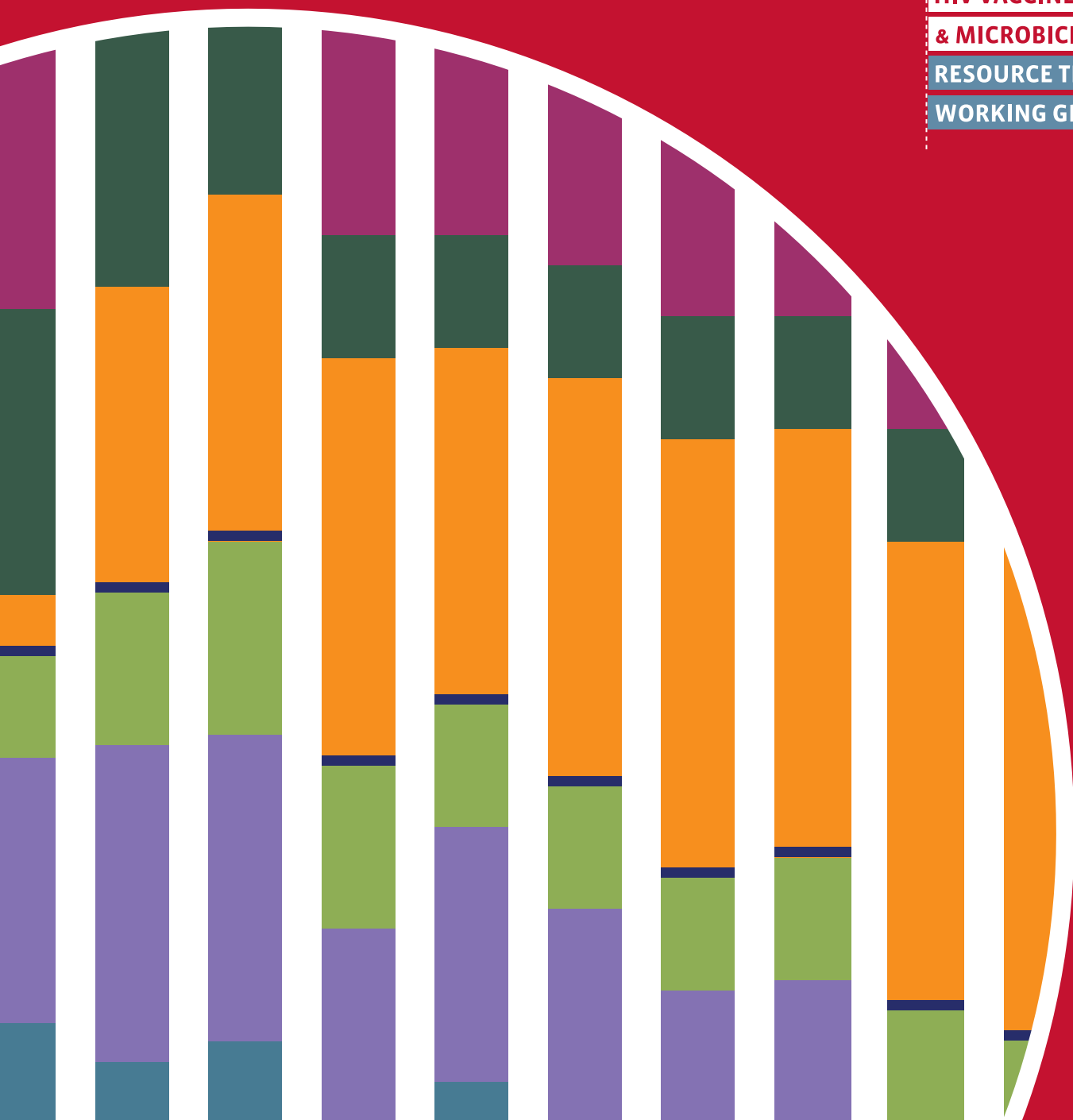


HIV Prevention Research & Development Funding Trends, 2000–2014

Investing in innovation in an evolving global health
and development landscape

HIV VACCINES
& MICROBICIDES
RESOURCE TRACKING
WORKING GROUP



HIV Prevention Research & Development Funding Trends 2000–2014
Investment priorities to fund innovation in an evolving global health and development
JULY 2015

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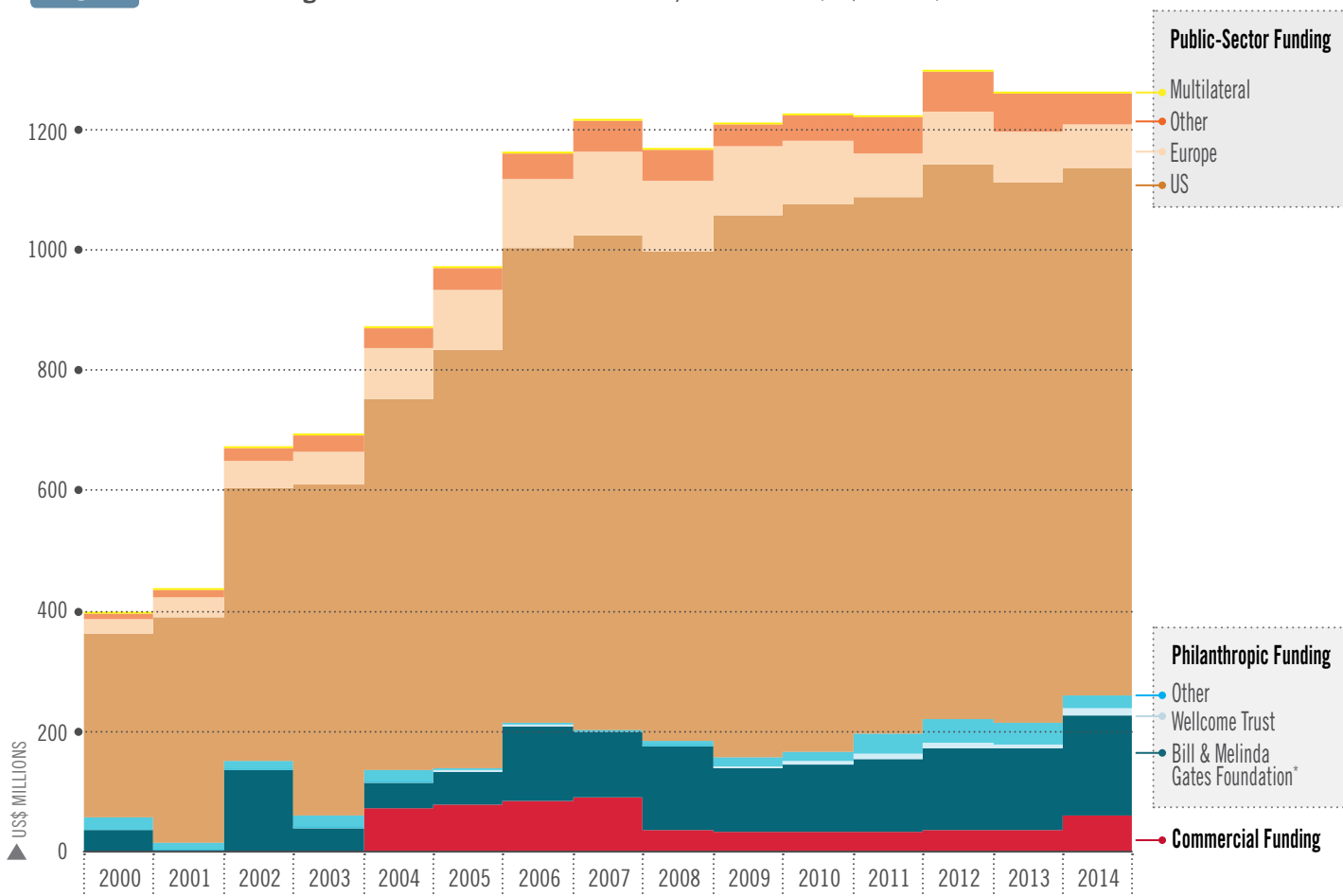
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In its eleventh annual report, the HIV Vaccines & Microbicides Resource Tracking Working Group (the “Working Group”) documents biomedical HIV prevention research and development (R&D)¹ spending for the calendar year 2014, as well as reports on an analysis of investment trends spanning fourteen years. The Working Group generates estimates of R&D investment that can be compared year to year across options and strategies and funding sources, helping assess the impact of public policies aimed at accelerating scientific progress and to provide facts for advocacy. This effort provides transparency for funders, policy makers and HIV/AIDS advocates so they can better understand and track investment flows.

The Working Group tracks trends in R&D investments and expenditures for biomedical HIV prevention options, including AIDS vaccines, microbicides, multipurpose prevention technologies, pre-exposure prophylaxis (PrEP), treatment as prevention, medical male circumcision, female condoms, HSV-2 vaccines, HIV cure and therapeutic vaccines.² From 2000 to 2014, the Working Group tracked over US\$15 billion in investments towards HIV prevention R&D (Figure 1).

Fig. 1 Global Funding Sources for HIV Prevention R&D, 2000–2014 (US\$ millions)



* Figures throughout the report may be amended following complete review of the data set from the BMGF.

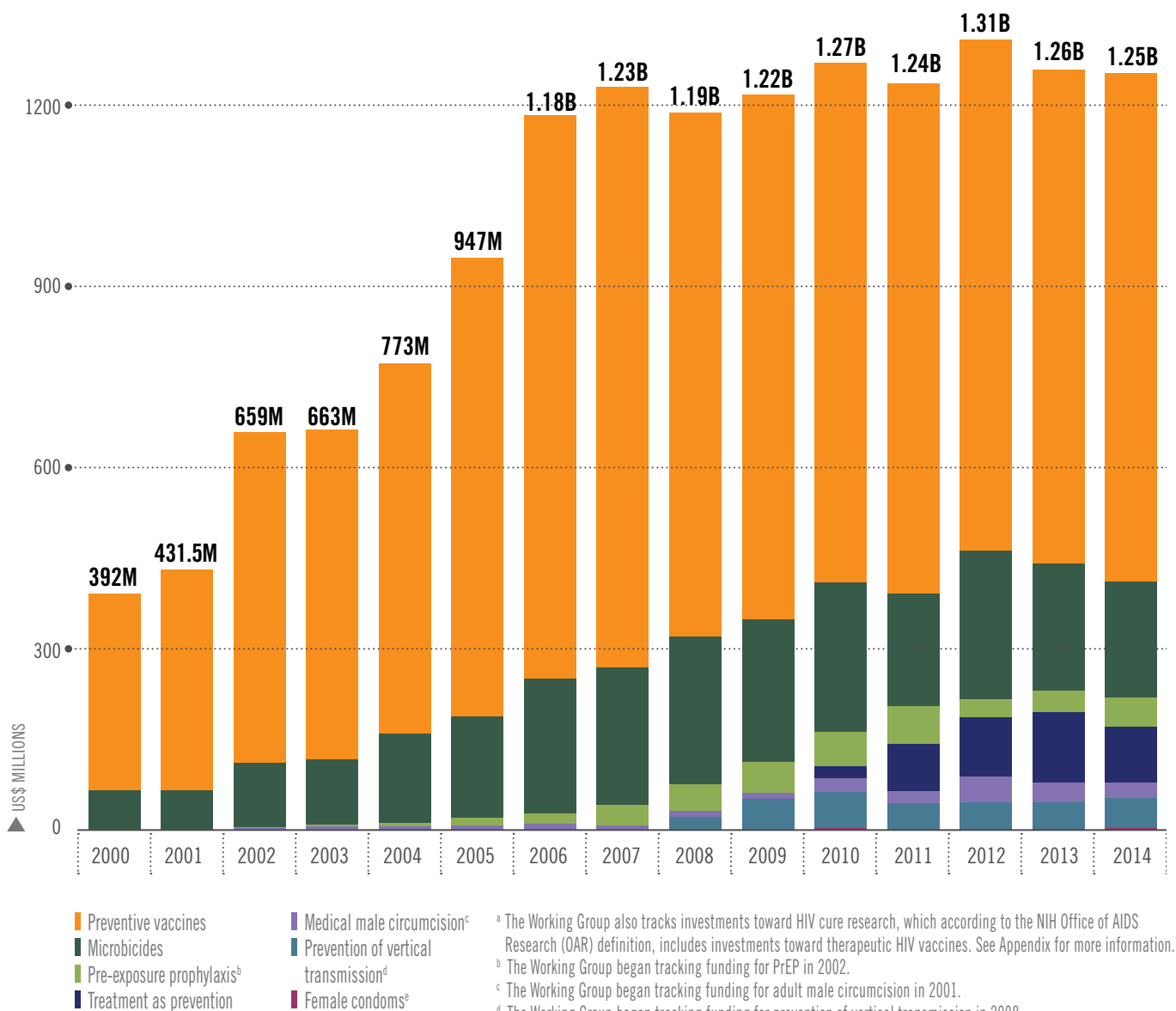
¹ For the purposes of this report, “research and development” or “R&D” and “research” both refer to the entire spectrum of research activities.

² The Working Group, in collaboration with the International AIDS Society (IAS), also tracks investments towards HIV cure research, which according to the NIH Office of AIDS Research (OAR) definition, includes investments toward therapeutic HIV vaccines. See Appendix for more information.

Trends in HIV Prevention R&D Funding

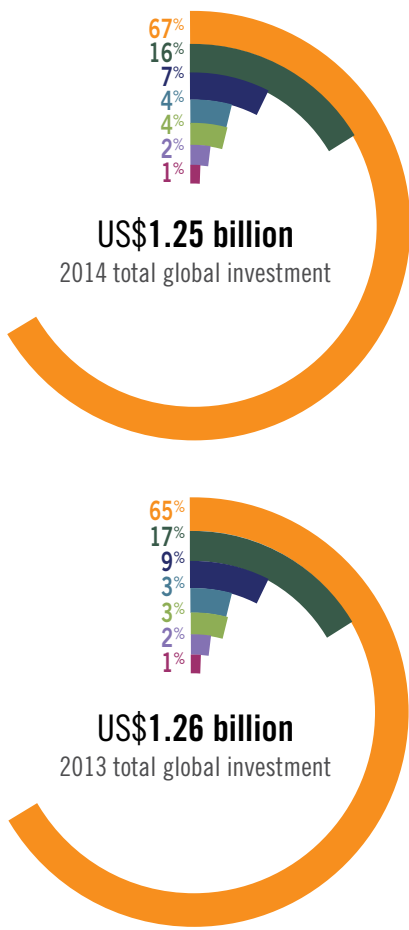
In 2014, the reported funding for HIV prevention R&D decreased by US\$10 million from the previous year to a total of US\$1.25 billion (Figure 2). While investments toward research in preventive vaccines, PrEP, female condoms and prevention of vertical transmission increased in 2014, investments towards microbicides, treatment as prevention and medical male circumcision decreased (Figure 3). Overall funding has remained at nearly the same level for approximately

Figure 2 Global HIV Prevention R&D^a Investment by Technology Category, 2000–2014 (US\$ millions)



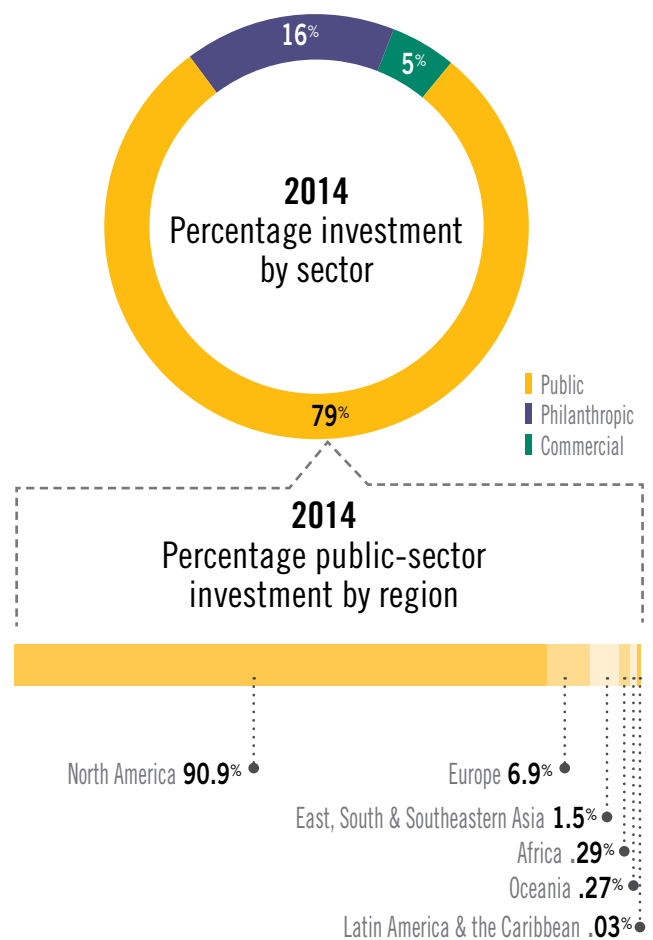
a decade. As in past years, the public sector made up the majority of total funding at US\$990 million (79 percent) (Figure 4), with the US public sector contributing US\$868 million (69 percent). European public-sector funding made up US\$69 million (five percent), public-sector investment from other countries made up US\$52 million (four percent), philanthropic investment was US\$200 million (16 percent) and investment from the commercial sector was US\$63 million (five percent).

Figure 3 Total Global HIV Prevention R&D Investment by Prevention Option, 2013–2014



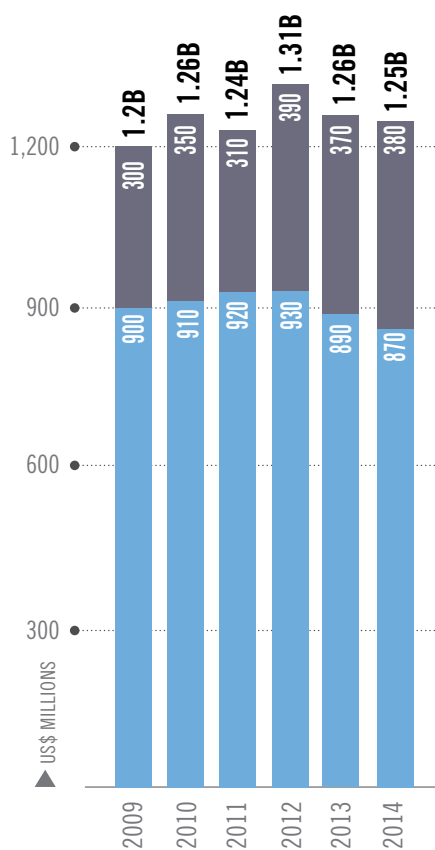
- Preventive vaccines
- Microbicides
- Pre-exposure prophylaxis
- Treatment as prevention
- Medical male circumcision
- Prevention of vertical transmission
- Female condoms

Figure 4 Total Global HIV Prevention R&D Investment by Sector, 2014



- US investment in HIV prevention R&D decreased by US\$19 million in 2014, from US\$887 million down to US\$868 million (Figure 5). Over the past ten years, annual US investment has increased by 43 percent, reaching its highest level in 2012, at US\$921 million. Overall, US public-sector investment in preventive vaccines, microbicides and prevention of vertical transmission increased in 2014, while investment in PrEP, treatment as prevention, medical male circumcision and female condoms decreased (Figure 6).
- European public-sector funding decreased between 2013 and 2014 by US\$9 million, down to US\$69 million (Figure 7). Over the past ten years, annual European investment has declined

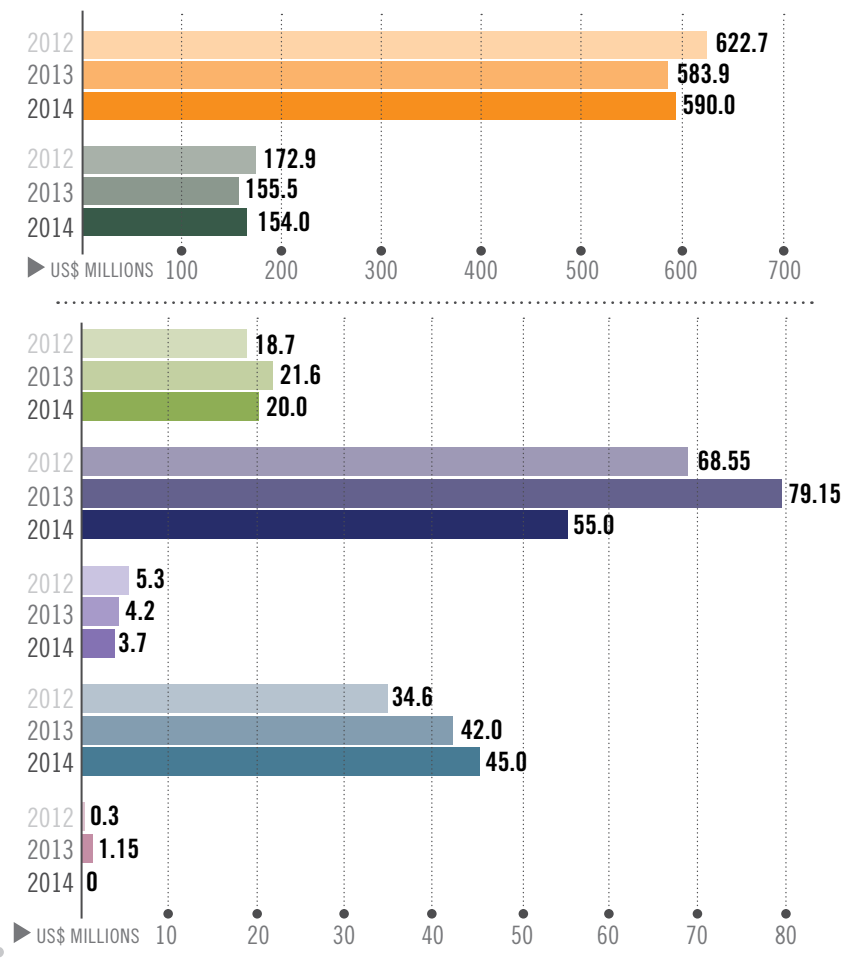
Figure 5 US Public-Sector Investment in HIV Prevention R&D Compared to Total Global Investment, 2009–2014* (US\$ millions)



■ US public sector
 ■ All other investment

* Figures are rounded.

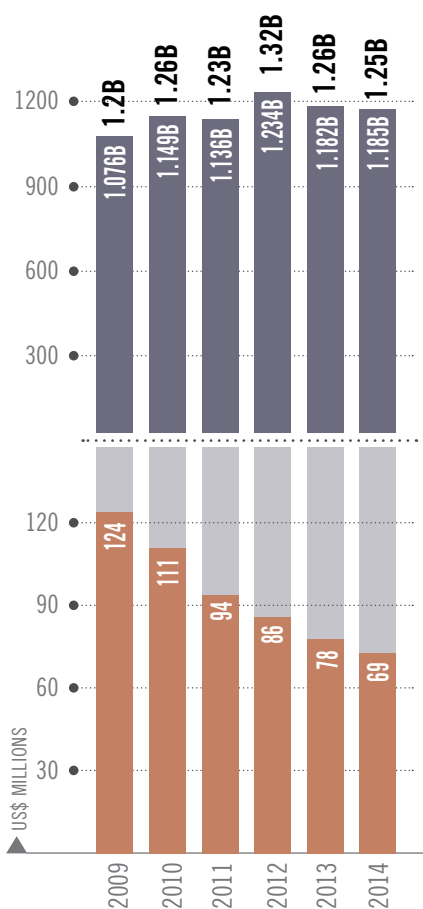
Figure 6 US Public-Sector Investment in HIV Prevention R&D, 2012–2014 (US\$ millions)



■ Preventive vaccines
 ■ Microbicides
 ■ Pre-exposure prophylaxis
 ■ Treatment as prevention
 ■ Medical male circumcision
 ■ Prevention of vertical transmission
 ■ Female condoms

by 16 percent, reaching its highest level in 2008, at US\$114 million. Overall, European public-sector investment declined with regards to research for preventive vaccines, microbicides and female condoms, while investment increased towards PrEP, treatment as prevention, medical male circumcision and prevention of vertical transmission (Figure 8). Investment by several European donors declined substantially, with the European Commission (EC), France, Denmark and Norway showing marked decreases in funding. Denmark and the EC decreased funding for both preventive vaccines and microbicides; funding from France decreased for preventive vaccines; and funding from Norway decreased for microbicides. However, several

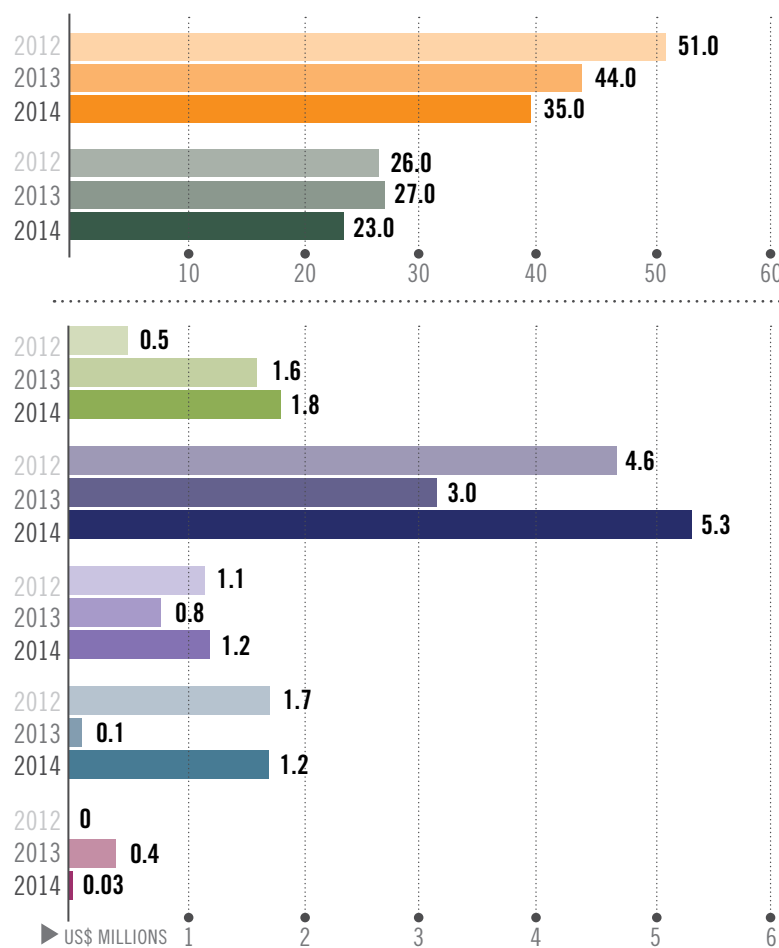
Figure 7 European Public-Sector Investment in HIV Prevention R&D Compared to Total Global Investment, 2009–2014* (US\$ millions)



European public sector
All other investment

* Figures are rounded.

Figure 8 European Public-Sector Investment in HIV Prevention R&D, 2012–2014 (US\$ millions)



Preventive vaccines
Microbicides
Pre-exposure prophylaxis
Treatment as prevention
Medical male circumcision
Prevention of vertical transmission
Female condoms

donors increased their funding in 2014, including Sweden, Switzerland and the UK. Sweden increased funding for preventive vaccines, microbicides and medical male circumcision; Switzerland increased funding for preventive vaccines, PrEP, treatment as prevention and prevention of vertical transmission and the UK increased funding for preventive vaccines, PrEP and treatment as prevention.

- Investment by other public-sector agencies declined substantially between 2013 and 2014 by US\$13 million, down to US\$52 million in 2014. From 2004 to 2014, annual investment from public-sector agencies outside of the US and Europe increased by 65 percent, reaching its highest level in 2012 at US\$69 million. However, in 2014 the largest declines in funding came from Australia, Canada and South Africa, with investments from India, Japan and Thailand declining nominally. Australia decreased investments in preventive vaccines and microbicides; Canada decreased investments in preventive vaccines, treatment as prevention and vertical transmission; and South Africa decreased investments in microbicides.
- Philanthropic support for HIV prevention R&D increased by US\$9 million, up to US\$200 million in 2014, reversing the trend of steady decline seen in the past few years. Over the past ten years, annual philanthropic support has increased significantly, reaching its highest level in 2012 at US\$203 million. Overall, philanthropic investments in preventive vaccines and PrEP increased, while investments in microbicides, treatment as prevention and medical male circumcision declined.
- Commercial sector funding saw a substantial increase, due to an increase in reported funding for preventive vaccine and female condom R&D.³

³ The Working Group receives responses from several commercial investors and combines these responses with estimates of investment from non-responders based on knowledge of ongoing research programs.

Key findings:

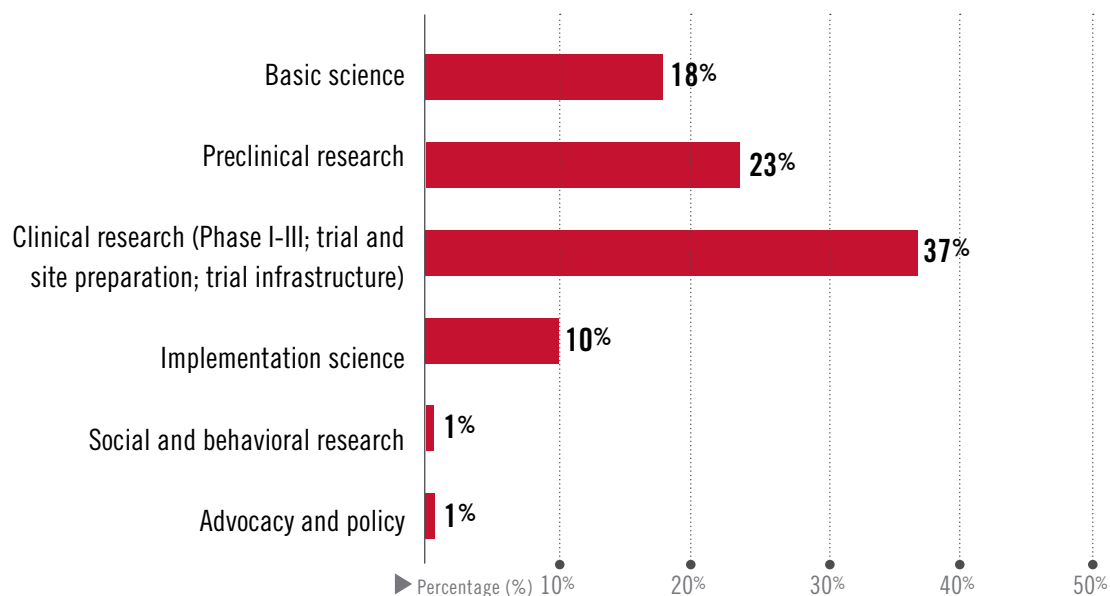
Each of the key findings that emerged from this year’s Working Group research, compilation and analysis reflects the state of funding for HIV prevention R&D and will be critical for HIV prevention R&D needs, priorities and responses going forward.

I R&D investment is expanding beyond research to rollout

Since the Working Group began tracking investments in HIV prevention, a number of options have moved through the pipeline from research to rollout (*Figure 9*). The importance of investing in products beyond bench science and clinical trials is expressed through the recent roll out and scale-up of options such as voluntary medical male circumcision⁴ and female condoms⁵, and in the demonstration project phase, PrEP.

Increasingly important to HIV prevention is research into the “science of delivery”, the study of the processes, context, and general determinants of the delivery of public services and goods. World Bank President Jim Kim explained that in aid-financed projects, “most failures happen at delivery”.⁶ It is important to consider how to deliver HIV prevention products and ensure that those products meet the needs of, and reach, end-users; otherwise products will not realize their full potential to reduce new HIV infections.⁷ Early investment to ensure the uptake of products is a growing part of HIV prevention R&D.

Figure 9 2014 HIV Prevention R&D Investment by Research Stage (Percentage %)



⁴ It is projected that circumcising 80 percent of all uncircumcised men in countries with high HIV rates and low male circumcision rates would avert one in five new HIV infections by 2025. Njeuhmeli, Emmanuel. 2011. *Voluntary Medical Male Circumcision: Modeling the the impact and cost of expanding male circumcision for HIV prevention in Eastern and Southern Africa*. PLOS Medicine. [journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001132](https://doi.org/10.1371/journal.pmed.1001132).

⁵ A Washington, DC female condom program has reduced new HIV infections and associated costs. 2012, July. Holtgrave, David. *Cost–Utility Analysis of A Female Condom Promotion Program in Washington, DC*. *AIDS and Behavior*. July 2012, Volume 16, Issue 5, pp 1115–1120. link.springer.com/article/10.1007%2Fs10461-012-0174-5.

⁶ “News.” *Remarks As Prepared for Delivery: World Bank Group President Jim Yong Kim at the Annual Meeting Plenary Session*. N.p., n.d. www.worldbank.org/en/news/speech/2012/10/12/remarks-world-bank-group-president-jim-yong-kim-annual-meeting-plenary-session.

⁷ USAID. *IDEA to IMPACT: A guide to introduction and scale of global health interventions*. www.usaid.gov/cii.

II Majority of investment from several large funders

In 2014, the US remained the largest public-sector and overall investor in HIV prevention R&D, with combined spending by the US National Institutes of Health (NIH), US Agency for International Development (USAID), US Centers for Disease Control and Prevention (CDC) and Department of Defense (DoD) totaling US\$868 million. Of the total funding tracked by the Working Group, the US invests nearly two-thirds. Sixty-six percent of all US public-sector funding comes from the US NIH. Combined, the US public sector (*Figure 10*) and the Bill & Melinda Gates Foundation (BMGF)* (*Figure 11*) account for 83 percent of all funding; potential reductions made by either could have a disproportionate impact on total funding.

While some funders increased their contribution in 2014, overall, fewer individual funders supported the HIV prevention research field than in previous years. Investment from emerging economies and countries hosting clinical trials and other HIV prevention R&D remains small. Expanding and diversifying the investment base could also provide a critical range of perspectives, human capacity and innovative concepts to the HIV prevention research agenda. A more diverse global cadre of funders, both involved in and dedicated to advancing HIV prevention R&D, would better assure sustained and consistent funding by reducing the risk that resource allocations by one or two primary donors would have a disproportionate impact on the whole field.

Figure 10 Top Five Countries Investing in HIV Prevention R&D, 2013–2014** (US\$ millions)

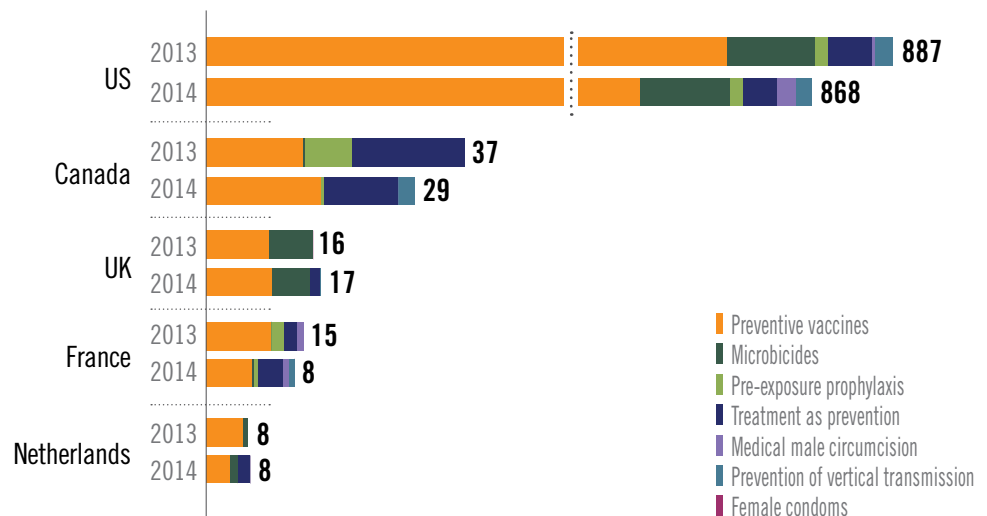
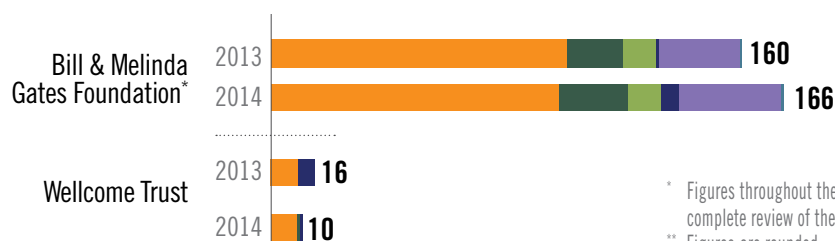


Figure 11 Top Philanthropic Organizations Investing in HIV Prevention R&D, 2013–2014** (US\$ millions)



* Figures throughout the report may be amended following complete review of the data set from the BMGF.

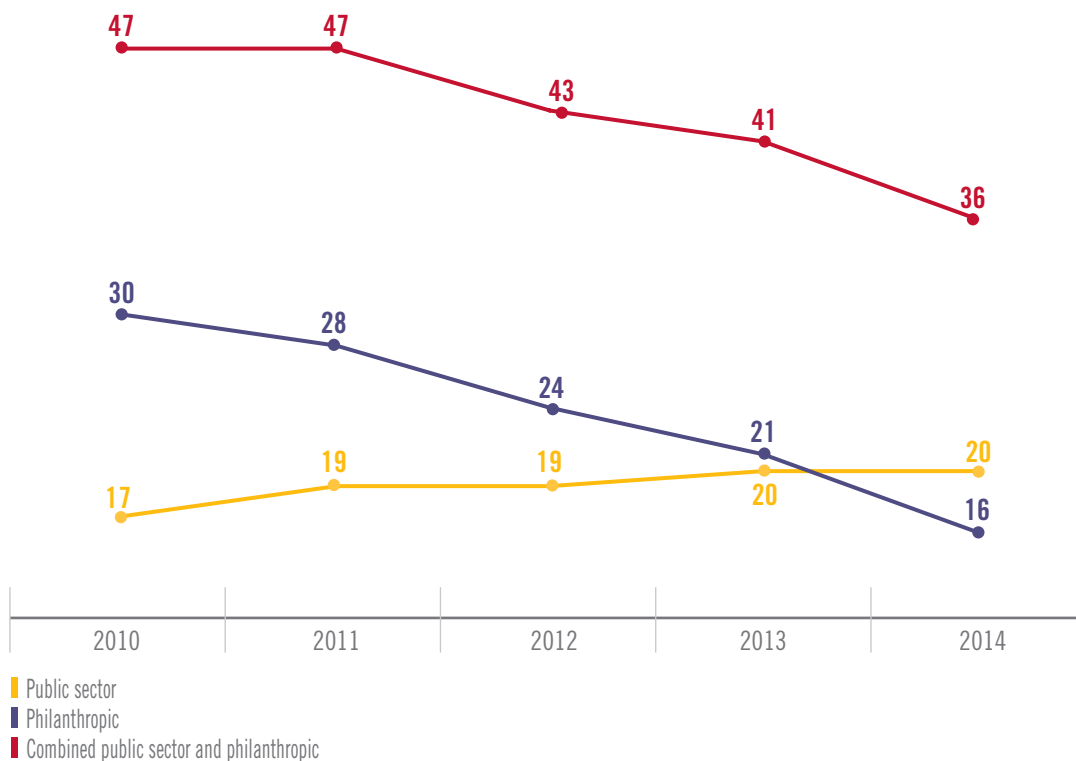
** Figures are rounded.

III Decrease in number of philanthropic funders engaged

While the total amount of philanthropic funding increased in 2014, the number of philanthropic funders engaged in HIV prevention research has been steadily declining since 2010. In 2014, 16 philanthropic funders invested in HIV prevention research, down from 30 in 2010 (Figure 12). In contrast, the number of countries investing public-sector funds in HIV prevention research has increased since 2010, from 17 to 20.

The BMGF and the Wellcome Trust make up nearly 90 percent of the total philanthropic investment in HIV prevention research. The importance of investments from these donors cannot be overstated. However, it is important to note that there has been a decrease in the number of philanthropic donors since 2010. Additionally, large decreases in philanthropic support from just a few funders have a large impact on the overall funding level.⁸ While overall philanthropic funding for HIV prevention R&D did not decrease in 2014, the wider AIDS philanthropic funding environment has felt these impacts in past years.

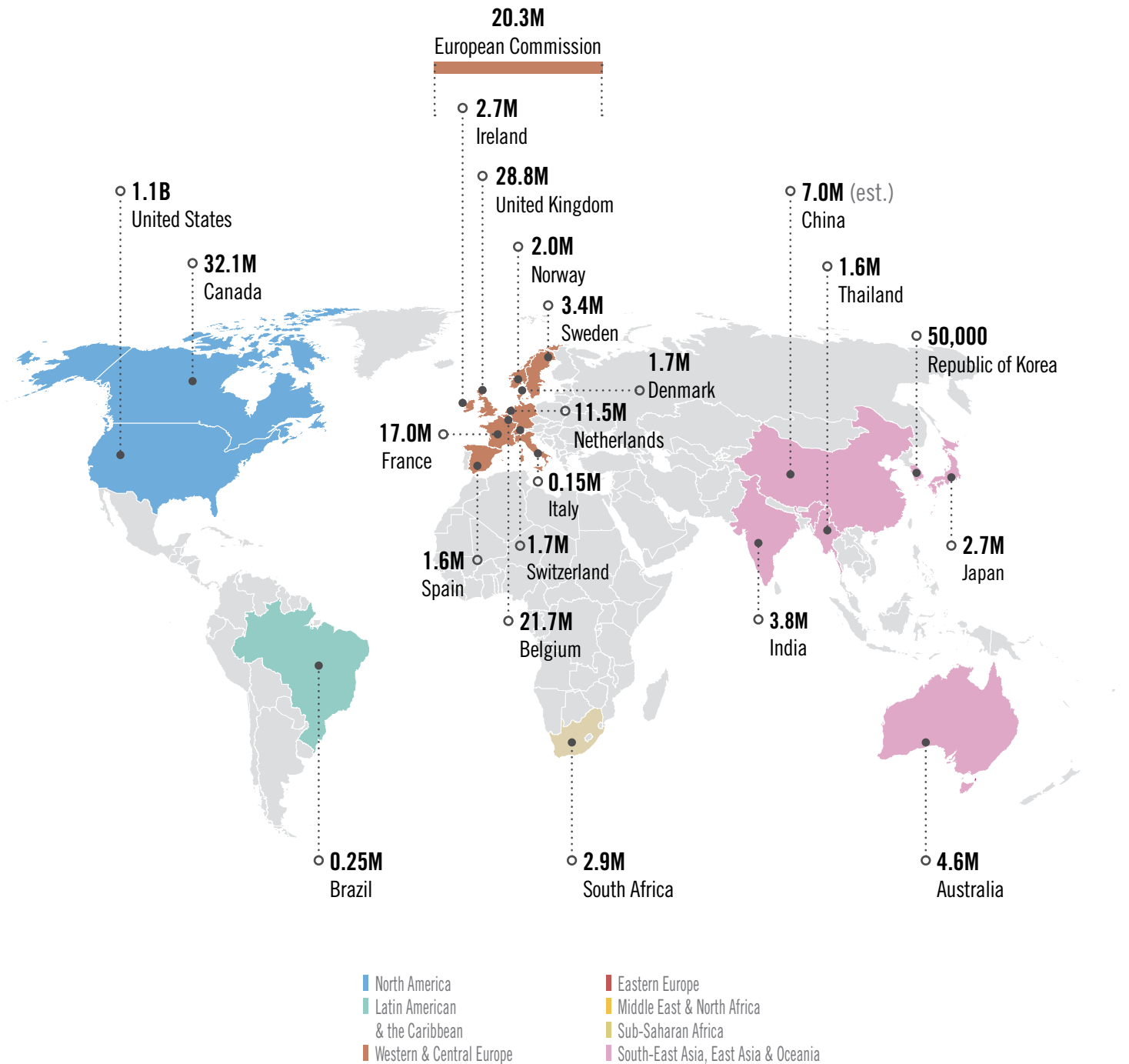
Figure 12 Number of Public Sector and Philanthropic Funders Investing in HIV Prevention R&D, 2010-2014



⁸ Funders Concerned About AIDS tracks global philanthropic support to address HIV/AIDS. *Global Philanthropic Support to Address HIV/AIDS in 2013*. www.fcaids.org/AIDSfunding/ResourceTrackingReport.

Figure 13 Total Global Investment in HIV Prevention R&D by Country, 2014 (US\$)

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



* 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 investment is allocated to a country based on the location of corporate headquarters and is underestimated due to a lack of reporting by companies. Not all commercial-sector estimates are able to be allocated by country.

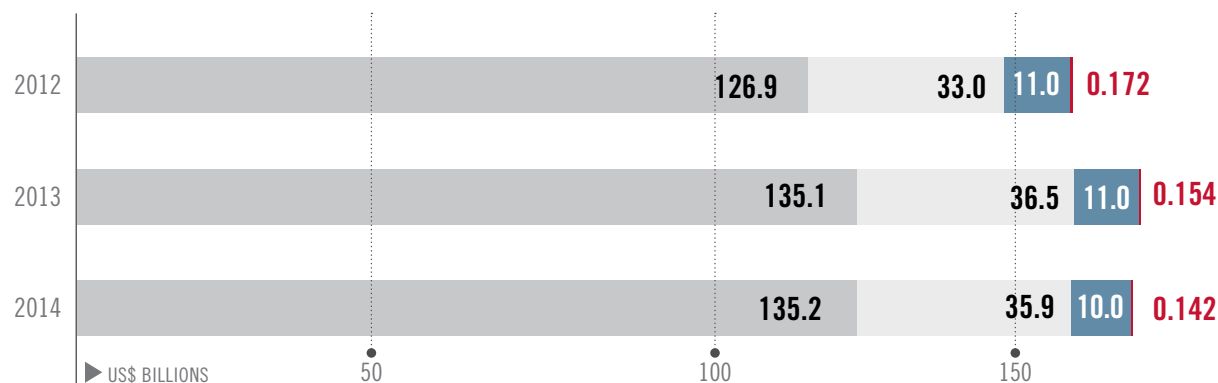
IV Development funding priorities are changing

In 2000, world leaders came together to adopt the United Nations Millennium Declaration to reduce extreme poverty and set targets, the Millennium Development Goals (MDGs)⁹, with a deadline of 2015. Building on the MDGs in 2001, the United Nations Declaration of Commitment on HIV/AIDS called for mobilizing new resources to mount an effective, comprehensive response to the epidemic. In particular, the Declaration called for increased investment in research related to HIV/AIDS and, more specifically, for the development of sustainable and affordable prevention options, such as vaccines and microbicides.

The MDGs expire in 2016 and the creation of the Sustainable Development Goals (SDGs) is in progress. The importance of investment in R&D as crucial to health gains articulated and reflected in the global goals can lead to increased political support and thus, investment, in global health R&D as has happened in past years. This is evidenced by a fourfold increase in the past 25 years in funding for health R&D resulting in improvements in health worldwide.¹⁰ The MDGs and Declaration have influenced large increases in investment in HIV/AIDS. This in turn led to greater overall HIV prevention R&D investment, an increase of threefold between 2001 and 2014.

After hitting an all-time high in 2013¹¹ overall development support in 2014 flatlined,¹² and development assistance for health (DAH) also remained level.¹³ However, development agency support for HIV prevention research declined by six percent (*Figure 14*). With the new SDGs set to be decided by mid-2015 and global financing for development also in a period of transition, it remains to be seen whether HIV prevention R&D, and global health R&D as a whole, will receive a prominent place in the new international development agenda.

Figure 14 HIV Prevention R&D in the Context of Development Assistance for Health and Total Official Development Assistance, 2012–2014 (US\$ billions)



- Development funding for HIV prevention R&D
- DAH focused on HIV/AIDS
- Development Assistance for Health (DAH)
- Official Development Assistance (ODA)

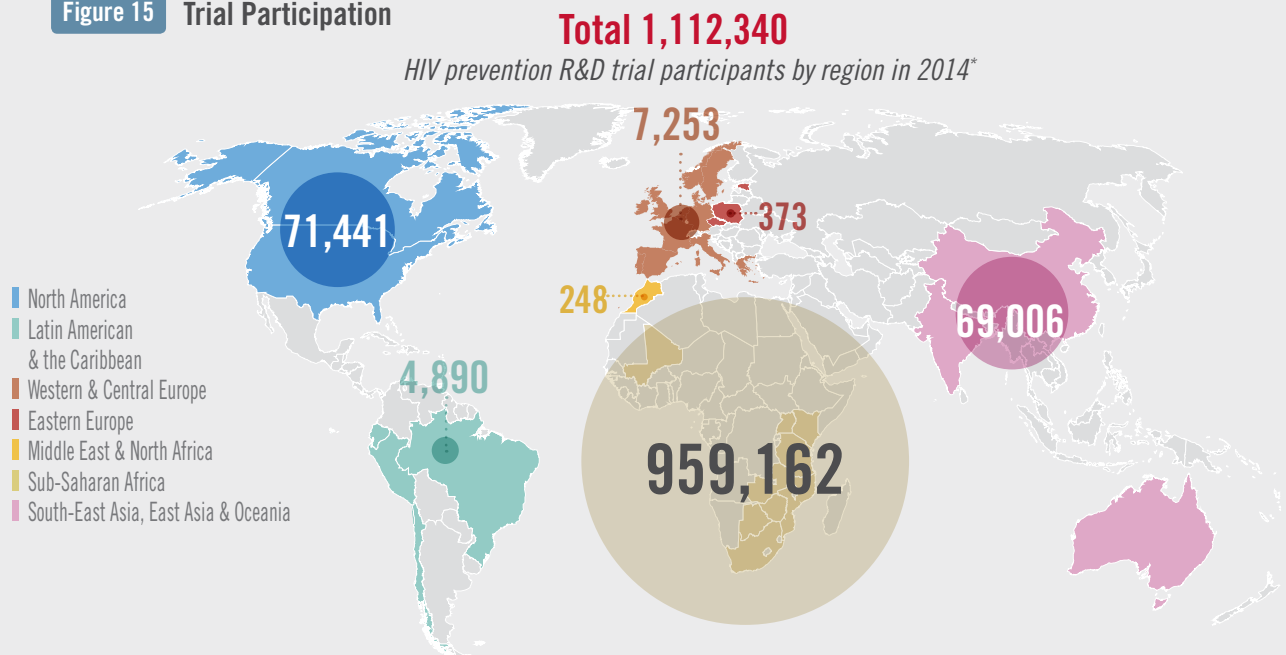
⁹ The MDGs consist of eight global goals, with goal six to combat HIV/AIDS, malaria and other diseases. www.un.org/millenniumgoals/aids.shtml.
¹⁰ Jamison, Dean T. 2013. *Global Health 2035: A world converging within a generation*. *The Lancet*. 382(9908). 1898-1955.
¹¹ Organisation for Economic Co-operation and Development (OECD). www.oecd.org.
¹² "Aid Statistics." *Development Aid Stable in 2014 but Flows to Poorest Countries Still Falling*.
¹³ *Financing of Health Care*. www.healthdata.org/sites/default/files/files/policy_report/2015/FGH2014/HME_PolicyReport_FGH_2014_0.pdf.

Trial participation

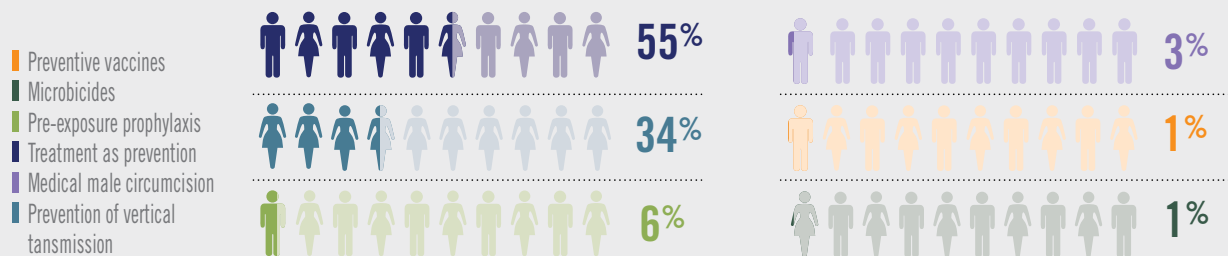
HIV prevention research cannot be accomplished without those who volunteer to participate in clinical trials, or without the engagement of communities in which those trials take place. In 2014, there were 1,112,340 participants in HIV prevention research trials, primarily based in sites with high HIV burdens in South Africa, Uganda and the US (Figure 15).

Trial participants gain access to HIV programs through trials in which they participate. Additionally, assuming the trial results are successful, these are the populations most likely to be the first to receive any new safe and effective HIV prevention method ensuing from such research. Importantly, they are also the populations that have taken on the risks inherent in biomedical research and have contributed their time, effort and commitment. Without their generous contributions to the field, research would not progress. There is no way to quantify the contribution of such participants in economic terms—it is both immeasurable and essential.

Figure 15 Trial Participation



Trial participants by prevention research area in 2014



*Countries by region follow UNAIDS regions and countries available at www.unaids.org/en/regionscountries/countries/.

Data Collection and Analysis Methodology

In order to generate investment estimates that can be compared from year to year from one option or strategy to another, across funding sources and longer term trend analyses, the Working Group developed a systematic approach to data collection and collation during the first iteration of this collaborative project in 2004. The same methods were employed to generate the estimates of funding for R&D presented here.

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 advocacy efforts to estimate annual investment in HIV prevention R&D. Investment trends were assessed and compared by year, prevention type, research phase, funder category and geographic location.

Comprehensive and consistent use of the 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 resource tracking. The primary limitation is that data collection largely depends on the response rate of public, private and philanthropic funders, and year-to-year variability is to a degree a reflection of this response rate. Funds are 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.¹⁴

Investment figures are rounded throughout the report. 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 figures in the report are reported in current US dollars and have not been adjusted for inflation.¹⁵

From a total of 150 surveyed organizations, institutions and companies, the Working Group received grant information from 110 responders. Information on a total of 1,342 grants were collected, of which 633 were allocated to HIV prevention research, with an average grant size of US\$2.2 million.

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 investment. Investment data also support the fact base for advocacy around spending levels, resource allocations, and messages about the value of sustained investment in the research required to build on the success of recent trials, bring novel HIV prevention candidates into the pipeline and support follow-on clinical trials to assure the safety, immunogenicity, efficacy and acceptability of new HIV prevention products.

¹⁴ 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.

¹⁵ Funding information in other currencies was converted into US dollars using the appropriate International Monetary Fund (IMF) annual average exchange rate for July 1, 2014, except for those funds where the Working Group had access to the actual rate received.

Table 1 | Global Investment in HIV Prevention R&D: 2014 funding map

| Funding type | 2013 | 2014 | % Change 2013-2014 | Funder | Total 2014 | Total 2013 | % Change |
|------------------------|-----------------------|---------------------|--------------------|-------------------------------------|---------------------|---------------------|-------------|
| US public sector | \$887 million | \$868 million | -2% | NIH | \$728.1 | \$750.0 | -2.9% |
| | | | | USAID/PEPFAR | \$84.5 | \$85.0 | -0.6% |
| | | | | CDC | \$24.3 | \$13.5 | 80.0% |
| | | | | MHRP | \$27.5 | \$38.4 | -28.4% |
| European public sector | \$77 million | \$69 million | -10% | Belgium | \$0.7 | \$1.1 | -36.4% |
| | | | | Denmark | \$1.7 | \$4.4 | -61.4% |
| | | | | EC | \$20.3 | \$25.1 | -18.7% |
| | | | | France | \$8.5 | \$15.1 | -43.0% |
| | | | | Germany | — | \$0.3 | — |
| | | | | Ireland | \$2.8 | \$2.6 | 3.8% |
| | | | | Italy | \$0.2 | \$0.1 | 100.0% |
| | | | | Netherlands | \$8.1 | \$8.9 | -8.7% |
| | | | | Norway | \$2.0 | \$2.5 | -20.0% |
| | | | | Spain | \$1.6 | \$0.2 | 675.0% |
| | | | | Sweden | \$3.4 | \$0.1 | 3300.0% |
| | | | | Switzerland | \$1.7 | \$0.7 | 150.0% |
| Other governments | \$65 million | \$52 million | -20% | Australia | \$4.6 | \$8.6 | -46.2% |
| | | | | Brazil | \$0.3 | \$0.4 | -37.5% |
| | | | | Canada | \$29.3 | \$37.1 | -21.3% |
| | | | | China | \$7.0 | \$7.0 | 0.0% |
| | | | | Cuba | — | \$0.2 | — |
| | | | | India | \$3.8 | \$1.9 | 100.0% |
| | | | | Japan | \$2.7 | \$3.0 | -10.0% |
| | | | | Russia | — | \$0.1 | — |
| | | | | South Africa | \$2.9 | \$4.0 | -25.0% |
| | | | | Taiwan | — | \$0.1 | — |
| | | | | Thailand | \$1.6 | \$2.8 | -42.9% |
| Philanthropic | \$193 million | \$200 million | 4% | BMGF | \$165.7 | \$160.0 | 4.1% |
| | | | | Wellcome Trust | \$10.4 | \$16.0 | -34.4% |
| | | | | Other | \$24.1 | \$17.0 | 42.4% |
| Industry | \$37 million | \$62 million | 68% | Commercial Sector | \$62.9 | \$37.0 | 70.0% |
| Total | \$1.26 billion | 1.25 billion | -1% | HIV prevention option totals | 1.25 billion | 1.26 billion | 1.0% |
| | | | | % Change 2013–2014 | | -1% | |

^a Where 100 increase in investment is noted, 2013 investment may not have been reported by the funder, and thus this is not necessarily indicative of a 100 percent increase in funding from 2013. Similarly, where a 100 percent decrease in funding is noted, the funder may not have reported investment for 2014. All figures are rounded. See Appendix for a detailed methodology section, including the limitations of data collection.

2014 Totals in US\$ millions (2013 investment, percentage change^a)

| Preventive AIDS vaccines | | | Microbicides | | | Pre-exposure prophylaxis | | | Treatment as prevention | | | Male circumcision | | | Female condoms | | | Prevention of vertical transmission | | |
|--------------------------|------------|-------------|--------------|------------|--------------|--------------------------|-----------|--------------|-------------------------|------------|---------------|-------------------|-----------|---------------|----------------|------------|--------------|-------------------------------------|-----------|--------------|
| 2014 | 2013 | Change | 2014 | 2013 | Change | 2014 | 2013 | Change | 2014 | 2013 | Change | 2014 | 2013 | Change | 2014 | 2013 | Change | 2014 | 2013 | Change |
| \$532.7 | \$518.2 | 2.8% | \$107.8 | \$111.2 | -3.1% | \$14.3 | \$14.2 | 0.7% | \$28.9 | \$64.8 | -55.4% | \$3.5 | \$1.2 | 191.7% | — | \$0.2 | — | \$40.9 | \$40.0 | 2.3% |
| \$28.7 | \$27.3 | 5.1% | \$45.0 | \$42.8 | 5.1% | — | \$1.0 | — | \$6.6 | \$11.3 | -41.3% | \$0.2 | \$0.5 | -60.0% | — | — | — | \$4.0 | \$2.0 | 100.0% |
| — | — | — | \$1.2 | \$1.5 | -20.0% | \$3.6 | \$6.4 | -43.8% | \$19.5 | \$3.1 | 529.0% | — | \$2.5 | — | — | — | — | — | — | — |
| \$27.5 | \$38.4 | -28.4% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$0.7 | \$1.0 | -30.0% | — | — | — | — | — | — | — | \$0.1 | — | — | — | — | — | — | — | — | — | — |
| \$0.9 | \$2.2 | -59.1% | \$0.8 | \$2.2 | -63.6% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$12.0 | \$16.2 | -25.9% | \$7.4 | \$8.9 | -16.9% | — | — | — | — | — | — | — | — | — | — | — | — | \$1.0 | — | — |
| \$2.7 | \$10.3 | -73.8% | \$0.3 | \$0.3 | 20.0% | \$1.6 | \$1.6 | 6.2% | \$2.7 | \$2.2 | 22.7% | \$1.2 | \$0.7 | 71.4% | — | — | — | — | \$0.01 | — |
| — | — | — | — | — | — | — | — | — | — | \$0.3 | — | — | — | — | — | — | — | — | — | — |
| \$1.4 | \$1.3 | 7.7% | \$1.3 | \$1.3 | 0.0% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$0.2 | — | — | — | \$0.1 | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$5.1 | \$4.9 | 4.1% | \$3.0 | \$3.6 | -16.7% | — | — | — | — | — | — | — | — | — | \$0.03 | \$0.4 | -92.5% | — | — | — |
| \$1.0 | \$1.0 | 0.0% | \$1.0 | \$1.5 | -33.3% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$1.5 | \$0.2 | 650.0% | — | — | — | — | — | — | \$0.1 | — | — | — | — | — | — | — | — | — | — | — |
| \$0.1 | \$0.0 | 400.0% | \$3.3 | \$0.02 | 16400.0% | — | — | — | — | — | — | — | \$0.1 | — | — | — | — | — | — | — |
| \$1.4 | \$0.6 | 133.3% | — | — | — | \$0.2 | — | — | — | \$0.1 | — | — | — | — | — | — | — | \$0.2 | — | — |
| \$8.6 | \$6.1 | 41.0% | \$6.2 | \$9.1 | -31.9% | \$0.4 | — | — | \$2.6 | \$0.5 | 420.0% | — | — | — | — | — | — | \$0.1 | \$0.1 | 0.0% |
| \$2.8 | \$7.2 | -61.1% | \$0.4 | \$0.7 | -42.9% | \$0.8 | \$0.3 | 166.7% | \$0.6 | \$0.4 | 50.0% | \$0.03 | \$0.03 | 0.0% | — | — | — | — | — | — |
| — | \$0.4 | — | — | — | — | \$0.3 | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$8.8 | \$16.3 | -46.0% | \$1.3 | \$0.2 | 550.0% | — | \$0.1 | — | \$18.9 | \$20.3 | -6.9% | \$0.2 | \$0.03 | 566.7% | — | — | — | — | \$0.2 | — |
| \$7.0 | \$7.0 | 0.0% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$- | \$0.2 | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$1.4 | \$1.5 | -6.7% | \$2.4 | \$0.3 | 757.1% | — | — | — | — | — | — | — | — | — | — | — | — | — | \$0.1 | — |
| \$2.7 | \$3.0 | -10.0% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$- | \$0.1 | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$2.6 | \$1.7 | 52.9% | \$0.4 | \$2.3 | -82.6% | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$- | \$0.1 | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| \$0.3 | \$0.4 | -25.0% | — | \$1.6 | — | — | — | — | \$1.3 | \$0.8 | 62.5% | — | — | — | — | — | — | — | — | — |
| \$114.0 | \$100.4 | 13.5% | \$7.6 | \$19.2 | -60.4% | \$23.4 | \$10.9 | 114.7% | \$2.5 | \$0.8 | 212.5% | \$18.1 | \$27.2 | -33.5% | — | — | — | \$0.9 | \$1.4 | -35.7% |
| \$6.3 | \$7.7 | -18.2% | \$0.002 | \$0.3 | -99.3% | — | — | — | \$0.6 | \$7.7 | -92.2% | \$2.7 | — | — | — | — | — | \$0.9 | \$0.2 | 350.0% |
| \$15.4 | \$12.4 | 24.2% | \$0.3 | \$0.4 | -25.0% | \$0.5 | — | — | \$7.9 | \$4.6 | 71.7% | \$0.1 | \$0.1 | 25.0% | — | — | — | — | \$0.1 | — |
| \$54.6 | \$31.0 | 76.1% | \$3.0 | \$3.0 | 0.0% | \$1.2 | \$1.7 | -29.4% | — | — | — | — | — | — | \$3.6 | \$1.6 | 125.0% | \$0.5 | — | — |
| 841 | 818 | 2.8% | 193 | 210 | -8.1% | 48 | 36 | 33.3% | 92 | 117 | -21.4% | 26 | 32 | -18.8% | 3.6 | 2.2 | 68.8% | 49 | 44 | 11.4% |
| 3% | | | -8% | | | 33% | | | -21% | | | -19% | | | 69% | | | 11% | | |

Global health and HIV

With the rapid emergence of Ebola in West Africa in 2014 and a few cases in the US and Europe, global health was placed firmly in the center of the public consciousness. Interest in global health spiked, in response to the increasing understanding that viruses and bacteria cross borders and oceans quicker than ever with increasing globalization and faster travel, affecting everyone regardless of geographic location and socioeconomic status.

In the wake of Ebola, the US galvanized support for the response to the epidemic on the ground in West Africa and for research into Ebola vaccine development across both the public and private sectors. The US National Institute of Allergy and Infectious Diseases (NIAID), along with GlaxoSmithKline, are advancing a vaccine developed by NewLink Genetics and Merck, with the Public Health Agency of Canada. A variety of other pharmaceutical, biotechnology companies and government agencies are also involved in the development of a vaccine—the Chinese Ministry of Health, Inovio, Johnson and Johnson with Bavarian Nordic, Novovax, Profectus Biosciences, Protein Sciences, the Russian Federal Ministry of Health and Vaxart—many of whom are also involved in AIDS vaccine R&D. The scientific overlaps are many, and in four out of five of the Ebola vaccines moving through the clinical pipeline, the vectors were originally developed and tested for HIV.¹⁶

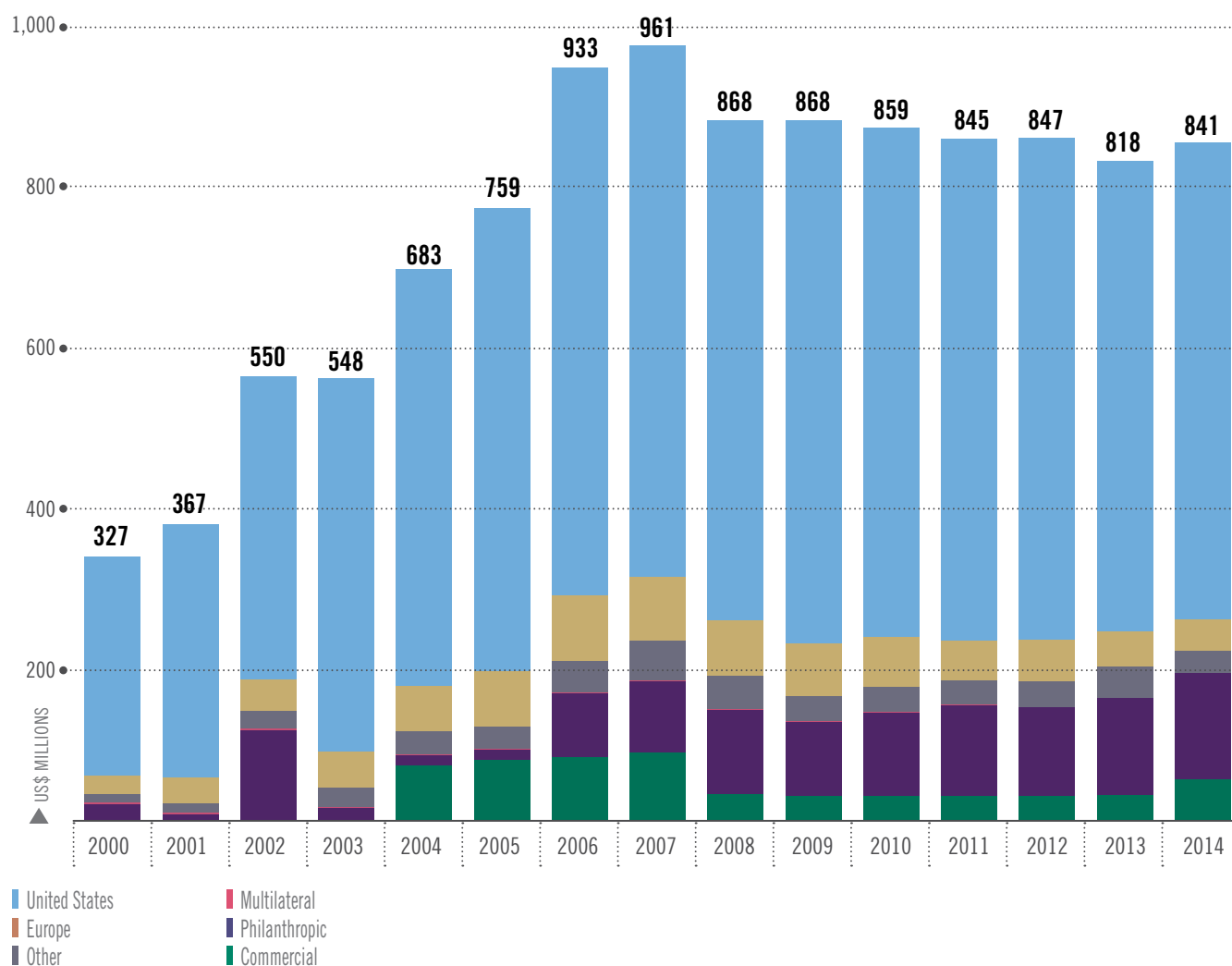
Additionally, investments made in the research capacity of many countries across Africa for HIV research enabled these same sites to be utilized quickly for Ebola research. Capacity building for HIV prevention trials has an impact beyond the HIV field, and allows for research to meet the current and evolving needs of populations and geographies.

¹⁶ Berkley, Seth. 2015. *Share the Risks of Ebola Vaccine Development*. *Nature*. 519–7543: 263.

2.0 Global investments in preventive AIDS vaccine research and development

In 2014, global investments in preventive AIDS vaccine R&D increased by US\$23 million, or 2.8 percent, from US\$818 million in 2013 to US\$841 million in 2014 (Figure 16). Funding in 2014 rebounded, despite the fact that 2013 saw the greatest year-to-year decrease in AIDS vaccine investment since 2008, following five years where funding had either declined or flatlined from a height of \$961 million in 2007.

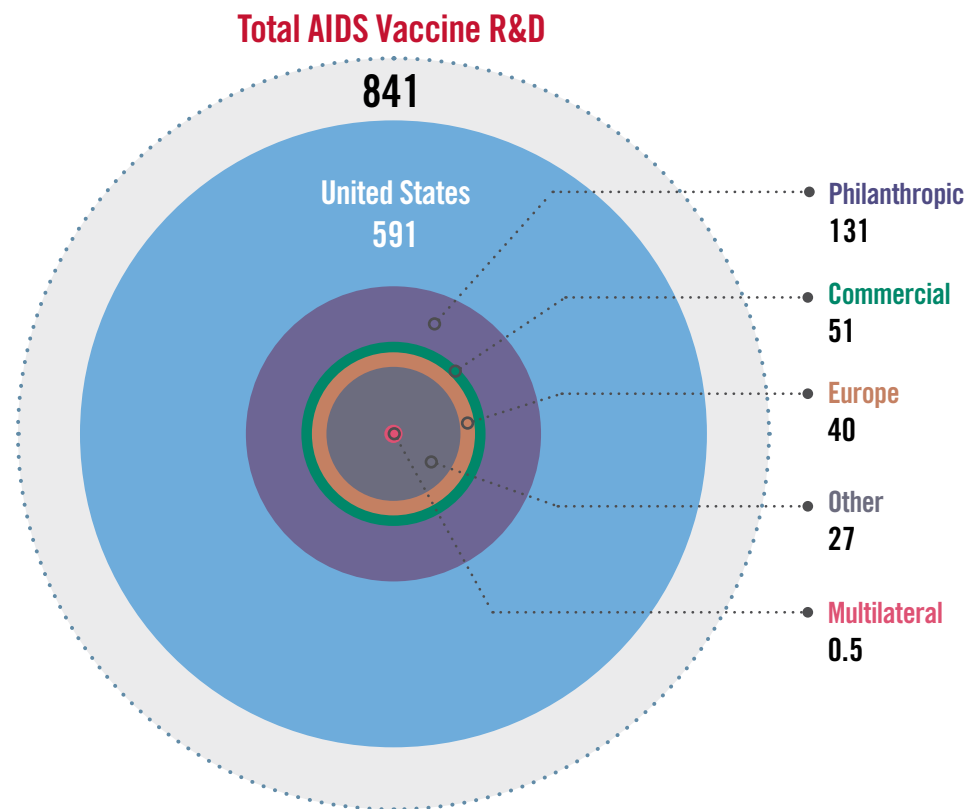
Figure 16 AIDS Vaccine R&D Funding by Sector, 2000–2014 (US\$ millions)



In 2013, mandated austerity measures taken by the US government caused a significant decline in funding. US sequestration policy mandated across-the-board budget cuts, affecting all aspects of the US fiscal environment in 2013 and not just HIV prevention research funding. While AIDS vaccine investments have yet to rebound to 2012 levels, 2014 saw a modest increase in investment over the previous year. While NIH investment did not return to 2012 levels, it did increase by US\$14.5 million from 2013, and USAID funding increased by nearly US\$1.4 million in 2014, regaining funding lost in 2013 due to sequestration (Figures 17 and 18).

Increases in funding from the US, the philanthropic-sector and commercial sector offset decreases by public-sector funders outside of the US. The philanthropic sector increased investment by US\$10.5 million (13 percent) and commercial sector increased investment by nearly US\$24 million (76 percent). Many public-sector agencies in Europe and other countries decreased their investment in 2014, including: Australia, Belgium, Canada, Denmark, EC, France, India, Japan and Thailand. Others increased their investment, including: Ireland, Italy, South Africa, Spain, Sweden, Switzerland and the UK.

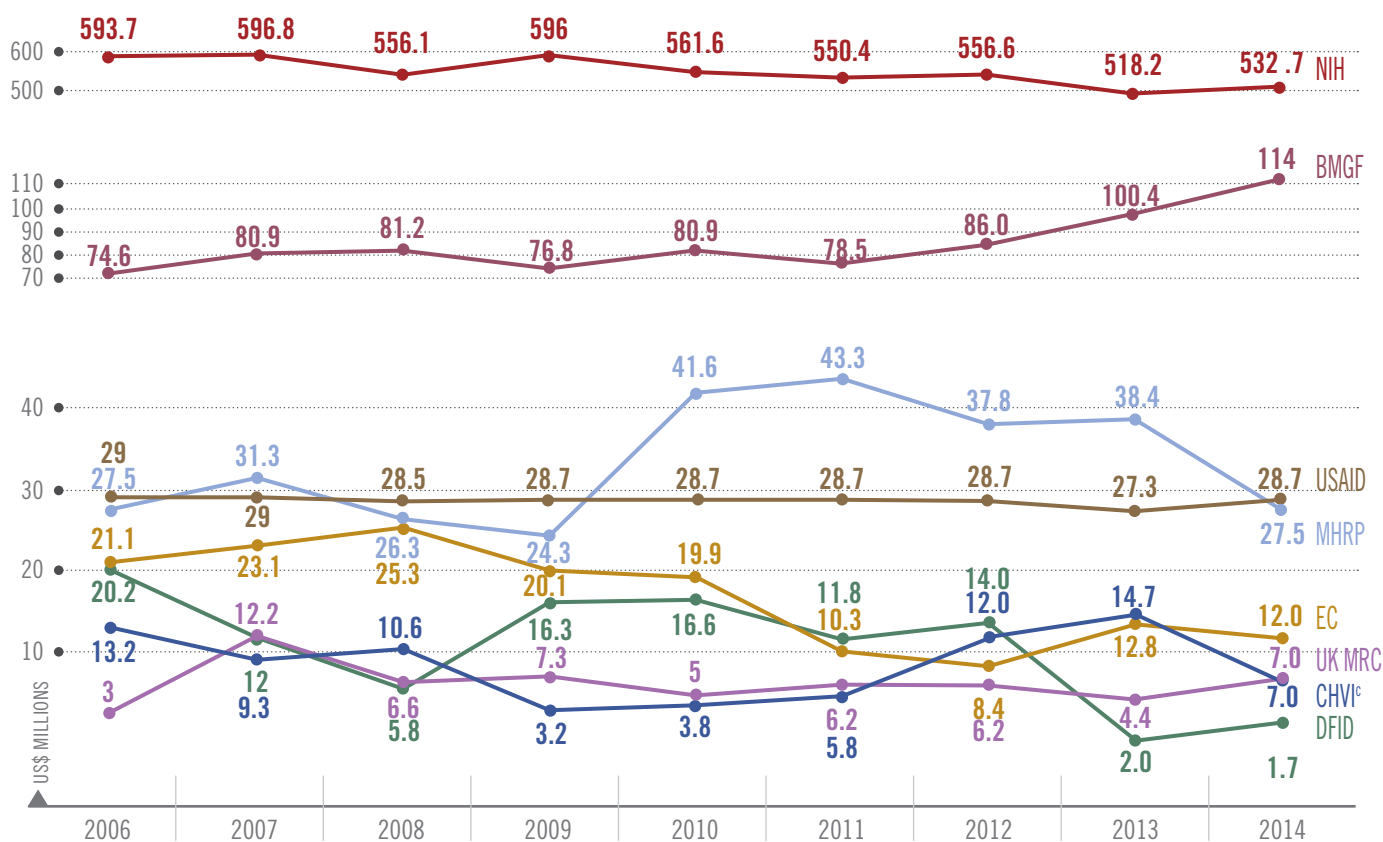
Figure 17 2014 Investment in AIDS Vaccine R&D by Sector (US\$ millions)



Progress towards an AIDS vaccine advanced substantially in 2014, with new data on a variety of strategies. Just a few of the advances include¹⁷:

- In December 2014, the Ad26 vector combined with mosaic modified vaccinia virus Ankara (MVA) boost vaccine started in a Phase I/II trial. Sponsored by Janssen, the trial is a partnership between the US NIH, US Military HIV Research Program (MHRP), International AIDS Vaccine Initiative (IAVI) and the Beth Israel Deaconess Medical Center in the US. In 2015 the trial will open in Rwanda, South Africa, Thailand and Uganda.
- The Pox-Protein Public-Private Partnership (P5) is funding a follow-up to the RV144 trial in Thailand, in which a similar pox-protein vaccine regimen was shown to reduce the risk of HIV infection by 31.2 percent. RV-144 follow-on trials are underway in Thailand. Additional P5 trials of attenuated vaccine candidates are underway and planned, starting in 2015 in Southern Africa. Organizational and financial support for the P5 comes from NIAID, the Bill & Melinda Gates Foundation, the US MHRP, Sanofi Pasteur, Novartis Vaccines and Diagnostics and the South African Medical Research Council in humans.
- Preclinical data on broadly neutralizing antibodies showed effectiveness in preventing infection in monkeys, and also showed evidence of therapeutic benefits. New target sites for neutralization and the isolation of even more powerful neutralizing antibodies were identified in 2014. The NIH supported clinical studies of passive immunization studies of broadly neutralizing antibodies, and a vectored immunoprophylaxis trial led by IAVI began in 2014.

Figure 18 AIDS Vaccine R&D Funder Trends, 2006–2014 (US\$ millions)



¹⁷ The advances discussed in this report are not meant to be comprehensive of all advances over 2014, but rather a summary with which to contextualize the funding data. For more information on these and other advances, see AVAC's 2015 HIV Vaccine Awareness Day Toolkit at www.avac.org/hiv-vaccine-awareness-day.

Table 2 | Annual Investments in AIDS Vaccine R&D, 2000–2014 (US\$ millions)

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| US | 272 | 314 | 376 | 463 | 516 | 574 | 654 | 659 | 620 | 649 | 632 | 615 | 623 | 584 | 591 |
| Europe | 23 | 32 | 39 | 44 | 57 | 69 | 82 | 79 | 69 | 65 | 61 | 48.5 | 52 | 44 | 40 |
| Other | 10 | 12 | 21 | 24 | 28 | 27 | 38 | 49 | 41 | 31 | 32 | 30 | 31 | 38 | 27 |
| Multilaterals | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 0.5 | 0.5 | 0.5 | 0.5 |
| Total public | 307 | 359 | 436 | 532 | 602 | 672 | 776 | 789 | 731 | 746 | 726 | 702 | 707 | 667 | 659 |
| Total philanthropic | 20 | 7 | 112 | 15 | 12 | 12 | 78 | 88 | 104 | 92 | 103 | 113 | 110 | 120 | 131 |
| Total commercial | – | – | – | – | 68 | 75 | 79 | 84 | 33 | 30 | 30 | 30 | 30 | 31 | 51 |
| Total global investment | 327 | 366 | 548 | 547 | 682 | 759 | 933 | 961 | 868 | 868 | 859 | 845 | 847 | 818 | 841 |

Table 3 | Top AIDS Vaccine Funders, 2010–2014 (US\$ millions)^{a,b}

| Rank | 2010 | | 2011 | | 2012 | | 2013 | | 2014 | |
|------|------------------|--------|------------------|--------|--------------------|--------|--------------------|--------|----------------------|--------|
| | Funder | Amount | Funder | Amount | Funder | Amount | Funder | Amount | Funder | Amount |
| 1 | NIH | 561.6 | NIH | 550.4 | NIH | 557 | NIH | 518.2 | NIH | 532.7 |
| 2 | BMGF | 80.9 | BMGF | 78.5 | BMGF | 86.0 | BMGF | 100.4 | BMGF | 114.0 |
| 3 | MHRP | 41.6 | MHRP | 43.3 | MHRP | 37.8 | MHRP | 38.4 | USAID | 28.7 |
| 4 | USAID | 28.7 | USAID | 28.7 | USAID | 28.7 | USAID | 27.3 | MHRP | 27.5 |
| 5 | EC | 19.9 | DFID | 11.8 | DFID | 14.0 | CHVI ^c | 14.7 | EC | 12.0 |
| 6 | China | 18.3 | EC | 10.3 | CHVI ¹⁹ | 12.0 | EC | 12.8 | Ragon Foundation | 10.0 |
| 7 | DFID | 16.6 | Ragon Foundation | 10.0 | Ragon Foundation | 10.0 | Ragon Foundation | 10.0 | CHVI ^c | 7.0 |
| 8 | Ragon Foundation | 10.0 | ANRS | 7.3 | EC | 8.4 | Wellcome Trust | 7.7 | China ^d | 7.0 |
| 9 | ANRS | 6.6 | China | 6.9 | Wellcome Trust | 8.2 | China ^d | 7.0 | UK MRC | 7.0 |
| 10 | Wellcome Trust | 5.1 | Wellcome Trust | 6.5 | China ^d | 7.0 | NHMRC | 6.8 | Wellcome Trust | 6.2 |
| 11 | UK MRC | 5.0 | UK MRC | 6.2 | UK MRC | 6.2 | ANRS | 5.3 | Netherlands | 5.1 |
| 12 | EDCTP | 4.5 | CHVI | 5.8 | Institute Pasteur | 4.8 | Netherlands | 4.9 | Institute Pasteur | 3.9 |
| 13 | CIDA | 3.8 | CIDA | 4.9 | Netherlands | 4.8 | Institute Pasteur | 4.8 | Sumagen Canada Inc. | 2.8 |
| 14 | AECID | 3.6 | NMHR | 3.9 | NHMRC | 4.4 | UK MRC | 4.4 | ANRS | 2.7 |
| 15 | NORAD | 2.5 | Netherlands | 3.8 | ANRS | 4.0 | EDCTP | 3.4 | South Africa DST/DOH | 2.5 |

^a See Appendix for list of acronyms.

^b 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.

^c 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.

^d The Working Group could not obtain a response from China for investments made in 2012 and 2013. 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*, with regards to a Phase II preventive AIDS vaccine trial started in August 2012, and other basic research that is underway.

Table 4 | **Philanthropic Investment in AIDS Vaccine R&D by Foundations and Commercial Philanthropy in 2014**

| Amount | Investors |
|---------------------------------|---|
| US\$114 million | Bill & Melinda Gates Foundation |
| US\$1 million to US\$10 million | Wellcome Trust, Ragon Foundation |
| US\$250,000 to US\$1 million | Immunity Project |
| <US\$250,000 | CANFAR, Broadway Cares, Korean Women Against AIDS |

Table 5 | **Estimated Commercial Sector Engagement in AIDS Vaccine R&D by Company in 2014**

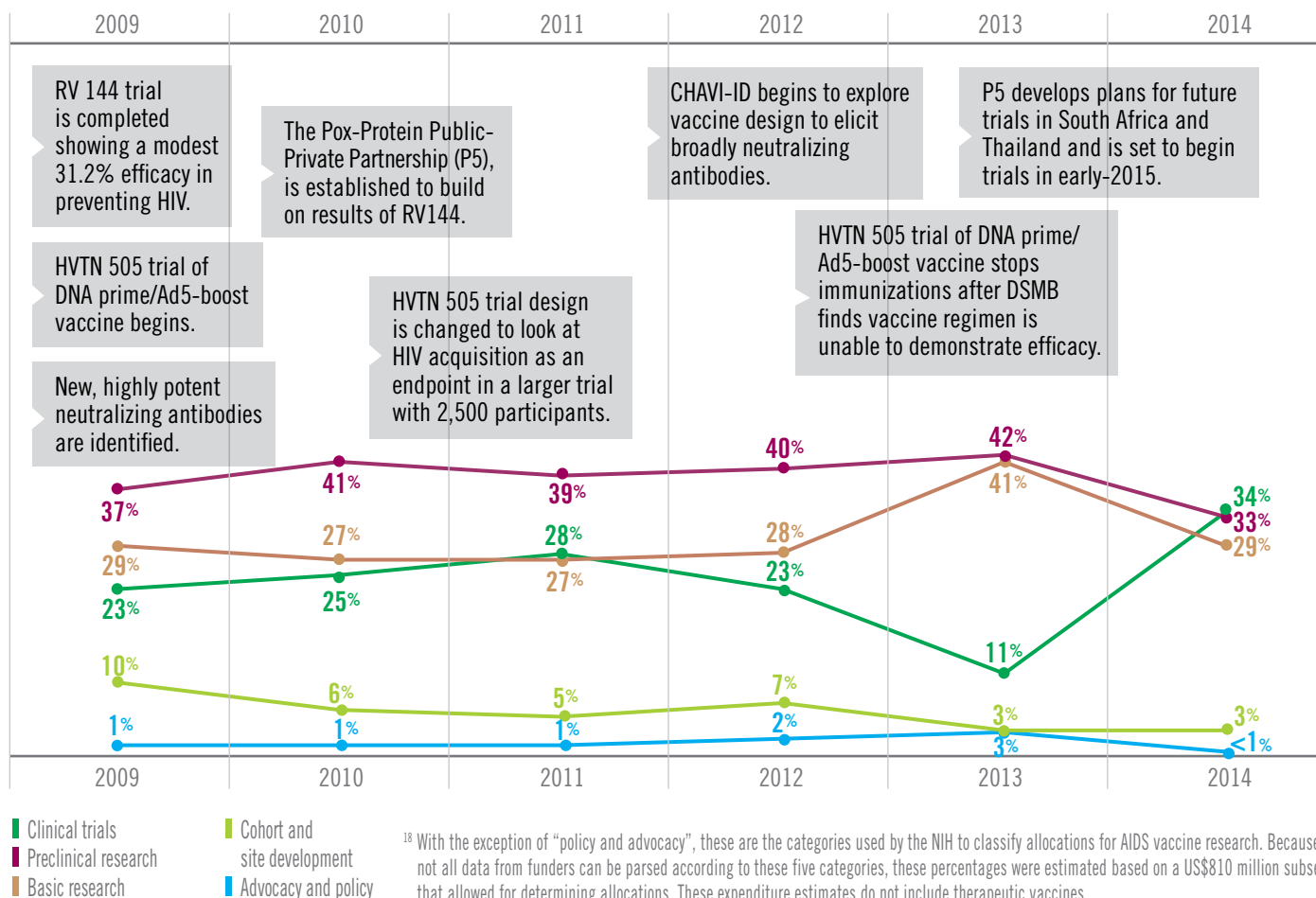
| Amount | Investors ^a |
|---------------------------------|--|
| US\$5 million to US\$10 million | Crucell, Novartis International AG, Sanofi Pasteur, Sumagen Canada Inc. |
| US\$1 million to US\$5 million | ESTEVE, GSK, Merck, Mymetics |
| US\$100,000 to US\$1 million | Advanced Biosciences, Argos Therapeutics, Bionor Immuno, FIT-Biotech, Genvec, GeoVax, Ichor, Inovio Pharmaceuticals, Vical |

^a 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.

2.1 Funding allocations for preventive AIDS vaccine research and development

In 2014, spending by the public and philanthropic sectors on preventive AIDS vaccine R&D was allocated to five categories: basic research (29 percent), preclinical research (33 percent), clinical trials (34 percent), cohort and site development (3 percent); and advocacy and policy (<1 percent). In 2014, the distribution of investment among the five categories shifted for the first time in five years (*Figure 19*). With several clinical trials getting ready to begin in late 2014 and early 2015, funding for clinical trials increased, which led in part to increased overall funding. Further information about the categories used to define R&D can be found in Table 13 of the Methodology section of the Appendix.¹⁸

Figure 19 **AIDS Vaccine R&D Funding Allocations by Percentage, 2009–2014**

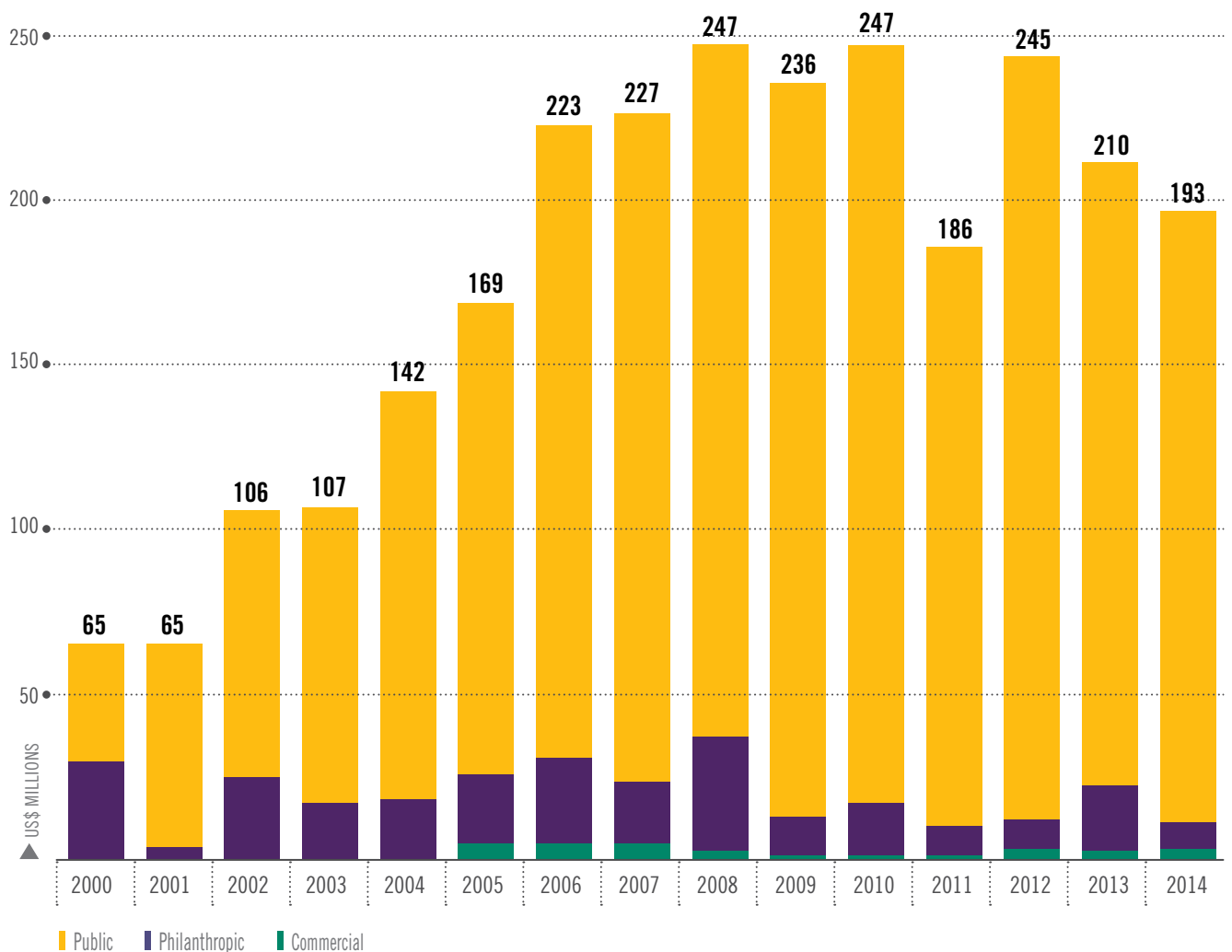


Microbicides

3.0 Global investments in microbicide research and development

Global investment in microbicide R&D declined overall in 2014 by US\$17 million, down to US\$193 million. Of the 2014 total, the public sector provided US\$182 million (94 percent), the philanthropic sector US\$8 million (4 percent) and industry US\$3 million (two percent) (*Figures 20 and 21*). The NIH was the predominant US public-sector contributor at US\$108 million (59 percent of all public-sector funding for microbicides), followed by US\$45 million from USAID). The European public sector followed at US\$23 million (12 percent); other individual country contributions constituted the remainder. Although the NIH reduced support for microbicide research in 2014 by US\$3.4 million, the US public sector remained the largest source of all microbicide investment globally, funding 80 percent of the 2014 total. *Figure 22* displays patterns of investment by individual key funders over the past eight years.

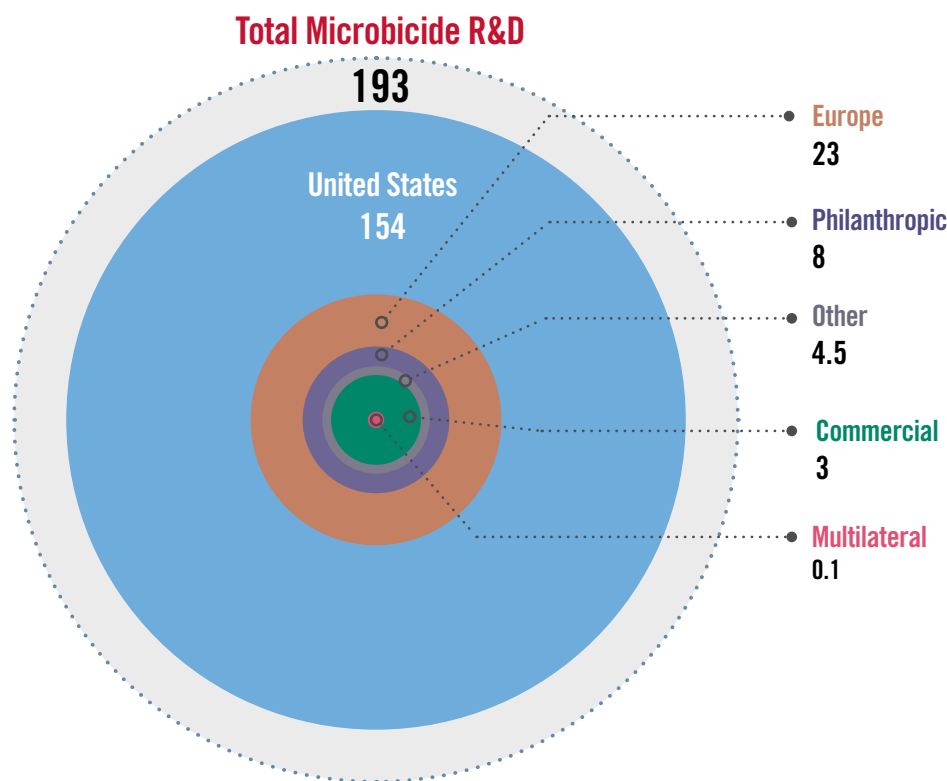
Figure 20 Microbicide R&D Funding by Sector, 2000–2014 (US\$ millions)



Philanthropic funding also declined in 2014, with the largest reductions in funding coming from the BMGF and the Wellcome Trust, whose combined participation fell by US\$12.5 million in 2014. Additionally, some philanthropic funders that had invested in microbicide research in previous years did not do so in 2014. Some European funders also decreased their funding in 2014, including Denmark, Norway and the UK, with a US\$4 million overall reduction from European public-sector donors.

2014 produced disappointing news for microbicide R&D when the FACTS 001 study of pericoital vaginal tenofovir gel failed to show efficacy. The design of this study built on the CAPRISA 004 trial, completed in 2010, which found a 39 percent decrease in HIV transmission in 2,059 Southern African women and a 51 percent reduction in genital herpes infections. Coupled with the fact that the VOICE trial of daily tenofovir gel had been closed in 2011 for lack of efficacy in a similar population, the net result has been that tenofovir gel is no longer in the pipeline for development as a vaginal microbicide.

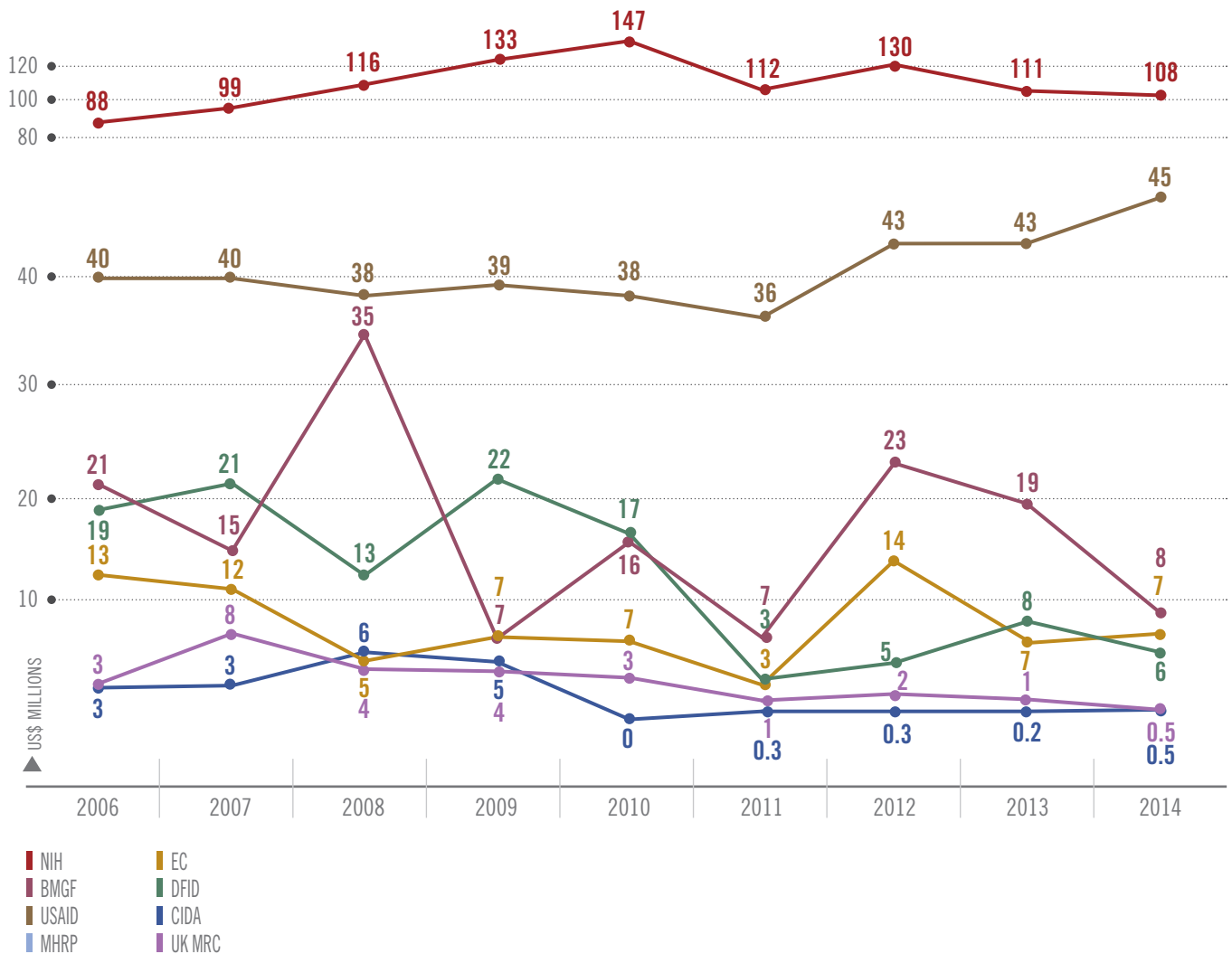
Figure 21 2014 Investment in Microbicide R&D by Sector (US\$ millions)



As a result, hope and investment in microbicides now resides in two parallel trials of a vaginal ring infused with the anti-HIV drug dapivirine and designed for one-month use: the ASPIRE trial being conducted by the Microbicide Trials Network and the RING Study proceeding under the aegis of the International Partnership for Microbicides (IPM). The first results are anticipated in early 2016, and further funding for topical microbicides is likely to hinge in some degree on the results of these trials.

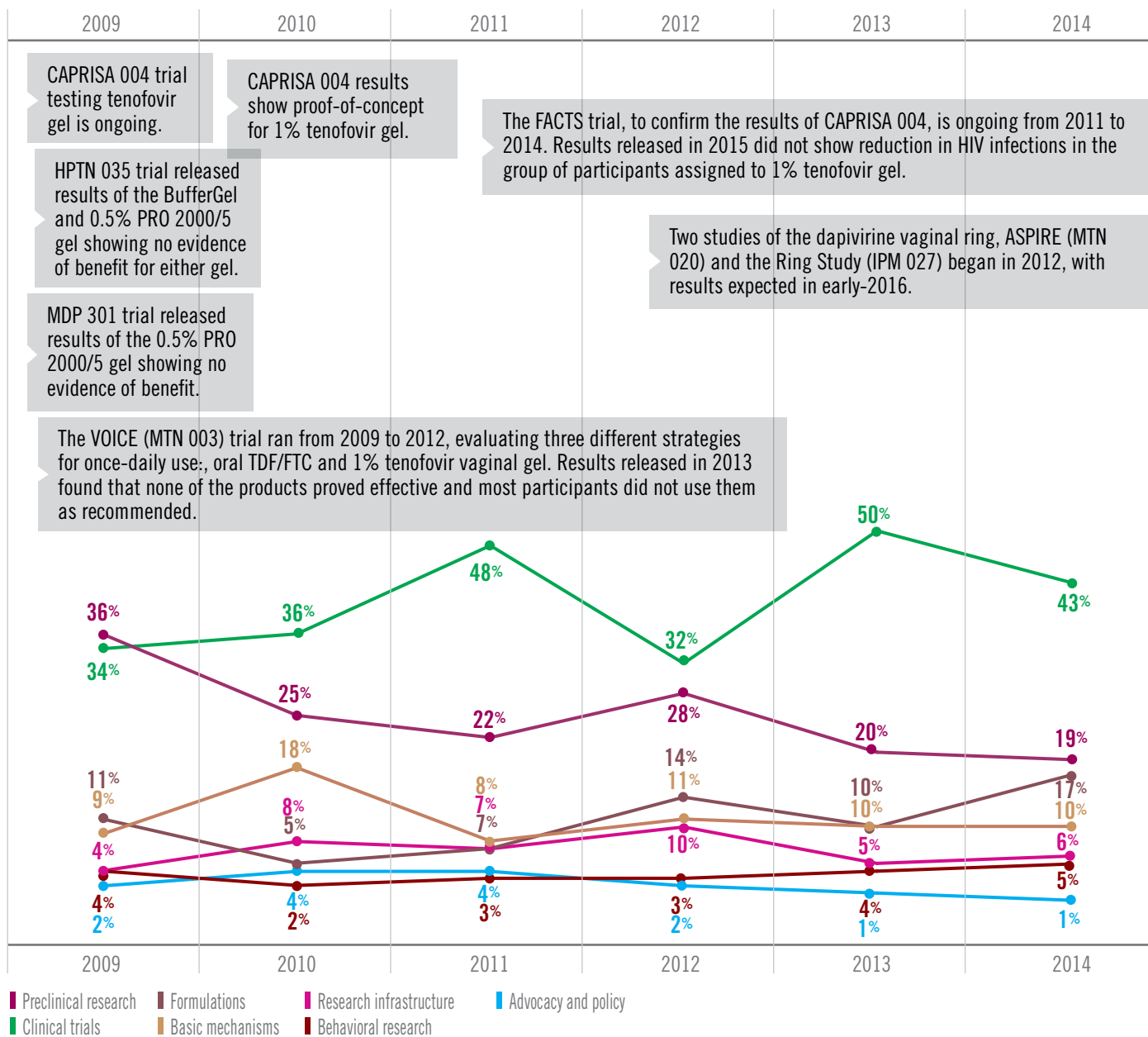
One of the consequences of these trial results, and other relevant results, is the recognition of the pivotal role of adherence to product use, particularly for young women in especially constraining trial environments. This has led to intensified behavioral research efforts around how to facilitate trial participation for such populations, as well as pharmacological approaches to assessing product use in more verifiable ways.

Figure 22 Microbicide R&D Funder Trends, 2006–2014 (US\$ millions)



Another outcome of these trial disappointments is the intensification of research into longer-duration methods of HIV prevention that do not require daily application or ingestion. Examples are the vaginal rings now in clinical trials, others containing different active compounds; and injectable PrEP, now in earlier-phase studies intended to lead to formulations that could be delivered at longer intervals. The earlier stages of the microbicide pipeline also contain efforts to develop improved vaginal rings, formulations for longer-acting topical applications, exploration of the potential of implant approaches and multipurpose prevention technologies (MPTs), discussed in section 3.2.

Figure 23 Microbicide R&D Funding Allocations by Percentage, Data Collection Category and Key Trials, 2009–2014



The microbicide pipeline also comprises ongoing work on rectal microbicides. Results from the MTN-017 trial of tenofovir, the first Phase II trial of a product intended for rectal use, are expected in early 2016 and will inform the way forward for the rectal microbicide R&D agenda. Research in the earlier stages of this pipeline is exploring potential for a dapivirine gel, douche microbicides, and non-ARV compounds such as Griffithsin. Total investment in rectal microbicide research in 2014 was US\$5.7 million; global investment between 2001 and 2014 totaled US\$43.7 million.

Table 6 | **Annual Investments in Microbicide R&D, 2006–2014** (US\$ millions)

| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|--------------------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| US | 129.7 | 139.8 | 154.4 | 172.6 | 181.7 | 148.0 | 173.0 | 155.0 | 154.0 |
| Europe | 56.3 | 59.6 | 39.9 | 44.4 | 40.3 | 16.0 | 27.0 | 27.0 | 23.0 |
| Other | 4.7 | 3.4 | 12.1 | 5.7 | 8.3 | 12.0 | 17.0 | 5.0 | 4.5 |
| Multilaterals | 1.4 | 0.2 | 0.2 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| Total Public | 192.1 | 203.0 | 206.6 | 222.9 | 230.4 | 176.0 | 217.0 | 187.0 | 182.0 |
| Total Philanthropic | 26.2 | 19.0 | 34.6 | 11.8 | 15.9 | 9.0 | 25.0 | 20.0 | 8.0 |
| Total Commercial | 4.5 | 4.5 | 2.5 | 1.0 | 1.0 | 1.0 | 3.0 | 3.0 | 3.0 |
| Total Global Investment | 222.8 | 226.5 | 243.7 | 235.7 | 247.3 | 186.0 | 245.0 | 210.0 | 193.0 |

Table 7 | **Top Microbicide Funders, 2010–2014** (US\$ millions)^a

| Rank | 2010 | | 2011 | | 2012 | | 2013 | | 2014 | |
|------|-------------|--------|-----------------------|--------|----------------|--------|----------------------|--------|----------------------|--------|
| | Funder | Amount | Funder | Amount | Funder | Amount | Funder | Amount | Funder | Amount |
| 1 | NIH | 147.0 | NIH | 111.8 | NIH | 129.9 | NIH | 111.2 | NIH | 107.8 |
| 2 | USAID | 38.0 | USAID | 36.0 | USAID | 43.2 | USAID | 42.8 | USAID | 45.0 |
| 3 | DfID | 16.5 | South African DST/DOH | 10.0 | BMGF | 22.9 | BMGF | 19.2 | BMGF | 7.6 |
| 4 | BMGF | 15.7 | BMGF | 7.0 | EC | 13.6 | DFID | 8.4 | EC | 7.4 |
| 5 | EC | 6.7 | DfID | 3.2 | CHVI | 9.2 | EC | 6.7 | DFID | 5.7 |
| 6 | China | 3.6 | Netherlands | 2.7 | South Africa | 7.0 | Netherlands | 3.6 | Sweden | 3.2 |
| 7 | UK MRC | 3.4 | NORAD | 2.5 | DFID | 4.7 | South Africa DST/DOH | 2.3 | The Netherlands | 3.0 |
| 8 | NORAD | 3.3 | Wellcome Trust | 1.6 | UK MRC | 2.2 | Denmark | 2.2 | ICMR | 2.3 |
| 9 | EDCTP | 2.0 | Irish Aid | 1.4 | Netherlands | 1.7 | EDCTP | 2.2 | Ireland | 1.3 |
| 10 | Spain | 1.9 | UK MRC | 1.3 | Ireland | 1.2 | Norway | 1.5 | CDC | 1.2 |
| 11 | Netherlands | 1.7 | Denmark | 0.9 | Norway | 1.0 | US CDC | 1.5 | NORAD | 1.0 |
| 12 | Denmark | 1.7 | NHMRC | 0.6 | OPEC | 1.0 | Ireland | 1.3 | DANIDA | 0.8 |
| 13 | Germany | 1.3 | OFID | 0.5 | Denmark | 0.9 | UK MRC | 0.8 | CIHR | 0.8 |
| 14 | Irish Aid | 1.1 | Spain | 0.4 | NHMRC | 0.5 | NHMRC | 0.5 | UK MRC | 0.5 |
| 15 | CDC | 0.7 | ARC | 0.4 | Wellcome Trust | 0.5 | Wellcome Trust | 0.3 | South Africa DST/DOH | 0.4 |

^a See Appendix for list of acronyms.

3.1 Funding allocations for microbicide research and development

In 2014, expenditures on microbicide R&D were allocated across the following seven categories: basic mechanisms of mucosal transmission (10 percent); preclinical testing (19 percent); formulations and modes of delivery (17 percent); clinical trials (43 percent); microbicide behavioral and social science research (5 percent); microbicide research infrastructure (6 percent); and policy and advocacy (1 percent) (*Figure 23*). Of particular interest are the persistently small size of allocations for behavioral research, especially given the awareness of the importance of adherence so sharply illuminated in the most recent clinical trials. Further information about the categories used to define R&D can be found in Table 14 of the Methodology section of the Appendix.

Research on HIV and the use of hormonal contraception

Since 1991, there has been debate around whether injectable progestin-based contraceptives, most specifically Depo-Provera/DMPA, increases a woman's risk of acquiring HIV—a question that has persistently troubled both research science and clinical practice. Efforts to answer this question by synthesizing data from observational studies, secondary analyses of trials, and systematic reviews have been burdened by significant study heterogeneity and uncontrolled risk of confounding cause and effect.

This history of uncertainty generated pressure for a randomized, controlled trial designed to resolve this crucial matter definitively. At the same time there have been counter-pressures arising from concerns that a definitive result from such research might narrow options for the millions of women at risk of both HIV infection and unintended pregnancy. The net result has been a revived sense of urgency for research toward new contraceptive agents and formulations, seen as desirable in any event.

Investment in HIV and hormonal contraceptive research is estimated at US\$5.5 million in 2014. Funders investing in research into hormonal contraception and HIV include: the BMGF, NIH, UK Medical Research Council and USAID.

After almost four years of debate, trial design and re-design, the ECHO trial—Evidence for Contraceptive Options & HIV Outcomes—is poised for implementation. A three-year open-label randomized clinical trial of DMPA, the levonorgestrel implant and the copper IUD, in 7,800 sexually active HIV-uninfected women ages 16-35 years, ECHO is scheduled to begin in late-2015 in 12 sites in east and southern Africa.

3.2 Investments in multipurpose prevention technology research and development

In 2014, total investment in multipurpose prevention technologies (MPTs) was US\$21 million. The US public sector funds most MPT research. Combined, the US NIH and USAID account for more than 50 percent of the total investment. CONRAD, IPM, PATH and the Population Council are the primary nonprofit entities working to advance MPTs. Other entities working at earlier points in the pipeline include biotechnology companies and university groups exploring individual MPT components.

The goal of this evolving area of research is development of technologies or strategies that combine protection against at least two of the following sexual and reproductive health indications: unintended pregnancy and sexually transmitted infections (STIs), including HIV. While HIV and contraception have been prioritized for regions of greatest need, MPTs will also need to respond to specific regional needs and epidemiologic profiles.

MPTs furthest advanced in the R&D pipeline include intravaginal rings combining different antiretroviral agents and hormonal contraception, and a combination topical gel designed to prevent HIV, herpes (HSV-2), and human papilloma virus (HPV). Clinical data from the recently completed VOICE and FACTS 001 trials and ongoing IVR trials, as well as continuing debate around hormonal contraception, will be consequential for MPT development and likely to affect funder strategies.

Data collection on multipurpose prevention technologies

In 2014, the Working Group partnered with CAMI Health to collect and analyze data on grants for MPT R&D relevant to prevention of HIV and at least one other sexual and reproductive health risk. Research categories collected by the Working Group under the MPT umbrella include microbicides and female condoms. They also capture data on funding for MPTs beyond the Working Group's standard collection parameters that, while lacking an HIV indication, are critically relevant. These grant data include pertinent investment in pregnancy, bacterial vaginosis, chlamydia, gonorrhea, hepatitis, HPV, HSV-2, syphilis, trichomoniasis, urinary tract infections, and "other STIs".

4.0 Investments in research and development related to pre-exposure prophylaxis

Global public, philanthropic and commercial sector investment in PrEP increased to US\$48 million in 2014, an increase of US\$12 million over 2013 (Figure 24). Investment increased by 33 percent in 2014 due in part to a number of new demonstration and implementation projects that began in 2014 focused on the use of PrEP in different settings and populations. Additionally, there are several ongoing studies testing long-acting PrEP formulations, with associated funding of approximately US\$13 million.

“PrEP works” was the resounding message from the PrEP research community in 2014. Results from several oral tenofovir-based PrEP studies showed the intervention to be effective at preventing HIV in 2010 and 2011, and research in 2014 moved towards demonstrating its use outside of a clinical trial setting.

- Evidence from two clinical studies—the PROUD study in the UK and the IPERGAY study in France and Canada—showed PrEP to be highly protective against HIV for gay men and other men who have sex with men (MSM) at high risk of infection.^{19, 20}
- A secondary analysis of the iPrEX trial provided further support for the efficacy of PrEP use among gay men and other men who have sex with men.²¹
- Additional results also showed that daily PrEP use in serodiscordant couples prevented herpes simplex virus infections.

Table 8 | Annual Investments in PrEP R&D, 2005–2014 (US\$ millions)

| | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|-------------------------|------|------|------|------|------|------|------|------|------|------|
| Public | 8.7 | 13.5 | 19.7 | 20.6 | 26.6 | 33.8 | 32.3 | 19.6 | 24.0 | 23.0 |
| Philanthropic | 2.4 | 2.4 | 12.6 | 22.5 | 24.6 | 23.2 | 28.7 | 10.9 | 11.1 | 24.0 |
| Commercial | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 1.3 | 0.5 | 2.0 | 1.0 |
| Total global investment | 12.4 | 17.2 | 33.6 | 44.4 | 52.5 | 58.3 | 62.3 | 31.0 | 37.1 | 48.0 |

Table 9 | PrEP Expenditures, 2014 (Percentage %)

| Research | Amount |
|---|--------|
| PrEP basic research | 12% |
| PrEP preclinical | 10% |
| PrEP clinical research | 39% |
| PrEP implementation research (post-trial access; demonstration projects; ancillary studies) | 38% |

¹⁹ McCormack, Sheena et al. *Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study*. CROI Presentation, February 2015.

²⁰ Molina, Jean-Michel et al. *On Demand PrEP With Oral TDF-FTC in MSM: Results of the ANRS Ipergay Trial*. CROI Abstract 23LB, February 2015.

²¹ Grant, Robert et al. *Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men*. *The New England Journal of Medicine*. 363.27 (2010): 2587–2599.

Figure 24 Investment in Pre-Exposure Prophylaxis R&D, 2005–2014 (US\$ millions)

DREAMS partnership

PrEP uptake and use by young women (ages 15 to 24) is one of the core indicators of the newly funded PEPFAR DREAMS Partnership. PEPFAR, with the Bill & Melinda Gates Foundation and the Nike Foundation, formed the US\$210 million partnership to reduce new HIV infections in adolescent girls and young women in ten countries in sub-Saharan Africa. The partnership “Determined, Resilient, AIDS-free, Mentored, and Safe (DREAMS)” will work to provide a core package of evidence-based interventions to address HIV risk and transmission and gender-based violence.

The PrEP indicator offers countries the opportunity to establish PEPFAR-supported demonstration projects by country teams aimed at young women, where seroprevalence is substantially higher than the national average. The indicator measures the uptake and utility of PrEP among young women.

5.0 Investment in research and development related to treatment as prevention

Investment in research into the early initiation of AIDS treatment drugs as a prevention strategy reached US\$92 million in 2014 (Figure 25). Four years after the release of trial data from HPTN 052, showing that people living with HIV who started ART at CD4 cell counts between 350 and 500 were significantly less likely to transmit HIV to their sexual partners, compared with people who started according to national guidelines, ongoing research seeks to answer questions about how best to implement treatment as prevention programmatically, and to address implementation in specific populations and settings.

Results released in 2014 showed the benefits of earlier initiation of treatment, modeling studies estimated the cost-effectiveness of earlier treatment initiation and implementation research addressed how to bring to scale treatment for prevention. Advances in 2014 include:

- Data from the Strategic Timing of AntiRetroviral Treatment (START) study released in May 2015 showed that HIV-infected individuals have a lower risk of developing AIDS if they start treatment earlier, when their CD4 count is higher, instead of waiting for CD4 levels to drop to lower levels. Along with data from previous studies showing that treatment reduced the risk of HIV transmission to uninfected sexual partners, the START findings support offering treatment to everyone with HIV and are further evidence supporting the expansion of ART access.²²
- Observational data from the PARTNER study showed no transmission events in serodiscordant couples in which the HIV-positive partner had a viral load of less than 200 copies/mL. The study includes both heterosexual participants and gay men and other men who have sex with men.²³
- A review and meta-analysis of studies of HIV transmission in serodiscordant heterosexual couples showed a very low transmission rate per unprotected sex act when the HIV-positive partner was on treatment for at least six months prior.

Table 10 | Annual Investments in Treatment as Prevention R&D, 2011–2014 (US\$ millions)

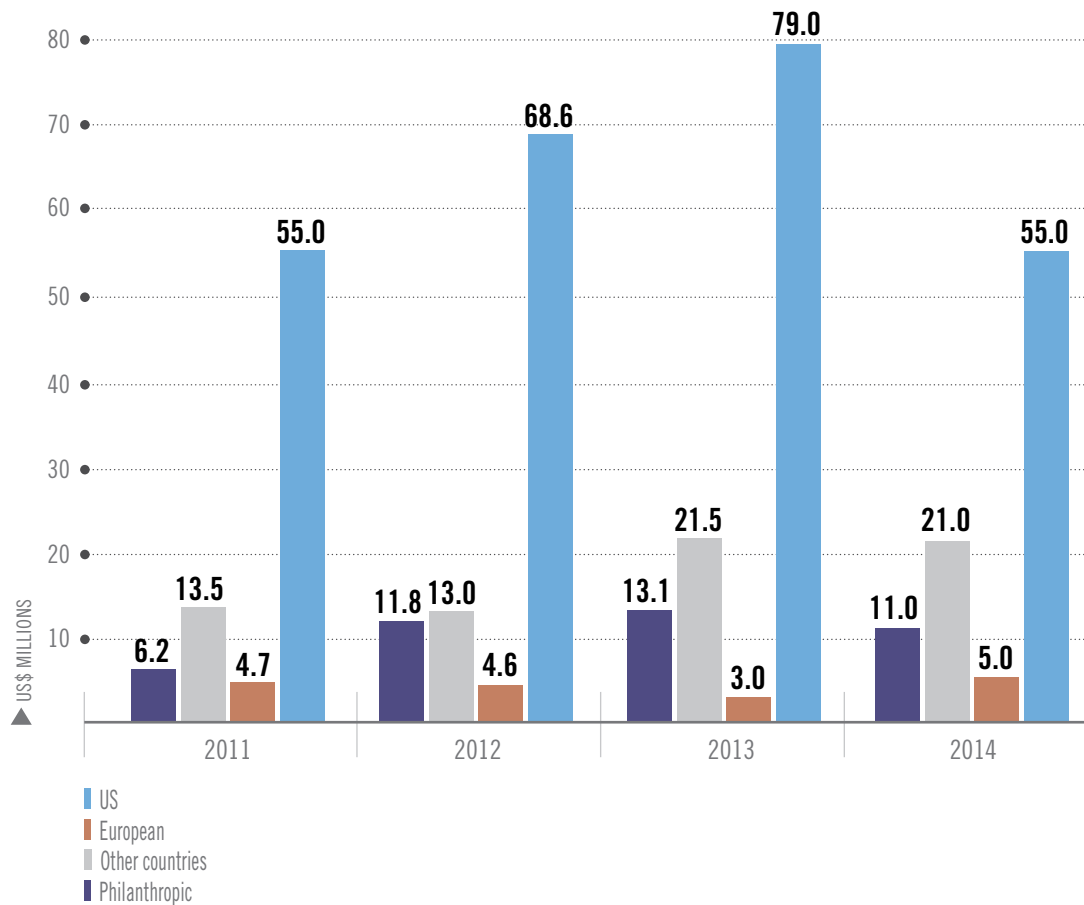
| | 2011 | 2012 | 2013 | 2014 |
|-------------------------|------|------|-------|------|
| US | 55.0 | 68.6 | 79.0 | 55.0 |
| Europe | 4.7 | 4.6 | 3.0 | 5.0 |
| Other | 13.5 | 13.0 | 21.5 | 21.0 |
| Total public | 73.2 | 86.2 | 103.5 | 81.0 |
| Total philanthropic | 6.2 | 11.8 | 13.1 | 11.0 |
| Total global investment | 79.4 | 98.0 | 117.0 | 92.0 |

²² NIAID press announcement and statement. Starting antiretroviral treatment early improves outcomes for HIV-infected individuals, study finds: trial results will likely impact global treatment guidelines, (27 May 2015). www.niaid.nih.gov/news/newsreleases/topics/Pages/aidsReleases.aspx.

²³ Rodger, Alison et al. HIV Transmission Risk Through Condomless Sex If HIV+ Partner On Suppressive ART: PARTNER Study. Conference on Retroviruses and Opportunistic Infections (CROI 2014). Boston, March 3-6. Abstract 153LB.

- The coming years will provide additional insights into the durability of treatment as prevention. In July 2015, the HPTN 052 trial is set to release results and will provide longer-term data on treatment as prevention among heterosexual couples. The START trial is expected to complete in the next few years, providing further evidence of the clinical benefits of early treatment initiation.²⁴

Figure 25 Investment in Treatment as Prevention R&D, 2011–2014 (US\$ millions)



²⁴ Strategic Timing of Antiretroviral Treatment (START). AVAC HIV Prevention Research & Development Database (PxRD). www.avac.org/trial/start.

6.0 Investments in follow-up studies and operations research related to voluntary medical male circumcision

Global public-sector and philanthropic investment in R&D and operations research related to voluntary medical male circumcision (VMMC) totaled US\$26 million in 2014, a decrease of US\$6 million from 2013.²⁵ For the past five years, the BMGF funded the majority of VMMC research, supporting research in 2014 at US\$18 million. The US public sector was the second largest funder, contributing US\$3.7 million in 2014. ANRS and Wellcome Trust also contributed to research efforts in 2014, by US\$1.2 million and US\$2.7 million respectively.

In 2014 several studies completed evaluation of strategies to increase the uptake of VMMC. Studies focused on financial compensation, a sports-based program, food vouchers and other methods.

- An economic incentive trial in Kenya showed that uptake of VMMC was higher among those receiving higher monetary compensation.
- A sports-based randomized trial in Zimbabwe showed increased uptake of VMMC, which was low overall, in the intervention arm.
- Several studies showing the safety and acceptability of new devices for VMMC completed in 2014, including studies using the ShangRing and PrePex devices. Further research is focused on the use of new VMMC devices in adolescents and by different types of providers.
- A comparative assessment of facilities in Kenya, South Africa, Tanzania and Zimbabwe was undertaken showing mixed results in terms of facility preparedness for VMMC delivery. Another study elucidated the challenges of rapid development of sites with all of the necessary equipment, supplies and protocols for effective VMMC delivery.

Table 11 | Funding for Medical Male Circumcision R&D, 2006–2014 (US\$ millions)

| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|-------------------------|------|------|------|------|------|------|------|------|------|
| Public | 6.9 | 4.8 | 6.2 | 7.5 | 5.0 | 6.1 | 7.2 | 5.0 | 5.2 |
| Philanthropic | 4.3 | 2.9 | 4.3 | 2.1 | 16.7 | 14.2 | 34.4 | 27.2 | 20.8 |
| Total global investment | 11.2 | 7.7 | 10.5 | 9.6 | 21.7 | 20.3 | 41.6 | 32.2 | 26.0 |

²⁵ While the Working Group tracks investment in R&D and operations research for adult male circumcision, it does not track investment in rollout and scale-up of the procedure. In the context of this report, “male circumcision” refers specifically to medical male circumcision performed for the purposes of reducing transmission of HIV and other sexually transmitted diseases. “Operations research” aims to develop solutions to current operational problems of specific health programs or specific service delivery components of the health system. “Implementation research” aims to develop strategies for available or new health interventions in order to improve access to and use of these interventions by the populations in need. Definitions from JHF Remme et al. Defining Research to Improve Health Systems. PLoS Med 7:11 (16 November 2010).

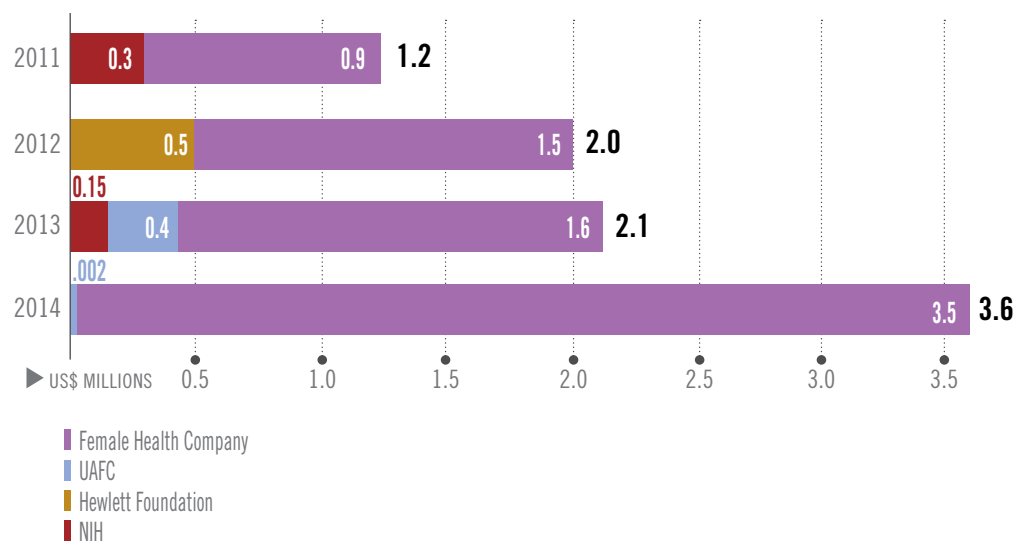
7.0 Investments in research and development and operations research related to female condoms

In 2014, global investment related to female condom R&D totaled US\$3.6 million, an increase of US\$1.5 million over 2013, from the Female Health Company and the Universal Access to Female Condoms (UAFC) Joint Programme, funded by the Netherlands Ministry of Foreign Affairs (Figure 26).

Female condoms have been available for over 20 years and are marketed in over 140 countries. As of March 2014, the FC2 and Cupid 1 are the only female condom products prequalified by the World Health Organization (WHO), while several other products are at various stages of development.

- A functionality study of the Cupid 2 was finished in 2014, and the results submitted to UNFPA. Cupid Ltd is also developing new varieties of female condoms.
- Velvet, developed by HLL Lifecare Ltd, finished in a functionality study in 2014, with the results submitted to UNFPA. Velvet is currently distributed in Australia, Bahamas, Brazil, India and Nepal.
- The Woman's Condom (also: O'Lavie, V female condom, Whisper, Maximum Diva), developed by the Dahua Medical Apparatus Company, is currently under review by the WHO and UNFPA for prequalification and undergoing an effectiveness study needed for USFDA approval.
- Other products in ongoing research include the FC3 from the Female Health Company.
- The Gates Foundation is providing support to several innovators to develop the Next Generation of male and female condoms.
- Ongoing clinical research included in the investment total is a clinical trial by the International Program for Microbicides (IPM) designed to assess use of the female condom when used in the presence and absence of a placebo vaginal ring.

Figure 27 Funding for Female Condom R&D, 2011–2014 (US\$ millions)



8.0 Investments in research related to vertical transmission prevention

Funding for research related to prevention of vertical transmission of HIV from mother to child at birth and during breastfeeding increased between 2013 and 2014, from approximately US\$44 million to US\$49 million. The public sector accounted for most of this funding, with the US, through NIH and USAID, contributing more than 91 percent.

Results in 2014 confirmed that triple antiretroviral therapy among pregnant women (i.e., Option B) is effective in prevention of vertical transmission. Several studies also released important findings in 2014, including:

- The PROMISE study, a multi-country randomized clinical trial, showed the Option B regimen superior to monotherapy during pregnancy for preventing vertical transmission. The study confirmed the 2013 WHO consolidated treatment guidelines recommending triple antiretroviral therapy for all pregnant and breastfeeding women.
- The Pediatric HIV/AIDS Surveillance Monitoring of Antiretroviral Therapy Toxicities Study, a prospective cohort study of HIV-exposed infants in the United States and the French Perinatal Cohort, released results showing low rates of congenital anomalies among babies exposed to antiretroviral medicine at the time of conception. However, the French Perinatal Cohort reported higher rates of heart defects among infants exposed in utero.
- In Botswana and Malawi, two additional studies showed the challenges of implementing programs to prevent vertical transmission, finding issues with the cascade of care.

Table 12 | Annual Investments in Prevention of Vertical Transmission R&D, 2008–2014 (US\$ millions)

| | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|--------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| US | 10.3 | 44.6 | 56.9 | 36.2 | 34.6 | 42.0 | 44.9 |
| Europe | 7.3 | 5.9 | 1.5 | 1.1 | 1.7 | 0.1 | 1.2 |
| Other countries | - | - | 1.3 | 5.1 | 6.7 | 0.2 | - |
| Total public | 17.6 | 50.5 | 59.7 | 42.6 | 42.9 | 42.4 | 46.6 |
| Total philanthropic | 3.6 | 0.9 | 0.0 | 0.5 | 0.8 | 1.7 | 2.5 |
| Total commercial | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.5 |
| Total global investment | 21.2 | 51.4 | 59.7 | 43.1 | 43.8 | 44.0 | 49.0 |

9.0 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 2014, a total of US\$9.9 million was provided for HSV-2 vaccine research from the US NIH and the Canadian Institutes of Health Research, an increase of US\$4.1 million over 2013. As in previous years, commercial investors were often subsidized by public-sector institutions, such as the US NIH. Pharmaceutical and biotechnology companies investing in HSV-2 vaccine R&D include Agenus Inc., Genoccea Biosciences, GSK, Juvaris and Vical.

10.0 Investments in cure and therapeutic vaccine research and development

The Working Group estimates that in 2014, US\$157.0 million was invested in cure research, an increase of 53 percent over the US\$102.7 million invested in 2013, and an increase of 79 percent over the US\$88.1 million invested in 2012. The majority of investments (88 percent) came from the public sector, with the US NIH contributing the majority of public funding, and the European Union, France, Australia and Canada also contributing significantly to HIV cure research.

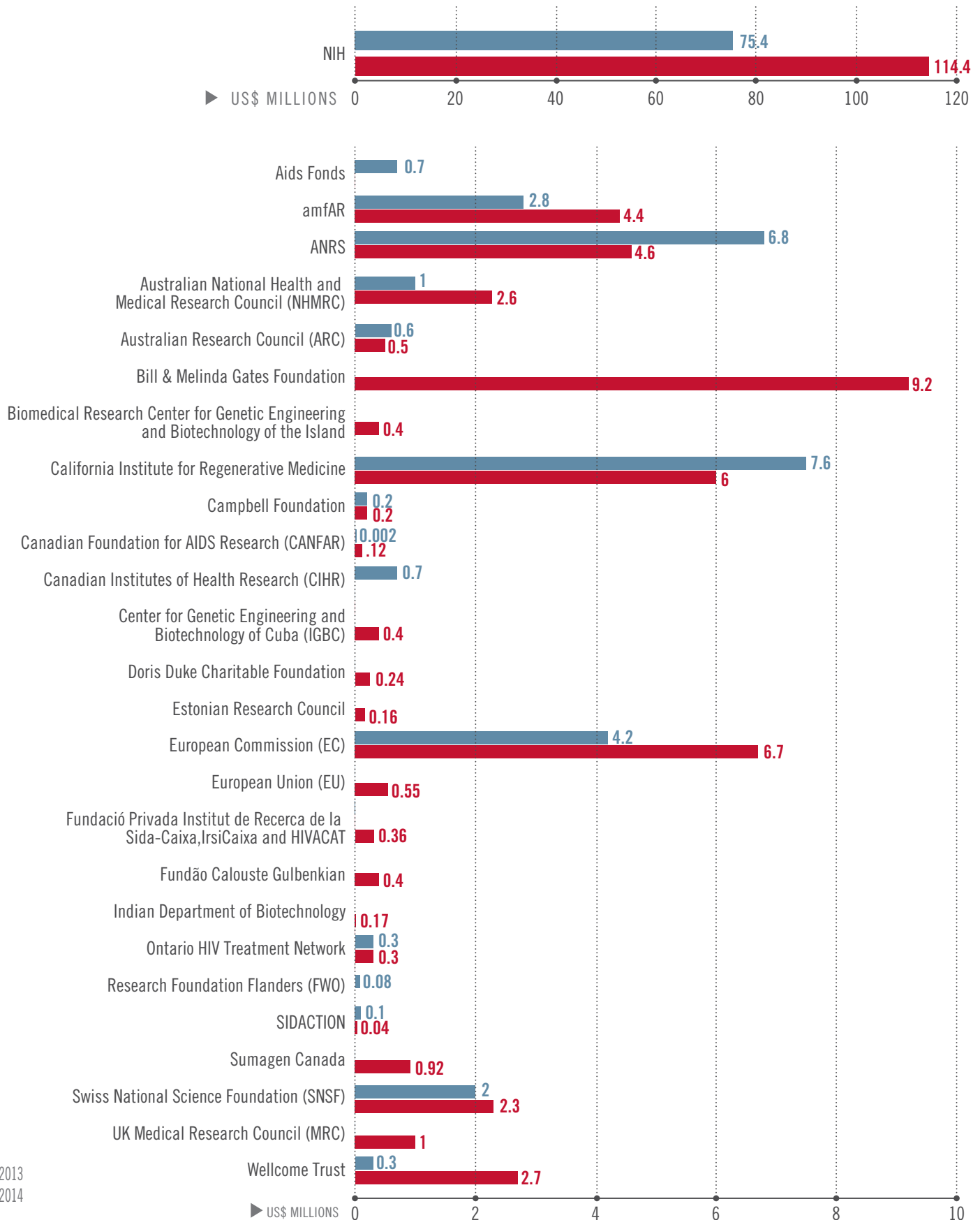
Approximately 11 percent of the total invested in 2014 came from philanthropies, such as Aides Fonds, amfAR, the Campbell Foundation, the BMGF and Sidaction. Several companies are known to have active cure research programs including Gilead, Janssen, Merck and Sangamo BioSciences, among several others. (Figures 27, 29, and 30).

In 2014, many initiatives towards cure research were ongoing. Through the IAS Towards an HIV Cure Initiative over 40 candidates were supported to attend the IAS symposium through the scholarship program. With the UNC Chapel Hill-GSK partnership, GSK will invest \$4 million per year for five years to accelerate the search for HIV cure and will also contribute personnel to UNC Chapel Hill. amfAR's Countdown to a Cure for AIDS plans to strategically invest \$100 million in cure research over the next six years aimed at finding a broadly applicable cure for HIV by 2020. The Canadian Initiative for HIV Cure Research, funding through the CIHR and Canadian Foundation for AIDS Research (CANFAR), awarded 10.7 million to two Canadian research teams. The HIV Cure Initiative, an international alliance of scientific, governmental, philanthropic, and industry organizations, launched in 2014 to identify, test, and distribute interventions that will lead to a cure. The Infectious Disease Research Institute is currently serving as the fiscal sponsor of the Initiative.

Table 13 | HIV Cure R&D (US\$ millions)

| Research | Amount |
|---------------|--------------|
| Public | 140.0 |
| Philanthropic | 16.9 |
| Commercial | 1.0 |
| Total | 157.9 |

Figure 27 Investments in HIV Cure R&D by Funder, 2013–2014 (US\$ millions)



Therapeutic vaccine research and development

Therapeutic vaccine research is defined by the Working Group as studies that increase scientific knowledge through research on protective immune responses and host defenses against HIV and is now included by the OAR as a subcategory of cure research. While in the past the Working Group has distinguished these studies from those that focus on cure research, the OAR has included these studies under the cure research umbrella.

The Working Group found a total of US\$13.2 million invested towards therapeutic vaccine research of the total US\$157.9 million invested in cure research in 2014. This represents an increase of US\$1.7 million from 2013 (Figure 28).

Figure 28 Investment in Therapeutic AIDS Vaccines, 2013–2014

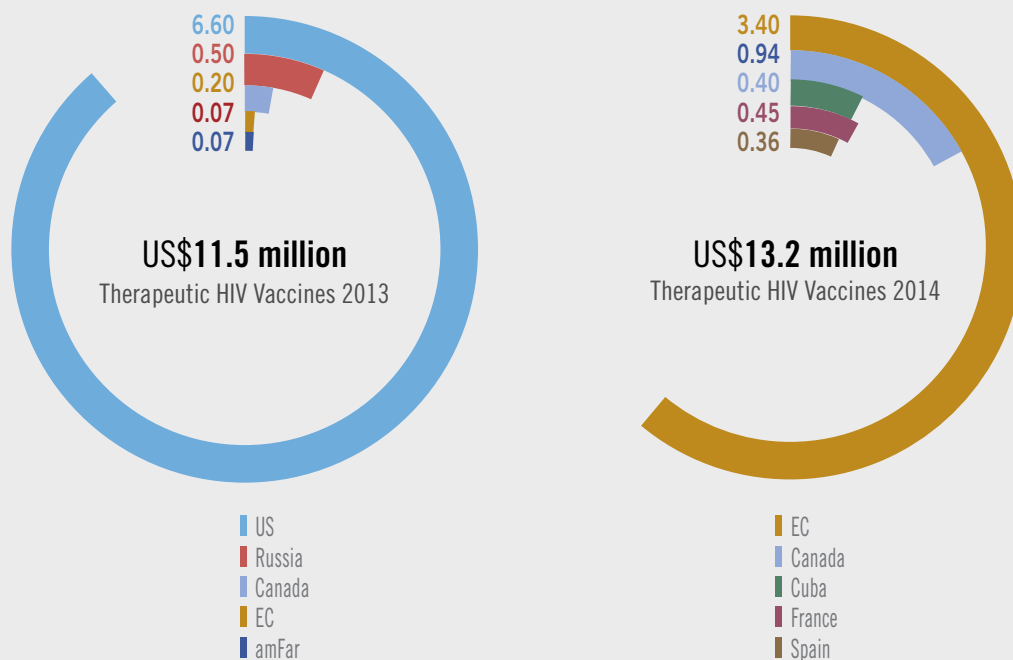


Figure 29 HIV Cure R&D Investments by Country, 2012–2014

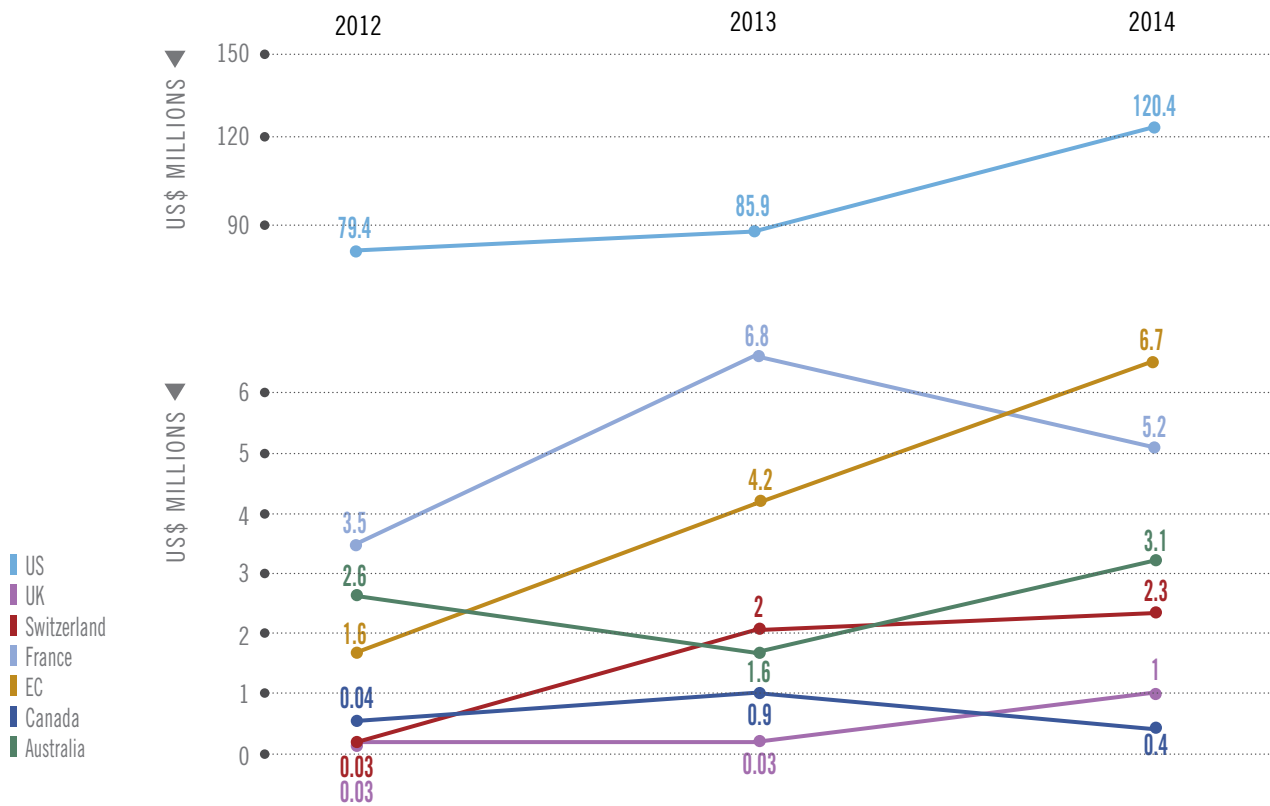
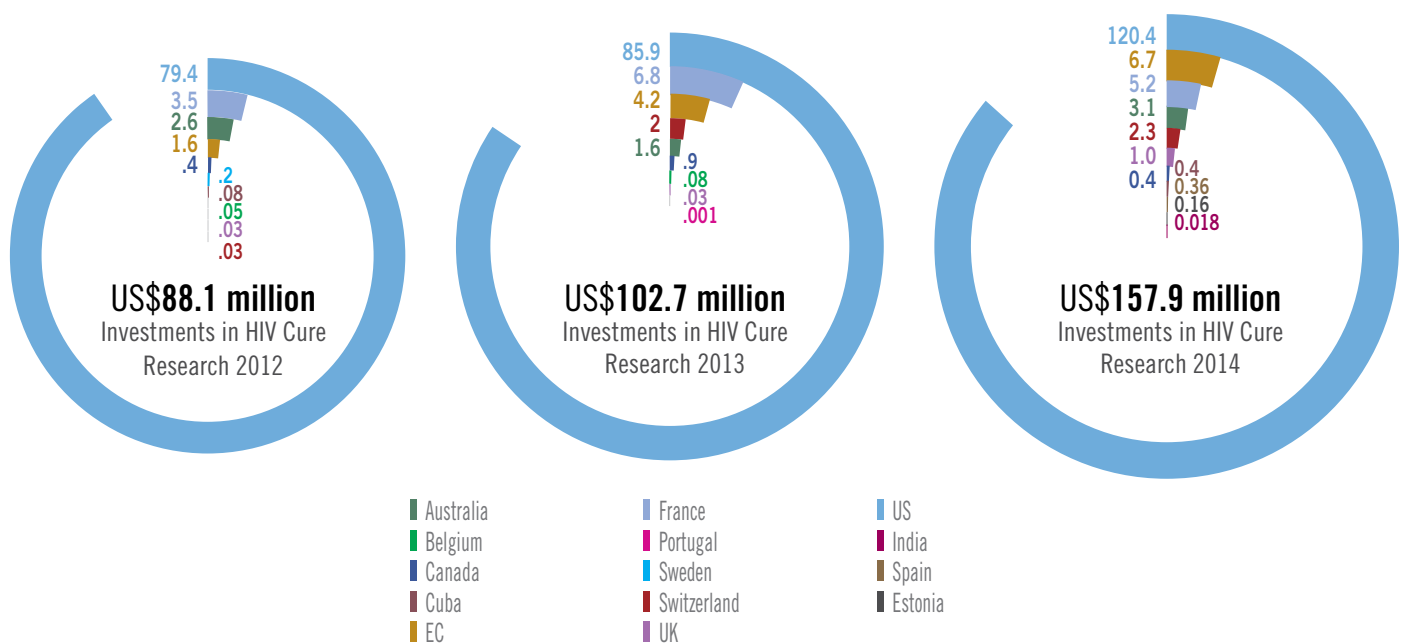


Figure 30 Investments in HIV Cure Research by Country, 2012–2014



Appendix

Appendix: Methodology

This report was prepared by Emily Donaldson (AVAC), with contributions from Kevin Fisher (AVAC), Thomas Harmon (IAVI), Polly Harrison (AVAC), Deepak Mattur (UNAIDS), José Antonio Izazola-Licea (UNAIDS) and Mitchell Warren (AVAC) of the HIV Vaccines & Microbicides Resource Tracking Working Group (herein referred to as “the Working Group”), with contributions from Kinan Lagast (AVAC) and 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.hivresourcetracking.org). The two sets of 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 Data Collection Categories section of the Appendix.

Data collection methods and fluctuation in investment levels

HIV prevention R&D investment figures are collected annually by the AIDS Vaccines & Microbicides Resource Tracking Working Group through an email survey. For the present report, the Working Group reached out from January to May 2015 to 300 funders in the public, philanthropic and commercial sectors and collected information on 596 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) 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.²⁶ 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.²⁷

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.

²⁶ 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, 2013 to March 31, 2014 was treated as 2013 and the fiscal year July 1, 2013 to June 30, 2014 was treated as 2014.

²⁷ 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.

Table 14 | **Public, Philanthropic and Commercial Sector Primary Funders**

| Total responders: 110 | |
|-----------------------|--|
| Sector | Type of Responders |
| Public | <ul style="list-style-type: none"> • National governments (including government research bodies, international development assistance agencies and other government funding agencies) • European Commission • Multilateral agencies |
| Philanthropic | <ul style="list-style-type: none"> • Private, not-for-profit organizations (e.g., foundations, trusts and non-governmental organizations) • Charities • Corporate donations • Individual gifts and bequests |
| Commercial | <ul style="list-style-type: none"> • Pharmaceutical companies • Biotechnology companies |

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 identified into categories based on NIH definitions.²⁸ As the largest funder of HIV prevention R&D and thus, with the majority of grants towards 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, 2014, 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 investment 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.

²⁸ See Data Collection Categories in the Appendix for expenditure categories.

Data Collection Categories:

- Preventive HIV 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 HIV vaccines
- Antiretrovirals (ARVs)
- Immune-based therapies & anti-inflammatory drugs
- Co-infection & opportunistic infection drugs
- Other HIV-associated drugs
- HIV diagnostics

Preventive and therapeutic HIV vaccine R&D

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

Microbicides R&D

| Category | Definition |
|---|---|
| Basic mechanisms of mucosal transmission | Elucidate basic mechanisms of HIV transmission at mucosal/epithelial surfaces. |
| Discovery, development and preclinical testing | Target R&D efforts at the discovery, development and pre-clinical evaluation of topical microbicides alone and or in combination. |
| Formulations and modes of delivery | Develop and assess acceptable formulations and modes of delivery for microbicides. |
| Clinical trials | Support for Phase I, II and III trials of candidate microbicides for safety, acceptability and effectiveness (including costs of candidate products). |
| Behavioral and social science research | Conduct applied behavioral and social science research to inform and optimize microbicide development, testing and acceptability and use. |
| Microbicide research infrastructure | Establish and maintain the appropriate infrastructure (including training) needed to conduct research. |
| Advocacy and policy development | The education and mobilization of public and political support for microbicides, and the targeting of potential regulatory, financial, infrastructure 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 |
|--|--|
| Basic research | Studies to increase scientific knowledge through research on protective immune responses and host defenses against HIV. |
| Preclinical research | Efforts to improve design, development and animal testing of experimental interventions. |
| Clinical trials | Support for Phase I, II and III trials (including the costs of candidate products). |
| Cohort and site development | Support to identify trials sites, build capacity, ensure adequate performance of trials, and address the prevention needs of the trial communities. |
| Advocacy and policy development | The education and mobilization of public and political support for new HIV prevention tools and the targeting of potential regulatory, financial, infrastructure or political barriers to their rapid development and use. |

Definitions

| Category | Definition |
|--|---|
| Treatment as prevention research | 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 ³ on HIV and/or TB-related morbidity and mortality or HIV transmission. |
| Multipurpose Prevention Technologies (MPTs) | Combine protection to prevent at least two sexual and reproductive health risks: unintended pregnancy, HIV and other sexually transmitted infections (STIs). Indications of interest include: <ul style="list-style-type: none"> • HIV • HSV • Pregnancy • Bacterial Vaginosis (BV) • Chlamydia • Gonorrhea • Hepatitis • HPV • Syphilis • Trichomoniasis • Urinary Tract Infections (UTI) • Other STIs |
| Cure research | 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

| | | | |
|-----------------|---|----------------|--|
| AECID | Spanish Agency for International Development Cooperation | IPM | International Partnership for Microbicides |
| amfAR | American Foundation for AIDS Research | IRMA | International Rectal Microbicides Advocates |
| ANRS | National Agency for Research on AIDS and Viral Hepatitis (France) | MHRP | US Military HIV Research Program |
| ANRS VRI | ANRS Vaccine Research Institute | MSF | Médecins Sans Frontières |
| ARC | Australian Research Council | MSM | Men who have sex with men |
| ART | Anti-retroviral therapy | MRC | UK Medical Research Council |
| ARV | Anti-retroviral | MTN | Microbicide Trials Network |
| BIDMC | Beth Israel Deaconess Medical Center | NAC | IAVI Neutralizing Antibody Consortium |
| BMGF | Bill & Melinda Gates Foundation | NHMRC | Australian National Health & Medical Research Council |
| BRICS | Brazil, Russia, India, China and South Africa | NIAID | US National Institute of Allergy and Infectious Diseases |
| CDC | US Centers for Disease Control and Prevention | NIH | US National Institutes of Health |
| CHAARM | Combined Highly Active Anti-Retroviral Microbicides Project | NIHR | UK National Institutes of Health Research |
| CHARM | Combination HIV Antiretroviral Rectal Microbicide Program | NSC | National Science Council of Taiwan |
| CHAI | Clinton Health Access Initiative | OAR | US NIH Office of AIDS Research |
| CHAVI-ID | Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery | OFID | OPEC Fund for International Development |
| CHVI | Canadian AIDS Vaccine Initiative | ORVACS | Objectif Recherche VACine Sida |
| CIDA | Canadian International Development Agency | P5 | Pox-Protein Public-Private Partnership |
| CIHR | Canadian Institutes of Health Research | PDP | Product development partnership |
| DAIDA | Danish International Development Agency | PEPFAR | US President's Emergency Plan for AIDS Relief |
| DBT | Department of Biotechnology at India's Ministry of Science and Technology | PHAC | Public Health Agency of Canada |
| DFID | UK Department for International Development | PMTCT | Prevention of mother-to-child transmission |
| DST | Department of Science and Technology, South Africa | PrEP | Pre-exposure prophylaxis |
| EC | European Commission | R&D | Research & development |
| EDCTP | European and Developing Countries Clinical Trials Partnership | SA DOH | South African Department of Health |
| EGPAF | Elizabeth Glazer Pediatric AIDS Fund | SIDA | Swedish Agency for International Cooperation Development |
| ESF | Estonia Science Foundation | SNSF | Swiss National Science Foundation |
| FACTS | Follow-on African Consortium for Tenofovir Studies | SRC | Swedish Research Council |
| FDA | US Food and Drug Administration | START | Strategic Timing of AntiRetroviral Treatment (START) study |
| FHI | Family Health International, US | TDF | Tenofovir |
| HPTN | Prevention Trials Network | TDF/FTC | Tenofovir/Emtricitabine |
| HVTN | HIV Vaccine Trials Network | UK | United Kingdom |
| IAVI | International AIDS Vaccine Initiative | UK HVC | UK AIDS Vaccine Consortium |
| ICMR | Indian Council of Medical Research | UNAIDS | Joint United Nations Programme on HIV/AIDS |
| IDRI | Infectious Disease Research Institute | US | United States |
| | | USAID | US Agency for International Development |
| | | VOICE | Vaginal and Oral Interventions to Control the Epidemic |
| | | VMMC | Voluntary Medical Male Circumcision |
| | | VRG | US Vaccine Research Center |
| | | WHO | World Health Organization |

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HIV Vaccines & Microbicides Resource Tracking Working Group

AVAC

www.avac.org

International AIDS Vaccine Initiative (IAVI)

www.iavi.org

Joint United Nations Programme on HIV/AIDS (UNAIDS)

www.unaids.org

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