations surrounding women's reproductive health which allowed for their evaluation of acceptance through "tangible methods rather than hypothetical" (Faundes et al., 1981). The results of the study indicate that with proper clinic personnel and education for users, women in Brazil and the Dominican Republic would use a contraceptive ring similar to DIAL 3D.

Ring Considerations and Concerns

Physical Ring Characteristics

The goal of an IVR is to provide a more diverse option of contraception for women. Data on ring acceptability is critical for new technologies to understand user needs, especially in lower income areas of the world. Each of the studies included in this literature review approached the physical characteristics of the ring in contrasting ways. Some studies targeted user perception heavily and other studies focused more on how comfortable women would feel using it.

However, all of these studies prioritized acceptability whether or not they were analyzing the same factors that make a woman want to use an IVR as her primary form of contraception.

Physically, IVRs are engineered and developed in different sizes, shapes, texture, design, color, and thickness.

One of the major production considerations of the DIAL 3D ring at UNC Chapel Hill is the use of color. A qualitative research study exploring IVR acceptability for contraception and STI protection in Delhi, India in lower-middle-class or slum areas is one of the few studies that inquired about color (Das et al., 2015). Across all focus groups, women were asked about ring colors and some participants inquired about white, purple, light brown, skin color, and transparent colored rings. Results indicated that not all women had a color preference as long as the ring was effective. Since the product would never be seen, transparent rings and white rings were most commonly preferred, especially with their association to "cleanliness" (Das et al., 2015). When informed about the color of the ring changing during menses most participants understood this possibility, but suggested proper instruction and warning on the packaging.

The systematic review on IVR acceptability and related preferences among women in low-and middle-income countries showcased an 88.3% baseline increase to 94.7% final follow up in terms of user acceptability for colored rings in observational studies (Griffin et al., 2019). By understanding the increase in user adherence based on color, we can use the results of this study to inform the DIAL 3D ring developers what features are acceptable for women to want to use the ring.

The size of the ring often has to do with its overall width and thickness, both of which play a major part in easy insertion and removal processes. The ring is pressed between the

pointer finger and thumb to push it into more of a linear shape and is then inserted. In the field study in Brazil and the Dominican Republic, participants were concerned with problems of "insertion, removal and expulsion of the ring" (Hardy et al., 1983). Insertion was not primarily difficult, but a few users had trouble related to the size as it was "too wide" and the rigidity which made the ring "difficult to fold."



A 2018 study in Kigali, Rwanda also evaluates size as an important feature, as some women noted that they were concerned with the size since they had no experience with IVR insertion (Kestelyn et al., 2018). While many studies' participants were concerned about the ring being too large, a few participants in Kigali were concerned about the ring being too small to fit into a woman's body. The systematic review on IVR acceptability and related preferences reported that 45.7% of participants initially stated that the ring was too big, but after physically using the ring, only 18.1% felt as though the ring was still too big to use (Griffin et al., 2019). The qualitative study in Delhi, India also studied size as most participants preferred thinner and smaller rings since the women felt like it would "fit better (Das et al., 2015)." The focus groups were encouraged to compare the size of NuvaRings to the diameter of the new prototypes, indicating concern about how size would affect where the ring would stay in the body and whether it would "move up and cause harm." By understanding the overall participant perspective on the size of rings, we can better inform the DIAL 3D ring developers what sizing features are necessary for women to accept and want to use the ring.

Partner Influence

This section will review participants' concerns and perspectives surrounding their partners' involvement with their birth control decision making process. Select women viewed partner involvement in IVR use as positive, wanting to share their learning experience with their partners in order to gain their support. Other women were nervous their partners would resort to violence or abuse if they did not support the use of contraceptives or HIV preventative technologies. Another group of participants just wanted to hide the decision from their partners and sought to independently explore what birth control method was best for them and their bodies. In the systematic review on IVR acceptability and related preferences, one randomized control trial showed that worries were significantly higher among women who had experienced a partner-related social harm, "defined by nonmedical adverse consequences from VR-use or trial participation more generally" (Griffin et al, 2019).

An HIV prevention ring study in Tanzania and South Africa study reported that 59% of study participants would use the vaginal ring (VR) without telling their partner and 62.6% of women reported that it was possible to use the VR without partner knowledge. Another study evaluated in the systematic review found that most women, roughly 80%, preferred partner approval of the VR; additionally, another study found that women were less likely to try the VR if they thought their partner might not like the method (Griffin et al, 2019). Overall, between 35-59% of women reported that it was important to be able to use a product without partner knowledge. The acceptability study in Africa focused on HIV prevention in Vaginal Rings found that 78% of women had disclosed study participation to their partner prior to ring use since 86% said their partner's approval of the ring was important. However, 59% thought it was important that the ring could be used without the partner's knowledge. Questions these studies sought to answer

surrounding partner support and influence included how important it is to participants that their main sexual partner accepts the vaginal ring and agrees that they can use it, and whether or not they believe their main sexual partner might become angry with them if they used the vaginal ring without telling him (Van der Straten et al., 2012). Results to these questions are as shown in

Figure 6.

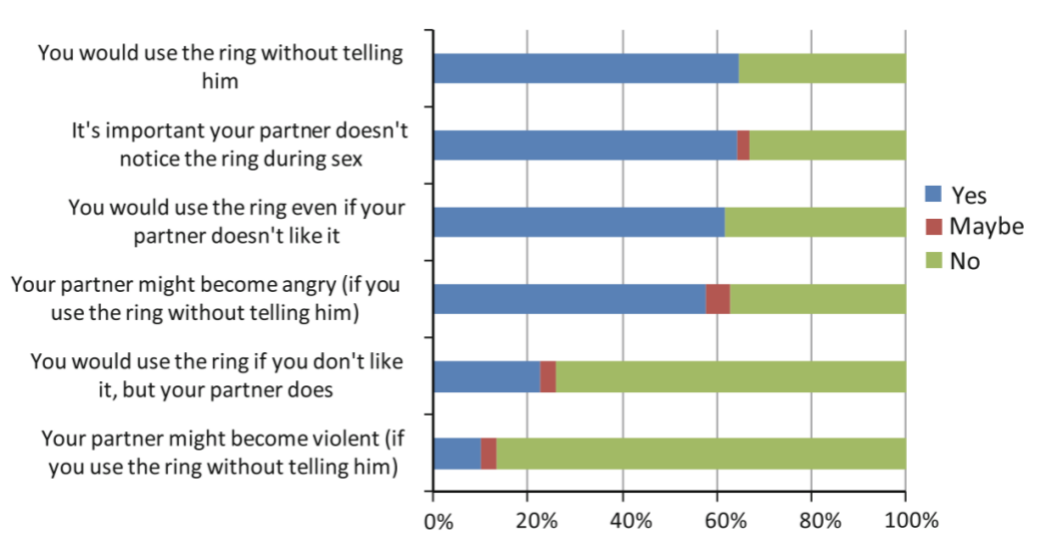


Figure 6. Women's reported Influence of partner on ring use at 12-week visit N= 151 (Van der Straten et al, 2012, p. 1783).

A similar study in Zimbabwe looked specifically at the importance of male partner involvement for women's acceptability and adherence in female-initiated HIV prevention methods. Results supported the need for more sophisticated measurements of how couples interact to make decisions to determine the extent to which women involved their partners in order for successful uptake (Montgomery, 2011). Another study exploring VR acceptability in India indicated that majority of participants felt that their husband or partner's consent was necessary because he was "the head of the household and controlled the finances (Das et al., 2015). While male partner consent was perceived to be very important, the participants shared that there could be situations where a woman might want to use the ring without confiding in her

husband, especially when there are differences of opinion over family planning. Understanding these concerns for women can help engineers and development companies create rings that women can feel comfortable about using privately and independently, taking into consideration financial equity.

Significant Concerns

Throughout the numerous studies reviewed in this chapter, there have been prominent concerns discussed regardless of where the study was conducted and participant demographics. The clearest concern was the detriment to women's health if the drug delivery process failed and ended up harming the body, alongside negative side effects and the body's rejection of the ring. If the drug delivery process fails, then there is no protection against pregnancy and no HIV or STI prevention, which would be a detrimental liability and could ruin the trajectory of a woman's life.

Additionally, many women were concerned about the ring getting lost in the body, coming out during sexual encounters, and having trouble with insertion, removal, and expulsion (Van der Straten et al., 2012; Faundes et al., 1981). Other female participants reported concerns about cleanliness based on odor, menstrual flow, discharge, and vaginal hygiene due to the long duration of the ring kept within a body cavity. This trend was especially clear in lower-income areas and for female sex workers (Faundes et al., 1981; Smith et al., 2008; Van der Straten et al., 2012; Das et al., 2015). Another significant concern revolves around worries that they did not or might not receive sufficient education and instruction on how to insert, remove, clean, and care for the ring expulsion, and daily use (Van der Straten et al., 2012; Faundes et al., 1981). These concerns will be addressed in chapters 4, 5, and 6 as I will discuss how women's opinions would

affect their use adherence. These findings indicate that the access to this technology must be paired with educational funding as women would not feel comfortable using the product without simultaneous instructional programming and support.

Future Considerations

With these concerns, participants provided suggestions and asked questions to help developers understand user needs based on acceptability outcomes. Participants emphasized the need for clinical assistance to inform women how to properly use the ring. They also asked for counseling and more educational resources to understand the functionality of the ring in order to take proper care and precautions while using it (Van der Straten et al., 2012). A 2012 trial in Sub-Saharan Africa studying vaginal ring adherence for expulsion, removal, and perfect use found that their results suggest the "need for enhanced counseling and instruction about management of menses and IVR use in future studies" (Montgomery et al., 2012).

The research suggests that counselors should build on the premise that women are familiar with inserting and removing vaginal products such as tampons. Alongside this consideration, this study signals a need to compare microbicide IVRs to tampons in future research, as this comparison can help explore whether "IVR efficacy is compromised by intravaginal product use (Montgomery et al., 2012)." Similarly, the findings from Van Der Straten's acceptability study for HIV prevention in African women indicate that concerns can be overcome through education, counseling at clinics, and direct experience of ring usage (Van der Straten et al., 2012).

Conclusion

While there is still a long way to go to fully understand how intravaginal rings and multi-purpose prevention technologies can help women find a sustainable, comfortable, and effective form of contraception, these studies have embarked on a promising journey to fulfill the full potential to help women's reproductive health worldwide. Researchers and women's health experts have started to understand the cultural implications and regional backgrounds that affect women's perception of these rings, and with these initial thoughts, there is a strong starting ground that can guide future research. As we have learned, contraceptive technology is not a "one-size-fits-all" model, and women have preferences that may change depending on their current needs. If we can develop an IVR that fits the majority of needs, there is a promising chance of helping women combat HIV, STI, and unwanted pregnancy risks. This literature review provided insight on how various women around the world have reacted to IVRs and what their initial thoughts and concerns were. After working on IVR research for the past 3 years, in the next sections I will compare our DIAL 3D ring developments to the studies discussed in this chapter.

Chapter 4: DIAL 3D Study

Introduction

Chapter 4 will focus on the data analysis portion of my research question to determine how DIAL 3D compares to other multipurpose technologies, specifically intravaginal rings, in order to globally progress women's health. As mentioned before, the intravaginal ring we are developing here at UNC aims to create a diverse and flexible option of birth control for women worldwide by 3D printing a ring that functions to prevent HIV and STIs and serves as contraception. Our engineering and qualitative team worked together to develop a ring that caters to women's needs and wants in terms of feel, look, design, color, and comfort. Our qualitative team conducted focus groups to obtain data on women's preferences, then presented this data to the engineering team to help them narrow down the selection on what the final prototype should look like. This chapter will explore the basics of our study design by first discussing the DIAL 3D study methodologies and results. The second half of this chapter will then compare these outcomes from DIAL 3D to previously existing intravaginal rings and MPTs that were explored in chapter 3's literature review.

Recruitment and Study Overview

In January of 2020, our research team began phase 1 of the qualitative portion of the DIAL 3D intravaginal ring project. While the engineering team was working on 3D printing techniques to develop rings in various designs, colors, and textures, and assess how changes in design affected rings' pharmacokinetic properties, we were facilitating focus groups with a diverse population of women in the area from the UNC Population Center database. Focus groups covered a wide range of demographics as seen in **Table 1**. Other screening information included recent sexual history, pregnancy status, history of contraceptives, history of vaginal

product use, self-reported HIV status, self-reported health status, and allergies or trauma that may interfere with prototype manipulation.

Demographic	Details
Age	18-25 group or 26-45 group
Race and Latina/Hispanic Ethnicity	White/Caucasian, Black and/or Hispanic/ Latinx
Location	Urban or rural
NuvaRing Use	Used before or never used

Table 1. Description of participant demographics for DIAL 3D focus groups and IDIs.

With a total of 37 participants, we held about 10 virtual focus groups with 3-6 women every few weeks throughout late 2020 and early 2021. Once participants logged on to Zoom, we put them in individual break rooms to complete the informed consent form with one member of our research team to provide an overview of the research project and its purposes to each participant. We then informed them about the discussion of the focus group, and remind them that they should feel free to skip any question or step out at any time. After they signed and consented, we asked that they fill out another questionnaire with more information about their reproductive history and experiences for our research team to have more context. Once again, we reminded participants to feel free to skip any questions that they did not want to answer. Once the ICF and questionnaire process were completed, we brought all participants back into the main zoom room. Many participants preferred an alias or only used their first names so we could protect all privacy and comfort during the focus groups.

Qualitative Focus Group Overview

Using a focus group guide to guide the discussions, a trained moderator and co-moderator facilitated the focus group discussions. Two notetakers took notes at each group and all focus groups were audio recorded. Based on the guide, the focus groups followed a similar pattern of discussion throughout phase 1 of this project. First, we introduced our team members and then did an icebreaker to help participants feel more comfortable with us and one another. Then, we jumped right into asking each participant about the previous vaginal product history, getting a feel for their likes and dislikes from products they have used in the past and thus, helping inform our research to understand why certain aspects of contraceptives and other feminine products would increase women's willingness to use them. During this part, women often discussed three categories: menstrual products, contraceptives, and other comfort products. When discussing menstrual products, participants shared likes or dislikes with pads, tampons, diva cups including applicators or brand influences. When discussing contraceptives, participants explained their history with a wide range of products from condoms to IUDs, birth control pills, an implant, tubal ligation, birth control patch, birth control injections, plan B and the NuvaRing. And lastly, comfort products they discussed included products such as lubricants and cleansing washes or wipes like Summer's Eve.



Figure 7. DIAL 3D Pink Ring Prototype

Color

Next, participants discussed the color of the ring, after we showed them slides of rings one at a time and heard their feedback on what they thought of that color as shown in the image

below of the pink ring slide in **Figure 7**. Sometimes participants piggy-backed off of one another, and other times, they could not have disagreed more. The colors included were gray, white, light purple, light pink, red, and light green as seen in the image below in **Figure 8**.



Figure 8. DIAL 3D Ring Prototype Colors

Through these focus groups and discussions specifically designed to hear opinions on color and design, we were able to obtain informative data on what women thought. They were honest and open, and provided great illustrative quotes surrounding each color. After going through all of the rings individually and together, we asked participants to rank the rings in order of which color they would prefer to use. We were ultimately able to eliminate certain ring colors from the final ring designs based on these rankings and this discussion through our coding process, which I will explain in a few sections. Color will also be a large component of my comparison of DIAL 3D to other rings since most other rings, similar to the NuvaRing, have

always been clear and never considered the option of color to enhance the choice of contraception for women.

Design

Following the color discussion, we moved on to the design portion. The design portion followed a similar structure: we went through each of the 6 designs one by one and probed participants with questions to understand their honest opinions of the rings. The rings were labeled by letters A-F, and each had a different design for drug delivery and insertion purposes, affecting the flexibility of the ring and feel as shown in **Figure 9**.

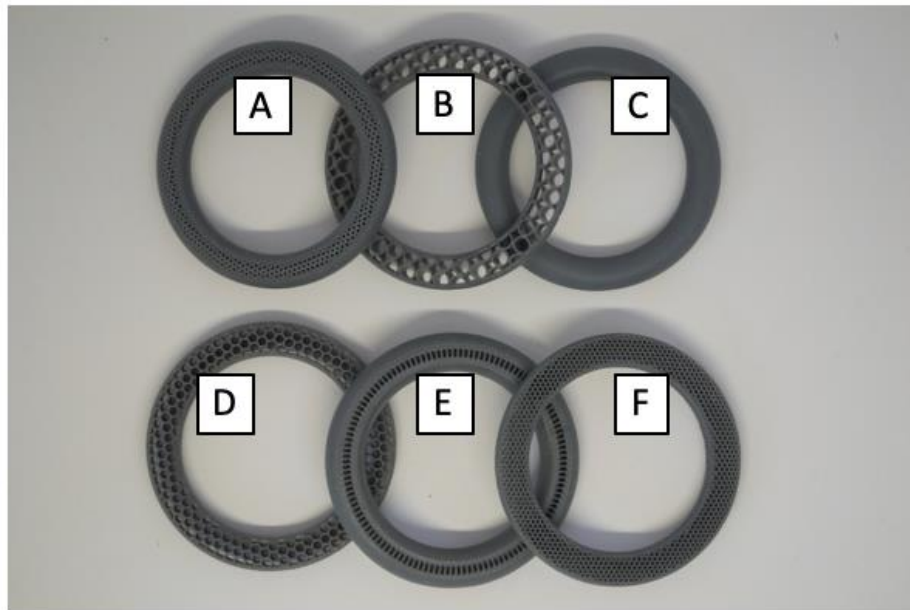


Figure 9. DIAL 3D Design Prototype Rings

After going through the individual slides, we showed all 6 rings together then showed some comparison pictures to show how big and wide the rings were in reality, comparing it with a side-by-side picture of a house key, pencil, and credit card (**Figure 10**). We also included a picture that compared the ring to a physical NuvaRing as seen in **Figure 11**. Since participants could not physically touch the ring in the virtual focus groups, we wanted to make sure they had

a strong understanding of the physical size of the ring. Along with this, we had one of our research team members show how flexible the ring was by using her set of the DIAL 3D prototypes in the zoom camera, flexing and folding the ring as if preparing for insertion. Our consultant advised our facilitators to make sure the participants initiated the need to see the ring,



Figure 10. Comparison of DIAL 3D Ring to house key for virtual size comparison

rather than offering so that we could ensure they were thinking through their own steps in regards to preference. Participants were surprised to see how pliable and flexible it was, which was helpful for gaining more insight on their interpretation of how the ring would work and whether or not they would want to use it in the future. Following

these slides, we had participants do a similar ranking exercise and rank the design in order of preference to use if given the prototype. In our next phase of research after eliminating a few colors and designs, we had participants rank designs and colors together to see if they influence each other in terms of preference.

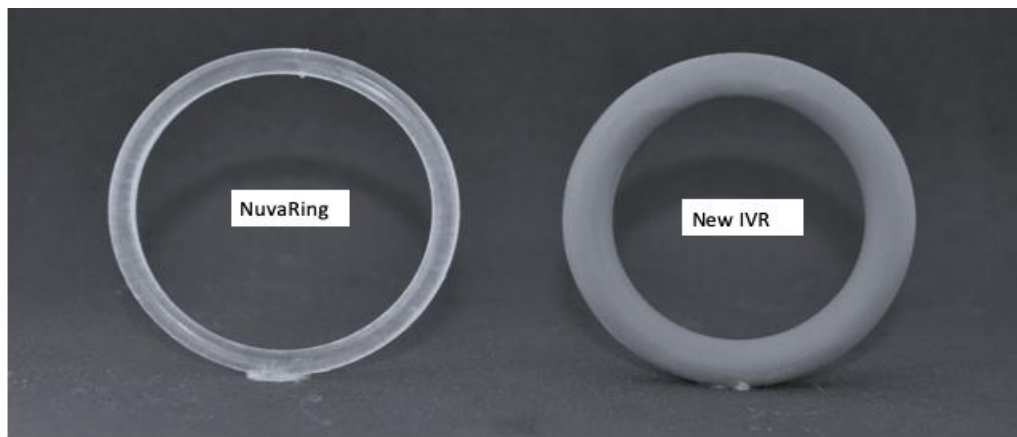


Figure 11. FG Slide Comparison of NuvaRing to DIAL 3D IVR Prototype

Coding and Analysis Matrix for Data Analysis

For every focus group, we had two notetakers to ensure we captured what each participant said, then crossed-check this with the transcription we received from a professional company. With these transcripts, we cleaned and labeled them to prepare them for our coding process. Over the course of phase 1, our qualitative team developed a codebook to guide our coding and data analysis in Dedoose, a cross-platform software developed to organize, analyze, and code-mixed methods research. This codebook had eight parent codes: prototypes, previous vaginal products, functions, sensation/experience, color, design, rank, and need to know. Within each of these umbrella parent codes, there are specific child codes that address the themes within each of those sections. For example, under the color parent codes, the child codes included each color of ring we showed participants.

The codebook included a definition for each code, and an example quote to ensure our code was capturing target phrasing or specific participant examples. For each focus group, we coded each relevant section of the transcript according to the parent and child codes the topic fit into based on the codebook. Multiple codes could be applied to the same utterance, and we would normally switch codes whenever the speaker or participant changed. For example, if a participant was comparing how both green and white rings make them feel unhygienic because the colors could look dirty after insertion and would not be a pleasant feeling, we could code that section of the transcript under codes: color, green, white, hygiene, and insertion.

Two people on our research team coded each transcript to make sure there were no major discrepancies and to ensure we had a strong inter-coder reliability within our coding process. Once this was completed, we created an analysis matrix to summarize the findings for color and design. The matrix included a summary and relevant quote for the many different codes, but I will only focus on the ones relevant to my research questions. By going through such a

systematic qualitative coding process, our matrix could be translated into succinct data to share with our engineering team to guide their decisions in terms of color and design.

In-Depth Interviews (IDI)

After completing the first phase of research with the focus groups, 3 ring colors were dropped and 1 ring color was added, and 3 designs were dropped, and 2 ring designs were added based on pharmacokinetic studies sheep study safety evaluation results. We had solid evidence for ring preferences in terms of color and design, and we had a better understanding of participants' main concerns related to the IVR. There was also a strong need for women to actually feel and hold the ring, so there was increased importance to include a tactile option in our next stages of research. Thus, the next phase of our study took place during the summer of 2021, as our research team conducted 1-on-1 and in-person in-depth interviews at UNC Gillings School of Public Health. The main focus for IDIs was to eliminate more colors and designs, as participants were shown five designs and four colors, and there was a new set of smaller rings in those designs.

IDIs were conducted in a similar structure: prior vaginal product history, participant evaluation of IVR designs and colors, followed by participant ranking of the designs and colors. The data analysis also followed the same process with transcription cleaning and coding, but the codebook was revised for emerging areas of interest. These codes were then summarized into another analysis matrix by key areas of interest, then ranking data was summarized to report back to the engineering team for testing. Testing was in the beginning stages, but we were able to inform our research with IDI outcomes to have more targeted testing for the next few rounds. The engineering team has been using female sheep for safety and pharmacokinetic testing since

their vaginal walls and tissues are relatively similar to humans in terms of pharmacokinetics, safety, tolerability, and local toxicity, so they were the most useful model of assessment for drug delivery for the vaginal ring (Holt et al., 2015).

Conclusion

From DIAL 3D, I have been able to understand women's needs and preference surrounding contraception with an IVR on a much smaller scale as all of our participants were located in North Carolina. From my literature review, I was given a deeper perspective on how women worldwide view intravaginal rings. Because our ultimate goal for DIAL 3D is to produce the ring on a global scale and impact women throughout the world to provide them with access to contraception and HIV and STI prevention, I will now compare the findings of DIAL 3D participants to women globally. The comparison will focus on factors such as size, texture and flexibility, hygiene, color, and functionality.

Chapter 5: DIAL 3D Ring in Comparison to other IVRs

Introduction

The second part of this chapter will focus on the comparison of DIAL 3D and our finding from our study to other intravaginal ring studies that were reviewed in chapter 3. When considering this analysis, it is important to note that the premise of my thesis is to explore how the findings from the DIAL 3D study serve to progress global women's health, based on the idea that in order to progress the state of reproductive health worldwide, women must be the ones who feel supported and seen. Thus, it is important to determine what features of the product will make women more likely to want to use the ring and empower them to feel most in control of their own bodies. In order to compare the DIAL 3D ring to other existing intravaginal rings, I will consider a number of factors that play a role in user preferences and product acceptability based on results of focus groups and IDIs across multiple studies. The factors or categories I will use to complete this analysis, all of which consider participants' first impressions of ring prototypes, include: size, texture and flexibility, hygiene, color, and functionality. I plan to break down the findings for each of these categories then share quotes and some examples to compare women's perceptions of the DIAL 3D ring with participant preferences for features of other IVRs worldwide.

Size

In Das et al.'s focus group study in India, size was a major point of discussion as participants across ALL groups preferred thin and small rings since they would likely fit better. Interestingly, the unmarried women found the size of any of the rings quite "alarming" when considering how it could fit inside their body. Since most of the participants were comfortable

with the size and diameter of the NuvaRing, they often used these measurements as a "benchmark" (Das et al., 2015). Participants also compared the NuvaRing in our DIAL 3D focus groups, especially with participants who were NuvaRing users. One participant (#8) said

"I can deal with the thickness/size. However, if we're looking at the two sizes together, the NuvaRing is more appealing with the size."

Another study reviewed in chapter 3 included an IVR acceptability review in Kigali, Rwanda in which women were concerned about size before insertion since they had no experience with IVR use (Kestelyn et al., 2018). This was also a concern in our DIAL 3D study especially in our focus groups, as participants who were not NuvaRing users had no concept of how insertion would work. An evaluation study in Urban Kenya provided informative quotes from their participants concerned about size (Smith et al., 2008, pp. 1030):

R5: The size is the biggest problem.

R6: She screams to express that it is big [parenthetical remark of one focus group participant to another].

R4: The size is very big.

R6: It will hurt us the first day but once we get used to it.

When participants were actually able to feel and play with our DIAL 3D ring prototypes in our IDIs, we were able to gain much more informative data on how they interacted with the ring during the first impression:

"this design looks smaller than the others which is more appealing since I think it would be more comfortable and less irritating while inserted for 90 days because of the size," said a participant from IDI 48 (DIAL 3D black, 26, NuvaRing user).

Another participant was on the fence about how big she preferred the ring to be, sharing that:

"the size seems fine, but it looks thicker than the NuvaRing, and I would prefer it to be thinner since the circumference is also larger than the NuvaRing. But, a bigger ring might prevent the ring from falling out (DIAL 3D, IDI 68)."

Overall, size was a salient feature for both groups and was important in how they expressed acceptability and user adherence. In terms of the comparison of DIAL 3D results to international IVR acceptability studies, DIAL 3D findings were very similar—women in both groups were commonly intimidated by too big of a ring, and preferred a smaller size since it seemed more comfortable to insert and keep in the body. Some women in both DIAL 3D and the international reviews were comfortable with big rings as long as they would still be easy to insert and comfortable to use. Thus, size perceptions in DIAL 3D were consistent with other studies, proving to be a salient feature of the ring in terms of user adherence for participants.

Texture and Flexibility (Insertion, Removal)

Das et al.'s study in India showed participants about six to eight various rings to focus group participants, and found that rings that felt thicker and heavier made women wary of using them, as one participant shared

"it is hard, too thick and uncomfortable which can cause irritation and discomfort and be difficult to insert (FGD #9, India study, pp.536)

Along with insertion, the participants were concerned about how flexible the ring would be once in the body, and if it could cause harm if it moved up in the body (Das et al., 2015). In Kigali, Rwanda, participants described the IVR as "soft and cold, with a pleasant smell (Kestelyn et al., 2018)." 96.7% of participants said that reinsertion would be easy based on the feel and flexibility of the ring. Women were able to insert the ring, so these studies are a bit more advanced in terms aspect of texture and flexibility they were able to assess and the results. Participants in the field study in Brazil and the Dominican Republic mostly agreed that insertion was not too difficult (Hardy et al., 1983). Women in this study who had concerns about size conveyed that the ring

"too wide and the rigidity made the ring difficult to fold" (Brazil and Dominican Republic Study, pp. 289).

The DIAL 3D IDIs were extremely informative for understanding user preference in texture and flexibility since we were able to conduct them in person and 1-on-1. Since our study is not in the insertion trial phase, we could only understand participant preferences by them feeling the ring with their hands. When asked about a specific ring design, one participant from IDI 39 (white, 39, NuvaRing user), said

"I'm really kind of taken with the thickness of it right now because the NuvaRing is fairly thin. I'm kind of interested in how aware I would be of it, and like, how this would feel– yeah, of whether or not I could feel it during the day (DIAL 3D)."

Flexibility proved to help participants rank the rings and compare them, as another participant (white, 41, NuvaRing user) when comparing two rings said,

"this seems softer and more pliable than rings 1 and 2. The holes make it seem less scary and bulky. 3 is my favorite because of flexibility and perceived ease of insertion. 3 and 4 are very close favorites... 3 is slightly more flexible (DIAL 3D IDI 49)."

A third participant (24, black, NuvaRing user) was focused on the thickness of a specific ring design, claiming that she:

"has a positive feeling about it. I think the thickness would possibly help with not only insertion but allowing it to stay up there. I do not have a concern about thickness in terms of wearing it (DIAL 3D, IDI 67)."

In DIAL 3D and international IVR acceptability studies, women were most concerned about the texture and flexibility of the ring in terms of insertion. As long as the ring was flexible enough to fold and soft enough to be comfortable within the body with minor irritation and discomfort, women were excited to use the ring. Rigidity and the diameter were important factors in all studies, as women wanted to ensure there would not be daily irritation and discomfort during use. So far, DIAL 3D participants are comfortable with the ring material and its flexibility. However, DIAL 3D is still in its early development stages, so insertion trials are a few years away from being completed. Thus, DIAL 3D should follow similar trial steps to the international IVR studies that have high rates of

acceptability in their insertion trial phases. If women are able to comfortably use and insert the ring in these trials, then the DIAL 3D ring will have promising potential to be successful in terms of user adherence.

Hygiene and Cleanliness

As mentioned in the size section, the NuvaRing was the benchmark for participants in Das et al.'s study in India, as all groups preferred thin and small rings. One participant even commented that *"a ring that looks like NuvaRing is preferable, they are thinner and more hygienic (FGD #1, married women with one or more children."* Color and hygiene are also considered to correlate, since women in this study preferred transparent or white rings due to their association to "cleanliness (Das et al., 2015)." A study reviewed in Chapter 3 on IVR adherence in Sub-Saharan Africa found that many women in the study were concerned about hygiene practices especially surrounding removal or expulsions, and menses-related management (Montgomery et al., 2012). Similar concerns were found in Smith et al.'s Urban Kenya study in which women were apprehensive about leaving the ring for extended amounts of time and the results on vaginal hygiene and collection of dirt or bodily fluids (Smith et al., 2008).

Hygiene was a prevalent topic of conversation during the DIAL 3D study's design portion of focus groups and IDI's. Women found that when they were comparing various drug delivery designs, a main concern was how the body's processes would affect the cleanliness of the product. With one design that had incredibly tiny holes throughout the ring as part of its design, one participant (white, 22, NuvaRing user) said

"the holes are a little worrisome. They're really small. I feel like that would probably trap a lot of bacteria (DIAL 3D)."

A second participant brought up holes and hygiene when ranking the ring designs, sharing that:

"For me it's all about comfort and how clean I can keep it. The holes are a lot bigger. I feel like it would be easier to clean and deal with hygiene wise. Same thing with [ring]. It still has those big holes. Even though it has some patterns in between that make it more intricate and maybe possible more difficult to clean (DIAL 3D IDI 64- Hispanic/Latin, 25, non-NuvaRing user)."

This same participant also considered the hygiene with color and design rankings as she felt more comfortable with a specific combination of a color and design, claiming that

"It is really pretty. I really, really like it a lot. It's very easy to see inside of it if you're trying to think of hygiene and cleanliness (DIAL 3D, IDI 64)."

In conclusion, Hygiene and cleanliness are significant points of concern for women in all of these studies. In both DIAL 3D and international IVR studies, the level of cleanliness of the ring inside the body and outside of the body post-removal strongly affected their level of acceptability and use. If the ring made them feel dirty or unsanitary, especially during menstrual cycles, women felt it would affect the comfort levels to use this product. In DIAL 3D and other studies, discussions heavily revolved around discoloration of the ring and how the color of the ring

impacts their perception of how hygienic it is. As we continue to develop the ring, it is important to keep these concerns in mind in order to help women feel as clean and sanitary as possible. If we can develop a ring that prevents major discoloration and is easy to clean, user adherence and acceptability will likely be more successful.

Color

When it comes to color, there is very little research on the development of colorful intravaginal rings. Much of the literature that has been published pertains to discoloration of the ring after being in the body, since women reacted negatively when they noticed a color change in the ring in the field study in Brazil and the Dominican Republic (Hardy et al., 1983). The ring model became light gray and looked dirty, which was not liked by about "one-third of users, who suggested that its correction may improve acceptance." Similarly, the acceptability study in Kigali, Rwanda found that "32% of participants did not like the discoloration of the ring, referring to it as dirty (Kestelyn et al., 2018)." Participants in DIAL 3D had mixed opinions on discoloration:

"a darker color would be really hard to tell I feel like, I don't like the darker for being able to see things when it comes out of the vagina. I like being able to see any discoloration that's concerning (DIAL 3D, IDI 49- white, 41, NuvaRing user)."

Another participant brought up discoloration as something she needed to know more about before deciding on whether or not she would use the ring, asking about

"if someone's pH is kinda off balance, how would that affect the color of it. I started thinking about discoloration cause I was pretty curious about that (DIAL 3D, FG 9)."

As mentioned in chapter 3, the qualitative research study exploring IVR acceptability in Delhi, India is one of the few studies that inquired about colors including white, purple, light brown, skin color, and transparent (Das et al., 2015). Results indicated that women generally did not have a strong color preferences as long as ring functions properly. In terms of color and hygiene, we have seen that transparent rings and white rings were associated with "cleanliness," but I also think the comparison to the NuvaRing's clear color causes women to prefer transparent rings. A DIAL 3D IDI 38 participant (white, 39, NuvaRing user) brought up her NuvaRing experience in reference to color, telling us that

"I think it would be great to pick a non-gendered color, like my NuvaRing is clear and I think that's just better than gray. Like grays and browns aren't colors we think of as being healthful. Whereas, kind of like clear, crisp, very light colors we associate with hygiene like blues." When looking at the light gray ring color, she said "I think it's closer to a white color, which again kinda evokes cleanliness and hygiene and things like that. Yeah I like that one (DIAL 3D)."

Overall, our DIAL 3D qualitative team was able to determine which colors were preferred over others in order to give our engineering team the data necessary to cut out certain

colors and try a few new ones. Participants definitely had a wide variety of preferences considering their backgrounds and emotional attachment to certain colors, especially in regards to how the color of a contraceptive technology would make them feel about using it. Thus, women had a wide variety of preferences for colors as some colors were clearly more preferred than others. For example, participants preferred the clean translucent and clear colors as mentioned above, while other participants wanted a colorful and bright IVR:

In reference to the light purple color one participant said she would want to:

“see how maybe the funner colors might make it better to use, it might be more appealing if it were a fun color. I just want it to do its job. I could see how for a younger audience they might want something that's colorful (DIAL 3D, IDI 50-white, 26, non-NuvaRing user).”

Another participant felt similarly when looking at the light gray ring:

"kinda dull, I feel more drawn to colors that are more vibrant or brighter (DIAL 3D IDI 51- black 23, non-NuvaRing user)."

In terms of color, DIAL 3D participants seem to be pleased with the various color options for the ring. When comparing these results to those found in the international IVR studies, it is important to consider the age and cultural differences among participants.

The perceptions of and preferences for color in the US, India, Brazil, Dominican Republic, and Rwanda are very different according to cultural norms and practices with more valued colors in terms of vibrancy or tone. Age also plays a role as younger women

may prefer a different mood or tone of color in comparison to elder women. All studies showcased a concern for discoloration, so as discussed in the hygiene and cleanliness section, as long as the DIAL 3D ring can prevent major discoloration and keep the ring color as close to the original color as possible, there is a higher likelihood for strong acceptability and user adherence rates.

Functionality

Overall, we have seen that the categories listed above are important, but do not take priority over the ring's functionality. Specifically, women have preferences regarding how the ring should look and feel, but they are more concerned about how well the ring will work in their bodies to protect from unintended pregnancy, HIV, and STIs. This notion was also perceived heavily through our DIAL 3D focus groups as many women were willing to compromise on size, color, and design. One participant (#8) said,

"However, if the new IVR can prevent HIV or AIDS, you can deal with certain things as well like thickness/size (DIAL 3D)."

This triple protection is a very appealing concept for many women since it is unique to multi-purpose prevention intravaginal rings (Das et al., 2015). The rings used in Das et al.'s study were monthly disposable IVRs, which women considered more comforting and easier compared to ones that could last for 3 to 6 months. The Urban Kenya evaluation study found that most women preferred an IVR with a "long-acting formulation," due to the convenience of not having to worry about HIV prevention (Smith et al., 2008). Their preferred duration of use would be 3 months to 1 year, similar to their preferred BC or injectable hormones, as one participant shared:

R: One year is good because once you insert it, you forget about it for a long time knowing that you are safe. You rest your head from worrying about HIV.

(Women's FG3, Urban Kenya, pp. 1030)

The DIAL 3D ring is supposed to last for 3 months. Then, women could remove it for the 4th month for their menstrual cycle, then insert another ring back in for their next 3 months. Thus, only using 3 rings per year is quite sustainable and equitable for birth control, especially for participants who were concerned about forgetting to take the ring out. One participant (white, 39, and a NuvaRing user) claimed in a focus group that it is

"phenomenal that the ring is designed to be inserted for 90 days at a time (DIAL 3D, IDI 22)."

Functionality is by far the most integral feature of intravaginal rings for all participants in these studies. Women in both DIAL 3D and all international IVR studies were like-minded in terms of valuing functionality over all other physical features such as size, color, texture, and hygiene. Most participants agreed that they were willing to overlook any undesirable physical features as long as the ring works successfully to protect them from unintended pregnancies, HIV, and STIs. DIAL 3D has promising potential to meet women's needs in terms of drug delivery and protection, which is currently undergoing testing in female sheep. DIAL 3D also received positive feedback on the duration of the ring as women were excited about the prospect of leaving the ring in 3 months at a time.

Conclusion

In conclusion, there is promising potential for the DIAL 3D ring to excite and empower women who are looking to use an intravaginal ring. Based on the comparison to other international IVR acceptability studies, the DIAL 3D ring showcases similar findings in terms of size, color, texture and flexibility, hygiene and cleanliness, and functionality. All studies consider functionality to be the most prioritized feature, as women internationally and in DIAL 3D just want a product that will do its job to protect from unintended pregnancies, HIV, and STIs. In the next chapter I will wrap up my thesis and its overall findings and results, then share some implications, lessons learned, and future uses.

Chapter 6: Discussion and Future Use

Since 1916, women have been fighting for their birth control rights, inspiring activism and family planning programs worldwide. From Margaret Sanger in the US to Alexandra Kollontai in the USSR to Raghunath Karve in India, leaders stepped up to actively work towards the legalization of contraception and dissemination of birth control information (Nichols, 2000). These initiatives led to FDA approval of birth control and contraceptives, the establishment of contraception for married couples in *Griswold vs. Connecticut*, WHO approval of the first birth control implant, and the creation of the UN Millennium Development Goals and Sustainable Development Goals that target gender equality and the improvement of women's health.

Despite major progress in family planning and contraception, there are still many barriers to improving reproductive health including access to care and clinics, risks of HIV and STI, male-dominated cultures, and the burden of cost. The impacts of these barriers vary based on women's demographics, since low-to-middle income countries suffer the greatest loss as roughly 817 women die each day from preventable pregnancy or child-birth causes (Boonstra, 2015). Thus, creating products like the DIAL 3D intravaginal ring and other multi-purpose prevention technologies can help women combat these barriers simultaneously. With protection from unintended pregnancy, HIV, and STIs, women are given control over their bodies and futures.

Findings: Lessons Learned through Comparisons of DIAL 3D and Other IVR Studies

My research question asks how the DIAL 3D technology we are developing serves to globally progress women's health in comparison to other multi-purpose prevention technologies as seen in international IVR acceptability studies. DIAL 3D will provide women with a unique product that fits a variety of needs to maximize protection from HIV and STIs and prevention of

unwanted pregnancies. As new IVRs with multi-purpose prevention functionalities continue to be developed, women will be presented with diverse and flexible options for birth control and family planning. There is not one current contraceptive technology that fits all needs. As the only approved intravaginal ring, the NuvaRing only targets the contraception for women. The DIAL 3D ring will release the same drugs as the NuvaRing for birth control purposes, but will also release drugs used for STI prevention and for Pre-exposure Prophylaxis (PREP) to prevent HIV.

To truly advance women's health, women must be in control of their own decisions regarding their bodies. When educated about these choices and their bodies, there is potential for women to choose a product that makes them feel comfortable and safe. In the last three years of studying qualitative data on women's preferences for intravaginal rings, we aimed to understand how a multitude of factors could affect women's acceptance of the ring. With all of our focus groups and discussions, our qualitative team was able to provide concrete feedback for the engineering team throughout the DIAL 3D ring development stage. Our results provided us with strong data in terms of users' likely uptake adherence for different features of the physical ring.

To fully answer my research question, the data analysis completed in this thesis not only focused on whether or not women would want to use the ring, but what features made them feel most excited and empowered to use it since that is ultimately what will progress women's health. By looking at size, texture and flexibility, hygiene and cleanliness, color, and ring functionality, I found that results from DIAL 3D are very consistent with the findings of other IVR studies in terms of acceptability. I have summarized the specific comparisons below.

Results and Lessons Learned

Functionality is the most integral feature for all participants in both DIAL 3D and the international IVR studies, as nearly all participants valued functionality over all other physical features such as size, color, texture, and hygiene. They shared that they did not care as much about the look of the ring and would overlook those features as long as the ring could protect them successfully. As we hope to continue conducting successful clinical trials, there is potential for the DIAL 3D ring to help women feel safe from unintended pregnancies, HIV, and STIs.

Size was another salient feature for participants in both DIAL 3D and other IVR acceptability studies and was an important in understanding their initial impressions and user adherence. Size perceptions in DIAL 3D were consistent with other studies, as our participants often expressed concern and intimidation by the size of the ring, feeling as though it would be too big to insert in their body. Participants in international IVR acceptability studies also preferred a smaller size since it seemed more comfortable to keep in the body. The NuvaRing was commonly used as a benchmark for size and color, as previous users or participants familiar with the NuvaRing continuously compared the prototype intravaginal ring to it in the focus group discussions.

Color is an interesting feature, as DIAL 3D is one of the very first rings to ever integrate color into the design. Most IVRs, like the NuvaRing, are transparent or clear, but the 3D printing engineering of the DIAL 3D ring requires it to be colored. One of the very few studies that looked at ring color was conducted in India on IVR acceptability and inquired about white, purple, light brown, skin color, and transparent colored rings (Das et al., 2015). So far, the DIAL 3D ring is still undergoing color analysis, but we

have eliminated ring colors that were disliked by the majority of participants. Certain “fun-colored” rings or “pretty and calming pastel colored” rings made women feel excited in our focus groups, giving them a chance to express themselves and feel in touch with their birth control technology. Another aspect of color that was found to be salient for women in the DIAL 3D and international IVR studies is discoloration. Women were concerned about the color of the ring changing after being inside the body. Participants in DIAL 3D inquired about how their bodily fluids would impact the color of the ring, so it is an important for the DIAL 3D team to keep in mind that we should prevent any discoloration as our engineering team continues to develop the ring features and color.

Similar to discoloration, hygiene and cleanliness were major points of discussion in both DIAL 3D and international IVR studies. If the ring made them feel dirty or unsanitary, especially during menstrual cycles, women said it would affect their level of ring acceptance and use. Since the duration of use varies by ring, DIAL 3D engineers should ensure that the ring can remain relatively clean during the 3 months of use. Cleanliness of the ring seemed to strongly impact user perceptions, so we must continue to develop a ring that prevents major discoloration and is easy to clean.

Based on all of these categories, there is a great window of opportunity for DIAL 3D to help women feel protected and excited about their birth control technology. Our ring can target and benefit a diverse group of women from those in lower income-countries at high risk for HIV to women in developed countries who worry about STIs from random partners. By considering the significant concerns from participants in the international IVR studies, we can focus on developing a ring that helps women feel comfortable and not worry about the physical issues with insertion and usage.

Limitations

The DIAL 3D study is still in its beginning stages of development as we have only conducted virtual focus groups to understand initial impressions and in-person IDIs. While our participants viewed the DIAL 3D ring very similarly to other international participants from studies whose development phases were more advanced than DIAL 3D, many of these studies are already in their insertion and clinical trial phases. Thus, the comparison was not as analogous since participants from the DIAL 3D study in North Carolina did not have the same lifestyle or experience as the participants in the other studies from Brazil, the Dominican Republic, Kenya and Sub-Saharan African countries, India, and select regions of Australia and Europe.

Cultural and regional differences play a large role in participant preferences and acceptability of the ring. The state of maternal health and gender equality varies significantly throughout the world, so comparing these results did not take into consideration all of the familial and community differences women faced. For example, some women do not use birth control methods because institutions, such as their government regime, religious practices, or family values prohibit their use. In DIAL 3D, our participants were all based in North Carolina so their life experiences are very different from women in any of the international studies. Thus, although despite the different settings, we were able to find many similarities among women in different studies regarding their preferences for IVR features, where we did find differences, such as in preferences for specific colors, we cannot disentangle the exact reasons for these differences, be they due to study design, cultural, or life experience differences.

Due to COVID-19, our study design and methods were completely adapted to take place virtually. While we tried to keep our research process as close to plan as possible, there were multiple limitations with participant recruitment, technology, virtual focus groups, and

impressions of the ring. Seeing a ring through a zoom screen results in very different feedback than holding the ring in-person and getting to play with it. The size, color, and designs were also harder to capture through a zoom screen, as we tried numerous ways to showcase the rings and pictures of them.

Future Use and Impact on Women's Global Health

Educate a girl, change the world (UN Women). From women's health to girls' education advocacy, this phrase indicates the power girls hold, especially educated girls. Educating girls promotes and improves gender equity by giving them the confidence and support to make decisions that will benefit their futures, especially in regards to their families and children (HIPs, 2014). Studies have shown that higher participation in school over time decreases fertility rates for girls as it has been estimated that an additional year of school for 1,000 women can prevent two maternal deaths (PRB, 2011; Summers, 1992). A comparative review found that women in about 32 countries who remained in secondary or higher education were five times more likely to know basic facts about HIV than illiterate women, reducing their chances of contracting HIV (Vandemoortele and Delamonic, 2000).

When given the resources and education they need, women are the ones in the best position to address the challenges they face (Cheney, 2022). New multipurpose prevention technologies can give women the tools necessary to protect their health and improve their quality of lives (Rosenburg, 2013). Over the years we have learned that contraceptive technologies are not one-size-fits-all products. Thus, the creation of MPTs address a multitude of risks and can provide protection that fits the needs of many women with various contraceptive preferences. Integrated solutions and multipurpose prevention technologies like DIAL 3D can expand

contraceptive options for women globally and, in conjunction with programs to broaden educational and consequent employment opportunities, advance progress in multiple development goals related to women's health—giving women and girls a chance to reach their full potential (Rosenburg, 2013).

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