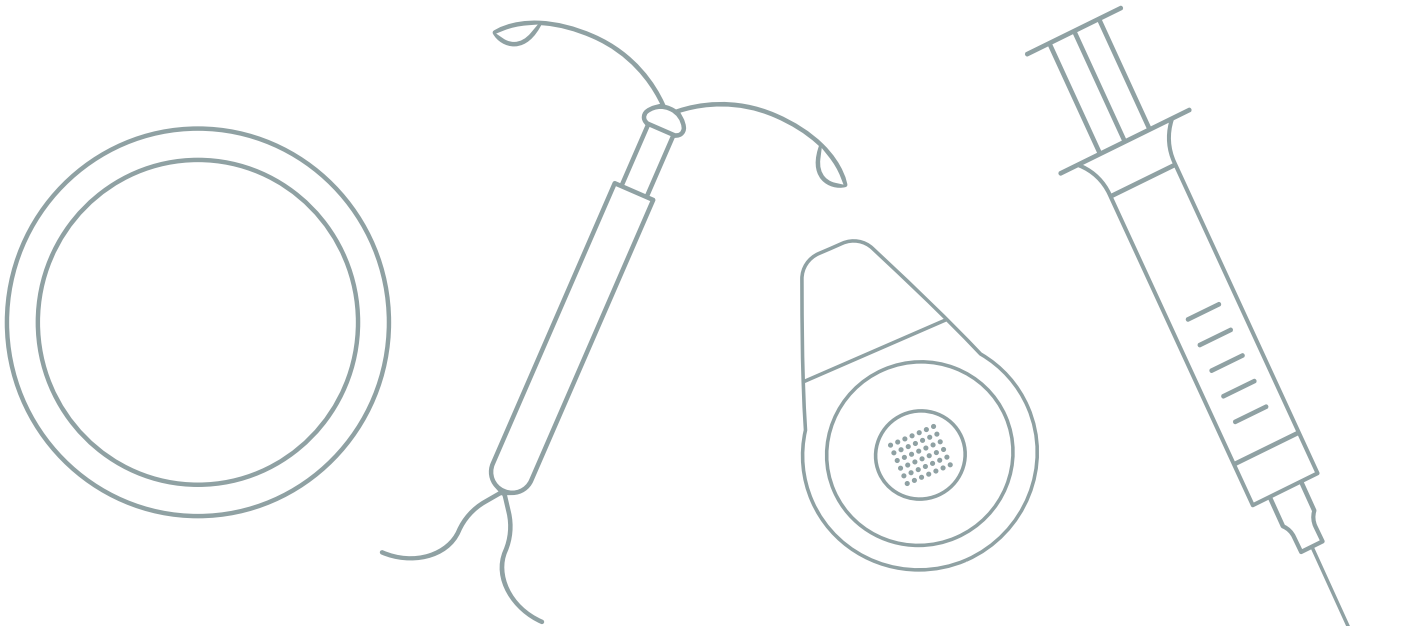
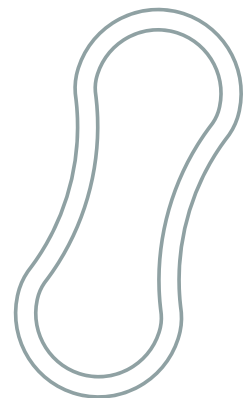
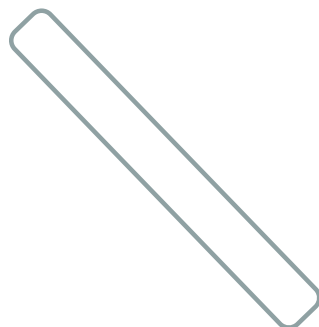
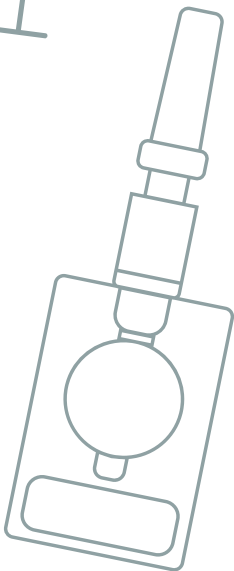
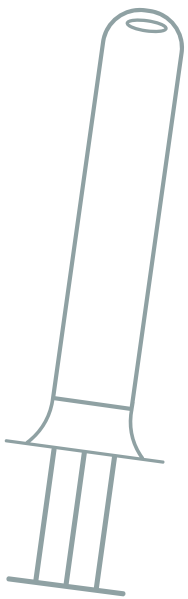




A series of case studies examining global health product innovations and R&D investment landscapes



CONTRACEPTION R&D: BROADENING HORIZONS TO MEET A DIVERSITY OF NEEDS



A need for better contraceptives

Access to modern contraceptives and sexual and reproductive health services is a fundamental human right. It is also critical to advancing health and economic wellbeing. Despite this, comprehensive access to and use of contraceptives remains unrealised, especially in low- and middle-income countries (LMICs) where approximately one-quarter of women of reproductive age still have an unmet need for modern contraception.¹

There are many reasons people may not use contraception, including a perception that they do not need it, opposition to its use, and cost barriers. Real or perceived side-effects, health risks, or inconvenience of available methods are, however, amongst the most common reasons cited by women for not using contraception, despite wanting to space or limit pregnancy.² This indicates a clear need for new methods that better meet the needs of contraceptive users, including those that are user-controlled, less or non-hormonal, or can be used by men, women, or both.³

Contraceptive R&D faces several challenges however, including a perceived low return on investment, regulatory hurdles and litigiousness. As such, the field is under-resourced in comparison to other areas of health and scientific research.^{4,5} Since 2018 Policy Cures Research has been tracking global investment in LMIC-appropriate product R&D for a range of sexual and reproductive health issues – including contraception – as part of the G-FINDER project.⁶ Using this data, this report analyses the funding landscape of contraceptive R&D from 2018 to 2021, assessing the scale and distribution of funding, as well as key funders and trends over time.

Global investment in contraceptive R&D

Global funding for contraception product development has averaged \$129m each year since 2018 – the first year of the G-FINDER sexual and reproductive health survey (Figure 1). Investment has fluctuated, and remained relatively stagnant overall. But it has also declined in recent years. In 2018, funding totalled \$114m, before jumping to \$143m in 2019 (up \$29m, 26%). Funding then fell for two consecutive years: marginally to \$140m in 2020 (down \$2.8m, -2.0% from 2019), then to \$117m in 2021 (down \$24m, -17% from 2020). The latter fall was driven by decreases in investment from several key funders, most noticeably industry, whose investment fell by 42% (down \$16m).

Multipurpose prevention technologies (MPTs) can also include products with contraceptive qualities since they are expressly designed to simultaneously provide protection – in various combinations – against pregnancy, STIs and/or HIV in a single product. However, because MPT R&D is a unique field – and doesn't always include a contraceptive element – we capture R&D funding for MPTs separately. But it is useful and interesting to review the investment portfolio of MPTs that include a contraception indication (abbreviated here to 'cMPTs') alongside the contraceptive-only space, to complete the picture of contraceptive R&D.

1 <https://www.guttmacher.org/report/adding-it-up-investing-in-sexual-reproductive-health-2019>

2 <https://www.guttmacher.org/report/unmet-need-for-contraception-in-developing-countries>

3 We acknowledge and support that gender identity is complex and non-binary. We use the terms 'male' and 'female' end-users or 'men' and 'women' to refer to a person's assigned sex characteristics at birth.

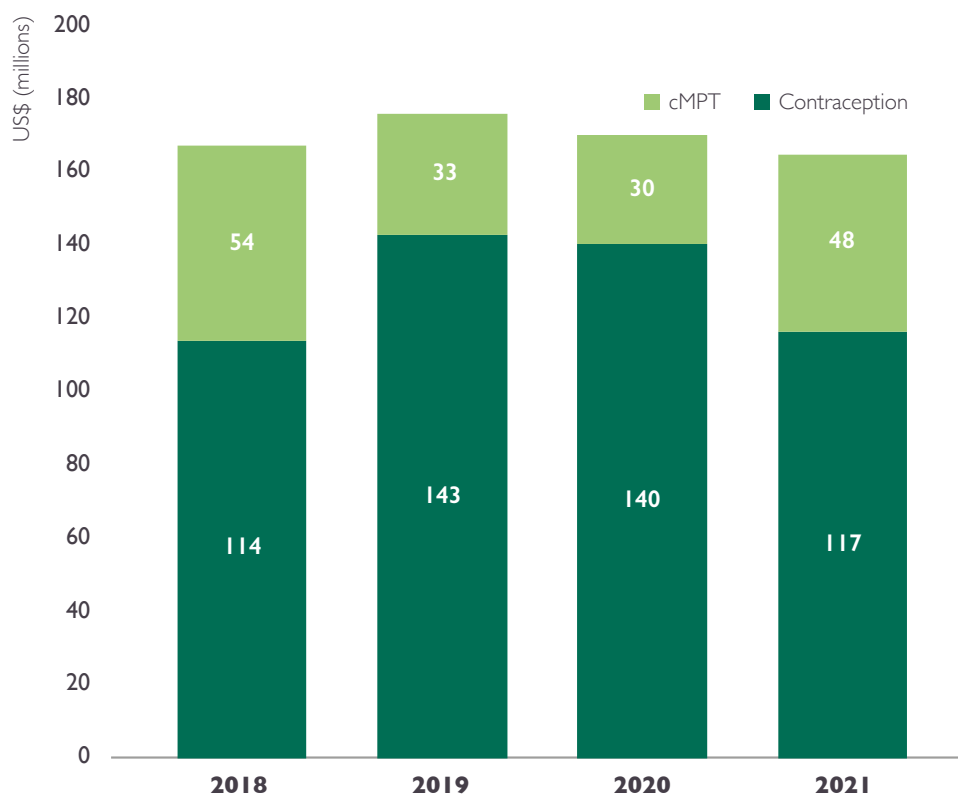
4 <https://www.thelancet.com/commissions/sexual-and-reproductive-health-and-rights>

5 <https://www.policycuresresearch.org/g-finder/>

6 <https://www.policycuresresearch.org/g-finder/>

If funding for cMPT R&D is included, the total contraceptive R&D investment figure for 2021 jumps 41% to \$165m (Figure 1). This ‘topped-up’ picture is similar across previous years, where the inclusion of cMPT funding raises total contraceptive investment by an average of 29%. It also reduces the apparent severity of the 2021 drop considerably, and softens year-on-year fluctuations in total contraception R&D funding.

FIGURE 1 Contraception and cMPT R&D funding 2018-2021



Funding by contraceptive type: where is the focus?

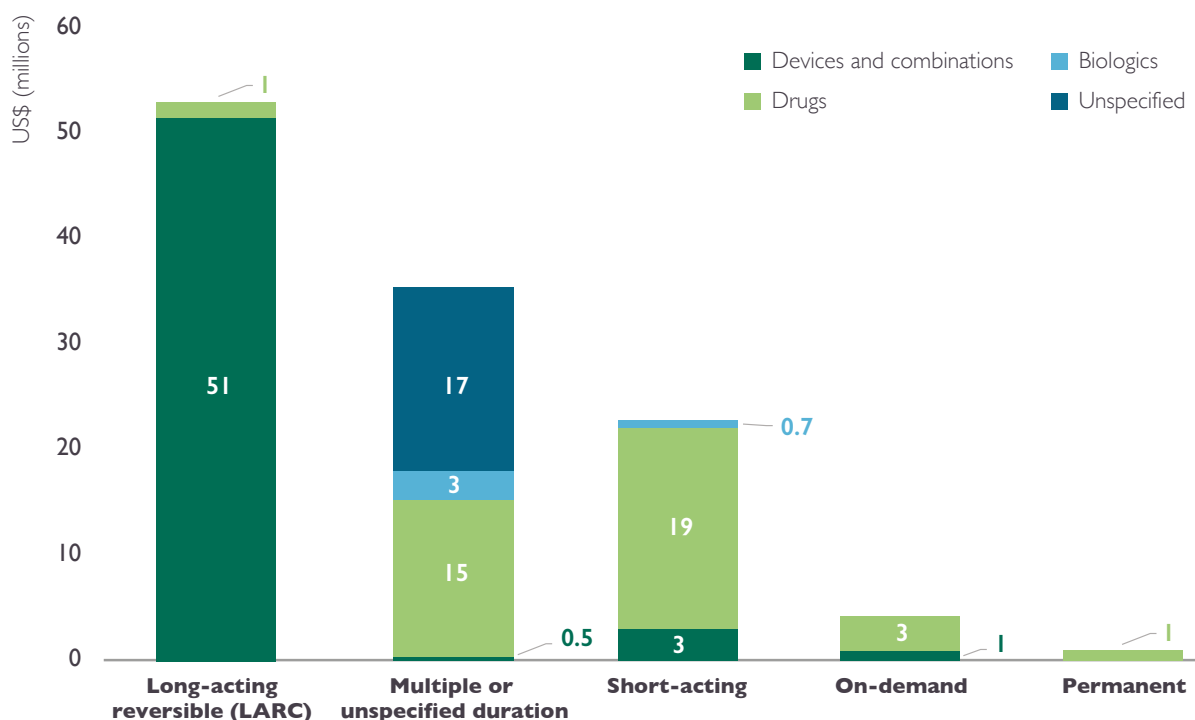
LONG-ACTING REVERSIBLE CONTRACEPTION

In 2021, the most recent year of data, 45% (\$53m) of total contraceptive funding was directed towards long-acting reversible contraception (LARCs), which was almost exclusively invested in devices & combination products⁷ (\$51m, 97% of LARC funding) (Figure 2). This is perhaps unsurprising given the technical need for delivery devices that can support sustained release of contraceptives for long-term prevention of pregnancy. Although this represented the third consecutive decrease in funding since a high of \$62m in 2018, LARCs still overwhelmingly dominate the contraceptive funding landscape, maintaining a position as top-funded method type across all four years since 2018, and marking a general trend towards highly effective, longer-term contraception.

⁷ The ‘device & combination product’ category includes either devices that prevent pregnancy directly (e.g., a copper IUD), or a device in combination with a pharmaceutical element that prevents pregnancy when used together (e.g., a levonorgestrel (hormone-releasing) IUD).

A big fall in industry funding more than accounted for the net drop in LARC funding, with its investment in LARC device & combination products more than halving from \$50m in 2018 to \$23m in 2021 (down \$28m, -54%). This was partially offset by an \$18m rise in funding from the Gates Foundation over the same period, including an \$8.9m funding boost in 2021 for an industry-led user-controlled hormonal implant. Despite falling, industry still remained a major investor in LARC devices & combination R&D however, particularly for entirely new or extended-duration hormone-releasing intrauterine devices (IUDs).

FIGURE 2 Contraception R&D funding by duration of action and product type 2021



CONTRACEPTION WITH MULTIPLE OR UNSPECIFIED DURATIONS

Contraception with multiple or unspecified durations received the next largest share of R&D funding in 2021 (\$36m, 30%), having remained at similar levels for the last three years after initially doubling between 2018 to 2019 to hit \$35m (up \$17m, 98%).

Most of this funding was dedicated to drugs (\$15m, 42% in 2021) and to R&D for multiple or unspecified product types (\$17m, 49% in 2021), which are largely geared towards multi-year, multi-method projects. This includes funding from the Gates Foundation to FHI 360 for the Contraceptive Technology Innovation Initiative and funding from the US NIH to the Contraceptive Clinical Trials Network (CCTN), where multiple methods of contraception are being developed and/or tried under several concurrent projects and trials. It also includes internal funding for Population Council’s Contraceptive Development program, which covers their range of contraceptive technologies currently under development, such as new and next generation intravaginal rings, microarray patches (MAPs), Nestorone injectables and Nestorone/testosterone gel.

Very little of the 2021 investment in contraception with multiple or unspecified duration was dedicated to biologics (\$2.8m, 7.9%), although this did represent 80% of all contraceptive biologics funding in the same year. As a relatively nascent area of R&D, funding for contraceptive biologics has been limited in the last four years and directed mostly towards early-stage research, including testing of Human Contraceptive Antibody (HCA) products.

SHORT-ACTING CONTRACEPTION

In 2021, short-acting contraception received \$23m, or 20% of contraceptive funding. As in previous years – and in contrast to LARC R&D – the vast majority of this was invested in drugs (\$19m, 83%).

However, 2021 also represented a near-halving of funding, as investment fell from a high of \$42m in 2020 (down \$19m, -46%). Nearly all of this was due to a \$17m drop in R&D funding for short-acting drugs, largely attributable to reductions in US NIH funding and a more than halving of Gates Foundation funding. While some of the latter was due to the completion of long-term projects, much of the drop from these two funders is likely due to cyclical fluctuations in funding, with several projects ongoing, multi-year investments.

Although only 14% of 2021 funding (\$3.2m) went to short-acting device & combination products such as intravaginal rings and MAP technology, this excludes an annual average of \$11m invested in – largely short-acting – cMPT device & combination products. Including these would significantly boost the measured investment in short-acting contraception.

ON-DEMAND CONTRACEPTION

On-demand contraception notched just \$4.4m (3.8% of total contraceptive funding) in 2021, roughly in line with its four-year average of \$5.0m.

For the third year running, the majority of 2021 funding for on-demand contraceptive R&D was invested in novel drugs (\$3.4m, 77%), up from just over a third (\$1.6m, 39%) in 2018. Most of this increased funding has come from the US NIH (peaking at \$3.1m, 91% in 2021), largely to Weill Cornell Medicine for the development of an on-demand pharmacological contraceptive that blocks sperm function via inhibition of the (non-hormonal) target ADCY 10.

Again, these figures do not capture the significantly larger investments in a variety of on-demand cMPTs, including vaginal gels, films, and fast-dissolve inserts, which, if included, would add at least another \$32m to on-demand investment in 2021, or an average of at least \$26m each year.

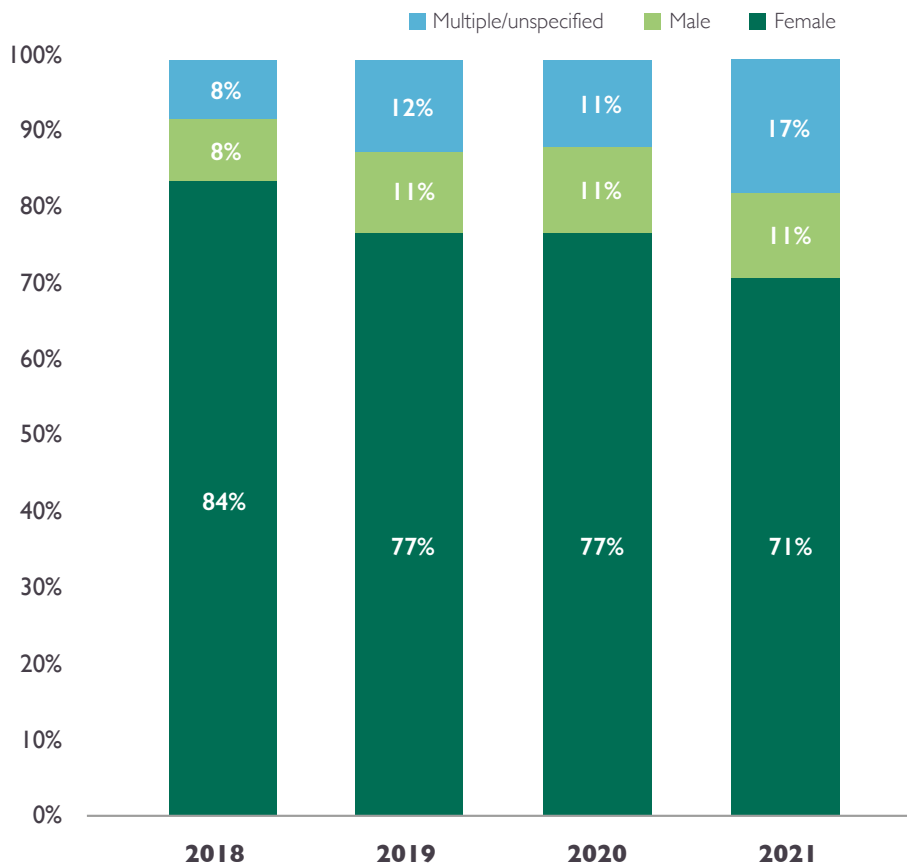
PERMANENT CONTRACEPTION

Novel permanent contraception has consistently represented the lowest share of contraception R&D funding since 2018. It received just \$1.1m (1.0% of contraception funding) in 2021, less than half of the previous year (\$3.2m), though more than the zero-value recorded in 2019. All investment reported has been via a single grant from the Gates Foundation to the Oregon Health and Science University for the development of a fallopian tube-directed sclerotising polidocanol foam.

A shift to more equitable and diverse end-user profiles

While R&D for contraceptive products targeting female end-users continues to dominate the contraceptive landscape, its share of overall funding has gradually declined, from 84% in 2018 to 71% in 2021 (Figure 3). Simultaneously there has been growth in funding specifically earmarked for male end-users, which rose from \$9.5m (8.3% of the total) in 2018 to \$13m (11%) in 2021 (though down slightly from its peak of \$16m in 2020). This was alongside even steeper growth in R&D targeting both male and female or as yet unspecified end-users (\$20m, 17% of the 2021 total). These trends offer promise of a growing interest in diversifying the contraceptive market.

FIGURE 3 Contraception R&D funding by end-user 2018-2021



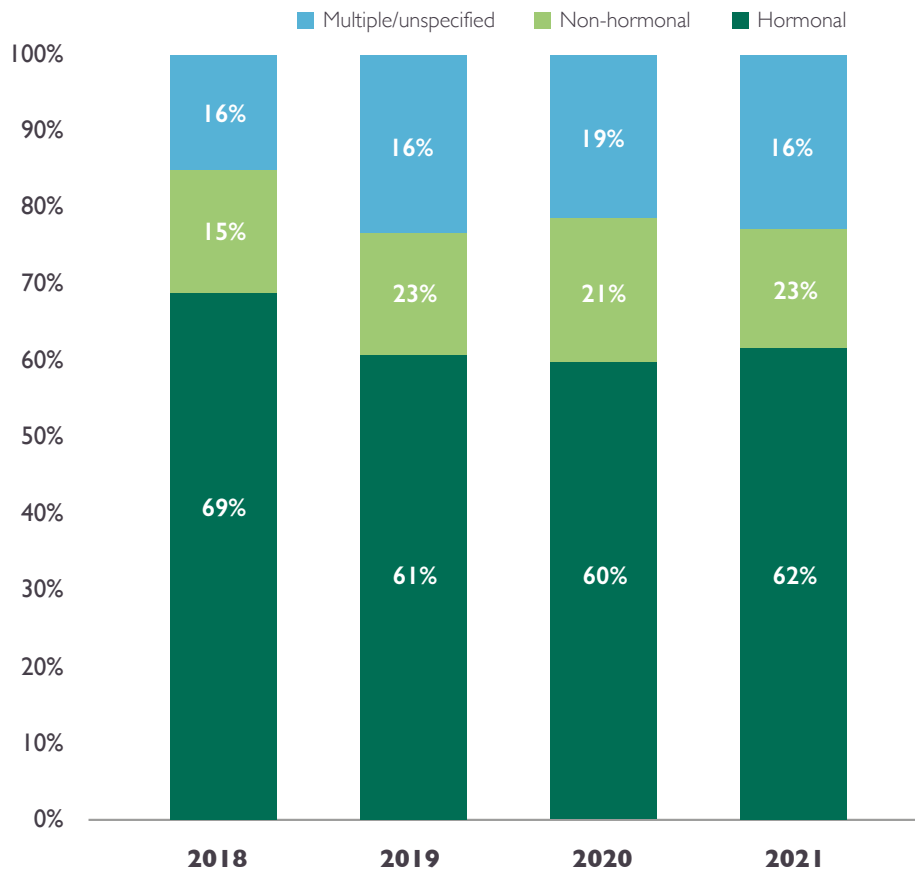
R&D targeting male end-users is primarily focused on short-acting contraception (\$7.4m, 57% of male contraceptive funding in 2021), which is exclusively focused on drugs. This dominance of short-acting methods has remained stable since 2018, albeit dropping from a peak of \$14m (86% of male contraceptive R&D) in 2020, and includes a range of innovative new products such as short-lived topical gels and sprays.

That said, 2021 also saw a half a million-dollar spike in funding to male-focused LARCs (up \$0.6m, 86%). This funding was directed towards first in-human studies of an industry-led vas-occlusive device with support from the Male Contraceptive Initiative. LARCs, together with contraception of multiple and unspecified durations – which more than doubled its funding between 2020 and 2021 to \$4.2m – now collectively account for 42% of male-focused contraception, up from an average of 21% across the preceding three years.

Slowly moving towards less or non-hormonal contraception

Given the well-documented side-effects of most currently available hormonal contraceptives, there has been an increasing demand for R&D into less or non-hormonal options. Despite this, research into hormonal contraception continues to represent 60% or more of investment in contraceptive R&D annually (Figure 4).

FIGURE 4 Contraception R&D funding by hormone profile 2018-2021



In value terms however, funding for hormonal contraceptive R&D has experienced two consecutive years of decline, hitting a low of \$72m in 2021, compared with a previous three-year average of \$83m. In addition, much of this funding is actually focused on R&D towards methods with reduced and ultra-reduced hormone levels, with the express intent of limiting unwanted side-effects while maintaining efficacy, particularly for existing products.

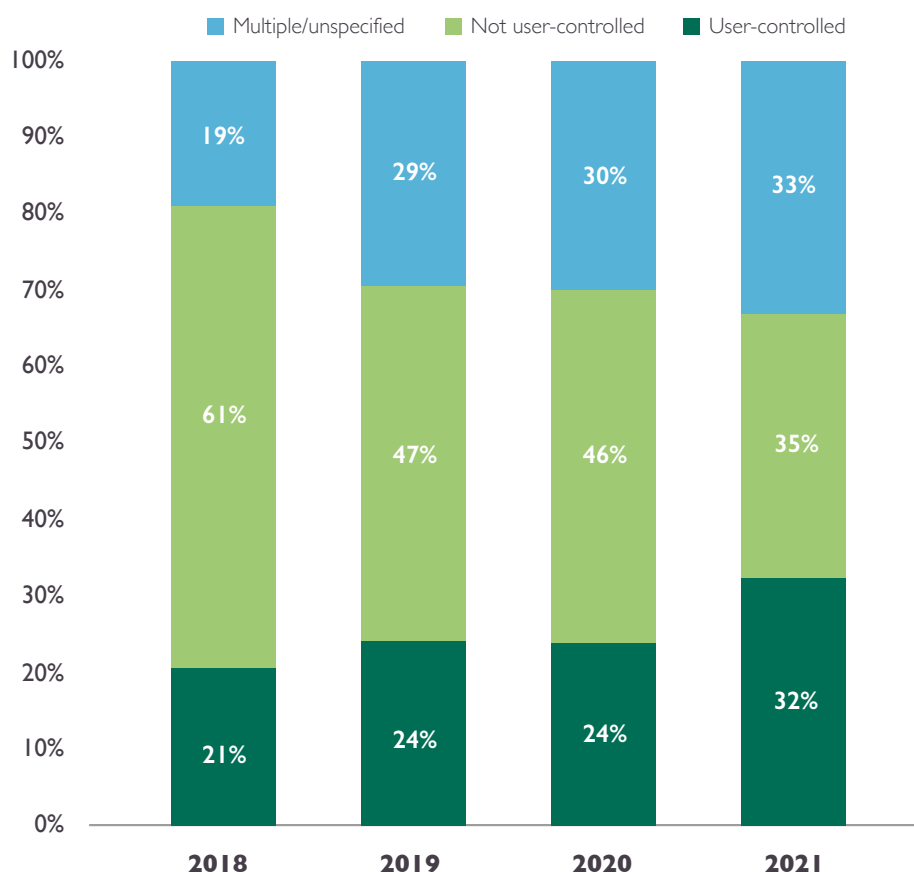
Funding specifically targeting non-hormonal contraception has in the meantime felt some (albeit slight) growth, increasing from \$18m in 2018 to \$26m in 2020, although it dropped back to \$18m in 2021. Together though, there does appear an evolving focus towards less- or non-hormonal contraceptives over the last few years.

Pivoting towards user-controlled contraception

Contraceptive methods that can be controlled by users themselves – when and wherever they want – and which do not require administration by medical professionals is a major impetus for new contraceptive development. Not only do these methods better reflect the actual preferences of contraceptive users, they also reduce some barriers to access – particularly in low-resource settings – by limiting or removing the need for health facility-based prescription or administration.

Encouragingly, the last four years have seen an increasing shift in focus towards this agenda. While non-user-controlled methods continue to receive the largest share of R&D funding, this proportion has decreased substantially over the last four years, declining progressively from a peak of 61% (\$69m) in 2018 to a low of 35% (\$40m) in 2021 (Figure 5).

FIGURE 5 Contraception R&D funding by administration type 2018-2021



Simultaneously, the relative proportion of funding for user-controlled methods has increased, climbing steadily from a low of 21% (\$23m) in 2018, to 32% (\$38m) in 2021. Much of this recent growth was driven by increased funding from the Gates Foundation for a range of projects, including MAP development, post-registration optimisation studies of DMPA-SC (Sayana Press), and industry-led development of a user-controlled implant and an 18-day extended-release oral contraceptive.

Funders are few, and investment is concentrated

Since 2018, 30 different organisations have reported funding contraception R&D. However, the Gates Foundation, the US NIH and industry have consistently represented 85% or more of total investment, occupying the top three funder positions every year (Table 1). In 2021, the Gates Foundation accounted for two-fifths (\$47m, 40%) of contraceptive R&D funding, positioning it as the top funder for the second year in a row. This was followed by the US NIH (\$29m, 24%) and industry (\$23m, 20%). Although industry funding dominated in previous years – at over \$50m in both 2018 and 2019 – it fell sharply to just \$23m in 2021, and was offset by a relatively sustained increase from the Gates Foundation starting in 2019.

While the Gates Foundation is the major supporter of early-stage R&D (averaging 50% of early-stage funding), the US NIH has every year bar one dominated funding for clinical development & post-registration studies (averaging 39% of clinical development funding) – the latter in large part due to support for the CCTN, which is trialling a number of novel female-targeted and male-targeted contraceptive methods across the US. The large proportion of funding that does not specify R&D stage (40% of total) is nearly all from industry (75%), covering undisclosed early and late-stage product development. Ultimately, whatever the order of funding or focus, there is a clear reliance on the interests of a handful of parties to carry contraceptive R&D forward.

TABLE 1 Funders of contraception R&D 2021

Funders	US\$ (millions)				% of total
	2018	2019	2020	2021	2021
Gates Foundation	26	45	49	47	40%
US NIH	26	35	33	29	24%
Aggregate Industry	51	52	39	23	20%
Population Council	3.5	2.9	2.9	10	8.9%
USAID	5.4	4.3	11	4.1	3.5%
Male Contraceptive Initiative (MCI)	0.6	0.8	1.4	1.7	1.4%
EC	0	0.2	1.5	1.2	1.1%
Children's Investment Fund Foundation (CIFF)			0.4	0.4	0.4%
Parsemus Foundation	<0.1	0.2	0.6	0.2	0.1%
Vinnova			<0.1	<0.1	<0.1%
Brazilian FAPESP		<0.1	<0.1	<0.1	<0.1%
TOTAL*	114	143	140	117	100%

*Totals in 2018-2020 reflect total funding for those respective years.

■ No reported funding.

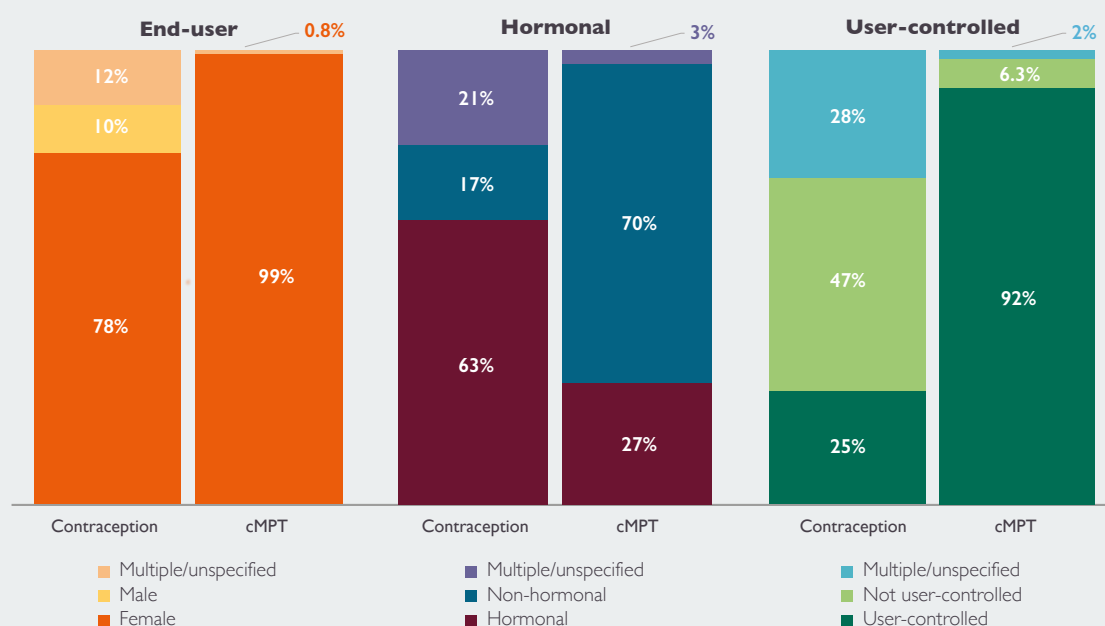
SPOTLIGHT: R&D funding for MPTs with a contraceptive indication

Overall, funding for cMPT R&D consistently represents over 90% of all investment in MPT R&D. Within the last four years, funding specifically for cMPTs fell for two years in a row, from a high of \$54m in 2018 to \$30m in 2020 (down \$24m, -44%), before partially recovering to \$48m in 2021. In 2021, \$30m (61%) of this funding was dedicated to cMPTs providing dual protection against pregnancy and STIs other than HIV, with \$12m (25%) going to cMPTs providing dual protection against pregnancy and HIV. The remaining \$6.5m (14%) went to cMPTs designed to protect against pregnancy, HIV and other STIs.

Across product types, microbicide cMPTs received two thirds (\$32m) of funding in 2021, a jump from the previous year's low of \$14m (up \$18m, 130%) – much of this for the commencement of pivotal late-stage trials of on-demand cMPTs with dual action against STIs and pregnancy. This was followed by device & combination cMPTs (\$12m, 24%) and drugs (\$4.7m, 9.8%), in line with previous years. Biologic cMPTs received no funding in 2021, after receiving a total of \$1.8m in prior years. Biologics employed in combination with devices – such as intravaginal rings – are however under development and included within the device & combination category.

Interestingly, unlike the rest of the contraceptive R&D landscape, nearly all funding for cMPTs over the last four years is for methods designed exclusively for female end-users, with just 1%-2% targeting multiple or unspecified users, and zero for men only (Figure 6). The vast majority is also for user-controlled (92%) and non-hormonal methods (68%). Although a contrast to straight contraceptive R&D, this is not that surprising for MPTs where the focus is for products that expressly address the diverse needs of women and girls.

FIGURE 6 Contraception and cMPT R&D funding by sex, hormone and user-control 2018-2021



Since 2018, there have been 15 reported funders of cMPT R&D. However, as with contraceptive-only R&D, actual funding is concentrated on a small pool. Industry has mostly remained the largest overall funder of cMPT R&D, contributing \$94m over four years – notably from women-centred, socially driven companies. The next highest funder of cMPTs was the US NIH, which has contributed \$40m across the last four years. Together, industry and the NIH accounted for more than 80% of its total funding since 2018. The remainder came from a limited group of funders – including the Gates Foundation, USAID and Children's Investment Fund Foundation – but even outside the top funders, the pool of interested parties is small.

Reflections

High rates of unmet need for contraception and stated dissatisfaction with current methods – particularly in LMICs⁸ – translates to an unequivocal need for new and better contraceptive methods. In reality, however, contraceptive R&D operates in a challenging space. A tricky regulatory environment (where products are developed for healthy people), heightened litigious potential, and perceived low returns make it an unattractive proposition for most investors. Indeed, this data shows that overall levels of funding for contraceptive R&D have largely stagnated since 2018, and have in fact declined over the last few years. They are also orders of magnitude lower than funding for other sexual and reproductive health issues: LMIC-relevant HIV/AIDS R&D, for example, sat at \$1,466m in 2021.⁹ Even more soberingly, more than twice as much (\$243m) was reported in R&D expenditure for cosmetics and personal care in 2021, from just one global company.¹⁰

Despite this, the data also shows some encouraging trends, particularly towards more human-centred, user-centric design in contraceptive innovation. A proportional fall in R&D investment for hormonal methods (from 69% to 62%) and non-user-controlled methods (from 61% to 35%) over the last four years is a positive move, and gives hope that an increasingly client-focused research agenda will deliver contraceptive products that meet the evolving needs and preferences of users. Likewise, a drop in the proportion of total funding geared towards female-only contraceptives (84% to 71%) within the same period reflects a move towards more gender-equitable healthcare, and acknowledges that a broader range of contraceptive options for men, women, or both, are needed to close gaps on unmet need.

On the other hand, these next-generation contraceptives remain at very early stages of development. While 38% of all contraceptive R&D funding over the past four years has been for early-stage research (a seemingly small slice, but still greater than just 23% for clinical development & post-registration studies, with the rest unspecified), this share increases when applied specifically to contraceptive R&D that is non-hormonal, user-controlled or male-only, rising to 91%, 58% and 68% respectively. Clearly, it will be some time before these types of contraceptive methods are in the hands of those that want and need them most.

Probably most concerning, however, is the dominance of the funding space by just a handful of players. Just under 90% of all funding between 2018 and 2021 came from the US NIH, the Gates Foundation and industry, nearly all of the latter from large multinational companies. In fact, less than 3% comes from small to medium-sized pharmaceutical and biotech companies, and there is effectively zero support from the public sector in LMICs or from public sector multilaterals. This begets a serious vulnerability to the interests, priorities and budgets of just a few parties, across limited sectors. New methods that better suit people's needs will undoubtedly play a role in the achievement of global sexual and reproductive health and contraception commitments¹¹ and targets¹², and if these are to meet their 2030 goals, the contraceptive R&D landscape will need continued and greater support from both existing and new funders, from all sectors, to drive progress forward.

⁸ <https://www.guttmacher.org/report/unmet-need-for-contraception-in-developing-countries>

⁹ <https://www.policycuresresearch.org/analysis/2022-G-FINDER-Neglected-Disease-report>

¹⁰ <https://www.statista.com/statistics/609083/randd-expenditure-of-estee-lauder-worldwide>

¹¹ <https://fp2030.org/FP2030-commitment-makers>

¹² <https://sdgs.un.org/goals/goal3>; <https://sdgs.un.org/goals/goal5>

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Published by Policy Cures Research
March 2023