

The Global Drug Gap

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Global inequities in access to pharmaceutical products exist between rich and poor countries because of market and government failures as well as huge income differences. Multiple policies are required to address this global drug gap for three categories of pharmaceutical products: essential drugs, new drugs, and yet-to-be-developed drugs. Policies should combine "push" approaches of financial subsidies to support targeted drug development, "pull" approaches of financial incentives such as market guarantees, and "process" approaches aimed at improved institutional capacity. Constructive solutions are needed that can both protect the incentives for research and development and reduce the inequities of access.

The 20th century created a multinational pharmaceutical industry with an extraordinary research and development (R&D) capacity to produce new drugs for many health conditions. But this R&D system remains focused primarily on the health issues of the world's affluent countries. The system depends on, for its financing, deriving large profits from the most successful products, which leads to high prices for these products and global inequities in access and health status. Recently, there has been increasing mobilization around the idea of a right to essential and new drugs and growing resistance to the notion that intellectual property rights should trump other policy considerations.

The global drug gap between rich and poor countries arises from multiple market and government failures as well as from huge income differences. Consequently, multiple policies are required to address this inequity. These efforts need to combine "push" approaches of financial subsidies to support targeted drug development, "pull" approaches of financial incentives such as market guarantees, and "process" approaches aimed at improved institutional capacity. Distinct policy mechanisms must address three categories: essential drugs, new drugs, and yet-to-be-developed drugs.

The concept of essential drugs, as unanimously endorsed by the World Health Assembly (1, 2), consists of "those that satisfy the health care needs of the majority of the population and should therefore be available at all times in adequate amounts and in appropriate dosage forms" (1). The World Health Organization (WHO) estimates that one-third of the world's population does not have access to essential drugs (this estimate has remained unchanged since the mid-1980s).

WHO has promoted the concept of essen-

tial drugs to advance health equity through expanded access to basic medicines for poor people in poor countries. Nearly 150 countries have adopted a national essential drugs list. The World Bank has promoted this concept to advance efficiency by focusing health expenditures on medicines likely to produce the most health benefits in a population (3).

Some controversy remains about whether a country's list of essential drugs should represent the maximum number of available drugs as a ceiling, or the minimum number of available drugs as a floor. Debate also persists about which products to define as essential and by whom. But enough consensus has emerged that even the International Federation of Pharmaceutical Manufacturers Associations, which initially opposed the idea, now accepts the principle of efficient provision of essential drugs in primary health care as a priority when resources are limited.

WHO's Eleventh Model List of Essential Drugs includes 302 active ingredients. Of these, 90% are off-patent and usually are available at reasonable prices. Typical examples are ibuprofen, morphine, mebendazole, and ampicillin. Several mechanisms are available to promote access to essential drugs.

First, a state's capacity to use the international market can be strengthened, resulting in more efficient procurement of essential drugs (for example, through competitive tenders). A related approach is the United Nations Children's Fund's (UNICEF's) procurement service, which offers to purchase essential drugs on the global market for governments of developing countries and other organizations on a cost-plus basis (4).

A second strategy is improving the state's capacity to manage the national pharmaceutical system. This strategy produces more efficient use of essential drugs within a country—for example, through improved warehousing and distribution systems and better control of corruption (5).

A third strategy is to focus on mechanisms that maintain effective supplies. Community-managed funds have been used to purchase

essential drugs for continuous local supply (6). International loans from the World Bank and aid agencies have supported the procurement of essential drugs. WHO and other international agencies have sought to direct in-kind donations toward essential drugs (7, 8).

A fourth strategy is to improve the rational use of essential drugs by health workers and consumers, especially in the private sector, because market purchases represent a major source of access to pharmaceuticals in developing countries.

Despite past controversies, a broad consensus has emerged on strategies to improve access to essential drugs in poor countries, and substantial progress has been achieved. Conflict subsided in part because most essential drugs are off-patent, and the implications for the global R&D system are minimal.

In contrast, major controversies exist over access to new drugs that have life-saving and welfare-enhancing consequences for diseases of public health importance in poor countries. These products are sometimes called "new essential drugs." With the availability of new antiretrovirals, the age-adjusted death rate for AIDS declined by 48% in the United States from 1996 to 1997, with similar decreases in Western Europe and Australia (9). But 95% of individuals worldwide who are infected with the human immunodeficiency virus (HIV) live in poor countries, with almost no access to these life-prolonging treatments because of programmatic and institutional problems as well as cost barriers (10, 11). At the end of 1998, 67% of the people in the world with HIV/AIDS lived in sub-Saharan Africa, where over 80% of the world's AIDS deaths have been recorded to date (Fig. 1).

Similar problems of access to new drugs have existed for other diseases, as illustrated by the case of praziquantel for schistosomiasis in the 1980s (12) and as illustrated for asthma treatments (13). What mechanisms could expand access to such new drugs in poor countries?

One option is to use the market. For example, a government can purchase the new drugs. In 1998, Brazil's federal government spent an estimated \$230 million on AIDS drugs, or over 30% of the government's budget for pharmaceuticals. Multinational companies could support a market-based approach through tiered pricing (14). The approach can work only if companies can protect their rich-country markets from parallel imports and if rich countries can accept the free-riding of poor countries on payments for R&D and innovation. A different (untested)

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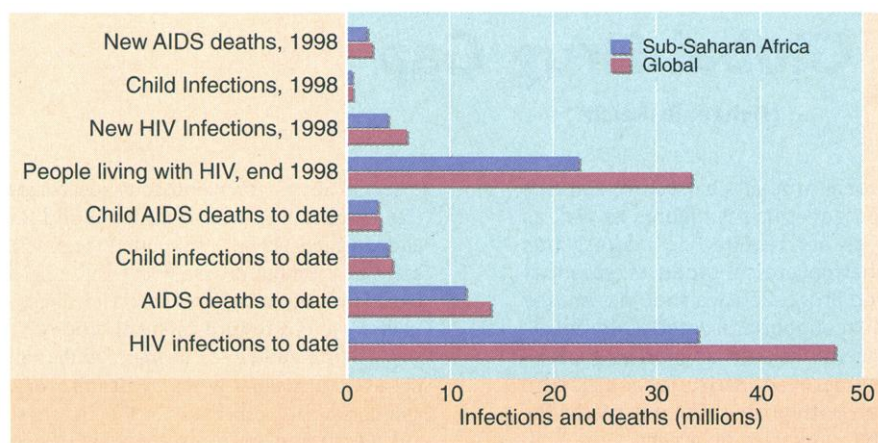
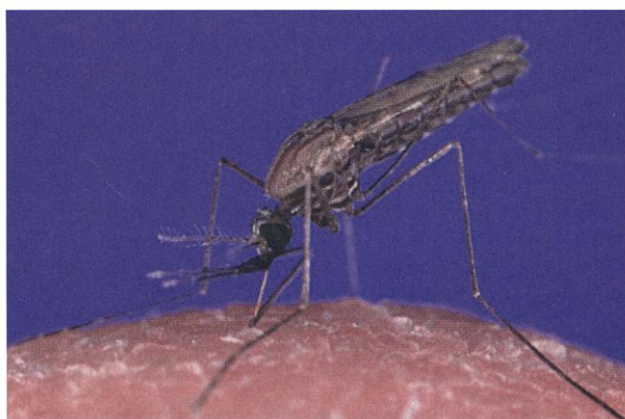


Fig. 1. HIV and AIDS estimates, sub-Saharan Africa and global (11).

Fig. 2. *Anopheles gambiae* mosquito, a major vector of malaria. About 500 million people in Africa, India, Southeast Asia, and South America are exposed to endemic malaria, and it is estimated to cause two-and-a-half-million deaths annually, one million of whom are children. [Image: James Gathany/CDC]



market-oriented approach would be to develop markets for patents for drugs that are of primary use to poor countries and sell the patents to producers (or to governments) in order to expand access to new products in poor countries (15).

Mandates are a second option. Health activists are pushing for legal mandates under the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement. Compulsory licensing would allow a national government to require licensing by a nonpatent-holder that would manufacture the new drugs within the country under certain conditions. Parallel imports (also allowed under TRIPS) let a country purchase new drugs from third parties in countries where the price is low in order to reduce the high prices of new drugs. So far, compulsory licensing has not been widely used to expand access to new drugs in developing countries. Most developing countries lack the regulatory and manufacturing capacity required for high-quality, cost-effective production of pharmaceuticals. A few middle-income countries with this capacity have encountered fierce political pressure from multinational pharmaceutical firms and the U.S. government when these countries have sought to pass national legislation for

compulsory licensing, as shown by the example of South Africa (16).

A third approach is to rely on munificence. Pharmaceutical manufacturers could expand product donation programs for new drugs that treat diseases of public health importance to poor countries. A well-known example is Merck's donation program of ivermectin for river blindness (17), which

provided products to treat about 30 million people in 20 countries in 1999. Other companies have recently adopted this strategy (including SmithKline Beecham for lymphatic filariasis, Pfizer for trachoma, and Glaxo-Wellcome for malaria), so far with mixed results (18). A related approach is to donate the patent rights for specific products, as Hoechst Marion Roussel has done to WHO for eflornithine to treat African trypanosomiasis or sleeping sickness (although a new manufacturer has yet to be found). Private foundations can also make significant contributions (e.g., the Gates Foundation for vaccines, the Clark Foundation for trachoma, and the Nippon Foundation for leprosy).

For markets, mandates, and munificence to work well, public and private actors must resolve their conflicting interests and establish partnerships and principles for access to new drugs. These issues inevitably connect to the R&D system for generating new products.

The world's major private pharmaceutical companies, the prime source of innovative pharmaceutical technology, do only limited research into new drugs to treat diseases in poor countries. For example, a lack of market incentives has stalled private research on new malaria drugs (Fig. 2) (19). Corporate research strategies typically follow the market incentives of global sales (Fig. 3). An assessment of 1233 new drugs that reached the market between 1975 and 1997 found only 13 products that were approved specifically for tropical diseases (20). Four types of fixes are commonly proposed to address yet-to-be-developed drugs.

The first is to provide public subsidies for R&D on new products through institutions such as the U.S. National Institutes of Health or the United Nations Development Program (UNDP)/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). These subsidies have contributed to the development of some new

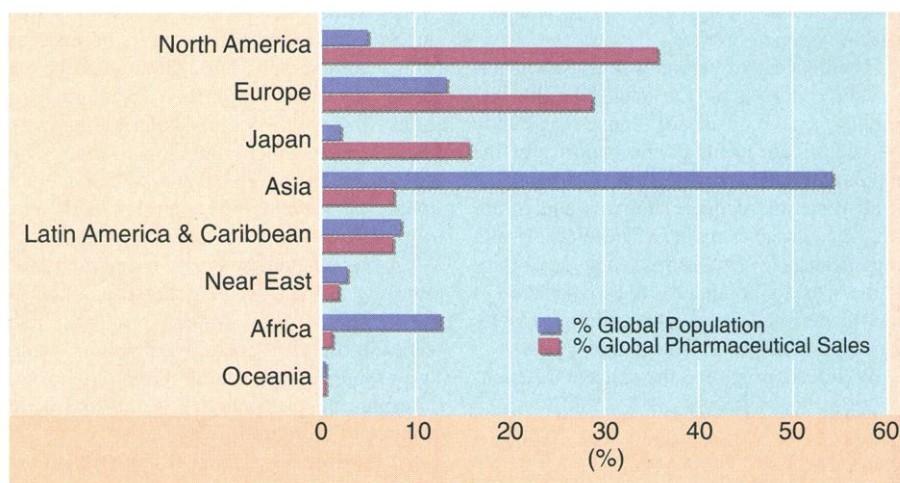


Fig. 3. Global population and pharmaceutical sales (by value), by region, 1997 (25).

drugs for people in poor countries. TDR helped develop 24 tropical disease drug products from 1974 to 1995; 14 were still in trials in 1995, and 10 were in clinical use (6 of these 10 products are included in the 13 new products noted above) (20, 21). TDR worked with private industry to develop most of these agents.

Second, new public-private partnerships for R&D on specific diseases or for specific types of products can be created. One recent example is the Medicines for Malaria Venture, which was initiated within the TDR program and WHO. This venture was recently spun off, with financial support from a consortium of donors, as an autonomous private foundation in Switzerland.

A third fix is to protect product patents in developing countries, as provided by the TRIPS Agreement, and thereby create incentives for private-sector R&D on drug therapies for diseases common in those countries. This approach is promoted by the multinational pharmaceutical industry. One study on the introduction of product patents in India concluded that implementation of the TRIPS Agreement could enhance R&D in that country not because of incentives but because Indian pharmaceutical companies would be blocked from following their previously profitable strategy of imitation (22).

A fourth fix is to create financial incentives for private corporate research by constructing "purchase funds" or guaranteed markets for future products (23). This approach has been recommended for vaccine development to induce private research on malaria, AIDS, and tuberculosis vaccines. A related approach is to provide incentives through orphan drug acts to spur development of drug therapies for rare diseases. Implementation of the U.S. orphan drug act

contributed to 10 new molecular entities for tropical diseases from a total of 152 new entities developed under the act between 1983 and 1997 (24).

These four strategies raise important questions about the accountability of public funds channeled to private companies and the fairness of the international distribution of research benefits. In addition, successful products from R&D become new drugs, with the potential for limited access in poor countries, unless effective mechanisms are built into the drug development process.

Strategies to expand access are generally better tested and more effective for essential drugs than for new drugs and yet-to-be developed drugs. But implicitly asking poor countries to wait for new drugs to go off-patent before gaining access seems profoundly unfair. New drugs are expensive, and poor people in poor countries cannot afford them without outside help. We need a constructive solution that can both protect the incentives for R&D and reduce the inequities of access. This requires forceful implementation of proven strategies, systematic experimentation with innovative ideas, and vast mobilization of financial resources (including debt forgiveness along with public and private funds).

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