

giene, and health systems, the international community can make an enduring, truly historical improvement in the lives of the world's least healthy people.

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COMMENTARIES

US Health Aid Beyond PEPFAR The Mother & Child Campaign

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ONE OF THE GEORGE W. BUSH ADMINISTRATION'S biggest successes has been the President's Emergency Plan for AIDS Relief (PEPFAR).¹ Even the president's critics acknowledge the important benefits PEPFAR has produced, both for those countries most seriously affected by human immunodeficiency virus (HIV)/AIDS and for the United States' moral legitimacy and diplomatic reputation. It was accordingly unsurprising that the president used his final State of the Union address to call for a doubling of PEPFAR's funds. Congress recently went even further, appropriating nearly \$50 billion for the program's renewal.¹

Yet doubling or tripling PEPFAR's funding is not the best use of international health funding. In focusing so heavily on HIV/AIDS treatments, the United States misses huge opportunities. By extending funds to simple but more deadly diseases, such as respiratory and diarrheal illnesses, the US government could save more lives—especially young lives—at substantially lower cost. Rather than inflating PEPFAR funding, the newly pledged billions could launch a new proposal program called the Mother & Child Campaign.

PEPFAR's Purview

In 2003, Congress appropriated PEPFAR \$15 billion over 5 years to combat HIV/AIDS in developing regions. By September 2007, the program had prevented mother-to-child transmission for 10 million pregnancies, supported outreach activities aimed at preventing transmission to 61.5 million people, and provided antiretroviral treatment (ART) to 1.45 million individuals.¹ United States citizens generally strongly support PEPFAR, partly because of the devastating effects of HIV/AIDS—the disease claims 1.9 million lives annually in lower-income countries—but also because HIV/AIDS is one of the few major health problems the United States shares with the developing world, and because it primarily affects adults, who have greater economic and political power.²

Yet despite being “the largest commitment ever by a single nation toward an international health initiative,”¹ PEPFAR fails to address many of the developing world's most serious health threats. In lower-income countries, mundane but deadly diseases cause more harm than HIV/AIDS. Respiratory infections alone claim 2.86 million lives

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each year.³ Another 2.2 million die annually from diarrheal diseases,⁴ and 1.24 million and 1.6 million die from malaria³ and tuberculosis,⁵ respectively. Even though a few smaller government-sponsored initiatives do target some of these illnesses, such efforts pale in comparison with the sheer funding and attention that PEPFAR provides for HIV/AIDS.

Principles for International Health Aid

International aid is inherently limited; it is impossible to address all health problems in developing countries simultaneously. Consequently, it is extremely important to consider how this finite aid is distributed. The allocation of international health aid should be guided by 3 fundamental principles: (1) to save the most lives; (2) to save young lives in particular; and (3) to do so using finite resources most effectively.

Saving the most lives has intuitive appeal: There are clear ethical obligations to help others, especially to avoid death, and it is imperative to meet that obligation for as many individuals as possible.⁶ This requires paying particular attention to the health problems inflicting the greatest burden on the greatest number of individuals.⁶

The focus on saving children reflects the particular need and condition of this population. Young children in developing regions have a proportionally greater disease burden than any other age group: 1 in 6 children born in sub-Saharan Africa dies before age 5 years.⁷ Furthermore, while every premature death is distressing, death in childhood is particularly tragic, as children lose more future years and stages of life than adults. Additionally, the effort required to prevent these deaths is small: of the 10 million annual deaths that occur among young children, 70% are attributed to easily avoidable causes such as pneumonia, diarrhea, malaria, and neonatal complications.⁷ Thus, children in developing regions likely represent the population most deserving of aid: a greater percentage die, losing more potential life, from causes that could be easily averted.

Because resources devoted to international health aid are inherently limited, seemingly economic considerations about cost-effectiveness actually reflect fundamental ethical principles. The more cost-effectively resources are used, the more lives can be saved.

Assessing PEPFAR

PEPFAR's strategy falls short of these 3 principles. Although annual mortality from HIV/AIDS is staggering, more lives could be saved by combating simple illnesses such as respiratory disease and diarrhea. PEPFAR also fails to focus on children: as Jones et al note, "levels of attention and effort directed at preventing the small proportion of child deaths due to AIDS with a new, complex, and expensive intervention seem . . . to be outstripping the efforts to save millions of children every year."⁸

Even though some HIV/AIDS-related interventions, such as condom distribution, are indeed cost-effective, other PEPFAR-funded interventions prove significantly less so. ART, for example, has a cost-effectiveness ratio between \$350 to \$2010 per disability-adjusted life-year (DALY) averted.^{9,10} Increasing US spending on such interventions means that health needs unrelated to HIV/AIDS will remain unmet.

The Mother & Child Campaign

What is the alternative? United States international health aid resources could launch a new program to provide a more comprehensive approach to health crises in developing countries: the Mother & Child Campaign.

This campaign would focus on the health needs of those hit hardest by simple but deadly diseases: young children and their mothers. Accordingly, the campaign would support efforts to prevent and treat diarrheal disease, respiratory infections, tuberculosis, malaria, vaccine-preventable diseases, neonatal conditions, and obstetric and maternal health problems.

Funding distribution would emphasize cost-effectiveness. For example, rather than financing treatments of neonatal jaundice (\$652 per DALY averted), the program would first provide community-based care for neonatal pneumonia (\$1 per DALY averted), nutritional supplements for anemic pregnant women (\$13 per DALY averted), and insecticide-treated bed nets in areas of endemic malaria (\$11-\$41 per DALY averted) (TABLE). Even anticipating start-up costs, these life-saving interventions would prove considerably more cost-effective than some currently funded interventions. Emerging cost-efficiency data would be incorporated into future Mother & Child Campaign funding decisions, continuously refining the program to maximize benefit.

To appreciate the potential health effects, compare the available treatment options under the 2 programs. In 2007, \$1.34 billion, nearly 50% of PEPFAR's annual budget, was spent supporting ART treatment for 1.45 million individuals.¹ For this same amount, the Mother & Child Campaign could vaccinate more than 44 million children against diphtheria, pertussis, polio, tetanus, and measles, and provide 134 million insecticide-treated bed nets to prevent malaria.^{11,12} PEPFAR has taken its \$15 billion far; the Mother & Child Campaign could take it even farther.

The Mother & Child Campaign also more fully meets the 3 evaluative principles. Addressing maternal and pediatric health works to save as many lives as possible by targeting 2 populations enduring much preventable morbidity and mortality; like young children, women of childbearing age in developing regions have a particularly great burden of disease.¹² The campaign also promotes children's health, both directly and by aiding mothers: motherless children are 10 times more likely to die within 2 years of their mother's death.¹⁵ Moreover, the Mother & Child Campaign overtly considers cost-effectiveness in distributing finite resources.

Table. Treatment Options and Cost-effectiveness in Lower-Income Regions

Annual Deaths in Lower-Income Regions	Sample Interventions	Cost-effectiveness Ratio, \$/DALY ^a	Cost per Intervention, \$	DALYs Averted for 1 Year of PEPFAR-Level Funding (\$3 Billion), in Millions
HIV/AIDS				
1.9 Million total (280 000 in children <15 y)	Condom promotion and distribution	1 (for sex workers) through 99 (medium-risk women)	11-17 per infection prevented	15-3 Billion
	Prevention of mother-to-child transmission	1-34	20-47 per infection prevented	250-600
	Voluntary counseling and testing	18-22, 82	393-1315 per infection prevented	36.6-167
	First-line ART	350-2010	28 038-185 396 per infection averted	1.5-8.5
Respiratory illness				
2.86 Million total (2 million in children <5 y)	Community-based case management for neonatal pneumonia	1		3 Billion
	Treatment of nonsevere pneumonia at the facility level	24-50	2 per treatment episode	125
	Case management of pneumonia	62-87	3-6 per treatment episode	34-48
Diarrheal disease				
2.2 Million total (1.9 million in children <5 y)	Oral rehydration therapy	24-139	0.50-6 per treatment for a child	125
	Water supply and sanitation: hygiene education, program design, and regulation added to existing infrastructure	20 (1.67-140)	NA	150
Malaria				
1.24 Million total (848 000 in children <5 y)	Case management with artemisinin-based combination therapy	12	NA	250
	Indoor residual spraying of long-lasting insecticides	9-41	NA	250-333
	Insecticide-treated bed nets	11-41	5 per insecticide-treated bed net	176-273
Vaccine-preventable disease				
2.1 Million total (1.4 million in children <5 y)	Traditional immunization program (diphtheria, pertussis, polio, tetanus, and measles)	7	14 per fully immunized child	429
Tuberculosis				
1.1 Million (100 000 child deaths)	DOTS treatment of new smear-positive cases only	6-8	443-590 per treatment	500
	DOTS therapy plus therapy for resistant cases	11-15	465-460 per treatment	200-273
Maternal conditions and neonatal complications^b				
529 000 Maternal and 4 million neonatal deaths	Community newborn care package	9	NA	333
	Antenatal tetanus toxoid immunizations	12	NA	250
	Iron and folic acid nutritional supplementation	13	NA	231
	WHO mother and baby package ^c	77-151	NA	20-39
	Routine maternity care ^d	86-125	NA	24-35

Abbreviations: ART, antiretroviral therapy; DALY, disability-adjusted life-years; DOTS, directly observed treatment, short-course; HIV, human immunodeficiency virus; NA, not found or available; PEPFAR, President's Emergency Plan for AIDS Relief; WHO, World Health Organization.

^aData in this column were calculated using information from references 9-15.

^bPrimarily neonatal sepsis/pneumonia, preterm delivery, and asphyxia at birth.

^cWHO mother and baby package with magnesium sulfate and active management of labor.

^dNinety percent coverage of prenatal care, normal delivery with skilled attendance, postnatal care, and treatment of sexually transmitted infections, syphilis, anemia, eclampsia, obstructed labor, postpartum hemorrhage, and sepsis.

It would be unethical and impractical to abandon or decrease programs developed under PEPFAR given fiduciary relationships, the threat of drug-resistant HIV/AIDS, and the devastation the disease wreaks on societal infrastructure. But the choices are not “double or nothing.” Government pledges to vastly increase PEPFAR funding create new options for international health aid. By allotting these newly pledged billions to the Mother & Child Campaign, the United States could continue PEPFAR programs at their current high level while using the newly committed funding to launch a more cost-effective program targeting basic health problems. This would respect the continuing need for HIV/AIDS work while acting upon the moral, economic, and practical advantages of devoting funding to diseases afflicting mothers and children in the developing world.

PEPFAR has been an important step for US international health aid, but multiplying its funding misses enormous opportunities to save lives, especially young lives, with more cost-effective interventions. By devoting the new funding to the Mother & Child Campaign, the United States could provide tremendous benefit to developing regions that experience great health burdens from common but deadly diseases. As President Bush said in his original PEPFAR announcement, “seldom has history offered a greater opportunity to do so much for so many.”¹

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Glucose Lowering to Control Macrovascular Disease in Type 2 Diabetes

Treating the Wrong Surrogate End Point?

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IN THE 1920S, THE USE OF INSULIN TO TREAT TYPE 1 DIABETES was lifesaving for children in diabetic ketoacidosis. Among the surviving patients with diabetes, the microvascular and macrovascular disease complications proved to be nonetheless devastating. The treatment of type 1 diabetes was revolutionized by the discovery that intensive glycemic control could prevent or delay the development of the microvascular complications of retinopathy, neuropathy, and nephropathy. Indeed, for patients with type 1 diabetes, aggressive insulin treatment also reduced the long-term risk of cardiovascular disease.¹

Therapeutic enthusiasm for intensive treatment expanded to include patients with type 2 diabetes, who typi-

cally have insulin resistance rather than the absence of insulin production characteristic of type 1 diabetes. Elevated glucose levels in patients with type 2 diabetes, like the high white blood cell counts in patients with bacterial pneumonia, are a consequence of insulin resistance together with inadequate compensatory hyperinsulinemia. Clinical trials of patients with type 2 diabetes demonstrated that improved glycemic control was associated with the prevention of microvascular complications. Numerous observa-

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