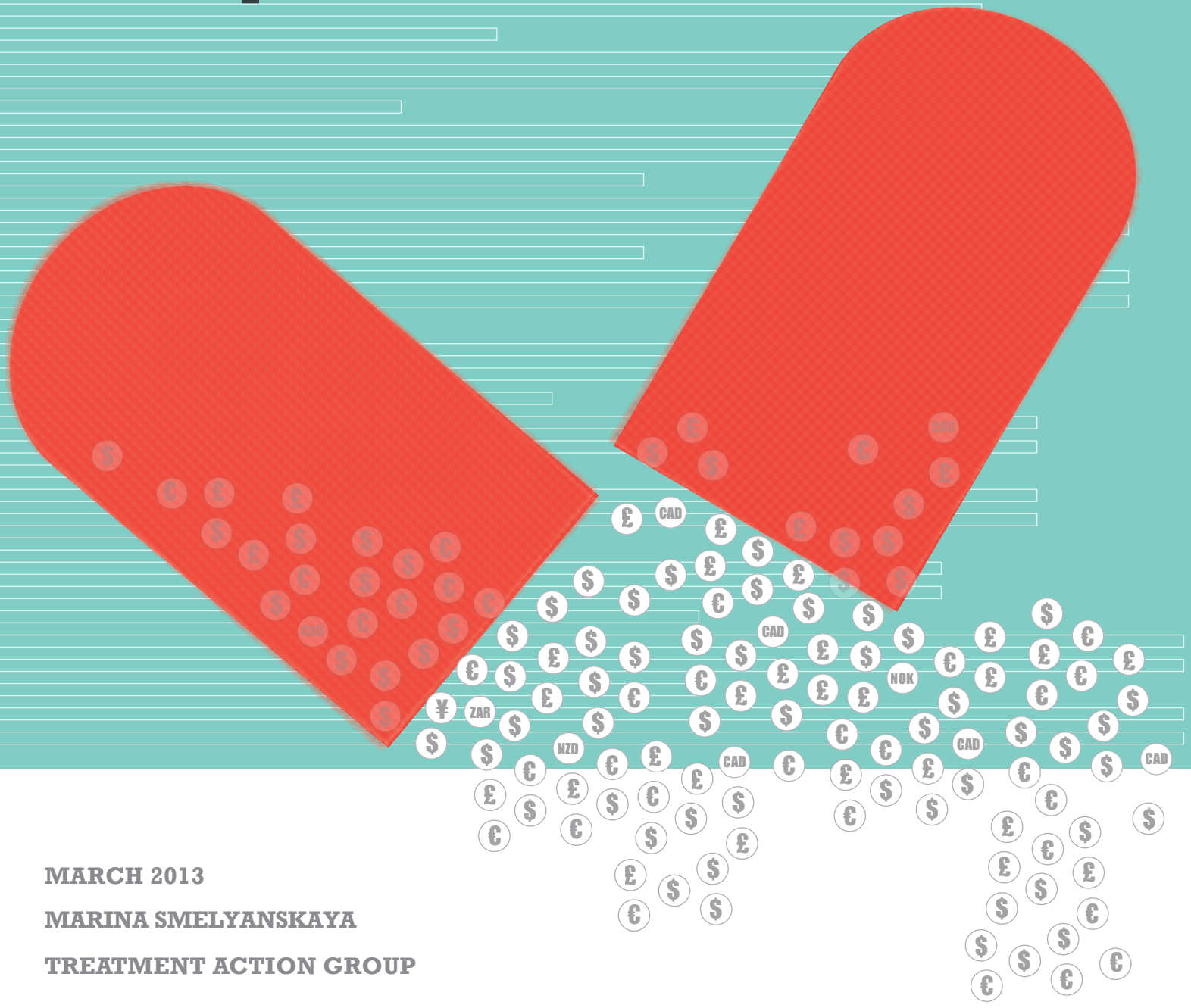
AVAC
Global Advocacy for HIV Prevention

TAG
Treatment Action Group

FUNDING SCIENTIFIC INNOVATION:

Global Investments in HIV Treatment Research and Development in 2010 and 2011



MARCH 2013

MARINA SMELYANSKAYA

TREATMENT ACTION GROUP

The HIV Treatment Research and Development Resource Tracking Project is a collaborative initiative of Treatment Action Group (TAG) and AVAC, directed and managed by TAG, with financial support from the Joint United Nations Programme on HIV/AIDS (UNAIDS).

About TAG

TAG is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS. TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action on the part of all affected communities, scientists, and policy makers to end AIDS.

About AVAC

AVAC is an international nonprofit organization that uses education, policy analysis, advocacy, and community mobilization to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. AVAC is the secretariat of the HIV Vaccines and Microbicides Resource Tracking Working Group.

About UNAIDS

UNAIDS leads and inspires the world to achieve its shared vision of zero new HIV infections, zero discrimination and zero AIDS-related deaths. UNAIDS unites the efforts of 11 UN organizations—UNHCR, UNICEF, WFP, UNDP, UNFPA, UNODC, UN Women, ILO, UNESCO, WHO and the World Bank—and works closely with global and national partners to maximize results for the AIDS response.

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Executive Summary

In 2009, Treatment Action Group (TAG) partnered with AVAC to collect baseline data on investments in HIV treatment research and development (R&D). These data provided an understanding of key funding streams in HIV treatment R&D and pointed at opportunities for further investment. Advances in HIV treatment science in 2010 and 2011 saw improvement in treatment regimens and strategies and reinvigorated optimism for finding a cure. In 2012, TAG and AVAC, with financial support from UNAIDS, put forth a collaborative effort to analyze trends in HIV treatment R&D investment in 2010 and 2011 to highlight gaps and encourage support in areas where it is most needed.

From 171 surveyed institutions, 41 funders reported investment in HIV treatment R&D in 2011 for a total of $2.6 billion. While more funders were identified in the 2009 survey (46), growth in investment was observed through both 2010 and 2011 with fewer funders reporting—34 in 2010 and 41 in 2011. This growth was due to actual funding increases from specific funders *and* to reports received from two large U.S. public-sector funders, whose data was not collected in 2009.

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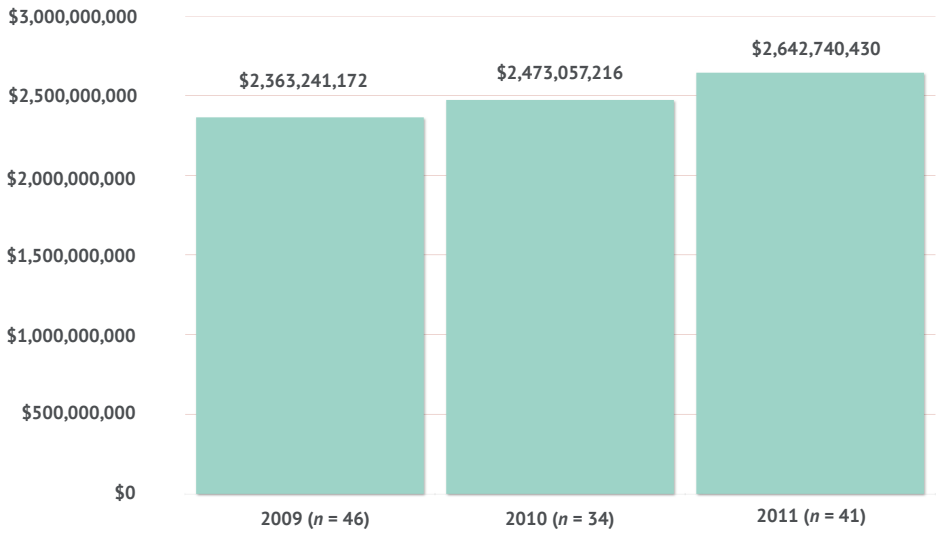
FIGURE 1 | **INVESTMENT IN HIV TREATMENT R&D: 2009–2011**



As in 2009, TAG collected data using electronic surveys from public, private, and philanthropic funding institutions. Funders were asked to report on their investments in HIV treatment R&D and classify them according to six research areas: basic science; applied/infrastructure/unspecified; drug discovery and development; diagnostics; therapeutic vaccines; treatment as prevention (TasP); and operational and implementation science.

The 2012 survey's key findings are as follows:

- Forty-one funders worldwide reported investing $2,642,740,430 (or $2.6 billion) in HIV treatment R&D in 2011. This investment represented an 11.8% increase from 2009 and a 6.9% increase from 2010, when 34 funders reported investing $2.5 billion in HIV treatment R&D projects.

- In 2011, 24 public-sector funders were responsible for the majority—$1.8 billion (or 70%)—of reported HIV treatment R&D. Eight private-sector funders contributed 26% of the 2011 total at $690 million, while nine philanthropic funders reported a contribution of $111 million accounting for 4% of the collected data on treatment R&D. While substantial, the private-sector figure is not representative of actual annual investments, as industry partners often decline participation or do not respond to TAG's requests for information.

- Public-sector funding increased 6.8% from 2009 to 2010 and decreased 1.2% from 2010 to 2011. The share of public-sector contribution to the total has also decreased—from 74.9% in 2010 to 69.2% in 2011. These findings indicate the overall trend of flat-lining and declining public-sector funds for key HIV treatment research areas.

- Investment increased across all research areas with the exception of therapeutic vaccines, where TAG recorded an investment decline of 22.2% since 2009.

- In both 2010 and 2011, investment in the development of new medications—at $1.24 billion (or 50.3%) and at $1.37 billion (or 51.8%), respectively—comprised the largest share of the total. Investment in basic science research was second largest—at 32.6% in 2010 and 31.7% in 2011.

- Investment in drug discovery increased by 13.8% since 2009 and by 10% since 2010 despite the fact that a larger number of funders reported in this category in 2009 (31 vs. 18 in 2010 and 20 in 2011). The total investment was $1.37 billion in 2011, $1.24 billion in 2010, and $1.2 billion in 2009. The area of research dedicated to developing new antiretroviral (ARV) medications received the largest amount of funding across all years.

- While TAG recorded an increase in the area of drug discovery, the figure in this area is likely misrepresented due to low reporting from industry leaders. Out of 41 pharmaceutical companies contacted by TAG, only five submitted completed surveys. Similarly impacted were therapeutic vaccine and diagnostics research categories, as the private sector plays an important role in these fields. In an attempt to provide up to date information on clinical activity, TAG presents an outline of the current antiretroviral therapy (ART) pipeline on page 43.

- The U.S. National Institutes of Health (NIH) remained the largest reporting donor in HIV treatment R&D, providing 67% of the total in 2010 and 62% in 2011. In 2011, the agency led investment in basic science and operational and implementation science, but fell behind private-sector partners in drug discovery (Gilead Sciences) and therapeutic vaccines (Company C).

- In 2011, TAG collected data from donors in 18 countries and classified funding from the European Commission (EC) as that coming from the European Region. While partial information was received from Brazil and South Africa, reports from countries like China and Russia, where research activity is taking place, were not obtained.

- Funders in the U.S. contributed the largest share (91.9%) to HIV treatment R&D. While U.S. funders might be more familiar with TAG's resource-tracking research and thus have a higher response rate, there is a need for other countries to step up in-

vestment in HIV treatment R&D and contribute meaningfully to ongoing resource-tracking efforts.

- It is rarely immediately clear which investments will prove to have the greatest impact on individual and public health, but there is no question that robust ongoing investment in novel HIV treatments and treatment strategies has played a key role in bringing lifesaving antiretroviral therapy to over 8 million people this year alone. Further improvements and innovations will be required to more easily, potently, durably, and safely treat the millions of people who already need HIV treatment or who will come to do so over the coming decade.

With marked advances in understanding viral destruction and the production of simpler and more effective drugs, HIV treatment science is focused on discoveries that will improve the lives of people living with HIV, rapidly scale up treatment, and reduce disease spread and mortality. While an increase in funding was recorded for 2010 and 2011, a trend in decreased investment from certain public-sector institutions was also observed.

The success of many lifesaving interventions and research projects depends on public-sector funding. Thus, stopping or flatlining investment now undermines this progress. Furthermore, the wide arsenal of interventions that are becoming available—thanks to rapid discovery—puts the end of the HIV epidemic within our reach. Given this scientific momentum, the world cannot afford to scale back investments in HIV treatment R&D.

1. Introduction and Information on Data and Methodology

1.1 Introduction

For 2011, TAG recorded a total investment of $2.6 billion in HIV treatment research and development (R&D) among 41 funders. As compared to the $2.4 billion total in 2009, the 2011 figure represents an 11.8% increase from 2009 and a 6.9% increase from 2010, demonstrating a steady growth in global contribution to HIV treatment R&D.

Two new compounds—the non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine and Complera (a fixed-dose combination of rilpivirine with emtricitabine and tenofovir)—were licensed in 2011, for an updated total of 32 medicines and fixed-dose ARV combinations available and approved for use by stringent regulatory authorities in the U.S. and other developed countries. Some developing countries have a broader array of fixed-dose combinations using drugs not combined in the U.S. or Europe due to intellectual property issues. Fourteen additional compounds, including a long-acting injectable formulation of rilpivirine, are currently in the pipeline.

Also in 2011, more than 8 million people were on antiretroviral therapy (ART)—a 20% increase from 6.6 million in 2010.[1] More people—58% in 2010 versus 33% in 2006—were accessing simpler drug regimens associated with decreased side effects. This progress would have been impossible without sustained investment in HIV treatment research and development over the past 25 years.

Development of new, simpler, more effective and affordable compounds will continue to be essential for attaining the goal of putting at least 15 million people on ART by 2015, as set forth in the 2011 *Political Declaration on HIV and AIDS*.[2] To this end, pharmaceutical industry leaders moved seven compounds into phase III studies in 2010 and 2011, and seven compounds into phase II. The focus of development is on compounds that can be taken as a single pill once daily, thus simplifying treatment, improving adherence, and reducing the risk of stockout-induced resistance to individual drugs. With an overwhelming majority of all HIV positive people living in resource-limited settings, affordability of medications will play a critical role in achieving universal treatment access, and safe, simple, durably effective single-pill combinations will help extend treatment success.

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1. UNAIDS. Together we will end AIDS. Accessed October 1, 2012, at http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/20120718_togetherwewillendaids_en.pdf.

2. Ibid.

A more effective version of tenofovir with a lower molecular weight is being developed by Gilead Sciences. This formulation has promise for resource-limited settings where stavudine, for which tenofovir is an effective and less toxic replacement, is now being phased out in many countries.[3] GS-7340 is currently in phase II of development and is being studied as a replacement for tenofovir in combinations such as elvitegravir/cobicistat/GS-7340/emtricitabine and darunavir/cobicistat/GS-7340/emtricitabine. A once-daily drug dolutegravir is being tested by ViiV along with a follow-up integrase inhibitor with a low molecular weight, a long half-life, and no need for pharmacokinetic boosting. Long-acting injectable formulations have been considered by both ViiV and Janssen, with the latter testing a long-acting injectable form of the NNRTI rilpivirine.

Oral and topical ARVs for preventing HIV transmission generated important research results in 2010 and 2011. In 2010, a groundbreaking multinational study known as IPrEx indicated that a daily combination of emtricitabine and tenofovir (brand name Truvada) could reduce the risk of HIV infection by 44% among sexually active HIV-negative men who have sex with men and transgender women who have sex with men.[4] IPrEx was supported by the National Institute of Allergy and Infectious Diseases (NIAID), Gilead Sciences, and the Bill & Melinda Gates Foundation (BMGF).

Perhaps the most important HIV prevention study of recent years was HIV Prevention Trials Network (HPTN) study 052, which in 2011 demonstrated a 96% reduction in HIV transmission among serodiscordant couples. In the experimental arm, HIV-positive partners were initiated on treatment immediately at enrollment with CD4 counts between 350 and 550 cells/mm^3 versus when their CD4 counts dropped below 250 cells/mm^3.[5]

Treatment as prevention (TasP), as in the case of HPTN 052, provides an unprecedented opportunity to roll back the HIV pandemic by initiating ART earlier. Further studies of various ARV combinations for the purpose of reducing HIV risk and preventing transmission are now taking place, and new compounds are being developed to perfect the interventions that would dramatically reduce the spread of HIV in communities most at risk. Availability of fixed-dose combination drugs that have lower toxicity and can be administered by lower level health care workers will become extremely important as more and more people living with HIV learn their status and access treatment earlier. Such improved regimens will allow access to treatment for the estimated 15 million HIV-positive persons who will need ART by the year 2015.

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3. Treatment Action Group. 2012 Pipeline. New York: Treatment Action Group, 2012.

4. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010 Dec 30;363(27):2587–99. doi: 10.1056/NEJMoa1011205.

5. Cohen, M et al. Prevention of HIV-1 Infection with early antiretroviral therapy. N Engl J Med. 2011 August 11; 365(6):493–505.

The years 2010 and 2011 also saw growing enthusiasm for HIV cure research. In December 2010, an article published by the journal *Blood* reported a case of a patient cured of HIV using CCR5 stem cell transplantation.[6] Earlier that year, another study suggested that introduction of ART in the very early stages of HIV infection could significantly halt viral spread.[7] Urged by these and other promising findings, the International AIDS Society launched its "Global Scientific Strategy: Towards an HIV-1 Cure"[8] initiative in 2012 that brings together HIV scientists, activists, and major research agencies and foundations in a cooperative effort to find a sterilizing or functional cure for HIV.

Despite this obvious progress and overall growth in support of HIV treatment R&D, research funding has declined and several reporting agencies deprioritized or significantly cut their HIV research budgets. The flatlining of the NIH budget, projected for 2013, will likely slow down development of new therapeutics and TasP[9] (see the discussion in section 2.12, Top 10 Funders in HIV Treatment R&D: 2011).

6. Allers K, Hutter G, Hoffman J, et al. Evidence for the cure of HIV infection by CCR5Δ32/Δ32 stem cell transplantation. Blood. 2011 Mar 10;117(10):2791–9. doi: 10.1182/blood-2010-09-309591. Accessed November 20, 2012, at http://bloodjournal.hematologylibrary.org/content/117/10/2791.full.pdf+html.
7. Hocqueloux L, Prazuck T, Avettand-Fenoel V, et al. Long-term immunovirologic control following antiretroviral therapy interruption in patients treated at the time of primary HIV-1 infection. AIDS. 2010 June 19;24(10):1598–1601.
8. International AIDS Society. "Towards an HIV Cure:" Global Scientific Strategy. Accessed October 25, 2012, at http://www.iasociety.org/Default.aspx?pageId=349.
9. National Institutes of Health. Office of AIDS Research trans-NIH AIDS research budget: FY 2013 budget. Accessed October 25, 2012, at http://www.oar.nih.gov/budget/pdf/2013_OARTransNIHAIDSResearchBudget.pdf.

TABLE 1

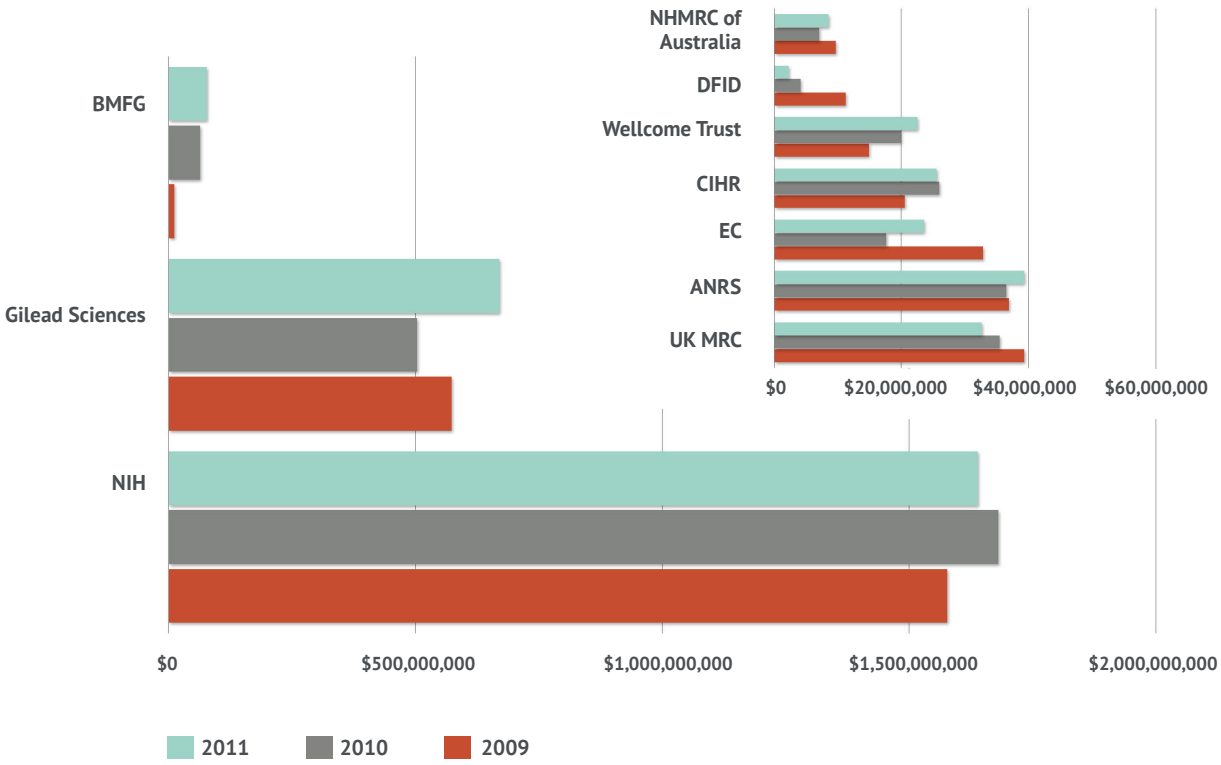
Top 10 Funders in HIV Treatment R&D: 2009–2011

2011 Rank	2010 Rank	2009 Rank	Funding Institution	Funder Type	2011 Total	2010 Total	2009 Total
1	1	1	U.S. National Institutes of Health (NIH)	P	$1,639,019,500	$1,681,033,862	$1,577,780,000
2	2	2	Gilead Sciences	C	$670,800,000	$503,340,000	$573,390,000
3	3	8	Bill & Melinda Gates Foundation (BMGF)	F	$78,423,625	$64,070,683	$11,583,996
4	4	4	Agence Nationale de Recherches sur le Sida et les Hépatites Virales (ANRS)	P	$39,291,029	$36,484,889	$36,930,094
5	5	3	UK Medical Research Council (UK MRC)	P	$32,671,670	$35,434,064	$39,300,905
6	6	6	Canadian Institutes of Health Research (CIHR)	P	$25,577,363	$25,969,285	$20,535,706
7	8	5	European Commission (EC)	P	$23,584,516	$17,641,172	$29,703,521
8	7	7	Wellcome Trust	F	$22,515,477	$19,962,890	$14,885,551
9	10	N/A	Office of the U.S. Global AIDS Coordinator (OGAC)	P	$15,213,509	$14,121,687	N/A
10	9	12	Japanese Ministry of Health, Labour and Welfare	P	$14,093,307	$14,121,687	N/A
15	13	10	National Health and Medical Research Council (NHMRC) of Australia	P	$8,593,257	$7,103,058	$9,739,226
20	18	9	Department for International Development (DFID)	P-D	$2,304,947	$4,160,928	$11,223,217

Note: P = public-sector funder C = private-sector funder P-D = public-sector development agency
F = philanthropic funder

A close look at the evolving top 10 funders from 2011 demonstrates a particular trend—significant contribution from the public sector, a growth in philanthropic investments and a decline in investments from bilateral agencies and some public funders.

FIGURE 2 **Snapshot: Top 10 Funders over the Years (2009–2011)**



A graphic review of the top 10 funders in 2009 and their contribution to the field between 2009 and 2011 also reveals that as top philanthropic donors (the BMGF, the Wellcome Trust) and some public-sector funders (the ANRS, the CIHR) increased their investment, others demonstrated unstable support (the NHRC of Australia, the EC) or decreased funding altogether (DFID, the UK MRC).

As public funding begins to decline, it is particularly important for private-sector, philanthropic and bi- and multilateral partners to pick up where public funders have left off. While larger private-foundation investors continue to play an important role in HIV treatment R&D, it is essential for new players to emerge and for coalitions of funders to form and support the most promising research in order to accelerate the development of better treatments and a cure.

In this year's report, TAG obtained investment data from fewer funders than in 2009—41 versus 46. Still, the total HIV R&D investment demonstrated growth due in part to actual growth from specific funders, and in part to reports received from two large U.S. public-sector funders, whose input was not recorded in 2009. TAG interprets available data to reflect actual investment trends and works to improve data collection for future reports.

1.2 Rationale

In 2011, 34 million people were living with HIV, 2.5 million were newly infected, and 1.7 million died from AIDS-related causes. While in some regions ART coverage reached 54%, in others it was as low as 13%.[10] And though UNAIDS is hopeful that the goal of putting 15 million people on ART by 2015 will be met, these projections might be offset by significant cuts to both the NIH budget and the budget of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). With studies indicating that treatment is also one of the most effective prevention interventions, the importance of developing cheaper and more effective medications is more vital than ever.

In 2011, public-sector donors from the U.S. supplied 63% of the $2.6 billion HIV treatment R&D total and PEPFAR supported treatment of 5.1 million children and adults[11]—64% of the global population receiving ART. Combined, these investments represent 0.05% of the U.S. 2011 GDP.[12] While other countries (excluding the European Union) have significantly lower GDPs, scaling up their investment in HIV research and treatment programs to match the U.S. contribution as a percentage of GDP could have a significant impact. Unless this occurs or substantial efficiencies are achieved in program implementation, the planned 11% reduction in PEPFAR funding threatens to significantly decrease support for ARV treatment and prevention of vertical transmission programs and other essential care interventions for affected populations.

As the United States and Europe struggle to regain economic stability, investment in treatment and intervention programs suffers—and with it the essential investment in HIV R&D. The unequivocal progress made in the battle against the epidemic would not be possible without expanding ART availability and introducing interventions, such as TasP more widely.

With support from UNAIDS, TAG and AVAC seek to understand the extent to which these transitions and funding shortages affect the HIV treatment R&D pipeline, where funding gaps lie and where donors must increase their investments to accelerate HIV research.

The HIV Treatment R&D Resource Tracking Project seeks to complement efforts undertaken by AVAC and the HIV Vaccines and Microbicides Resource Tracking Working Group, which focuses on funding for HIV prevention research and development.

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10. UNAIDS. Together we will end AIDS. Accessed October 1, 2012, at http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/20120718_togetherwewillendaids_en.pdf.
11. President's Emergency Plan for AIDS Relief. PEPFAR blueprint: creating an AIDS-free generation. Accessed December 10, 2012, at http://www.pepfar.gov/documents/organization/201386.pdf.
12. Calculated using TAG data, 2011 GDP data from the World Bank retrieved from http://data.worldbank.org/indicator/NY.GDP.MKTP.CD, and Fiscal Year 2011 Budget Tracker by the Kaiser Family Foundation retrieved from http://www.kff.org/globalhealth/upload/8045_FY2011.pdf.

1.3 | Methodology

In 2012, TAG surveyed key HIV treatment R&D funders to assess the state of global investments in the development of innovative strategies to treat and control HIV. The first HIV treatment R&D survey was conducted in 2009 among 140 philanthropic, public, private, and bilateral and multilateral agencies and institutions, yielding data from 46 donors and a collective HIV treatment R&D investment total of $2.4 billion.[13]

For this report, TAG solicited data for years 2010 and 2011. Electronic surveys were sent to 171 potential contacts, including the comprehensive database of 140 key HIV R&D treatment donors developed in 2009, and an additional 31 contacts acquired through desktop research or recommended by AVAC and other participating funders. A new reporting template was developed that invited participants to report the 2010 and 2011 research disbursements, funding trends, and the HIV treatment R&D funding priorities they considered of utmost importance.

Unless otherwise specified, data for all the charts and tables presented in this report were collected by TAG and AVAC in August–October 2012 from U.S. and international funders. Data were analyzed by TAG and presented to best represent current and past trends.

Funding data reported in non-U.S. currency were converted to U.S. dollars using the July 1, 2011, currency exchange rate for 2011 amounts and the July 1, 2010, amounts provided by the OANDA Corporation at http://www. oanda.com/currency/converter.[14]

Respondents were asked to classify the awards into seven research categories. Category definitions were revised, but closely aligned with those provided in 2009. The therapeutic vaccines category, previously included under the drug discovery category in immune-based therapies (IBTs) and anti-inflammatories, was separated into its own category for this report.

This year, TAG also revised its initial definition of treatment as prevention (TasP), to exclude other ARV-based prevention research such as preexposure prophylaxis (PrEP). While the development of new compounds and the use of existing ARVs for preventing transmission in communities with elevated HIV risk are extremely important, they are not within the scope of TAG's research and thus PrEP projects were excluded from this report.[15]

13. See corrections to 2009 reported data.

14. All monetary amounts in this report are calculated in U.S. dollars.

15. Information on investments in PrEP research can be found in the HIV Vaccines and Microbicides Resource Tracking Working Group's annual reports at www.hivresourcetracking.org.

The following are the seven research categories where investments were collected for 2010 and 2011:

- **Basic Science:** Scientific research that uncovers or enhances fundamental knowledge about the HIV virus, pathogenesis, and the immune response but is not linked to a product or treatment therapy.

- **Applied/Infrastructure/Unspecified:** All transitional research relevant to HIV treatment or HIV research that funders were not able to categorize.

- **Drugs:** Scientific research to develop new drugs or enhance existing compounds used to treat HIV. Projects listed included investment in preclinical or clinical research on
  - anti-retroviral drugs (ARVs);
  - medicines for treatment of coinfection and opportunistic infections;
  - immune-based therapies including anti-inflammatory drugs; and
  - other HIV-associated treatments.

- **HIV Diagnostics:** Research related to development of new diagnostic tools, including rapid, point-of-care tools that can detect and characterize the virus in blood and mucosal fluids.

- **Therapeutic Vaccines:** Preclinical or clinical research on vaccines that treat HIV infection by enhancing immune responses to HIV.

- **Treatment as Prevention:** Research aimed at understanding the role of antiretroviral therapy in reducing viral load and curbing viral transmission in HIV-positive individuals.[16]

- **Operational and Implementation Science:** Randomized, controlled, or prospective and/or retrospective observational studies of existing interventions within routine program settings as well as epidemiology, surveillance, or targeted evaluation of new or existing HIV treatments.

Of 171 funders, 58 responded: 10 reported no investments in 2010 and 2011, 32 completed the survey, and 16 either supplied unclear explanation of their portfolios or submitted incomplete surveys. Data from the NIH and Swiss National Science Foundation were accessed from publicly available sources. TAG also secured data from its partner, AVAC.

As a result, a total of 38 surveys were processed by TAG and resulted in 42 unique global R&D funders. Of the 42 donors, 34 supplied their 2010 investment data, and 41 provided their 2011 data. As in 2009, reporting from the private sector was extremely low, with only five companies submitting data.

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16. Information on investments in TasP research can also be found in the HIV Vaccines and Microbicides Resource Tracking Working Group's annual reports at www.hivresourcetracking.org. The Working Group's definition of TasP research includes implementation and operations research, as well as some research into the health effects of early or immediate treatment.

1.4 | Limitations of Data Collection and Analysis

TAG is committed to collecting the most comprehensive data from key HIV funders. Still, we acknowledge that this report captures only a portion of global support for HIV treatment R&D and leaves room for adjustment and improvement as more data emerge. As in 2009, certain factors limited the scope of data captured in this report such as:

- The private-sector response rate remained low. Forty-one private sector companies were asked to submit data: 5 submitted surveys, 3 reported no investment, 1 company declined to participate, and 5 companies responded to the survey request but provided no data. Twenty-seven companies did not respond to multiple requests from TAG, despite being offered an option to report anonymously. As in 2009, TAG presents the scope of the missing data by charting out private-sector involvement in ART development on page 43.

- Eight funders who participated in the 2009 survey were unresponsive this year, while several funders with substantial investments in the field participated in this year's survey for the first time and provided 2010 and 2011 data. This limits TAG's ability to track yearly trends for particular funders.

- Large multilateral agencies, including the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), UNITAID, USAID, and the World Health Organization either did not respond to the survey or could not provide data due to insufficient internal tracking resources. These agencies invest in a variety of treatment R&D, particularly operational and implementation research and their contribution is extremely important to the field. Where it was possible, TAG contacted grant recipients and/or collaborators to obtain funding data. In this year's report, TAG also discusses the Global Fund's activities in operational research on page 36.

- TAG attempts to preserve consistency in year-to-year donor reporting. However, timing restrictions and other issues prevent some funders from reporting in time for the release of this report. Thus, year-to-year variations in donor reporting are inevitable.

- This year, TAG was able to capture only partial investment data from Brazil and South Africa. We were unable to obtain funding data from China, India, or Russia. TAG will continue monitoring reports from countries whose investment in HIV treatment R&D might be less evident, but where meaningful progress is taking place.

- As in 2009, TAG attempted to capture information on investment in TasP research. The number obtained by TAG is misleadingly low and does not reflect the actual investment in this area. We summarize the scope of the projects dedicated to this important topic in a section dedicated to TasP (section 2.5).

1.5 | Corrections to 2009 Reported Data

European Commission Data

The European Commission (EC) submits its investment data by sharing the total grant amount, grant duration and grant start and end dates. To calculate the annual investment, TAG divides the total grant amount by the total number of years the grant is active.

In the 2012 EC survey submission, TAG became aware that several awards were not included in the 2009 EC total. As such, the 2009 EC grant total has been adjusted upward, from $32.9 million to $34.6 million.

Company C

Since 2009, Company C has reported data on HIV vaccine investments. However, according to this year's correspondence with the company representative, the company began separating therapeutic vaccine investment from other research investments in 2011. Since the company does not know what proportion of funding was dedicated to therapeutic vaccines in 2009 and 2010, TAG corrected the 2009 total from $1.2 million to $0 to avoid inflating the funding totals.

GeoVax Labs

GeoVax Labs funding was overreported in 2009. In 2012, the company stated that it had no proprietary funding for therapeutic vaccines in 2009. The amount of $3 million originally reported in 2009 included NIH and other outside funding that the company could not comment on with precision. The company's contribution in 2009 was thus reduced to $0.

These amendments mostly concern the therapeutic vaccines funding total and the overarching area of IBTs and anti-inflammatories. All 2009 revisions were subsequently adjusted in this report to present an updated analysis.

Corrections to TAG Coding and Analysis

- In 2009, entries from the European and Developing Countries Clinical Trial Partnership (EDCTP) were included in the global HIV treatment R&D total. However, since the EDCTP is not an original source funder but instead receives money from various funding sources, TAG excluded the 2009 EDCTP investment from the global total to avoid double counting and tracked these funds separately.

- In 2009, the EC was incorrectly categorized as a multilateral agency, thus contributing to the multilateral total. In this report, EC awards were classified as public-sector investments. Only four categories were considered for sectorial contribution in 2009—public-sector funders (P), private-sector funders (C), public-sector development agencies (P-D), and philanthropic funders (F).

- In 2009, a grant from the Canadian Institutes of Health Research (CIHR) was not categorized into any research category. The grant was related to comorbidities and thus placed into the drugs: coinfection and opportunistic infections category. The grant total of $36,743 was added to represent the correct total for that category.

- TAG collects data from NIH public databases and compares the agency's general definitions against a wide multitude of grants. In 2009, two NIH categories—one referring to "approaches to interrupt vertical transmission" characterizing research in the area of vertical transmission, and another to "therapeutic approaches to prevent horizontal transmission" addressing PrEP research—were erroneously counted as TasP research. As a result, 2009 public-sector and overall totals have been corrected.

As a result of the above-mentioned corrections, the 2009 total decreased 4% from $2.5 billion to $2.4 billion.

TAG welcomes corrections and comments from participating donors as well as from colleagues in the funder and activist communities. If you have comments regarding collected data or suggestions on survey methodology, please contact TAG at **hivrdtracking@treatmentactiongroup.org.**

2. Results

TABLE 2 | Reporting Funders in HIV Treatment R&D (2010–2011)*

#	Funding Institution	Funder Type	2010 Total	2011 Total
1	NIH	P	$1,681,033,862	$1,639,019,500
2	Gilead Sciences	C	$503,340,000	$670,800,000
3	BMGF	F	$64,070,683	$78,423,625
4	ANRS	P	$36,484,889	$39,291,029
5	UK MRC	P	$35,434,064	$32,671,670
6	CIHR	P	$25,969,285	$25,577,363
7	EC	P	$17,641,172	$23,584,516
8	Wellcome Trust	F	$19,962,890	$22,515,477
9	OGAC	P	$14,121,687	$15,213,509
10	Japanese Ministry of Health, Labour and Welfare	P	$14,826,097	$14,093,307
11	U.S. National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention (CDC)	P	$4,267,419	$9,988,798
12	Swiss National Science Foundation	P	$7,907,323	$9,918,255
13	Company A	C	$7,845,000	$9,576,000
14	Company C	C	$6,314,197	$9,042,805
15	NHMRC of Australia	P	$7,103,058	$8,593,257
16	Canadian International Development Agency (CIDA)	P-D	$5,682,269	$7,872,931
17	Institut Pasteur	F	$4,261,203	$5,226,180
18	amfAR, the Foundation for AIDS Research	F	$2,051,956	$3,039,211
19	Department of Science and Technology, South Africa	P	$2,390,700	$2,893,500
20	DFID	P-D	$4,160,928	$2,304,947
21	Australian Research Council	P	$1,157,631	$2,216,344
22	Swedish Research Council	P	$1,718,730	$2,111,696
23	Research Council of Norway	P	$1,047,945	$2,099,215
24	Doris Duke Foundation	F	$324,000	$1,536,664

Notes: * Rank, based on 2011 totals; P = public-sector funder; C = private-sector funder; P-D = public-sector development agency; F = philanthropic funder.

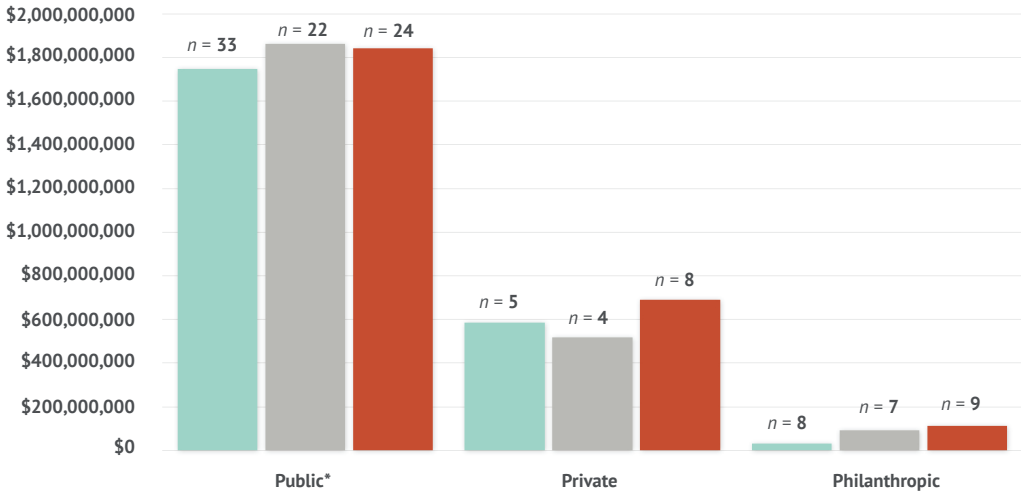
TABLE 2 | Reporting Funders in HIV Treatment R&D (2010–2011)*

#	Funding Institution	Funder Type	2010 Total	2011 Total
25	Swedish International Development Agency (SIDA)	P-D	$966,355	$1,003,360
26	Italian Ministry of Health	P	N/A	$764,863
27	Carlos III Health Institute	P	$894,138	$731,487
28	Company D	C	$507,302	$634,008
29	"Médecins Sans Frontières (Doctors Without Borders)	F	N/A	$424,314
30	Dutch Ministry of Foreign Affairs	P-D	$491,511	$344,825
31	Swiss Agency for Development and Cooperation (SDC)	P	N/A	$295,000
32	Company E	C	$174,000	$151,000
33	Academy of Finland	P	$2,098	$147,770
34	SIDACTION	F	$59,320	$141,970
35	Biogen	C	$0	$137,025
36	Health Research Council of New Zealand	P	$216,608	$123,419
37	Canadian Foundation for AIDS Research	F	$299,250	$120,360
38	Fondazione Cariplo	F	N/A	$50,750
39	Estonian Science Foundation	P	N/A	$36,120
40	Mundipharma	C	N/A	$13,703
41	Pfizer	P	N/A	$10,658
42	Brazilian Ministry of Health	P	$329,646	N/A
	Grand Total		$2,473,057,216	$2,642,740,430

Notes: * Rank, based on 2011 totals; P = public-sector funder; C = private-sector funder; P-D = public-sector development agency; F = philanthropic funder.

2.1 | Investment by Funding Sector

FIGURE 3 | HIV R&D Funding by Sector: 2009–2011



	Public*	Private	Philanthropic
2009	$1,745,956,951	$586,612,844	$30,671,377
2010	$1,863,847,416	$518,180,498	$91,029,301
2011	$1,840,896,680	$690,365,199	$111,478,552

*Including International Development Agencies

In 2011, as in previous years, the majority (70%) of reported HIV treatment R&D funding originated from public-sector funders in the amount of $1.8 billion. Reported private-sector funding amounted to $690 million and accounted for 26% of the collected data on treatment R&D.17 The philanthropic contribution represented 4% of the total at $111 million.

17. Private-sector funding is significantly underreported, since only a few pharmaceutical companies responded to TAG's request for information.

TABLE 3 | Percent Change in Investment of Different Donor Sectors: 2009–2011

Sector	2009	2009 to 2010 % Change	2010	2010 to 2011 % Change	2011	2009 to 2011 % Change
Public *	$1,745,956,951	6.8%	$1,863,847,416	-1.2%	$1,840,896,680	5.4%
Private	$586,612,844	-11.7%	$518,180,498	33.2%	$690,365,199	17.7%
Philanthropic	$30,671,377	196.8%	$91,029,301	22.5%	$111,478,552	263.5%

Note: * Public total includes international development agencies.

While R&D investment experienced steady growth over three years, a 1.2% decrease was experienced in the public sector from 2010 to 2011. This decline is possibly due to the fact that the U.S. government stimulus funding, received by the NIH in 2010 and totaling $47 million, expired that year. Because the NIH is such a significant funder, this large sum offsets the 2010 to 2011 increase in yearly contribution from other public-sector funders (ANRS, the EC, the CDC, OGAC, the Swiss National Science Foundation, the NHMRC, CIDA, and some others). Also of note is that a smaller number of public-sector funders (22 and 24 in 2010 and 2011, respectively, as opposed to 33 in 2009) reported this year, yet large contributions from two U.S. public-sector funders—the CDC and the Office of the U.S. Global AIDS Coordinator (OGAC)—were recorded for 2010 and 2011.

From 2009 to 2010, a 11.7% funding decline was observed in the private sector. Since relatively few companies report data to TAG, the significance of this discrepancy is hard to evaluate. In 2010, TAG was not able to report Company C data, since the company could not provide the exact amount contributed to therapeutic vaccine development.

The most significant increase is observable in the philanthropic sector—263.5% from $30.7 million in 2009 to $111.5 million in 2011. The significant influx of funding from the BMGF caused the sector's threefold increase from the baseline. The foundation is known for cyclical funding and channeling large amounts of funds at the start of grant awards, which results in fluctuating awards year-to-year. The BMGF has a broad portfolio of grants in HIV treatment R&D with a large focus on developing drugs for coinfections—tuberculosis (TB) in particular. In addition to the BMGF, other philanthropic funders (Wellcome Trust, amfAR) increased their contribution in 2011, as can be seen in table 4.

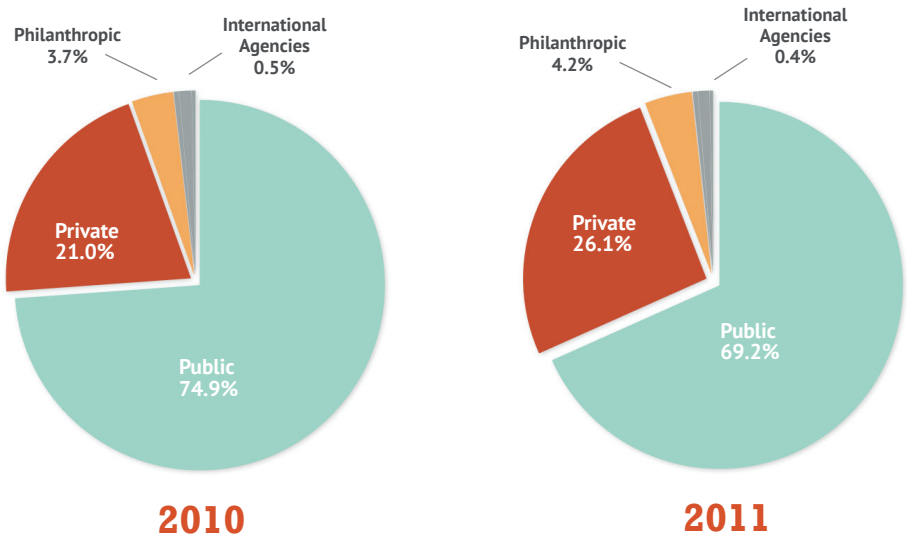
TABLE 4 | **Top 5 Philanthropic Funders: 2010–2011**

#	Funding Institution	2010 Total	2011 Total
1	BMGF	$64,070,683	$78,423,625
2	Wellcome Trust	$19,962,890	$22,515,477
3	Institut Pasteur	$4,261,203	$5,226,180
4	amfAR	$2,051,956	$3,039,211
5	Doris Duke Foundation	$324,000	$1,536,664

In 2012, TAG collected data from nine foundation partners. Six submitted data, and three were reported by other funders. While some of the reporting foundations (amfAR, Institut Pasteur) focus on HIV treatment R&D, others have broader portfolios and invest in different areas of scientific foray. With flagging investment from the public sector, foundation funders potentially have to switch course from pure prevention interventions to investment in treatment R&D.

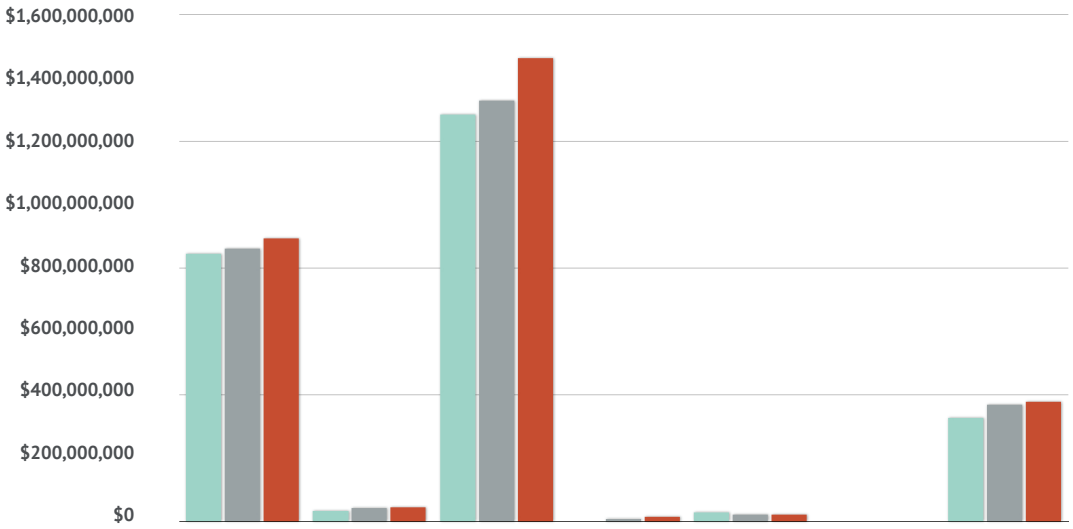
While public-sector donors make up the largest portion of the R&D budget, it is troubling that the overall percent growth of 5.4% from 2009 to 2011 is the smallest in this sector. Public-sector investment increased by 6.8% from 2009 to 2010, but decreased 1.2% from 2010 to 2011. The overall share of public-sector contribution has also decreased from 74.9% of the total (contributed by 33 funders) in 2010 to 69.2% of the total (contributed by 41 funders) in 2011.

FIGURE 4 | **Share of Contribution by Sector: 2010–2011**



2.2 | Investment by Research Area

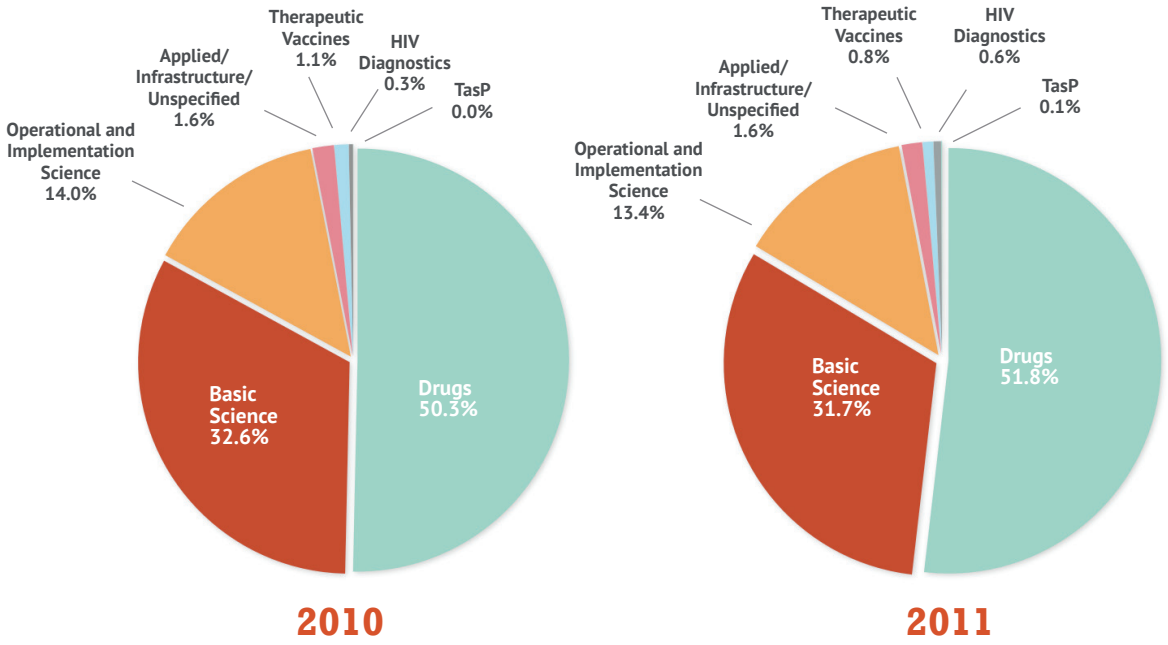
FIGURE 5 | Investment by Research Area: 2009–2011



	Basic Science	Applied/Infrastructure/ Unspecified	Drugs	HIV Diagnostics	Therapeutic Vaccines	TasP	Operational and Implementation Science
2009	$792,360,123	$30,612,268	$1,203,818,202	$2,108,014	$26,846,664	$111,996	$307,383,905
2010	$806,839,484	$40,568,291	$1,244,887,871	$7,792,157	$20,389,280	$591,321	$345,674,615
2011	$838,467,322	$41,182,642	$1,369,976,845	$14,977,906	$20,894,265	$2,137,183	$355,104,269

Investment increased across all research areas with the exception of therapeutic vaccines, where TAG recorded an investment decline since 2009. While the contribution toward development of HIV diagnostics was smallest in all years, the most dramatic increase in year-to-year funding was observed in that area.

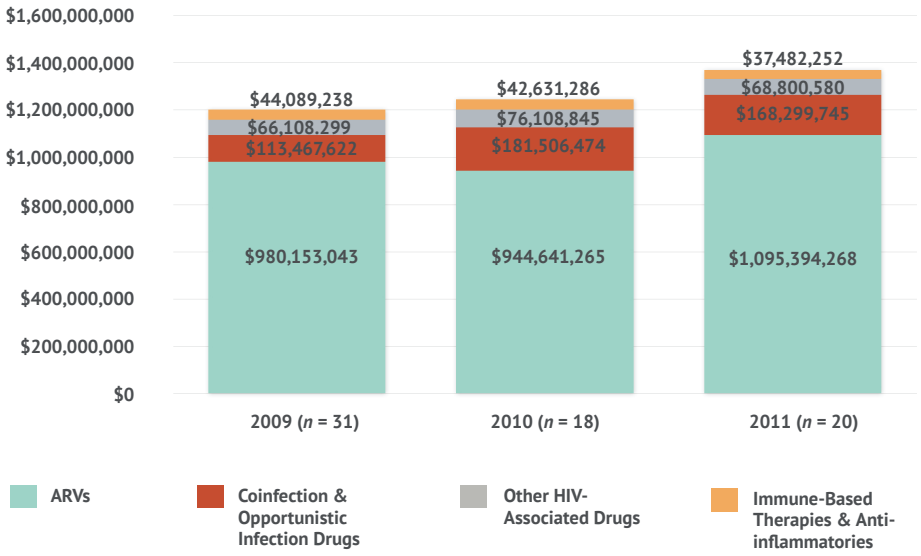
FIGURE 6 | **Percent Investment by Research Area: 2010–2011**



Both in 2010 and 2011, investment in the development of new medications at $1.24 billion and at $1.37 billion, respectively, comprised the largest share of the total. Investment in basic science research was second largest, and the development of new HIV diagnostics and TasP received the lowest amounts from HIV treatment donors.

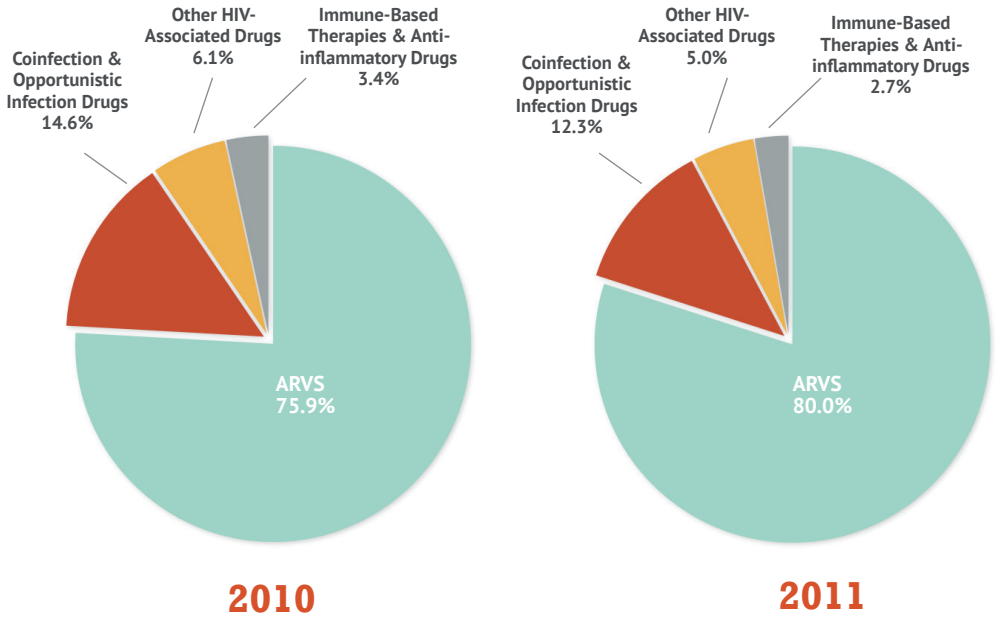
2.3 | Investment in Drug Discovery and Development

FIGURE 7 | **Investment in Drug Discovery: 2009–2011**



Investment in drug discovery increased by 13.8% since 2009 and by 10% from 2010, despite the fact that a larger number of funders reported in this category in 2009 (31 vs. 18 in 2010, and 20 in 2011). The total investment was $1.37 billion in 2011, $1.24 billion in 2010, and $1.2 billion in 2009. The area of research dedicated to developing new ARV medications received the largest amount of funding across all years.

FIGURE 8 | **Investment in Drug Discovery by Subcategory: 2010–2011**



The share of investment in ARV drug discovery was largest in 2011. Drugs for the treatment of coinfections and opportunistic infections were the second largest area of investment.

TABLE 5 | Top 10 Drug Discovery Funders: 2010–2011

2010 Top 10 Drug Discovery Funders			2011 Top 10 Drug Discovery Funders		
1	NIH	$646,142,387	1	Gilead Sciences	$670,800,000
2	Gilead Sciences	$503,340,000	2	NIH	$612,859,296
3	BMGF	$49,949,413	3	BMGF	$39,504,089
4	Japanese Ministry of Health, Labour and Welfare	$12,171,366	4	Japanese Ministry of Health, Labour and Welfare	$10,155,588
5	ANRS	$9,733,885	5	Company A	$9,576,000
6	Company A	$7,845,000	6	ANRS	$8,382,475
7	CIHR	$5,432,351	7	EC	$5,194,419
8	EC	$5,149,628	8	CIHR	$5,073,165
9	Wellcome Trust	$1,361,912	9	Wellcome Trust	$1,906,522
10	UK MRC	$724,808	10	UK MRC	$1,542,174

In 2011, the estimated R&D contribution to ARV development from Gilead Sciences was higher than that of the NIH. As in 2009, Gilead supplied TAG with the company's total R&D investment. To determine the company's investment in ARV development, TAG used the company's Securities and Exchange Commission (SEC) filings, publicly available on the company's website, and pipeline data on ARVs and other non-HIV-related medicines in development by Gilead. Yearly, the company makes over 70% of its profits on the sale of Truvada and Atripla. This large income from ARV drug sales translates into a substantial portfolio of new ARV development. In 2010 and 2011, Gilead moved three ARVs—QUAD (already approved by the FDA as Stribild and pending approval in Europe), and the single agents elvitegravir (an integrase inhibitor) and cobicistat (a pharmacokinetic booster), both also submitted to regulators.

Along with development of new ARV drugs, the company also invests in development of medicines for treatment of viral hepatitis, diabetes drugs, and oncological agents. Other nonviral disease medicines, including ranolazine for cardiovascular disease and diabetes, aztreonam for cystic fibrosis, and a leukemia agent, also moved into phase II and III trials in those years. Considering that phases II and III of drug development are the most costly, and that the company's portfolio was split among ARV and nonviral medications in 2010 and 2011, TAG estimated Gilead's contribution to ARV development at 60%.

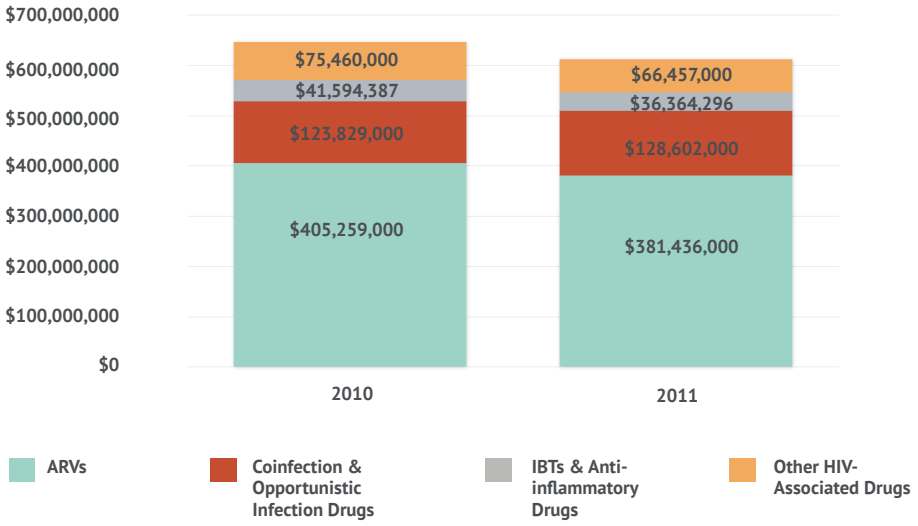
In 2012, only five private-sector funders reported directly to TAG; investments from three additional companies were reported by other funders. Thus, pharmaceutical industry

contribution to drug discovery and development is underrepresented in this report. Later in the report, in section 2.10, TAG provides a detailed pharmaceutical-sector pipeline to ensure discourse on the issue.

Development of new compounds for treatment of HIV, use of existing and new medications for attacking HIV reservoirs, and studies supporting research of HIV gene therapy and stem cell engineering for the treatment of HIV were funded by donors in the ARV development category in 2010 and 2011.

Along with Gilead and, potentially, other private-sector investors, the NIH supports an extensive portfolio of research grants in drug discovery and consistently remains a leading donor in this area.

FIGURE 9 | **NIH Investment in Drug Discovery: 2010–2011**



The NIH drug discovery portfolio focuses on research that investigates new targets critical for HIV replication, discovery of new therapeutics, and evaluation of the effectiveness of these new medications in lab cell cultures and animal models.

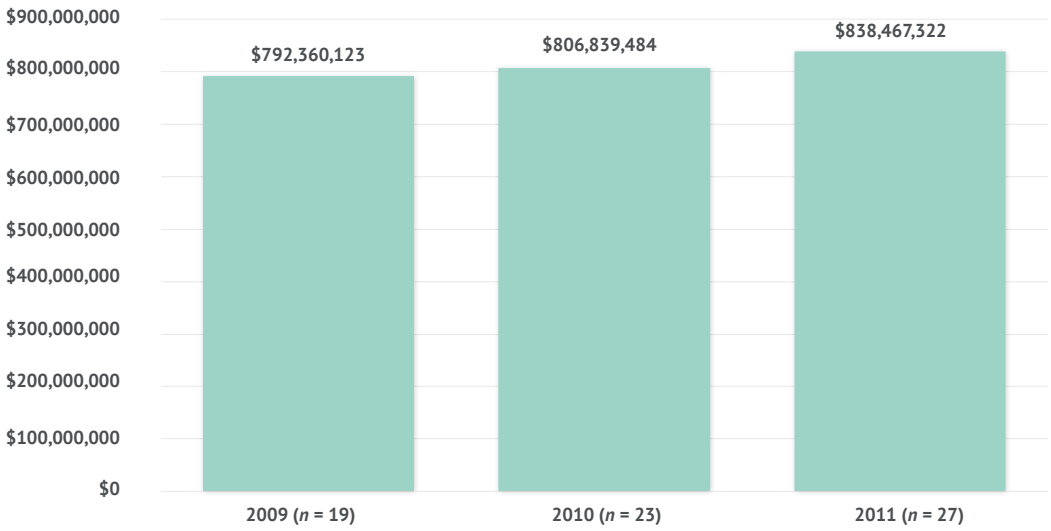
After the NIH, the BMGF was the largest funder of development of drugs for coinfection and opportunistic infections. In 2010, 100% of the foundation's portfolio in drug discovery went to that area. A large portfolio of grants investigating new medications and strategies for TB treatment among people with HIV comprise the foundation's commitment.

Along with new TB treatment regimens, donors investing in coinfection drugs supported research in treatment of *Cryptococcus* and fungal infections associated with HIV, Kaposi's sarcoma, hepatitis B and C, and toxoplasmosis.

TAG accounted for investment in HIV-associated cancers and neurological diseases under the "other drugs" category and immune reconstruction approaches under the "IBT" category.

2.4 | Investment in Basic Science

FIGURE 10 | **Investment in Basic Science: 2009–2011**



Investment in basic science has grown steadily and increased by 5.8% since 2009, and 3.9% since 2010. More funders reported investment in this category in 2011 than in other years: 27 in 2011, 23 in 2010 and 19 in 2009. This increased donor interest could be the result of excitement over cure research and some other areas of scientific promise.

Viral entry, interactions, and survival have been the focus of basic science research since the discovery of HIV. In recent years, basic science research has narrowed in on several promising topics. High on the priority list were projects dedicated to viral latency and eliminating viral reservoirs. HIV hides in reservoirs in various parts of the human body, thus maintaining a latent status in the infected person. Identifying and characterizing reservoirs and learning ways of extracting the virus from these cell and tissue populations, as well as understanding chemical and biological pathways used by the virus to establish latency, could provide clues to better therapies and eventually a cure. Development of better therapies was also the goal of projects investigating potential HIV inhibitors responsible for virus assembly (Vif-APOBEC3G) and virus uncoating (TRIM5alpha).

Additional research in basic science included the studies of viral entry into the body. Several projects focused on dendritic cells—forming blocks of the human immune system that assist T cells with recognizing antigens—and their role in HIV pathogenesis. Studies seeking to unearth how HIV interacts with other pathogens, particularly hepatitis and TB, were also numerous.

TABLE 6 | Ranked Investment in Basic Science: 2011

#	Funding Institution	2011 Total
1	NIH	$744,649,000
2	BMGF	$13,775,398
3	CIHR	$11,663,820
4	UK MRC	$11,627,606
5	ANRS	$10,989,586
6	EC	$8,344,912
7	Wellcome Trust	$8,041,630
8	NHMRC of Australia	$7,357,968
9	Swiss National Science Foundation	$5,330,626
10	Japanese Ministry of Health, Labour and Welfare	$3,937,719
11	Institut Pasteur	$2,866,562
12	amfAR	$2,070,432
13	Swedish Research Council	$1,923,856
14	Doris Duke Foundation	$1,293,664
15	Australian Research Council	$1,214,108
16	Italian Ministry of Health	$764,863
17	Research Council of Norway	$678,648
18	SIDA	$652,800
19	Carlos III Health Institute	$625,766
20	Academy of Finland	$147,770
21	SIDACTION	$141,970
22	Biogen	$137,025
23	Canadian Foundation for AIDS Research	$120,360
24	Fondazione Cariplo	$50,750
25	Estonian Science Foundation	$36,120
26	Mundipharma	$13,703
27	Pfizer	$10,658

The NIH is the top investor in basic science research, providing 92% and 89% of the global contribution to the area in 2010 and 2011, respectively. CIHR, the BMGF, and the UK Medical Research Council (UK MRC) have been among the top investors, and contributions from these institutions grew from 2010 to 2011.

In the U.S., the NIH, BMGF, the Doris Duke Foundation, and amfAR supported basic science projects in 2010 and 2011, with the NIH funding 99.4% of the total recorded U.S. basic science budget in 2010 and 97.8% in 2011.

TABLE 7 | **U.S. Donors in Basic Science: 2010–2011**

#	Funding Institution	2010 Total	% of Total	2011 Total	% of Total
1	NIH	$744,649,000	99.4%	$744,649,000	97.8%
2	BMGF	$3,241,947	0.4%	$13,775,398	1.8%
3	amfAR	$1,064,559	0.1%	$2,070,432	0.3%
4	Doris Duke Foundation	$324,000	0.0%	$1,293,664	0.2%
	Total	$749,279,506	92.9%	$761,788,494	90.9%

Because of the large NIH investment, the U.S. is the leading donor in the area of basic science. However, contribution from donors in other parts of the world grew in 2011.

FIGURE 11 | **Basic Science Contribution by Country: 2010**

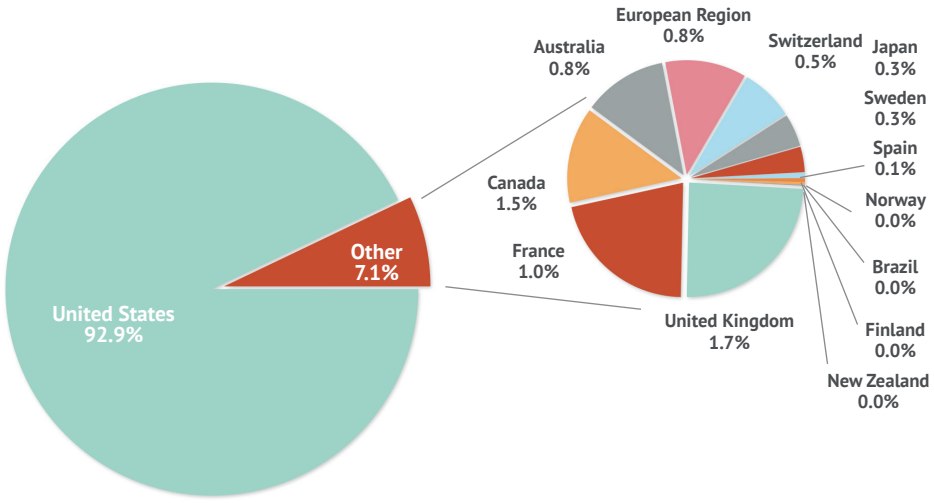
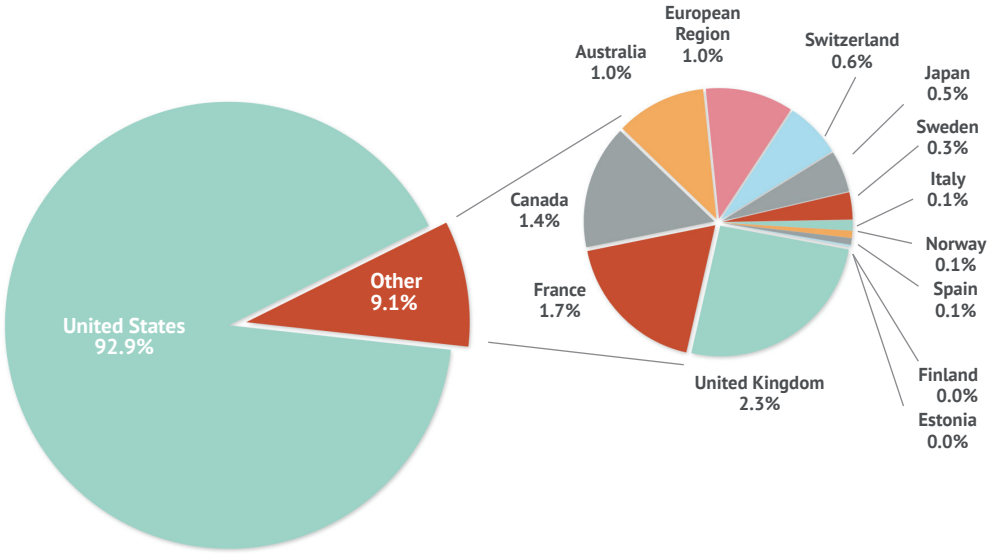


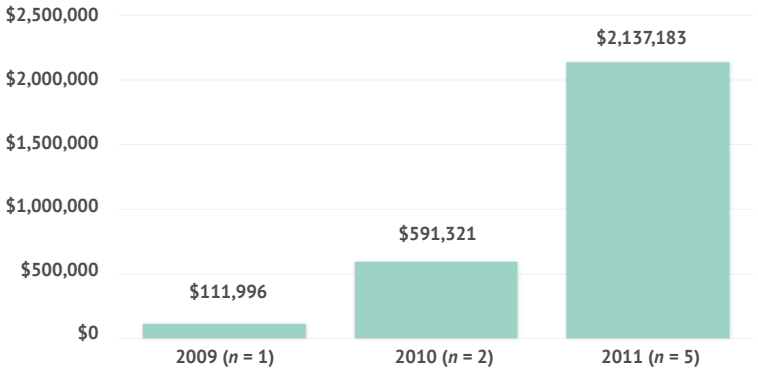
FIGURE 12 | **Basic Science Contribution by Country: 2011**



2.5 | Investment in Treatment as Prevention (TasP)

In response to the potential of TasP in reducing infection on the individual *and* community level, there is evidence of funders scaling up investment in this area.

FIGURE 13 | Investment in TasP: 2009–2011



Investment in TasP research increased 20-fold since 2009 and almost quadrupled since 2010. Still, numbers reported by TAG are not representative of the actual investment in the area. In all years, TAG recorded investment in TasP research among very few funders—a total of two in 2010 and five in 2011.

TABLE 8 | TasP Funders: 2010–2011

TasP Funders	2010 Total	2011 Total
ANRS	$0	$1,762,983
BMGF*	$460,795	-$72,790
CDC	$0	$146,242
CIHR	$130,526	$95,434
NHMR of Australia	$0	$205,315
Total	$591,321	$2,137,183

Note: * The Bill & Melinda Gates Foundation reported negative funding on a grant that carried over from 2010 to 2011.

There is evidence that other agencies are investing more substantive sums of money in this field. For example, in 2010 and 2011, the NIH reported investing $67,734,000 and $65,064,000, respectively, in the area of therapeutics as prevention.[18] From the agency's public reporting it is difficult to estimate which portion of the funding goes to TasP and which to PrEP, so in an effort to provide the most accurate data, TAG does not report these numbers. However, table 9 below provides a summary of ongoing efforts in TasP research supported by NIH and other funders.

TABLE 9 | **TasP Studies in 2010 and 2011**[19]

Study Name	TasP Intervention	Conducting Institution(s)	Supporting Institution(s)	Timeline
Sustainable East Africa Research in Community Health (SEARCH) Collaboration	ART for all CD4 counts	University of California, San Francisco, International Development Research Centre (IDRC), Kenya Medical Research Institute (KEMRI)	NIAID	2010 onward
An HIV Prevention Program for Mochudi, Botswana	ART for high viral loads	Harvard School of Public Health	NIAID	2009–2013
Iringa Combination Prevention Trial	ART for CD4 counts <340 cells/mm^3	Johns Hopkins School of Public Health	USAID	2011 onward
PopART (HPTN 071)	ART for all CD4 counts	HIV Prevention Trials Network	OGAC, NIH, BMGF	2011 onward
Médecins Sans Frontières (MSF) TasP study	Immediate ART initiation after diagnosis, regardless of CD4 count	MSF	MSF	2011 onward
Impact of Immediate vs. World Health Organization Recommendations–Guided ART Initiation on HIV Incidence—Feasibility Phase (TasP)	Immediate ART initiation after diagnosis, regardless of CD4 count	Africa Centre for Health and Population Studies	ANRS	2011 onward
Strategic Timing of Antiretroviral Treatment (START)	ART initiation at CD4 count >500 cells/mm^3	University of Minnesota	NIH, NIAID, Abbott, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Merck, Tibotec	2009–2015

18. National Institutes of Health. Office of AIDS Research trans-NIH AIDS research budget: FY 2013 budget. Accessed December 29, 2012, at http://www.oar.nih.gov/budget/pdf/2013_OARTransNIHAIDSResearchBudget.pdf.

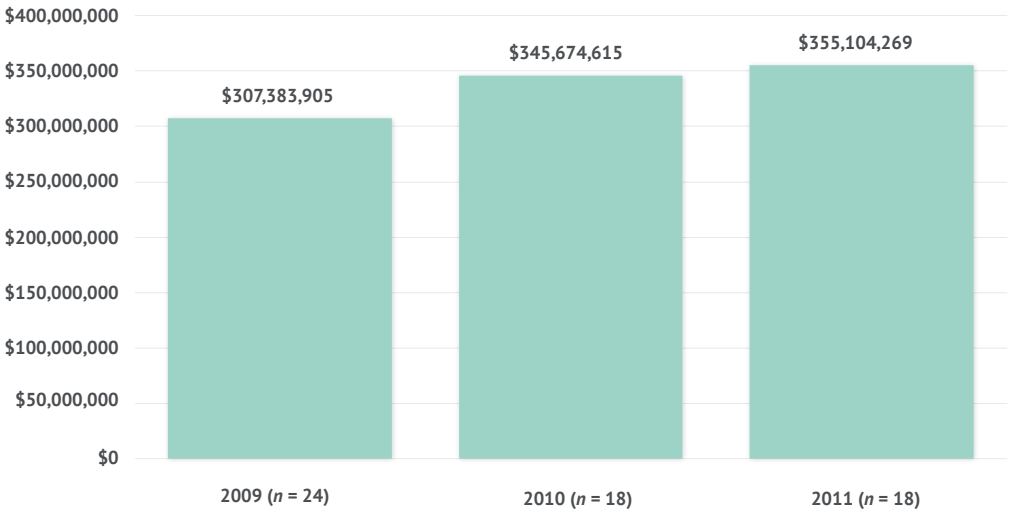
19. Data for this table have been obtained using information in Granich R. et al. Antiretroviral therapy in prevention of HIV and TB: update on current research efforts. Curr HIV Res. 2011 Sep;9(6):446–469, and publicly available information on ongoing trials at http://www.clinicaltrials.gov.

The majority of studies described in table 9 include TasP in a broader spectrum of interventions; thus, it might be difficult for funders and implementers to report on separate funding streams. Additional studies are also being conducted in the U.S. with support from various academic institutions—the majority of these trials target the "seek, test, and treat" approach of treatment initiation immediately after testing. The studies focus on vulnerable populations of injection drug users and incarcerated individuals.[20]

With so few funders reporting on TasP funding and NIH only planning to increase investment in the area of therapeutics as prevention by 0.3% from 2012 to 2013,[21] more donors need to turn their attention to promising research in TasP.

2.6 | Investment in Operational and Implementation Science

FIGURE 14 | **Investment in Operational and Implementation Science: 2009–2011**



Investment in operational research grew steadily over the last three years with a 15.5% increase from 2009 to 2011 and a 2.7% increase from 2010 to 2011. In 2011 and 2010, a smaller number of funders (18 vs. 24 in 2009) reported in this category. However, investments from large public-sector funders in the U.S. were captured in those years, providing for a higher total. This growth could also potentially be explained by growing interest in ART efficiency and safety as more individuals begin receiving treatment.

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20. Granich R et al. Antiretroviral therapy in prevention of HIV and TB: update on current research efforts. Curr HIV Res. 2011 Sep;9(6):446–69.

21. National Institutes of Health. Office of AIDS Research Trans-NIH AIDS Research Budget. Fiscal Year 2013. Accessed October 25, 2012, at http://www.oar.nih.gov/budget/pdf/2013_OARTransNIHAIDSResearchBudget.pdf.

Investigation in operational and implementation science supports studies monitoring ART resistance, side effects, and interactions with other drugs, particularly those used for treatment of coinfections. The BMGF, the Dutch Ministry of Foreign Affairs (through amfAR), the CIHR, and OGAC all supported studies in these areas. OGAC also supported multiple evaluations and cost-effectiveness studies of various treatment interventions. The CDC supported several large studies monitoring HIV testing technologies and along with UK MRC, invested in studies striving to understand the course of HIV disease in the era of ART. The Wellcome Trust supported research looking into the effects of ART on pregnancy and childbirth, and the trust and UK MRC supported several pediatric ART studies.

TABLE 10 | Funders in Operational Research: 2010–2011

Funders in Operational and Implementation Science 2010			Funders in Operational and Implementation Science 2011		
1	NIH	$275,098,000	1	NIH	$275,098,000
2	UK MRC	$16,775,832	2	UK MRC	$18,492,408
3	OGAC	$14,121,687	3	OGAC	$13,244,944
4	Wellcome Trust	$9,515,491	4	BMGF	$10,062,434
5	CIDA	$5,682,269	5	CDC	$9,842,556
6	CDC	$4,267,419	6	Wellcome Trust	$9,253,485
7	DFID	$4,160,928	7	Swiss National Science Foundation	$4,309,215
8	ANRS	$3,669,087	8	CIDA	$4,232,931
9	Swiss National Science Foundation	$3,230,485	9	CIHR	$3,329,125
10	BMGF	$3,152,474	10	ANRS	$2,656,374
11	CIHR	$3,058,791	11	DFID	$2,304,947
12	EC	$653,571	12	EC	$776,785
13	Dutch Ministry of Foreign Affairs	$491,511	13	SIDA	$350,560
14	amfAR	$450,542	14	Dutch Ministry of Foreign Affairs	$344,825
15	NHMRC of Australia	$400,620	15	NHMRC of Australia	$324,670
16	SIDA	$342,355	16	Doris Duke Foundation	$243,000
17	Carlos III Health Institute	$320,933	17	Swedish Research Council	$187,840
18	Swedish Research Council	$282,620	18	amfAR	$50,171

The NIH was the largest investor in operational research in 2010 and 2011, with the UK MRC and OGAC also contributing substantive amounts both years.

Global Fund Investment in Operational Research

As one of the major global donors in HIV prevention and treatment, the Global Fund to Fight AIDS, Tuberculosis and Malaria contributes a significant amount of funding to evaluate and assess HIV treatment programs.

The Global Fund defines operational research as follows:

Any research producing practically-usable knowledge (evidence, findings, information, etc.) which can improve program implementation (e.g., effectiveness, efficiency, quality, access, scale-up, sustainability) regardless of the type of research (design, methodology, approach) falls within the boundaries of operations research.

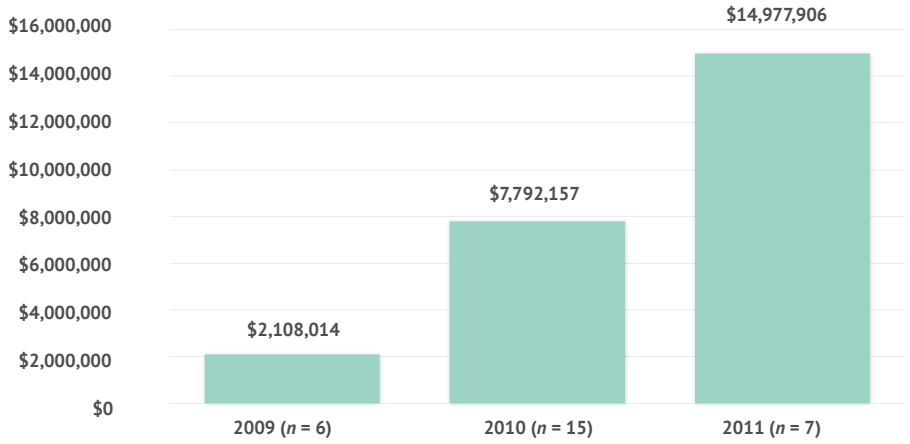
The Global Fund supports social, behavioral, and epidemiological research, and as it relates to TAG's resource-tracking efforts, the fund also invests in the assessment of treatment programs, monitoring of treatment and treatment resistance, and the participation of persons living with HIV/AIDS (PLWHAs) in treatment effectiveness research. Operational and implementation research is supported through country-led proposals and as a part of a proposed monitoring and evaluation framework. Thus, it is difficult for the fund to parse out this investment—it comes as a part of a general operational support/project monitoring funding stream with exact spending, documented only at the country level. Because of this, TAG was unable to track the Global Fund's investment, but we are eager to highlight the agency's investment in operational research.

Here, several examples are listed of the Global Fund's support for programs related to HIV treatment R&D:

- Lesotho Round 8 Grant: Annual cohort survey of survival rates for PLHWAs on treatment regimens and study of ART resistance.
- Moldova and Ukraine Rounds 8–9: Monitoring of ART treatment resistance
- Burkina Faso Round 6 Grant: Monitoring of TB and antimalarial drugs on ART treatment outcomes and adherence

2.7 | Investment in HIV Diagnostics

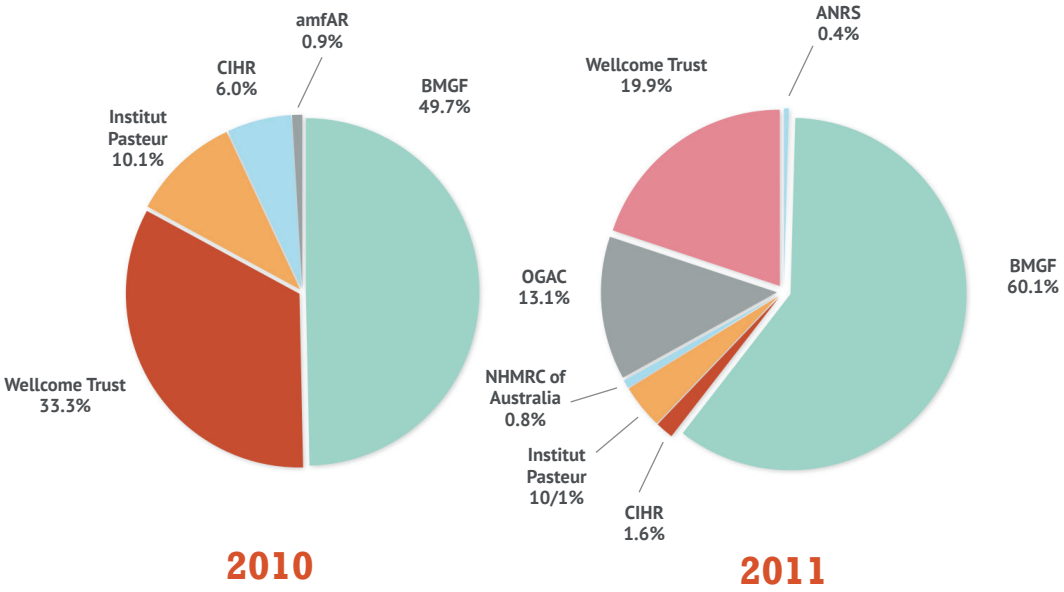
FIGURE 15 | Investment in HIV Diagnostics: 2009–2011



Investment in HIV diagnostics R&D has increased sixfold since 2009. In 2009, TAG did not originally include this research category in the resource-tracking survey. Only after reviewing the data and realizing that several funders reported funding activity in HIV diagnostics did TAG decide to begin tracking this important work. In 2012, TAG requested specific reporting on diagnostics development encouraging funders to include this investment. The number of funders reporting in this category was only slightly higher in 2011—seven as opposed to five in 2010 and six in 2009—but the large increase in investment is evidence of this area's importance.

Funders reported investment in new diagnostic tools that would simplify and accelerate HIV testing for low-resource settings, as well as improve testing strategies to ensure timely ARV initiation. For example, the BMGF supported development of two new rapid point-of-care tests for measuring CD4+ T cells in people living with HIV in resource-poor settings, as well as an early infancy HIV test. In turn, the Wellcome Trust invested in the development of affordable tests for HIV and sexually transmitted illnesses through a product development partnership, and in research investigating the use of low-cost dried blood spot testing for determining levels of ART in HIV-positive individuals to asses ART adherence and resistance.

FIGURE 16 | **HIV Diagnostics Funders: 2010–2011**

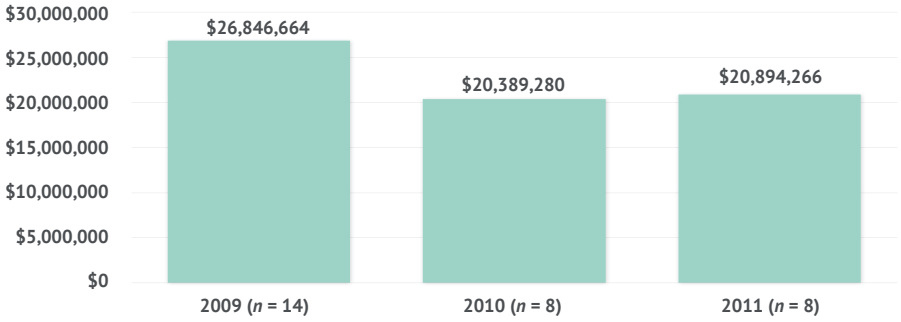


In 2010 and 2011, the BMGF was the leading donor in HIV diagnostics R&D.

2.8 | Investment in Therapeutic Vaccines

The resurgence of hope in cure research has reinvigorated the field of therapeutic vaccine development. Two recent studies[22,23] have noted viral-load reduction while testing vaccine candidates. In 2012, 25 therapeutic vaccine compounds were in the clinical pipeline, however, with regard to funding, TAG documented a decline in the overall contribution to the field—a 22.2% reduction in funding from 2009 to 2011.

FIGURE 17 | Investment in Therapeutic Vaccines: 2009–2011

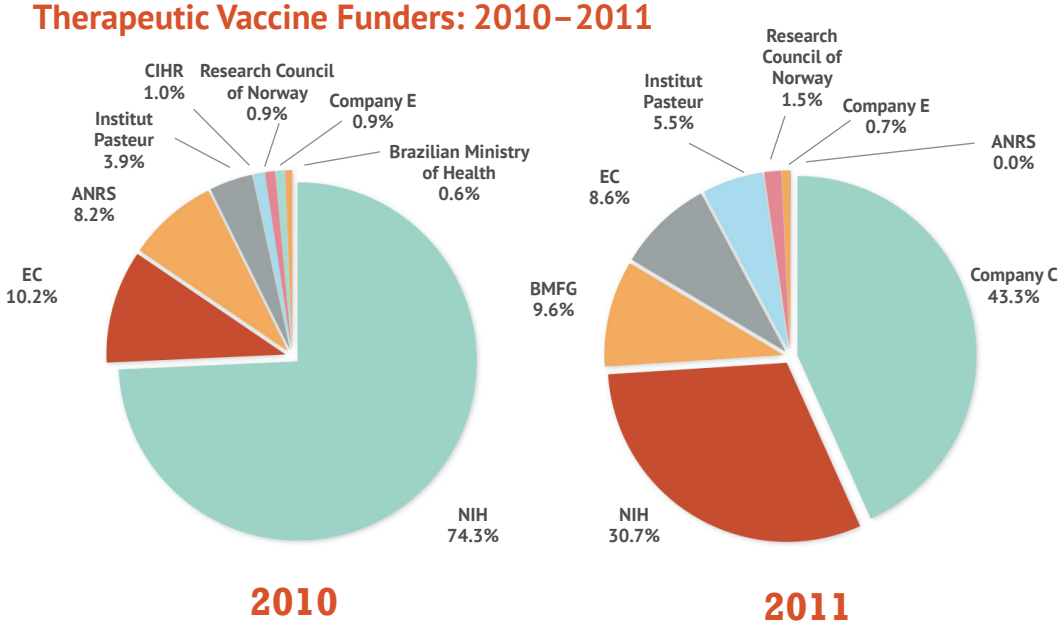


While in 2010 the NIH was the largest funder in therapeutic vaccine development, in 2011 Company C made the largest contribution. This indicates the overall trend in the corporate sector dominating in such areas as ART and vaccine development. In fact, of the current 25 therapeutic vaccine pipeline candidates, the grand majority receives private-sector support. Hence, TAG concludes that the 2010 and 2011 investment figures in therapeutic vaccines are woefully underreported.

22. Vardas E, Stanescu I, Leinonen M, et al. Indicators of therapeutic effect in FIT-06, a phase II trial of a DNA vaccine, GTU(®)-Multi-HIVB, in untreated HIV-1 infected subjects. Vaccine. 2012 Jun 8;30(27):4046–54.

23. Rockstroh JK, Pantaleo G, Pollard R, et al. A phase II, randomized, double-blind, multicenter, immunogenicity study of Vacc-4x versus placebo in patients infected with HIV-1 who have maintained an adequate response to ART (Abstract #TULBPE028). Poster session presented at: 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention; 2012 July 17–20; Rome. Accessed October 12, 2012, at http://pag.ias2011.org/abstracts.aspx?aid=4727.

FIGURE 18 | **Therapeutic Vaccine Funders: 2010–2011**



2.9 | European and Developing Countries Clinical Trials Partnership (EDCTP) Data

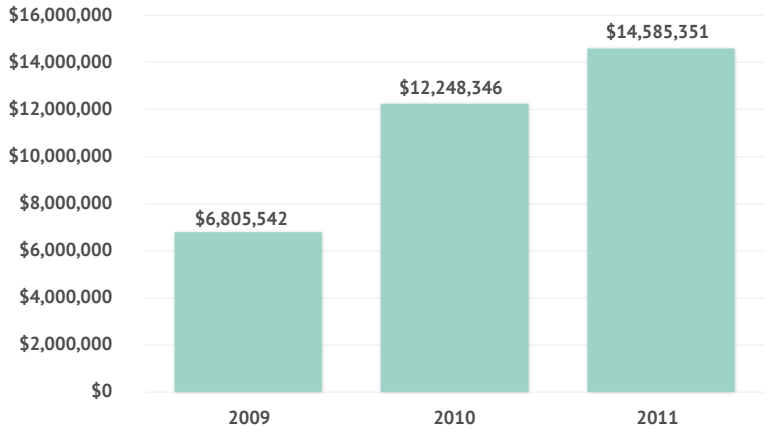
The EDCTP was created in 2003 as a European response to HIV, TB, and malaria. The partnership seeks to accelerate development of new drugs, vaccines, microbicides, and diagnostics against the three diseases through support of phase II and III clinical trials in sub-Saharan Africa. The EDCTP currently unites 14 European Union member states (Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom), as well as Norway and Switzerland. Combining resources from these countries, the EDCTP supports activities aimed at eradicating the three diseases.[24] TAG collects annual data on EDCTP's investment in HIV treatment R&D via its publicly available website.

Some countries that contribute to the EDCTP have several portfolios as HIV funders, others direct the majority of their HIV research funding to the EDCTP. For example, in its report to TAG, the Dutch Ministry of Foreign Affairs confirmed that 3% of its 2011 funding directed at global health research was allocated to the EDCTP. The agency also reported contribution to other large product development partnerships (PDPs). This could indicate a particular trend among E.U. members of supporting R&D via large PDPs. The Swedish International Development Cooperation Agency also reported significant contribution to EDCTP that far exceeds the amount the agency contributed to the field of HIV treatment R&D documented in this report.

24. European and Developing Countries Clinical Trials Partnership. Joint Programme of the Action. Accessed November 29, 2012, at http://www.edctp.org/fileadmin/documents/about_edctp/JP_public_version.pdf.

TAG carefully analyzes EDCTP data and E.U. member states submissions to avoid double counting. Since the EDCTP is a funding recipient, the funding described below is not included in any of the annual funding totals. The chart below represents the EDCTP's investment in trials relevant to HIV treatment R&D between 2009 and 2011. EDCTP investment more than doubled in 2011 compared to the baseline year and grew 57% between 2010 and 2011.

FIGURE 19 | **EDCTP Contribution to HIV Treatment R&D Trials: 2009–2011**



2.10 | Private-Sector Pipeline

Out of 171 surveys circulated by TAG, 41 were sent to private-sector companies. Only 5 pharmaceutical companies submitted completed surveys, 3 reported no investment, and 1 company declined participation. Five other companies responded to the initial request, but ended up not providing data. The remaining 27 industry representatives produced no response.

To better understand the private sector's activity in HIV treatment R&D, TAG conducted extensive desktop research and found a total of 14 new ART compounds in the pipeline in 2011.[25] Two new compounds went into the pipeline in 2011 and another 11 compounds were in phase II or phase III trials (these are the phases that are most financially taxing, and thus require a substantial investment).

Desktop research also found pharmaceutical-sector investment in the development of rapid and more efficient HIV diagnostics. Two fourth-generation HIV diagnostic tests were approved by the U.S. Food and Drug Administration (FDA) in 2010 and 2011.[26,27] Both are assays that allow viral detection in the acute earlier stages of infection. One was designed by Abbott Laboratories and the other by Bio-Rad Laboratories.

Considering the significant pharmaceutical-sector investment in various research areas, lack of reporting provides for a large gap in the reported HIV treatment R&D funding total. In figure 20, TAG traces the pharmaceutical ART pipeline to demonstrate the scale of the sector's investment activity.

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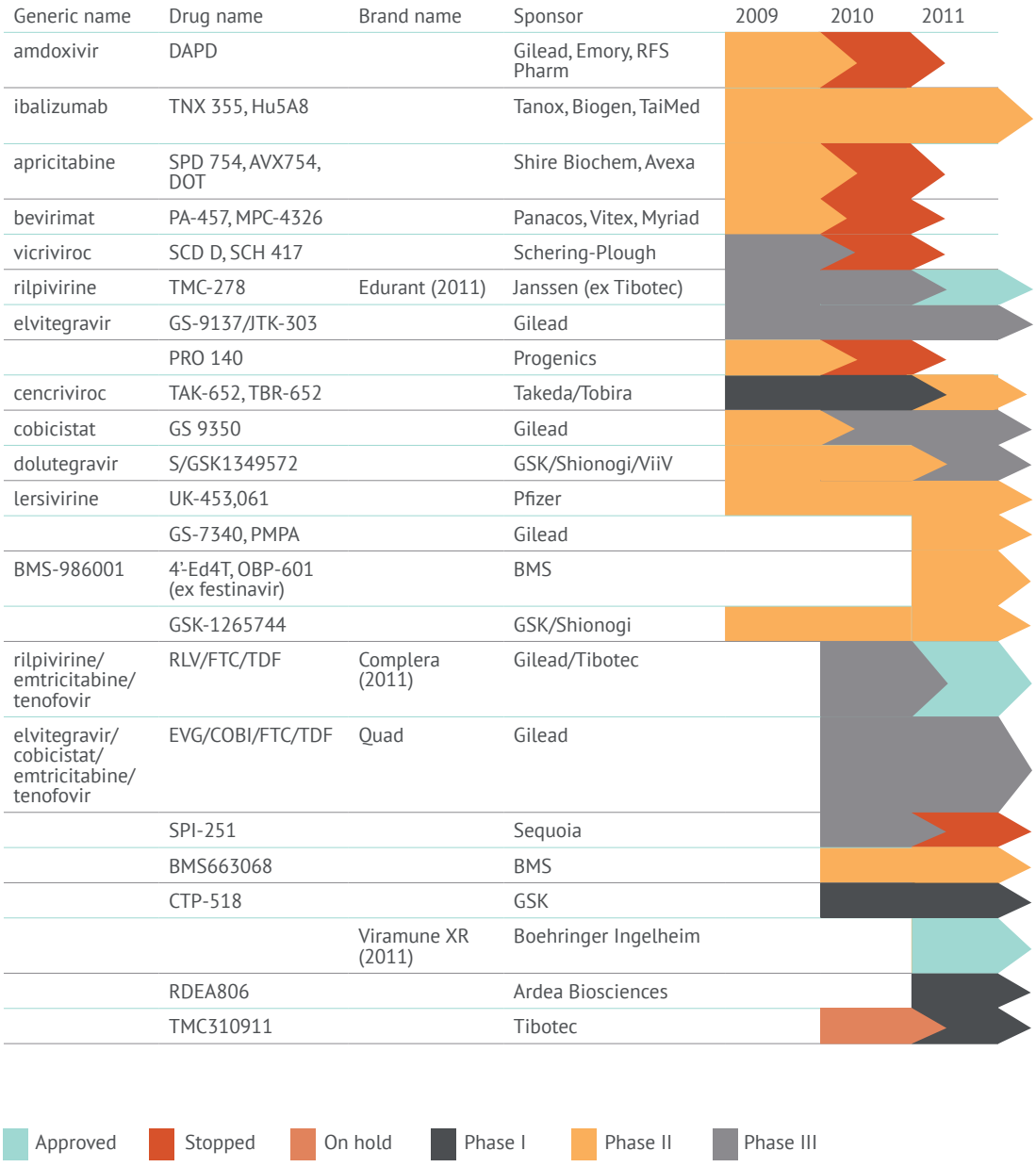
25. Collins S. The antiretroviral pipeline. 2012 Pipeline Report. New York: Treatment Action Group, 2012. Accessed December 29, 2012, at http://www.pipelinereport.org/toc/arv.

26. U.S. Food and Drug Administration. Fourth Generation HIV Diagnostic Test Approved, permitting earlier detection of infection. Accessed November 12, 2012, at http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm216409.htm.

27. U.S. Food and Drug Administration. Approval of 2nd fourth generation HIV diagnostic test for earlier detection of infection. Accessed November 12, 2012, at http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm272914.htm.

FIGURE 20 | **Pharmaceutical Sector ART Pipeline: 2009–2011**

Generic name	Drug name	Brand name	Sponsor
amdoxivir	DAPD		Gilead, Emory, RFS Pharm
ibalizumab	TNX 355, Hu5A8		Tanox, Biogen, TaiMed
apricitabine	SPD 754, AVX754, DOT		Shire Biochem, Avexa
bevirimat	PA-457, MPC-4326		Panacos, Vitex, Myriad
vicriviroc	SCD D, SCH 417		Schering-Plough
rilpivirine	TMC-278	Edurant (2011)	Janssen (ex Tibotec)
elvitegravir	GS-9137/JTK-303		Gilead
	PRO 140		Progenics
cencriviroc	TAK-652, TBR-652		Takeda/Tobira
cobicistat	GS 9350		Gilead
dolutegravir	S/GSK1349572		GSK/Shionogi/ViiV
lersivirine	UK-453,061		Pfizer
	GS-7340, PMPA		Gilead
BMS-986001	4'-Ed4T, OBP-601 (ex festinavir)		BMS
	GSK-1265744		GSK/Shionogi
rilpivirine/ emtricitabine/ tenofovir	RLV/FTC/TDF	Complera (2011)	Gilead/Tibotec
elvitegravir/ cobicistat/ emtricitabine/ tenofovir	EVG/COBI/FTC/TDF	Quad	Gilead
	SPI-251		Sequoia
	BMS663068		BMS
	CTP-518		GSK
		Viramune XR (2011)	Boehringer Ingelheim
	RDEA806		Ardea Biosciences
	TMC310911		Tibotec



2.11 | Discussion

The field of HIV treatment R&D remains dynamic, with new challenges constantly arising on the scientific frontier and viral eradication strategies coming tantalizingly within scientific reach. As evidenced by the data in this report, significant contributions are being made to HIV treatment R&D. Still, with major funders, such as the NIH, the UK MRC, the CIHR, and others flatlining or decreasing funding, the field could be faced with a situation in which discovery begins to outpace available resources. Such a scenario would be unacceptable and unethical at a time when TasP effectiveness and the opportunity for a cure promise a significant reduction in the number of new HIV infections and complete viral eradication.

Furthermore, in order to achieve the goal set forth in the 2011 *Political Declaration on HIV/AIDS* that calls for placing 15 million people on treatment by 2015, cheaper, less toxic medications will be in high demand. Despite a heightened number of people on treatment reported in 2011, in the same year only 8 million people in low- and middle-income countries were receiving ART, while another 7 million who were medically eligible to start treatment, were not accessing it.[28] This 46% discrepancy can be eliminated if cheaper, more effective regimens are introduced. In the United States—the country with the largest HIV budget—2,000 patients were on a waiting list to receive federally subsidized ART in 2011. Additionally, with early ART initiation indicated as one of the single most effective preventive interventions, access to ART, must be expanded further.

Simpler, more efficient ART formulations are in high demand, but their costs are still prohibitive for the majority of those in need of treatment. In a recent study, combination ART drugs taken once daily were shown to be more effective for ensuring patient adherence than multiple pills that have to be taken throughout the day.[29] Gilead—the only large pharmaceutical company that reported to TAG—dominates the HIV medication market producing the only three currently available once-daily combination formulations and two NNRTIs. Gilead/BMS's Atripla costs over $20,000 per year to U.S. patients.[30] As recently as November of 2012, the FDA issued a "tentative" approval of the generic

28. UNAIDS. Together we will end AIDS. Accessed December 1, 2012, at http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/JC2296_UNAIDS_TogetherReport_2012_en.pdf.

29. Sax PE, Meyers JL, Mugavero M, Davis KL. Adherence to antiretroviral treatment and correlation with risk of hospitalization among commercially insured HIV patients in the United States. PLoS One. 2012;7(2):e31591. doi: 10.1371/journal.pone.0031591.

30. Pricing can be obtained online from various pharmacies and varies from $1,800 to over $2,000 for a monthly dosage.

version of Atripla for PEPFAR to purchase and use in countries where the agency supports treatment programs.[31] Some sources estimate this generic formulation to cost $200 per patient per year.[32]

Gilead is also developing a prodrug version of tenofovir, which could be more potent and less expensive. The prodrug—GS-7340—could prove to be a cost-effective replacement for tenofovir, but it's not yet clear whether the drug will have lower toxicity than tenofovir.[33] Two long-lasting drugs are being investigated by ViiV, among them a once-monthly injectable formulation. If they become widely available, these medications could help bring a dramatic scale-up of treatment and TasP that is urgently needed to halt the epidemic.

However, the increased availability of generics and the drive to produce simpler and long-lasting drug formulations may be resulting in a smaller number of innovator companies (in recent years, Boehringer Ingelheim, Pfizer, and Roche have each downsized or eliminated their HIV R&D departments). Still, the combined brand-name and generic HIV medication market was valued at $11.3 billion in 2010 and is expected to reach $11.8 billion in 2011 and $14.1 billion in 2016.[34] This projected growth is not a likely indicator of single-pill combination ART becoming financially accessible for the purposes of treatment and prevention. However, this decade will see a wave of patent expiries on drugs licensed in the late 1990s and early 2000s, enabling some combinations to come down drastically in price.

2.12 | Top 10 Funders in HIV Treatment R&D: 2011

The National Institutes of Health (NIH)

The NIH is the largest public global investor in HIV research. For 2010 and 2011 its contribution is almost twice that of reporting corporate funders. The NIH supports projects that involve basic science, prevention methodologies, drug development, and social and behavioral research, as well capacity building for HIV research dissemination.

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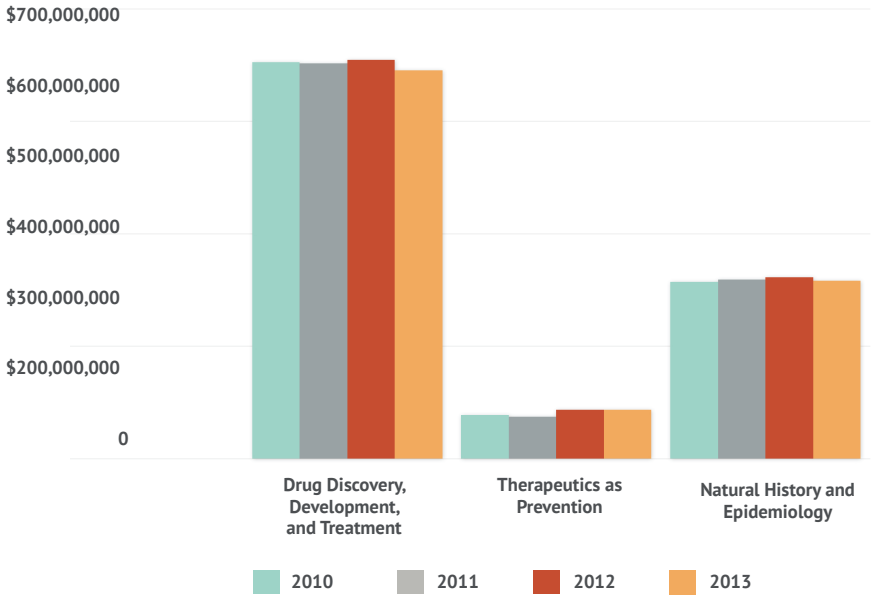
31. U.S. Food and Drug Administration. International programs. Accessed December 18, 2012, at http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119231.htm.
32. Sanders B. The high cost of high prices for HIV/AIDS drugs and the Prize Fund alternative: opening statement of Chairman Sanders Subcommittee on Primary Health and Aging hearing. Accessed December 18, 2012, at http://www.sanders.senate.gov/newsroom/news/?id=c8d9b29a-723f-4f29-b4e1-78c61c99a35f.
33. Ryom L; the D:A:D Study Group. Exposure to ARV and the risk of renal impairment among HIV+ persons with normal baseline renal function: the D:A:D study (Abstract 865). Poster session presented at: 19th Conference on Retroviruses and Opportunistic Infections; 2012 March 5–8; Seattle, WA. Accessed December 15, 2012, at http://www.retroconference.org/2012b/Abstracts/45437.htm.
34. BCC Research. The Global Market for AIDS/HIV testing and treatment. Accessed December 10, 2012, at http://www.bccresearch.com/report/aids-hiv-testing-treatment-market-phm058a.html.

To pace discovery with the pandemic's growth, the agency also focuses on certain high-priority areas of research. For example, projects focused on developing and testing biomedical prevention technologies and treating HIV comorbidities were outlined as critical for AIDS research funding in 2010.[35] In 2009 and 2010, the NIH received additional resources from the American Recovery and Reinvestment Act stimulus package. These funds ended in 2011, and while the agency's funding for HIV treatment R&D has been steadily increasing through 2012, the 2013 budget proposal requests the same amount as in 2012 thus decreasing NIH's investment in the area of drug development by 2.3% as well as flatlining and/or decreasing funding for other areas of HIV research. Funding cuts will result in the drug discovery budget to fall below 2010 levels. In 2011, NIH funding decreased 2.7% as compared to 2010, from $1.75 billion to $1.70 billion.

FIGURE 21 | **NIH – Key Budget Cuts to HIV Treatment R&D Funding 2010–2013***



Note: *** The 2013 data reflect the preliminary figures from the 2013 congressional budget justification, while prior years reflect approved and actual spending.[36]**

35. NIH Office of AIDS Research. FY 2010 trans-NIH plan for HIV-related research. Accessed October 25, 2012, at http://www.oar.nih.gov/strategicplan/fy2010/index.asp.

36. National Institutes of Health. Office of AIDS Research Office of AIDS Research trans-NIH AIDS research budget: FY 2013 budget. Accessed December 7, 2012, at http://www.oar.nih.gov/budget/pdf/2013_OARTransNIHAIDSResearchBudget.pdf.

Gilead Sciences

Gilead Sciences produces five of the 32 approved HIV compounds and in 2012 has three additional compounds seeking regulatory approval in the United States and Europe, and one antiretroviral product in the pipeline. In 2010, the company made 85.7% of its profits from the sales of Atripla, Truvada, Viread, and Emtriva, and in 2011, 85.2% was made from the sales of these four ARVs with the newest rilpivirine and Complera, added to that list.[37] Gilead Sciences also works on producing and developing medications for liver disease, cardiovascular and respiratory problems, treatment of fungal infections, and controlling cytomegalovirus in HIV-positive adults. The company is also expanding its oncological medication portfolio. According to TAG's estimations of Gilead's HIV treatment R&D portfolio, the company's investment increased 33.3%, from $503 million in 2010 to $671 million in 2011.

TABLE 11 | **The Gilead Sciences Pipeline**

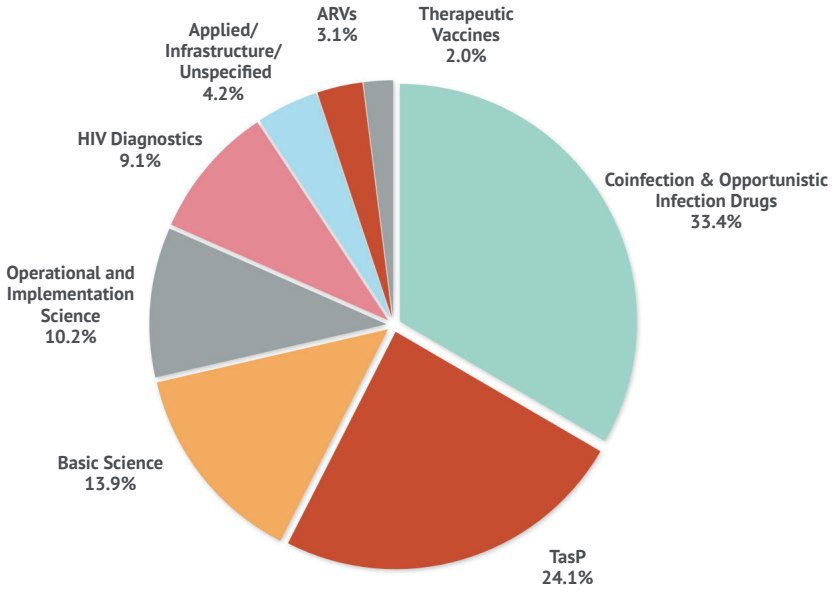
Compound	Status
"Quad" integrase STR (elvitegravir/FTC/TDF/cobicistat)	FDA approved in U.S. and E.U. dossier submitted
Elvitegravir (integrase inhibitor)	U.S. FDA and E.U. dossiers submitted
Cobicistat (formerly GS-9350) (PK enhancer)	U.S. FDA and E.U. dossiers submitted
GS-7340 (nucleotide reverse transcriptase inhibitor)	Phase II

The Bill & Melinda Gates Foundation (BMGF)

The BMGF is the largest philanthropic investor in HIV treatment R&D. The BMGF's HIV program supports efforts that contribute to reducing global incidence of HIV and treatment optimization. The program focuses on six research areas that advance development and delivery of new HIV prevention methods and makes investments in improving the efficiency and effectiveness of existing prevention and treatment efforts. Intersecting with the BMGF's HIV research portfolio is the funder's commitment to TB reduction through extensive investment in the development of affordable and safer shorter-term TB regimens. In fact, 34% of BMGF's disbursements reported in 2011 are related to the development of drugs for TB and TB/HIV coinfection. The BMGF's funding cycles also make for a varied yearly contribution, resulting in spikes in funding evident by a 7.5-fold increase from the 2009 baseline to 2011. Between 2010 and 2011, the foundation's funding increased 16.5%, from $85.1 million to $99.1 million.

37. Gilead Sciences, Inc. Annual filings to the United States Securities and Exchange Commission form 10-K. Accessed November 1, 2012, by searching for most recent (2/23/12) SEC annual filing at http://investors.gilead.com/phoenix.zhtml?c=69964&p=irol-sec.

FIGURE 22 | **The 2011 Bill & Melinda Gates Foundation Portfolio**



Agence Nationale de Recherche sur le Sida et les Hépatites Virales (ANRS)

The ANRS focuses on treatment and prevention research for HIV and viral hepatitis in France and in resource-limited settings. For HIV treatment, the agency prioritizes testing of novel therapeutic combinations, evaluation of simplified drug regimens, and HIV and aging. The ANRS invests in basic science and clinical trials of HIV and hepatitis C coinfection. A significant portion of its portfolio is dedicated to prevention, vaccine trials, and sociobehavioral research related to HIV. Funded by the French government and receiving 8% of its total budget from the philanthropic and pharmaceutical sector, the agency has consistently invested in innovative HIV science. In 2011, the ANRS reported that it experienced a slight funding decline, which is not reflected in the agency's support to HIV treatment R&D. In this area, ANRS investment increased 7.7% from $36.5 million in 2010 to $39.3 million in 2011.

The UK Medical Research Council (UK MRC)

The UK MRC supports world-class medical research to improve human health. In 2009 the organization published a five-year strategy entitled *Research Changes Lives* that aims to accelerate discovery in the most pressing health issues facing society.[38] The strategy does not have a specific HIV focus. HIV and AIDS are envisioned in the strategy in the realm of global health and addressing issues facing the developing world. In this strategic objective, the UK MRC also invests in TB and malaria research as well as research related to noncommunicable diseases in developing countries. The steady decline of funding to

38. UK MRC. Research changes lives: MRC strategic plan 2009-2014. Accessed October 1, 2012, at http://www.mrc.ac.uk/About/Strategy/StrategicPlan2009-2014/index.htm.

HIV treatment R&D in 2009–2011 and a large number of projects in the area of HIV prevention supported in the last two years could be a sign of the agency's prioritization in prevention research. UK MRC's investment decreased 7.8% from $35.4 million in 2010 to $34.7 million in 2011.

The Canadian Institutes of Health Research (CIHR)

The CIHR's HIV/AIDS Research Institute manages the government of Canada's investment in HIV research. The institute's budget totals over $22 million annually and supports projects in five funding areas: biomedical and clinical research, health services and population health research, community-based research, the CIHR Canadian HIV Trials Network, and the Canadian HIV Vaccine Initiative.[39] In 2011, the CIHR funded all areas of HIV treatment R&D tracked by TAG except for therapeutic vaccines. In both 2010 and 2011, the agency was among the top supporters of basic science and operational research. Since 2010, the total amount of HIV treatment R&D funding provided by the CIHR decreased slightly by 1.4% from $26.0 million in 2010 to $25.6 million in 2011.

The European Commission (EC)

The EC contributes to HIV research through one of its framework programs: multiannual programs agreed on by the E.U. member states. The EC's Research Framework Program 7 (FP7) funds research aimed at combatting the three major infectious diseases—HIV, TB, and malaria—for 2007–2013. Research in the area of HIV/AIDS remains a high priority for the commission. While several large projects supported by the FP7 in 2010 and 2011 were dedicated to preventive vaccine research, others focused on design and development of new ARV drugs and other scientific methods and strategies that could lead to combating the virus. EC funding increased 33.7% from $17.6 million in 2010 to $23.6 million in 2011.

The Wellcome Trust

The Wellcome Trust was started by Henry Wellcome, the founder of the Wellcome pharmaceutical company, which after several sales and mergers became GlaxoSmithKline. Henry Wellcome's legacy of promoting human and animal health remains the trust's main mission. HIV research is not a specific priority of the trust, but in its 2010–2020 strategy, it highlights the virus under a priority to "combat infectious disease." The aim of this priority is to understand the emergence, transmission, pathogenesis, and control of acute and chronic infections at the global level. As such, the Wellcome Trust responds to the needs of AIDS researchers and continuously supports innovative projects in HIV science, treatment, and prevention.[40] In 2011, the Wellcome Trust was one of the major philanthropic contributors, with the largest investments directed to basic science and operational research. The trust also contributed a significant amount to HIV diagnostics, making it the second largest global contributor to the design of new diagnostic tools. From $20 million in 2010 to $22.5 million in 2011, the trust's annual investment increased 13.0%.

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39. Canadian Institutes of Health Research. HIV/AIDS Research Institute. Accessed October 9, 2012, at http://www.cihr-irsc.gc.ca/e/25832.html.

40. Wellcome Trust Strategic plan 2010–20: extraordinary opportunities. Accessed October 25, 2012, at http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/WTDV027438.pdf.

The U.S. National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Division of HIV/AIDS Prevention (NCHHSTP), Centers for Disease Control and Prevention (CDC)

One of the largest centers at the CDC, with an annual budget of approximately $1 billion, the center is comprised of four divisions, each of which is defined by the disease that it addresses. The Division of HIV/AIDS Prevention supports programs and research that aim to prevent and control HIV. The majority of the division's funding in 2011 was dedicated to operational research and supported studies that evaluate new testing and treatment methodologies as well as assessing other ART interventions. Along with the NIH and BMGF, the CDC was also one of the key supporters in the area of TasP research. The CDC did not participate in TAG's 2009 assessment, but its investment in operational research and TasP did increase 37% from $12.4 million in 2010 to $17 million in 2011.

The Office of the U.S. Global AIDS Coordinator (OGAC)

OGAC invests in research to assess the effectiveness and progress of interventions supported by PEPFAR. In 2011, OGAC was the third largest contributor to operational research. Supporting studies in the treatment of opportunistic infections and coinfections, monitoring of drug resistance, and interventions improving HIV/TB coinfection effectiveness, OGAC aims to use operational and implementation science findings to guide interventions and policies both locally and abroad. From $14.1 million in 2010 to $15.2 million in 2011, TAG recorded a 7.7% increase in OGAC's contribution to the field of HIV treatment R&D.

3 | Conclusion and Recommendations

3.1 | Conclusion

From 2009 to 2011, TAG recorded an 11.7% growth in HIV treatment R&D investment. For both 2010 and 2011, investment in ART development received the largest contribution across all research areas. Among the 33 funders reporting in 2010, 14 reported investment in ART development for a total of $944 million (or 37%) of that year's total, and among the 41 funders reporting in 2011, 17 reported contributing to ART research for a total of $1.09 billion (or 40%) of that year's total. Considering that only three private-sector funders reported their contributions to ART development, and that the actual number of private-sector companies supporting clinical ART development is far greater, the HIV drug development total and the overall HIV treatment R&D total is likely to be much higher than that presented in this report.

In 2010, five funders reported a $7.89 million total contribution to the development of new HIV diagnostics, and in 2011, seven funders reported contributing $14.98 million in this area. HIV diagnostics comprised 0.3% and 0.5% of the total investment in the corresponding years. As with ART development, private-sector companies are extensively involved in research and production of diagnostic tools. No private-sector reports were received in the area of diagnostics, again demonstrating an underrepresentation of HIV treatment R&D totals.

As in the baseline year, the public-sector was the leading sector supporter of HIV treatment R&D, contributing 75.2% of the total in 2010, and 69.5% in 2011. Funders from the U.S. contributed 92.6% of the total calculated by TAG in 2010, and 92.2% in 2011. With reports from 18 other countries, TAG was not able to collect data from China, India, Russia, and Thailand, and only partial input was collected from Brazil, Japan, and South Africa. These countries are making an important contribution to HIV treatment R&D, and TAG will make every effort to collect this information for future reports.

The years 2010 and 2011 saw some significant scientific progress in HIV treatment R&D: reports of the effectiveness of existing ART as TasP; prospects of long-acting HIV medications and expansion of availability of once-daily combinations; development of diagnostic tools capable of detecting the virus at the earlier stages of infection; and promise of a cure. If a collaborative, multisectorial approach is chosen to make more effective medications accessible and boost investment to the most promising research areas, the HIV epidemic can be reversed and possibly halted once and for all.

3.2 | Recommendations:

- Public-sector donors are critically important as the key funders to all areas of HIV treatment R&D. With the current momentum in HIV treatment discovery, flatlining major public-agency funding will delay delivery of cheaper, more effective treatment and prevention tools to those most in need.

- Donors facing recent funding shortages have urged prominent scientists and research institutions to collaborate. Competition doesn't benefit HIV research: on the contrary, it disperses limited resources instead of focusing them on areas of greater promise. Consortiums have been created around cure and HIV vaccines, and other areas of HIV treatment R&D could benefit from collaborations—particularly across multiple sectors and countries.

- If public-sector funding declines, philanthropic and private-sector funders will need to step up to the challenge of supporting promising research. In turn, both pharmaceutical and biotech companies investing in HIV R&D should contribute funding data to this report to help us create a more accurate account of the world's investment in HIV treatment R&D.

- More resources need to be directed at developing diagnostic tools and at research evaluating the effectiveness of initiating HIV-positive individuals on existing and new formulations of ARV drugs early for the sake of prevention. These two areas of HIV treatment R&D are underfunded and seem to be less supported by funders.

- Investment in three major areas of HIV treatment R&D—drug discovery, therapeutic vaccines, and HIV diagnostics—has not been properly represented due to the lack of private-sector response. The private sector should report annual investments in HIV treatment R&D to achieve transparency and maximize collaboration with other donor sectors.

- Obtaining the most current information on investment in HIV treatment R&D in developed and developing countries is impossible without the involvement of local advocates. TAG calls on partners in Africa, Asia, Eastern and Western Europe, and South America to collaborate and advocate for public- and private-sector transparency on lifesaving research investments.

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