G-FINDER METHODOLOGY

Background to the G-FINDER survey

Each year since 2007, the G-FINDER project has provided policy-makers, donors, researchers and industry with a comprehensive analysis of global investment into research and development (R&D) of new products to prevent, diagnose, control or cure neglected diseases in developing countries. It provides an up-to-date analysis of how R&D investments are being allocated across diseases and product types, funding trends over time, and where the potential gaps lie.

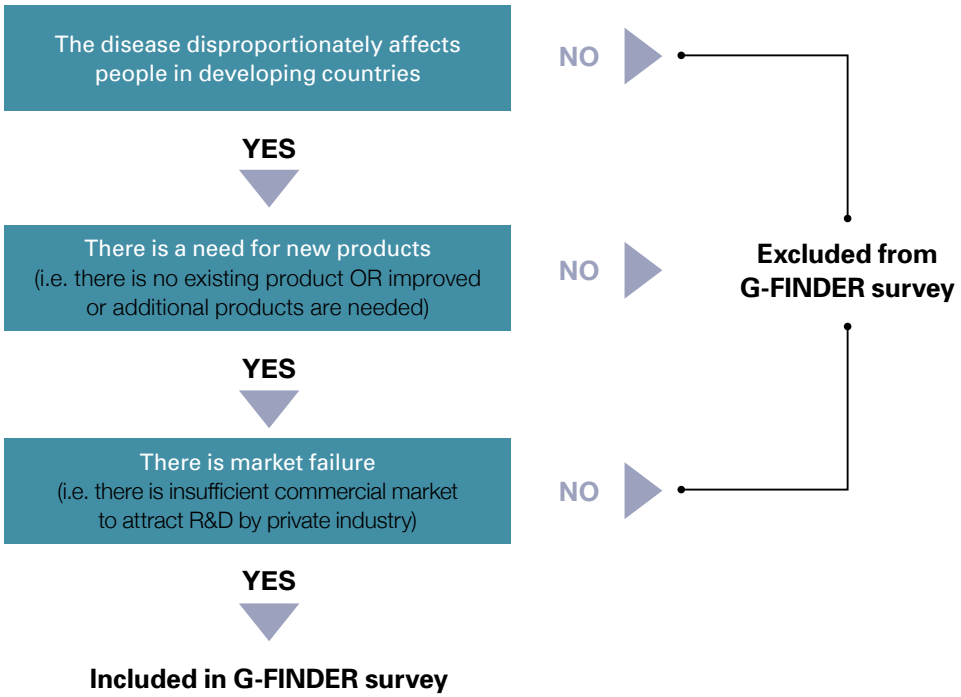
G-FINDER is recognised as the gold standard in tracking and reporting global funding for neglected disease R&D. The World Health Organization (WHO) Expert Panel's Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPOA) includes a recommendation for Member States to commit to providing information to G-FINDER, and G-FINDER has been included – as both a primary source and an indicator – in agenda items presented at the WHO Executive Board meeting and World Health Assembly.[1,2] G-FINDER is the primary source of neglected disease R&D funding data for both the WHO's Global Observatory on Health R&D and Donor Tracker, and helps support the work of many other groups in the broader global health community.

The survey scope

DEFINING NEGLECTED DISEASES AND PRODUCTS

The scope of the G-FINDER survey is determined in consultation with the G-FINDER Advisory Committee, which is made up of a broad cross-section of international experts in neglected diseases and product development (see Annexe 1 for the list of current Advisory Committee members). When defining the G-FINDER scope at the project's inception, and at all subsequent reviews, three key criteria (see Figure 1) have been applied in order to establish a list of neglected diseases and products for which R&D would cease or wane if left to market forces.

Figure 1. Filter to determine G-FINDER neglected disease inclusions



Although all basic research and all relevant product types – drugs, vaccines (preventive and therapeutic), diagnostics, microbicides and vector control products (chemical and biological control agents, and reservoir targeted vaccines) – were considered for all diseases, it is important to note that not all areas are included in the G-FINDER scope for all diseases, and some are included only with restrictions. For example, pneumonia drugs are excluded because there is a sufficient commercial market; while pneumonia vaccine investments are only included if they meet G-FINDER requirements for strain, vaccine type and target age group.

Platform technologies (adjuvants, diagnostic platforms and delivery devices) and multi-disease vector control products (VCPs) are also included in the scope of G-FINDER. Platform technologies can potentially be applied to a range of neglected diseases and products, but have not yet been linked to a specific product for a specific disease. Multi-disease VCPs target vectors capable of transmitting several different diseases.

Investments that do not meet the G-FINDER scope are excluded from the results. This includes activities such as advocacy and behavioural research, which are critical to effecting change, but which are distinct from product development and fall outside the G-FINDER criteria.

A comprehensive explanation of all inclusions, exclusions and restrictions is outlined in the detailed G-FINDER R&D scope document, which is available online. A matrix summarising the neglected diseases, products and technologies included in this year's G-FINDER report is shown in Table 1.

TYPES OF RESEARCH INCLUDED

G-FINDER quantifies neglected disease R&D investments into two overarching categories, each broken down into a number of further categories:

- Basic and early-stage research, including:
  - Basic research
  - Discovery and pre-clinical development
- Clinical or field development and post-registration studies, including:
  - Baseline epidemiology in preparation for product trials
  - Clinical or field trials
  - Phase IV/pharmacovigilance studies of new products

A detailed explanation of what types of R&D activities are included in each of these categories, as well as specific inclusions and exclusions related to the G-FINDER scope, is provided in the G-FINDER neglected disease R&D scope document.

The purpose of G-FINDER is to track and analyse global investment in the research and development of new health technologies for neglected diseases. **G-FINDER does not, and is not intended to, capture investment in the entire spectrum of neglected disease research.** Many research activities that are extremely important for global health are excluded from this report because they are not related to the development of new tools for neglected diseases; this includes health systems and operations/implementation research (for example, research into health systems or policy issues, or research into the programmatic delivery of non-product interventions, or existing health technologies), and sociological, behavioural and epidemiological research not related to the development of new health technologies. We also exclude investment into non-pharmaceutical tools such as untreated bed nets, or interventions such as circumcision. General therapies such as painkillers or nutritional supplements are also excluded, as these investments cannot be ring-fenced to neglected disease treatment only. Investment that is not research-related is similarly excluded: although we recognise the vital importance of activities such as health programme delivery, advocacy, routine disease surveillance programmes, community education and general capacity building to address neglected diseases, investment in these activities falls outside the scope of G-FINDER.

CHANGES TO THE G-FINDER R&D SCOPE FOR NEGLECTED DISEASES

Although maintaining a consistent scope is important in order to allow analysis of multi-year R&D funding trends, the scope of the G-FINDER survey is reviewed annually in consultation with the Advisory Committee.

In year two of the G-FINDER survey (FY2008), the typhoid and paratyphoid fever disease category was expanded to include non-typhoidal *Salmonella enterica* (NTS) and multiple *Salmonella* infections, while R&D for lymphatic filariasis diagnostics was added.

In FY2013 (the seventh survey year), the survey was expanded to include three additional diseases: cryptococcal meningitis, hepatitis C (genotype 4) and leptospirosis. Dengue vaccines were determined to no longer fit the criteria for inclusion in the G-FINDER survey given the emergence of a commercial market, and dengue vaccine R&D funding (including all previously reported investment) was removed from the survey. All other dengue product areas were retained.

In FY2014 (the eighth survey year), the hepatitis C category was expanded to capture investment in R&D for two additional genotypes (genotypes 5 and 6) that disproportionately affect people in developing countries.

In FY2016 (the tenth survey year), the bacterial pneumonia & meningitis category was expanded to explicitly include developing country-focused basic research for both *Streptococcus pneumoniae* and *Neisseria meningitidis*. Developing country-specific research into therapeutic vaccines for HIV/AIDS was also added as a restricted category, reflecting emerging research into broadly neutralising anti-HIV antibodies (bNAbs) and their potential use in developing countries.

In FY2017, Policy Cures Research changed how funding for vector control R&D and funding targeted at multiple diseases is reported by G-FINDER. Some of these changes result in funding falling into different categories than it would have in previous years, while other changes expand the scope of funding included in G-FINDER.

In conjunction with our ongoing collection of emerging infectious disease (EID) R&D investment data, the latest version of our survey (FY2017) allowed participants to provide separate information on funding intended to support research applicable to *both* neglected diseases and EIDs, under core funding, platform technologies and other R&D. Our inclusion of this funding results in an expanded scope for each of these categories in FY2017. Funding for R&D targeted *exclusively* at EIDs continues to be excluded from G-FINDER.

In FY2017 a new category, multi-disease vector control products, was created to capture funding for R&D not targeted at one specific vector-borne disease. This category includes funding that cannot be allocated to a single neglected disease, resulting in a change to how grants are classified, but not to G-FINDER's overall scope. However, the new category also captures funding for R&D applicable to *both* neglected diseases and EIDs, which would not have been included in previous years.

For example, the *Aedes aegypti* mosquito transmits both the dengue virus (a neglected disease) and the Zika virus (an EID). Funding for R&D targeted at controlling the *Aedes aegypti* mosquito has historically been divided between the two diseases, with only the portion notionally allocated to dengue included in G-FINDER. Under the new approach, the full value of this kind of funding is included under the new category for multi-disease vector control products.

The FY2017 report also added R&D stage categories to the biological vector control products and reservoir targeted vaccine categories, reflecting the developing international consensus on the R&D pathways for these products. These changes affect the way funding is categorised, but do not expand the scope of G-FINDER

Finally, in FY2017 the G-FINDER scope was expanded to include R&D investments in chemical vector control products for Chagas' disease and diagnostics for tapeworm infections; and the chemical vector control product category now explicitly includes funding of novel insecticide-based tools for controlling outdoor transmission, provided they are designed for use in developing countries.

Table 1. G-FINDER neglected diseases, products and technologies

Disease		Basic research	Drugs	Vaccines (preventive)	Vaccines (therapeutic)	Diagnostics	Microbicides	Vector control products
HIV/AIDS		Restricted	Restricted	✓	Restricted	✓	✓	-
Malaria	*P. falciparum*	✓	✓	✓	-	✓	-	✓
	P. vivax	✓	✓	✓	-	✓	-	✓
	Multiple / other malaria strains	✓	✓	✓	-	✓	-	✓
Tuberculosis		✓	✓	✓	✓	✓	-	-
Diarrhoeal diseases	Rotavirus	-	-	Restricted	-	-	-	-
	Shigellosis	✓	Restricted	✓	-	✓	-	-
	Cholera	✓	Restricted	✓	-	✓	-	-
	Cryptosporidiosis	✓	Restricted	✓	-	✓	-	-
	Enterotoxigenic *E. coli* (ETEC)	-	-	✓	-	✓	-	-
	Enteroaggregative *E. coli* (EAEC)	-	-	✓	-	✓	-	-
	Giardiasis	-	-	-	-	✓	-	-
	Multiple diarrhoeal diseases	✓	Restricted	✓	-	✓	-	-
Kinetoplastid diseases	Leishmaniasis	✓	✓	✓	✓	✓	-	-
	Sleeping sickness (HAT)	✓	✓	✓	-	✓	-	✓
	Chagas' disease	✓	✓	✓	✓	✓	-	✓
	Multiple kinetoplastid diseases	✓	✓	✓	✓	✓	-	✓
Helminth infections (worms & flukes)	Schistosomiasis (bilharziasis)	✓	✓	✓	-	✓	-	✓
	Lymphatic filariasis (elephantiasis)	✓	✓	-	-	✓	-	✓
	Onchocerciasis (river blindness)	✓	✓	✓	-	✓	-	✓
	Tapeworm (taeniasis / cysticercosis)	✓	✓	-	-	✓	-	✓
	Hookworm (ancylostomiasis & necatoriasis)	✓	✓	✓	-	-	-	-
	Strongyloidiasis & other intestinal roundworms	✓	✓	✓	-	✓	-	-
	Roundworm (ascariasis)	✓	✓	-	-	-	-	-
	Whipworm (trichuriasis)	✓	✓	-	-	-	-	-
	Multiple helminth infections	✓	✓	✓	-	✓	-	✓
***Salmonella* infections**	Typhoid and paratyphoid fever (*S.* Typhi, *S.* Paratyphi A)	✓	✓	✓	-	✓	-	-
	Non-typhoidal *S. enterica* (NTS)	✓	✓	✓	-	✓	-	-
	Multiple *Salmonella* infections	✓	✓	✓	-	✓	-	-
Dengue		✓	✓	-	-	✓	-	✓
Bacterial pneumonia & meningitis	*S. pneumoniae*	Restricted	-	Restricted	-	✓	-	-
	N. meningitidis	Restricted	-	Restricted	-	✓	-	-
	Both *S. pneumoniae* and *N. meningitidis*	Restricted	-	-	-	✓	-	-
Hepatitis C (genotypes 4, 5 & 6)		-	Restricted	✓	-	✓	-	-
Leprosy		✓	✓	-	-	✓	-	-
Cryptococcal meningitis		-	✓	-	-	-	-	-
Leptospirosis		-	-	-	-	Restricted	-	-
Buruli ulcer		✓	✓	✓	-	✓	-	-
Trachoma		-	-	✓	-	✓	-	-
Rheumatic fever		-	-	✓	-	-	-	-

Investment applicable to more than one neglected disease, or to both neglected and emerging infectious diseases				
Platform technologies			Multi-disease vector control products	Core funding of a multi-disease R&D organisation
General diagnostic platforms	Adjuvants and immunomodulators	Delivery technologies and devices		
Restricted	Restricted	Restricted	✓	✓

HANDLING OF EMERGING INFECTIOUS DISEASE R&D FUNDING

In response to the 2014 West African Ebola epidemic, the G-FINDER survey scope was expanded for FY2014 (the eighth survey year) to capture investments in Ebola R&D for diagnostics, drugs and preventive vaccines, as well as basic research. For FY2015 (year nine), the survey scope was further expanded to include other African viral haemorrhagic fevers (VHFs). In addition to Ebola, this new category allowed respondents to report R&D funding for Marburg and other African VHFs. In FY2016 (year ten), a separate scope definition was developed to identify investment in R&D for all priority emerging infectious diseases (EIDs) identified in the WHO R&D Blueprint for action to prevent epidemics.

Although EID funding data continues to be collected alongside investments in R&D for neglected diseases, the analysis of this data will be reported separately. The only exception is investment in R&D that is applicable to both neglected and emerging infectious diseases, the full value of which will be included in both analyses, as described earlier.

Conducting the survey

IDENTIFICATION OF SURVEY RECIPIENTS

In FY2007 (the first year of the survey), recipients were identified through various avenues including our own contacts database; previous neglected disease surveys in HIV/AIDS, tuberculosis (TB), and malaria; and research to find previously unknown funding organisations in countries with high research and development expenditure as a percentage of gross domestic product.

In FY2008, we focused on groups and countries that were missing or poorly represented in year one, developing proactive strategies to both increase the number of survey recipients and improve response rates in these areas. Major Indian public agencies involved in funding R&D for neglected diseases were identified and incorporated in our list of participants, and additional diagnostics organisations and small pharmaceutical and biotechnology firms (SMEs) were also included.

In FY2009, the survey was expanded to capture major public funding agencies in an additional three developing countries - Ghana, Colombia and Thailand - and in FY2010 expanded again to reach public funders in Argentina, Chile, Malaysia, Mexico, Nigeria and Uganda.

In FY2011, several organisations known to be active in malaria R&D were surveyed for the first time as part of a project to measure R&D funding into malaria elimination- and eradication-specific activities conducted on behalf of the Malaria Eradication Scientific Alliance (MESA).

In FY2016 and FY2017, in response to stakeholder feedback, we put in place a number of targeted strategies to further increase survey participation in low- and middle-income countries, with a particular focus on African countries, as well as Brazil and China.

Any time that new diseases have been added to the survey scope, organisations known to be active in these areas have been identified and surveyed.

DATA COLLECTION

Over the past decade, the G-FINDER survey has operated according to two key principles: capturing and analysing data in a manner that is consistent and comparable across all funders and diseases; and presenting funding data that is as close as possible to 'real' investment figures.

G-FINDER was originally designed as an online survey. An online survey platform was developed to capture grant data and is still used by the majority of survey participants. An offline grant-based reporting tool is also available. Industry (pharmaceutical companies and biotechnology firms) investment in R&D is not grant-based, so the reporting tool has been tailored for these participants. Instead of grants, companies enter the number of staff working on neglected disease programmes, their salaries, and direct project costs related to these programmes. Companies are required to exclude 'soft' figures such as in-kind contributions and costs of capital.

For some organisations with very large datasets, the online survey and equivalent offline reporting tool are difficult to use. The G-FINDER team was therefore asked to use publicly available databases to identify the relevant funding. For the US National Institutes of Health (NIH), grants are collected using the Research Portfolio Online Reporting Tools (RePORTER) and the Research, Condition and Disease Categorization (RCDC) process. For the Biomedical Advanced Research and Development Authority (BARDA), funding information is identified using the international and domestic 'Project Maps' retrieved from the Medical Countermeasures website. Information on funding from the US Department of Defense (DOD) is collected using the Defense Technical Information Center's 'DOD investment budget search' tool. Funding from the European Commission (EC)* is retrieved from the Community Research and Development Information Service (CORDIS) public database and the Innovative Medicines Initiative's (IMI) online project list. Supplementary data is provided by the EC. Information about the R&D projects funded by Innovate UK is extracted from spreadsheets available on its website.

All participating organisations are asked to only include disbursements (or receipts), rather than commitments made but not yet disbursed. In general, only primary grant data is accepted; the only exception is in the case of data collection collaborations between G-FINDER and other R&D funding surveys, such as AVAC. Data from all sources is subject to verification using the same processes and inclusion criteria.

THE SURVEY PLATFORM

Survey recipients are asked to enter grant-by-grant expenditures incurred during their financial year that had the largest overlap with the relevant G-FINDER year (as opposed to the last calendar year). Intermediaries and product developers are also asked to enter grant-by-grant revenue during the same period.

Survey recipients are asked to enter details for every neglected disease investment they disbursed or received, including:

1. a specific disease or sub-disease, from a predefined list
2. a product type (e.g. drugs, vaccines, microbicides), from a predefined list
3. a research activity within the product type (e.g. discovery and pre-clinical, clinical development), from a predefined list
4. the name of the funder or recipient of the grant
5. a brief description of the grant
6. a grant identification number
7. the grant amount

Where survey recipients cannot provide data to this level of detail, they are asked to provide the finest level of granularity they can. If survey recipients are not able to allocate the grant to a single disease, four options are available:

1. 'Core funding of a multi-disease organisation' (e.g. funding to an organisation working in multiple diseases, where the expenditure per disease was not known to the funder)

* The term 'EC' used here and throughout the report refers to funding from the EU budget that is managed by the European Commission or related EU partnerships and initiatives, such as the European and Developing Countries Clinical Trials Partnership (EDCTP) and IMI

2. 'Platform technologies', further allocated as investment into diagnostic platforms; adjuvants and immunomodulators; or delivery technology and device platforms. These categories capture investments into technologies which were not yet directed towards a specific disease or product
3. 'Multi-disease vector control products', which captures funding for vector control product R&D that is not yet targeted at a specific disease, or that is targeted at multiple vector-borne diseases
4. 'Unspecified R&D' for any grants that still cannot be allocated

New survey recipients are also asked to confirm their organisation details such as their role in funding (e.g. funder, fund manager, product developer), financial year, currency used, type of organisation (e.g. private sector firm, academic institution, multilateral organisation), and country where they are located.

Validation and analysis

VALIDATION

All entries over $0.5m are verified against the inclusion criteria. Cross-checking is conducted using automated reconciliation reports – which match investments reported as disbursed by funders with investments reported as received by intermediaries and product developers – followed by a manual grant-level review of the report outputs. Any discrepancies are resolved by contacting both groups to identify the correct figure. For grants from the US NIH, funding data is supplemented and cross-referenced with information received from the Office of AIDS Research (OAR) and the National Institute of Allergy and Infectious Diseases (NIAID).

Industry figures are reviewed against industry portfolio information held by Policy Cures Research and against full-time equivalent (FTE) and direct costs provided by other companies. Costs that fall outside the expected range, for example, above average FTE costs for clinical staff, are queried and corrected with the company.

UNSPECIFIED FUNDING

A small proportion of funding (typically less than 3%) is reported to the survey each year as 'unspecified', usually for multi-disease programmes where investment cannot easily be apportioned by disease. A proportion of funding for some diseases is also 'unspecified', for instance, when funders report a grant for research into TB basic research and drugs without apportioning funding to each product category. This means that reported funding for some diseases and products will be slightly lower than actual funding, with the difference being included as 'unspecified' funding.

Another small fraction (typically less than 5%) of global funding is given as core funding to R&D organisations that work in multiple disease areas, for example, the European and Developing Countries Clinical Trials Partnership (EDCTP) and the Foundation for Innovative New Diagnostics (FIND). As this funding cannot accurately be allocated by disease it is reported as unallocated core funding. In cases where grants to a multi-disease organisation are earmarked for a specific disease or product, they are included under the specific disease-product area.

DATA AGGREGATION

All pharmaceutical industry funding data is aggregated and anonymised for confidentiality purposes. Rather than being attributed to individual companies, pharmaceutical company investment is instead reported according to the type of company, with a distinction made between multinational pharmaceutical companies (MNCs) and small pharmaceutical and biotechnology firms (SMEs).

INFLATION ADJUSTMENTS

Funding data is adjusted for inflation and converted to US dollars (US$) for the relevant financial year to eliminate artefactual effects caused by inflation and exchange rate fluctuations, allowing accurate comparison of year-on-year (YOY) changes. Due to these adjustments, historical G-FINDER data in tables and figures in the current report will differ to data in previous G-FINDER reports.

All reported data is adjusted for inflation using consumer price index (CPI) estimates from the International Monetary Fund (IMF)[3] and any data entered by survey participants in their local currency is converted to US$ based on the average annual exchange rate of the relevant financial year as reported by the IMF,[4] Bank of England,[5] United Nations Treasury[6] and OANDA.[7]

ANNUAL CHANGES IN R&D FUNDING

To avoid reporting on artefactual variations related to survey participation, year-on-year (YOY) funding analysis was previously based only on funding reported by organisations that had participated in every year of the survey – referred to as 'YOY funders'.

G-FINDER is now in its eleventh year, and survey participation from the major funders has stabilised. Therefore annual changes mentioned in the FY2017 report are based on funding reported by all survey participants. In instances where changes were materially influenced by survey participation, an explanation has been provided.

Limitations

While the survey methodology has been refined over the past decade, there are limitations to the data presented, including survey non-completion, time lags in the funding process, an inability to disaggregate some investments, and non-comparable or missing data.

SURVEY NON-COMPLETION

Some neglected disease R&D funding may not be captured because organisations are not identified as active in this field and are therefore not invited to participate, or are invited to participate, but do not respond. Despite this, we are confident that the majority of neglected disease R&D funding is captured by G-FINDER because large funders active in this area and target groups identified by the Advisory Committee are prioritised on follow-up.

TIME LAGS IN THE FUNDING PROCESS

Time lags exist between disbursement and receipt of funding as well as between receipt of funds and the moment they are actually spent. Thus, grants by funders will not always be recorded as received by recipients in the same financial year and there may be a delay between R&D investments as reported by G-FINDER and actual expenditure on R&D programmes by product developers and researchers. Nevertheless, as this report analyses trends over an extended period, the impact of time lags is minimal.

INABILITY TO DISAGGREGATE INVESTMENTS

Funding allocated to some diseases and products may be slightly underestimated due to:

- Multi-disease organisations: Core funding grants to organisations working on multiple diseases, such as the EDCTP, are not counted within the funding figures for specific diseases
- Multi-disease grants: When funders are unable to disaggregate multi-disease grants, these investments are included in the 'Unspecified R&D' category or the new 'multi-disease vector control products' category.

NON-COMPARABLE DATA

Due to a significant increase in the size of the survey in FY2008, data from FY2007 is the least comparable to other years. Furthermore, the current public official databases for the US NIH data, the RCDC and RePORTER, used for data collection between FY2008 and FY2017, use a different structure than the US NIH database used in FY2007. This means reports obtained from RCDC and RePORTER in years two to eleven are not directly comparable to those used in year one.

MISSING AND INACCURATE DATA

G-FINDER can only report the data as it is given to us. Although strenuous efforts are made to check the classification, accuracy and completeness of grants, in a survey of this size it is likely that some data will still have been incorrectly entered or that funders may have accidentally omitted some grants. We periodically amend historical G-FINDER data after the publication of the report if better data is provided or errors are identified. We believe that the checks and balances built into the G-FINDER process mean that mistakes, if present, have a minor overall impact.

Variation between surveys

Other groups also publish annual surveys of global R&D investment into selected neglected diseases, such as HIV/AIDS and TB. Although G-FINDER works in close collaboration with some of these groups, both to ease survey fatigue on the part of participants and to clarify any major variance in our findings, each survey nevertheless has slightly different figures. This is chiefly due to differences in scope, in particular inclusion in other surveys of funding for advocacy, capacity building and operational studies – all excluded from G-FINDER. Methodological differences also lead to variations, in particular that G-FINDER figures are adjusted for inflation and exchange rates, which is not always the case for other surveys. As mentioned before, classification of some funding as ‘unspecified’ in G-FINDER (e.g. multi-disease programmes) may in some cases also lead to different figures than those published in disease-specific surveys.