The Initiative for Multipurpose Prevention Technologies (IMPT) advances the development of MPTs to address the interlinked risks of unintended pregnancy and sexually transmitted infections (STIs) including HIV, believing that the availability of desirable methods that deliver an array of prevention combinations will improve the lives of women and families worldwide. Established in 2009, the IMPT is a collaborative network that engages product developers, scientific researchers, healthcare providers, funders, and community-based advocates in Africa, China, India, the United States, and Western Europe. Leveraging the multidisciplinary expertise of this diverse network, the IMPT works to advance the science to support the development of MPTs and their successful introduction into target populations with high unmet need.

Multipurpose Prevention Technologies (MPTs) are an innovative class of products that deliver varied combinations of HIV prevention, other STI prevention, and contraception and will improve the lives of women and families worldwide.

The project on which this document reports was conducted by the IMPT Secretariat team and technical consultant Chelsea B. Polis (Guttmacher Institute/IMPT). This document was prepared by Laura Dellplain (IMPT), Diane Royal (IMPT), and Chelsea B. Polis (Guttmacher Institute/IMPT). This work could not have been completed without the valuable insights and contributions from key informants.

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**Introduction**

The multipurpose prevention technology (MPT) field, formalized in 2009 with the inception of the product-neutral Initiative for MPTs (IMPT), has grown substantially over a relatively short period. The MPT product development pipeline is diverse, with nearly a dozen products in various stages of clinical trials, including intravaginal rings (IVRs), vaginal inserts, vaginal gels, and vaginal films. There is widespread recognition that the impact potential of MPTs could be immense, but to ensure the successful development and introduction of the first MPT product and subsequent products, there is much more that needs to be understood and addressed across several key research areas.

The IMPT provides guidance to the MPT field through working groups that are all overseen by a steering committee. In January 2015, the IMPT Steering Committee elevated modelling as a key priority research area. More specifically, the IMPT recommended accelerated action around modelling efforts to robustly assess public health impact and cost-effectiveness of MPT product options in specific target populations.

Data on the potential public health impact and cost effectiveness of MPTs are critical in building the case for MPT development, investment, commercialization, advocacy, and policy support. Given that MPTs are still largely undergoing clinical trials, however, the field does not have access to such data through robust surveillance efforts as would be the case for products already on the market. Modelling is thus an important strategy in generating this evidence base. Moreover, modelling may be a useful tool in determining the appropriate impact targets, including the balance of public health efficacy and cost-effectiveness (though not mutually exclusive attributes) when developing and planning the introduction of a health intervention.

Having identified this research priority for the MPT field, from September to November 2016, the IMPT conducted a landscape review of relevant MPT modelling activities to begin to assess specific gaps and next steps. The IMPT first identified what modelling has already been done for MPTs as well as ongoing MPT-relevant modelling activities. A summary, including methods and findings, is detailed below.

**Methods**

To produce this landscape review, we conducted a comprehensive literature review and key informant interviews. Prior to launching the literature review, we connected with the OPTIONS consortium to align methodologies with their pre-exposure prophylaxis (PrEP) modelling landscape analysis, which they had conducted in Fall 2015. We searched PubMed and Google Scholar for articles that published data on modelling efforts in the context of MPT development. More specifically, we included articles that examined factors relevant to the likely uptake, public health impact, cost-effectiveness, or other forecasting of products with multiple sexual and reproductive health prevention indications (which were not necessarily labeled in all articles as “MPTs”), aside from male or female condoms. An example of an excluded publication was a study that modelled the pharmacokinetic properties of an MPT product. Key search term themes included: modelling, multipurpose prevention technologies (MPTs)/ dual protection, sexually transmitted infections/ diseases (STIs/ STDs), HIV/AIDS, and contraception/ family planning/ unintended pregnancy.

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1 The OPTIONS (Optimizing Prevention Technology Introduction on Schedule) consortium led by Wits Reproductive Health Institute, AVAC, and FHI 360, aims to provide targeted support to expedite and sustain access to ARV-based HIV prevention products in countries and among populations where most needed, including South Africa, Kenya, and Zimbabwe.
We selected key informants (n=6) for their expertise in modelling in the MPT and/or biomedical HIV prevention context (see bios below); all key informants were identified through recommendations from experts within the IMPT network. Drawing on initial recommendations from the IMPT Steering Committee, we developed a set of interview questions and then vetted them with several committee members. We conducted key informant interviews over the phone as semi-structured interviews, a qualitative research methodology that includes open-ended questions on pre-identified themes. Two of the four semi-structured interviews were conducted in pairs (i.e., two key informants were interviewed at the same time). An hour was allotted for each interview. Interview notes were then coded for further analysis of key themes.

**Key Informant Interviewee Bios (in alphabetical order)**

Ume L. Abbas, MD is an infectious disease specialist and Assistant Professor at Baylor College of Medicine in Houston, Texas, USA.

Idé Cremin, MSc, PhD has a research interest in mathematical modelling and is a Research Associate within the Faculty of Medicine, School of Public Health at Imperial College London, UK.

Katharine Kripke, PhD is a Senior Health Policy Analyst with Avenir Health – a global health organization that works to enhance social and economic development by providing tools and technical assistance in policy, planning, resource allocation and evaluation.

Martha Larson is the Project Manager of OPTIONS consortium, housed at FHI 360.

Jennifer A. Smith, MSc, DPhil has a research focus on developing models to understand the implications of the potential association between injectable hormonal contraceptives use and HIV risk. Dr. Smith is a Research Fellow within the Faculty of Medicine, School of Public Health at Imperial College London, UK.

David van de Vijver, PhD is an epidemiologist with a specialty in virology based at Erasmus Medical Center in Rotterdam, Netherlands.

**Findings**

We identified several relevant modelling projects, both published and ongoing. Of seven citations identified through the literature search, we excluded four as they pertained only to animal modelling. We added one additional citation suggested by a key informant, bringing the total number of published works on MPT modelling for the purposes of this project to four citations (n=4), representing three modelling projects (two publications discussed the same project). Other projects described during the interviews either added further detail to identified citations or outlined additional ongoing work. Most identified modelling projects are in progress.

**Published MPT Modelling Work**

One published, peer-reviewed article described a discrete choice experiment conducted in 2005 by the London School of Hygiene and Tropical Medicine, which investigated preferences of sexually active South African women aged 18-45 for new HIV prevention technologies (including microbicides, diaphragms, and female condoms), compared against what, if anything, they had used for HIV prevention at last sex. Microbicides were chosen as preferred product (48% of respondents), followed by the diaphragm (28%), followed by female and male condoms (13% and 10%, respectively). While 74% of women said they would prefer to change to...
using a new HIV prevention technology (i.e., either a microbicide, diaphragm, or female condom), this proportion was lower (56%) among women currently using male condoms. The most important characteristics to women in considering these new HIV prevention technologies were the level of protection against pregnancy and HIV. Price and the ability to use the product in secret also had a significant (though smaller) impact on the probability of saying that they would choose one of these three new HIV prevention methods. The predicted population level uptake of microbicides ranged from 11% (for a microbicide with 55% effectiveness at HIV prevention, no pregnancy prevention, and priced at 10 rand) up to 56% (for a free microbicide that was 95% effective against both HIV and pregnancy) and even higher (65%) among women not currently using male condoms. These estimates should be considered upper bounds, given the potential for upward bias in reported likelihood of using new products. It is also important to bear in mind that these data were collected in 2005, when the HIV prevention landscape was different from present day.

**Ongoing MPT Modelling Work**

Another discrete choice experiment for new HIV prevention technology product types (also led by the London School of Hygiene and Tropical Medicine and conducted in South Africa), was published in a study protocol and as a conference abstract in 2016. Due to its nature as an abstract, we are not able to report as much detail on this project as with other projects. The study examined demand for oral PrEP, vaginal microbicide gel, IVRs, diaphragm plus microbicide gel, and a long-acting ARV-based injectable among four populations in South Africa: women, adolescent girls aged 16-17, men, and female sex workers. This study found that injectable PrEP was favored over other studied product options by all groups, as well as multipurpose prevention for HIV, other STIs, and pregnancy over single-indication prevention. Additionally, this study found that adolescent women were most responsive to multipurpose protection when compared to predicted uptake of single-indication HIV prevention products (approximately between 3-14% versus 1-3% respectively); but predicted uptake for single-indication HIV prevention products among this group was lower than other groups (approximately between 1-3% versus 1.5-16% respectively).

Another study, led by Imperial College London in 2016 and published as a conference abstract, looked specifically at the potential health impact and cost effectiveness of multipurpose IVRs with HIV and pregnancy indications among women aged 15-49 in South Africa. As described during the interview with Drs. Idé Cremin and Jennifer A. Smith, the team developed and analyzed a model of HIV prevalence and incidence in South Africa. This detailed model included a long list of assumptions regarding demographics, sexual behavior, HIV transition and progression, treatment, other interventions (e.g., male circumcision), maternal mortality, reproductive health outcomes, efficacy, costs, and DALYS. This modelling research found that, even where other HIV prevention strategies such as male circumcision and treatment as prevention are being used, a multipurpose IVR could have the potential to “avert 1.6-2.9% of new HIV infections among women aged 15-49 years, 4.3-4.6% of maternal deaths and 1.5-1.6% of DALYS among women aged 15-49 years that would occur between 2018 and 2025 using a delivery strategy that targets 10% of 15-29-year-olds and 5% of 30-49-year-olds.” Preliminary findings also suggested that such an IVR could be cost-effective when delivered through horizontal or vertical programs, at an estimated $200 to $2,700 per DALY, although the researchers noted caveats such as a lack of real world data and unknown unit cost (see section below for additional detail). Moreover, as Drs. Cremin and Smith noted, there is broader applicability of their work to the MPT field: “…we [could] model other MPTs in the same way, but with different assumptions about coverage.”
Finally, Dr. David van de Vijver’s recent work in collaboration with Chelsea Polis (Guttmacher Institute) and colleagues aims to model the health impacts of long-acting injectable PrEP co-administered or co-formulated with DMPA in Mopani, South Africa. The model considers the impact of age and gender categories, assumptions about assortative mixing between various groups, and the long-term impact of DMPA on the HIV/AIDS epidemic in Mopani (i.e., given the potential association between DMPA and increased risk of HIV acquisition in women, if DMPA is substituted with a different contraceptive, whether HIV-infection rates will decrease). While there are no injectable MPTs currently in clinical development, this assessment of an injectable contraceptive method combined or co-administered with long acting injectable PrEP, such as cabotegravir, which is now in clinical trials, and the subsequent impact on HIV-infection rates and rates of unintended pregnancy, may help to answer questions relevant to the entire MPT field.

Challenges and Research Gaps

The primary challenge discussed across all interviews are the assumptions currently required to develop a model predictive of MPT impact, when no physical product yet exists on the market (other than male or female condoms). This lack of “real-world data” requires making assumptions about factors such as product uptake, adherence, and costs when modelling the overall public health impact of MPTs. The validity of these assumptions is unknown until a physical product is available and the relevant data have been gathered. Several interviewees cited these issues as a primary research gap within the MPT modelling field. For example, estimates of unit costs, including how costs might vary and costs to reach various subgroups, are currently unknown, but would be important to produce cost-effectiveness analyses that could influence policy-makers. Similarly, several interviewees discussed the importance of understanding projected MPT uptake and adherence, and how various MPT product attributes might affect these estimates. One researcher noted that this is also a data gap for PrEP, as it remains unclear how people in different populations may value PrEP in comparison to other HIV prevention approaches, or other things on which people may want to spend their time and resources. The assumption for MPTs is that people will want to use products with two or more indications, but we need to know more about who wants to use these products, why, and when. For age and/or gender specific models, assumptions about product usage need to be even more specific to desires of various population subgroups.

In some countries, there is also a lack of current, reliable contraceptive use data. For example, while some models can use contraceptive data from Demographic and Health (DHS) surveys, there has been no DHS survey conducted in South Africa since 2003 (although one is currently ongoing). For models that would consider the various impacts of introducing a new MPT product that included a pregnancy prevention indication, it would be necessary to understand how many women are already using contraception, and which kind of method, to model the impact of introducing a new product in the existing contraceptive method mix context (i.e., whether it would cause contraceptive method migration, and if/how this may impact rates of unintended pregnancy). Similarly, understanding whether the introduction of MPTs would displace other existing HIV prevention approaches, such as use of condoms, would be important – including potential impacts on rates of other STIs not prevented by that MPT.

Finally, to model the effectiveness of various MPTs for HIV, STI, or pregnancy prevention, we need to understand the varied synergistic or antagonistic effects of combining multiple drugs (e.g., a hormonal contraceptive and an ARV) within a single product in terms of potential impacts on the effectiveness of either medication. A recent systematic review, led by FHI 360 and commissioned by the WHO, addresses the issue of drug interactions amongst combinations of hormonal contraceptives and antiretroviral drugs studied to date.
All interviewed researchers agreed that additional research is needed to address these data gaps and that financial support would be needed to expand MPT modelling efforts. There has been some recent interest and investment in modelling work for PrEP, and current funding partnerships may indicate who may have future interest in supporting modelling work.

Extensions from single-indication HIV prevention modelling to MPT modelling

As HIV prevention product development is already a primary driver in MPT development, modellers associated with HIV prevention product impact modelling are well-positioned to contribute to MPT modelling. In addition to the overlap in stakeholders, HIV prevention modelling is highly relevant to MPT modelling, thus relevant single-indication HIV prevention modelling efforts are further described below.

As previously mentioned, the IMPT connected with the OPTIONS consortium to align our MPT modelling landscape with their PrEP modelling landscape. Resources related to their modelling analysis can be accessed here. In a more in-depth interview with OPTIONS consortium members Dr. Kripke and Ms. Larson highlighted a few other related ongoing projects (some of which are cited in the OPTIONS modelling landscape), including: CASPR - USAID’s new initiative led by AVAC around the search for an HIV vaccine which includes a modelling component; a PrEP access project in Kenya called Bridge to Scale, led by Jhpeigo; and a collaboration with IPM and Avenir Health to develop a business case for the IVR. These three modelling projects are filling critical data gaps on uptake, product use, and cost for the HIV prevention field and will be helpful to future MPT models.

Another critical body of work is from Dr. Ume L. Abbas and her group out of Baylor University, USA, who has been modelling PrEP for the past several years. They were one of the first groups to model oral PrEP and have published a relevant paper on injectable PrEP, focused primarily on rilpivirine PrEP in Kwa-Zulu Natal, South Africa, which suggested cost-effectiveness or cost-savings of prioritized scale-up when compared with no PrEP. Currently, Dr. Abbas and her team are completing impact and cost effectiveness modelling work on the dapivirine IVR. Within this analysis, the team has been able to include recent efficacy data and is also considering drug resistance. As the results from this research are currently being analyzed, the IMPT’s interview with Dr. Abbas focused primarily on research gaps and challenges. The future paper on impact and cost effectiveness modelling of the dapivirine IVR, however, will be an eventual core contributor to the MPT modelling literature.

Next steps

As the MPT field expands and evolves, the IMPT will continue to track the growing body of MPT modelling work from its product-neutral, strategic platform. While the field is nascent with products still in clinical trials, modelling analyses will help to illuminate the path ahead for the MPT field by both making the case for MPT development as well as supporting the identification of ideal target product profiles for MPTs.

In future phases of this exercise, the IMPT will develop an appropriate action plan for the MPT field around the identified priority next steps for MPT modelling, which may include strategies to conduct extensions from single-indication HIV prevention modelling. To this end, the IMPT will continue to engage with HIV prevention modellers who are well-positioned to conduct extensions into MPT modelling in their work.


