

POLICY CURES RESEARCH.

SEXUAL AND REPRODUCTIVE HEALTH RESEARCH AND DEVELOPMENT: **BEYOND SPILLOVERS**

POLICY CURES RESEARCH

ACKNOWLEDGEMENTS

This is the third report providing a consolidated picture of investment in research & development for reproductive, sexual, maternal or women's health issues – with a focus on products and technologies applicable to low- and middle-income country settings – produced by Policy Cures Research through the G-FINDER project. We are very grateful to all of the survey participants who have contributed to this effort. With their commitment, we have been able to continue to provide accurate, up-to-date financial information on research and development for sexual & reproductive health issues. The patience and engagement of the participating government and multilateral agencies, academic and research institutions, product development partnerships, philanthropic institutions and pharmaceutical and biotechnology companies have made this project possible.

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INTRODUCTION

Sexual and reproductive health: A pivotal moment

Sexual and reproductive health covers a variety of needs and issues spanning from adolescence (including menarche), through the reproductive years (including sexual health, reproductive cancers, pre-pregnancy, pregnancy and birth), and into mature or post-reproductive life (including menopause).

The right to good sexual and reproductive health (SRH) is enshrined in numerous international and national agreements, including twice within the 2030 Agenda for Sustainable <u>Development</u>, and is widely recognised as a pressing global health <u>issue</u>. Despite this, progress has been slow globally in meeting the SRH needs of people, particularly those in low- and middle-income countries (LMICs), and especially those of women and <u>girls</u>*. In many instances, this is due to weak health systems, political and cultural opposition, or limited access to information. In others however, research and development (R&D) gaps remain a problem. LMIC-predominant issues generally suffer from an insufficient market to attract commercial R&D. On top of this, SRH issues – while not exclusive to women and girls – suffer from pervasive gender-related biases in biomedical research, which play a key role in market failures for SRH products and technologies.

In fact, despite a period of 30 years since the US NIH Revitalization Act mandated inclusion of women and minorities in federally funded clinical research, biological sex differences and gender dimensions in R&D have continued to be sidelined, with implications not only for proper representation in clinical trials, and for meaningful sex disaggregation in the interpretation of results, but also for research prioritisation from the get-go. As a result, many biomedical products are either sub-optimal for use amongst half the population, or entirely lacking.

This third iteration of the G-FINDER report on SRH issues comes amidst a recent, collective surge of interest and attention to the 'gender data gap' and prioritisation of 'women's health' R&D. Women's health includes a wide range of issues (such as infectious diseases, non-communicable diseases, chronic conditions) that affect women and girls exclusively, disproportionately, or differently. The scope of this G-FINDER report includes **R&D for SRH products or technologies that are relevant to, fill gaps and are appropriate for people in LMIC contexts – particularly women and girls – where the need is greatest.** As such, its intersection with women's health R&D is significant and growing.

To shift the needle in both women's health and SRH, there is a critical need for relevant and timely data and analysis to inform policy agendas, budgets, and priority setting. The purpose of this report is, in service of all these goals, to capture details on investments in SRH R&D, as well as share information and resources on related product pipeline landscapes being researched by Policy Cures Research and other global health R&D organisations.

Table 1. G-FINDER sexual and reproductive health issues, products and technologies

Healthissue			•	Basic reser	prugs	Microbicide	is Vaccines	Biologics	Diagnostic	evices & orbination
Sexually transmitt	Gonorrhoea			Restricted	Restricted	~	~	~	~	-
infections (STIs)	Herpes simp	olex virus 2 (HSV-2)		Restricted	~	~	~	~	~	-
	Chlamydia			Restricted	-	~	~	~	~	-
	Syphilis			Restricted	Restricted	~	~	~	Restricted	-
	Human T-lyr	mphotropic virus 1 (H	TLV-1)	~	~	~	~	~	~	-
	Hepatitis B			Restricted	Restricted	-	-	Restricted	~	-
	Multiple STIs*			Restricted	Restricted [†]	-~	~	~	~	-
	Other STIs			Restricted	Restricted	~	~	~	~	-
HIV/AIDS			Restricted	Restricted	~	~	Restricted	~	-	
Human papillomavirus (HPV) and related cervical cancer			Restricted	Restricted	~	Restricted	~	✓**	✓ ^{††}	
Contraception	Long-acting	reversible (LARC) [≈]		-	~	-	\checkmark	~	-	~
	Short-acting) ^{\$\$}		-	~	-	\checkmark	~	-	~
	On-demand	***		-	~	-	-	~	-	~
	Permanent ⁺	t†		-	~	-	-	-	-	~
	Multiple or u	inspecified duration		-	~	-	~	~	-	~
Multipurpose prev	vention technologie	s (MPTs)		-	~	~	-	~	-	~
Preeclampsia & ec	clampsia			Restricted	Restricted	-	-	~	~	-
Postpartum haem	orrhage (PPH)			-	~	-	-	-	-	Restricted
Inve	estment applicable		<u> </u>	disease,	or to mor	re than on	e global	health ar	ea#	
Vaccine-related platform technologies	Pl Drug-related platform technologies	Adjuvants & immunomodulators	General platforr	diagnostic m & multi- diagnostics Biologics-related platform technologies		s		nding of an organisatic	n	
~	~	~		~		~			~	

denotes a category where a disease or product is included in the survey

Restricted denotes a category where only some investments are eligible

The G-FINDER project covers three global health areas: neglected diseases, emerging infectious diseases, and sexual & reproductive health issues. Please note HIV, Hepatitis B, and general diagnostic platforms & multi-disease diagnostics (except for multiple STIs) are captured through the G-FINDER neglected disease survey.

Multiple STIs: two or more STIs, including but not limited to chlamydia, gonorrhoea, syphilis, and HIV

- Includes therapeutic drugs for the treatment of two or more STIs. Preventive drugs that address two or more STIs are captured under the MPT section (MPTs > drugs)
- Microbicides for the treatment of two or more STIs are in scope, but are captured under the MPT section (MPTs > microbicides) ş
- Other STIs: STIs that disproportionately affect populations in LMICs, including but not limited to trichomoniasis, chancroid, Mycoplasma genitalium, lymphogranuloma venereum, and granuloma inguinale (donovanosis)
- ** Includes both diagnostics for HPV infection and diagnostics for cervical lesions
- ^{††} Includes devices that either clear HPV infection or treat cervical lesions
- LARC: long-acting reversible contraceptives that work for \geq 1 year (e.g. implants; IUDs)
- Short-acting: methods that work for < 1 year but do not require action at the time of intercourse (e.g. injectable hormones)</p> *** On-demand: methods that require action at the time of intercourse or pericoitally for efficacy (e.g. emergency contraception)

*** Permanent: irreversible methods

Background to the G-FINDER sexual and reproductive health project

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into R&D of new products to prevent, diagnose, control or cure neglected diseases in developing countries, making it the gold standard in tracking and reporting global funding for neglected disease R&D.

The G-FINDER project first collected data on global funding for sexual & reproductive health (SRH) R&D as a one-off report covering funding from the 2013 financial year ('FY2013'). We began gathering SRH data on an ongoing basis in 2018, culminating in the 2020 release of our previous report, *Understanding the Spectrum*, which covered FY2018 funding data. This report – overall the third iteration of a G-FINDER report covering sexual and reproductive health issues – revisits those findings from FY2018, with the addition of three further years of data from FY2019 to FY2021.

The scope of this report

In line with the G-FINDER project's primary focus on areas which are neglected due to market failure, **this report is not intended to capture investment in the entire global spectrum of SRH R&D**. It is focused specifically on the SRH needs of people in low- and middle-income countries (LMICs), particularly women and girls, that are not being met because of a lack of appropriate products or technologies, or the absence of fundamental scientific knowledge.

OUR FIGURES INCLUDE BOTH 'LMIC-TARGETED' AND 'LMIC-APPROPRIATE' R&D

For some SRH R&D investments, the product or technology is clearly only intended and suitable for high-income country (HIC) markets. For example, overly 'high-tech' innovations in diagnostics that would require deep cold storage, complex laboratories and comprehensive public programs to operate would only be feasible in high-resource HIC settings. R&D investments like these are excluded from this report since they are driven by, targeted at and currently useful only to people in HICs.

On the other hand, some investments are specifically aimed at LMIC needs. These target people living in LMICs who suffer disproportionately from unintended pregnancies, death and disability during pregnancy and childbirth, sexually transmitted infections (STIs), and other SRH issues. This includes research aimed at developing new or adapted products that are heat stable or 'low-tech', for example, inhaled rather than intravenous oxytocin for the treatment of postpartum haemorrhage (PPH); or at measuring or improving the safety and efficacy of products in LMIC populations. These investments clearly target the needs of people in LMICs and are therefore included in this report.

However, while people in HICs and LMICs can and do have different SRH needs, there are also particular needs that span low-, middle- and high-income settings. For example, women and girls in HICs have similar desires to women and girls in LMICs for a broad choice of contraceptives, including those that are affordable, safe, easy-to-use and have minimal side effects. In cases like these, with obvious dual markets, it is not easy to disentangle R&D that may *benefit* populations in LMICs from R&D that is *explicitly designed* for populations in LMICs. Some SRH products developed initially with HIC markets in mind, like some contraceptives, may also be applicable to people in LMICs. Recognising this shared market, investments like these are also included in the report.

To determine if a R&D investment is in scope or not, this report therefore required all investments – regardless of intended market – to answer yes to an overarching filter:

▶ Is this product appropriate to and suitable for use in LMIC contexts?

Examples of 'LMIC-appropriate' products include (but are not limited to) those that are heat stable, easy-to-use, or which do not require a skilled professional to administer. Although cost is an acknowledged practical barrier to access for many health products, it was not used as a limiting criterion to determine LMIC-appropriate R&D.

This approach was validated with advice from an Expert Advisory Group convened at the start of the project in 2018.

HOW WE IDENTIFY SRH R&D GAPS IN LMIC CONTEXTS

Based on this overarching principle, with the help of our Expert Advisory Group we reviewed a range of SRH issues, and filtered them based on two criteria:

- ▶ Is the issue a significant health issue affecting people in LMICs?
- Is there a need for new products? (i.e. there is no existing product, or improved or additional products are needed to meet the needs of people in LMICs)

The resulting scope of SRH issues, products and technologies included is presented in Table 2.

Although basic research and all relevant product types – drugs, microbicides, vaccines, biologics, diagnostics, and devices & combinations – were considered for inclusion in relation to every SRH issue, not all were included in the scope for all issues, and some were included only with restrictions. For example, syphilis diagnostics were excluded, because cheap, easy-to-use, point-of-care diagnostics already exist and are appropriate for use in low- and middle-income settings. Syphilis drugs, on the other hand, *were* included; but only those that target latent, tertiary, maternal or congenital syphilis, since drugs to treat early-stage syphilis are effective and readily available.

Along with core funding disbursed to SRH-focused R&D organisations, our scope also includes platform technologies – technologies which can potentially be applied to a range of health issues but have not yet been attached to a specific product for a specific issue or disease, specifically, in the case of SRH, adjuvants and immunomodulators, and delivery technologies for drugs or vaccines. Both these categories include funding aimed at more than one of the overarching global health areas (GHAs) covered by the G-FINDER survey – neglected disease, emerging infectious disease and SRH – provided it was judged to have significant potential application to SRH as well.

A comprehensive explanation of all inclusions, exclusions and restrictions is outlined in the detailed G-FINDER SRH R&D scope document, which is available online at <u>www.policycuresresearch.org/g-finder</u>.

Table 2. Sexual and reproductive health issue and product R&D funding 2021 (US\$ millions)

atth issue or roduct	Basic resear	ch	unes.	aics,	hicides	ostics	wices & ions	cified	
odue	Basicie	orugs ,	laccines F	Biologics	Nicrobicides	biagnos D	evices & ions	nspecified	iotal
Sexually transmitted infections (STIs)	30.66	14.53	49.85	39.72	0.24	10.74		0.58	146.3
Gonorrhoea	5.29	10.71	35.94	2.42	0.24	3.98		0.11	58.6
Herpes simplex virus 2 (HSV-2)	2.08	1.14	3.16	36.26	-	0.03		0.46	43.1
Chlamydia	10.34		7.34	-	-	1.43		-	19.
Syphilis	4.46	0.35	2.79	0.54	-	0.33		-	8.4
Human T-lymphotropic virus 1 (HTLV-1)	5.43	0.79	0.62	0.50	-	-		-	7.:
Multiple STIs	2.86	0.19	-	-	^	2.84		0.01	5.9
Other STIs	0.20	1.34	-	-	-	2.14		-	3.
Human papillomavirus (HPV) and related cervical cancer	13.51	0.92	64.73	18.78	0.53	27.02	14.16	2.81	142.
Contraception		39.66	-	3.51			56.21	17.40	116.
Long-acting reversible (LARC)		1.43	-	-			51.48	-	52
Short-acting		18.94	-	0.69			3.20	-	22.
On-demand		3.37		-			1.01	-	4.
Permanent		1.14					-	-	1
Multiple or unspecified duration		14.78	-	2.82			0.52	17.40	35.
Nultipurpose prevention technologies MPTs)		4.72		-	32.40		12.24	0.51	49.
Preeclampsia & eclampsia	14.10	4.88		1.52		0.19		0.04	20
Postpartum haemorrhage (PPH)		0.91					-	-	0
Platform technologies									92.
Vaccine-related platform technologies									47
Drug-related platform technologies									14
Adjuvants and immunomodulators									13.
General diagnostic platforms & multi- disease diagnostics									10.
Biologics-related platform technologies									6.
Core funding									11.
Other R&D									11.
Fotal SRH R&D funding									593.

No reported funding
 Category not included in G-FINDER
 Microbicides for the treatment of two or more STIs are in scope, but are captured under multipurpose prevention technologies

DISEASES WITH SRH ELEMENTS CAPTURED IN OUR OTHER REPORTS ARE NOT INCLUDED

In addition to being primarily or potentially sexually transmitted, HIV/AIDS, hepatitis B, and hepatitis C are also defined by G-FINDER as neglected diseases, with their R&D funding captured in the G-FINDER neglected disease report. Other diseases, such as schistosomiasis, can have a significant reproductive dimension (i.e., genital schistosomiasis), but are also considered primarily neglected diseases and captured in the corresponding G-FINDER report. Likewise Zika – a primarily vector-borne disease which can also be transmitted sexually – is included in our report on emerging infectious disease R&D funding. To avoid double counting, funding for these diseases is *not* included in this report. This means that the overall totals reported here should not be characterised as the global total for *all* G-FINDER-relevant SRH R&D, since some relevant funding is instead captured in our other reports.

FUNDING FOR SRH ALONGSIDE NEGLECTED OR EPIDEMIC DISEASE IS INCLUDED

Some funders reported investments targeted at SRH issues alongside neglected diseases and/ or emerging infectious diseases. These included platform technologies where the product could feasibly be used for SRH as well as neglected and/or emerging infectious diseases, such as general drug or vaccine delivery platforms. These are included in this report.

We also capture some investments that are applicable to more than one SRH issue, such as novel contraceptives also designed to provide protection against one or more STIs. Where the intended outcome of such R&D is a single 'multi-purpose technology' (MPT) its funding is treated as being for MPTs and not included in the totals for contraception or STIs.

Please refer to the G-FINDER SRH and G-FINDER neglected disease survey R&D scope documents for scope detail, available at www.policycuresresearch.org/g-finder.

TYPES OF RESEARCH INCLUDED

Funding included in this report covers the spectrum from basic research to post-registration studies of new products. We break these activities down into the broad categories of basic & early-stage research, and clinical or field development & post-registration studies.

- Basic & early-stage research, including:
 - Basic research
 - · Discovery and pre-clinical development
- Clinical development & post-registration studies, including:
 - · Baseline epidemiology in preparation for product trials
 - Clinical development
 - Post-registration studies of new products, including Phase IV/pharmacovigilance, and operational research for diagnostics and devices & combinations

The purpose of this report is to track and analyse global investment in R&D of new products and technologies to address SRH issues disproportionately affecting people in LMICs. **The report does not, and is not intended to, capture investment in the entire spectrum of SRH research**. Many research activities that are extremely important for global health are excluded because they are not related to the development of new tools; this includes health systems and operations/implementation research (for example, research into health systems or policy issues, or research into the programmatic delivery of non-product interventions, or existing health technologies), and sociological, behavioural and epidemiological research not related to the development of new health technologies.

General therapies such as painkillers or nutritional supplements were also excluded, as these investments cannot be ring-fenced to SRH. Investment that is not research-related was similarly excluded. Although we recognise the vital importance of activities such as health program delivery, advocacy, routine disease surveillance programs, community education and general capacity building in addressing SRH issues, investment in these activities falls outside the scope of this report.

We have conducted significant retrospective data mining following the publication of the previous edition of this report in 2020, leading to significant improvements to the 2018 funding totals reported there. We also began excluding funding for HIV and hepatitis from the reported SRH totals, meaning the overall figures we quote here are much lower than those provided in 2020.

We also made some changes to the inclusions in our survey scope starting in 2019, which have not been retrospectively applied to the 2018 data – leading to some minor artefactual growth between 2018 and 2019. The newly included categories and other changes were: microbicides as a distinct product category (preciously captured under 'drugs') across issues; devices for HPV; biologics for preeclampsia; biologics and vaccines for contraception; biologics for MPTs; and an expansion of preeclampsia drug restrictions (see scope document).

The scope of this report, and that of the 2020 edition, differ significantly from that of the earlier report on reproductive health R&D we published in 2014, meaning figures in the latter are not meaningfully comparable to the ones included here, and are therefore not included in this report.

INFLATION ADJUSTMENTS AND AGGREGATION OF INDUSTRY DATA

Funding data is adjusted for inflation and converted to US dollars (US\$) to eliminate artefactual effects caused by inflation and exchange rate fluctuations.

All pharmaceutical industry funding data is aggregated and anonymised for confidentiality purposes, with a distinction made between multinational pharmaceutical companies ('MNCs') and small pharmaceutical and biotechnology firms ('SMEs').

USE OF ESTIMATED FUNDING DATA

The Indian ICMR has been a consistent provider of SRH core funding, investing an average of \$7m yearly in intramural funding to their Reproductive Health Institute. However, in the (temporary) absence of ICMR funding data for 2021, and to avoid showing an artefactual fall, we have imputed an estimate for its intramural core funding for that year only based on the average nominal value of funding over the preceding three years. Subsequent reports will be updated on the basis of the true 2021 ICMR funding value once it becomes available.

SUPPLEMENTARY MATERIAL

A detailed methodology is available at: https://www.policycuresresearch.org/analysis

All of the data behind G-FINDER SRH report is available through the online data portal: https://gfinderdata.policycuresresearch.org

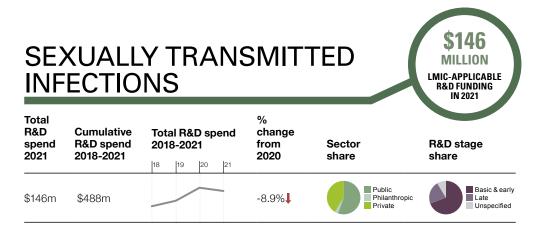
Table 3. R&D funding by condition 2018-2021^

realth issue or P&D area	US\$ (million	15]	C	umulative tote	
Rau	2018	2019	2020	2021	
Sexually transmitted infections (STIs)	78	103	161	146	488
Human papillomavirus (HPV) and related cervical cancer	90	103	121	142	456
Contraception	114	144	141	117	516
Multipurpose prevention technologies (MPTs)	56	37	33	50	176
Preeclampsia & eclampsia	18	35	28	21	101
Postpartum haemorrhage (PPH)	7.5	5.6	2.1	0.9	16
Platform technologies	24	51	73	93	241
Vaccine-related platform technologies	9.0	24	40	47	120
Drug-related platform technologies	1.4	4.7	7.3	15	28
Adjuvants and immunomodulators	14	22	18	14	68
General diagnostic platforms & multi-disease diagnostics	<0.1	0.6	7.2	11	18
Biologics-related platform technologies				6.2	6.2
Core funding	11	39	14	12	76
Other R&D	1.3	8.6	11	12	33
Total SRH R&D funding	401	525	584	594	2,103

Biologics-related platform technologies were moved to a separate category in 2021.

Please note that some of the health issues listed are actually groups of conditions, such as the sexually transmitted infections (STIs). This reflects common practice and also the shared nature of research in some areas.

- No reported funding



Global funding for LMIC-relevant sexually transmitted infections (STIs) R&D totalled \$488m over the four years from 2018 to 2021. This figure excludes HIV, hepatitis B, and other potentially sexually transmitted infections such as hepatitis C and Zika, which are included in our other reports – see box overleaf.

Funding for STIs has nearly doubled since 2018, rising by 86% to reach \$146m by 2021. This is mostly thanks to an ongoing increase in industry funding (including a \$14m jump in 2021 alone), combined with consistent support from the US NIH. The NIH has remained the largest single funder of STI R&D every year, providing a total of \$253m.

The distribution of funding across the STIs included in this report has remained relatively constant, with gonorrhoea consistently receiving by far the most funding (\$59m in 2021), followed every year by herpes simplex virus 2 (HSV-2) (\$43m in 2021) and chlamydia (\$19m in 2021). The remaining two individual STIs captured through G-FINDER – syphilis (\$8.5m) and HTLV-1 (\$7.3m) – each received significantly less funding each year. Funding for multiple STIs (\$5.9m) has typically been in line with these two smaller diseases, while the Other STIs category (\$3.7m) usually receives the smallest share of STI funding.

Antimicrobial resistance (AMR) poses a major threat to effective treatment of STIs, with increasing emergence of resistant strains no longer susceptible to existing antibiotics. However, the novel drug pipeline is largely empty or immature. Gonorrhoea is the only STI with drug candidates in late-stage trials. Preventive and therapeutic vaccines are therefore also urgently required. Currently however, there are no approved vaccines for syphilis, gonorrhoea, HTLV-1, HSV-2 or chlamydia. Development of vaccines to clear or prevent infection with HSV-2 is advancing despite setbacks, while several novel preclinical candidates for gonorrhoea is also ongoing, alongside recruitment for Phase I trials of an entirely new gonorrhoea vaccine from <u>GSK</u>. Diagnostics to identify AMR and guide treatment are also needed. Diagnosis still relies on costly laboratory testing: low-cost rapid point-of-care tests are needed for all STIs except for <u>syphilis</u>. There is also a need for tests that can simultaneously diagnose co-existing <u>STIs</u>.



Unmet R&D need

The novel antibiotic <u>zoliflodacin</u> for gonorrhoea, is in Phase III clinical development through a partnership between <u>GARDP</u> and Entasis Therapeutics (now a subsidiary of Innoviva), with topline results expected end of 2023. A second novel antibiotic, GSK's <u>gepotidacin</u>, is also in Phase III trials expected to conclude in October 2023.

Table 4. Sexually transmitted infection R&D funding 2021 (US\$ millions)

Healthissue	Basic rese	arch	Jaccines	Biologics	Nicrobicid	es Diagnostic	Jnspecifie	id iotal o	10
Gonorrhoea	5.3	11	36	2.4	0.2	4.0	0.1	59	40
Herpes simplex virus 2 (HSV-2)	2.1	1.1	3.2	36	-	<0.1	0.5	43	29
Chlamydia	10		7.3	-	-	1.4	-	19	13
Syphilis	4.5	0.4	2.8	0.5	-	0.3	-	8.5	5.8
Human T-lymphotropic virus 1 (HTLV-1)	5.4	0.8	0.6	0.5	-	-	-	7.3	5.0
Multiple STIs	2.9	0.2	-	-	^	2.8	<0.1	5.9	4.0
Other STIs	0.2	1.3	-	-	-	2.1	-	3.7	2.5
Total	31	15	50	40	0.2	11	0.6	146	100

^ Microbicides for the treatment of two or more STIs are in scope, but are captured under multipurpose prevention technologies.

Category not included in G-FINDER
 No reported funding

Reported funding for **gonorrhoea** peaked in 2020, jumping 77% from \$41m in 2019 to \$73m in 2020, spurred on by industry's commencement of early-stage vaccine R&D. In 2018, the \$31m in total gonorrhoea R&D funding was shared near equally between basic research (\$8.2m, 26%), drugs (\$7.9m, 25%), vaccines (\$7.2m, 23%) and diagnostics (\$6.7m, 22%). By 2021, the landscape looked very different, with vaccine funding having increased four-fold (\$36m, 61% of the 2021 total). This was driven by increases in vaccine funding from both industry and US NIH, part of a global focus on prevention, given the serious threat posed by antimicrobial resistance in gonorrhoea infections.

Gonorrhoea drug development was the only other area to receive even 10% of 2021 funding (\$11m, 18%). This was largely driven by NIH support for discovery of novel therapeutics, as well as UK DHSC and German BMBF funding to GARDP for its ongoing Phase III trials of the novel antibiotic zoliflodacin – the first antibiotic trial fully sponsored by a non-profit. After representing greater than 20% of gonorrhoea funding each in 2018, basic research and diagnostic R&D have both fallen, each accounting for less than 10% of funding in 2020 and 2021.

While gonorrhoea funding remains focused on early-stage research, which accounted for nearly three quarters of 2021 funding (\$44m, 74%), clinical development has also risen from \$4.3m in 2018 to \$13m in 2021, thanks to both new vaccine development and GARDP's ongoing zolifidacin trials.

R&D for **herpes simplex virus 2 (HSV-2)** continues to be dominated by, and dominate, funding for biologics, with HSV-2 biologics R&D receiving \$96m, the most biologics funding of any single disease-specific product area. Funding for HSV-2 biologics – largely for therapeutic vaccines – increased from \$10m in 2018, to \$36m in 2021, representing more than 80% of total HSV-2 funding, and 91% of all funding for STI biologics. This biologics funding was driven by industry, which provided well over 90% of the total. Remaining funding was focused on preventive vaccine research – though current R&D avenues offer opportunities for preventive use of therapeutic vaccines and vice versa. Vaccine funding averages around \$3m each year, exclusively from the NIH for early-stage discovery and preclinical work.

As with most STIs, **chlamydia** funding has seen a comfortable increase, nearly doubling from \$10m in 2018 to \$19m in 2021. With chlamydia drug R&D excluded from scope, and no recorded in-scope funding for microbicide R&D, funding has been mostly split between basic research (a total of \$30m, 48%), and vaccines (\$26m, 24%). Almost all the remaining funding went to diagnostics R&D (\$6.1m, 9.9%), which also received the only recorded funding for chlamydia clinical development: just \$0.4m.

Funding for chlamydia basic research experienced a sharp increase starting in 2020 (up \$3.8m, 68%), thanks to the US NIH, which has provided 98% of all historical chlamydia basic research funding. The picture is similar for other product areas, with the US NIH providing 87% (\$23m) of vaccine funding, and 80% (\$4.9m) for diagnostics. The EC has been the only other reliable funder, committing \$2.4m for chlamydia vaccine basic research since 2019 via its VacPath project.

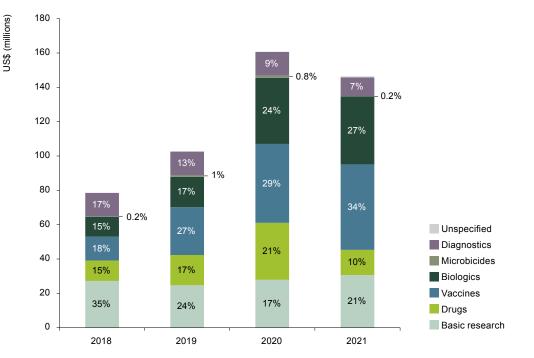


Figure 1. Sexually transmitted infection R&D funding by product type 2018-2021

Funding for **syphilis** R&D rose more than four-fold from \$2.0m in 2018 to \$8.5m in 2021. It saw a sharp increase in 2021 (up \$2.6m, 44%) to \$4.5m, which represents nearly 40% of the historical total. This growth was thanks to several new funders, headlined by a new \$2.5m Gates Foundation funding stream for basic research and translational science on *T. pallidum* to inform vaccine development, and the first ever funding reported for syphilis diagnostics (\$0.3m), almost exclusively from the Thrasher Research Fund.

Prior to 2021, 93% of total syphilis R&D funding had been provided by the US NIH, split roughly equally between early-stage vaccine R&D and basic research. As with chlamydia, there has been next to no clinical development funding; and no recorded syphilis funding from industry.

Human T-cell lymphotropic virus type 1 (HTLV-1) is the only disease to receive less funding in 2021 than in 2018, falling slightly from \$8.6m to \$7.3m. The vast majority of HTLV-1 funding is provided by the US NIH, largely for basic research (76%), with much of the remainder from Wellcome (\$3.5m), also mostly (84%) for basic research.

Japan's JSPS has played a small but consistent role in HTLV-1 basic research, its provision of just over \$1m indicative of the prevalence of the disease in the Japanese population, while Australian funding (\$0.3m), reflects the prevalence of HTLV-1 in Australian Indigenous communities.

Funding for **multiple STIs** – including R&D targeting more than one STI – has remained relatively stable over the last four years, averaging \$8.1m. Basic research accounted for just under half the total (\$14m, 42%), slightly below the share for diagnostics (\$17m, 54%) – in line with a global push towards multi- over single-STI panels. Diagnostic programmes largely focused on chlamydia/ gonorrhoea multi-diagnostics, most of which came from CARB-X (\$5.9m) and industry (\$2.3m).

Other STI R&D fell to a low of \$1.5m in 2020 but rebounded in 2021 with the commencement of \$2.1m in diagnostic R&D by industry, taking funding to a record \$3.7m. Funding for Other STI R&D has typically centred around drug research, and came mostly from the US NIH, for discovery research into lower burden STIs such as Trichomoniasis and *Mycoplasma genitalium*.

Table 5. Top funders of sexually transmitted infection R&D 2021

Je ^r -	15\$ (million	15]	c	cumulative total		
Funder	2018	2019	2020	2021		
US NIH	54	60	72	67	253	46
Aggregate industry	12	17	47	60	136	41
Gates Foundation	2.7	6.5	6.3	4.1	20	2.8
UK DHSC	1.8	6.0	5.4	2.9	16	2.0
German BMBF	-	-	-	2.7	2.7	1.8
Australian NHMRC	<0.1	<0.1	0.8	1.8	2.7	1.2
EC	0.1	1.5	1.9	1.8	5.2	1.2
Wellcome	0.7	1.3	1.7	1.6	5.3	1.1
Swiss SNSF	0.4	0.4	0.2	0.7	1.7	0.5
Canadian CIHR	-	<0.1	<0.1	0.6	0.8	0.4
UKNHS	0.6	0.8	0.8	0.4	2.6	0.3
Thrasher Research Fund				0.3	0.3	0.2
Subtotal of top 12^	77	101	159	144	481	99
Total	78	103	161	146	488	100

^ Subtotals for 2018-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.

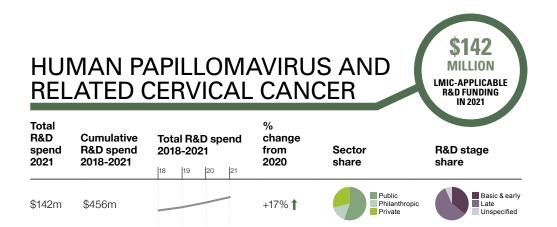
- No reported funding

FUNDING FOR SEXUALLY TRANSMITTED INFECTIONS COVERED IN OUR OTHER REPORTS

The figures presented above, and throughout this report, exclude funding for some STIs (or potential STIs) which we treat primarily as neglected diseases, such as HIV, hepatitis B and C, and which are covered in our G-FINDER ND reports – or as emerging infectious diseases, such as Zika, which are covered in our EID reports.

For context, comparable figures for these excluded STIs are included here:

- LMIC-relevant R&D funding for **HIV/AIDs** was just over \$6bn between 2018 and 2021. This was nearly 30 times the total for the top funded SRH STI, gonnorhoea (\$205m), and more than 12 times the total funding of all SRH STIs put together over the same period (\$488m). As with the SRH STIs, HIV funding was dominated by the US NIH (65% of the HIV total, 52% for SRH STIs). HIV funding was significantly more skewed towards vaccines, which received 51% of the in-scope funding, than the SRH STIs, for which vaccine R&D received 28% of total funding.
- Funding for **hepatitis B** R&D totalled \$55m between 2018 and 2021, roughly in line with the total for chlamydia (\$62m). With vaccine development out of scope for hepatitis B, the included funding was split fairly equally between basic research, biologics and drug R&D.
- **Hepatitis C** received a total of \$97m, substantially below the total for HSV-2 (\$126m) but well above the \$62m received by chlamydia. Industry provided the largest total share of hepatitis C funding over that period, with almost all of it coming in 2018 in support of late-stage drug trials.
- Research & development funding for **Zika** a primarily mosquito-borne pathogen which can also be transmitted sexually was \$525m between 2018 and 2021, more than double the \$205m total for gonorrhoea and slightly higher than the \$488m received by all SRH STIs put together. Global funding for Zika spiked in response to the 2015 South American epidemic, and has broadly trended down since, falling from \$215m in 2018 to \$80m in 2021.



Total funding for human papillomavirus (HPV) and HPV-related cervical cancer R&D in 2021 was \$142m. Funding rose by \$21m (17%), capping three consecutive years of growth which have seen funding rise by more than 50% since 2018 – an overall increase of \$53m over three years.

The majority of 2021's growth, and much of the total increase since 2019, is thanks to Unitaid, which has increased its HPV funding every year since its initial investment of \$11m in 2019. An upward trend in funding from the US NIH and industry – which collectively accounted for a quarter of total funding between 2018 and 2021 – has also contributed to the long-term increase in HPV R&D.

Historically, a little under half of HPV R&D funding has gone to vaccines, and around a quarter to diagnostics. Most of the remaining funding has been split fairly evenly between basic research, biologics and – since their 2019 inclusion – devices. While this pattern broadly continued to hold in 2021, with vaccines receiving 45% of the total, there were big swings in other product areas: the share for biologics (13%) and devices (10%) surged to record highs, while diagnostics (19%) reached a record low.

The rise in vaccine R&D funding focused on early-stage research and was mostly due to industry, which provided nearly half of the 2021 total. Industry's vaccine funding has grown from just \$6.2m in 2018 to \$32m in 2021, a result of substantial increases from ongoing industry players for both novel vaccines and improvements to existing products. Vaccines also continued to receive the largest share of clinical development funding in 2021, at 44% of the total, but this share represents a record low, mostly due to the growth in biologics clinical development. Industry-driven vaccine increases were followed by fairly steady contributions from the US NIH and the Gates Foundation (up \$1.9m to \$15m in 2021), the latter focusing on post-registration dose-reduction studies of existing preventive vaccines, which preceded the WHO announcement in 2022 that a single-dose HPV vaccine delivers substantial protection. Vaccine funding from the German BMBF to PATH also continued, supporting Phase III safety and efficacy trials of the bivalent HPV vaccine, Cecolin, which is registered in China and which received WHO pre-approval in 2021.

Unmet R&D need Given the absence of HPV-specific drug treatments and availability of highly effective preventive vaccines, current global approaches focus on prevention. This remains a challenge in LMICs, however, due to inequity of access to existing vaccines and challenging dosing regimens. While three vaccines have received WHO prequalification, these follow a two- or three-dose schedule, do not protect against all high-risk HPV strains and are unable to eliminate pre-existing infection. Following a number of dose-reduction studies of existing HPV vaccines, the WHO formally recommended a single-dose schedule in Dec 2022, but its guidance has yet to be fully implemented. Screening is also instrumental in the timely implementation of adequate surveillance and treatment. Current screening technologies, including DNA tests, are resource intensive, reaching only 5% of women in LMICs. The most widely used screening method, visual inspection with acetic acid, offers poor specificity and high observer variability. Several technologies in development aim to provide simpler, more reliable, and safe point-of-care use in LMICs.

pipeline spotlight India's Drugs Controller General granted market authorisation to the Serum Institute of India for India's first Quadrivalent Human Papillomavirus vaccine, <u>CERVAVAC</u>, against HPV-related cervical cancer.

The therapeutic vaccine candidate, TG4001, a modified vaccinia virus Ankara (MVA)-based vaccine is due to complete Phase Ib/II testing for HPV-16 positive metastatic cervical cancer by late <u>2024</u>.

The rapid growth in device R&D funding has been driven by Unitaid, which has directed half of its funding each year to devices, providing nearly 88% of HPV device funding since they were first added to the survey scope in 2019. All of Unitaid's funding to date has gone to the Clinton Health Access Initiative, with half of the funding allocated to implementation research on handheld thermal ablation devices, and the other half allocated to diagnostic funding for a novel Al-based tool.

The sharp growth in biologics R&D, on the other hand, is more recent, and the result of several converging trends. These include a more than 70% increase in funding from the US NIH, new 2021 streams of funding from the Gates Foundation, and ongoing growth from SME funders – all largely focused on therapeutic HPV vaccines.

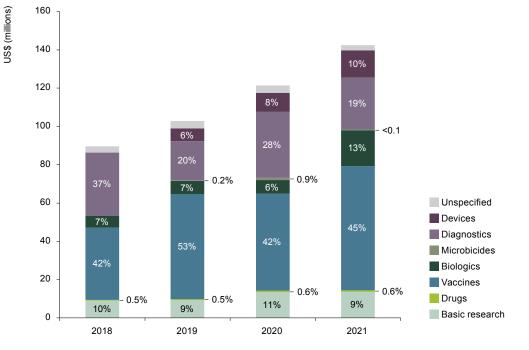


Figure 2. Human papillomavirus and related cervical cancer R&D funding by product 2021

While the complex physiobiology of the virus and its possible clinical manifestations mean that basic research continues to be an important area for investment, 2021 saw static funding for basic research and a significant shift towards clinical development. The big increase in funding for later-stage R&D – which jumped to a record \$82m in 2021 (up \$24m, 41%) – was thanks to substantial increases across all product categories, but headlined by clinical trials for biologics – which saw their clinical development funding nearly triple to \$14m in 2021.

Funding for diagnostic R&D fell 22% in 2021 and is down 19% since 2018. The overall drop is the result of steep industry spending cuts (down \$14m, -78%) driven by pipeline progression of a commercially available HPV assay. But diagnostic R&D remained relatively robust thanks to its receipt of the other half of Unitaid's 2019 funding stream, which has left Unitaid responsible for about a third of post-2018 diagnostics R&D. The actual drop in diagnostics funding since 2018 is likely to be slightly overstated, since a substantial share of 2018 funding came from two organisations for which data was not available post-2019.

Both drug and microbicide R&D continue to be exclusively funded by the US NIH and each received less than \$1.0m in 2021 – with the former rising for a third consecutive year to \$0.9m (up another \$0.2m, 31%) and the latter dropping by half to \$0.5m. Persistently low funding for drug R&D reflects both restrictive inclusion criteria (only those that target HPV infection are included, while anti-neoplastic drugs are not), as well as a general R&D focus on preventive vaccines, biologics and device-based treatments over small molecule approaches. What little drug funding there is remains almost entirely in early-stage research (95% of cumulative drug R&D total), with no reported funding specifically for clinical development.

Public funders from high-income countries – particularly the US NIH – have historically provided most of HPV R&D funding: 43% of the total since 2018. Though 2021's NIH funding declined slightly (by \$2.7m, down 6.0%) from its 2020 peak, it remained the top funder for HPV R&D, having now provided a third of total funding between 2018 and 2021. Private MNCs – following four consecutive years of increases – were responsible for just under a fifth of funding in 2021, with much of the remainder coming from the public multilateral Unitaid. Contributions from SMEs dropped sharply in 2021 following pipeline progression in diagnostic development, which accounted for a substantial share of their pre-2021 funding. Involvement from LMICs – just 2.4% of the historical total, mostly from India – remains quite limited.

Table 6. Top funders of HPV and related cervical cancer R&D 2021

	JS\$ (million	15)			umulative	total
Funder	2018	2019	2020	2021	2	<u>Or</u>
US NIH	30	39	45	42	156	30
Aggregate industry	23	15	34	41	114	29
Unitaid	-	11	16	27	54	19
Gates Foundation	17	24	13	22	76	15
German BMBF	-	0.6	5.1	3.5	9.2	2.5
EC	2.0	2.5	2.2	2.1	8.7	1.5
Indian BIRAC	1.7	0.2	<0.1	1.4	3.4	1.0
UK NHS	-	0.3	0.5	0.6	1.5	0.4
Canadian CIHR	0.4	0.5	0.3	0.4	1.6	0.2
UK MRC	1.0	1.5	1.2	0.3	4.1	0.2
Wellcome	0.3	0.4	0.3	0.3	1.3	0.2
Colombian Minciencias	-	0.2	<0.1	0.3	0.5	0.2
Subtotal of top 12^	88	100	119	141	449	99
Total	90	103	121	142	456	100

^ Subtotals for 2018-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.

- No reported funding



Global funding for contraception product development has averaged \$129m each year since 2018. Funding peaked at \$144m in 2019, before falling for two consecutive years: marginally to \$141m in 2020 (down \$2.5m, -1.7% 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 funding fell by 42% (down \$16m).

%

change

Sector

Public Philanthropic

Private

share

from

2020

-17% 👃

Total R&D spend

21

2018-2021

19 20

118

\$117 MILLION

LMIC-APPLICABLE R&D FUNDING IN 2021

R&D stage

Basic & early Late

Unspecified

share

In 2021, 45% (\$53m) of contraceptive funding was directed towards long-acting reversible contraception (LARCs), which was almost exclusively invested in devices & combination products (\$51m, 97% of LARC funding). This represented the third consecutive decrease in LARC funding since its high of \$62m in 2018 and was driven by a big fall in funding from industry, whose investment in LARC device & combination products more than halved from \$50m in 2018 to \$23m in 2021. Thanks to an \$18m rise in funding from the Gates Foundation, though, which partially offset the fall in industry funding, LARCs still overwhelmingly dominate the contraceptive funding landscape.

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

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 represented by multi-year, multimethod projects. This includes funding from the Gates Foundation to FHI 360 for the Contraceptive Technology Innovation Initiative and multi-product clinical trial funding from the US NIH for the Contraceptive Clinical Trials Network.

Unmet R&D needs

Meeting global contraceptive needs requires the provision of a diverse range of options. Although several effective products are available, global unmet need for modern contraception persists, particularly in LMICs. This unmet need is in major part due to a lack of contraceptives that meet the spectrum of needs of individual users. Different product profiles are required, including less- or non-hormonal products, male contraceptives and user-controlled options, allowing for greater usability and user autonomy. There is also a particular unmet need for novel products that overcome additional barriers faced by users in low-resource settings and in diverse cultural contexts. This includes products that offer LMIC-appropriate alternatives to cold-chain transport and storage or administration by skilled health professionals, and those that acknowledge the cultural significance of menstruation via options that are non-hormonal or do not disturb usual bleeding patterns.

FHI 360's levonorgestrel, a six-month contraceptive, is approaching Phase 1 trials. Its microsphere technology allows users to self-inject, reducing the need for regular medical consultations.

Population Council and the US NIH are developing the male contraceptive NES/T gel, currently in Phase 2b trials. It uses a combination of Nestorone and testosterone to reversibly suppress spermatogenesis via daily topical application.

pipeline ource

pipeline spotliaht

Calliope - available here - provides an interactive database of the R&D pipeline for contraceptives. It is coordinated by FHI 360 as part of the Contraceptive Technology Innovation (CTI) Exchange.

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

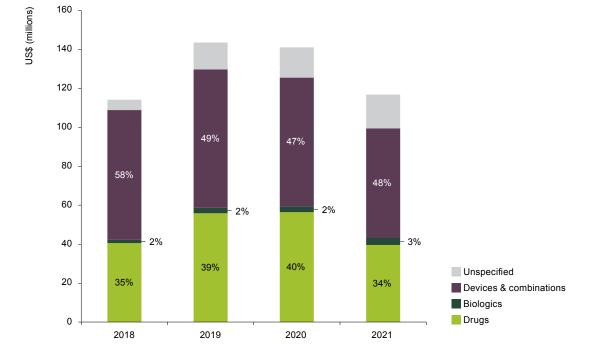


Figure 3. Contraception R&D funding by product type 2018-2021

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

However, 2021 also saw a near-halving of short-acting contraceptive 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 funding for short-acting drugs, largely attributable to reductions in US NIH and Gates Foundation funding.

On-demand contraception notched just \$4.4m (3.8% of 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 on-demand drug funding has come from the US NIH (peaking at \$3.1m, 91% in 2021), largely for the development of an on-demand pharmacological contraceptive that blocks sperm function via inhibition of the target ADCY 10.

Novel **permanent contraception** has consistently represented the lowest share of contraception R&D funding. 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 reported investment in permanent contraceptives has been from the Gates Foundation to the Oregon Health and Science University for the development of a fallopian tube-directed sclerotising polidocanol foam.

Table 7. Contraception R&D funding by duration 2018-2021

Duration	JS\$ (million	15)		C	Sumulative 2	total 021 % of total
Duit	2018	2019	2020	2021		
Long-acting reversible (LARC)	62	62	58	53	235	45
Short-acting	26	39	42	23	130	20
On-demand	4.1	7.3	4.1	4.4	20	3.8
Permanent	3.9	-	3.2	1.1	8.2	1.0
Multiple or unspecified duration	18	35	34	36	122	30
Total	114	144	141	117	516	100

- No reported funding

While R&D for contraceptive products targeting female end users continues to dominate, its share of overall funding has gradually declined, from 84% in 2018 to 71% in 2021, as the contraceptive market shows promising signs of diversification. This is thanks to growth in funding specifically earmarked for male end users, which rose to \$13m (11%) in 2021, alongside steeper growth in R&D targeting both male and female (or as yet unspecified) end users (\$20m, 17% of the 2021 total).

R&D targeting male end users is primarily focused on short-acting contraception (\$7.4m, 57% of male contraceptive funding in 2021). That said, 2021 also saw a spike in funding to male-focused LARCs (up \$0.6m, 85%). This funding was directed towards first in-human studies of an industry-led vas-occlusive device with support from the Male Contraceptive Initiative.

Research into hormonal contraception continues to represent 60% or more of investment in contraceptive R&D annually. However, funding specifically targeting non-hormonal contraception has felt some (albeit slight) growth, increasing from \$18m in 2018 to \$27m in 2020, although it dropped back to \$18m in 2021. Much of the funding for hormonal contraception is in fact focused on methods with reduced or ultra-reduced hormone levels, with the express intent of limiting unwanted side-effects while maintaining efficacy.

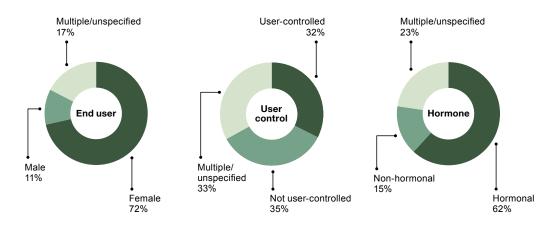


Figure 4. Contraception R&D funding by product end user, user-control, and hormone 2021

Encouragingly, the last four years have seen an increasing shift in focus towards user-controlled contraceptive methods. While non-user-controlled methods continue to receive the largest share of funding, this proportion has decreased substantially to a low of 35% (\$40m) in 2021. As a result, the relative proportion of funding for user-controlled methods has increased, climbing steadily 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 and post-registration optimisation studies of DMPA-SC (Sayana Press).

Duration	Drugs	Vaccines	Biologics	evices &	unspecifie	iotal o	10
Long-acting reversible (LARC)	1.4	-	-	51	-	53	45
Short-acting	19	-	0.7	3.2	-	23	20
On-demand	3.4		-	1.0	-	4.4	3.8
Permanent	1.1			-	-	1.1	0.9
Multiple or unspecified duration	15	-	2.8	0.5	17	36	30
Total	40	-	3.5	56	17	117	100

Table 8. Contraception duration R&D funding by product type 2021 (US\$ millions)

Category not included in G-FINDER

- No reported funding

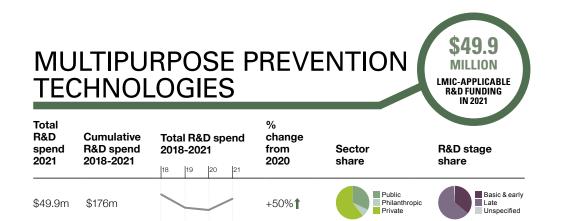
Since 2018, 30 different organisations have reported funding contraception R&D. However, the Gates Foundation, the US NIH and industry have consistently represented 85% or more of total investment. In 2021, the Gates Foundation accounted for two-fifths (\$47m, 40%) of contraceptive R&D funding, positioning it as the top funder for the second year in a row.

The Gates Foundation is the major supporter of early-stage R&D (averaging nearly 50% of early-stage funding), while the US NIH has, every year bar one, dominated funding for clinical development (averaging 51% of clinical development funding). Funding from industry makes up nearly three-quarters the 40% of funding that does not specify an R&D stage, representing an undisclosed mix of early and late-stage product development.

Table 9. Top funders of contraception R&D 2021

- del	US\$ (million	19	cumulative total			
Funder	2018	2019	2020	2021		
Gates Foundation	26	45	50	47	169	40
US NIH	26	36	34	29	124	24
Aggregate industry	51	52	39	23	166	20
Population Council	3.6	2.9	2.9	10	20	8.9
USAID	5.4	4.3	11	4.1	25	3.5
Male Contraceptive Initiative (MCI)	0.6	0.8	1.4	1.7	4.5	1.4
EC	<0.1	0.2	1.5	1.2	3.1	1.1
Children's Investment Fund Foundation (CIFF)	-	-	0.4	0.4	0.8	0.4
Parsemus Foundation	<0.1	0.2	0.6	0.2	1.0	0.1
Vinnova	-	-	<0.1	<0.1	0.1	<0.1
Brazilian FAPESP	-	<0.1	<0.1	<0.1	<0.1	<0.1
Research Council of Norway	0.2	0.2	<0.1	-	0.4	-
Subtotal of top 12^	114	143	141	117	515	100
Total	114	144	141	117	516	100

 $^{\wedge}$ Subtotals for 2018-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021. - No reported funding



Global funding for multipurpose prevention technology (MPT) product development over the last four years was \$176m. Funding returned to \$50m in 2021, a near complete recovery from its low of \$33m in 2020 (up \$17m, 50%), which itself followed two consecutive years of decline from the peak of \$56m in 2018.

The peaks and troughs in MPT funding over the past four years have largely been driven by changes in industry investment, particularly fluctuations in funding for MPTs that provide dual protection against pregnancy and STIs, as industry-backed candidates moved through the pipeline. These types of MPTs – indicated for pregnancy and STI prevention – have received over half of all investment in MPT R&D since 2018 (\$95m, 54%) and just under 60% of funding in 2021 (\$30m), the majority of which went to industry-led development of topical microbicides.

The next largest share of funding was dedicated to MPTs providing dual protection against pregnancy and HIV (\$47m, 27%), followed by MPTs designed to protect against pregnancy, HIV and other STIs (\$23m, 13%). Less than 5% (\$6.2m) went to non-contraceptive MPTs intended to protect against HIV and other STIs simultaneously. While no funding was reported for non-contraceptive MPTs designed for prevention of multiple non-HIV STIs, R&D for products intended to *treat* multiple STIs does exist, and is captured under our measure of STI funding (see page 5). Overall, this distribution of MPT funding has remained consistent over time, with contraceptive MPTs ('cMPTs') receiving 90% of all MPT investment.

Currently, the only available multipurpose prevention technologies (MPTs) are condoms, but progress in microbicide, biologic and drug R&D for contraceptives and STIs has spurred the development of products combining their prophylactic uses, especially via novel delivery methods. The MPT sector is user-centric and many products offer innovative user-controlled administration via topical gels, films or inserts. Some MPTs in development provide advantages specifically for people in LMICs: heat-stable vaginal rings and on-demand fast-dissolving inserts or topical gels may help solve storage and accessibility difficulties, since they can be distributed without requiring regular access to skilled health workers or cold chain. On-demand products provide unprecedented levels of agency, enabling consistent and discreet use. The potential of MPTs is generating momentum but most products are still in early development; out of 28 products in development, only six have reached clinical trials.



Unmet R&D need

Population Council is conducting preclinical evaluations for an on-demand non-hormonal contraceptive and anti-STI fast-dissolving insert. It combines <u>Q-Griffithsin</u>, a non-antiretroviral lectin with potent anti-HIV activity, with anti-sperm and other excipients providing protection against pregnancy, HIV and bacterial vaginosis, chlamydia, gonorrhoea and HSV-2. Its use of a non-ART anti-HIV agent helps address risks of ART resistance.

pipeline source The iMPT Product Development Database – <u>available here</u> – is an interactive database of the R&D pipeline for MPTs. It is coordinated by iMPT, a project of CAMI-health.

Table 10. Multipurpose prevention technology indication R&D funding by product type 2021

Indication	Drugs F	Biologics	Nicrobicid	es evices & combinations	ons Unspecifie	iotal o	10
Contraception + STI	-	-	29	0.8	-	30	59
Contraception + HIV	4.6	-	1.3	6.2	-	12	24
Contraception + STI + HIV	0.1	-	1.7	4.6	-	6.5	13
STI + HIV	-	-	0.6	0.5	-	1.1	2.2
Unspecified	-	-	-	0.1	0.5	0.6	1.3
Total	4.7	-	32	12	0.5	50	100

- No reported funding

Indication	JS\$ Imillion	19		C	Sumulative 2	total 021 % of tot	a
Indi	2018	2019	2020	2021			
Contraception + STI	40	15	11	30	95	59	
Contraception + HIV	7.9	14	13	12	47	24	
Contraception + STI + HIV	5.5	4.6	6.3	6.5	23	13	
STI + HIV	0.6	2.8	1.8	1.1	6.2	2.2	
Unspecified	2.1	0.8	1.6	0.6	5.1	1.3	
Total	56	37	33	50	176	100	

Table 11. Multipurpose prevention technology R&D funding by indication 2018-2021

In 2021, cMPT funding focused on microbicides, which received two-thirds (\$32m) of cMPT funding – an \$18m (130%) jump from 2020's low of \$14m. Much of this sudden growth was driven by funding for pivotal late-stage trials testing the STI element of on-demand cMPTs with dual action against STIs and pregnancy. The next largest share of 2021 funding went to device & combination cMPTs (\$12m, 24%), covering development of products such as intravaginal rings, microarray patches and other devices combined with drugs, microbicides or biologics. cMPT drugs received \$4.7m (10%), in line with previous years, including funding for a daily oral cMPT that dually protects against HIV and pregnancy. Finally, biologic-based cMPTs received no funding at all in 2021 and a total of just \$1.8m between 2018 and 2020, all of which was from the NIH to Boston University, to determine if human contraceptive antibody (HCA) has dual activity as a contraceptive agent and STI microbicide. The lack of biologic-based MPT funding in 2021 reflects the subsequent evolution of this program to combine HCAs with intravaginal rings, shifting its funding to our devices & combinations category for 2021.

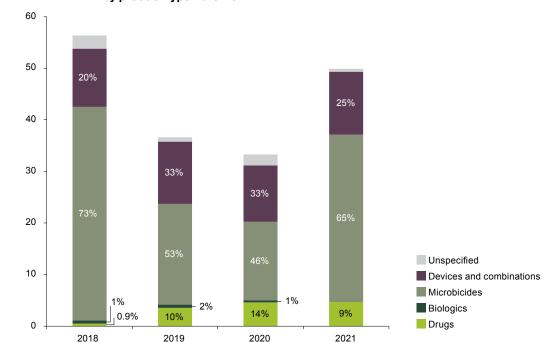


Figure 5. Multipurpose prevention technology R&D funding by product type 2018-2021

US\$ (millions)

Unlike the rest of the contraceptive R&D landscape, nearly all funding for cMPTs over the last four years was for methods designed exclusively for female end users, with just 1-2% targeting multiple or unspecified users, and none for male end users only. A clear majority of cMPTs were also usercontrolled (92%) and non-hormonal (70%). Although this is a contrast to straight contraceptive R&D (see page 22), this makes sense in the context of MPTs, which typically focus on products that expressly address the needs of women and girls, particularly their need for discretion and autonomy.

As with cMPTs, funding for non-contraceptive MPTs is focused on topical microbicides, which have received just over two-thirds of funding since 2018 (\$4.1m). The majority of this is intramural funding from Population Council for the development of a fast-dissolving insert containing Q-Griffithsin that protects against HIV, HSV-2 and HPV (\$2.8m). The remaining third of funding for MPTs that protect against HIV and other non-HIV STIs went towards devices & combination products (\$2.1m), of which almost all was provided by the US NIH for the development of an intravaginal ring that protects against gonorrhoea and HIV.

Multiple/unspecified Female Not user-controlled 100% 10% 3% 1 I Hormonal 20% llear End user Hormone control T User-controlled Non-hormonal 90% 76%

Figure 6. Multipurpose prevention technology R&D funding by product end user, user-control, and hormone 2021

Across all MPTs, 61% of funding since 2018 has been directed towards clinical development (\$107m), compared to 35% for early-stage research (\$61m). Industry is the predominant funder of clinical development, mostly focused on late-stage development of microbicides with dual contraceptive and STI protective qualities. In contrast, the US NIH has funded two-thirds of early-stage research (\$40m), supporting a larger and more diverse slate of candidates than those that have advanced to clinical development.

Since 2018, there have been 19 reported funders of MPT R&D. However, as with other areas of sexual and reproductive health R&D, actual funding is concentrated on a small pool of major contributors. Industry has remained the largest overall source of MPT R&D funding, providing \$95m over four years (54% of the total) - mostly from women-centred, socially conscious companies. The next largest funder of MPTs was the US NIH, which has contributed a total of \$46m. Together, industry and the NIH accounted for 80% of total funding since 2018.

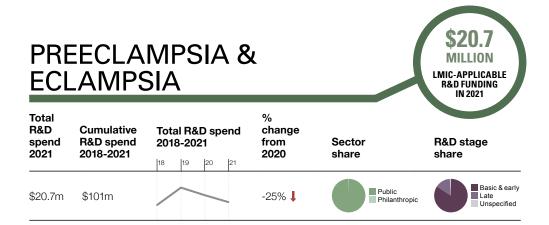
Beyond these, USAID and Population Council have been the next largest public HIC funders. Combined, public HIC funders altogether contributed 40% (\$71m) of overall funding. Much of the remainder came from philanthropic organisations (\$8.4m, 4.8%), with falling funding from the Children's Investment Fund Foundation (down \$1.4m from 2019 to 2021) more than offset by an increase from the Gates Foundation (up \$2.9m over the same period).

٨٥٢.	US& Initional			C	cumulative total			
Funder	2018	2019	2020	2021				
Aggregate industry	41	15	11	29	95	58		
US NIH	7.4	9.8	14	14	46	29		
Gates Foundation	-	0.5	1.0	3.3	4.8	6.7		
Anonymous funder(s)				2.0	2.0	4.1		
Population Council	-	2.3	1.2	0.7	4.2	1.4		
Canadian CIHR	-	0.3	0.4	0.4	1.2	0.9		
Children's Investment Fund Foundation (CIFF)	0.2	1.7	1.4	0.3	3.6	0.6		
USAID	6.6	5.6	1.8	-	14	-		
French ANRS	0.9	<0.1	1.0	-	2.0	-		
UK FCDO	-	1.4	0.7	-	2.1	-		
Australian MRFF		-	0.5	-	0.5	-		
Colombian Minciencias	-	-	0.2	-	0.2	-		
Total	56	37	33	50	176	100		

Table 12. Top funders of multipurpose prevention technology R&D 2021

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.

- No reported funding



Global funding for preeclampsia & eclampsia (PE&E) basic research and product development totalled \$101m in the four years from 2018 to 2021. Annual funding has ranged from a low of \$18m in 2018 to a peak of \$35m the following year, growth that was mostly due to 2019 changes in survey scope, with the addition of biologics and broader inclusion criteria for drugs. From 2019, funding steadily declined, falling by \$7.4m (-21%) in 2020 and a further \$6.9m (-25%) in 2021. While basic research continued to dominate the funding landscape, the major fluctuations were mostly driven by a 2019 spike in reported biologics funding and the sharp 2021 decline in funding for diagnostics.

Basic research accounted for nearly three-fifths of historical PE&E funding (\$60m) and has remained relatively stable, ranging \$14m (in 2018 and in 2021) to \$17m (in 2020) with a little over three-quarters of the total provided by either the US NIH (\$47m) or the Canadian CIHR (\$2.9m). This basic research-dominated landscape reflects a growing interest in filling critical knowledge gaps as to the underlying pathophysiology of preeclampsia, as well as identifying genetic and environmental risk factors as possible avenues of prediction and prevention.

Preeclampsia and eclampsia are placental-mediated multisystem disorders that cause hypertension and organ dysfunction during pregnancy or post-partum, responsible for 10-15% of maternal deaths globally, with 99% occurring in LMICs. Current management relies on specialist healthcare: detection of elevated blood pressure and urinary protein assumes regular antenatal monitoring; measurement of biomarkers in urine or blood requires laboratory facilities; and definitive treatment – delivering the placenta – requires skilled obstetric care.

Unmet R&D needs

Only one medicine – magnesium sulphate – is specifically indicated for PE&E (for eclamptic seizures) with safe administration requiring skilled healthcare practitioners. No other medicines are currently available for prevention or treatment, and none address the underlying aetiology. Low-dose aspirin and calcium supplementation are, however, recommended by the WHO for prevention in high-risk women; but identifying those at risk is challenging without expert medical assessment. Medicines based on improved understanding, and applicable to LMICs, are required. Since timely detection is essential, there is also an unmet need for diagnostics applicable to low-resource settings, especially point of care tests.

MZe786 is a novel hydrogen sulfide-releasing molecule with an aspirin structure 'backbone' being developed by MirZyme Therapeutics. The drug offers improved maternal and fetal outcomes over aspirin alone, and is intended to be taken once daily by women at risk of PE&E. It is the first pregnancy drug to be granted fast-track approval by the UK regulatory body (in 2022).

The University of Technology Sydney has developed low-cost lateral flow assays targeting novel biomarkers for preeclampsia. Use on clinical samples demonstrated improved sensitivity and specificity over standard <u>ELISA</u>.

pipeline source

pipeline spotliaht

The AIM maternal health database – <u>available here</u> – is an interactive database of the R&D pipeline for preeclampsia/eclampsia medicines and diagnostics over the last two decades. It is part of the Accelerating Innovations for Mothers (AIM) project, a partnership between Policy Cures Research, Concept Foundation and Burnet Foundation. A brief overview of this analysis can be found overleaf.

Investment in drug R&D was (narrowly) the second largest area of total funding and, like basic research, has also remained relatively stable. The sharp apparent increase in drug R&D in 2019 was actually driven by an expansion in our survey scope aimed at capturing therapeutic alongside preventive drug R&D and broadening eligibility for dosing trials and studies using repurposed drugs. Setting aside the effects of scope changes, the true value of PE&E drug R&D probably remained mostly unchanged at around \$5m between 2018 and 2019 and in the years since. Funding for drug R&D has explored several avenues, including, for example, at least \$6.7m in NIH support for randomised controlled trials of pravastatin for prevention of PE&E in high-risk women, \$1.3m from the Australian NHMRC for Phase II trials of esomeprazole, as well as funding from Merck for Mothers to WHO HRP for the STEP-Mag Trial dose reduction studies on magnesium sulphate for eclampsia.

The introduction of the biologics category in 2019 also contributed to the substantial increase in that year's measured funding, thanks to \$12m in newly-included biologics funding – 34% of the 2019 total. This was largely driven by \$11m of industry investment in clinical development of polyclonal antibodies for the treatment of preeclampsia. However, late-stage trials were ultimately terminated in 2020 for futility, explaining the big drop in biologics funding from 2020 onwards. Outside of this, reported preeclampsia biologics R&D has remained relatively stable at between \$1m to \$2m each year, almost entirely provided by the US NIH. However, our analysis of the PE&E pipeline – see overleaf – shows significant additional product development activity by organisations which do not report their funding to the G-FINDER survey.

Diagnostics R&D funding decreased significantly in 2021, receiving just \$190k (down \$2.6m, -93%) after consistently averaging around \$3m over the preceding three years. This sudden fall was mostly due to absence of investments from three of the major pre-2021 funders for preeclampsia diagnostics: the US NIH, Grand Challenges Canada and the European Commission. Their reductions followed the completion of major projects, including the wrap-up in 2020 of the EC-funded PEDPOC project, aimed at developing a novel test for rapid early diagnosis and continual monitoring of preeclampsia, as well as the 2020 conclusion of NIH funding to industry for point-of-care tests, which had totalled more than \$4.2m over the previous three years. The small amount of remaining 2021 diagnostics investment was thanks to a new stream of funding from Australian NHMRC to the University of Melbourne for a preeclampsia predictive test, leaving the NHMRC as the only funders of PE&E diagnostics.

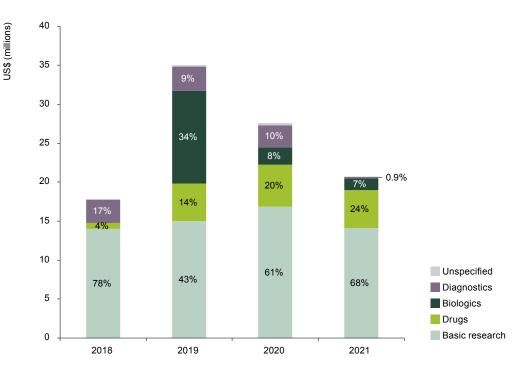


Figure 7. Preeclampsia & eclampsia R&D funding by product type 2018-2021

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A substantial portion preeclampsia clinical development funding had been devoted to the industryled late-stage polyclonal antibody trials discontinued for futility in 2020. Since then, clinical development has accounted for less than 20% of overall funding, mostly for drug development, and almost entirely provided by the NIH (\$3.0m, 98%). The near absence of ongoing clinical development left the bulk of funding in 2021 targeted at basic research (\$14m, 68%) and earlystage development of drugs (\$1.7m, 8.0%) and biologics (\$1.5m, 7.3%).

Thirteen organisations provided funding for preeclampsia in 2021 – down from a peak of 24 in 2020. More than three-quarters of 2021 funding came from the US NIH (\$17m, 82%), which has remained the single largest contributor to preeclampsia R&D since 2018, providing two-thirds of the overall total. It was followed in 2021 by two consistent contributors: the Australian NHMRC – with support across basic research and diagnostics – and Canadian CIHR – mostly for basic research – each contributing \$1.0m (5% of the 2021 total). Several previously reliable funders ceased backing PE&E R&D in 2021, headlined by the Gates Foundation – which provided a little over \$1.2m between 2018 and 2020 – and Grand Challenges Canada (\$1.3m total). Their absence meant that, in 2021, only one other funder provided more than \$250k: the Swedish Research Council, which more than doubled its initial 2020 investment to \$0.7m, making it the fourth largest contributor behind the NIH, CIHR and NHMRC.

Table 13. Top funders of preeclampsia & eclampsia R&D	2021
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	US\$ (million	nsi			umulative	total 021 % of tot
under	2018	2019	2020	2021		
US NIH	12	19	20	17	68	82
Australian NHMRC	1.4	1.6	0.9	1.0	4.9	4.8
Canadian CIHR	0.5	0.7	1.1	0.9	3.3	4.8
Swedish Research Council	-	-	0.3	0.7	1.1	3.5
Health Research Council of New Zealand (HRC)	0.2	0.2	0.3	0.2	0.9	1.2
Brazilian FAPESP	<0.1	<0.1	<0.1	0.2	0.4	0.9
Chilean FONDECYT	-	0.2	0.3	0.2	0.6	0.8
Swedish SIDA	-	0.2	0.1	0.1	0.5	0.6
Indian DBT	-	<0.1	0.9	<0.1	1.0	0.4
German BMBF	-	<0.1	0.1	<0.1	0.2	0.4
Swedish Heart-Lung Foundation		-	<0.1	<0.1	<0.1	0.3
EC	0.2	1.3	1.1	<0.1	2.6	0.3
Subtotal of top 12^	18	35	27	21	100	100
Total	18	35	28	21	101	100

^ Subtotals for 2018-2020 top 12 reflect the top funders for those respective years, not the top 12 for 2021.

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.

- No reported funding

The public sector has been largely responsible for providing preeclampsia R&D funding (\$88m, or 87% of the historical total), of which the vast majority was invested by HICs (\$83m, 94%). The only consistent LMIC public funder was the Brazilian FAPESP (a total of \$0.4m), but nine other LMIC organisations provided at least some funding, across a variety of product areas. The complete absence of industry funding meant that, by 2021 essentially all funding (99.7%) came from the public sector.

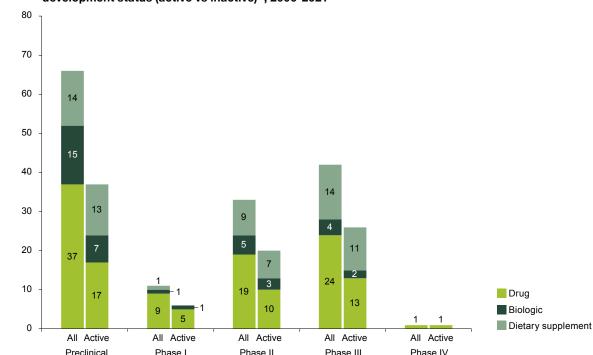
THE PREECLAMPSIA PIPELINE

Through the AIM project, PCR researched the landscape of biomedical products under investigation or in use for a number of pregnancy-specific conditions since 2000. Unlike the figures elsewhere in this report, these findings include *all* products whether or not they are LMIC-appropriate. They are intended to provide useful context on the broader landscape of R&D for these important health issues, but do not correspond directly to the (scope-restricted) funding estimates.

In total, we identified 153 candidates in use or investigated for preeclampsia & eclampsia (PE&E) between 2000 and 2021.* Ninety are drugs (59% of the total), 25 (16%) biologics, and 38 (25%) dietary supplements. Overall, 90 (59%) candidates had evidence of R&D activity since 2019, and the remaining (63 candidates, 41%) were inactive.

Just one candidate – magnesium sulphate – has been approved for use for PE&E, and only for the prevention or treatment of eclamptic seizures. The 152 remaining medicines were under investigation for PE&E, including 12 candidates already being used off label (8% of candidates), the majority of which (10) are antihypertensives for the symptomatic treatment of preeclampsia-induced hypertension. Purely investigational candidates include diverse avenues of R&D, such as inflammation and immune modulators (e.g. sulfasalazine, celecoxib and polyclonal antibodies); angiogenic balancing medicines (e.g. biologics such as vascular endothelial growth factor, placental growth factor, etc.); vasoconstriction and vasodilation balancing drugs, such as nitric oxide donors or precursors (e.g. glyceryl trinitrate, sildenafil citrate) and hydrogen sulphide-based therapies (e.g. sodium hydrosulphide); proton pump inhibitors (e.g. esomeprazole); lipid lowering molecules/statins (e.g. pravastatin) and candidates targeting oxidative stress (e.g. melatonin, antioxidant vitamins, plant extracts).

A quarter of candidates are either new chemical entities or novel biologics (38), including cuttingedge siRNA-based therapies and other biologics with novel delivery mechanisms (nanoparticle and viral vector). While almost all of these have remained in preclinical development, some have seen very recent progress, including the sFIt-1-targeting siRNA – CBP-4888 – which as of mid-2023 has just entered Phase I. The remaining 115 (75%) are repurposed medicines, 75 (65%) reaching Phase II or Phase III clinical trials, a little over half of which were ongoing at the time the database was finalised.

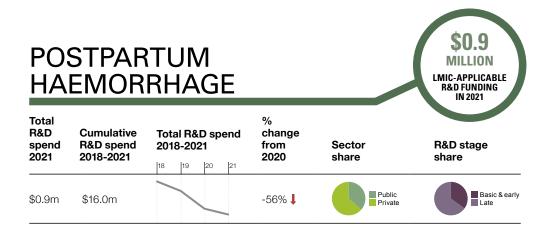


Preeclampsia & eclampsia medicines by R&D stage, product type and development status (active vs inactive)[^], 2000-2021

^AThe preeclampsia & eclampsia medicines pipeline was updated as of May 2021. Active candidates are candidates with evidence of R&D activity since 2019.

* The preeclampsia & eclampsia medicines pipeline was updated as of May 2021. Information is accurate up until this date

Number of PE/E medicines



Global funding for postpartum haemorrhage (PPH) product development dropped to a new low of \$0.9m in 2021. This represented a fall of more than half from the previous year (down \$1.1m, -56%), and cemented a worrying downward trend from a peak of \$7.5m in 2018. Funding across both drugs and devices has now fallen every year since 2018. Industry, as PPH's largest investor, has mostly been responsible for the overall state of PPH R&D, contributing the majority of funding during the 2018 and 2019 peak, and a narrow majority of what little funding remained in 2021.

Just 12% of the total \$16m invested in PPH R&D over the past four years went to devices, with the remaining 88% (\$14m) directed towards drugs. The share of drug funding rose to 100% in 2020 and 2021 as there has been no reported funding *specifically* for PPH devices since 2019, when they received \$0.7m. However, these figures do not include self- and onward funding from the WHO Human Reproductive Programme (HRP), since funding from these kinds of 'intermediary organisations' (organisations which both give and receive funding) is already accounted for in any R&D funding specifically directed to them by funders. In 2021, this WHO HRP onward funding for PPH device R&D totalled \$0.4m and was earmarked for a Phase III clinical trial in Vietnam evaluating the comparative effectiveness and safety of four uterine balloon tamponade devices.

Although PPH affects one in six women giving birth, generalised use of high quality uterotonic agents in prevention and treatment, ready access to second line therapeutics such as hemostatic agents and blood products, and provision by highly skilled practitioners has virtually eliminated maternal deaths from PPH in high-income countries. However, it remains the leading cause of maternal mortality in LMICs. Oxytocin is the uterotonic of choice for management of PPH, but in its standard form requires refrigerated transport and storage, and administration by skilled health workers; neither of which are consistently available in low-resource settings. Reducing maternal mortality from PPH in LMICs requires novel approaches tailored to low-resource contexts. There is ongoing development of alternative preparations of oxytocin and other medicines that are heat-stable, easy-to-administer and affordable. Low-tech devices that control bleeding have also been specifically developed for the treatment of PPH as adjunct therapies, or when first line treatments have <u>failed</u>.

Monash University and industry partners have been developing heat stable inhaled oxytocin, recently announcing a Phase I trial of the <u>ICOone</u> inhaler, developed by Sweden's <u>Iconovo</u>.

Medicated gauze repurposed from topical wound care are in development for PPH. The PPH-specific Celox chitosan gauze, CELOX PPH Uterine Hemostatic Tamponade, received CE certification in Europe in November <u>2022</u>.

pipeline source

pipeline spotliaht

Unmet R&D need

The AIM maternal health database – <u>available here</u> – is an interactive database of the R&D pipeline for postpartum haemorrhage medicines and devices over the last two decades. It is part of the Accelerating Innovations for Mothers (AIM) project, a partnership between Policy Cures Research, Concept Foundation and Burnet Foundation. A brief overview of this analysis can also be found overleaf.

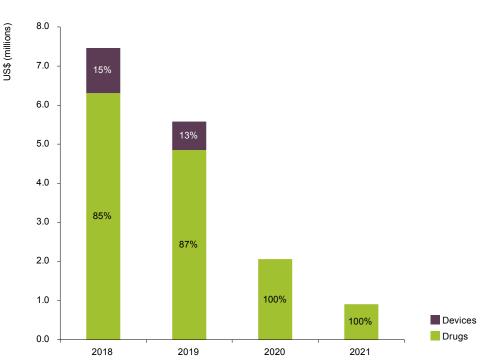


Figure 8. Postpartum haemorrhage R&D funding by product type 2018-2021

Our PPH device R&D figures also do not include funding for PATH's Devices, Diagnostics, and Drugs to Address Women's Needs programme (D3AWN), which funds development of a mix of products which target either PPH or preeclampsia/eclampsia and which is therefore captured under the heading of non-issue-specific funding elsewhere in this report (see page 38). Over the past four years, D3AWN received \$6.9m in funding from the UK FCDO to advance its portfolio of four products. Two of these products were for the management of PPH: the Ellavi uterine balloon tamponade device and sublingual oxytocin. The latter, however, has since been removed from its portfolio, after failing to meet thresholds for clinical relevance.

Much of the \$1.9m of total funding for PPH devices that *was* captured across 2018 and 2019 also went towards the Ellavi uterine balloon tamponade. Grand Challenges Canada provided \$0.8m over two years, (44% of device funding) to Sinapi Biomedical for Ellavi operational research, alongside the unknown share of FCDO funding provided by PATH via D3AWN. The UK NHS provided the second largest total share of device funding (\$0.6m, 33%), all of which went to the University of Liverpool for the development of the PPH Butterfly – an intravaginal device consisting of a perforated platform and folding handle, for which promising Phase II clinical trial results were published in 2023. Almost all of the remaining device funding came from industry in 2018 (\$0.4m, 21%), including funding from MSD for Mothers for the development of a uterine suction tamponade device.

The wind-down in funding for PPH device R&D may partly reflect the advancement of several devices through the pipeline: following the completion of the PEARLE study, for example, the JADA system – a uterine suction tamponade device – gained FDA approval in 2020. However, our analysis of the PPH pipeline – see overleaf – shows significant additional product development activity by organisations which do not report their funding to the G-FINDER survey.

Of the 88% of PPH funding which has been directed to drug R&D since 2018, just under 75% – a total of \$11m – was directed towards the development of inhaled oxytocin, being developed by the Monash University Institute of Pharmaceutical Sciences in partnership with GlaxoSmithKline and Johnson & Johnson. However, with industry funding tapering over the past four years, the project has also begun to receive support from other philanthropic and public HIC funders, including \$0.3m from Australia's Victorian state government.

FINDINGS

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Practically all remaining funding reported for PPH drug R&D (\$3.0m, 21%) was for the MSD for Mothers-funded, WHO-coordinated Phase III clinical trials to evaluate heat-stable carbetocin. This funding was largely concentrated in 2018, after which – in 2019 – heat stable carbetocin was added to the WHO Essential Medicines List, and in 2020 received its first approval. MSD for Mothers continues to fund post-registration studies of heat-stable carbetocin, including in combination with other drugs such as tranexamic acid.

With heat-stable carbetocin, Monash's inhaled oxytocin and almost all devices in clinical trials over the past four years, clinical development comprised 94% (\$15m) of PPH R&D funding. Just \$0.9m (5.6%) went towards early-stage research. This included <\$0.1m for the development of microarray patch technology for the delivery of oxytocin.

Industry has provided the lion's share of all PPH product development funding over the years (\$14m, 87% of the total), including all of the funding captured in 2020. Most of the remainder came from public HIC funders – mainly from the UK and Australia – which provided 6.7% (\$1.1m) of the total, and Grand Challenges Canada, a public multilateral organisation (\$0.8m, 5.2%). Philanthropic and public LMIC funders provided just 1.1% (\$0.2m) between them, and none at all over the last two years.

Table 14. Top funders of postpartum haemorrhage R&D 2021

Funder	US\$ (millions)			cumulative total		
-une	2018	2019	2020	2021		
Aggregate industry	6.6	4.7	2.1	0.6	14	64
Victorian Department of Jobs, Precincts and Regions				0.3	0.3	36
Grand Challenges Canada (GCC)	0.4	0.4	-	-	0.8	-
UK NHS	0.3	0.3	-	-	0.6	-
Indian BIRAC	<0.1	<0.1	-		<0.1	-
SFI	-	0.1	-		0.1	-
Gates Foundation	0.2	-	-	-	0.2	-
Wellcome	<0.1	-	-	-	<0.1	-
Total	7.5	5.6	2.1	0.9	16	100

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.

- No reported funding

THE POSTPARTUM HAEMORRHAGE PIPELINE

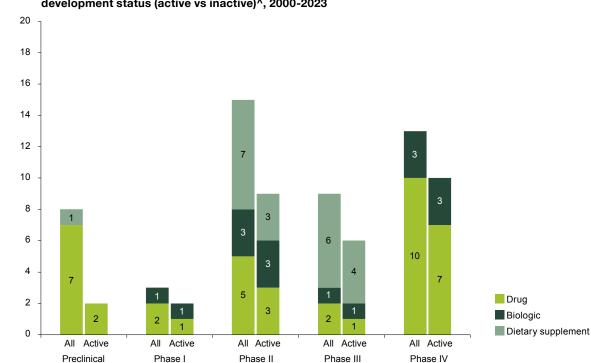
Through the AIM project, PCR researched the landscape of biomedical products under investigation or in use for a number of pregnancy-specific conditions since 2000. Unlike the figures elsewhere in this report, these findings include all products whether or not they are LMIC-appropriate. They are intended to provide useful context on the broader landscape of R&D for these important health issues, but do not correspond directly to the (scope-restricted) funding estimates.

Medicines

In total, we identified 49 medicines in use or under investigation for the prevention and/or treatment of postpartum haemorrhage (PPH) between 2000 and 2023*. 26 are drugs (53% of the total), 14 dietary supplements (29%), and 9 biologics (18%). Well over half of the medicines (29 candidates, 59%) are in active development (post-2020), with the remaining 20 (41%) currently inactive.

Nearly three-quarters of all medicines (36, 73%) are investigational, of which eight are also already used off-label for PPH, including the oral prostaglandin, misoprostol (indicated for gastric ulcers). Purely investigational candidates include an array of herbs and polyphenols, oxytocin formulations in new delivery devices, repurposed small molecules, as well as one new candidate – CT-001 – a next generation biological therapy which received Orphan Drug Designation from the US FDA for the treatment of postpartum haemorrhage in January 2022, and is now entering Phase I trials. The remaining 13 (27%) are already approved for use in the management of PPH, covering several uterotonics and hemostatic agents, as well as the newly approved medicines eptacog alfa and LMIC-focused heat stable carbetocin.

Nearly two-thirds of all medicines identified are repurposed, with the remaining 18 new chemical or biological entities (NCEs). However, over half of these NCEs (10 candidates, 56%) are already approved for use in PPH, meaning the remaining pool of NCEs still under investigation for PPH is quite small – just 8 candidates. Furthermore, 5 of these candidates are inactive, leaving just 3 novel medicines in active development for PPH: CT-001, heat stable inhaled oxytocin, and heat stable oxytocin via microarray patch.



Postpartum haemorrhage medicines by R&D stage, product type and development status (active vs inactive)^, 2000-2023

^The PPH medicines pipeline was updated as of February 2023. Active candidates are candidates with evidence of R&D activity since 2020.

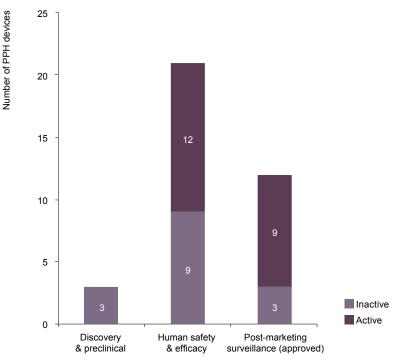
Number of PPH medicines

Devices

We identified 36 devices in use or under investigation for treatment and management of PPH between 2000 and 2023*. Half of these are intrauterine balloons (18 candidates, 50%). External compressive devices comprise the next largest share (5 candidates, 14%), followed by vacuum/ suction devices (4 candidates, 11%), gauze (3 candidates, 8.3%) and intravaginal clamps (2 candidates, 5.6%). Across all 36 devices, 21 (58%) had evidence of R&D activity since 2020, whereas the remaining 15 (42%) are currently inactive.

One-third of devices are already approved for use (12 products, 33%) – such as the Bakri balloon and the newer JADA system – with two-thirds in development (24 candidates, 67%). Of the latter, 88% (21) were in clinical development, with just 3 in discovery or preclinical stages, but only 12 are under active investigation. Active candidates include balloon tamponades already used off label for PPH (e.g. condom catheter, glove tamponade, foley catheter, and Cook Cervical Ripening Balloon), as well as a range of other investigational devices including the Mini-Sponge Tamponade Device, Suction Tube Uterine Tamponade (STUT) (with Levin tube), PPH butterfly, Hemostatic Intra-Uterine Suction Cup, and ultra-low-tech devices such as ice packs and a ball and binder.

Just over two-fifths of the devices identified (15 candidates, 42%) are designed and developed specifically to treat and control PPH, such as the Ellavi Uterine Balloon Tamponade, and the Every Second Matters for Mothers and Babies - UBT device. Of the remaining 21 repurposed or improvised devices, 6 are routinely used off label for PPH in clinical practice, including condom catheters, which are frequently used in low-resource settings where purpose-built UBTs may be too expensive.



Postpartum haemorrhage devices by R&D stage and development status (active vs inactive)^, 2000-2023

[^]The PPH devices pipeline was updated as of February 2023. Active candidates are candidates with evidence of R&D activity since 2020.

	D FOR E ISSL	\$117 MILLION LMIC-APPLICABLE R&D FUNDING IN 2021						
Total R&D spend 2021	Cumulative R&D spend 2018-2021	Total R&D spend 2018-2021 18 19 20 21				% change from 2020	Sector share	R&D stage share
\$117m	\$349m		_	_	-	+20%	Public Philanthe Private	ropic

G-FINDER includes three categories of funding that cannot be allocated to a specific SRH issue: platform technologies; core funding of an SRH R&D organisation; and Other R&D.

Platform technologies are tools or technologies that can be applied to a range of areas but are not yet focused on a single SRH area or product. The platform technology category includes: vaccine, drug and biologics platforms; adjuvants and immunomodulators; and general diagnostic platforms.

Core funding refers to non-earmarked funding given to organisations that work in multiple SRH areas, where the expenditure on each disease or issue is not determined by the funder.

Other R&D captures any grant that cannot otherwise be allocated, such as multi-dimensional projects covering a number of SRH issues, products and thematic areas at the same time.

Global funding for R&D that was not specifically targeted at a single SRH issue has been trending upwards since 2018, increasing by a total of \$80m to reach \$117m in 2021. A rise in platform technology funding accounted for the majority of the growth, receiving relatively consistent annual increases totaling \$69m since 2018.

By 2021, more than three-quarters (80%) of non-issue-specific funding was invested in SRHapplicable platform technologies (\$93m, up \$20m from 2020). This was followed by funding for 'Other R&D' (10%) – which has increased from a low of \$1.3m in 2018, to reach \$12m in 2021. The remaining 10% (\$12m) of non-issue-specific funding came via core funding to organisations involved in SRH R&D, which slumped further in 2021 after dropping sharply in 2020 (down by \$26m) from a one-off \$28m spike in 2019.

Because our multi-STI and multipurpose prevention technology (MPT) categories typically capture funding which is directed to multiple specific issues in sexual & reproductive health, most of the activity included here is more broadly applicable R&D potentially relevant to all three of the global health areas covered by the G-FINDER survey: neglected disease, emerging infectious disease and sexual & reproductive health. Such funding might include, for example, a vaccine adjuvant which can be administered alongside vaccines against COVID-19, HPV and leishmaniasis – diseases which fall under each of our three global health areas. Just 1% of funding listed here is focused purely on multiple sexual & reproductive health issues, with the vast majority (97%) being categorised as potentially applicable to all three global health areas. Another 2% covers R&D which applies to both neglected diseases and SRH issues, much of which involves research with potential application to HIV, which we treat as both a neglected disease and a sexual & reproductive health issue. While R&D for HIV alongside other STIs is included here, funding which is *exclusively* relevant to HIV R&D is instead covered in our G-FINDER neglected disease report.



Rice University, with support from the Bill & Melinda Gates Foundation, will develop a once-a-year treatment for patients infected with HIV and other infectious diseases. These employ cells engineered to make therapeutic substances, in this case monoclonal antibodies (mAbs), to be delivered to patients through protective biopolymer <u>shells</u>.

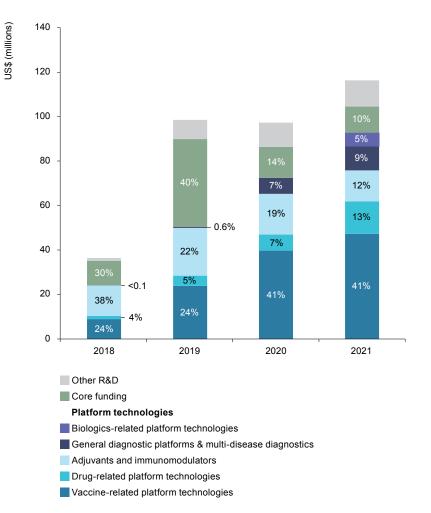


Figure 9. Non-issue-specific R&D funding by product type 2018-2021

Platform technologies

Funding for SRH-applicable platform technologies reached \$93m in 2021, a \$20m increase from 2020, following an ongoing upward trend. Half of this funding in 2021 was invested in vaccinerelated platform technologies (\$47m, 51%), with most of the remainder split relatively evenly between drug-related platforms (\$15m, 16%), adjuvants & immunomodulators (\$14m, 15%), and general diagnostic platforms (\$11m, 11%). The remaining 6.7% was invested in biologics-related platforms, a new category introduced in 2021, which serves to highlight a growing category of funding that was previously included under drug or vaccine platform R&D.

Almost all areas of platform technology saw increased investment in 2021, after increasing steadily since 2018. The sole exception was funding for adjuvants & immunomodulators, which returned to its 2018 level of \$14m after a two-year peak averaging nearly \$20m. The sharp overall growth in (non-adjuvant) platform technologies has been experienced across all global health areas, even prior to the COVID pandemic – which helped drive a sharp increase in EID-relevant platforms, including many which are also relevant to SRH.

Two-thirds of all this 2021 platform technology funding came from the Gates Foundation, which has gradually increased its (SRH-relevant) platform funding from \$12m in 2018 to \$62m in 2021, with investments across all platform types. As in the previous two years, over half (59%) of Gates funding was for vaccine platforms, along with substantial investments across drug-, diagnostic- and biologics-related platforms, such as assays to improve the speed of manufacturing vaccines, and a low-cost manufacturing process for monoclonal antibodies.

The majority of the remaining platform funding came from the US NIH (14%) and the EC (8.1%). 2021 saw a four-fold increase in EC funding for platform technologies, linked to new investment in vaccine-related platforms, and first-time investment in SRH-applicable platforms from the Mexican CONACYT and US DOD.

Core funding

Core funding of SRH R&D organisations totalled \$12m in 2021, roughly in line with previous years, with the exception of 2019 when a large (\$24m), one-off grant from the German BMZ to Adjuvant Capital boosted the total to \$39m.

The Indian ICMR has been a consistent provider of SRH-related core funding, investing an annual average of \$7.1m in intramural funding to their Reproductive Health Institute. However, in the (temporary) absence of ICMR funding data for 2021, and to avoid showing an artefactual fall, we have imputed an estimate for its intramural core funding – for 2021 only – based on the average nominal value of funding over the preceding three years. Subsequent reports will be updated on the basis of the true 2021 ICMR funding value once it becomes available.

Other than ICMR, the top core funders have shifted from year to year: the UK FCDO was a top core funder of SRH R&D in 2018 and 2019, providing over \$4m in each year to Bangladesh's icddr,b, for research across multiple SRH issues. This funding dropped sharply in 2021 (along with the FCDO's overall R&D funding across all global health areas) falling to just \$52k.

In 2020, there was a one-off jump in Gates core funding (\$4.9m) – predominantly to the Scripps Research Institute, and PATH's One Billion Lives Fund – which then dropped below 2019 levels in 2021. The decline in 2021 funding from Gates and the FCDO left the Norwegian MOFA – which had not previously provided any funding in this area – as the second largest core funder, thanks to the \$3.5m it provided to the Research Council of Norway for SRH-related research.

These figures do not include the significant SRH-focused core funding provided to large organisations, such as the WHO, which are not primarily devoted to R&D, and where R&D expenditure cannot be apportioned. Instead, we count only the funding they receive which is specifically devoted to or including R&D activities.

Other R&D

Funding for SRH-related 'Other R&D' has increased every year to reach \$12m in 2021, up from just \$1.3m in 2018. This is due to both entirely new funding streams and increased funding from ongoing funders, especially the Gates Foundation and the US NIH.

The Gates Foundation saw a third consecutive year of stable funding with their contribution of \$3.5m in 2021 making them the single biggest funder of Other R&D. Industry provided its first ever funding to this area in 2021, supporting early-stage research covering multiple disease areas and indications.

The UK FCDO had been a consistent funder in this area, providing over 80% of the 2018 total. Their funding, though, fell by almost two-thirds (\$1.6m) in 2021, alongside deep cuts across almost all areas of the FCDO's support for global health R&D. Their \$0.9m in remaining funding went entirely to PATH, directed towards their Devices, Diagnostics, and Drugs to Address Women's Needs Product Development ('D3AWN') project. As with many of the funding streams included under the heading of Other R&D, this money will ultimately be divided across a portfolio of individual products, in this case to prevent or manage either preeclampsia & eclampsia (PE&E) or postpartum haemorrhage (PPH); but the original disbursement is not earmarked for specific candidates or even areas, meaning it cannot be attributed to the totals for either PE&E or PPH.

Table 15. Top non-issue-specific R&D funders 2021 (US\$ millions)

Funder P	atform echnologi	core fundi	ng Other R&D	iotal o	10
Gates Foundation	61	0.5	3.5	65	56
US NIH	14	0.3	2.5	16	14
EC	7.6	-	-	7.6	6.5
Indian ICMR		6.5	-	6.5	5.6
Norwegian Ministry of Foreign Affairs	-	3.5	-	3.5	3.0
Mexican CONACYT	2.6		-	2.6	2.2
US DOD	2.5	-	-	2.5	2.2
Aggregate industry	-	-	2.2	2.2	1.8
UK FCDO	0.5	<0.1	0.9	1.5	1.2
Indian DBT	1.3	-	-	1.3	1.1
South African MRC	0.6	-	0.6	1.2	1.0
Anonymous funder(s)		0.9	-	1.0	0.8
Subtotal of top 12	92	12	9.7	112	96
Total	93	12	12	117	100

Funding organisation did not participate in the survey for this year. Any contributions listed are based on data reported by funding recipients so may be incomplete.
 No reported funding

DISCUSSION

Funding is not equal: non-maternal SRH R&D funding has enjoyed robust growth since 2018, while investment in maternal health has languished

Funding for the range of sexual and reproductive health issues included in this report has grown by nearly \$200m since we began collecting data in 2018, an increase of nearly 50%. But this growth has not been distributed equally.

Much of the overall rise was in funding not specific to a single issue, which we will discuss in more detail below. But most of the actual issue-specific funding growth – another \$121m of the \$193m overall increase – was geared towards R&D for sexually transmitted infections or issues related to them. Human papillomavirus and HPV-related cervical cancer R&D, for example, rose by \$53m (up 59%). Meanwhile the other major STIs covered in this report also received an additional \$68m (up 86%), mostly via big boosts in funding for gonorrhoea and genital herpes ('HSV-2') R&D. These three areas – HPV, gonorrhoea and HSV-2 – accounted for 94% of the net growth in issue-specific SRH funding between 2018-2021.

In fact, overall funding for non-maternal SRH issues – STIs, HPV, contraception, and multipurpose prevention technologies (MPTs) – rose by \$117m (34%) between 2018 and 2021. In stark contrast, funding for the maternal health issues included in the report – postpartum haemorrhage and preeclampsia & eclampsia – *fell* by a combined \$3.7m, together receiving just \$22m in 2021. This is a drop of nearly 15% from budgets which were already dangerously light even in 2018.

While funding for maternal health remains unacceptably low, our data probably underestimates the true level of funding. Our review of the product development pipeline for maternal health – see the boxouts in individual chapters – reveals a significant amount of ongoing activity in areas for which we received little or no funding data. While our survey coverage is broad, we do still have gaps in participation and data from key players in maternal health-related R&D, which may be contributing to an underestimate of maternal health investment.

The other reason that funding for maternal health R&D is much lower than for other issues is, however, likely due to the different reasons *why* funders support SRH R&D. Many SRH issues have a 'dual market', with new technologies needed and potentially useful in both high-income and low- and middle-income countries. We recognise this, and include funding for developing these kinds of products – as long as they are 'LMIC-appropriate' – even if they are not developed specifically with LMIC populations in mind. While this excludes R&D which can only work in high-resource settings, it does however ignore funders' motives. And typically, not much mystery surrounds which side of the dual market product developers are most interested in: funding is far more likely to focus on tapping high-income country commercial potential, by addressing high-income country problems. Comparing the R&D needs and burden of maternal versus non-maternal SRH issues thus partly explains the gap in funding between them.

High-income countries, for example, experience more than 15% of the global burden of genital herpes, but less than 1% of the burden of maternal health issues. The difference in their respective funding likely reflects this difference in burden and market potential: HSV-2 R&D received twice as much funding as maternal health, despite maternal health being responsible for more than ten times the global burden, almost exclusively in LMICs. Funding for gonorrhoea – another area with a relatively substantial burden in HICs and seen as posing a global threat due to antimicrobial resistance – was even higher: more than two and a half times the total for maternal health, addressing an issue with less than a thirtieth of maternal health's global burden.

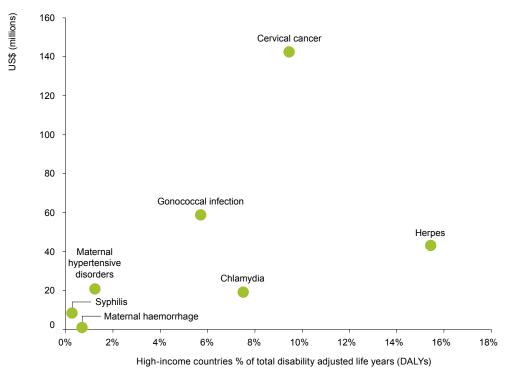


Figure 10. Total R&D funding and the burden of sexual and reproductive health issues in high-income countries 2021

Moreover, many maternal health issues – like postpartum haemorrhage – really *do* require specific LMIC-*targeted* interventions, such as low-tech devices or heat-stable drug formulations to replace drugs like oxytocin – responsible for saving countless lives in high income countries but often inappropriate for low-resource settings. Given comparatively limited funding in this space, it does seem that where there is little dual market potential to drive investment, some funders and developers – except those driven by a global health agenda – appear less inclined to support purely LMIC-targeted technologies.

LMICs cannot subsist on the spillovers from HIC-focused R&D

The recent trends in SRH R&D funding strongly suggest that, for much of the funding included in this report, helping LMIC populations may just be a byproduct of the primary goal to deliver improved products for high-income country markets.

While funders' true motives are hard to judge, there is no question that many of the SRH products we see being developed will ultimately be brought to market in HICs. If these products spill over into LMICs eventually, they will still deliver real benefits. But it *does* matter that so much of the global funding reported focuses primarily – and sometimes exclusively – on the needs of HICs. It distorts the distribution of funds away from areas like maternal and pregnancy-related conditions, the burden of which has been significantly reduced in most HICs. And, perhaps more importantly, it means there is no guarantee that the potentially beneficial technologies we see in the pipeline will reach people in LMICs within a reasonable timeframe.

A pipeline built from the perspective of HIC needs will produce products which require further testing in, and adaptation to, low-resource environments. Technologies with on-paper applications to LMIC as well as HIC needs will also require additional funding to deliver that impact in practice, and may end up being abandoned if they fail to secure that investment or generate LMIC commercial demand. The sharp rise in funding for biologics – which has more than doubled as a share of SRH funding – is a likely case in point. Biologics funding is mostly devoted to HSV-2, which offers a strong commercial incentive in high-income settings, especially given biologics are typically more costly than small molecule drugs, and more reliant on stable infrastructure for transport, storage and administration. Translating this to LMIC access may therefore be some time away. Similarly, large investments in new contraceptives geared towards and now available in high-income markets, but ideal for low-resource settings – such as on-demand, non-hormonal and user-controlled contraception like Phexxi – are likely to be some way off reaching LMIC markets.

While 'spillover' from HIC-targeted products is obviously a good thing, it will not replace the need for R&D that targets the specific needs of individuals in low-resource settings. Unfortunately, investment in genuinely LMIC-focused R&D – in areas like PPH devices or drugs, preeclampsia point of care diagnostics or new medicines – is unacceptably low, and seems to be falling.

There are growing concerns about drug resistance, but a decline in diagnostic funding suggests a missed opportunity to help combat the issue

The period since 2018 has seen big rises in the share of funding going to vaccines – which rose from 14% to 24% of total funding. Almost half of this increase (\$29m, 46%) was focused on gonorrhoea, largely in response to the rise of serious antimicrobial resistance (AMR) to existing drug treatments, and which was naturally coupled with the 2020 spike in next generation gonorrhoea drug funding, which more than tripled from \$7.9m in 2018 to \$29m in 2020.

At the same time, the share of funding for SRH diagnostics fell by nearly half, from 12% in 2018 to 6.4%, offset only partly by the rapid rise in general diagnostic platforms potentially relevant to SRH. This represents a missed opportunity to maintain the effectiveness of existing drug treatments and control the spread of resistance by identifying it at the point-of-care and adapting treatments accordingly. Moreover, even with the inevitability of rising drug resistance, particularly for gonorrhoea, funding appropriate diagnostics will be critical to reduce transmission, and allow health systems more time to prepare for widespread use of new therapies and preventive and therapeutic vaccination. Unfortunately, despite solid global efforts in support of STI diagnostics R&D, particularly point-of-care tests for STIs – this lack of investment remains concerning.

On the positive side, some SRH funding is becoming more user-focused and more diverse

Promisingly, growth in funding for contraception and MPTs is, at least, one area where innovations are meaningfully moving towards meeting the specific needs of users, especially those in LMICs.

In LMICs – and in indeed HICs – unmet need for contraception is driven by issues of access and cost, but also, and to a large extent, acceptability. In these settings, meeting the needs of users requires more than simply achieving clinical efficacy. There is demand for user-controlled products which can be obtained and used without the need for administration by a medical professional; and for a wider variety of options, especially low- or non-hormonal contraceptives; those that cater to male users; or those that limit disruption to menstrual bleeding patterns.

Encouragingly, there are clear signs of progress in these areas: a proportional fall in R&D investment for hormonal methods of contraception (from 69% to 62%) and non-user-controlled methods (from 60% to 35%) over the last four years points to an increasingly user-focused research agenda. Likewise, a drop in the proportion of total funding geared towards female-only contraceptives (84% to 71%) reflects a move towards more gender-equitable healthcare, and acknowledges that a broader range of contraceptive options for all sexes and genders are needed. This progress of contraceptive R&D towards greater user control mirrors the gains already made in funding for MPTs, where almost two-thirds of historical funding has gone to products which are both non-hormonal and user-controlled.

However, research into more diverse and user-controlled contraceptives remains very much at earlystages of development with, for example, 91% of non-hormonal contraceptive funding directed towards early-stage research. Given the higher costs of later-stage trials, much more funding will be needed to transform the product pipeline and, ultimately, the range of products available in LMICs.

As with other global health areas, sexual and reproductive health R&D has benefited from COVID-driven increases in funding for platform technologies

Non-issue-specific (NIS) funding represented the single biggest area of growth in SRH R&D between 2018 and 2021 – particularly in R&D for platform technologies – technologies that can be applied to a range of areas but are not yet focused on a single area or product. But the impact of this growth on our measure of SRH funding doesn't necessarily reflect a deliberate commitment from funders.

While overall NIS funding has more than tripled since 2018 (up by a total of \$80m), mostly thanks to a nearly fourfold increase in funding for platforms (up \$69m), the vast majority of this growth was in funding – and platforms – relevant to neglected and epidemic diseases, but with the *potential* to impact sexual or reproductive health. Broadly-applicable platform technologies can count as 'SRH R&D' without actually being *intended* to address sexual and reproductive health issues. Indeed, many platform technologies are ultimately used in ways not originally conceived of by their inventors – like the ChAdOx1 adenoviral vector, which was quickly repurposed in 2020 from Ebola and Crimean Congo Haemorrhagic Fever to form the basis of AstraZeneca's COVID vaccine.

So, while shared technologies are always welcome, we should celebrate this particular growth area cautiously, with the knowledge that the single biggest rise in SRH funding is actually a global spike in funding for tools for a variety of different diseases, most of them unrelated to sexual and reproductive health. Whether the political will exists to move beyond the creation of these platforms to actually fund their application to SRH, and especially to the specific needs of low-resource settings, is another story.

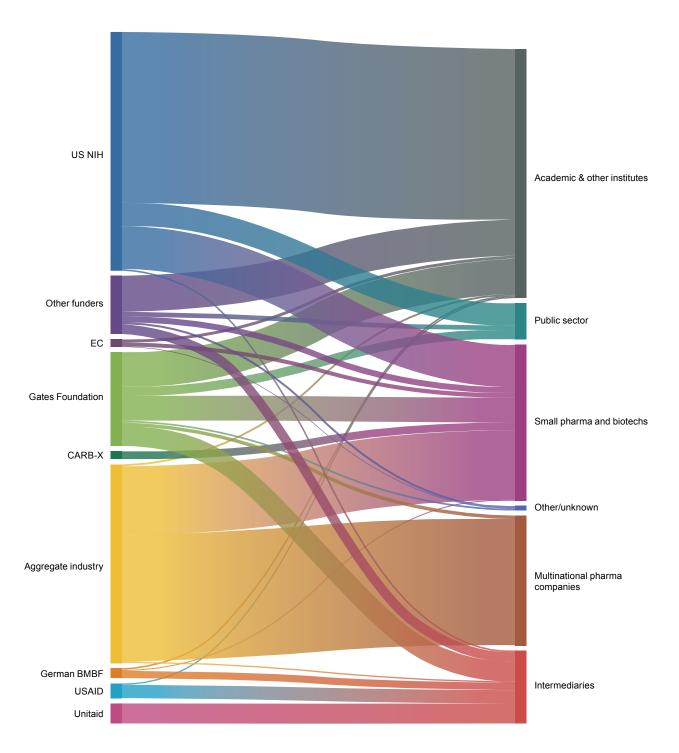
Funding for SRH has become less reliant on a handful of dominant funders, but remains too concentrated

The US National Institutes of Health (NIH) has consistently been the largest single funder of SRH R&D, providing more than 30% of the total each year. Another quarter of 2021's total funding came from industry, which is encouraging given it has traditionally been more cautious in its funding for SRH R&D, typically perceiving it as unlucrative, political, and litigious. Together, these top two funders have consistently comprised more than half of the global share of SRH R&D funding each year.

However, although NIH and industry continue to dominate SRH R&D, their combined share fell from 68% in 2018 to 57% in 2021. This reflects growth in funding from several other sources, most notably Unitaid, the European Commission, the German BMBF and the Gates Foundation. But, even with this diversification, funding remains very concentrated amongst the top 10 funders overall, who accounted for more than 93% of the 2021 total, narrowly their largest annual share on record.

Figure 11. SRH funding flows 2018-2021





A moment in the spotlight: there is hope that a pivotal global focus on women's health will lead to increased investment in SRH R&D, and a genuine focus on LMIC needs

The last few years has seen increased discussion of and attention to key problems facing women's health, namely the critical lack of interest and investment in innovations to address health issues that affect women exclusively, disproportionately, or differently, as well as the near absence of attention to the intersection of gender and sex in global health R&D. This inattention has not only blockaded women and girls from study designs and outcome measures – for example, through the exclusion of pregnant and lactating women from clinical trials – it has also removed them from the research agenda at large.

At a time now where 'women's health' is receiving the attention it deserves, including within the global health sector, we can be optimistic that enthusiasm for progress will translate to funding to drive action. And given most SRH issues *do* affect women and girls exclusively, disproportionately or differently – with a particular burden for those in LMICs – there is hope that funding for LMIC-applicable SRH products will rise, and soon.

Ultimately, however, talk is cheap, and late-stage clinical development is expensive. The \$594m in 2021 funding across all SRH R&D remains just a small fraction of the amounts devoted to, for example, HIV (\$1.5bn) and COVID-19 (\$5.6bn). If the scores of products waiting in early-stage development are to advance through the pipeline and begin addressing the burden of sexual and reproductive health issues, increased attention needs to bring with it a genuine increase in funding. And to be successful, a genuine commitment to the specific, individual needs of people in low- and middle-income countries will be critical.

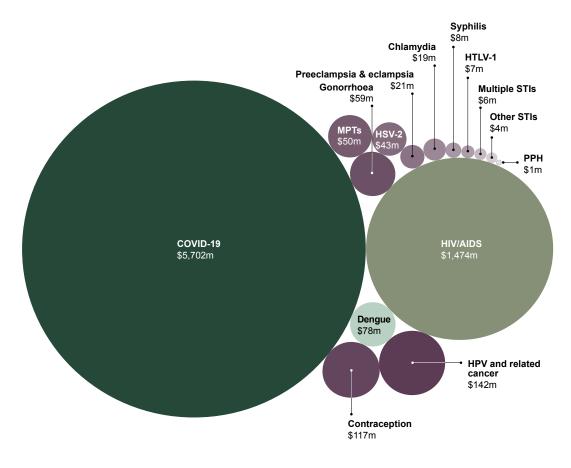


Figure 12. R&D funding to SRH versus COVID-19, HIV/AIDS and dengue 2021 (US\$ millions)

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