

# HIV Prevention Research & Development Investments, 2000–2015

*Investment priorities  
to fund innovation in a challenging  
global health landscape*



RESOURCE TRACKING  
FOR HIV PREVENTION  
RESEARCH & DEVELOPMENT

**HIV Prevention Research & Development Investments, 2000–2015**  
Investment priorities to fund innovation in a challenging global health landscape  
OCTOBER 2016

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## *Reflecting the Evolving Field of Biomedical HIV Prevention*

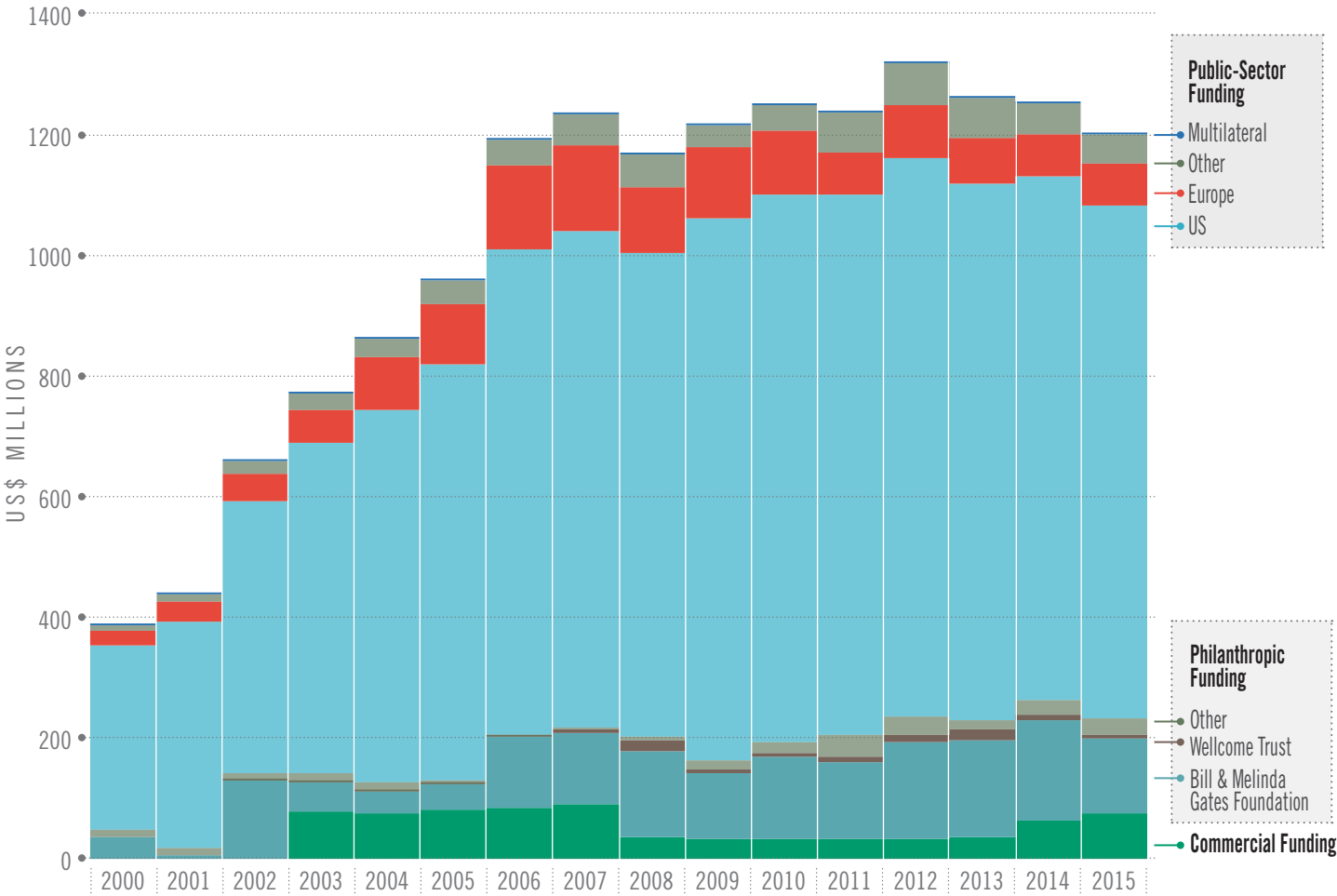
In 2016, the HIV Vaccines & Microbicides Resource Tracking Working Group was renamed the “Resource Tracking for HIV Prevention Research & Development Working Group” in order to accurately convey the full scope of the report to those who use and supply the data on which the report depends. The group’s revised name also reflects the evolution of the prevention field, provides flexibility as that field continues to evolve and allows for adjustment as individual prevention options proceed from research to the various phases of rollout and research and development investment emphases shift accordingly.

# Introduction

Since 2004 the Resource Tracking for HIV Prevention Research and Development Working Group (“Working Group”) has employed a comprehensive methodology to track trends in research and development (R&D) investments and expenditures for biomedical AIDS prevention options, including AIDS vaccines, microbicides, pre-exposure prophylaxis (PrEP), treatment as prevention (TasP), medical male circumcision (VMMC), female condoms, prevention of vertical transmission (PMTCT) and HSV-2 vaccines. The Working Group also tracks investments toward HIV cure research which, under the National Institutes of Health (NIH) Office of AIDS Research (OAR) definition include investments in therapeutic AIDS vaccines.<sup>2</sup>

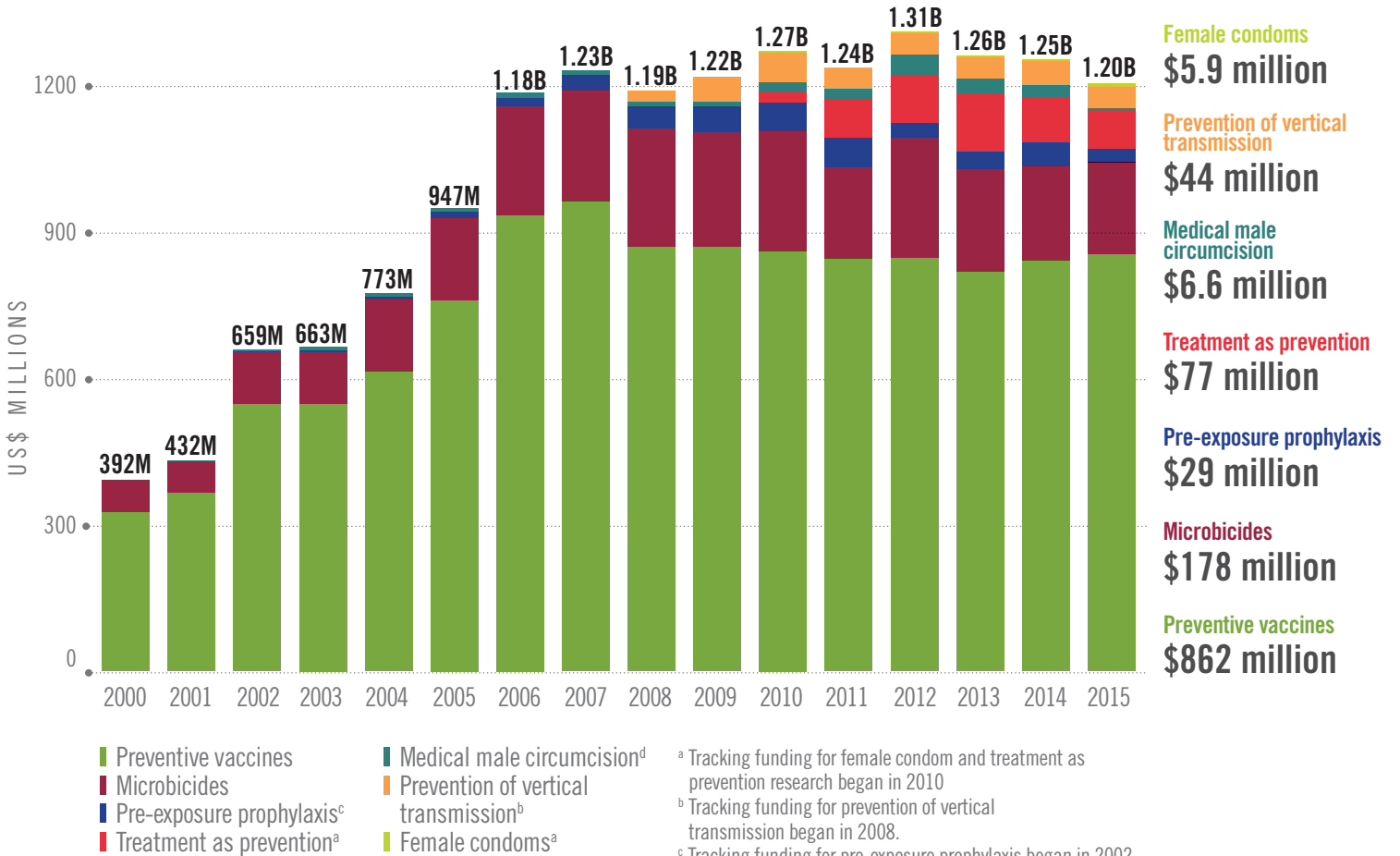
The Working Group generates estimates of R&D investments that can be compared year to year across options, strategies and funding sources, helping assess the impact of public policies aimed at accelerating scientific progress and furnish facts for advocacy. This effort provides transparency for funders, policy makers and HIV/AIDS advocates, enabling increased

**FIGURE 1 Global Funding Sources for HIV Prevention R&D, 2000–2015 (US\$ millions)**



understanding of HIV prevention R&D investment flows. In this, its twelfth annual report, the Working Group documents R&D spending for the calendar year 2015, and analyzes investment trends spanning fifteen years (Figure 1).

**FIGURE 2 Global HIV Prevention R&D Investments by Technology Category, 2000–2015**  
(US\$ millions)



## ● Trends in HIV Prevention R&D

In May of 2016, UNAIDS released its *Global AIDS Update*.<sup>3</sup> The *Update* highlighted the fact that 17 million people were on antiretroviral treatment at the end of 2015 — two million people ahead of the 15 million target set within the *2011 UN Political Declaration on HIV and AIDS*. However, it also underlined that there have been no declines in HIV acquisition rates among adults for the past several years. The net effect of these countervailing trends is that since 2010, the number of annual new HIV infections among adults has remained unchanged from 1.9 million, with some countries actually experiencing increases in incidence.<sup>4</sup>

The implications of these dynamics for the funding of HIV prevention R&D, the core purpose of which is to continue producing innovative approaches to reducing new infections, are sizable. So too, is the importance of tracking the volumes and directions of that funding.

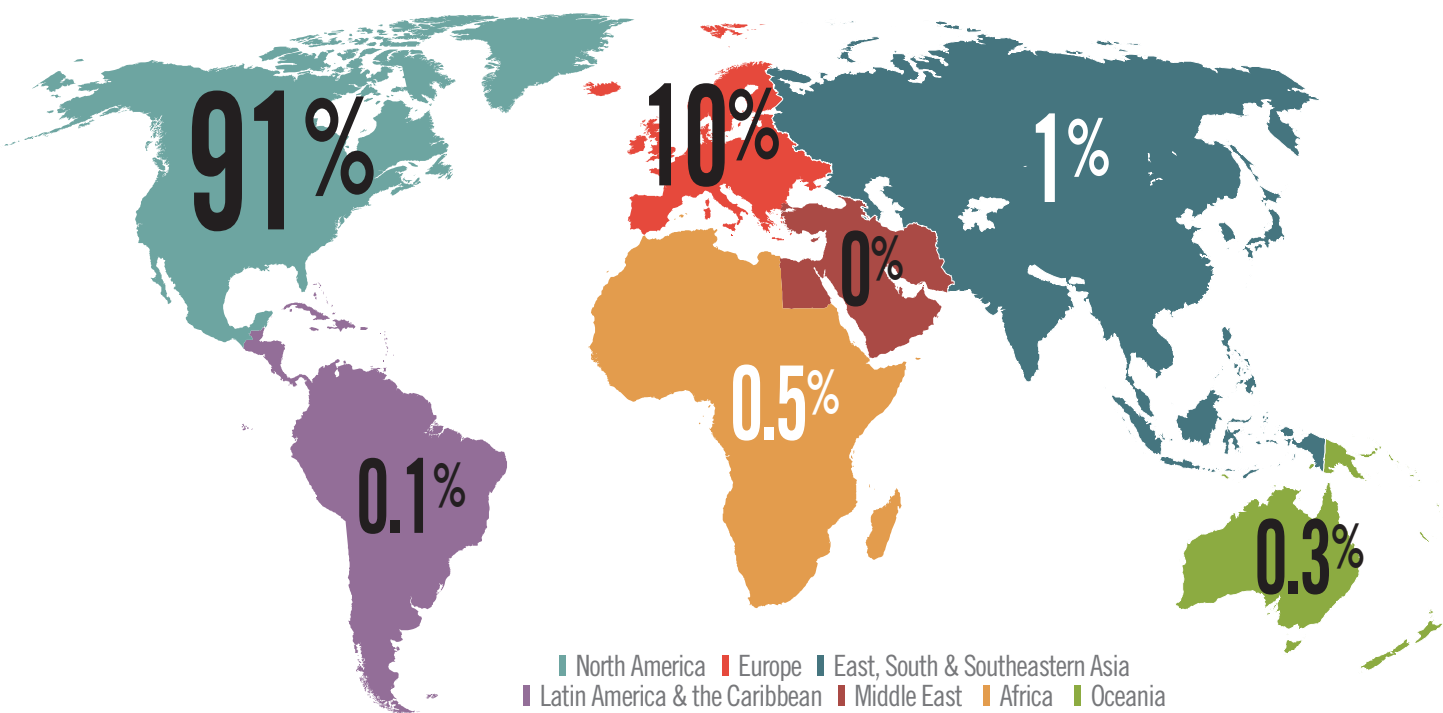
In 2015, reported funding for HIV prevention R&D decreased slightly from US\$1.25 billion in 2014 to US\$1.20 billion<sup>5</sup> after more than a decade, during which overall funding remained essentially flat (*Figure 2*).

FIGURE 3 2015 Global HIV Prevention R&D Investments By Sector & Region

### 2015 HIV prevention R&D investments by sector



### 2015 public-sector investments by region



Within that trend, while investments toward research for preventive vaccines and female condoms increased from 2014 levels, investments toward microbicides, PrEP, TasP, VMMC and PMTCT declined. In that same decade, investment contributions by sector (Figure 3) also varied. See Table 2 for more specific data behind the analysis presented below.

- United States public-sector funding dropped by 2.1 percent from 2014 to 2015, and in 2015 HIV research was flat-funded at the NIH. Still, the US public sector remained the single largest source of funding for HIV prevention R&D, with a total investment of US\$850 million. There was also variation within sector contributions by technology category: investments in preventive vaccines saw a slight increase over 2014 levels of US\$590 million. PrEP, VMMC and female condom R&D also increased slightly, but microbicides, TasP and PMTCT saw a decline in US public-sector funding in 2015 (Figure 4).

FIGURE 4a US Public-Sector Investments in HIV Prevention R&D, Compared to All Other Funding, 2011–2015 (US\$ billions)

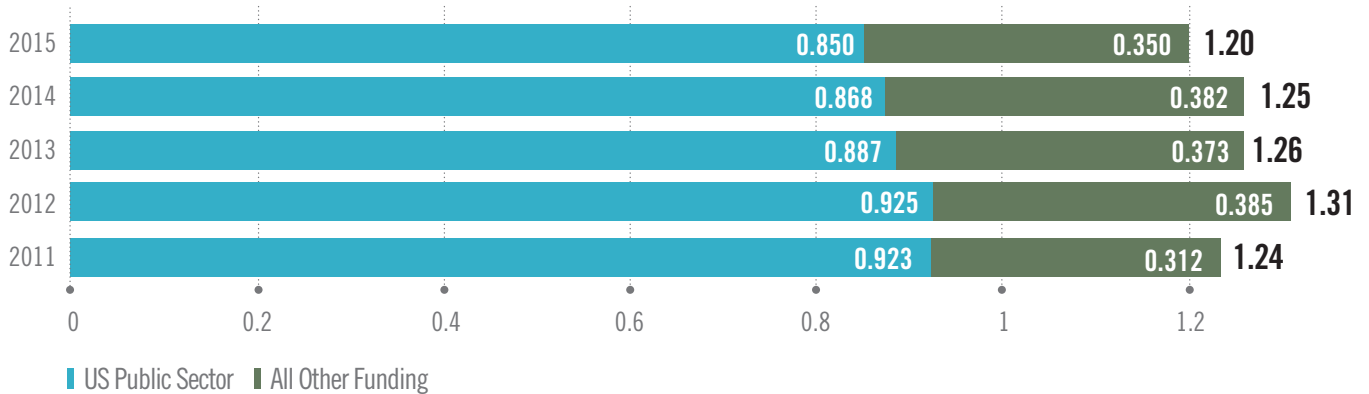
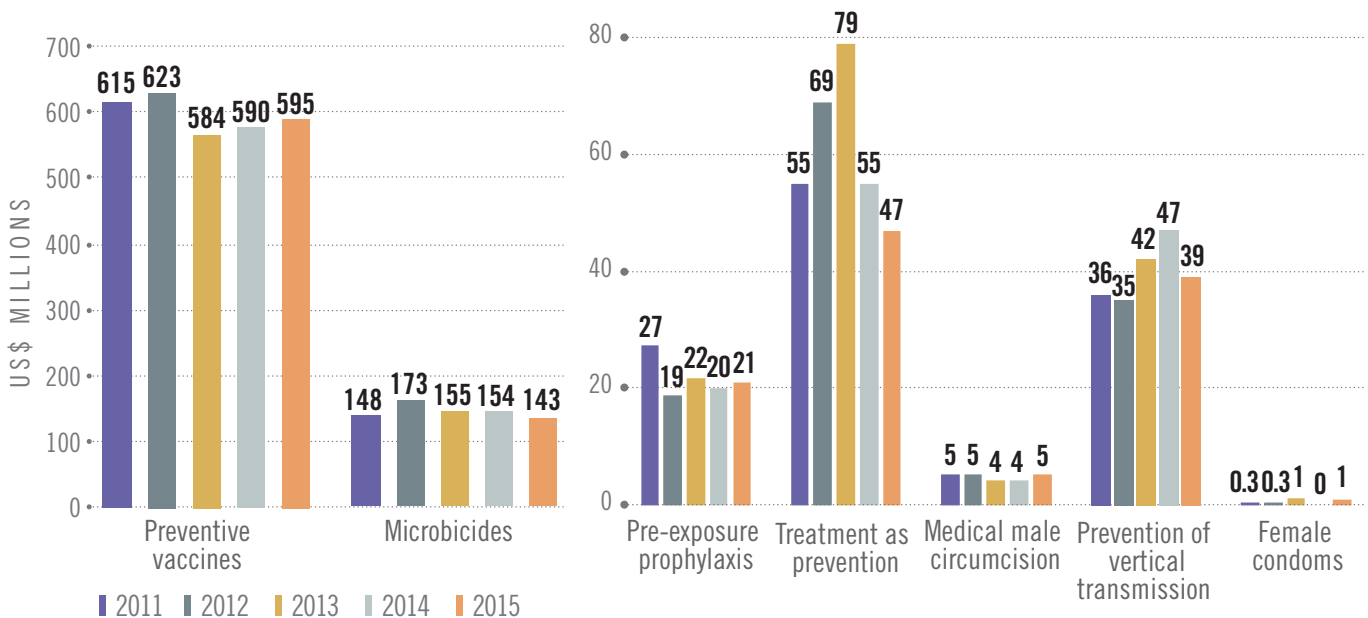


FIGURE 4b US Public-Sector Investments in HIV Prevention R&D, by Technology, 2011–2015 (US\$ millions)





➤ The European public sector contributed seven percent of total public-sector investments in HIV prevention R&D, at US\$69 million. This is the same amount invested as in 2014. Several new investors entered the field in 2015, but their contributions were offset by reductions from existing funders. European public investments in female condoms, PMTCT and PrEP increased (by two percent, 31 percent and 27 percent, respectively), while investments in male circumcision, microbicides and TasP decreased (by 96 percent, 27 percent and 13 percent, respectively). Funding for preventive vaccine R&D experienced a significant increase, from US\$35 million in 2014 to US\$44 million in 2015, due to the European Commission’s Horizon 2020 initiative<sup>6</sup> (Figure 5).

FIGURE 5a European Public-Sector Investments in HIV Prevention R&D, Compared to All Other Funding, 2011–2015 (US\$ billions)

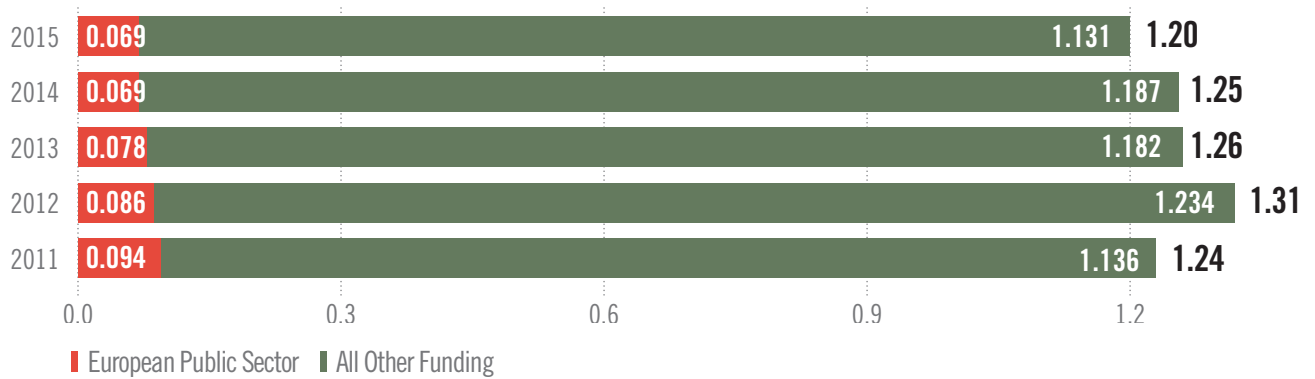
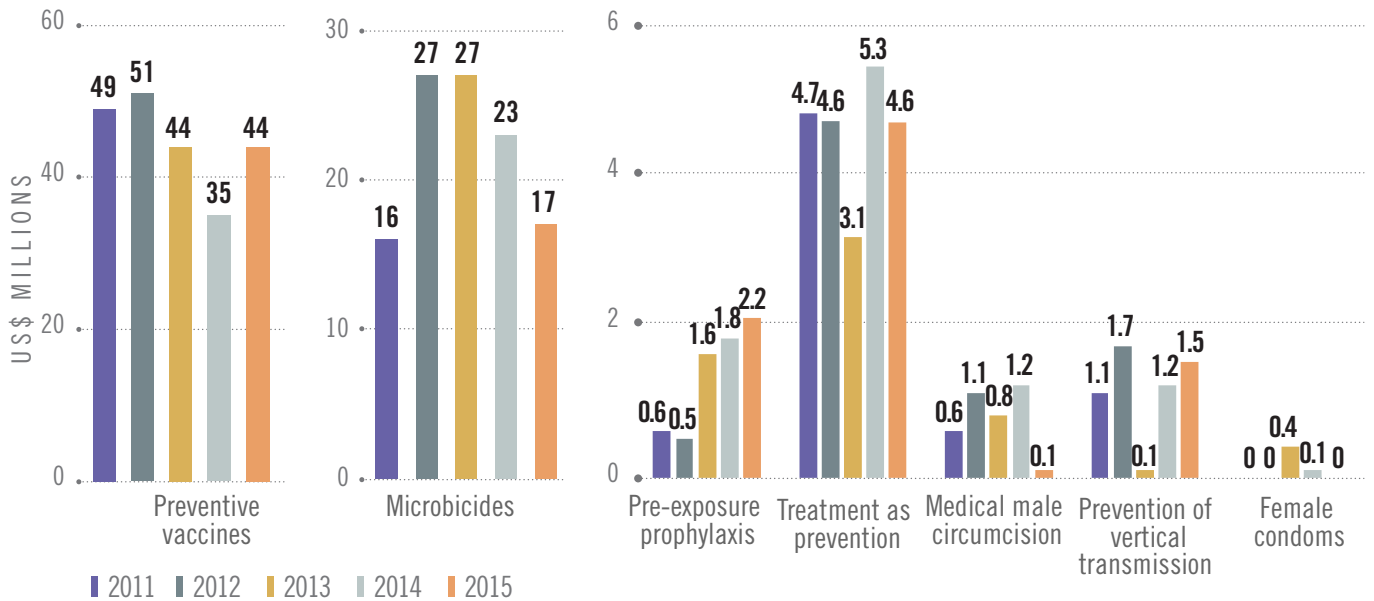
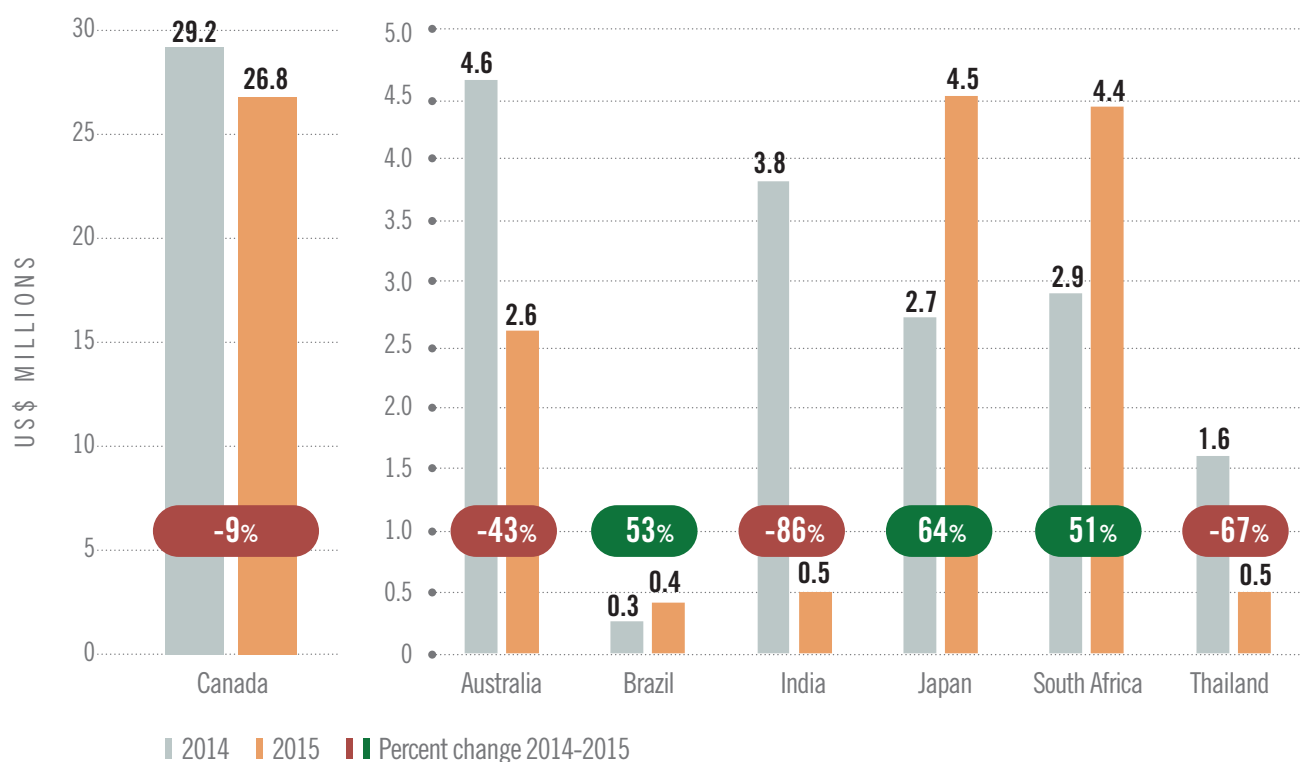


FIGURE 5b European Public-Sector Investments in HIV Prevention R&D, by Technology, 2011–2015 (US\$ millions)



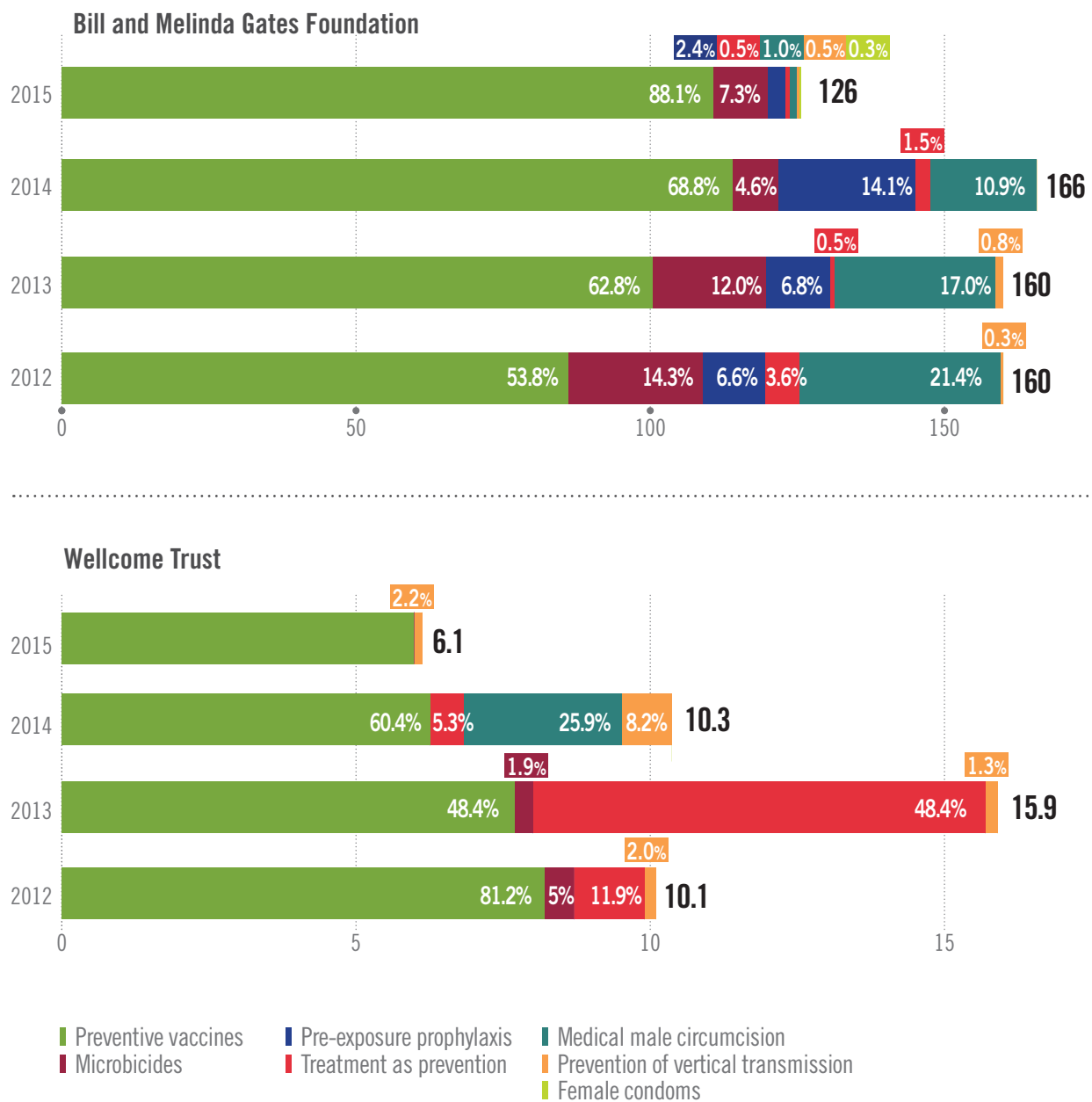
- Public-sector funding outside the US and Europe also declined slightly, falling another US\$2 million in 2015, down from US\$52 million. Brazil, Japan and South Africa increased their public investments in HIV prevention by 53 percent, 64 percent and 51 percent respectively, while Australia, Canada, India and Thailand reduced their levels by 43 percent, 9 percent, 86 percent and 67 percent, respectively (Figure 6). Funding reductions were seen in VMMC (89 percent), microbicides (46 percent), PrEP (26 percent) and TasP (16 percent). Funding for preventive vaccines remained essentially unchanged at US\$26 million. PMTCT and female condoms experienced a boost in funding due to new investments from India for implementation research into female condom R&D and renewed interest from Australia, Brazil, Canada and South Africa in funding research on PMTCT.

FIGURE 6 Changes in Public-Sector Investments Outside the US and Europe, 2014–2015 (US\$ millions)



➤ Global philanthropic funding declined dramatically from 2014 to 2015, with the two traditionally largest funding sources, the Bill and Melinda Gates Foundation (BMGF) and the Wellcome Trust, reducing their contributions to biomedical HIV prevention by 24 percent and 41 percent, respectively (Figure 7). This continued a multi-year downward trend in philanthropic support which had reversed briefly in 2014. The number of philanthropic funders participating in HIV prevention R&D funding increased slightly, however, from 16 funders in 2014 to 20 in 2015.<sup>7</sup> In 2015 the philanthropic sector comprised 13 percent of all funding at US\$157 million, a 22 percent decrease from its 2014 contribution level. It is possible that such decreases could simply be due to the cyclical nature of philanthropic research funding.







FIGURE 7 Investments in R&D Prevention by Top Philanthropic Funders (US\$ millions)



- Somewhat in contrast, the commercial sector is estimated to have increased its contribution to HIV prevention R&D by 18 percent over 2014 levels, continuing a modest trend of steady increases over several years. In 2014 the Working Group received information from nine companies about HIV prevention R&D investments, while in 2016 it received data from 15 companies. Estimates of commercial contributions to all areas of HIV prevention R&D tracked by the Working Group have been steadily increasing for several years, as industry has played a larger role not only in product development, but also in providing funding and expertise for implementation and rollout.<sup>8</sup>

Highlighting the cyclical nature of R&D is critical to understanding some of the funding ebbs and flows presented in this report. While many expensive efficacy trials were undertaken in the 2010-2015 period, several others are only just getting underway (*Table 1*).

TABLE 1 Ongoing and Planned Efficacy Trials (July 2016)

Strategy	Trial	Product	Number ppts	Population	Status (start-end)	Location
 Antibody	<b>HVTN 704/ HPTN 085</b>	VRC01 antibody, infused every two months	2,700	Men and transgender persons who have sex with men	Enrolling: Apr. 2016–Sept. 2020	Brazil, Peru, US
 Antibody	<b>HVTN 703/ HPTN 081</b>		1,500	Sexually active women	Enrolling: May 2016–Jul. 2020	Botswana, Kenya, Malawi, Mozambique, Tanzania, South Africa, Zimbabwe
 Preventive HIV vaccine	<b>HVTN 702</b>	ALVAC/gp120 MF59 adjuvant boost, five doses over 12 months	5,400	Sexually active heterosexual women and men	Projected start Nov. 2016–End 2020	South Africa
 Long-acting injectable	<b>HPTN 083</b>	Cabotegravir injections every two months	4,500	Men and transgender persons who have sex with men	Projected start Q3/4 2016; projected end June 2020	~40 sites in North and South America, South Africa and Asia
 Long-acting injectable	<b>HPTN 084</b>	Cabotegravir injections; schedule to be confirmed, either every two or three months	TBD	Sexually active women	Potential start in 2017	Southern and East African countries TBD
 Preventive HIV vaccine	<b>TBD</b>	Ad26/MVA boost	TBD	TBD	Potential start in 2017	US, Latin American, Southern and East African countries TBD

For the latest trial updates visit [www.avac.org/pxrd](http://www.avac.org/pxrd).

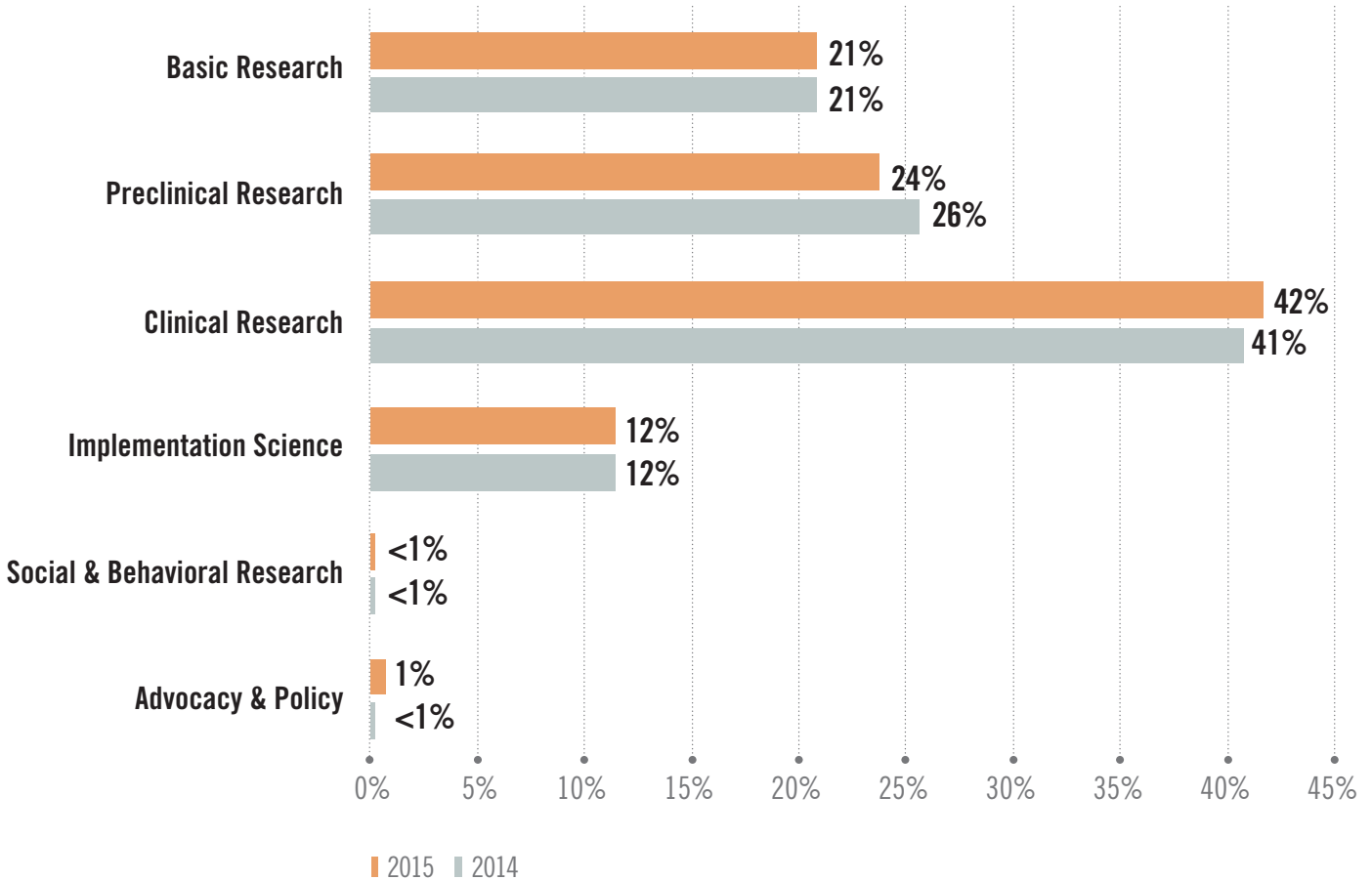
## ● Key Findings

Each of the key findings that emerged from this year’s resource tracking, ancillary research, data compilation and analysis reflects not only the status of investments for HIV prevention R&D, but also the sources and foci of these investments.

**I Investments have expanded to develop, demonstrate and deliver HIV prevention options**  
 HIV prevention R&D spans the various stages of research, reflecting continued momentum to develop new prevention options and excitement about expanding implementation of the existing prevention toolbox. In 2014 and 2015, basic research held steady at 21 percent of all investments while clinical research (Phases I to III) increased slightly between 2014 and 2015 (Figure 8).

Tracking investments in the “science of delivery”, or the study of processes, context and various other determinants of effective HIV prevention programming, began in 2014, and remained high on funders’ agendas in 2015. Roughly 12 percent of all investments in 2014 were directed to “implementation science” and held steady at the same level in 2015.

FIGURE 8 Research to Rollout: Investments by research stage, 2014–2015



## **II Industry is expanding its contributions to HIV prevention R&D**

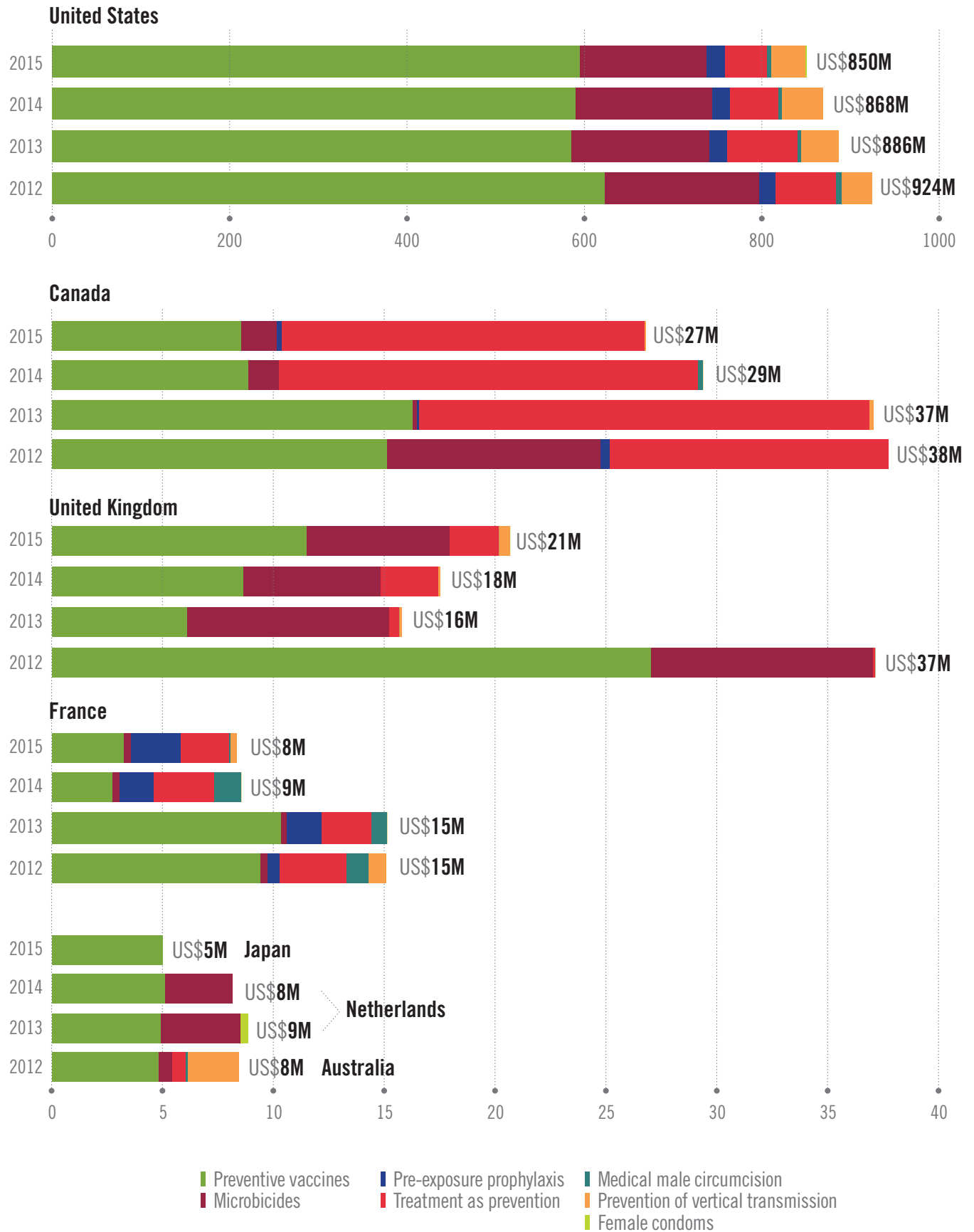
2015 saw industry play a greater role in HIV prevention across the continuum from research to rollout. Not only were product donations crucial to improving accessibility of biomedical prevention options, but commercial entities also increased investments in implementation and demonstration research. Commercial-sector investments in implementation science increased 36 percent from 2014 to 2015. Industry contributions to basic and clinical research have also remained critical to advancing future prevention options, and investments in these phases of the R&D pipeline received funding boosts from industry in 2015 accordingly.

Following efficacy results for the dapivirine ring, some commercial-sector entities have also provided technical expertise to support movement toward the next steps, with critical emphasis on needs and challenges for the ring's primary end-user populations.

## **III Funding remains concentrated among a small number of large investors**

Of the US\$1.20 billion total investments in 2015, US\$850 million (or 70 percent) came from the US public sector (*Figure 9*), with the NIH producing the majority. Philanthropic-sector investments continue to be dominated by the BMGF, which produced 80 percent of philanthropic contributions in 2015. Together the US public sector and the BMGF constituted 81 percent of all funding in 2015, down only slightly from 83 percent in 2014. A more diverse base of funders could increase the stability and continuity of R&D financing, and could help cushion the impact if one or two large donors were to make reductions in their investments.

FIGURE 9 Top Countries Investing in HIV Prevention R&D, 2012–2015 (US\$ millions)



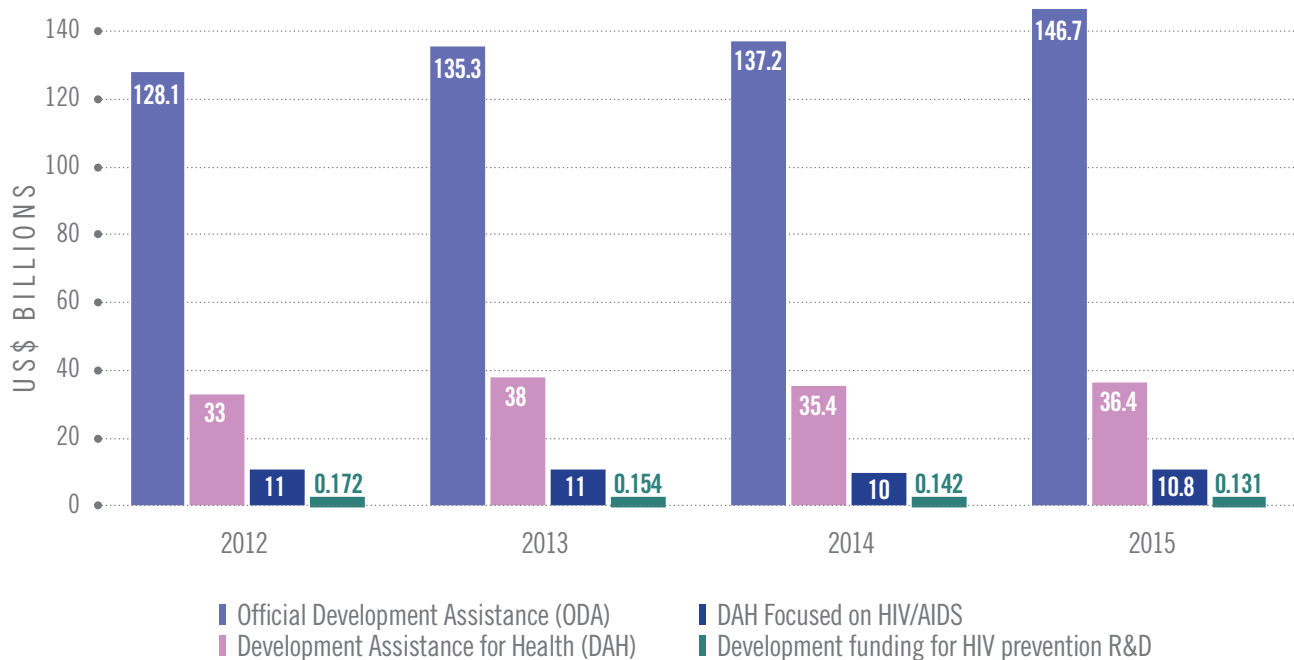
#### IV It remains to be seen whether global commitments will translate to action

The expiration of the Millennium Development Goals (MDGs) in 2015 marked the end of an unprecedented effort to mobilize resources in service of a vast number of health and development initiatives. Development assistance for health (DAH) grew 11 percent annually from 2000-2010.<sup>9</sup> In 2015, however, DAH was US\$36 billion, down from its peak of US\$38 billion in 2013 and essentially flat from 2014.<sup>9</sup> The MDGs precipitated significant investment in HIV/AIDS. Even with DAH flat-lining in 2015, the amount allocated to HIV actually increased by 2.5 percent.

With the closure of the MDG era comes the inception of the Sustainable Development Goals (SDGs). The ambitious program of 17 goals and 169 targets is aimed at continuing and accelerating the momentum engendered by the MDGs. SDG 3 is dedicated specifically to health, with health R&D included in target 3b.<sup>10</sup> While not explicitly related to health, targets 9.5 and 9.b of “Goal 9: Industry, Innovation and Infrastructure” support capacity building for technology R&D and innovation in all countries with a special emphasis on lower- and middle-income countries — capacity which can, in turn, be applied to HIV prevention R&D.

In 2015, development agency support for HIV prevention R&D was US\$131 million (*Figure 10*), declining from US\$142 million in 2014. Monitoring HIV prevention funding data can contribute to ensuring progress toward target 3b and other relevant targets of the SDGs. For lasting achievements toward ending the HIV epidemic by 2030 to be made, HIV prevention R&D must regain and retain prominence on the global development agenda.

FIGURE 10 HIV Prevention R&D in the Context of Development Assistance for Health and Total Official Development Assistance, 2012–2015 (US\$ billions)



Sources: AVAC: [www.AVAC.org](http://www.AVAC.org); Institute for Health Metrics and Evaluation (IHME). [www.healthdata.org](http://www.healthdata.org); Organisation for Economic Co-operation and Development (OECD). [www.oecd.org](http://www.oecd.org); Resource Tracking for HIV Prevention R&D Working Group 2015 data collection.



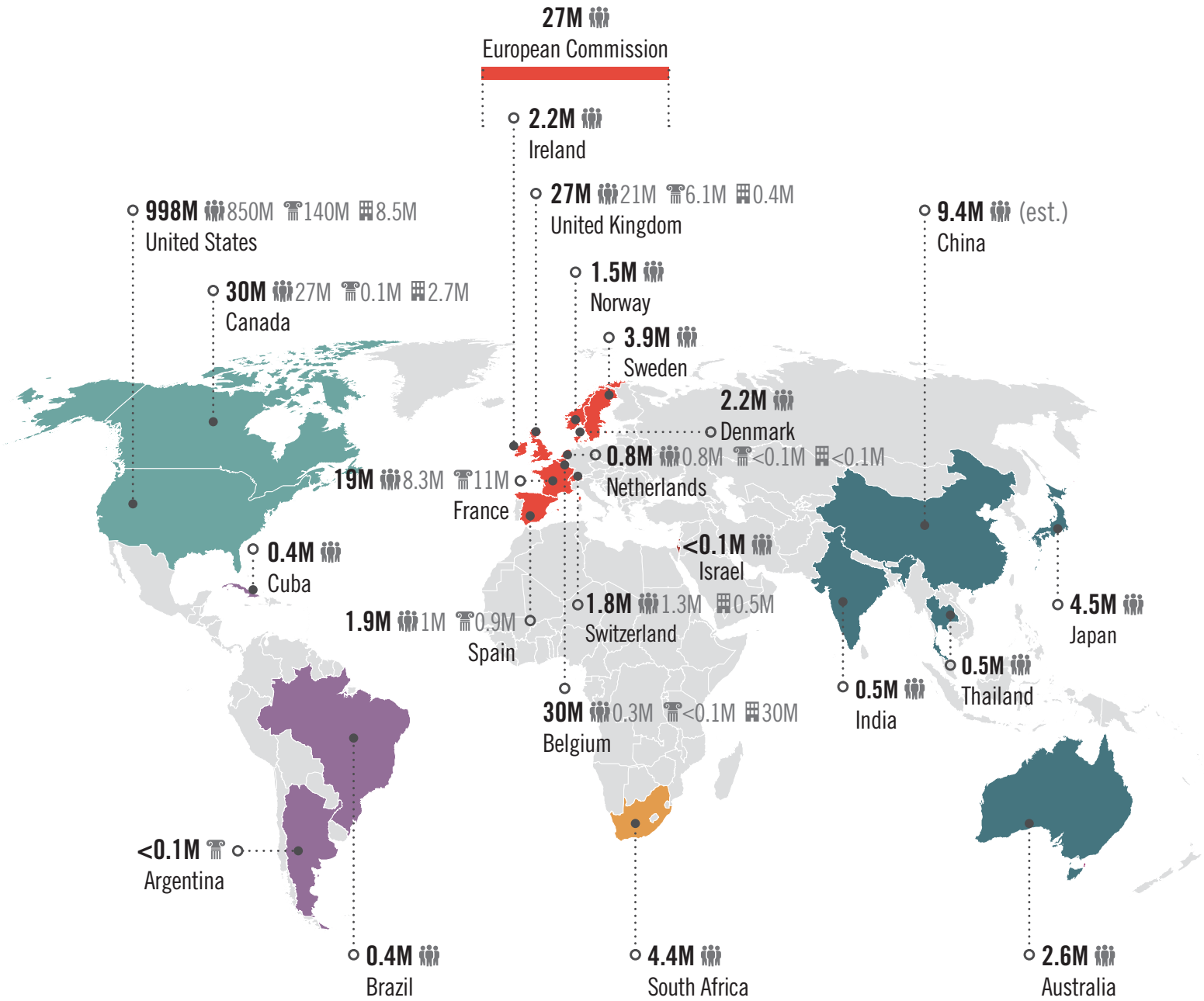
**V Support for continued mobilization of MIC and LMIC resources is imperative**

Of all global HIV prevention R&D funding in 2015, 1.6 percent came from upper-middle-income countries (UMICs), up from 1.2 percent in 2014, while 0.05 percent (down from 0.4 percent in 2014) came from India as the sole lower-middle-income country (LMIC) from which the Working Group was able to collect investment data (*Figure 11*). The bulk of India's funding was allocated to its basic preventive vaccine efforts. UMIC funding went to preclinical vaccine research, spearheaded primarily by South Africa's public sector research institutions and their contributions to the development and testing of a clade C AIDS vaccine candidate.

Reliance on donor funding in LMICs and UMICs remains high, despite steady upward economic growth in these countries.<sup>11</sup> Beyond South Africa, African government-backed programs for science, including HIV prevention R&D, are in various early stages.<sup>12</sup> In the face of a slowing decline of HIV incidence rates among adults globally,<sup>4</sup> countries may not be able to rely on the sustainability of external funding sources; UNAIDS has estimated that total resources from international sources for HIV service delivery in low-and-middle-income countries declined to US\$8.1 billion in 2015, the lowest level since 2010.<sup>13</sup> Countries must instead be supported in efforts to mobilize a diversity of domestic resources for HIV prevention R&D. The import of domestic resource mobilization and enhanced access to science, technology and innovation has been acknowledged by the global community through the commitments made to the SDGs, and specifically SDG 17.<sup>14</sup> Realizing these goals through concrete global action and the necessary associated funding commitments will further progress within HIV prevention R&D and global health R&D as a whole.

FIGURE 11 Total Global Investments in HIV Prevention R&D by Country, 2015 (US\$)

Public, philanthropic and commercial-sector funding from countries investing in HIV prevention R&D\*



- North America
- Latin America & the Caribbean
- Western & Central Europe
- Middle East
- Sub-Saharan Africa
- Southeast Asia, East Asia & Oceania
- Public
- Philanthropic
- Commercial

\* Information collected includes funding from those countries that responded to the Working Group's annual survey, or where public information on sources of funding was available. Totals include public, philanthropic and commercial sector funding from each country. Commercial-sector investments are allocated to a country based on the location of corporate headquarters and are underestimated due to a lack of reporting by companies. Not all commercial-sector estimates are able to be allocated by country.

## *Creative Investing in HIV Prevention R&D*

With traditional funding channels shrinking and shifting research priorities, development organizations, research entities and implementing agencies alike are facing the need to be more efficient with available yet stagnating or dwindling funds. Concurrently, private capital markets are recognizing the vast economic potential of investing for impact, or investing to link social with financial returns. Impact investing provides capital and leverages resources to build capacity and achieve gains in scale that may not be realized through conventional grant-making alone.<sup>15,16,17</sup> As a financing model for R&D related to HIV prevention, impact investing may be worth exploration.

Development Impact Bonds (DIBs) are one model through which private investors seek to have a greater impact on community outcomes. Through DIBs, private investors work with partners such as government agencies, non-profit and other service providers to furnish financing to achieve a shared goal. If the goal is achieved, an “outcomes funder” repays the investments, with more successful programs usually leading to greater return on investments. Investments are not of money alone, but also of skills and expertise aimed at driving results and creating lasting improvements in the lives of affected communities.

The US-based think tank, the Center for Global Development, and the UK-based Social Finance developed a case study for mobilizing private resources through a DIB for TasP in Swaziland. This was built upon the successful outcome of HPTN 052, which demonstrated significant HIV transmission reduction risk in serodiscordant couples upon early ART initiation.<sup>18</sup> A DIB would provide the approximately US\$10 million needed to fund a three-year implementation study, the outcomes being measured through viral suppression and reduced HIV transmission, as well as estimated future gains such as financial savings from decreased medical needs and improved economic productivity. The DIB provides incentives for private investors to assist in sustainable systems building for the coordination and integration of multilevel interventions for maximum efficiency.<sup>15</sup>

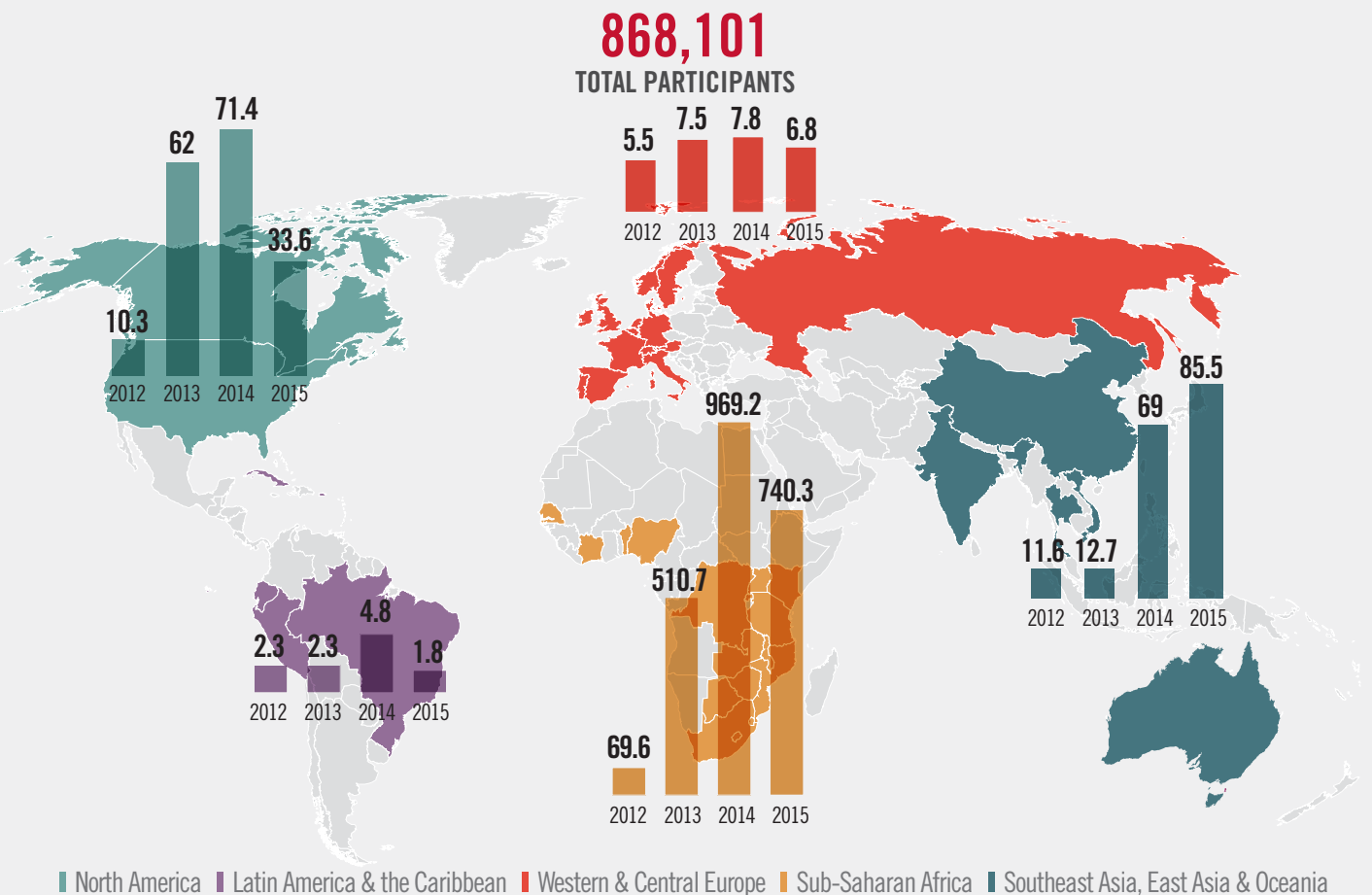
The risks and challenges of DIBs and similar financing models remain great. Investors must ensure that interventions and deal structures create lasting improvements, making responsible funding choices and entrusting in local expertise. The private sector is notoriously risk-averse, and impressing upon it the benefit of investing for impact versus return in nontraditional enterprise is something with which the cash-strapped global health sector has scant experience. However, the increasing importance of the “impact economy” sees consumers holding corporations accountable to interests other than their bottom line. In this light, DIBs may be further explored as a way to sustainably finance future HIV prevention R&D.

## Trial Participation

HIV prevention research cannot be conducted without those who volunteer to participate in clinical trials, or without the engagement of communities in which those trials take place. In 2015, there were over 868,000 participants in HIV prevention research trials, primarily based in sites with high HIV/AIDS burdens in South Africa, Uganda and the US (Figure 12).

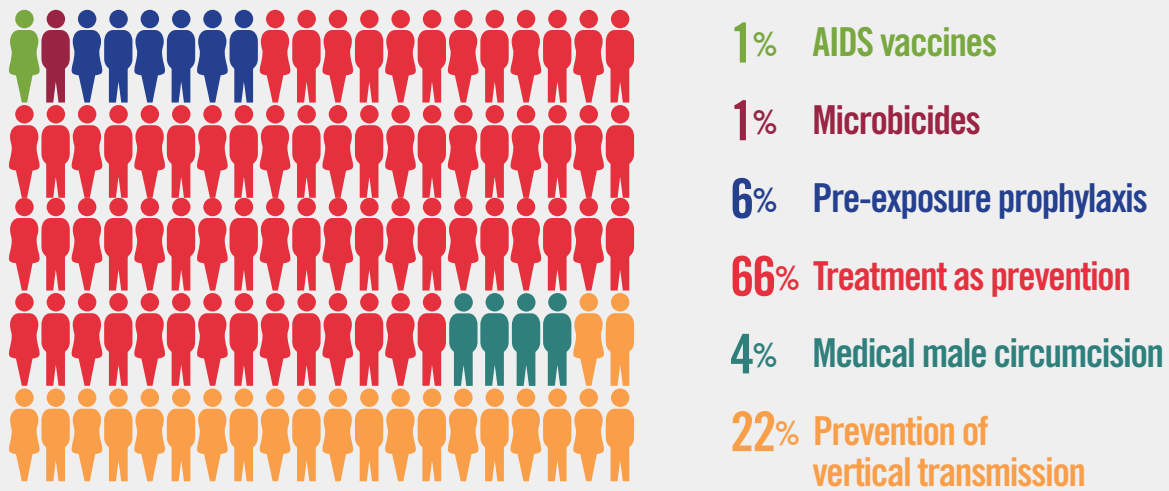
It is important to note the dearth in enrollment of members of key populations (KPs) (Figure 13). While there are trials aimed specifically at men who have sex with men (MSM), transgender individuals and people who inject drugs (PWID), and hence require their participation, the preponderance of trials do not specify the need to include members of KPs. Without specific outreach to members of these populations, as well as to adolescent girls and young women, and without assistance in overcoming the various barriers to participation such as criminalization laws, trial sponsors cannot guarantee that research outcomes will meet a diversity of needs.

FIGURE 12 HIV Prevention R&D Trial Participants by Region, 2015 (thousands)



Trial participants gain access to HIV programs through trials in which they participate, and assuming successful trial results, they are hopefully the populations most likely to be the first to receive any new safe and effective HIV prevention methods ensuing from such research. Failing to ensure that members of KPs are able to engage meaningfully with the prevention research pipeline may also prevent them from reaping the potential benefit of scientific progress. Greater efforts must be made to include KPs in these essential processes for the HIV prevention response to be truly impactful.

FIGURE 13 Trial Participants by Prevention Research Area, 2015



Key Population Representation in Clinical Trials , 2015



## ● Collection and Analysis Methodology

In order to generate investment estimates that can be compared from year to year, from one technology to another and across funding sources, a systematic approach to data collection and collation was developed at the establishment of this collaborative project in 2004. Its fundamental premise is that monitoring HIV prevention R&D investment trends permits the identification of investment needs, prioritization of research areas and assessment of the impact of public policies that increase or decrease investments. Investment data also provide the fact base for advocacy around spending levels, resource allocations, the value of sustained investments in research building on trial successes, attracting novel HIV prevention candidates to the pipeline, and follow-on trials to assure the safety, immunogenicity, efficacy and acceptability of new HIV prevention products.

The same methods were employed to generate the estimates of funding for R&D presented in this year's report. R&D data were collected on annual disbursements by public, private and philanthropic funders for product development, clinical trials and trial preparation, community education and policy and advocacy efforts to estimate annual investments in HIV prevention R&D. In 2015, the Group also began tracking data on funding toward implementation science for HIV prevention. Investment trends were assessed and compared by year, prevention type, research phase, funder category and geographic location.

Comprehensive and consistent use of this methodology enables data comparisons across organizations, countries and years. The Working Group makes every effort to maintain a comparable data set, while allowing for the limitations inherent to global investment tracking styles and timing. Its primary limitation is that data collection largely depends on the response rate of public, private and philanthropic funders, and year-to-year variability is partly a reflection of this response rate. Funds were allocated to the year in which they were disbursed by the donor, irrespective of whether the funds were expended by the recipient in that year or in future years.<sup>19</sup>

Investment figures are rounded throughout the report. In order to minimize double-counting, the Working Group distinguishes between primary funders and intermediary organizations. "Intermediary" organizations receive resources from multiple funders and use these resources to fund their own work, as well as the work of others. All figures in the report are reported in current US dollars and have not been adjusted for inflation. Because of this, investments in later years may be overvalued relative to investments in earlier years due to inflation.<sup>20</sup>

From a total of 215 surveyed organizations, institutions and companies, 112 funders reported their investments. A total of 1,752 grants were collected, of which 485 were allocated to HIV prevention research, with an average grant size of US\$1,099,050 million.

## *Global Health and HIV: Lessons from Ebola and Zika*

If 2014 was the year of Ebola, 2015 was that of Zika, a virus which is spread through infected *Aedes* mosquitoes and which has been linked to the congenital birth disorder microcephaly, along with a host of other conditions. While the international health community was slow to declare the spread of Ebola an emergency, officials reacted swiftly to Zika.

The outbreaks of Ebola and Zika have served to reignite public health awareness of the potential for global health pandemics borne of today's interconnectedness. These outbreaks have further emphasized that the global health R&D and funder communities cannot afford to deprioritize research investments in diseases of the developing world. In the case of Ebola, an effective vaccine for monkeys was developed over a decade ago, but the relative rarity of the virus — and the economic realities of the countries typically affected — prevented further investments and development.<sup>21</sup> The recently-convened public-private Coalition for Epidemic Preparedness (CEPI) aims to facilitate the movement of vaccines with limited commercial value but powerful population-level benefits through R&D to market. Its inception was inspired by the awareness that the neglect of this Ebola candidate — and its subsequent devastating toll on West African countries — cannot be repeated.<sup>22</sup>

Nevertheless, efforts to contain the dual outbreaks of Ebola and Zika have underlined the importance of investments in HIV prevention R&D. While support for capacity building in countries across Africa for HIV research enabled these same sites to be utilized quickly for Ebola, the hunt for an effective Zika vaccine has been boosted by expertise and research along the HIV vaccine pipeline.<sup>23</sup>

Failing to invest adequately in comprehensive prevention R&D for Zika and Ebola — as with HIV — is to the detriment of global public health. Investing in prevention R&D has an impact beyond the HIV field, and allows for research to meet the current and evolving needs of the global community.

TABLE 2 Global Investments in HIV Prevention R&amp;D: 2015 funding map

Funding type	2014	2015	% Change 2014-2015	Funder	Total 2015	Total 2014	% Change
US Public Sector	\$868 million	\$850 million	-2.1%	NIH	\$729.9	\$728.1	0.2%
				USAID/PEPFAR	\$74.7	\$84.5	-11.6%
				CDC	\$15.7	\$24.3	-35.4%
				MHRP	\$26.6	\$27.5	-3.3%
European Public Sector	\$69 million	\$69 million	0%	Belgium	\$0.3	\$0.7	-57.1%
				Denmark	\$2.2	\$1.7	29.4%
				EC	\$27.3	\$20.3	34.5%
				France	\$8.3	\$8.5	-2.4%
				Germany	—	—	—
				Ireland	\$2.2	\$2.8	-21.4%
				Italy	—	\$0.2	—
				Netherlands	\$0.8	\$8.1	-90.2%
				Norway	\$1.5	\$2.0	-25.0%
				Spain	\$1.0	\$1.6	-35.5%
				Sweden	\$3.9	\$3.4	14.7%
				Switzerland	\$1.3	\$1.7	-23.5%
Other Governments	\$52 million	\$50 million	-3.8%	Australia	\$2.6	\$4.6	-43.8%
				Brazil	\$0.4	\$0.3	60.0%
				Canada	\$26.8	\$29.2	-8.2%
				China	\$9.4	\$7.0	34.3%
				Cuba	\$0.4	—	—
				India	\$0.5	\$3.8	-86.8%
				Israel	\$0.04	—	—
				Japan	\$4.5	\$2.7	66.7%
				Russia	—	—	—
				South Africa	\$4.4	\$2.9	51.7%
				Taiwan	—	—	—
				Thailand	\$0.5	\$1.6	-68.8%
Philanthropic	\$200 million	\$157 million	-21.5%	BMGF	\$125.7	\$165.7	-24.1%
				Wellcome Trust	\$6.1	\$10.4	-41.3%
				Other	\$25.4	\$24.1	5.4%
Industry	\$63 million	\$75 million	18.4%	Commercial Sector	\$74.5	\$62.9	18.4%
<b>Total</b>	<b>\$1.25 billion</b>	<b>\$1.20 billion</b>	<b>-1.6%</b>	<b>HIV prevention option totals</b>	<b>\$120 billion</b>	<b>\$125 billion</b>	<b>-1.6%</b>
				<b>% Change 2014–2015</b>		<b>-2%</b>	

<sup>a</sup> Where 100 percent increase in investments is noted, 2014 investments may not have been reported by the funder, and thus this is not necessarily indicative of a 100 percent increase in funding from 2014. Similarly, where a 100 percent decrease in funding is noted, the funder may not have reported investments for 2015. All figures are rounded. See Appendix for a detailed methodology section, including the limitations of data collection.



2015 totals in US\$ millions (2014 investments, percent change<sup>a</sup>)

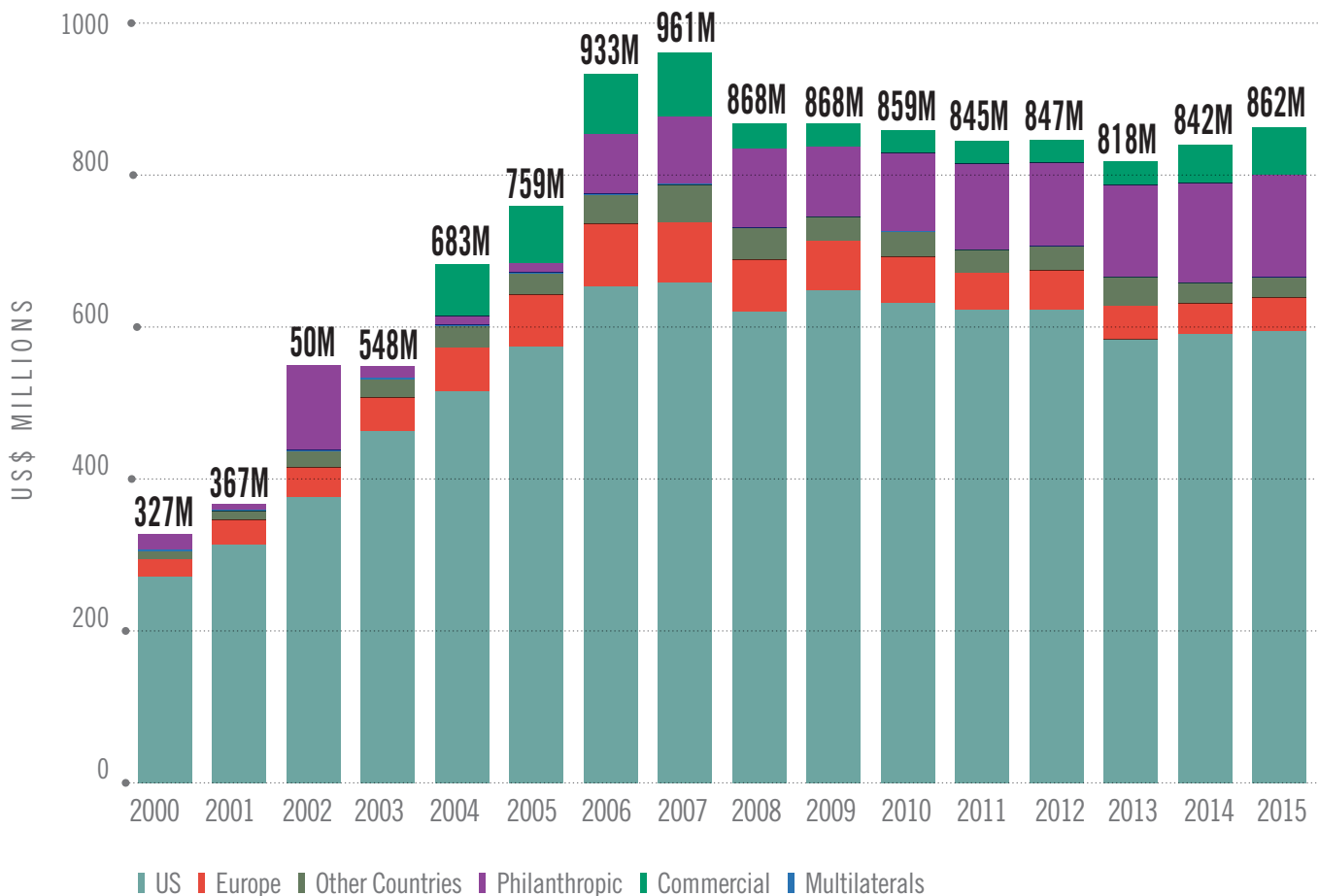
Preventive AIDS vaccines			Microbicides			Pre-exposure prophylaxis			Treatment as prevention			Male circumcision			Female condoms			Prevention of vertical transmission		
2015	2014	Change	2015	2014	Change	2015	2014	Change	2015	2014	Change	2015	2014	Change	2015	2014	Change	2015	2014	Change
\$538.0	\$532.7	1.0%	\$106.3	\$107.8	-1.4%	\$16.4	\$14.3	14.7%	\$28.7	\$28.9	-0.7%	\$1.6	\$3.5	-54.3%	\$0.6	—	—	\$38.4	\$40.9	-6.1%
\$28.7	\$28.7	0.0%	\$35.0	\$45.0	-22.2%	\$3.9	—	—	\$6.3	\$6.6	-4.5%	—	\$0.2	—	—	—	—	\$0.7	\$4.0	-82.5%
—	—	—	\$1.0	\$1.2	-16.7%	\$0.5	\$3.6	-86.1%	\$10.7	\$19.5	-45.1%	\$3.5	—	—	—	—	—	—	—	—
\$26.6	\$27.5	-3.3%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$0.1	\$0.7	-85.7%	\$0.1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$0.7	\$0.9	-22.2%	\$1.4	\$0.8	75.0%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$22.8	\$12.0	90.0%	\$3.9	\$7.4	-47.3%	—	—	—	—	—	—	—	—	—	—	—	—	\$0.6	\$1.0	-39.0%
\$3.2	\$2.7	18.5%	\$0.3	\$0.3	0.0%	\$2.2	\$1.6	37.5%	\$2.2	\$2.7	-18.5%	\$0.05	\$1.2	-95.8%	—	—	—	\$0.3	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$1.1	\$1.4	-21.4%	\$1.1	\$1.3	-15.4%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	\$0.2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$0.7	\$5.1	-86.3%	\$0.01	\$3.0	-99.7%	—	—	—	—	—	—	—	—	—	\$0.03	\$0.03	0.0%	—	—	—
\$0.7	\$1.0	-30.0%	\$0.8	\$1.0	-20.0%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$1.0	\$1.5	-33.3%	—	—	—	—	—	—	—	\$0.1	—	—	—	—	—	—	—	—	—	—
\$0.9	\$0.1	800.0%	\$2.9	\$3.3	-11.0%	—	—	—	—	—	—	—	—	—	—	—	—	\$0.1	—	—
\$1.0	\$1.4	-28.6%	—	—	—	—	—	—	\$0.2	—	—	—	—	—	—	—	—	\$0.1	\$0.2	-50.0%
\$11.5	\$8.6	33.7%	\$6.4	\$6.2	3.2%	—	—	—	\$2.3	\$2.6	-11.5%	—	—	—	—	—	—	\$0.5	\$0.1	400.0%
\$0.9	\$2.8	-67.9%	\$0.2	\$0.4	-50.0%	\$0.3	\$0.8	-62.5%	\$0.7	\$0.6	16.7%	\$0.01	\$0.03	-66.7%	—	—	—	\$0.5	—	—
\$0.01	—	—	—	—	—	\$0.3	\$0.3	0.0%	—	—	—	—	—	—	—	—	—	\$0.04	—	—
\$8.5	\$8.8	-3.4%	\$1.6	\$1.3	23.1%	\$0.2	—	—	\$16.3	\$18.9	-13.8%	\$0.02	\$0.2	-90.0%	—	—	—	\$0.1	—	—
\$7.0	\$7.0	0.0%	—	—	—	—	—	—	\$2.4	—	—	—	—	—	—	—	—	—	—	—
\$0.4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$0.3	\$1.4	-78.6%	\$0.1	\$2.4	-95.8%	—	—	—	—	—	—	—	—	—	\$0.07	—	—	—	—	—
\$0.04	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$4.5	\$2.7	66.7%	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$3.9	\$2.6	50.0%	\$0.5	\$0.4	25.0%	—	—	—	—	—	—	—	—	—	—	—	—	\$0.01	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
\$0.03	\$0.3	-90.0%	—	—	—	\$0.02	—	—	\$0.5	\$1.3	-61.5%	—	—	—	—	—	—	—	—	—
\$110.7	\$114.0	-2.9%	\$9.2	\$7.6	21.1%	\$3.1	\$23.4	-86.8%	\$0.7	\$2.5	-72.0%	\$1.3	\$18.1	-92.8%	\$0.4	—	—	\$0.4	\$0.9	-55.6%
\$6.0	\$6.3	-4.8%	—	\$0.002	—	—	—	—	—	\$0.6	—	—	\$2.7	—	—	—	—	\$0.1	\$0.9	-88.9%
\$18.5	\$15.4	20.1%	\$0.1	\$0.3	-66.7%	\$0.1	\$0.5	-60.0%	\$4.8	\$7.9	-39.2%	\$0.2	\$0.1	100.0%	—	—	—	\$1.8	—	—
\$62.2	\$54.6	13.9%	\$6.0	\$3.0	100.0%	\$1.6	\$1.2	33.3%	\$0.03	—	—	—	—	—	\$4.4	\$3.6	22.2%	\$0.5	\$0.5	0.0%
<b>862</b>	<b>842</b>	<b>2.4%</b>	<b>178</b>	<b>193</b>	<b>-7.8%</b>	<b>29</b>	<b>48</b>	<b>-39.6%</b>	<b>77</b>	<b>92</b>	<b>-16.3%</b>	<b>6.6</b>	<b>26</b>	<b>-74.6%</b>	<b>5.9</b>	<b>3.6</b>	<b>62.5</b>	<b>44</b>	<b>49</b>	<b>-9.8%</b>
2%			-8%			-40%			-17%			-75%			63%			-10%		

## AIDS Vaccines

### 1.0 Global investments in preventive AIDS vaccines research and development

In 2015, investments in preventive AIDS vaccine R&D increased two percent from 2014 to US\$862 million. This is the greatest absolute amount of investments seen in AIDS vaccines since 2008/2009 but is still far from the 2007 peak of US\$961 million. The US remained the largest global contributor to R&D, increasing its investments less than one percent, to US\$595 million (Figure 14 and Table 3).

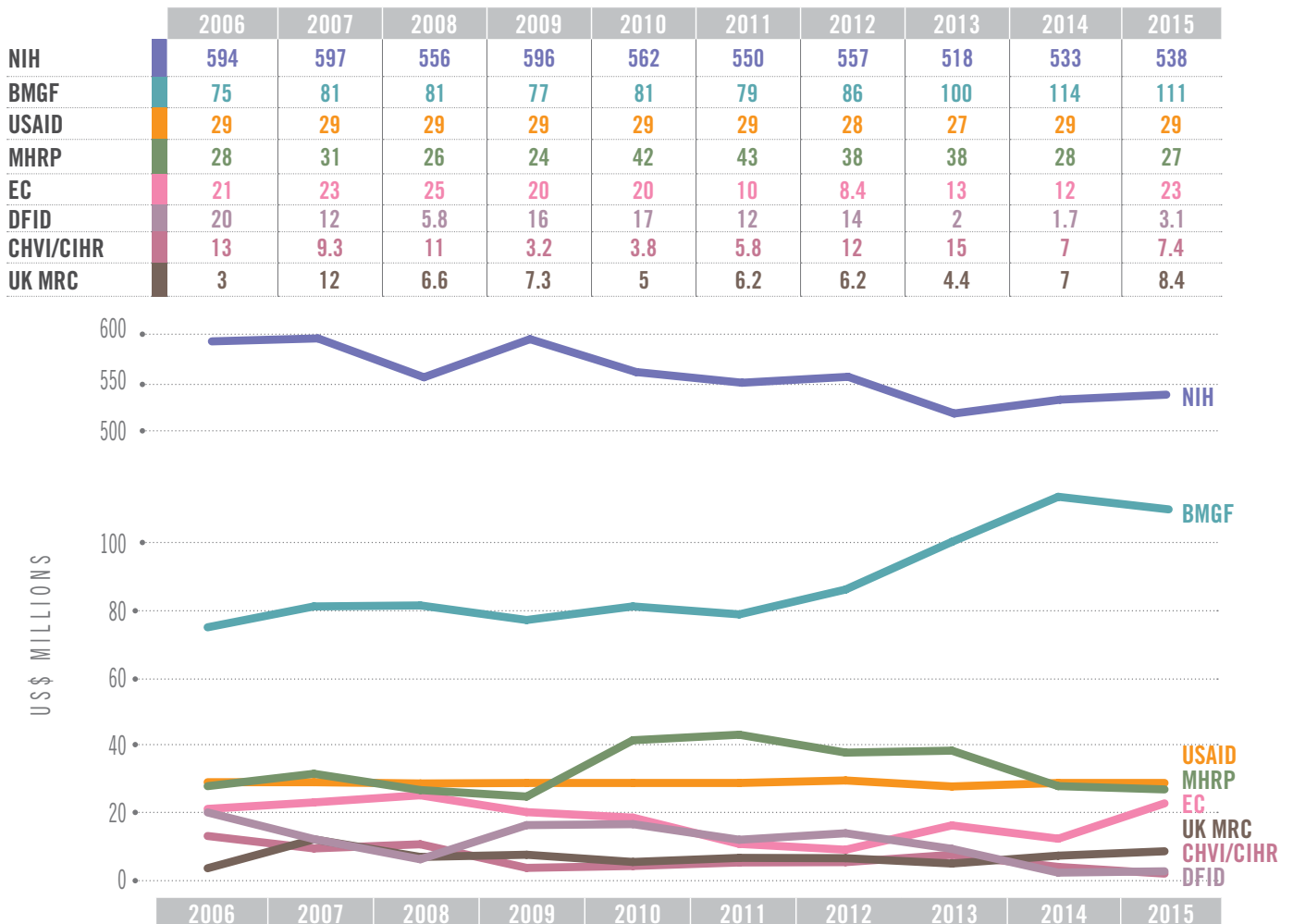
FIGURE 14 AIDS Vaccine Funding, 2000–2015 (US\$ millions)



European funding also increased substantially, from US\$35 million in 2014 to US\$44 million in 2015 (Figure 14 and Table 3). This can be attributed to a significant expansion of HIV research in Europe through two major initiatives under Horizon 2020:

- In November of 2015 the European Commission (EC) launched the European AIDS Vaccine Initiative (EAVI2020). This roughly US\$26 million (€23 million) global initiative, coordinated by Imperial College London, unites leading scientists and researchers from both public and private organizations<sup>24</sup> in a targeted effort to bring both therapeutic and preventive AIDS vaccines to clinical human trials within the next five years.
- In early 2016 the EC also granted over US\$24 million (€22 million) to form the European HIV Vaccine Alliance (EHVA). EHVA is a five-year, multidisciplinary platform that draws on industrial and academic expertise from Europe, the US and Africa and utilizes state-of-the-art technologies to develop innovative preventive and therapeutic AIDS vaccine concepts. The effort is co-led by the directors of the French Institute of Health and Medical Research (INSERM) and the Swiss Vaccine Research Institute at Lausanne University Hospital (CHUV).<sup>25</sup>

FIGURE 15 Top AIDS Vaccine R&D Funder Trends, 2006–2015 (US\$ millions)



AIDS vaccine R&D funding from the philanthropic sector remained flat at US\$135 million in 2015 (Tables 3 and 4), while industry increased its contribution by an estimated 13 percent (Tables 3 and 5). This, along with increases in US financing and European Commission-specific funding for AIDS vaccine R&D, offset decreases from several other public entities. Australia, Belgium, Canada, Denmark, India, Ireland, Italy, the Netherlands, Norway, Spain, Switzerland and Thailand all decreased public funding in 2015. Other countries increased their commitments, including Brazil, Cuba, Israel, Japan, South Africa, Sweden and the UK.

Other developments in the AIDS vaccine sphere include:

- Increasing progress made on broadly neutralizing antibodies (bNABs), with the pipeline moving from preclinical to Phase I and II clinical trials. Sister Phase II safety and efficacy studies (The AMP Study) of the human monoclonal antibody VRC01 began in 2016: the first evaluating HIV prevention in MSM and transgender women in North and South America and the second in women in several African countries.

TABLE 3 Annual Investments in AIDS Vaccine R&D by Sector, 2006–2015 (US\$ millions)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
US	272	314	376	463	516	574	654	659	620	649	632	615	623	584	590	595
Europe	23	32	39	44	57	69	82	79	69	65	61	48.5	52	44	35	44
Other Countries	10	12	21	24	28	27	38	49	41	31	32	30	31	38	26	26
Multilaterals	2	2	2	2	2	2	2	2	1	1	1	0.5	0.5	0.5	0.5	0.5
Total Public	307	359	436	532	602	672	776	789	731	746	726	702	707	667	651	664
Total Philanthropic	20	7	112	15	12	12	78	88	104	92	103	113	110	120	136	135
Total Commercial	–	–	–	–	68	75	79	84	33	30	30	30	30	31	55	62
Total Global Investments	327	366	548	547	682	759	933	961	868	868	859	845	847	818	842	862

TABLE 4 Philanthropic Investments in AIDS Vaccine R&D by Foundations and Commercial Philanthropy in 2015

Amount	Investors
US\$111 million	Bill & Melinda Gates Foundation
US\$1 million to US\$10 million	Wellcome Trust, Ragon Foundation
US\$250,000 to <US\$ 1 million	amfAR, La Caixa Banking Foundation, SIDACTION
<US\$250,000	Merck Foundaton, Hearst Foundation, Google AdWords, Broadway Cares, Fondation pour la Recherche Médicale

TABLE 5 Estimated Commercial Sector Engagement in AIDS Vaccine R&D by Company in 2015

Amount	Investors <sup>a</sup>
US\$5 million to US\$10 million	Novartis International AG, Sanofi Pasteur
US\$1 million to US\$5 million	Sumagen Canada Inc., GSK, Merck, Mymetics
US\$100,000 to US\$1 million	Cepheid, Emmes

<sup>a</sup> The Working Group provided “Company X” with a confidential disclosure agreement. Investments from Company X are not reflected on Table 5, but are included in the total commercial and global investment figures.

- The Pox-Protein Public-Private Partnership (P5), a body comprised of organizations working to build on the Thai RV144 clinical trial, was given the go-ahead and funding by the NIH to proceed with a large-scale prime-boost efficacy trial of a vaccine candidate that is a modified version of RV144. The trial, HVTN 702, is the first large-scale AIDS vaccine trial to take place in South Africa in almost a decade. It is expected to begin recruitment in late-2016 and data are not expected to be available for at least four years.
- LMIC sponsorship of bNAB R&D also increased in 2015; India and the Netherlands strengthened their existing collaboration with a further initiative tasking governmental and non-governmental entities from both countries with the development, trialing and potentially ultimate manufacture of preventive and therapeutic bNABs.<sup>26</sup> Future funding reviews should expect to see increased investments from India in this burgeoning area of R&D.

TABLE 6 Top AIDS Vaccine R&D Funders, 2011–2015 (US\$ millions)<sup>a,b</sup>

Rank	2011		2012		2013		2014		2015	
	Funder	Amount	Funder	Amount	Funder	Amount	Funder	Amount	Funder	Amount
1	NIH	550	NIH	557	NIH	518	NIH	533	NIH	538
2	BMGF	79	BMGF	86	BMGF	100	BMGF	114	BMGF	111
3	MHRP	43	MHRP	38	MHRP	38	USAID	29	USAID	29
4	USAID	29	USAID	29	USAID	27	MHRP	28	MHRP	27
5	DFID	12	DFID	14	CHVI <sup>c</sup>	15	EC	12	EC	23
6	EC	10	CHVI <sup>c</sup>	12	EC	13	Ragon Foundation	10	Ragon Foundation	10
7	Ragon Foundation	10	Ragon Foundation	10	Ragon Foundation	10	CHVI <sup>c</sup>	7	UK MRC	8.4
8	ANRS	7.3	EC	8.4	Wellcome Trust	7.7	China <sup>d</sup>	7	CHVI/CIHR	7.4
9	China	6.9	Wellcome Trust	8.2	China <sup>d</sup>	7	UK MRC	7	China <sup>d</sup>	7
10	Wellcome Trust	6.5	China <sup>d</sup>	7	NHMRC	6.8	Wellcome Trust	6.2	Wellcome Trust	6
11	UK MRC	6.2	UK MRC	6.2	ANRS	5.3	Netherlands	5.1	Institut Pasteur	5.5
12	CHVI <sup>c</sup>	5.8	Institut Pasteur	4.8	Netherlands	4.9	Institut Pasteur	3.9	South Africa DST/SAMRC	3.9
13	CIDA	4.9	Netherlands	4.8	Institut Pasteur	4.8	Sumagen Canada Inc.	2.8	DFID	3.1
14	NMHC	3.9	NHMRC	4.4	UK MRC	4.4	ANRS	2.7	Japan AMED	2.4
15	Netherlands	3.8	ANRS	4.0	EDCTP	3.4	South Africa DST/DOH	2.5	ANRS	2.4

<sup>a</sup> See Appendix for list of acronyms.

<sup>b</sup> A portion of the significantly lower contribution to AIDS vaccine R&D by DFID in 2013 can be attributed to a difference in funding cycles: a £5m disbursement was recognized as 2012 funding according to Working Group methodology.

<sup>c</sup> Participating CHVI Government of Canada departments and agencies are: the Canadian International Development Agency (CIDA), the Public Health Agency of Canada (PHAC), Industry Canada, the Canadian Institutes of Health Research (CIHR) and Health Canada. CIHR grants are reported separately.

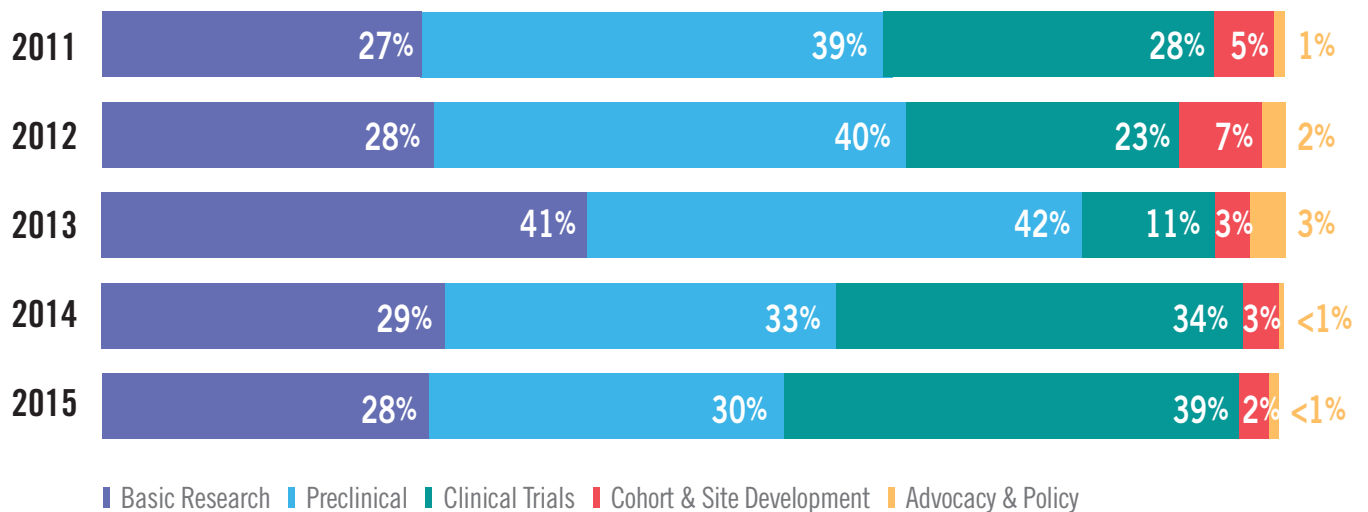
<sup>d</sup> The Working Group could not obtain a response from China for investments made in 2012–2015. Thus, an estimate was developed and sent to China's National Center for AIDS/STD Control and Prevention. The estimate was developed based on public information submitted by the National Center for AIDS/STD Control and Prevention and China's Center for Disease Control and Prevention on [clinicaltrials.gov](http://clinicaltrials.gov), with regards to a Phase II preventive AIDS vaccine trial that started in August 2012 and other research that is underway.

## 1.1 Funding allocations for preventive AIDS vaccine research and development

In 2015, funding for preventive AIDS vaccine R&D was allocated to the following categories: basic research (28 percent), preclinical research (30 percent), clinical trials (39 percent), cohort and site development (two percent) and advocacy and policy (less than one percent) (Figure 16). These allocations have shifted only slightly from 2014, continuing the emphasis on clinical trials engendered by the start of several new trials in late 2014 and early 2015.

Further information about the categories used to define vaccine R&D can be found in Table 10 in the “Methodology” section of the Appendix.

FIGURE 16 AIDS Vaccine Funding Allocations, 2011–2015 (US\$ millions)

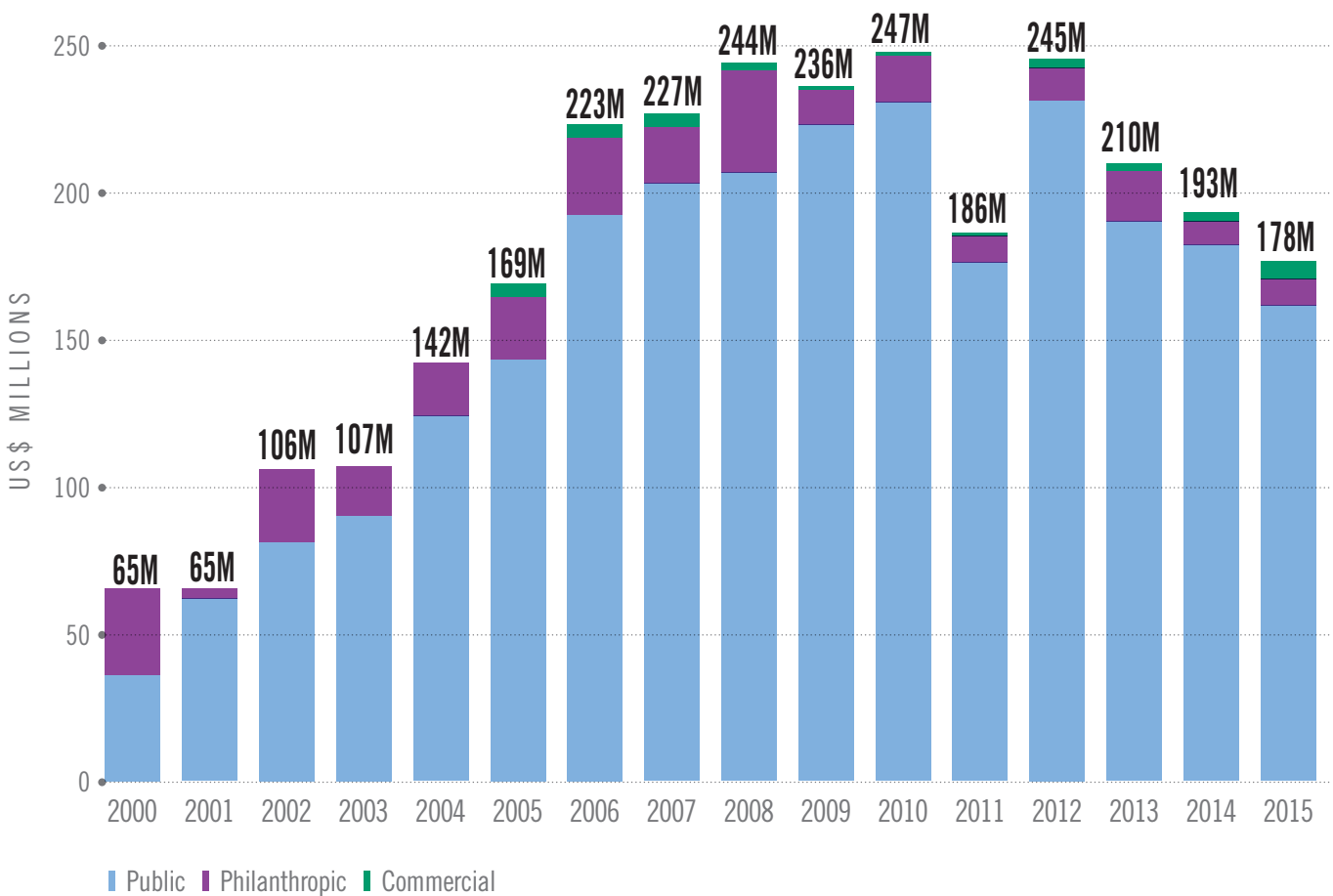


# Microbicides

## 2.0 Global investments in microbicide research and development

Global investments in microbicide R&D decreased in 2015 by US\$16 million to a total of US\$178 million. Of the 2015 total, the public sector was once again the greatest contributor, at US\$162 million, or 91 percent of the total. This is a decline from the 2014 public-sector investment level of US\$182 million. The philanthropic sector followed at US\$9.3 million, or 5.2 percent of the total, representing an increase over its 2014 levels of US\$7.9 million. The commercial sector contributed \$6 million, representing 3.3 percent of total microbicide investments in 2015 and doubling its 2014 contribution (Figure 17).

FIGURE 17 Microbicide Funding, 2000–2015 (US\$ millions)



The NIH remains the largest public-sector funder of microbicide R&D, providing US\$106 million in 2015, just slightly below its 2014 amount of US\$108 million. USAID was the next largest funder with US\$45 million, equal to its 2014 contribution, followed by the UK Department for International Development (DFID), which decreased its contribution by nine percent from 2014 levels, down to US\$5.2 million (*Figure 19 and Table 7*).

US public-sector investments comprised 80 percent of all public funding for microbicide R&D, followed by European public-sector investments at 11 percent, which at US\$17 million was a 26 percent decrease from the 2014 level (*Figure 18*). Other major European public-sector funders in 2015 were the European Commission (US\$3.9 million), the Swedish Embassy (US\$2.6 million) and the Ministry of Foreign Affairs of Denmark (Danida, US\$1.4 million) (*Table 8*).

The sole philanthropic investment in microbicide R&D in 2015 was US\$9.3 million from the BMGF, which was, in fact, a 16 percent increase over the total philanthropic contribution in 2014.<sup>27</sup>

TABLE 7 Annual Investments in Microbicide R&D by Sector, 2006–2015 (US\$ millions)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
US	130	140	154	173	182	148	173	155	154	143
Europe	56	60	40	44	40	16	27	27	23	17
Other Countries	4.7	3.4	12	5.7	8.3	12	17	5	4.5	2.4
Multilaterals	1.4	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.1	0.1
Total Public	192	203	207	223	230	176	217	187	182	162
Total Philanthropic	26	19	35	12	16	9	25	20	8	9.3
Total Commercial	4.5	4.5	2.5	1	1	1	3	3	3	6
Total Global Investments	223	227	244	236	247	186	245	210	193	178

### *Donor Allocations: Microbicides and PrEP*

Just as the HIV prevention field evolves to provide new strategies and options for those who need and want them, so too does the language used to describe the facets composing that field. With any evolution, convergence to a single point takes time. To this end, funding entities often describe the direction of their donations differently, with some preferring to categorize all PrEP and microbicide R&D funding under the umbrella of “ARV-based prevention”. The Working Group makes every effort to allocate such projects in a consistent manner methodologically, but it is important to highlight that donor allocations may not necessarily conform.



FIGURE 18 2015 Investments in Microbicide R&amp;D by Sector (US\$ millions)

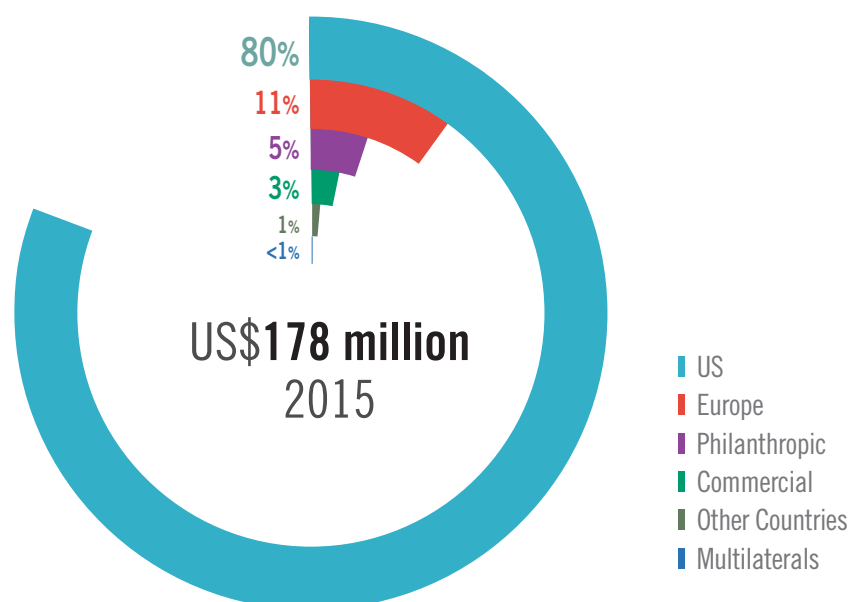


TABLE 8 Top Microbicide R&amp;D Funders, 2011–2015 (US\$ millions)

Rank	2011		2012		2013		2014		2015	
	Funder	Amount	Funder	Amount	Funder	Amount	Funder	Amount	Funder	Amount
1	NIH	112	NIH	130	NIH	111	NIH	108	NIH	106
2	USAID	36	USAID	43	USAID	43	USAID	45	USAID <sup>a</sup>	35
3	South Africa DST/DOH	10	BMGF	23	BMGF	19	BMGF	7.6	BMGF	9.2
4	BMGF	7	EC	14	DFID	8.4	EC	7.4	DFID	5.2
5	DFID	3.2	CHVI	9.2	EC	6.7	DFID	5.7	EC	3.9
6	Netherlands	2.7	South Africa	7	Netherlands	3.6	Sweden	3.3	Sweden	2.9
7	Norad	2.5	DFID	4.7	South Africa DST/DOH	2.3	Netherlands	3	CHVI/CIHR	1.5
8	Wellcome Trust	1.6	UK MRC	2.2	Denmark	2.2	ICMR	2.3	DANIDA	1.4
9	Irish Aid	1.4	Netherlands	1.7	EDCTP	2.2	Ireland	1.3	UK MRC	1.2
10	UK MRC	1.3	Ireland	1.2	Norway	1.5	CDC	1.2	IrishAid	1.1
11	Denmark	0.9	Norway	1	US CDC	1.5	Norad	1	CDC	0.9
12	NHMRC	0.6	OPEC	1	Ireland	1.3	DANIDA	0.8	Norad	0.8
13	OFID	0.5	Denmark	0.9	UK MRC	0.8	CIHR	0.8	South Africa DST/SAMRC	0.5
14	Spain	0.4	NHMRC	0.5	NHMRC	0.5	UK MRC	0.5	ANRS	0.2
15	ARC	0.4	Wellcome Trust	0.5	Wellcome Trust	0.3	South Africa DST/DOH	0.4	NHMRC	0.2

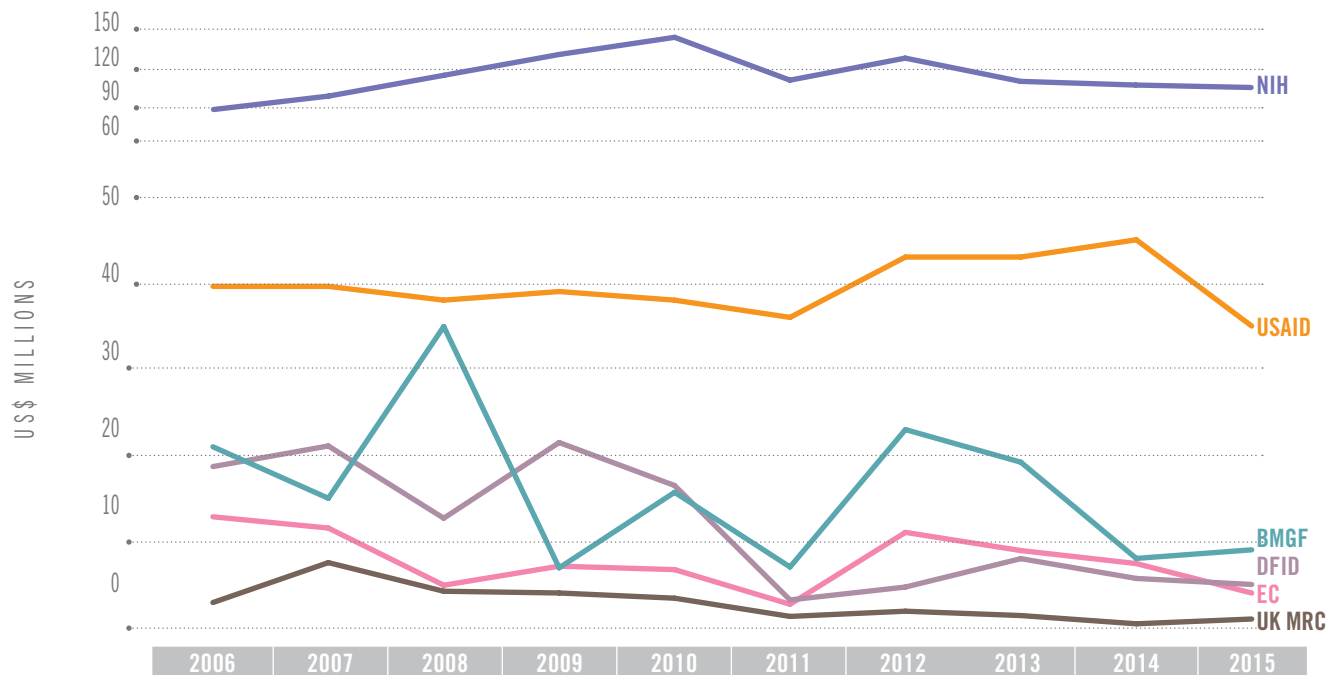
<sup>a</sup> USAID allocated US\$45 million to microbicides in 2015, but US\$10 million of this was allocated to PrEP and multipurpose prevention technologies. Hence, overall funding has not decreased, but rather, additional information has caused allocations to shift.

## Major microbicide developments in 2015

2015 was a productive year for microbicide research and development. Multiple trials of rectal and vaginal products were ongoing, two of which would produce positive results and be presented at the Conference on Opportunistic Infections (CROI) in early 2016: the “sister” efficacy trials of a monthly dapivirine-containing vaginal ring, ASPIRE and The Ring Study, which showed modest HIV protection of 27 percent and 31 percent, respectively. This news would soon be followed by NIH approval for ASPIRE to proceed with HOPE, the HIV Open-label Prevention extension trial designed to understand critical differences in age group-related adherence and efficacy revealed in the ring studies, in which younger and therefore epidemiologically more vulnerable<sup>28</sup> women (under 21) failed to benefit from protection.

FIGURE 19 Top Microbicide R&D Funder Trends, 2006–2015 (US\$ millions)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
NIH	88	99	116	133	147	112	130	111	108	106
USAID	40	40	38	39	38	36	43	43	45	35
BMGF	21	15	35	7	17	7	23	19	8	9
DFID	19	21	13	22	16	3	5	8	8	5
EC	13	12	5	7	7	1	14	7	7	4
UK MRC	3	8	4	4	3	1	2	1	0.5	1



The HOPE and ongoing Ring Study teams will also combine and further analyze their data to attempt to understand issues specifically confronting younger women that might have contributed to this disappointing discrepancy. NIAID also plans to sponsor MTN 034/IPM 035, a Phase IIa crossover study, to assess whether failure of the ring to protect the youngest women was due to lack of adherence, biological factors or some combination of both.<sup>29</sup> It is reasonable to expect future funding reviews to trend toward adherence-related behavioral research and biometrics, as dose-dependent microbicide options advance along the product pipeline.

Research on rectal microbicides also advanced in 2015. Results of MTN 017, a Phase II safety and acceptability study, demonstrated that a rectal tenofovir gel-based microbicide would be safe and acceptable when used daily and pericoitally by MSM and transgender women. Results are expected to open the door to future options for rectal microbicide products and delivery routes.<sup>30</sup>

## ***ECHO: Evidence for Contraceptive Options & HIV Outcomes***

In late 2015, the ECHO trial, a three-year open-label randomized clinical trial of three contraceptive technologies — Depo-Provera/DMPA, the levonorgestrol implant and the copper IUD — began. The purpose of the trial, funded by the BMGF, Swedish International Development Cooperation Agency (SIDA), Wellcome Trust and USAID, is to answer the critical question of how hormonal contraceptives affect a woman's risk of acquiring HIV.

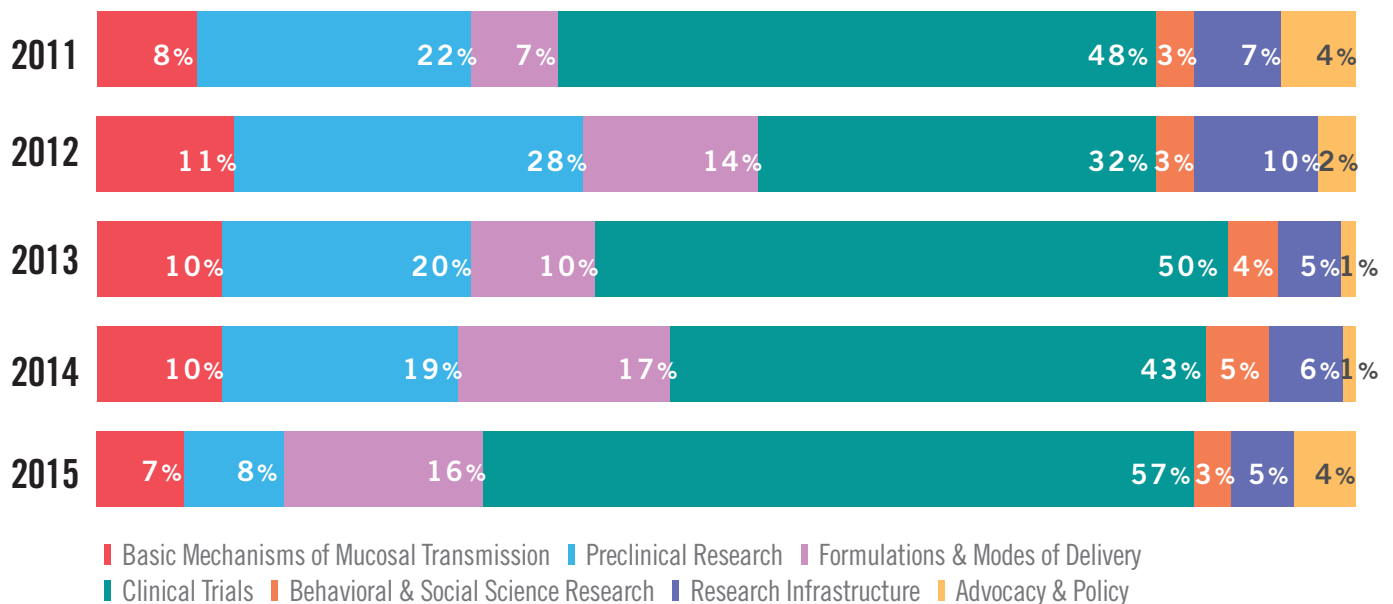
In addition to post-enrollment HIV seroconversion, the trial endpoints include pregnancy, serious adverse events and method continuation. A total of 7,800 sexually active, HIV-uninfected women in 12 sites in East and Southern Africa will participate. The hope is that definitive results from a well-executed trial that has retained meaningful engagement with key civil society stakeholders will provide the evidence needed for policymakers and implementers alike to help women make fully informed choices about their sexual and reproductive health.<sup>31,32,33</sup>

Other funders of HIV and hormonal contraceptive research in 2015 included the CDC, the NIH, the Ontario HIV Treatment Network (OHTN), Swedish Research Council, the US FDA and PATH International. In 2015 the Working Group tracked US\$9.6 million in disbursements supporting this area of research.

## 2.1 Funding allocations for microbicide research and development

In 2015 microbicide R&D expenditures were allocated as follows: basic mechanisms of mucosal transmission (seven percent), preclinical research (eight percent), formulations and modes of delivery (16 percent) clinical trials (57 percent), social and behavioral research (three percent), research infrastructure (five percent) and advocacy and policy (three percent) (Figure 20). These allocations represent a sizeable shift since 2014 toward greater investments in the later stages of the pipeline and diminished investments in the earlier stages. Social and behavioral research investments fell to the low 2011/2012 level, but as adherence has proved consistently vital to the outcomes of all major microbicide trials completed to date, allocations to understanding the determinants of adherence and efficacy and their interdependence may increase.

FIGURE 20 Microbicide R&D Funding Allocations by Percentage, 2011–2015 (US\$ millions)



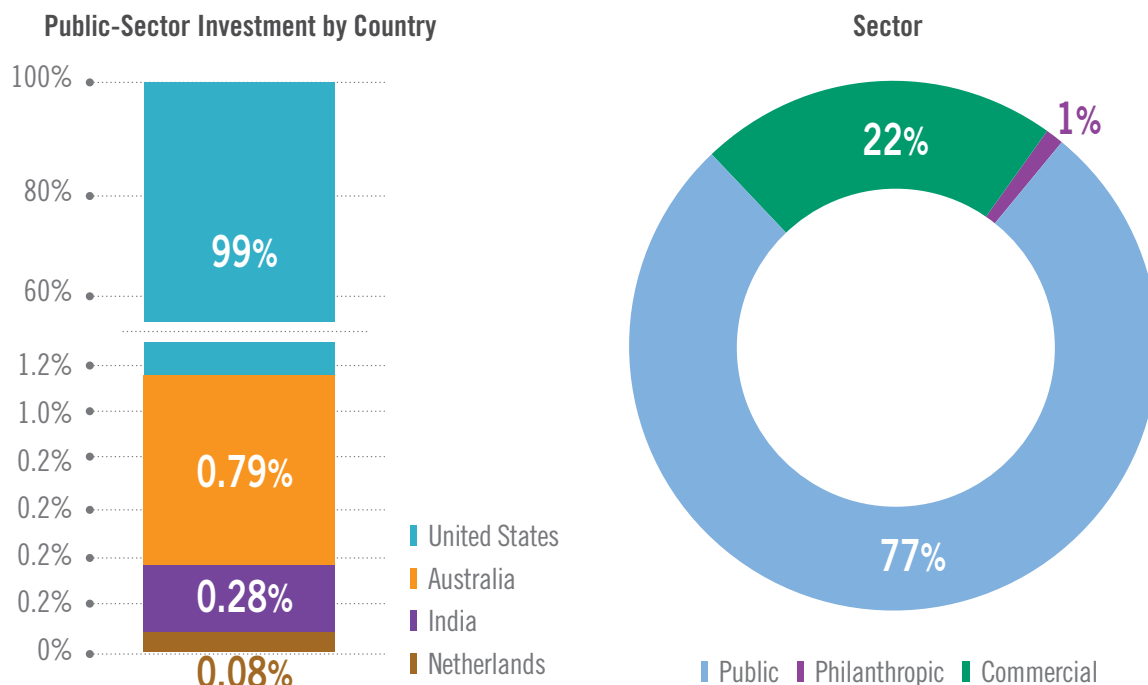
## 2.2 Global investments in multipurpose prevention technology research and development

In 2015, as in 2014, the Working Group partnered with CAMI Health to collect and analyze data on grants for multipurpose prevention technologies (MPTs). In 2014, overall investments totaled US\$32 million, a 39 percent increase from the US\$22.8 million reported in 2013.<sup>34</sup> As of 2015, that investment figure had risen to US\$48 million, 1.5 times the 2014 investment level.

The US public sector provided more than half of MPT funding (59 percent) in 2014, and an even higher proportion in 2015 when it accounted for 86 percent of the total and 99 percent of public funding (Figure 21). In both years, as well as in 2013, USAID and NIH were the primary US public-sector MPT R&D funders; the European public sector, primarily the European Commission, accounted for 3.1 percent in 2014 and dropped its support to less than one percent in 2015, when it was represented solely by the government of the Netherlands. The predominant philanthropic source of MPT R&D support in 2013, 2014 and 2015 was the BMGF, with the Wellcome Trust the source of European philanthropic-sector support in 2014. The Female Health Company was the major source of commercial investments in MPTs from 2013 through 2015.

In sum, the United States, primarily its public sector, accounted for over 85 percent of all investments in multipurpose prevention technologies in 2013, 2014 and 2015, with the NIH being the largest contributor in all three years. The primary recipients of this public-sector support continue to be nonprofit entities such as CONRAD and the Population Council; academic research groups, such as the Albert Einstein College of Medicine, University of Louisville and University of Pittsburgh; and small biotechs such as Auritec, ImQuest and Mapp Biopharmaceutical.

FIGURE 21 Investments in Multipurpose Prevention Technologies by Country and Sector, 2015



The goal of MPT research is the development of single products that simultaneously protect women from multiple health risks by combining protection from unintended pregnancy and protection from one or more sexually transmitted infections, importantly, though not exclusively, HIV. The only prevention technologies available in today's marketplace that can be defined as MPTs are male and female condoms, which can provide protection against both HIV and pregnancy — of particular importance in countries heavily burdened by HIV and maternal and infant mortality — but they have limitations in use that constrain their effectiveness.

MPT R&D is taking place from the earliest stages of preclinical testing and into Phase I trials, and includes a wide range of formulations and delivery systems for both sustained-release and on-demand use.<sup>35</sup> These include combinations of antiviral agents, including lectins and monoclonal antibodies; intravaginal rings in various configurations, vaginal gels, vaginal and rectal films and fast-dissolving tablets; and new delivery strategies, such as nanofiber platforms and long-acting PrEP formulations that could form the basis for long-acting injectables. The MPT pipeline also includes modifications of female condoms to incorporate protection against HIV and other STIs known to facilitate HIV transmission.

Attention to and progress in MPT R&D have been considerable, especially over the past three years. Still, this new field confronts the usual dilemmas in the development of any new health technology, especially combination products with their particular regulatory implications. It also faces inherently difficult questions in fields traditionally unlinked from one another, each with its own complex history and realities, including the need to rely so critically on user behavior. To address these challenges with maximum rigor and bring clarity and focus to the path ahead, special effort has been devoted to specifying Target Product Profiles (TPP) for the desired attributes of each MPT prevention indication and corresponding dosage form for specific user populations. These are already proving useful in collaboration and communication among donors and developers and with representatives from prospective user settings, and they should continue to inform investment decisions going forward.

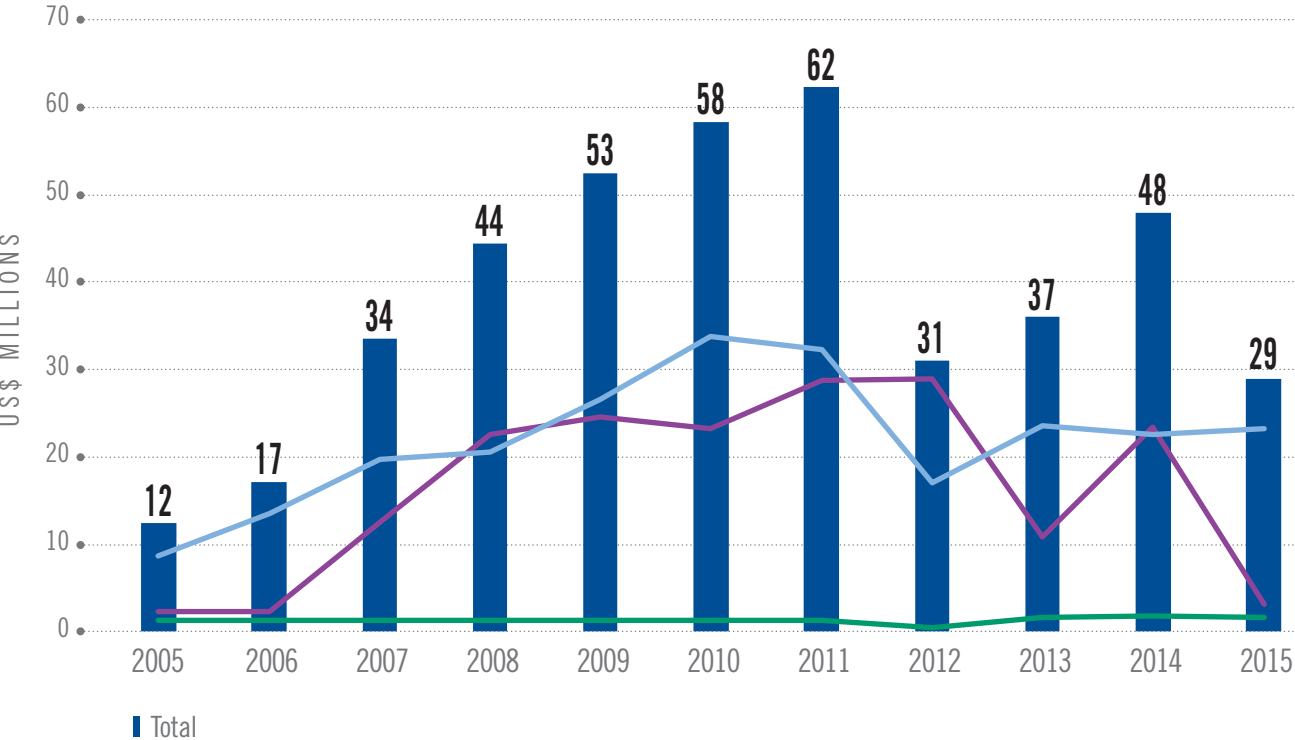
## Other HIV Prevention Options

### 3.0 Global investments in research and development related to pre-exposure prophylaxis

Global public, philanthropic and commercial investments in pre-exposure prophylaxis (PrEP) R&D contracted by 40 percent under 2014 levels in 2015. This was driven largely by a decline from the philanthropic sector as the BMGF decreased its investments in PrEP by almost 90 percent from 2014. While public investments in PrEP R&D remained at US\$24 million, commercial investments increased by 33 percent to US\$1.6 million, driven entirely by Gilead’s increased investments in implementation and demonstration projects (Figure 22). It is important to note that much funding is focused on other aspects of PrEP, such as guidelines and delivery mechanisms that are not tracked as R&D or captured in this report.

FIGURE 22 Investments in Pre-Exposure Prophylaxis, 2005–2015 (US\$ millions)

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Public	8.7	14	20	21	27	34	32	20	24	23	24
Philanthropic	2.4	2.4	13	23	25	23	29	11	11	24	3.2
Commercial	1.3	1.3	1.3	1.3	1.3	1.3	1.3	0.5	2.0	1.2	1.6



Implementation and demonstration projects in 2015 spanned a wide variety of target audiences and potential beneficiaries. Some of the 26 global projects ongoing in 2015 include:

- ▶ POWER: Prevention Options for Women's Evaluation Research combines microbicides and oral PrEP to assess young (age 16-29) women's preferences, uptake and adherence, in addition to identifying cost-effective delivery strategies. This trial is taking place in Kenya and South Africa.<sup>36</sup>
- ▶ NYC PrEP (PrEPared and Strong) explores structural, social and cultural factors that are relevant to Black MSM engagement with PrEP in New York City. Community-based research with 200 Black MSM will inform the design of a PrEP adherence support intervention for the targeted population.<sup>37</sup>
- ▶ A demonstration project among FSW in Dakar, Senegal aims to build a sustainable PrEP program for FSW, establishing that the provision of daily oral PrEP as an HIV prevention strategy is feasible and acceptable and has high uptake among this population.<sup>38</sup>

In late 2015, the WHO expanded its recommendation on PrEP to include all populations at substantial risk of HIV (i.e., those in which HIV incidence is three per 100 person-years or higher).<sup>39</sup> In its guidelines the WHO stressed that its revision was based on an array of high-quality evidence speaking to the efficacy, acceptability and real-world applicability of PrEP, and that it should be considered and offered as an additional tool in a comprehensive HIV prevention package. Following the revised WHO guidelines, in March 2016 South Africa revealed plans to offer daily oral PrEP to at least 3,000 female sex workers. This declaration follows South Africa's decision in late 2015 to become the first country in southern Africa to register Truvada as PrEP.<sup>40</sup>

The release of these guidelines cemented an increasing trend toward the widespread favorability and acknowledgement of the protective potential of PrEP, a trend which is possibly reflected in funding allocations for 2015.



### 3.1 Funding allocations for PrEP research and development

Allocations to PrEP R&D outside of implementation and demonstration projects were as follows: basic research (less than one percent), preclinical research (six percent), clinical research (37 percent) and advocacy (three percent).

Fully 53 percent was invested in PrEP implementation and demonstration projects — attempts to determine appropriate delivery and adherence support modalities for the full spectrum of global populations who stand to benefit.

#### *Long-Acting Injectables (LAIs): What are they and where is the science?*

Long-acting injectables (LAIs) are antiretroviral drugs designed to be delivered by injection, remain slowly effective after initial dosage, and maintain their effects over long periods of time. Antiretroviral drugs formulated as LAIs would require dosing every few months rather than daily, and would have the potential to simplify both treatment and prevention, improve uptake and reduce the burden of adherence. However, many existing ARVs cannot yet be formulated to be suitable for injection, and LAIs for prevention still require regular testing to monitor for HIV infection to lessen the potential for ARV-resistant HIV transmission. LAIs now in clinical trials include GSK744, an integrase strand transfer inhibitor, and TMC278, a nonnucleoside reverse transcriptase inhibitor. A Phase IIb trial is also testing a combination of these two drugs as “maintenance” therapy for people living with HIV who have already achieved virologic suppression through the use of traditional ARVs.<sup>41,42</sup> Results from the Phase IIa ECLAIR study presented at the 2016 Conference on Retroviruses and Opportunistic Infections (CROI) suggested that intramuscular injections of GSK744 were preferable to an oral formulation.<sup>43</sup>

Current funding for LAIs comes from both the public and commercial sphere, with the US NIH and UK Medical Research Council providing the bulk of the almost US\$1.3 million investment in 2015. Several commercial entities are funding R&D of long-acting treatment using the drugs mentioned above. Those funds are not included within the scope of this report.

## *Industry and HIV Prevention: Investments in PrEP and DREAMS*

In December 2015, it was announced that Gilead, along with Johnson & Johnson and Viiv Healthcare, would be joining PEPFAR's DREAMS Partnership to reduce new HIV infections in adolescent girls and young women. Gilead will be donating over US\$6.5 million during the course of the three-year initiative to enhance PrEP programs for young women in select DREAMS countries.

Other work by Gilead includes both early and late-clinical research into novel treatment and cure strategies, efforts to enhance testing and linkages to care globally and engaging in new partnerships with other invested entities such as pharmacies and sexual health clinics to develop awareness of Truvada as PrEP and create innovative PrEP delivery systems.

Gilead remains the largest corporate HIV funder in the world, with a current contribution of US\$73 million to HIV annually.<sup>44</sup>

## *WHO Endorsement: What lessons can we learn from VMMC?*

In 2007, the WHO and UNAIDS issued an official recommendation on VMMC, asserting the procedure's power as an additional prevention tool against HIV/AIDS.<sup>45</sup> In 2013 and 2015, the WHO then prequalified the nonsurgical circumcision devices PrePex and Shang Ring respectively.<sup>46</sup> Contrary to expectations, these guidelines did not lead to an immediate increase in the funding made available for VMMC in regions of high HIV prevalence — skepticism based on limited acceptability and concerns about the practical reality of widespread scale-up of services stymied investments into this key area of prevention.<sup>47</sup> A meta-review from 2014 showed that low demand has indeed contributed to missed VMMC coverage targets, with stakeholder engagement and formative research into community preferences proving critical to success.<sup>48</sup>

With the issuance of WHO guidelines on PrEP in 2015, are there lessons to be gleaned from the experience of VMMC, such as where along the research continuum funding might — or should — begin to flow in order to truly maximize the effect of these game-changing recommendations? The Working Group will be looking at this fulcrum point in PrEP R&D to determine the effect on investments in the coming years and assess if and how past mistakes have been avoided.

## 4.0 Global investments in research and development related to treatment as prevention

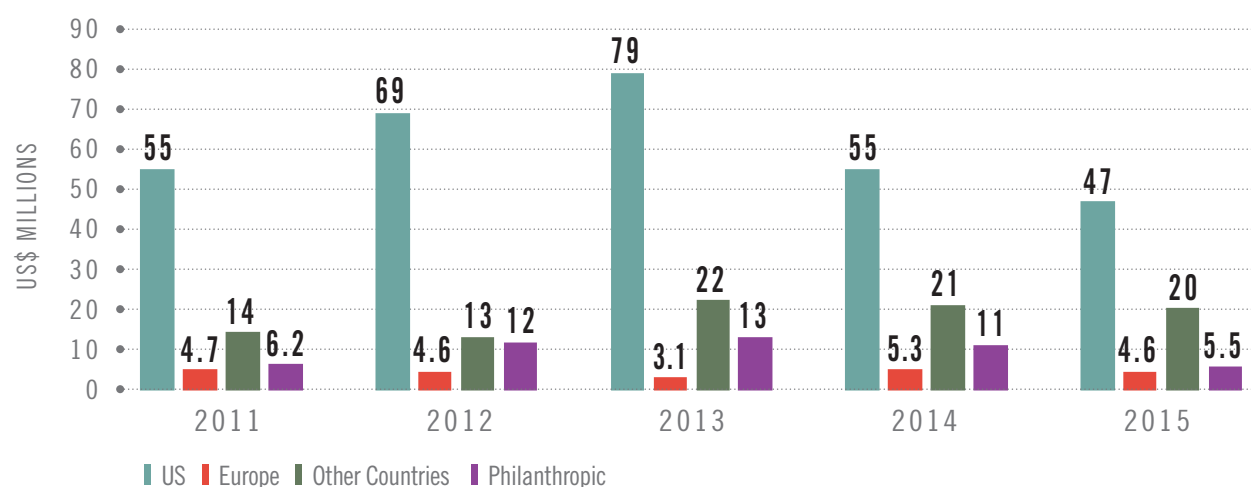
Global investments in treatment as prevention (TasP) fell 17 percent from 2014 levels to US\$77 million in 2015, led by declines in public-sector investments (12 percent). US public-sector investments fell 15 percent, as the Centers for Disease Control and Prevention (CDC) cut its contribution by 45 percent from 2014. The philanthropic sector also experienced a decline of 50 percent even though more funders overall invested in TasP in 2015 (*Figure 23*).

Average 2015 grant size from all funders was a little over half that of 2014, which resulted in lower total funding despite a slightly higher number of funders. Investments into implementation research remained high — 90 percent of funding was designated for implementation science in 2015, down only slightly from 93 percent in 2014. For the first time, investments in TasP were also tracked from the commercial sector.

2015 saw the release of new WHO guidelines adopting a new strategy for treatment: rather than initiate ARV treatment after CD4 T-cell counts have fallen below 500, all individuals living with HIV should be started on therapy, regardless of CD4 count (or, “test and start”).<sup>49</sup> Prior to the WHO guidance, PEPFAR’s Expert Working Group had recommended rollout of test and start across all sites where PEPFAR was providing support. The Expert Working Group determined that the positive results of the Strategic Timing of AntiRetroviral Treatment (START), TEMPRANO and HPTN 052/A5345 studies provided ample evidence that the benefits of immediate ARV initiation outweighed any evidence of harm.<sup>50</sup>

FIGURE 23 Investments in Treatment as Prevention by Sector, 2011–2015 (US\$ millions)

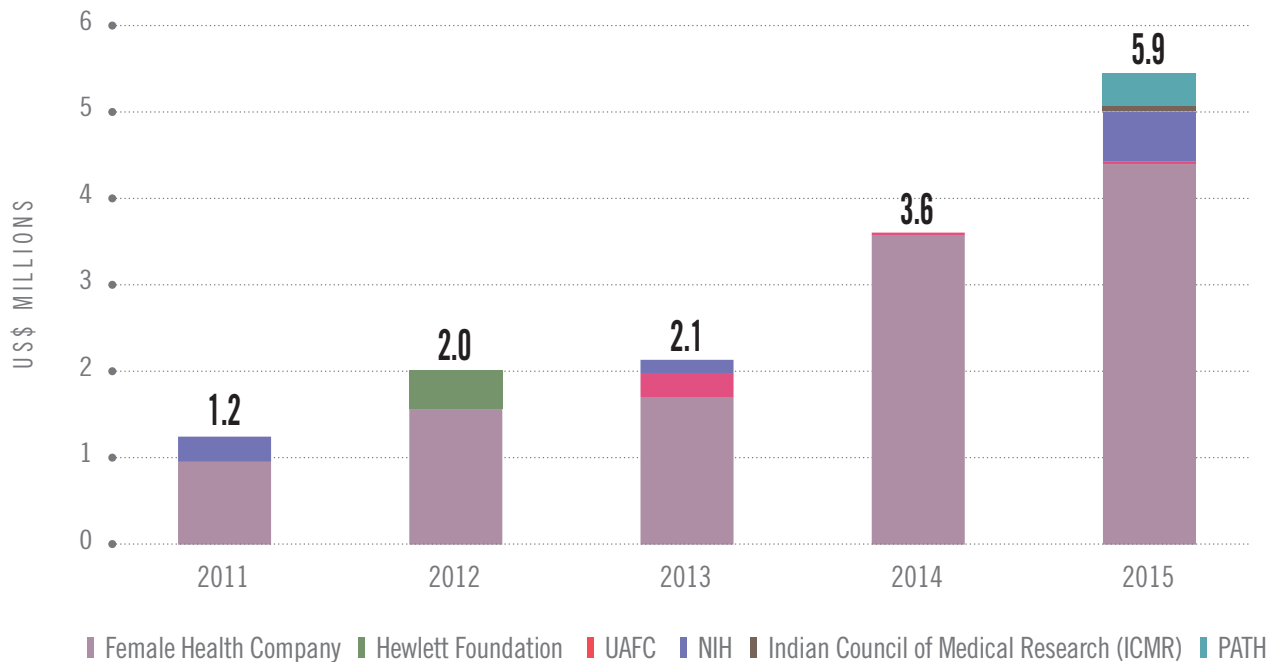
	2011	2012	2013	2014	2015
US	55	69	79	55	47
Europe	4.7	4.6	3.1	5.3	4.6
Other Countries	14	13	22	21	20
Total Public	73	86	104	81	71
Total Philanthropic	6.2	11.8	13	11	5.5
Total Commercial	—	—	—	—	<0.1
Total Global Investments	79	98	117	92	77



## 5.0 Global investments in female condom research and development

Funding for female condoms has seen a significant increase every year since 2011 (Figure 24). In 2015 investments in female condoms reached almost US\$5.9 million, contributed principally by one US commercial entity, the Female Health Company. In 2015, funding was invested primarily in acceptability and uptake research, i.e., implementation factors. Public-sector investments, at 18 percent of all investments (Figure 25), were provided by the NIH (56 percent), PATH (36 percent), Universal Access to Female Condoms (UAFC) Joint Programme, funded by the Netherlands Ministry of Foreign Affairs (2.7 percent) and investments by the Indian Council of Medical Research (6.7 percent).

FIGURE 24 Investments in Female Condoms by Funder, 2011–2015 (US\$ millions)

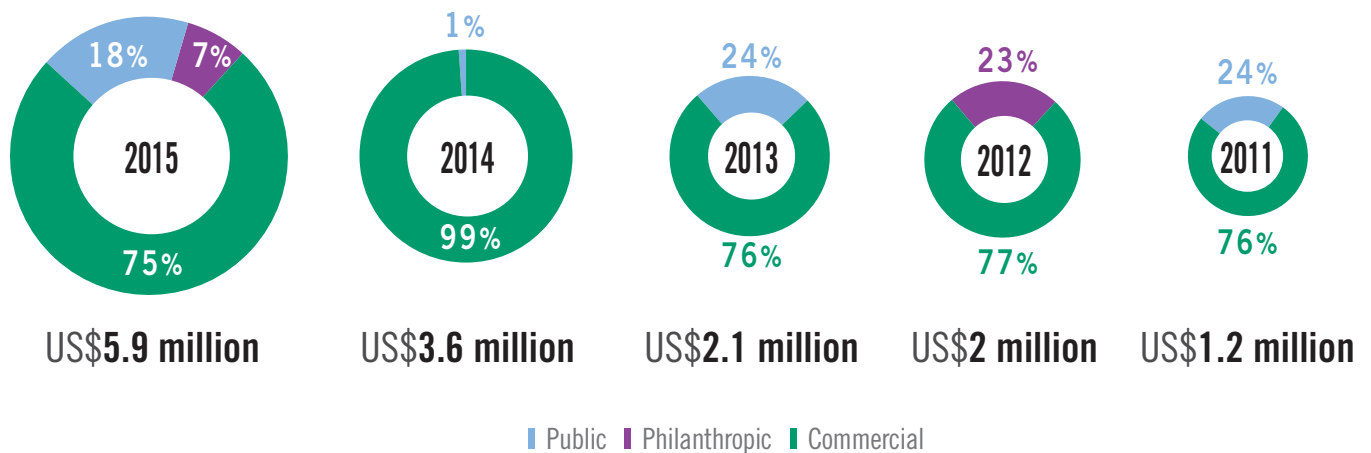


In order to improve upon the variable acceptability rates<sup>51</sup> of the female condom amongst both males and females and to increase uptake, innovation produces a varied and interesting landscape in the current market.<sup>52</sup>

- A performance and safety trial of the Wondaleaf®, an ultra-thin polyurethane product with an adhesive shield to cover and protect the external genitalia, is ongoing in Malaysia.
- Several implementation studies are ongoing in India to assess acceptability and factors associated with uptake of the female condom in various settings.
- A mapping study using geographic information systems (GIS) conducted in Philadelphia determined that, compared to 77 percent area availability of the male condom, only 1 percent of service providers sold or provided the female condom.
- A clinical trial sponsored by the International Partnership for Microbicides (IPM) released results at CROI in February 2015 showing that female condom use was safe with concurrent use of a placebo vaginal ring.
- The Gates Foundation is providing support to several innovators to develop the Next Generation of male and female condoms.

Funding by the public and commercial sectors for the female condom in 2015 was allocated predominantly to implementation research (90 percent), with the remainder going to clinical trials (2.5 percent), advocacy and policy (6.8 percent) and social and behavioral research (0.8 percent). This represents a change from 2014, in which funding was directed entirely toward implementation research. Increased clinical research may indicate heightened interest in expansion of available options.

FIGURE 25 Investments in Female Condoms by Sector, 2011–2015 (US\$ millions)

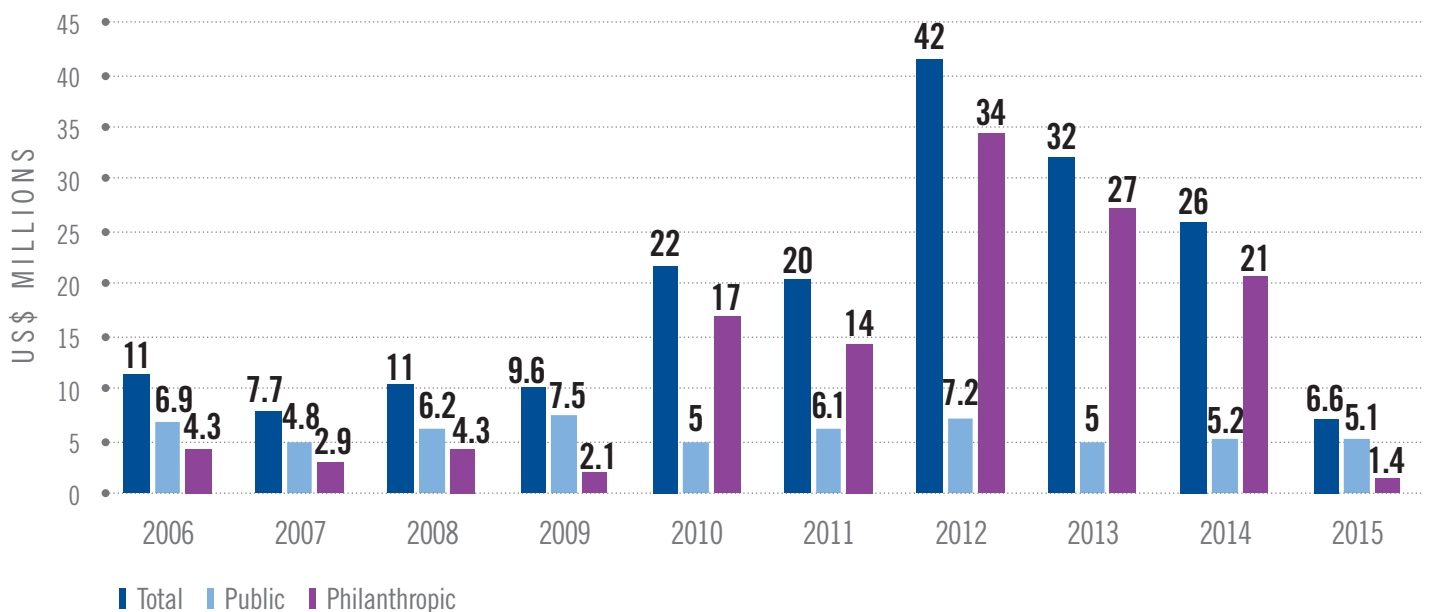


## 6.0 Global investments in implementation and expansion of voluntary medical male circumcision

Global investments in R&D, operations and implementation research related to voluntary medical male circumcision (VMMC) drastically declined in 2015 (Figure 26), led by a significant decrease in contributions from the BMGF.<sup>53</sup> Disbursements to VMMC-related projects by the BMGF totaled US\$1.3 million, down from US\$18 million in 2014. The US public sector was the largest funder in 2015, and at US\$5.1 million, its contribution was 37 percent greater than that of 2014. It is possible that as empirical evidence mounts for VMMC as an effective HIV prevention option, such reductions in investments will be natural as funders turn their attention to more nascent technologies. Uptake of VMMC remains low in many priority countries, however, and research into improving access to and use of this effective tool appears to be threatened by competing donor priorities.<sup>54</sup> In response to concerns by advocates in 2015, funding for VMMC implementation research may experience an upswing in 2016.<sup>55,56</sup>

FIGURE 26 Investments in Voluntary Male Medical Circumcision by Sector, 2006–2015 (US\$ millions)

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Total Public	6.9	4.8	6.2	7.5	5	6.1	7.2	5	5.2	5.1
Total Philanthropic	4.3	2.9	4.3	2.1	17	14	34	27	21	1.4
Total Global Investments	11	7.7	11	9.6	22	20	42	32	26	6.6



While several VMMC projects assessing uptake strategies ended in 2014, important work was still being completed in this field:

- In Zambia, results from the Spear & Shield project demonstrated the importance of female partner acceptance as an indicator of men’s likelihood to undergo VMMC.<sup>57</sup> Similarly, in Tanzania qualitative research revealed the import of mothers and female partners in young men’s decisions to seek VMMC.<sup>58</sup>
- A non-inferiority trial of the AccuCirc device versus the Mogen clamp for early infant male circumcision (EIMC) in Zimbabwe demonstrated no difference in adverse events, safety or parental acceptability.<sup>59</sup> The AccuCirc was selected in 2014 by the Botswana Ministry of Health for use in their national newborn male circumcision program, which was one of the first to be implemented in Africa.<sup>60,61</sup>

## 7.0 Investments in research related to prevention of vertical transmission

R&D funding related to the prevention of vertical HIV transmission from mother to child (PMTCT) at birth and during breastfeeding decreased from US\$49 million in 2014 to US\$44 million in 2015, led by declines from the US public sector. Contributions from the philanthropic sector declined by eight percent despite a more diverse cadre of contributors (*Table 9*).

2015 saw a major global breakthrough in PMTCT; Cuba was declared the first country on earth to have functionally eradicated vertical transmission.<sup>62</sup> Eradication is considered accomplished when new pediatric infections due to vertical transmission are less than 0.05 percent of live births and transmission rate is less than five percent in non-breastfeeding populations or less than three percent in breastfeeding populations.<sup>63</sup> In mid-2016, Cuba was joined by Thailand, Belarus and Armenia in achieving this milestone.<sup>64</sup>

TABLE 9 Annual Investments in Prevention of Vertical Transmission by Sector, 2008–2015 (US\$ millions)

	2008	2009	2010	2011	2012	2013	2014	2015
US	10	45	57	36	35	42	47	39
Europe	7.3	5.9	1.5	1.1	1.7	0.1	1.2	1.6
Other Countries	–	–	1.3	5.1	6.7	0.2	–	0.7
Total Public	18	51	60	43	43	42	47	41
Total Philanthropic	3.6	0.9	0.0	0.5	0.8	1.7	2.5	2.3
Total Commercial	–	–	–	–	–	–	0.5	0.5
Total Global Investments	21	51	60	43	44	44	49	44

Other notable results from the field include:

- The National Evaluation of Malawi's PMTCT programme (NEMAPP), a two-year cohort study comprising 1851 HIV-positive mothers of 4- to 12-week-old infants revealed dramatic cuts in transmission with the utilization of lifelong antiretroviral therapy (ART, formerly known as Option B+).<sup>65</sup>
- An analysis of vertical transmission data from 2000-2011 in France documented no transmission among women who conceived while on ART and maintained viral suppression throughout pregnancy, providing further evidence for the prevention benefits of lifelong ART provision.<sup>66</sup>
- Two observational studies provided positive evidence for the safety of ART during pregnancy. In Botswana, a birth outcomes study amongst 10,000 women reported no increased risk of adverse events associated with the currently recommended triple therapy regimen. In Zambia there was no increased risk of low birth outcomes associated with ART initiation or duration during pregnancy amongst 4,000 women.<sup>66</sup>

## **8.0 Investments in HIV prevention research and development related to HSV-2 prevention**

Prevention of herpes simplex virus type 2 (HSV-2) infections in HIV-negative people may prove to be an effective element in an HIV prevention strategy. While HSV-2 suppression with acyclovir and its analogues has not been shown to affect HIV acquisition, research on other therapeutic and prophylactic methods is ongoing and some basic questions continue to be pursued.

In 2015, a total of US\$5.5 million was provided for HSV-2 vaccine research, down \$4.4 million from 2014 levels. The two largest funders, the NIH and Canadian Institutes of Health Research, remained the same as 2014, with the bulk of the decrease attributable to lower NIH contributions to this area of research. As in previous years, commercial investors were often subsidized by public-sector institutions, such as the NIH. Pharmaceutical and biotechnology companies investing in HSV-2 vaccine R&D include Agenus Inc., Genoccea Biosciences, GSK and Juvaris.



## 9.0 Investments in cure and therapeutic vaccine research and development

The Working Group estimates that in 2015, US\$202 million was invested in cure research, representing a substantial increase of 25 percent over the US\$161 million invested in 2014, and an increase of 129 percent over the US\$88 million invested in 2012 (*Figures 27 and 28*). The majority of investments (US\$182 million) came from the public sector, with US\$18 million invested by philanthropies such as amfAR, CANFAR, Fair Foundation, the BMGF and Wellcome Trust. Despite outreach by the Working Group this year, only one company, Cooper Human Systems, responded to the survey, so this estimate undercounts commercial investments in cure research (*Figure 29*). Several companies are known to have active cure research programs, including BMS, Gilead, Janssen, Merck and Sangamo BioSciences, among others. In 2015, the United States through the NIH contributed the majority of public funding, with the European Union, Australia, France and Canada also providing significant contributions to HIV cure research (*Figure 30*). In 2014, non-US countries invested 12 percent of global HIV cure research funding, while in 2015, these countries increased their investments to 14 percent of global HIV cure research. Recent initiatives include:

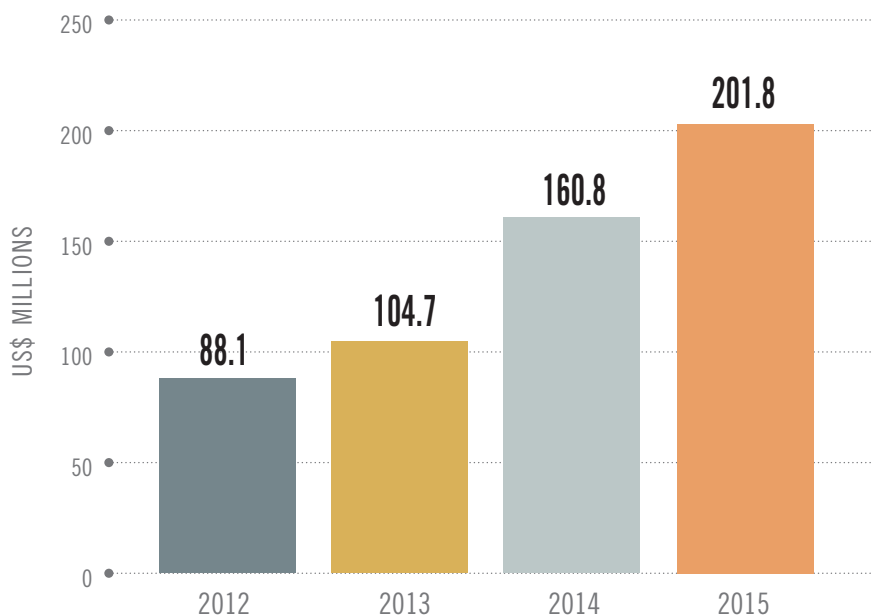
### ➤ IAS Towards an HIV Cure initiative

At the end of 2014, a new international scientific working group was convened to update and revise the IAS Towards an HIV Cure Global Scientific Strategy. The revised Global Scientific Strategy was launched in Durban at the AIDS 2016 conference.

### ➤ Martin Delaney Collaboratories

Announcement of newly funded Martin Delaney Collaboratories, dedicated to supporting new cure strategies, by the National Institutes of Health.

FIGURE 27 **Current Cure Research Investments, 2012–2015** (US\$ millions)



➤ **amfAR Countdown to a Cure for AIDS**

amfAR is beginning investments over six years aimed at finding a broadly applicable cure for HIV by 2020 with partners Qura Therapeutics and the University of California, San Francisco.

➤ **The FRESH and ECHO early capture cohorts**

Early capture cohorts in South Africa through the Ragon Institute (FRESH) and in Thailand and East Africa through the Military HIV Research Program (ECHO) collect critically important data on early immune responses and viral reservoirs in very early infection.

FIGURE 28 **Investments in HIV Cure Research by Country, 2012–2015** (US\$ millions)

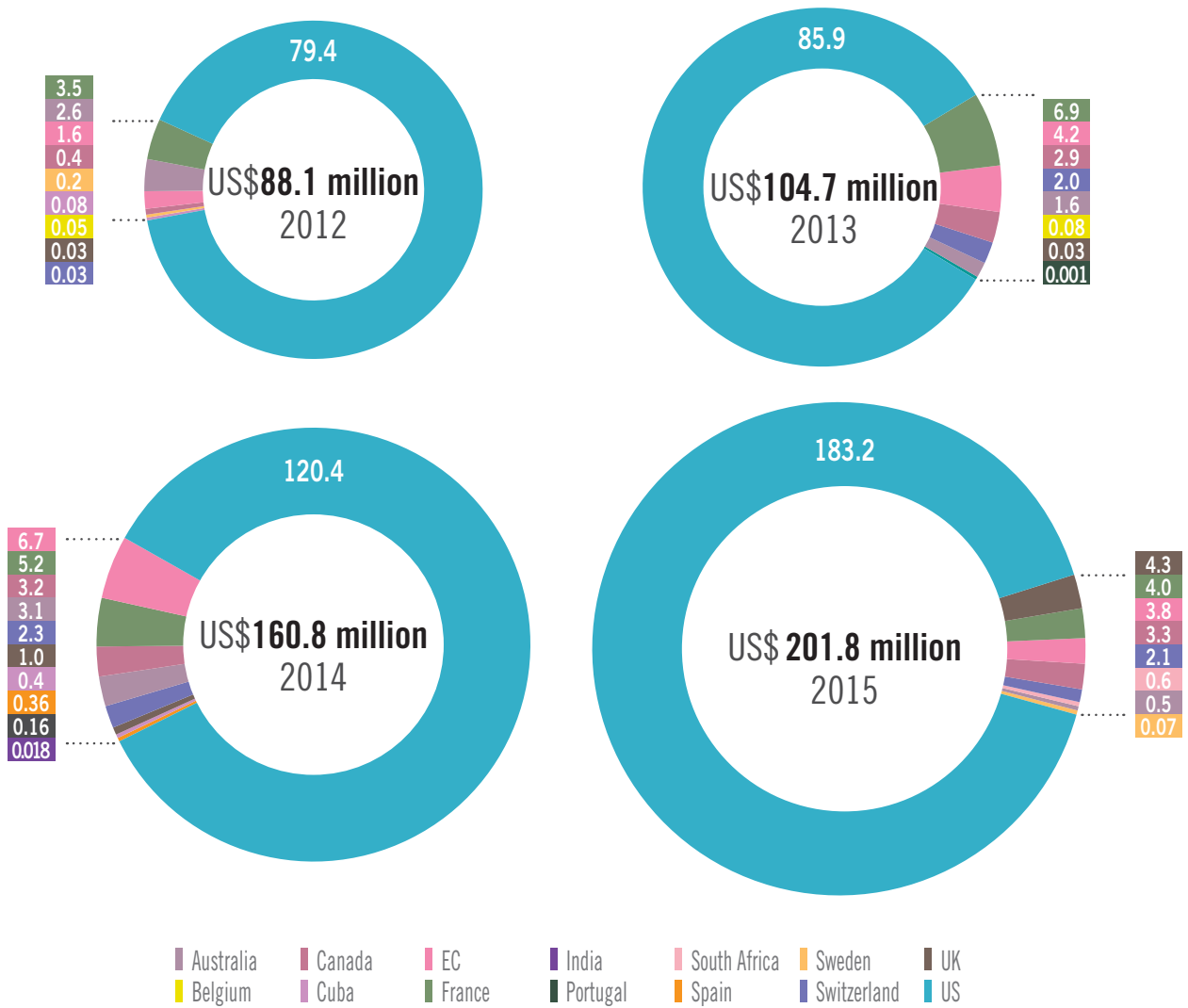


FIGURE 29 Investments in HIV Cure R&D by Funder, 2013–2015 (US\$ millions)

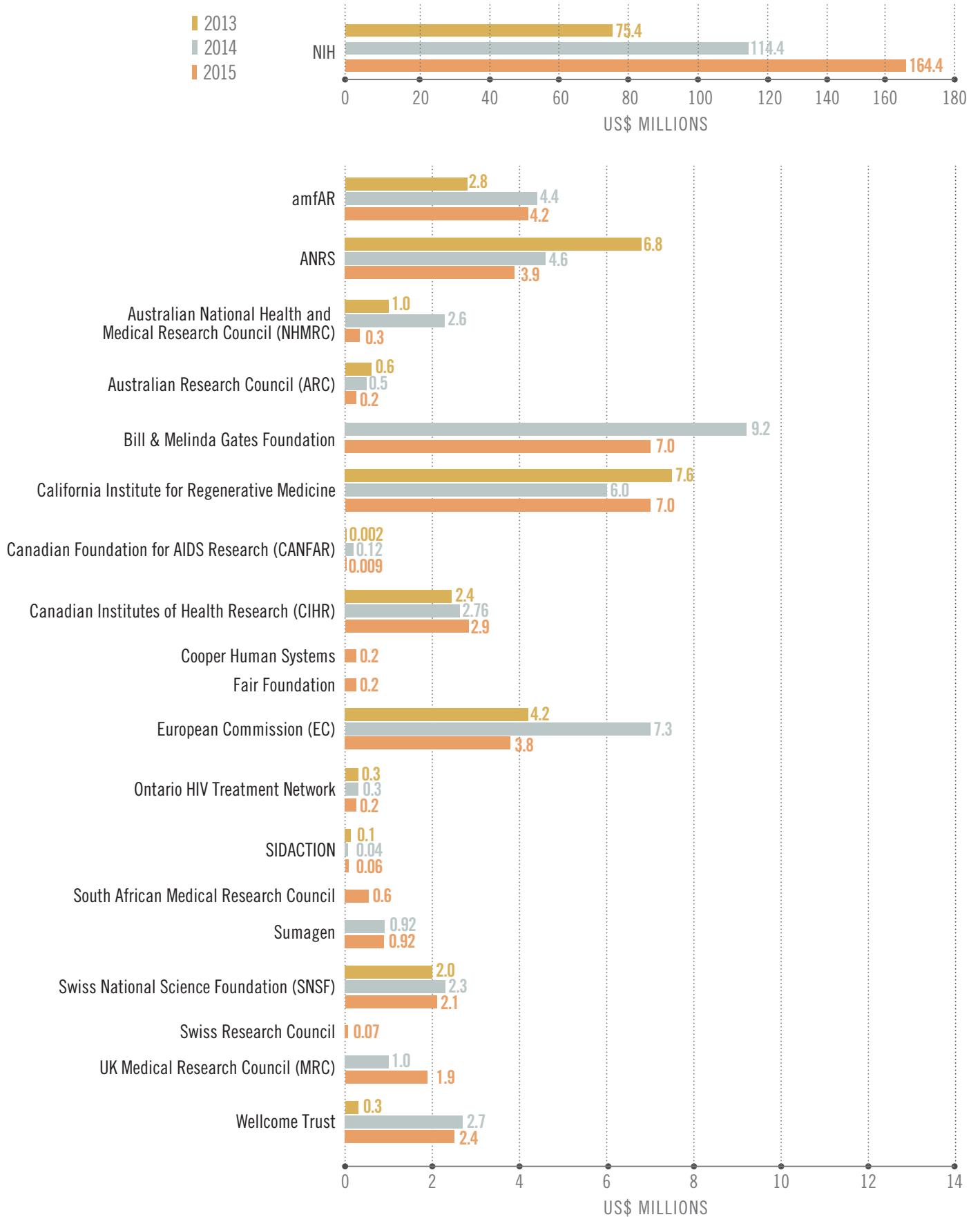
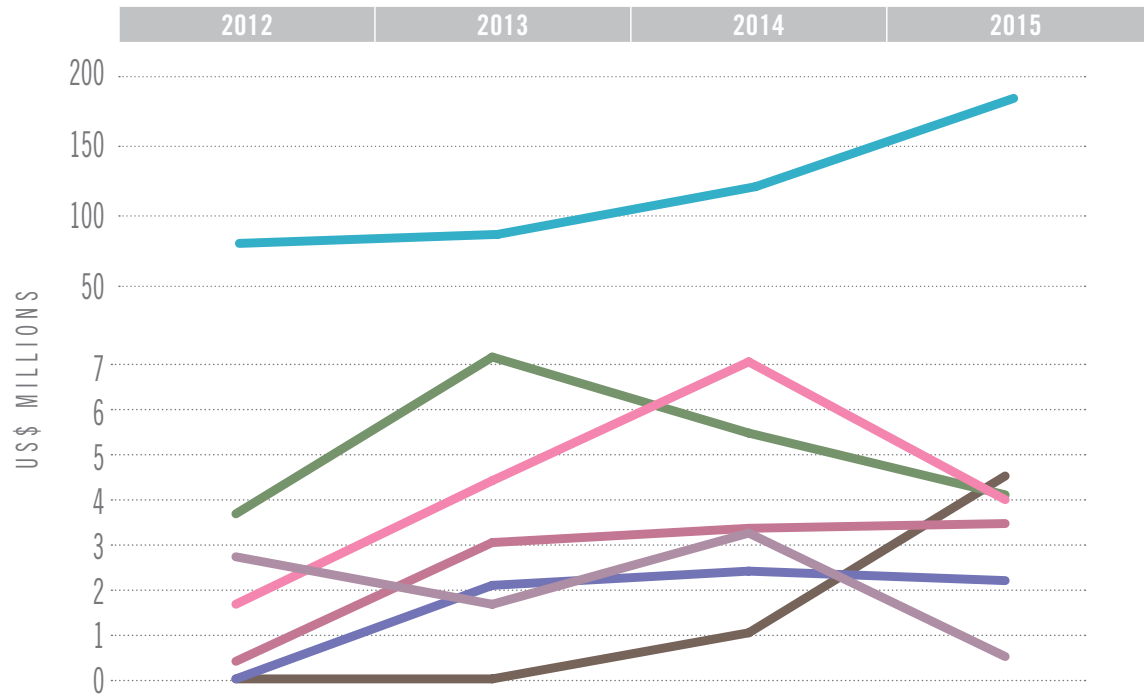


FIGURE 30 HIV Cure R&amp;D Investments by Country, 2012–2015



	2012	2013	2014	2015
United States	79.4	85.9	120.4	183.2
European Commission	1.6	4.2	6.7	3.8
Canada	0.4	2.9	3.2	3.3
Switzerland	0.03	2.0	2.3	2.1
United Kingdom	0.03	0.03	1.0	4.3
France	3.5	6.8	5.2	4
Australia	2.6	1.6	3.1	0.5

# Endnotes

- <sup>1</sup> For the purposes of this report, the terms “research and development, or “R&D” and “research” are used interchangeably and all refer to the entire spectrum of research activities.
- <sup>2</sup> See Appendix for more information.
- <sup>3</sup> UNAIDS. 2016. *Global AIDS Update*. [http://www.unaids.org/sites/default/files/media\\_asset/global-AIDS-update-2016\\_en.pdf](http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf).
- <sup>4</sup> UNAIDS. 2016. *Prevention Gap Report*. [http://www.unaids.org/sites/default/files/media\\_asset/2016-prevention-gap-report\\_en.pdf](http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf).
- <sup>5</sup> Some portion of these declines can perhaps be accounted for by the significant appreciation of the US dollar in 2015. Currency equivalents provided to the Working Group fell an average of 10 percent from 2014 to 2015 relative to the US dollar. However, even when comparing investments made in non-USD currencies between the two years, global funding for HIV prevention R&D was still found to have declined overall.
- <sup>6</sup> Horizon 2020 is the European Union's largest research and innovation financing program in its history. Its goal is to facilitate world-class science and public-private partnership, engendering sustainable and inclusive economic growth in addition to breakthroughs in science and industry. Funding is available for a wide range of areas, from agriculture and forestry to transport, health and wellness. <https://ec.europa.eu/programmes/horizon2020/>.
- <sup>7</sup> Please refer to the Appendix for a comprehensive explanation of data collection methodology used and its associated limitations.
- <sup>8</sup> The Working Group receives responses from several commercial investors and combines these responses with estimates of investments from non-responders based on knowledge of ongoing research programs.
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- <sup>19</sup> Any instances in which funds were reported in the year they were spent rather than disbursed are clearly noted, with the rationale behind this decision indicated.
- <sup>20</sup> Funding information in other currencies was converted into US dollars using the appropriate International Monetary Fund (IMF) annual average exchange rate for July 1, 2015, except for those funds where the Group had access to the actual rate received.
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- <sup>27</sup> This outcome does not necessarily represent a de-prioritization of microbicide investments in the philanthropic sector. For example, the majority of grants from the Wellcome Trust – a major contributor of microbicide funding in past years – are made solely in response to investigator applications, which vary from year to year.
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- <sup>32</sup> ECHO. 2016. *ECHO Consortium*. <http://echo-consortium.com/>.
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- <sup>35</sup> IMPT. 2015. *The MPT Pipeline by Indication Combination*. <http://www.theimpt.org/documents/MPT-Pipeline-Table.pdf>.
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- <sup>40</sup> More information on global PrEP availability can be found on [prepwatch.org](http://prepwatch.org). At the time of publication, the following countries have registered Truvada, TDF/FTC or tenofovir disoproxil fumarate and emtricitabine as PrEP: Australia, Canada, France, Kenya, Peru, South Africa, Taiwan, Thailand, United States.
- <sup>41</sup> Arya, Au, Belew, Miele, Struble. 2015. *Regulatory Challenges in Developing Long-Acting Antiretrovirals for Treatment and Prevention of HIV Infection*. *Current Opinion in HIV & AIDS*. 10(4).
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- <sup>52</sup> FCMI+. 2016. *Other Female Condoms*. <http://fcmi.org/fcmi-product-briefs/other-female-condoms.html>.
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- <sup>64</sup> Agence France-Presse. 2016. *Thailand First Asian Nation to Eliminate Mother-to-Child HIV Transmission; Belarus, Armenia Also Reach Milestone, WHO says*. <http://kff.org/news-summary/thailand-first-asian-nation-to-eliminate-mother-to-child-hiv-transmission-belarus-armenia-also-reach-milestone-who-says/>.
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- <sup>67</sup> Organizations were asked to provide data based on the calendar year if possible and, if not, by their fiscal year. For organizations for which the fiscal year and the calendar year did not match, the Working Group treated the fiscal year as equivalent to the calendar year in which it predominantly occurs. For example, the fiscal year April 1, 2014 to March 31, 2015 was treated as 2014 and the fiscal year July 1, 2014 to June 30, 2015 was treated as 2015.
- <sup>68</sup> Any instances in which funds were reported in the year they were spent rather than disbursed are clearly noted, with the rationale behind this decision indicated.
- <sup>69</sup> See Data Collection.

## Appendix: Methodology

This report was prepared by Laura Lazar (AVAC), with contributions from Emily Donaldson (AVAC), Kevin Fisher (AVAC), Thomas Harmon (IAVI), Polly Harrison (AVAC), UNAIDS staff and Mitchell Warren (AVAC) of the Resource Tracking for HIV Research and Development Working Group (herein referred to as “the Working Group”), with contributions from Emily Hayman. The Working Group developed and has utilized a systematic approach to data collection and collation since 2004. These methods were employed to generate the estimates of funding for R&D presented in this report. A detailed explanation of the methodology can be found on the Working Group website ([www.hivresourcectracking.org](http://www.hivresourcectracking.org)). Categories used to describe different R&D activities — one for AIDS vaccines and one for HIV microbicides — were derived from those developed by the US NIH and are shown in the following tables.

TABLE 10 **Public, Philanthropic and Commercial Sector Primary Funders**

Total responders: 112	
Sector	Type of Responders
<b>Public</b>	<ul style="list-style-type: none"> <li>• National governments (including government research bodies, international development assistance agencies and other government funding agencies)</li> <li>• European Commission</li> <li>• Multilateral agencies</li> </ul>
<b>Philanthropic</b>	<ul style="list-style-type: none"> <li>• Private, not-for-profit organizations (e.g., foundations, trusts and non-governmental organizations)</li> <li>• Charities</li> <li>• Corporate donations</li> <li>• Individual gifts and bequests</li> </ul>
<b>Commercial</b>	<ul style="list-style-type: none"> <li>• Pharmaceutical companies</li> <li>• Biotechnology companies</li> </ul>

## *Data Collection Methods and Fluctuation in Investment Levels*

HIV prevention R&D investment figures are collected annually by the Resource Tracking for HIV Prevention R&D Working Group through an email survey. For the present report, the Working Group reached out from January to May 2016 to 215 funders in the public, philanthropic and commercial sectors and collected information on 485 grants and line-item investments that the Group then allocated to HIV prevention R&D.

Two different types of resource flows were tracked: investments, defined as annual disbursements by funders; and, when available, expenditures, defined as the level of resources directly spent on R&D activities by funding recipients in a particular year. The main reasons for differentiating between these two resource flows were: (1) some funders may forward fund (i.e., disburse funding in one year to be expended over multiple years); (2) research projects may be delayed and (3) entities such as the increasingly important product development public-private partnerships (PDPs) often receive funds in one year but expend them over a period of time or may hold funds to sustain multi-year contracts.

Investment figures were based on estimates of the level of funds disbursed each year and generated from the perspective of the funder.<sup>67</sup> As such, funds were allocated to the year in which they were disbursed by the donor, irrespective of whether the funds were expended by the recipient in that year or in future years.<sup>68</sup>

In order to minimize double-counting, the Working Group distinguished between primary funders and intermediary organizations. “Intermediary” organizations receive resources from multiple funders and use these resources to fund their own work as well as the work of others. All identified primary funders were categorized as public, (such as government research bodies, international development agencies and multilaterals), philanthropic, (such as foundations, charities and corporate donors) or commercial, (pharmaceutical and biotechnology companies) sector funders.

While limitations exist in developing a method for breaking down funding allocations by type of activity or stage of product development, the Working Group allocates resources into categories based on NIH definitions.<sup>69</sup> As the largest funder of HIV prevention R&D and thus, with the majority of grants toward HIV prevention research allocated based on NIH definitions, this allows for the most accurate possible analysis of the largest portion of grants. For grants received outside of NIH funding, the allocation of funding was based on the information provided by the intermediaries or funders. When this information was not available, the Working Group reviewed the descriptions of the projects funded and, based on the description of each project, allocated the funds across the expenditure categories.

All figures in the report are given in current US dollars and have not been adjusted for inflation. Funding information in other currencies was converted into US dollars using the appropriate International Monetary Fund (IMF) annual average exchange rate for July 1, 2015, except for those funds where we had access to the actual rate received.

Every effort was made to obtain a comprehensive set of data that was comparable across organizations and countries. However, the data presented in this report are subject to a number of limitations:

- Requests for information were directed to all public, philanthropic and commercial organizations identified as providing funding for HIV prevention R&D. However, not all entities contacted responded or provided financial information with their response. For the private sector, annual investments and funding estimates were extrapolated based on qualitative data collection on R&D programs and expert opinions.
- The Working Group provides R&D allocation definitions in the survey sent to funders. However, most funders and intermediary organizations do not break down their expenditures and investments by type of activity or stage of product development, and definitions often vary among funders.
- The Working Group attempted to reduce the potential for double-counting and to distinguish between funders and recipients of funding. However, all financial information is “self-reported” by organizations and not independently verified.



## Data Collection Categories:

- Preventive AIDS vaccines
- Microbicides
- Multipurpose prevention technologies
- Pre-exposure prophylaxis (PrEP)
- Treatment as prevention
- Male circumcision
- Female condom
- HSV-2
- Prevention of vertical transmission
- HIV cure
- Therapeutic AIDS vaccines
- Antiretrovirals (ARVs)
- Immune-based therapies & anti-inflammatory drugs
- Co-infection & opportunistic infection drugs
- Other HIV-associated drugs
- HIV diagnostics

Preventive and therapeutic AIDS vaccine R&D	
Category	Definition
<b>Basic research</b>	Studies to increase scientific knowledge through research on protective immune responses and host defenses against HIV.
<b>Preclinical research</b>	Efforts to improve preventive AIDS vaccine design, development and animal testing.
<b>Clinical trials</b>	Support for Phase I, II and III trials (including the costs of candidate products).
<b>Cohort and site development</b>	Support to identify trial sites, build capacity, ensure adequate performance of trials and address the prevention needs of the trial communities.
<b>Advocacy and policy development</b>	Education and mobilization of public and political support for preventive AIDS vaccines and the targeting of potential regulatory, financial, infrastructural or political barriers to their rapid development and use.

Microbicides R&D	
Category	Definition
<b>Basic mechanisms of mucosal transmission</b>	Elucidate basic mechanisms of HIV transmission at mucosal/epithelial surfaces.
<b>Discovery, development and preclinical testing</b>	Target R&D efforts at the discovery, development and pre-clinical evaluation of topical microbicides alone and or in combination.
<b>Formulations and modes of delivery</b>	Develop and assess acceptable formulations and modes of delivery for microbicides.
<b>Clinical trials</b>	Support for Phase I, II and III trials of candidate microbicides for safety, acceptability and effectiveness (including costs of candidate products).
<b>Behavioral and social science research</b>	Conduct applied behavioral and social science research to inform and optimize microbicide development, testing and acceptability and use.
<b>Microbicide research infrastructure</b>	Establish and maintain the appropriate infrastructure (including training) needed to conduct research.
<b>Advocacy and policy development</b>	Education and mobilization of public and political support for microbicides, and the targeting of potential regulatory, financial, infrastructural or political barriers to their rapid development.

### Other prevention tools: male circumcision, treatment as prevention, treatment of herpes simplex virus type 2 (HSV-2), cervical barriers and pre-exposure prophylaxis (PrEP)

Category	Definition
<b>Basic research</b>	Studies to increase scientific knowledge through research on protective immune responses and host defenses against HIV.
<b>Preclinical research</b>	Efforts to improve design, development and animal testing of experimental interventions.
<b>Clinical trials</b>	Support for Phase I, II and III trials (including the costs of candidate products).
<b>Cohort and site development</b>	Support to identify trials sites, build capacity, ensure adequate performance of trials and address the prevention needs of the trial communities.
<b>Advocacy and policy development</b>	Education and mobilization of public and political support for new HIV prevention tools and the targeting of potential regulatory, financial, infrastructural or political barriers to their rapid development and use.

### Definitions

Category	Definition
<b>Treatment as prevention research</b>	Research evaluating the impact of early/expanded ART (at any CD4 count), ART initiation strategies (e.g., Seek, Test, Treat and Retain) or ART adherence strategies on HIV incidence, HIV transmission risk, HIV risk behavior and/or community viral load; and impact of ART at CD4 count $\geq$ 350 cells/mm <sup>3</sup> on HIV and/or TB-related morbidity and mortality or HIV transmission.
<b>Multipurpose Prevention Technologies (MPTs)</b>	<p>Combine protection to prevent at least two sexual and reproductive health risks: unintended pregnancy and HIV and other sexually transmitted infections (STIs). Indications of interest include:</p> <ul style="list-style-type: none"> <li>• HIV</li> <li>• HSV</li> <li>• Pregnancy</li> <li>• Bacterial Vaginosis (BV)</li> <li>• Chlamydia</li> <li>• Gonorrhea</li> <li>• Hepatitis</li> <li>• HPV</li> <li>• Syphilis</li> <li>• Trichomoniasis</li> <li>• Urinary Tract Infections (UTI)</li> <li>• Other STIs</li> </ul>
<b>Cure research</b>	Research conducted on viral latency, elimination of viral reservoirs, immune system and other biological approaches, as well as therapeutic strategies that may lead to either a functional (control of virus rather than elimination, without requirement for therapy) or sterilizing (permanent remission in absence of requirement for therapy) cure of HIV infection.

## **Toward a Cure Program Definition: US NIH eradication of viral reservoirs**

Research conducted on viral latency, elimination of viral reservoirs, immune system and other biological approaches, as well as therapeutic strategies that may lead to either a functional (control of virus rather than elimination, without requirement for therapy) or sterilizing (permanent remission in absence of requirement for therapy) cure of HIV infection.

### **Pathogenesis studies**

Basic research on viral reservoirs, viral latency and viral persistence, including studies on genetic factors associated with reactivation of the virus, and other barriers to HIV eradication.

### **Animal models**

Identification and testing of various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.

### **Drug development and preclinical testing**

Programs to develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system.

### **Clinical trials**

Studies to evaluate lead compounds, drug regimens and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.

### **Therapeutic vaccines**

Design and testing of vaccines that would be capable of suppressing viral replication and preventing disease progression.

### **Adherence/compliance**

Development and testing of strategies to maintain adherence/compliance to treatment, in order to improve treatment outcomes and reduce the risk of developing HIV drug resistance.

## Appendix: List of acronyms

<b>amfAR</b>	The Foundation for AIDS Research	<b>LAI</b>	Long-acting injectable
<b>ANRS</b>	National Agency for Research on AIDS and Viral Hepatitis (France)	<b>LMIC</b>	Lower-middle-income country
<b>ARC</b>	Australian Research Council	<b>MDG</b>	Millennium Development Goal
<b>ART</b>	Anti-retroviral therapy	<b>MHRP</b>	US Military HIV Research Program
<b>ARV</b>	Anti-retroviral	<b>MPT</b>	Multipurpose prevention technology
<b>ASPIRE</b>	A Study to Prevent Infection with a Ring for Extended Use	<b>MRC</b>	UK Medical Research Council
<b>BMGF</b>	Bill & Melinda Gates Foundation	<b>MSM</b>	Men who have sex with men
<b>BMS</b>	Bristol-Meyers Squibb	<b>MTN</b>	Microbicide Trials Network
<b>bNAB</b>	Broadly neutralizing antibody	<b>NEMAPP</b>	National Evaluation of Malawi's PMTCT programme
<b>BV</b>	Bacterial vaginosis	<b>NHMRC</b>	Australian National Health & Medical Research Council
<b>CANFAR</b>	Canadian Foundation for AIDS Research	<b>NIAID</b>	US National Institute of Allergy and Infectious Diseases
<b>CDC</b>	US Centers for Disease Control and Prevention	<b>NIH</b>	US National Institutes of Health
<b>CEPI</b>	Coalition for Epidemic Preparedness	<b>Norad</b>	Norwegian Agency for Development Cooperation
<b>CHVI</b>	Canadian HIV Vaccine Initiative	<b>OAR</b>	US NIH Office of AIDS Research
<b>CIDA</b>	Canadian International Development Agency	<b>ODA</b>	Official Development Assistance
<b>CIHR</b>	Canadian Institutes of Health Research	<b>OECD</b>	Organisation for Economic Co-operation and Development
<b>COP</b>	Country Operational Plan	<b>OFID</b>	OPEC Fund for International Development
<b>CROI</b>	Conference on Retroviruses and Opportunistic Infections	<b>OHTN</b>	Ontario HIV Treatment Network
<b>DAH</b>	Development assistance for health	<b>OPEC</b>	Organization of the Petroleum Exporting Countries
<b>DANIDA</b>	Danish International Development Agency	<b>P5</b>	Pox-Protein Public-Private Partnership
<b>DBT</b>	Department of Biotechnology at India's Ministry of Science and Technology	<b>PDP</b>	Product development partnership
<b>DFID</b>	UK Department for International Development	<b>PEPFAR</b>	US President's Emergency Plan for AIDS Relief
<b>DIB</b>	Development Impact Bond	<b>PHAC</b>	Public Health Agency of Canada
<b>DOH</b>	Department of Health	<b>PMTCT</b>	Prevention of vertical transmission
<b>DREAMS</b>	Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe women	<b>POWER</b>	Prevention Options for Women's Evaluation Research
<b>DST</b>	Department of Science and Technology, South Africa	<b>PrEP</b>	Pre-exposure prophylaxis
<b>EAVI2020</b>	European AIDS Vaccine Initiative	<b>R&amp;D</b>	Research & development
<b>EC</b>	European Commission	<b>SA DOH</b>	South African Department of Health
<b>ECHO</b>	Evidence for Contraceptive Options and HIV Outcomes	<b>SDG</b>	Sustainable Development Goal
<b>EDCTP</b>	European and Developing Countries Clinical Trials Partnership	<b>SIDA</b>	Swedish Agency for International Cooperation Development
<b>EHVA</b>	European HIV Vaccine Alliance	<b>SIDACTION</b>	Association de lutte contre le sida
<b>EIMC</b>	Early infant male circumcision	<b>SNSF</b>	Swiss National Science Foundation
<b>FDA</b>	US Food and Drug Administration	<b>START</b>	Strategic Timing of AntiRetroviral Treatment study
<b>FRESH</b>	Females Rising through Education, Support, and Health	<b>TasP</b>	Treatment as prevention
<b>FSW</b>	Female sex workers	<b>TDF</b>	Tenofovir
<b>GIS</b>	Geographic information systems	<b>TDF/FTC</b>	Tenofovir/Emtricitabine
<b>GSK</b>	Glaxo SmithKline	<b>TEMPRANO</b>	A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa
<b>HOPE</b>	HIV Open-label Prevention extension trial	<b>TPP</b>	Target Product Profiles
<b>HPTN</b>	HIV Prevention Trials Network	<b>UAFC</b>	Universal Access to Female Condoms Joint Programme
<b>HPV</b>	Human papillomavirus	<b>UK</b>	United Kingdom
<b>HSV</b>	Herpes simplex virus	<b>UMIC</b>	Upper-middle-income country
<b>HVTN</b>	HIV Vaccine Trials Network	<b>UNAIDS</b>	Joint United Nations Programme on HIV/AIDS
<b>IAS</b>	International AIDS Society	<b>US</b>	United States
<b>IAVI</b>	International AIDS Vaccine Initiative	<b>USAID</b>	US Agency for International Development
<b>ICMR</b>	Indian Council of Medical Research	<b>USD</b>	United States dollar
<b>IHME</b>	Institute for Health Metrics and Evaluation	<b>UTI</b>	Urinary tract infections
<b>IMF</b>	International Monetary Fund	<b>VMMC</b>	Voluntary Medical Male Circumcision
<b>IMPT</b>	Initiative for Multipurpose Prevention Technologies	<b>VOICE</b>	Vaginal and Oral Interventions to Control the Epidemic
<b>IPM</b>	International Partnership for Microbicides	<b>VRC</b>	US Vaccine Research Center
<b>KP</b>	Key population	<b>WHO</b>	World Health Organization

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