

The role of advocacy in sustaining male contraceptive research and development

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Abstract

Novel male contraceptives have been in development for well over half a century, and despite a robust predicted global market for new methods, funding for research and development has been extremely limited. While the pharmaceutical industry previously supported male contraceptive research and development, industry partners are only spectators in the current space, awaiting a product that has been de-risked by the public sector before re-entering the field. Current male contraceptive development efforts are thus primarily funded by nonprofit, non-governmental, and government agencies who also act as the primary advocates for the field. Specific organizations include the International Consortium on Male Contraception, the Population Council, the Male Contraceptive Initiative, the World Health Organization, and the US National Institutes of Health. The funding provided by these public agencies, alongside their social and policy-based advocacy efforts such as market research, public education, and calls to action have kept the male contraceptive product development space afloat, resulting in a pipeline of potential products advancing towards market approval. However, as these products mature into more expensive clinical stages of development, they continue to face significant funding challenges, which many programs may not overcome. To fully realize the benefits of novel male contraceptive options, it is incumbent on philanthropic entities, impact investors, venture capital, and/or the pharmaceutical sector to provide significant and timely support for male contraceptive research and development.

KEYWORDS

impact investing, innovation, male contraception, reproduction, reproductive autonomy, unintended pregnancy

Despite the glaring unmet need for novel methods of male contraception as well as a robust global market^{1,2} funding for research and development has been significantly lacking. Given the lack of involvement from the pharmaceutical industry over the past 30 years,³ the nearly exclusive historical focus on developing female methods has

meant that male contraception has struggled with even less funding for decades.

While it is logical that initial efforts would focus on the development of female methods, given that women carry a significantly greater burden in the case of unintended pregnancy, the role of men in

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contraception and, indeed, the reproductive health of men in general, has been all but lost since the introduction of the female contraceptive pill in the 1960s. Notably, despite the multiple methods of female contraception currently on the market, the unmet need for contraception is still significant. United Nations estimates for 2023 indicate that, globally, 10.6% of women of reproductive age (15–49) who wish to stop or delay childbearing are not currently using a method of contraception. Rates vary dramatically by region, with Central, Western, and East Africa reported at 26.2%, 21.9%, and 19.0%, respectively; Southern, Central, and Western Asia reported as 10.3%, 12.6%, and 14.6%, respectively; and the Caribbean at 17.8%.⁴

What progress has been made in continuing the development of novel male contraceptive methods over the past decades has been supported primarily by nonprofit or government agencies. Hormonal contraception for men has largely been supported by the World Health Organization, Human Reproduction Special Program, and the Population Council, in collaboration with the Contraceptive Development Program (CDP), Contraceptive Clinical Trials Network (CCTN), and the Contraceptive Research Branch (CRB) of the National Institutes of Health (NIH) Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

In the early 2000s, uncertainty about the market for male contraceptives and the lack of guidelines from the major regulatory agencies, including the US Food and Drug Administration (FDA), resulted in a lack of involvement from the pharmaceutical industry. One exception is from the early 2000s when the companies Organon and Schering Pharma worked collaboratively to advance a combined method comprised of an annual implant of progestin and three monthly injections of testosterone (T).⁵ Soon after, individual contraceptive development programs became at risk due to shifting business landscapes. Schering's program ended when Bayer acquired the company in 2007. Organon's work ended by 2009 when Merck bought Schering-Plough, who acquired Organon in 2007.⁶ In the midst of mergers and acquisitions, male contraceptive development programs were the casualty of industry business decisions that determined the combined development, regulatory, market, and other risks were not worth the possible financial return. Some companies redirected part of their research investments to female contraceptives to improve safety and develop user-controlled delivery systems, but the male contraceptive field was largely neglected throughout the early 2000s 's.

The acceptability and demand for male contraception have evolved over the last two decades. In 2005, a multinational survey suggested that about 50% of men across four continents (nine countries) would use a male hormonal contraceptive.⁷ In 2019, a consumer research study conducted by the Male Contraceptive Initiative (MCI) indicated that 82 percent of US men aged 18–44, with partners who experienced an unplanned pregnancy in the past, would be interested in new methods of male contraception. The majority of these men also said they want to share contraceptive responsibility with their partner.⁸ A multinational survey of 19,000 adult men from seven countries (Bangladesh, Democratic Republic of Congo, Côte d'Ivoire, Kenya, Nigeria, Vietnam, and the United States) was co-funded by the Bill & Melinda Gates Foundation and MCI in 2022. This survey showed that men and their

partners are strongly in favor of new forms of male contraception and that women trust their partners to use them responsibly. The study found that 78%–98% of men, depending on the country, would take a male contraceptive pill, with up to 76% of men saying they would use a method within the first 12 months that it was available on the market.²

However, in a world where half of all pregnancies are unintended, it is more important than ever to consider the broader societal implications of a groundbreaking class of therapeutics like male contraceptives, which would offer reproductive autonomy to men but would also present an opportunity for shared contraceptive responsibility among couples. As such, socially minded or otherwise public organizations have largely shouldered the responsibility of male contraceptive research and development, and with it, the role of the field's primary advocates. Here we briefly describe the efforts of these organizations to advocate for and in some cases fund the development of male contraceptives. Please note that we do not detail the contributions of the World Health Organization (WHO) or NIH Eunice Kennedy Shriver NICHD here as their efforts are detailed in other manuscripts published within this same issue.

1 | THE POPULATION COUNCIL

Established in 1952, the Population Council has played a significant role in the development of modern contraceptive methods, including long-acting reversible methods (LARCs), like the TCU 200 intrauterine device introduced in the late 1970s.⁹ With seven reproductive health products developed or brought to market to date (Paragard, Norplant, Jadelle, Progering, Mifeprex, Mirena, and Annovera),¹⁰ the Population Council's track record of success in contraceptive advocacy and product development in the female contraceptive space has led to their co-development of a hormonal contraceptive gel for men containing Nestorone (segesterone acetate) and testosterone (NES/T). Nestorone was first approved for use as a vaginal contraceptive system in 2018 and is currently being developed in other formulations for both women and men. It exhibits high antigonadotropic activity leading to full suppression of spermatogenesis. The first formulation of the gel was created in the laboratories at the Population Council and then transferred to contract manufacturing organizations for scale-up under good manufacturing practice conditions. The combined NES/T male contraceptive product, developed in collaboration with Eunice Kennedy Shriver NICHD CDP, is currently in Phase IIb of the US FDA clinical trial process (NCT03452111).¹¹ Currently, NES/T is the closest drug-based, investigational male contraceptive product to market. In addition to the direct development of the NES/T product, the Population Council has also served an important role in funding the development of seven alpha-methyl-19-nortestosterone (MENT), a promising male contraceptive implant.

The Population Council's mission to support vulnerable populations and gender equity initiatives is a major driver of the organization's efforts in the male contraceptive space. Through active advocacy efforts and collaborations with key stakeholders, the Population Council aims to increase awareness and support for male contraceptive

product development to help men share responsibility for contraceptive decision-making.

2 | THE INTERNATIONAL CONSORTIUM OF MALE CONTRACEPTION

The International Consortium of Male Contraception (ICMC) was founded in 2013 by Dr. David Serfaty, a founding member and Honorary President of the European Society of Contraception and Reproductive Health, and Dr. Regine Sitruk-Ware, a Distinguished Scientist, from the Population Council. Drs. Serfaty and Sitruk-Ware approached stakeholders from across academia, government, and non-government agencies to join forces and follow recommendations from the 10th Summit Meeting on Hormonal Male Contraception, a series of meetings organized by investigators that included government and non-government agencies, as well as representatives from the pharmaceutical industry.¹²

The mission of ICMC is to advocate for the advancement of male contraception and promote collaboration among investigators, government and non-government agencies, industry, and other interested groups. The ICMC was established as an international network to address the medical and socio-cultural aspects of male contraception, current and future hormonal and non-hormonal male contraceptives, and the improvement of surgical methods related to male contraception.

The consortium organizes a biennial Congress as well as scientific sessions and symposia in the programs of major congresses of andrology, gynecology, and endocrinology, with the goal of disseminating the most recent findings on male contraceptive research and development. In 2024, the fourth congress of the ICMC was hosted by the Population Council in New York and attracted a record number of attendees as well as multiple media outlets, thus indicating increasing visibility and public interest in male contraception.

Together, ICMC and the MCI (see below) organized and participated in several meetings and co-signed manifestos with renowned scientists in 2016 and 2018 to urge the pharmaceutical industry and health agencies to become actively involved in the development of male contraceptives. These organizations were also urged to join and collaborate with other stakeholders and advocacy groups, as was successfully done in the development of the first contraceptive pill for women. An appeal was also made to women's health groups and male health advocates to demand active involvement from industry and politicians in supporting male contraceptive research and development.¹³

3 | PARSEMUS FOUNDATION

The Male Contraception Information Project was formed by the Parsemus Foundation in the early 1990s and served as a clearinghouse for information related to new methods of male contraception. Eventually, this project was succeeded by MCI, a nonprofit established with initial support from the Parsemus Foundation.

The Parsemus Foundation also has a history of advocacy and financial support for non-hormonal male contraception. The foundation supported and promoted work on several contraceptive targets as well as allocating funding and efforts toward the development of Vasalgel,¹⁴ a hydrogel material injected into the vas deferens that acts as a LARC for men. The foundation has now partnered with NEXT Life Sciences to bring the Vasalgel product to market as Plan A.¹⁵ In addition to supporting the development of Vasalgel, the Parsemus Foundation has provided advocacy support through sensitizing and educating the public on the need for new methods of male contraception, primarily through web-based educational content.¹⁶

4 | MALE CONTRACEPTIVE INITIATIVE

MCI was founded in 2014 as an organization dedicated to raising awareness and advocating for the need for non-hormonal, reversible male contraceptive methods. MCI's mission is to empower men, and couples, to fully contribute to family planning goals by providing them the resources they need for reproductive autonomy. Since 2017, MCI has received funding from an anonymous donor in support of a grant-making program that, as of 2024, has awarded over \$14 million in funding to product developers, making MCI currently the second-largest funder of male contraceptive development activities behind the NICHD.¹⁷

In addition to grant-making, MCI supports a broad range of advocacy efforts globally including community engagement, policy advocacy, and research community support. Operating as an ecosystem coordinator, MCI works to assess the needs of researchers and the male contraceptive research and development space more broadly. Often these efforts identify the need for supplemental activities or services that may not routinely be included in technical grant applications but are still a critical need to ensure the success of a product (e.g., market research and regulatory strategy guidance).

MCI's communications outreach strategy has also played a vital role in the organization's advocacy efforts. Providing a global audience with accurate information about the status of product development efforts is at the core of these efforts; however, engagement with the general public has identified a need for additional educational information about basic male reproductive function and health. To address this need, the outreach and advocacy strategy was designed with four tiers: educate, inform, inspire, and convert:

1. **Educate:** This base tier provides the foundational understanding of male reproductive biology, primarily focusing on the general public as the target audience. Providing the basic knowledge necessary to understand male biological functioning ensures that the public understands how the next generation of male contraception works. This is accomplished through videos, primers, podcasts, and other informative web-based content, and is primarily designed to sensitize the public to the language and necessary underlying information required to know how male contraception works.

2. Inform: The second tier seeks to build upon the foundational knowledge and share details about male contraceptive methods (how they work, what's in development, etc.). This stage is key to ensuring that there is early adoption of products. By working hand-in-hand with grantees and other product developers, an up-to-date repository of information is broadcast to the public regarding the position of products in development, their characteristics, and their timeline to market. In addition to these passive broadcasts, MCI works to engage the media, acting as a resource for news outlets, documentarians, and other communications partners.
3. Inspire: The third tier makes direct connections between male contraceptive methods and the multitude of societal challenges they can/will address while focusing on mission-driven individuals and organizations. For example, connecting male contraception to the UN Sustainable Development Goals, a globally recognized agenda for achieving peace and prosperity through strategies that "improve health and education, reduce inequality, and spur economic growth",^{18,19} thus demonstrating the broad and meaningful impact that investment in this space can realize.
4. Convert: The final tier focuses on bringing people into the fold to advocate for male contraception, support advocacy organizations, and invest directly in product developers. This has resulted in outreach from a broad audience which includes the general public, youth advocates, funding sources, and potential providers of male contraception such as urologists, family practice providers, and obstetrician-gynecologists.

Youth engagement is also a priority for MCI as the current generation of young people will be the ultimate users of products currently in development. The MCI Youth Advisory Board (YAB) is comprised of young people (aged 16–27) from around the world who work to advocate for male contraception in their local communities and contribute their perspectives to MCI advocacy activities. As future scientists, policymakers, physicians, and reproductive health advocates, YAB members participate in activities including presenting at conferences, leading undergraduate research grants, and conducting community-based advocacy efforts such as peer conversations, workshops, and other means of communicating the needs and priorities of young people with respect to contraception.

5 | CONCLUSION

Advocacy efforts have played a critical role in keeping the hope of male contraceptive methods alive, yet the consistent lesson over the past five decades is that we will not be able to achieve timely success through advocacy alone. Activities such as market research, public education, and promotion efforts are supportive of and indeed may be required for successful market introduction; however, identifying the levels of funding that will be required to take products to market remains a challenge, especially as programs advance to more expensive clinical stages of development.

Male contraceptive research and development is still almost entirely supported through the public and philanthropic sectors, with some advocacy groups listed here serving in dual roles, also acting as primary funders of the space. Although these organizations work closely with one another and with the larger community, even their combined resources are not sufficient to see this robust product pipeline through to market. In recent years, some programs nearing or entering clinical trials have attracted venture capital, indicating a potential opportunity for more funding for the field, but the absence of substantial support from the pharmaceutical industry, which typically has the resources to conduct large-scale clinical trials and bring such products to market, has been a major obstacle.

The potential benefits of novel male contraceptives extend far beyond individual reproductive autonomy, which is in and of itself a noble and worthy goal. Male contraception represents an opportunity to address broader societal challenges such as reducing the number of unintended pregnancies for women and the associated health system and financial burdens and promoting shared contraceptive responsibility for men and women, which ultimately serves to advance gender equity in family planning. Given the potential market size and opportunity, advocates should work to not only change the mindset of profit-minded companies by highlighting the societal benefits of male contraceptives but also work to highlight the untapped demand and global market opportunity.

The persistent efforts and successes of organizations such as WHO, NICHD, the Population Council, ICMC, the Parsemus Foundation, and MCI demonstrate the value and impact of continued investment in male contraceptive product development. Together, their commitment has supported the promise of male methods since the 1970s 's and has led to significant scientific advances. However, the call to action is clear: for novel methods of male contraception to become a reality, there must be a commitment from other philanthropic entities, impact investors, venture capital, or the pharmaceutical sector to provide significant funding to support male contraceptive research and development, particularly through clinical phases, to product introduction, manufacturing, marketing, and distribution. Without this dedication, we risk recession in the progress we have seen over the past decade. It should be noted that for some development programs, this is not merely a concern, but an imminent reality. Only through collective action and substantial investment can we hope to achieve the transformative impact that novel male contraceptives promise.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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