EMBO reports

viewpoint

The grand impact of the Gates Foundation

Sixty billion dollars and one famous person can affect the spending and research focus of public agencies

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In an ideal world, scientific research would be free from constraints; the professional interests of the scientific community and individual scientists would determine research topics and directions, and funding would be limitless. In the real world, however, factors such as the economy, health and social interests also have an influence and eventually limited financial resources must be prioritized. Public agencies and private benefactors support research with the expectation that the results will translate into tangible benefits such as economic growth, health products, or solutions to social problems. Given that much of academic research is predominantly funded by public money, funding agencies frequently determine the direction of research.

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In the USA, the National Institutes of Health (NIH; Bethesda, MD, USA) has an annual budget of approximately US$30 billion and influences biomedical research extensively by setting funding priorities. Given that the NIH distributes taxpayers' money, it predominantly supports research that targets health problems affecting US citizens. However, more recently, the US Federal Government's funding allocations through the NIH have been influenced by private foundations, shifting their focus and resources towards addressing the problems of global health. Most notable of these foundations has been the Bill & Melinda Gates Foundation (BMGF; Seattle, WA, USA; www.gatesfoundation.org), which was set up by the couple in 2000.

Here, we review the impact of the Grand Challenges for Global Health (GCGH) initiative that was started by the BMGF in 2003 and that managed to influence the NIH's funding priorities. We found that the NIH supplemented the GCGH with increased funding of approximately US$1 billion for global health issues at a time when the overall NIH budget experienced little growth. Interestingly, this redirection of resources towards global health by the NIH and the BMGF contradicted the traditional wisdom: that increases in funding from one agency in a particular area of research will lead other agencies to reduce their financial support for the same field.

The BMGF is the largest charitable foundation in the USA. It came into existence in 2000 when the William H. Gates Foundation, founded in 1994, merged with the Gates Learning Foundation, founded in 1997. As of March 2007, the BMGF's endowment was estimated to be US$33 billion, of which it awards approximately US$1.6 billion in grants (BMGF, 2006). The endowment and number of grants will continue to increase steadily after US investor Warren Buffet announced in June 2006 that he would contribute another US$30 billion over the next decades (BMGF, 2006).

According to its website, the goal of the BMGF is to "reduce inequities and improve lives around the world." To achieve this, the Foundation concentrates on three main areas: global health, global development, and the US program that includes education and access to technology for low-income communities in the USA. The Foundation's global programmes focus on: "improving health, reducing extreme poverty, and increasing access to technology in public libraries." These priorities were greatly influenced by the year 2000 United Nations' Millennium Development Goals (Sidebar A), which identified eight action items to be completed by 2015. Over the past 13 years, the BMGF—and its predecessor, the William H. Gates Foundation—distributed more than US$7.8 billion, including more than US$2 billion for work combating HIV/AIDS, tuberculosis (TB) and malaria; approximately US$1.9 billion for immunizations; and US$448 million for the GCGH projects (www.gatesfoundation.org).

Bill and Melinda Gates envisioned the GCGH as a way "to identify research areas with the greatest promise for saving and improving lives in the developing world; to fund novel, interdisciplinary approaches

Sidebar A | The UN millennium development goals

Goal 1: Eradicate extreme poverty and hunger
Goal 2: Achieve universal primary education
Goal 3: Promote gender equality and empower women
Goal 4: Reduce child mortality
Goal 5: Improve maternal health
Goal 6: Combat HIV/AIDS, malaria and other diseases
Goal 7: Ensure environmental sustainability
Goal 8: Develop a global partnership for development

(Source: www.un.org/millenniumgoals)

Sidebar B | The Grand Challenges in Global Health

Goal 1: Improve childhood vaccines
Grand Challenge 1: Create effective single-dose vaccines
Grand Challenge 2: Prepare vaccines that do not require refrigeration
Grand Challenge 3: Develop needle-free vaccine delivery systems

Goal 2: Create new vaccines
Grand Challenge 4: Devise testing systems for new vaccines
Grand Challenge 5: Design antigens for protective immunity
Grand Challenge 6: Learn about immunological responses

Goal 3: Control insects that transmit agents of disease
Grand Challenge 7: Develop genetic strategy to control insects
Grand Challenge 8: Develop chemical strategy to control insects

Goal 4: Improve nutrition to promote health
Grand Challenge 9: Create a nutrient-rich staple plant species

Goal 5: Improve drug treatment of infectious diseases
Grand Challenge 10: Find drugs and delivery systems to limit drug resistance

Goal 6: Cure latent and chronic infection
Grand Challenge 11: Create therapies that can cure latent infection
Grand Challenge 12: Create immunological methods to cure chronic infections

Goal 7: Measure health status accurately and economically in developing countries
Grand Challenge 13: Develop technologies to assess population health
Grand Challenge 14: Develop versatile diagnostic tools

(Source: www.gcgh.org)

among researchers seeking solutions; and to get the 'rich-world' scientific community to apply its experience to pivotal health questions of the developing world" (Gates, 2003). The initiative aims to challenge and encourage researchers in the biomedical field to apply their knowledge and expertize to diseases and conditions that disproportionately affect the developing world. In doing so, the initiative aims to alleviate the so-called 90–10 gap in biomedical research; each year, US$70 billion are spent on research worldwide, but only 10% of this money is used for research on diseases that affect 90% of the world's population.

The Grand Challenges were inspired by the German mathematician David Hilbert (1862–1943), who, at the International Congress of Mathematics in Paris, France, in 1900, presented 23 unsolved problems in mathematics (Hilbert, 1902). Hilbert's challenge ultimately guided mathematical research for the following century and many of the problems were eventually solved, although a few remain unanswered. Unlike Hilbert, Gates did not propose a list of specific challenges himself, but asked a group of experts to compile a list of 10 main issues for global health that his foundation would attempt to solve by targeting its funds. The objective of the initiative was to support high-risk research with a high potential impact on public health.

The BMGF donates the GCGH funds to the Foundation at the National Institutes of Health (FNIH; Bethesda, MD, USA), which manages the research projects. The FNIH is a non-profit organization established by the US Congress in 1996 to promote collaboration between non-profit charities, industry and academia, "to support the NIH mission of improving health through scientific discovery" (www.fnih.org). Other partners include the Wellcome Trust (London, UK) and the Canadian Institutes of Health Research (Ottawa, ON, Canada). Although the FNIH manages and administers the grants, the GCGH scientific board oversees and selects the projects to be funded. The board is led by Nobel laureate Harold Varmus—President of the Sloan–Kettering Cancer Center (New York, NY, USA) and former director of the NIH—and consists of 20 leading scientists from industry, academia, philanthropic organizations and government with expertize in biomedical research (Varmus *et al*, 2003; www.gcgh.org).

On the basis of solicitations to biomedical researchers, which resulted in 1,048 submissions from scientists and institutions in 75 countries, the GCGH board agreed on seven long-range goals with 14 grand challenges (Sidebar B). These challenges or goals do not address individual diseases; instead, they concentrate on crucial research problems that affect multiple disorders. However, the goals are heavily slanted towards infectious diseases, which the board believe have the greatest impact on health conditions in the developing world. "These are all very significant and difficult scientific problems," commented Varmus in a *Science* article, which published the challenges (Varmus *et al*, 2003). "If we could solve any one of these grand challenges, the impact on health in the developing world could be dramatic, and we hope to solve several in the course of this new initiative."

> **…this sudden interest and financial support for global health research at the NIH was largely due to the BMGF, and its strong outreach to both the scientific community and the public**

Following the announcement of the GCGH, the FNIH issued a request for proposals, and reviewed more than 1,500 letters of intention and 445 project proposals. The BMGF first proposed to spend US$200 million on the project, but eventually decided to inject an additional US$250 million after receiving and reviewing the large number of grant applications. In July 2005, the FNIH awarded grants to 43 projects totalling US$437 million. These ongoing five-year grants range from US$579,000 to US$20 million, and the grant recipients come from 33 countries, although more than half of the grants are to researchers in the USA (Cohen, 2005). The last grant was awarded in September 2005, making a total of 44 projects funded with US$448 million (www.gatesfoundation.org). The BMGF acknowledged that this would not be a one-shot deal, and that they expect successful projects to request and receive additional funding in the future.

Unlike traditional grants from the NIH or many other funding agencies, GCGH grants also require researchers to define specific milestones, and scientists could potentially lose funding if they do not accomplish them. Applicants must also submit a plan that explains how their product, once it has been developed, will be made available and affordable to people in developing countries.

The foundation frequently stated that the goal was not only to solve global health challenges, but also to attract new scientists to the field (Gates, 2003). The BMGF realized that, in order to do so, the field needed new investment. Ultimately and interestingly, this came not only from the BMGF and other private donors but also from the NIH.

The 2006 fiscal year budget for the NIH was US$28.5 billion. After several decades of steady growth—

including a doubling of the budget between 1998 and 2003—the figures have been relatively constant since 2003 (Fig 1) with only small increases each year. The NIH itself consists of various institutes at the Bethesda campus, and the one that has the most responsibility for research into infectious diseases and funding such projects is the National Institute for Allergies and Infectious Diseases (NIAID). Of the main institutes at the NIH—the National Cancer Institute (NCI), the National Institute for Heart, Lung and Blood (NHLBI), and the NIAID—it was the NIAID that was least affected by the stagnating budget. In fact, its budget has increased by 23% since 2003, whereas the NCI and NHLBI each saw increases of only 4.7% (Intersociety Working Group, 2007).

Some of this increased funding since 2003 can be explained by new initiatives—such as a focus on bioterrorism and preparedness in light of a possible flu pandemic—but other diseases that are addressed by the GCGH have also experienced remarkable increases in funding. Research in infectious diseases increased by 26%: research on malaria and tuberculosis in particular increased by 40% and 22%, respectively. The biggest winners were vaccines (Fig 2): the funds for general vaccine-related research increased by 41%, and research on vaccines against malaria and tuberculosis increased by 96% and 62%, respectively. These changes are even more remarkable when compared with other disease-related research: anthrax-related research saw a reduction in funding of 49%; asthma increased by only 15%; and heart disease—the leading cause of death in the USA, which is funded by NHLBI—saw only a 3% increase during this time.

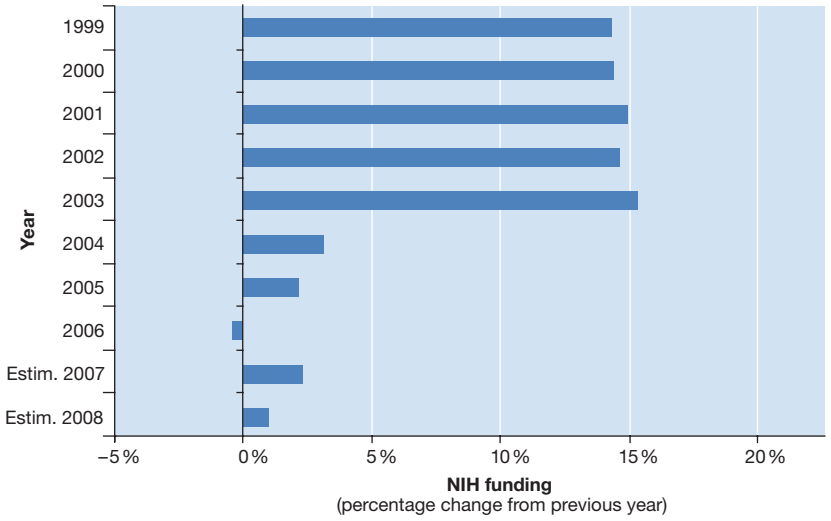

Fig 1 | National Institutes of Health funding: percentage change from previous year, financial years 1999–2008. Source: American Association for the Advancement of Science; NIH budgets by institute and funding mechanism, financial years 1998–2008 (www.aaas.org/spp/rd). Estimated budgets are given for 2007 and 2008.

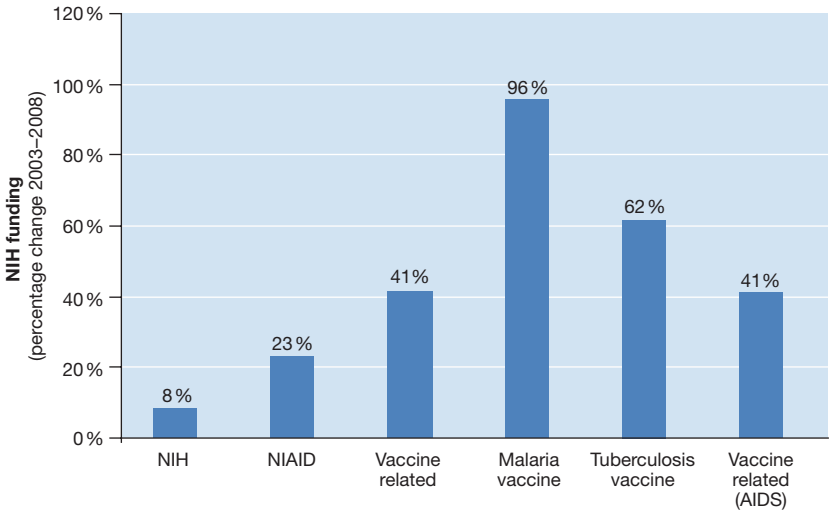

Fig 2 | Estimates of funding for specific diseases and research: percentage change between 2003 and 2008, by research area. Source: National Institutes of Health (NIH); estimates of funding for various diseases, conditions, research areas (www.nih.gov). Estimated budgets are given for 2007 and 2008. NIAID, National Institute for Allergies and Infectious Diseases.

In our view, this sudden interest and financial support for global health research at the NIH was largely due to the BMGF, and its strong outreach to both the scientific community and the public. First, the Foundation encouraged scientists to get involved in the whole process to address challenges in global health research; this is in stark contrast to the NIH Roadmap, in which only a select 300 scientists were asked for input. Although Gates had a few preconceived ideas about what the GCGH should fund—such as finding new approaches to preventing and treating HIV—it was the Foundation's scientific board that chose the specific challenges and projects to be awarded.

The strong response from the scientific community confirmed their interest in the project: more than 1,000 responses and more than 1,500 letters of inquiry were submitted. "The overwhelming response demonstrates that when scientists are given a chance to study questions that could save millions of lives, they eagerly rise to the challenge," Gates commented in 2005 when he announced the additional US$250 million for the project (Cohen, 2005).

Second, the BMGF engaged the media. At the World Economics Forum Annual Meeting in Davos, Switzerland, in January 2003—a gathering of leaders from business, government, international institutions, non-governmental organizations, universities and other communities to discuss global

issues—Bill Gates announced that the BMGF intended to create and sponsor the GCGH, and his appearance at the meeting guaranteed worldwide press coverage (Butler, 2003). The following day, Gates published a commentary in the *Wall Street Journal* outlining the concept and the reasoning behind it (Gates, 2003).

Third, the BMGF used and continues to use the GCGH to "advocate—vigorously but responsibly—in [its] areas of focus": research focused on diseases that predominately affect developing countries. In addition, the Foundation supports other advocate groups with similar aims such as the ONE Campaign (www.one.org), which actively lobbies for increased US federal funding to combat global poverty and global health challenges.

Many health advocates believe that the push for global health and research on diseases affecting developing countries was long overdue

By reaching out to the press and creating enthusiasm among the scientific community, the BMGF has been able to translate their own contribution into a significant increase in federal research in this area. The BMGF's fund of US$450 million over five years for research related to global health issues was eventually supplemented by approximately US$1 billion from the NIH for the period 2004–2008. By encouraging an increase in NIH funding, the BMGF also succeeded in recruiting additional researchers into the field who would be hesitant to rely on Foundation support alone for biomedical research.

The BMGF prides itself on making bold choices and pushing researchers to find ways around impediments—whether a lack of collaboration between AIDS vaccine researchers or the lack of researchers in global health research. By aggressively promoting their aims and research, and by making the GCGH grants prestigious as well as generous, the BMGF was able to raise the profile of global health research in the USA, which encouraged legislators in Congress to notice global health as a priority and helped to increase similar research at the NIH.

Furthermore, the BMGF gained a disproportionate influence on public health policy (Wadman, 2007). One example is the requirement that all GCGH grantees must draft a plan of how to make health products resulting from their research affordable to people in developing countries. Furthermore, in 2006, the BMGF dictated that all AIDS-vaccine grantees share their results in order to help the field move forward (Chase, 2006).

The experience of the BMGF and its GCGH illustrates how strong advocacy can influence public research policies and budgets (Brower, 2005). Of course, the NIH does not directly change its funding priorities based on pressure from advocacy groups. However, politicians—members of Congress—are more receptive to campaigns from patient groups. Congress then directs the NIH, through the appropriation process, to target specific areas for increased funding. Such was the case for HIV/AIDS in the 1990s, in which advocacy groups managed to increase HIV/AIDS funding at the NIH to approximately US$3 billion by 2006, as well as breast cancer research, which obtained more than US$700 million from NIH in the same year.

Many health advocates believe that the push for global health and research on diseases affecting developing countries was long overdue. In fact, the BMGF has found a niche that was not previously supported: high-risk, high-impact projects in the context of infectious diseases. One of the BMGF principles is to "take risks, make big bets, and move with urgency." To this end, the BMGF announced a new US$100 million programme in October 2007 to fund 1,000 new high-risk research projects under the title "Grand Challenges Explorations". This new programme will complement the GCGH projects with US$100,000 awards that enable scientists to test new ideas by using a faster approval process than a traditional NIH grant (Cohen, 2007). "The scientific community has shown tremendous interest in the Grand Challenges initiative, and the projects funded so far are beginning to show important progress," commented Varmus. "The new Explorations initiative will help to further increase innovation in global health research" (www.gatesfoundation.org).

Although the BMGF should be commended for their role in raising the profile of research into infectious diseases that predominantly affect the developing world, the true impact of the GCGH will only be realized after the initial grants run out. Is five years enough time to expect projects to yield conclusive results? Will they lead to new products that benefit people in developing countries? Will promising projects find new funding if the BMGF does not continue to support them through its GCGH? Are the GCGH projects focused on the right priorities? Only time will tell if the GCGH initiative and its goals are an efficient strategy to improve global health. In the meantime, they serve to focus the attention of policy-makers, scientists, the media and the general public on the particular health problems that still affect the majority of people on this planet—a worthwhile goal indeed.

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